for the United Kingdom and Ireland

2023 edition







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What's new in the 2023 edition

Out of 538 recommendations in this guideline, almost 300 have been updated, added or endorsed since the 2016 edition. Here are highlights of some of the changes, together with the change to the geographical remit of the guideline, which now covers the four nations of the United Kingdom, and the Republic of Ireland.

Organisation of stroke services

Hyperacute, acute and rehabilitation stroke services should provide specialist medical, nursing and rehabilitation staffing levels matching the recommendations in Table 2.5. [see 2.5 B and Table 2.5]

A stroke rehabilitation unit should have access to a consultant specialising in stroke rehabilitation (medical or non-medical, i.e. nurse or therapist, where professional regulation permits). [see 2.5 K]

Stroke rehabilitation units with non-medical consultant leadership should have daily medical cover (ward doctors, GPs), enabling admissions and discharges 7 days a week. [see 2.5 L]

People undergoing rehabilitation after stroke who are not eligible for early supported discharge should be referred to community stroke rehabilitation if they have ongoing rehabilitation needs when transferred from hospital. [see 2.8 B]

The intensity and duration of intervention provided by the community stroke rehabilitation team should be established between the stroke specialist and the person with stroke and be based on clinical need tailored to goals and outcomes. [see 2.8 E]

A multidisciplinary service providing early supported discharge and community stroke rehabilitation should adopt a minimum core team structure. [see 2.8 F]

In the case of people with stroke with limited life expectancy, the multidisciplinary team should establish whether there is any existing documentation of the patient's wishes regarding management of risks associated with continued eating and drinking. [see 2.15 E]

Acute care

Dual antiplatelet therapy with either aspirin and clopidogrel, or aspirin and ticagrelor, should be considered in patients presenting within 24 hours of TIA and minor stroke. [see 3.3 B]

Patients with acute ischaemic stroke within 4.5 hours of known onset should be considered for thrombolysis with alteplase or tenecteplase. [see 3.5 A]

Patients with acute ischaemic stroke who were last known to be well more than 4.5 hours earlier should be considered for thrombolysis with alteplase between 4.5-9 hours of known onset, if there is evidence of the potential to salvage brain tissue on CT perfusion or MRI (DWI-FLAIR mismatch). [see 3.5 B]

Patients eligible for mechanical thrombectomy should receive prior intravenous thrombolysis as rapidly as possible (unless contraindicated), irrespective of whether they have presented to an acute stroke centre or a thrombectomy centre. [see 3.5 F]

Patients presenting with acute anterior circulation ischaemic stroke and large artery occlusion between 6 and 24 hours previously, including wake-up stroke, should receive mechanical thrombectomy on the basis of a combination of ASPECTS score and target or clinical imaging mismatch. [see 3.5 I]

Patients presenting with acute ischaemic stroke in the posterior circulation within 12 hours of onset should be considered for mechanical thrombectomy if they have a confirmed intracranial vertebral or basilar artery occlusion. [see 3.5 K]

Patients with acute spontaneous intracerebral haemorrhage with a systolic BP of 150-220 mmHg should be considered for urgent treatment within 6 hours of symptom onset, aiming to achieve a systolic BP of 130-139 mmHg within one hour and sustained for at least 7 days. [see 3.6 C]

Early non-invasive cerebral angiography (CTA/MRA within 48 hours of onset) should be considered for patients with acute spontaneous intracerebral haemorrhage where a macrovascular cause is likely to be identified. [see 3.6 H]

Rehabilitation and recovery

People with stroke should be considered to have the potential to benefit from rehabilitation at any point after their stroke. [see 4.1 A]

People with stroke should be routinely screened for delirium. [see 4.29 B]

People with stroke should be screened for cognitive problems as soon as it is medically appropriate and they are able to participate in a brief interaction, usually within the initial days after onset of stroke. [see 4.29 C]

People with stroke should be routinely screened for anxiety and depression using standardised tools, the results of which should be used alongside other sources of information. [see 4.39 B]

People with motor recovery goals following stroke should receive at least 3 hours a day of therapy (therapist-delivered) and should be supported to remain active for up to 6 hours a day. [see 4.2 A].

For people with stroke who show diminished motivation, reduced goal-directed behaviour or decreased emotional responsiveness that is persistent and affects engagement with rehabilitation or functional recovery, apathy should be considered alongside other cognitive and mood disorders. [see 4.40 A]

People with some upper limb movement, or impaired mobility or balance after stroke, should be offered repetitive task practice as the principal rehabilitation approach, in preference to other therapy approaches including Bobath. [see 4.18 A, 4.20 B and 4.22 C]

People with mild-moderate arm weakness after stroke may be considered for transcutaneous vagus nerve stimulation in addition to usual therapy. Implanted vagus nerve stimulation should only be used in the context of a clinical trial. [see 4.18 H]

Stroke rehabilitation services should ensure they have adequate equipment, including the technology requirements to provide telerehabilitation, to enable provision of the treatments recommended within this guideline. [see 6.4 D]

Stroke services should consider building links with recreational fitness facilities such as gyms or leisure centres, or providing equipment in outpatient departments, to enable people with stroke to access treadmills and other relevant fitness equipment. [see 4.221]

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People with stroke should be offered cardiorespiratory training or mixed training once they are medically stable, regardless of age, time since stroke and severity of impairment. [see 4.17 E]

People with stroke should be assessed and periodically reviewed for post-stroke fatigue, including for factors that might precipitate or exacerbate fatigue (e.g. depression and anxiety, sleep disorders, pain) and these factors should be addressed accordingly. Appropriate time points for review are at discharge from hospital and then at regular intervals, including at 6 months and annually thereafter. [see 4.25 C]

People with aphasia after stroke should be given the opportunity to improve their language and communication abilities as frequently and for as long as they continue to make meaningful gains, including access to appropriate practice-based digital therapies. [see 4.43 B and C]

Long-term management and secondary prevention

Home blood pressure monitoring should be considered for guiding the management of BP-lowering treatment, with a typical home systolic BP target below 125 mmHg. [see <u>5.4 A and F</u>]

Lipid-lowering treatment for people with ischaemic stroke or TIA and evidence of atherosclerosis should aim to reduce fasting LDL-cholesterol below 1.8 mmol/L (equivalent to a non-HDL-cholesterol below 2.5 mmol/L in a non-fasting sample). [see 5.5 C]

People who have an intracerebral haemorrhage whilst taking an antithrombotic medication to prevent vascular occlusive events may be considered for restarting antiplatelet treatment. [see <u>5.6 C</u>]

People with ischaemic stroke and atrial fibrillation or flutter should be considered for anticoagulation within 5 days of onset for mild stroke and may be considered for anticoagulation from 5-14 days of onset for moderate to severe stroke. Wherever possible people in the latter category should be offered participation in a trial of the timing of initiation of anticoagulation after stroke. [see <u>5.7 A</u>]

Selected people below the age of 60 with ischaemic stroke or TIA of otherwise undetermined aetiology, in association with a patent foramen ovale (PFO) and a right-to-left shunt or an atrial septal aneurysm, should be considered for endovascular PFO device closure within 6 months of the index event to prevent recurrent stroke. [see 5.10 B]

People with lobar intracerebral haemorrhage (ICH) associated with probable cerebral amyloid angiopathy (CAA) may be considered for antiplatelet therapy for the secondary prevention of vaso-occlusive events, and those with atrial fibrillation (AF) may be considered for oral anticoagulation. Wherever possible these people should be offered participation in a randomised controlled trial of antithrombotic treatment after ICH associated with CAA. [see 5.19 B and C]

People with CADASIL should be considered for intensive cardiovascular risk factor management, including antiplatelet therapy to prevent secondary vascular events. [see <u>5.20 B and C</u>]

In people with ischaemic stroke or TIA requiring antithrombotic treatment the presence of cerebral microbleeds (regardless of number or distribution) need not preclude the use of such treatment. [see 5.21 A]

People with stroke should be offered cardiorespiratory training or mixed training, for at least 30-40 minutes, 3 to 5 times a week for 10-20 weeks regardless of age, time since stroke onset or severity of impairments, guided by their goals and preferences. [see <u>5.23 C</u>]

People with stroke should be supported to develop their own self-management plan, based on their individual needs, goals, preferences and circumstances. [see 5.27 F]

1 Guideline development

1.0 Introduction

Purpose of guideline

The National Clinical Guideline for Stroke provides authoritative, evidence-based practice guidance to improve the quality of care delivered to every adult who has a stroke in the United Kingdom and Ireland, regardless of age, gender, type of stroke, location, or any other feature. The guideline is intended for:

- those providing care nurses, doctors, therapists, care staff;
- those receiving care patients, their families, their carers;
- those commissioning, providing or sanctioning stroke services;
- anyone seeking to improve the care of people with stroke. [2023]

Parties responsible for guideline

The 2023 edition, like the previous editions of this guideline, was produced by the Intercollegiate Stroke Working Party. The Working Party was originally set up by the Royal College of Physicians and is a group of senior representatives from the professional bodies in England, Wales and Northern Ireland involved in stroke care, as well as the voluntary sector and patient voice representatives. For this edition encompassing the whole of the UK and Ireland, the Working Party established a Guideline Development Group with representatives from the Working Party, from the Scottish Intercollegiate Guidelines Network (SIGN) and from the Irish National Clinical Programme for Stroke. Production of the 2023 edition was supported by a project team based at the Sentinel Stroke National Audit Programme (SSNAP), King's College London. More information about contributors to the guideline is in Section 1.9 Contributors. [2023]

The 2023 guideline is endorsed for use in clinical practice by the Royal College of Physicians of London, the Scottish Intercollegiate Guidelines Network (SIGN) and the Royal College of Physicians of Ireland. [2023]

Relationship to guidance from NICE and SIGN

In appraising the updated evidence base the Guideline Development Group has paid close attention to the content of the most recent NICE guidance on stroke:

- NICE guideline [NG128] Stroke and transient ischaemic attack in over 16s: diagnosis and initial management (last updated in 2022) https://www.nice.org.uk/guidance/ng128;
- NICE quality standard [QS2] Stroke in adults (last updated in 2016)
 https://www.nice.org.uk/guidance/qs2/chapter/Quality-statement-2-Intensity-of-stroke-rehabilitation;
- NICE guideline [CG162] Stroke rehabilitation in adults (last updated in 2013, update due late 2023) https://www.nice.org.uk/guidance/cg162. [2023]

This guideline is referred to as SIGN 166 and replaces the following SIGN guidelines:

- SIGN 119: Management of patients with stroke: Identification and management of dysphagia (published 2010, withdrawn 2020);
- SIGN 118: Management of patients with stroke: Rehabilitation, prevention and management of complications, and discharge planning (published 2010, withdrawn 2020);
- SIGN 108: Management of patients with stroke or TIA: Assessment, investigation, immediate management (published 2008, withdrawn 2018). [2023]

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1.1 Scope

This guideline covers the management in adults (i.e. people aged over 16 years) of:

- stroke (ischaemic stroke and primary intracerebral haemorrhage [ICH]) and transient ischaemic attack (TIA), including ocular or retinal stroke and amaurosis fugax;
- subarachnoid haemorrhage (SAH): immediate management required at an admitting hospital. [2016]

The guideline does not cover:

- primary prevention of stroke;
- detailed recommendations on (neuro-)surgical techniques (but the role of surgery is addressed);
- management of children with stroke;
- surgical or neuroradiological interventions for SAH;
- general aspects of healthcare, unless there are specific issues relating to stroke. [2016]

2023 edition

The 2023 edition is a partial update of the 2016 edition. The scope of the update is available here. This edition includes updated evidence published since 2015, with literature searches completed up to September 2022 and with some major publications since that date also included. [2023]

This 2023 edition of the guideline includes Scotland and the Republic of Ireland for the first time, as well as England, Wales, Northern Ireland, and the Isle of Man. This expansion of the guideline's remit will affect some of the nomenclature, which differs between nations and health systems, and clinicians may need to interpret recommendations in the context of their healthcare system. [2023]

1.2 Context and use of this guideline

This guideline relates to those aspects of clinical management that are specific to stroke; it does not seek to address areas of routine clinical practice and good governance such as courtesy and respect for the individual, shared decision making and supporting patient choice, accurate record keeping etc. [2016]

This guideline is not intended to overrule regulations or standards concerning the provision of services and should be considered in conjunction with them. In considering and implementing this guideline, users are advised to also consult and follow all appropriate legislation, standards and good practice. [2023]

No clinical guideline can account for every eventuality, and recommendations should be taken as statements that inform and guide the clinician, the patient and any other user, and not as rigid rules. The clinician remains responsible for interpreting the recommendations taking into account the circumstances at hand (e.g. medical, psychosocial, cultural) and including competing priorities for the patient and co-morbidities such as frailty, and for considering whether new evidence might exist that could alter the recommendation. In doing so, clinicians should consider Sweeney's three levels of significance when applying the evidence to the person in front of them: statistical significance (is the evidence valid?), clinical significance (does the evidence apply to this clinical situation?) and personal significance (does the evidence apply to this person's particular circumstances and priorities?) (Sweeney et al, 1998). Clinicians can reasonably expect guidelines to be unambiguous about the first and to give guidance about the second, but the third level of significance can only be understood within the relationship between the treating clinician and their patient, and may provide the justification for deviations from recommended management in particular cases. [2016]

1.3 Models underpinning guideline development

This guideline has used several models or frameworks to structure its recommendations and layout. In summary these are:

- the Donabedian model (Donabedian, 1978) for considering healthcare: structure, process and outcome;
- the healthcare process: diagnosis, assessment, intervention (treatment and support), and evaluation;
- the WHO international classification of functioning, disability and health (WHO ICF) model (World Health Organization, 1978; Wade & Halligan, 2004);
- time: prevention, acute, post-acute/recovery and long-term. [2016]

The WHO ICF model is a useful conceptual framework for disease management, particularly one with such long-term impact as stroke. This framework is articulated in terms of:

- pathology (the disease processes within organs);
- impairment (symptoms/signs; the manifestations of disease in the individual);
- activities (the impact of impairments on the person's usual activities);
- participation (the impact of activity limitations on a person's place in family and society). [2016]

1.4 Methodology of guideline development

The same methodology was followed for the 2023 update as for the 2016 edition. It includes seven distinct steps to ensure a thorough and rigorous process. The detailed methodology is available in the methodology overview [here]. The seven steps are:

- 1. Development of scope (see process and final scope, including research questions, here);
- 2. Searching the scientific literature (see search strategies here);
- 3. Selection of studies for inclusion;
- 4. Assessment of the quality of the evidence (see evidence tables here);
- 5. Moving from evidence to recommendations;
- 6. Health economic considerations;
- 7. External peer review and public consultation (see peer review and public consultation document here, and peer review comments and responses in the peer review report here). [2023]

Grading of recommendations and consensus recommendations

As with the 2016 and earlier editions, the methodology followed has:

- not graded recommendations. In many clinical guidelines, recommendations are given a grade which derives entirely from the design of the studies providing the evidence. Methodologically strong evidence for less important interventions gives the linked recommendation an apparently higher priority than an important recommendation where the evidence is weaker. The strength depends solely upon the study design and ignores other important features of the evidence such as its plausibility, generalisability, and the absolute benefit to the total population of people with stroke; [2016]
- used quantitative and qualitative evidence where appropriate. In choosing between making a
 recommendation based on less than perfect evidence and making no recommendation at all,
 the guideline seeks to guide practice using the best available evidence; [2016]
- allowed for recommendations to be developed by consensus:
 - in areas of practice where evidence is absent or of such poor quality or quantity that a recommendation cannot be derived; [2016]

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 where formal literature searching of a narrowly defined research question would not have adequately encompassed the clinical implications of the topic. (See the methodology guide here for more details). [2023]

Strength of recommendations

Depending on the strength of the evidence, recommendations in this guideline are either strong (a treatment or service 'should be provided/offered') or conditional (a treatment 'should be considered' or 'may be considered'). More detail about the wording of recommendations can be found in the methodology overview here. [2023]

NICE accreditation

The 2016 edition was accredited by NICE. NICE has agreed to extend the accreditation to the 2023 edition. This applies until December 2023. NICE accreditation processes are changing and the accreditation status of this guideline may change in future. [2023]

1.5 Funding and conflicts of interest

Funding for the guideline project team was received from the following external sources on condition that the Guideline Development Group retained complete editorial independence over the guideline development process and content:

- Stroke Association;
- Johnson & Johnson Medical Ltd (through an educational grant agreement);
- Welsh Assembly Government;
- NIMAST (Northern Ireland Multidisciplinary Association for Stroke Teams). [2023]

The editors and the Intercollegiate Stroke Working Party wish to express their immense gratitude and appreciation for the financial support granted freely by these organisations, without which production of this edition would not have been possible. [2023]

The policy on declarations of interests is here. [2023]

1.6 Treatments not mentioned in this guideline

Users of this guideline should apply the general rule that if an intervention covered by the scope of this guideline is not mentioned, then it is not recommended for use, and commissioners and service planners are not obliged to obtain it for the populations they serve. [2016]

1.7 Participation in clinical research

A small number of specific recommendations that patients should not be offered a treatment except 'in the context of clinical trial' have been included. This has been done when there is already some research which leaves uncertainty about the benefits and harms, but there is insufficient evidence to either recommend an intervention, or to avoid its use. [2016]

1.8 Licensing and approval of medication

Recommendations in this guideline about the use of specific medicines (and devices) do not specify whether the medicine is licensed or approved by the Medicines and Healthcare products Regulatory

Agency (MHRA) or European Medicines Agency (EMA) for that particular use. It is the responsibility of the individual clinician and their healthcare provider to decide whether to permit the unlicensed/off-label use of medication in their formulary, including by referring to the source data from the appropriate regulator. The Guideline Development Group may have considered it appropriate to recommend medication which has not been licensed for specific situations (e.g. aspirin in acute ischaemic stroke) or is not available in certain jurisdictions (e.g. injectable lipid-lowering therapies in the Republic of Ireland). Additional advice on the use of new and existing medicines is provided by the National Institute for Health and Care Excellence (NICE), which evaluates technologies for the NHS in England and Wales, the Scottish Medicines Consortium (SMC) for NHSScotland and the National Centre for Pharmacoeconomics (NCPE) for the Health Service Executive (HSE) in Ireland. [2023]

1.9 Contributors

The Intercollegiate Stroke Working Party is extremely grateful to the following groups who contributed their time and expertise (considerably above and beyond the usual call of duty) to producing this edition:

- the four guideline editors;
- members of the Guideline Development Group;
- topic group leads;
- members of topic groups and other contributors. [2023]

In addition, the Working Party is grateful to all those who contributed to their organisation's peer review of the draft guideline and those who submitted public consultation comments. Finally, the Working Party thanks the members of the stroke guideline project team and SIGN. The guideline would not exist without the hard work of all the contributors, who are listed here. [2023]

1.10 Notes on the text

Unchanged text from the 2016 edition is marked [2016]. Text is marked [2023] when:

- the recommendation and supporting text are new since the 2016 edition;
- the recommendation and supporting text have been updated since the 2016 edition as a result of new evidence;
- the recommendation was reviewed but not amended from the 2016 edition since the new evidence did not support a change. The supporting text has been updated. [2023]

The 2016 edition was prepared by the Intercollegiate Stroke Working Party ('Working Party'). The 2023 edition is the responsibility of the Guideline Development Group. In the case of consensus recommendations, sources for 2016 recommendations refer to 'Working Party consensus', whereas sources for 2023 recommendations refer to 'Guideline Development Group consensus'. [2023]

Some 2016 text has been changed to ensure it is applicable to Scotland and Ireland as well as to England, Wales and Northern Ireland, without changing the sense. These changes are not marked [2023]. [2023]

This edition is published online only. Apart from as indicated above, the text from 2016 is unchanged but may be in a different order from the 2016 publication. Sections may also have been re-titled and renumbered (particularly in the Rehabilitation and Recovery chapter). [2023]

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2 Organisation of stroke services

2.0 Introduction

This chapter considers stroke management from a population perspective, addressing the means of organising services to deliver high quality stroke care. If services for people with stroke are poorly organised, outcomes will also be poor despite the evidence-based practice and best endeavours of individual clinicians. Furthermore, if clinical teams do not have sufficient knowledge and skills, and are not consistent in their clinical practice, many people will receive sub-optimal care. [2016]

The recommendations in this chapter affect the full range of services within a comprehensive acute and community stroke service, and many of them have a strong evidence base and are among the most important contained in this guideline. [2016]

2.1 Public awareness of stroke

In recent years mass media campaigns such as the Face Arm Speech Time (FAST) campaign, have been delivered with the aim of increasing public awareness of the symptoms and signs of stroke (available at https://www.nhs.uk/actfast/Pages/know-the-signs.aspx; https://irishheart.ie/campaigns/fast/; https://www.thinkfast.org.uk/). Public awareness of stroke prevention and treatment are also important. [2016]

2.1 Recommendation

A Public awareness campaigns of the symptoms of stroke should be recurrent, targeted at those most at risk of stroke, and formally evaluated. [2016]

2.1 Sources

A Lecouturier et al, 2010a,b; Working Party consensus

2.1 Evidence to recommendations

The available research indicates some trends with regard to mass media campaigns, for example: television may be more effective than posters and newspaper advertisements; campaigns need to be repeated rather than short-term and one-off, and there are methodological weaknesses in the research (Lecouturier et al, 2010a). The evidence for a direct link between awareness and recommended behaviour is weak, especially among older members of the population, minority ethnic groups and those with lower levels of education, all of which are population groups at greater risk of stroke (Jones et al, 2010). Campaigns aimed at both public and healthcare professionals may have more impact on professionals than the public (Lecouturier et al, 2010b). More research in the area of improving public awareness and appropriate action is needed. [2016]

2.2 Definitions of specialist stroke services

- A specialist is defined as a healthcare professional with the necessary knowledge and skills in managing people with stroke and conditions that mimic stroke, usually by having a relevant further qualification and keeping up to date through continuing professional development. This does not require the healthcare professional exclusively to manage people with stroke, but does require them to have specific knowledge and practical experience of stroke. [2016]
- A specialist team or service is defined as a group of specialists who work together regularly managing people with stroke and conditions that mimic stroke, and who between them have the

knowledge and skills to assess and resolve the majority of problems. At a minimum, any specialist unit, team or service must be able to deliver all the relevant recommendations made in this guideline. This does not require the team exclusively to manage people with stroke, but the team should have specific knowledge and practical experience of stroke. Types of acute stroke service are described in Section 2.4 Organisation of inpatient stroke services. [2016]

2.3 Transfer to acute stroke services

2.3 Recommendations

- A Community health services and ambulance services (including call handlers and primary care reception staff) should be trained to recognise people with symptoms indicating an acute stroke as an emergency requiring transfer to a hyperacute stroke centre with prealert notification to the stroke team. [2023]
- B People with an acute neurological presentation suspected to be a stroke should be admitted directly to a hyperacute stroke unit that cares predominantly for patients with stroke, with access to a designated thrombectomy centre 24 hours a day, 7 days a week for consideration of mechanical thrombectomy. [2023]
- C Acute hospitals receiving medical admissions that include people with suspected stroke should have arrangements to admit them directly to a hyperacute stroke unit on site or at a designated neighbouring hospital as soon as possible to monitor and regulate basic physiological functions such as neurological status, blood glucose, oxygenation, and blood pressure. [2016]
- D Acute hospitals that admit people with stroke should have prioritised access to a specialist stroke rehabilitation unit on site or at a neighbouring hospital. [2016]
- E Local health economies/health boards (geographic areas or populations covered by an integrated group of health commissioners/service planners and/or providers) should aim to have a specialist neurovascular service capable of assessing and treating people within 24 hours of transient cerebrovascular symptoms. [2016]
- F Public and professional education programmes should be run to increase awareness of stroke and the need for urgent diagnosis and treatment. [2016]

2.3 Sources

- A, B Follows from the evidence concerning the emergency diagnosis and treatment of stroke (Section 3.4 Diagnosis and treatment of acute stroke imaging, Section 3.5 Management of ischaemic stroke, Section 3.6 Management of intracerebral haemorrhage, Section 3.7 Management of subarachnoid haemorrhage)
- C Follows from the evidence concerning acute stroke care (Section 3.10 Acute stroke care)
- D Follows from the evidence concerning specialist stroke units (<u>Section 2.2 Definitions of specialist stroke services</u>, <u>Section 2.4 Organisation of inpatient stroke services</u>)
- E Follows from the evidence concerning TIA diagnosis and treatment (Section 3.2

 Management of TIA and minor stroke assessment and diagnosis, Section 3.3

 Management of TIA and minor stroke treatment and vascular prevention)
- Follows from the evidence concerning the emergency diagnosis and treatment of stroke (Section 3.4 Diagnosis and treatment of acute stroke imaging, Section 3.5 Management of ischaemic stroke, Section 3.6 Management of intracerebral haemorrhage, Section 3.7 Management of subarachnoid haemorrhage)

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2.3 Evidence to recommendations

Effective stroke care needs an organisational structure that facilitates best treatments at the right time. This section makes recommendations that follow from studies of treatment efficacy; e.g. intravenous thrombolysis can only be given within the eligible time window if people arrive in the appropriate setting within that time. Major urban reorganisations of stroke services have taken place in some parts of the UK and Ireland to improve access to hyperacute stroke unit care. Evidence from Manchester and London suggests that such care should be in hyperacute stroke centres available 24 hours a day, 7 days a week, and should be for all people with acute stroke, not just those who might be suitable for intravenous thrombolysis (Ramsay et al, 2015). [2016]

The RACECAT trial in Catalonia, Spain tested whether transporting people with acute stroke suspected to be due to large artery occlusion directly to a thrombectomy centre (ambulance redirection or bypass) improves outcomes compared with being taken to the patient's nearest acute stroke centre (Pérez de la Ossa et al, 2022). This multi-centre, cluster RCT did not demonstrate a clinical outcome advantage from redirection, but in many respects RACECAT is not directly applicable to many parts of the UK and Ireland. The strategy for adopting either a secondary transfer or an ambulance redirection service model for thrombectomy will depend upon local and regional services and the population served (Ford et al, 2022). There is an urgent need for research addressing this question that is directly applicable to the NHS and HSE. Processes of care are important for optimising patient outcomes and these apply at both the referring acute stroke centre and the receiving thrombectomy centre. If local acute stroke centre workflow cannot be optimised, then redirection to a thrombectomy centre may be better and should be considered regionally. For secondary transfers that are longer than one hour, helicopter-based transfer may improve speed of access to thrombectomy and associated patient outcomes (Coughlan et al, 2021). [2023]

Mobile stroke units (MSUs) are ambulances equipped with brain imaging equipment and specialist staff that are capable of delivering thrombolysis or identifying large artery occlusion when equipped with CT angiography. In data largely from non-randomised trials with a standard ambulance comparator group and blinded outcome assessments, after deployment of an MSU, patients with ischaemic stroke had a better clinical outcome, were more likely to receive thrombolysis and incur shorter onset to thrombolysis times (Turc et al, 2022a). However, it is uncertain what the effects of MSUs are on an unselected stroke population, the cost-effectiveness of MSU care, how to integrate MSUs into pre-hospital pathways and how these might be applied across both rural and urban regions. Ongoing randomised trials may answer some of these questions, although modelling of costs and benefits applied across different regions and service models is likely to be required (Chen et al, 2022). [2023]

2.3 Implications

These recommendations have significant implications for the organisation of acute medical services within any 'health economy' (locality). At a regional or subregional level, those who commission and provide stroke services are required to configure these services to achieve the maximum benefit to the population from the delivery of time-sensitive treatments, and to consider issues relating to the colocation of other emergency services that are beyond the scope of this guideline. It is important that, with such reconfiguration of services, there is a robust governance infrastructure in place to monitor the quality of stroke services delivered. [2023]

2.4 Organisation of inpatient stroke services

There is strong evidence that specialised stroke unit care initiated as soon as possible after the onset of stroke provides effective treatments that reduce long-term brain damage, disability and healthcare costs. An acute stroke service consists of either: a) a comprehensive stroke centre (CSC) providing hyperacute, acute and inpatient rehabilitation including thrombectomy (thrombectomy centre) and neurosurgery; or b) an acute stroke centre (ASC) providing hyperacute, acute and inpatient

rehabilitation. A stroke rehabilitation unit (SRU) provides inpatient rehabilitation only. All components of a specialist acute stroke service should be based in a hospital that can investigate and manage people with acute stroke and their medical and neurological complications, but this requirement does not apply to services designed to provide stroke care only in the rehabilitation phase. [2023]

2.4 Recommendations

- A People with the sudden onset of focal neurological symptoms seen by community-based clinicians (e.g. ambulance paramedics) should be screened for hypoglycaemia with a capillary blood glucose, and for stroke or TIA using a validated tool. Those people with persisting neurological symptoms who screen positive using a validated tool should be transferred to a hyperacute stroke unit as soon as possible with pre-alert notification to the admitting stroke team. [2016]
- B People with suspected acute stroke (including people already in hospital) should be admitted directly to a hyperacute stroke unit and be assessed for emergency stroke treatments by a specialist clinician without delay. [2016]
- C Acute stroke services should provide specialist multidisciplinary care for diagnosis, hyperacute and acute treatments, normalisation of homeostasis, early rehabilitation, prevention of complications and secondary prevention. [2016]
- Acute stroke services should have management protocols for the admission pathway including links with the ambulance service, emergency stroke treatments, acute imaging, neurological and physiological monitoring, swallowing assessment, hydration and nutrition, vascular surgical referrals, rehabilitation, end-of-life (palliative) care, secondary prevention, the prevention and management of complications, communication with people with stroke and their family/carers and discharge planning. [2016]
- E Acute stroke services should have continuous (24/7) access to brain imaging including CT or MR angiography and perfusion when necessary and should be capable of undertaking immediate brain imaging when clinically indicated. [2023]
- Acute stroke services should have protocols for the monitoring, referral and transfer of patients to thrombectomy centres for mechanical thrombectomy and regional neurosurgical centres where available for decompressive hemicraniectomy, surgical management of intracranial haemorrhage and the management of symptomatic hydrocephalus including external ventricular drain insertion. [2016]
- G Acute stroke services should ensure that people with conditions that mimic stroke are transferred without delay into a care pathway appropriate to their diagnosis. [2016]
- H People with a diagnosis of stroke that was not made on admission should be transferred without delay into that part of the stroke service most appropriate to their needs. [2016]
- Patients with acute neurological symptoms that resolve completely within 24 hours of onset (i.e. suspected TIA) should be given aspirin 300 mg immediately, unless contraindicated, and be assessed urgently within 24 hours by a stroke specialist clinician in a neurovascular clinic or an acute stroke unit. [2023]
- J Acute stroke services should have an education programme for all staff providing acute stroke care (including ambulance services and the emergency department as appropriate) and should provide training for healthcare professionals in the specialty of stroke. [2016]
- K Acute stroke services should participate in national and local audit, multicentre research and quality improvement programmes. [2016]

2.4 Sources

A, B Follows from the evidence concerning emergency stroke treatments (Section 3.4)

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- <u>Diagnosis and treatment of acute stroke imaging, Section 3.5 Management of ischaemic stroke, Section 3.6 Management of intracerebral haemorrhage, Section 3.7 Management of subarachnoid haemorrhage)</u>
- C Follows from the evidence concerning emergency treatments and monitoring (Section 3.5 <u>Management of ischaemic stroke</u>, Section 3.6 <u>Management of intracerebral haemorrhage</u>, Section 3.7 <u>Management of subarachnoid haemorrhage</u>, Section 3.10 <u>Acute stroke care</u>)
- D Follows from the evidence concerning specialist stroke units (<u>Section 2.5 Resources:</u> inpatient stroke services)
- E Wardlaw et al, 2004; follows from the evidence concerning emergency stroke treatments (Section 3.5 *Management of ischaemic stroke*)
- Follows from the evidence concerning emergency stroke treatments (<u>Section 3.5</u> <u>Management of ischaemic stroke</u>, <u>Section 3.6 Management of intracerebral haemorrhage</u>)
- G, H Working Party consensus
- I Follows from the evidence concerning TIA diagnosis and treatment (Section 3.2

 Management of TIA and minor stroke assessment and diagnosis, Section 3.3

 Management of TIA and minor stroke treatment and vascular prevention)
- J Follows from the evidence concerning specialist stroke units (<u>Section 2.5 Resources:</u> inpatient stroke services)
- K Obligations under the NHS Standard Contract; Working Party consensus

2.4 Evidence to recommendations

Given that 1 in 20 strokes occur in people already in hospital (Intercollegiate Stroke Working Party, 2016), clinicians in high-risk clinical areas (e.g. cardiology or renal wards, cardiothoracic units) should have a high level of awareness of acute stroke and the time-critical nature of interventions to improve outcome, including how to contact a stroke specialist for advice, arrange imaging and transfer patients to a hyperacute stroke unit. [2023]

Any person with the acute onset of a focal neurological syndrome with persisting symptoms and signs (i.e. suspected stroke) needs urgent diagnostic assessment to differentiate between acute stroke and other causes. Progress in the medical management of acute stroke demands a corresponding increase in the availability of advanced imaging techniques, and all hyperacute stroke services will need immediate and timely access to multi-modal brain imaging including CT or MR angiography and perfusion when necessary. [2023]

2.4 Implications

These recommendations have significant implications for the organisation of clinical services within acute hospitals. Systems need to be adapted to ensure that people with acute stroke have rapid access to an acute stroke unit and to facilitate rapid transfer out of the unit once acute management is complete. [2016]

2.5 Resources – inpatient stroke services

Leadership and culture are important contributors to delivering high quality stroke care, and they should be evident at all levels, e.g. individual professionals, teams, units, trusts/hospitals and across networks. Culture and tone 'from the top' matters and are key enablers of joint working across professional and organisational boundaries and important to the provision of holistic and compassionate care to patients and their families (Francis, 2013; Getting it Right First Time, 2022). A well-led, appropriately staffed and skilled multidisciplinary stroke unit is the cornerstone of holistic and compassionate care for people with

stroke. In parts of the UK, legislation is due to be implemented in 2024 to ensure 'safe staffing' for nurses and medical practitioners in health and social care settings (Scottish Government, 2019). [2023]

2.5 Recommendations

- A People with stroke should be treated in a specialist stroke unit throughout their hospital stay unless their stroke is not the predominant clinical problem. [2016]
- B A hyperacute, acute and rehabilitation stroke service should provide specialist medical, nursing, and rehabilitation staffing levels matching the recommendations in Table 2.5 below.

Table 2.5 Recommended levels of staffing for hyperacute, acute and rehabilitation units

	Physio- therapy	Occupation al therapy	Speech and language therapy	Clinical psychology / neuro- psychology	Dietetics	Nursing	Consultant stroke physician	Consultant- level practitioner- led ward rounds
Umman	Whole-time equivalents (WTE) per 5 beds*				WTE per bed	24/7 availability; minimum		
Hyper- acute stroke unit	1.02	0.95	0.48	0.28	0.21	2.9 (80:20 registered: unregis- tered)	6.0 thrombolysis trained physicians on rota	Twice daily ward round
Acute stroke unit & stroke rehab- ilitation unit	1.18	1.13	0.56	0.28	0.21	1.35 (65:35 registered: unregis- tered)	Acute stroke unit: 7 day cover with adequate out of hours arrange- ments**	Acute stroke unit: daily ward round** Stroke rehabilit- ation unit: twice- weekly ward round**

^{*} WTE figures are for 7-day working for registered staff and include non-clinical time (such as supervision and professional development) as well as non-face-to-face clinical activity. Registered staff should be augmented by support workers and rehabilitation assistants to achieve the intensity and dose of therapy recommended in Section 4.2 Rehabilitation approach – intensity of therapy (motor recovery and function).

[2023]

- C A hyperacute stroke unit should have immediate access to:
 - specialist medical staff trained in the hyperacute and acute management of people with stroke, including the diagnostic and administrative procedures needed for the safe and timely delivery of emergency stroke treatments;
 - specialist nursing staff trained in the hyperacute and acute management of people with stroke, covering neurological, general medical and rehabilitation aspects;
 - stroke specialist rehabilitation staff;

^{**} Consultant stroke physician input may need to be adjusted according to the acuity of the unit. All acute and rehabilitation units should have at least 2 ward rounds per week led by a consultant-level practitioner (physician, nurse or therapist; see Recommendation 2.5K). For recommendations regarding orthoptist staffing, see Section 4.48 Vision.

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- diagnostic, imaging and cardiology services;
- tertiary services for endovascular therapy, neurosurgery and vascular surgery. [2016]
- D A hyperacute stroke unit should have continuous access to a consultant physician with expertise in stroke medicine, with consultant review 7 days per week. [2016]
- E An acute stroke unit should provide:
 - specialist medical staff trained in the acute management of people with stroke;
 - specialist nursing staff trained in the acute management of people with stroke, covering neurological, general medical and rehabilitation aspects;
 - stroke specialist rehabilitation staff;
 - access to diagnostic, imaging and cardiology services;
 - access to tertiary services for neurosurgery and vascular surgery. [2016]
- An acute stroke unit should have continuous access to a consultant physician with expertise in stroke medicine, with consultant review 5 days per week. [2016]
- G Where telemedicine is used for the assessment of people with suspected stroke by a specialist physician, the system should enable the physician to discuss the case with the assessing clinician, talk to the patient and/or family/carers directly and review radiological investigations. Telemedicine should include a high quality video link to enable the remote physician to observe the clinical examination. [2016]
- H Staff providing care via telemedicine (at both ends of the system) should be appropriately trained in the hyperacute assessment of people with suspected acute stroke, in the delivery of thrombolysis and the use of this approach and technology. The quality of care and decision making using telemedicine should be regularly audited. [2016]
- A stroke rehabilitation unit should predominantly care for people with stroke, and should maintain the staffing and skill levels required of a stroke unit regardless of size, location or mix of conditions of the patients being treated. [2023]
- J A stroke rehabilitation unit should have a single multidisciplinary team including specialists in:
 - medicine;
 - nursing;
 - physiotherapy;
 - occupational therapy;
 - speech and language therapy;
 - dietetics;
 - clinical psychology/neuropsychology;
 - social work;
 - orthoptics;

with timely access to rehabilitation medicine, specialist pharmacy, orthotics, specialist seating, assistive technology and information, advice and support (including life after stroke services) for people with stroke and their family/carers. [2023]

- A stroke rehabilitation unit should have access to a consultant specialising in stroke rehabilitation (medical or non-medical, i.e. nurse or therapist, where professional regulation permits) at least 5 days a week, with twice weekly consultant-led ward rounds.

 [2023]
- L Stroke rehabilitation units with non-medical consultant leadership should have daily medical cover (ward doctors, GPs), enabling admissions and discharges 7 days a week, with support available from stroke physicians as required. 24 hour on-site medical cover may not be required depending on patient admission criteria, with adequate out of hours arrangements. [2023]
- M A facility that provides treatment for inpatients with stroke should include:

- a geographically-defined unit;
- a co-ordinated multidisciplinary team that meets at least once a week for the exchange of information about inpatients with stroke;
- information, advice and support for people with stroke and their family/carers;
- management protocols for common problems, based upon the best available evidence;
- close links and protocols for the transfer of care with other inpatient stroke services,
 early supported discharge teams and community services;
- training for healthcare professionals in the specialty of stroke. [2016]
- N Specialist inpatient stroke services should include sufficient administration and management (including data management) support. [2023]

2.5 Sources

- A Stroke Unit Trialists' Collaboration, 2013
- B Bray et al, 2014; Ramsay et al, 2015; Guideline Development Group consensus
- C-F Follows from the evidence and recommendations concerning emergency treatments and monitoring (Section 3.5 Management of ischaemic stroke, Section 3.6 Management of intracerebral haemorrhage, Section 3.7 Management of subarachnoid haemorrhage, Section 3.10 Acute stroke care)
- G, H Meyer et al, 2008; Working Party consensus
- I-L Stroke Unit Trialists' Collaboration, 2013; NICE, 2016d; Guideline Development Group consensus
- M Working Party consensus
- N Guideline Development Group consensus

2.5 Evidence to recommendations

The previous sections have been concerned with the organisational structure of stroke services. It is equally important to have appropriate resources available for the care of people with stroke: the workforce, buildings, and technological support required. Minimum staffing levels on stroke units were originally defined in hyperacute stroke service reconfigurations such as that in London, and are supported by observational evidence from UK registries about acute care processes that are associated with substantial benefits to patients, including those admitted outside office hours and at weekends (Ramsay et al, 2015; Turner et al, 2016). The evidence regarding the optimal size of a hyperacute stroke unit was similarly confined to observational studies, reflecting a level of institutional experience and competence in the provision of specialist hyperacute treatments such as intravenous thrombolysis (Bray et al, 2013) that corresponds with a volume of at least 500 acute stroke admissions per year. [2023]

The evidence supporting stroke unit care from the stroke unit trialists in the 1990s was updated in a 2013 Cochrane review, which found that people with stroke who receive organised inpatient care in a stroke unit are more likely to be alive, independent, and living at home one year after their stroke (Stroke Unit Trialists' Collaboration, 2013). The benefits were only apparent in units based in a discrete ward. Increased access to stroke unit care has made a vital contribution to reducing stroke mortality and remains an imperative for all inpatients with stroke. [2023]

The Guideline Development Group endorses an updated recommendation regarding staffing levels of registered staff on inpatient stroke units expressed as whole-time equivalents (WTE) in Table 2.5. These recommendations take into account therapy delivered across seven days. Achieving the recommendations in <u>Section 4.2 Rehabilitation and recovery – intensity of therapy (motor recovery and function)</u> will also require unregistered support workers and rehabilitation assistants delivering

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rehabilitation under the supervision of registered staff. SSNAP reports 2021-22 (Sentinel Stroke National Audit Programme, 2022) indicate that for suitable patients, up to a third of physiotherapy and occupational therapy is currently being delivered by unregistered rehabilitation assistants. An understanding of the local context, together with these recommendations, will be required to inform more detailed service specifications (including banding/seniority), which may include increased staffing if deemed appropriate. [2023]

Staffing recommendations also include non-clinical time (such as supervision and professional development) as well as non-face-to-face clinical activity such as environmental visits, family contact and equipment ordering. Units with a small bed base may need to consider revisions to these staffing levels to ensure adequate registered staffing cover across the week, taking account of rotas and days off for weekend working. Recommendations for orthoptist staffing levels in hyperacute and acute stroke units are made in Section 4.48 Vision. Sufficient administrative and management support (including data management) is essential to the efficiency and governance of the core stroke unit team and should also be included. [2023]

Telemedicine is used in some centres to support decision making in the hyperacute management of people with stroke because of significant practical or geographical obstacles. Observational evidence suggests that telemedicine is associated with more protocol violations and longer treatment times (Meyer et al, 2008; Dutta et al, 2015). Furthermore, unless telemedicine is used as part of an otherwise well-developed acute stroke service, outcomes may suffer (Heffner et al, 2015). [2016]

2.5 Implications

These recommendations will require a considerable increase in the provision of some specialties in stroke services, including clinical psychology/neuropsychology and social work. The Guideline Development Group is concerned by the findings from national registries indicating continued poor provision of these specialties for people with stroke. Patterns of work need to be reviewed to deliver sufficient direct therapy by removing some administrative duties and ensuring that time is not spent by registered therapists on tasks that could be done by unregistered staff. Restoring adequate social work provision will require close integration with social services. [2023]

2.6 Location of service delivery

Stroke services should be organised to treat a sufficient number of patients to ensure that the specialist skills of the workforce are maintained. At the same time, the closer a rehabilitation service is to the person's home the more that family/carers can be engaged and the more targeted the rehabilitation can be. This section provides a recommendation on the location of delivery of services, aiming for an appropriate balance between care in hospital, on an outpatient basis and at home. **[2016]**

2.6 Recommendation

A People with acute stroke who cannot be admitted to hospital should be seen by the specialist team at home or as an outpatient within 24 hours for diagnosis, treatment, rehabilitation, and risk factor management at a standard comparable to that for inpatients. [2016]

2.6 Source

A Working Party consensus

2.7 Transfers of care – general principles

After stroke, many people will interact with several different services during their recovery: primary care, specialist acute stroke services, specialist rehabilitation services, social services, housing, generic community services etc. This section covers general principles around the transfers of care between these agencies. Transfers of care out of hospital are covered in <u>Section 2.8 Transfers of care from hospital to home – community stroke rehabilitation</u>. [2016]

2.7 Recommendations

- A Transfers of care for people with stroke between different teams or organisations should:
 - occur at the appropriate time, without delay;
 - not require the person to provide information already given;
 - ensure that all relevant information is transferred, especially concerning medication;
 - maintain a set of person-centred goals;
 - preserve any decisions about medical care made in the person's best interests. [2016]
- B People with stroke should be:
 - involved in decisions about transfers of their care if they are able;
 - offered copies of written communication between organisations and teams involved in their care. [2016]
- C Organisations and teams regularly involved in caring for people with stroke should use a common, agreed terminology and set of data collection measures, assessments and documentation. [2016]

2.7 Sources

- A Working Party consensus
- B Asplund et al, 2009; Working Party consensus
- C Working Party consensus

2.7 Implications

These recommendations require those who commission and provide services across health and social care to consider the current situation and how it might be redesigned to reduce transfers of care between organisations and improve continuity. The person recovering from stroke and their family should experience seamless care without artificial distinctions between service providers or between health and social care. [2016]

2.8 Transfers of care from hospital to home – community stroke rehabilitation

The most common transfer of care, and the most stressful for people with stroke and their family/carers, is that from in-hospital care to their home or to a care home. Many people report feeling afraid and unsupported, and carers report feelings of abandonment (Stroke Association, 2015). There is much that services can do to support and reassure people with stroke and their family/carers regarding the smooth transfer of care into the community. [2016]

Community stroke rehabilitation services, including delivery of early supported discharge, are required to co-ordinate the transfer of care from hospital to home, working collaboratively with people with stroke and family members, stroke inpatient unit staff and informed by an assessment of the person's home environment (Drummond et al, 2013). Through a specialist multidisciplinary team structure, early, effective community specialist stroke rehabilitation and disability management needs to be

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provided to all people with stroke leaving hospital who need it. Stroke rehabilitation should be provided in the person's own home or place of residence, including residential or nursing homes (Fisher et al, 2011; Fisher et al, 2013; NHS England, 2022). [2023]

2.8 Recommendations

- A Hospital inpatients with stroke who have mild to moderate disability should be offered early supported discharge, with treatment at home beginning within 24 hours of discharge. [2023]
- B Patients undergoing rehabilitation after stroke who are not eligible for early supported discharge should be referred to community stroke rehabilitation if they have ongoing rehabilitation needs when transferred from hospital. [2023]
- C Early supported discharge and community stroke rehabilitation should be provided by a service predominantly treating people with stroke. [2023]
- D Therapy provided as part of early supported discharge should be at the same intensity as would be provided if the person were to remain on a stroke unit. [2023]
- E The intensity and duration of intervention provided by the community stroke rehabilitation team should be established between the stroke specialist, the person with stroke and their family/carers, and be based on clinical need tailored to goals and outcomes. [2023]
- F A multidisciplinary service providing early supported discharge and community stroke rehabilitation should adopt a minimum core team structure matching the recommendations in Table 2.8 and below.

Table 2.8 Recommended levels of staffing for multidisciplinary services providing early supported discharge and community stroke rehabilitation

alsonarge and community stroke renabilitation				
Discipline	WTE per 100 referrals to service p.a.			
Physiotherapy	1.0			
Occupational therapy	1.0			
Speech and language therapy	0.4			
Casial warker	Up to 0.5 and at least 0.5 WTE per team			
Social worker	recommended locally			
Rehabilitation assistant/assistant practitioners	1.0			
Clinical psychology/neuropsychology	0.2-0.4*			
Nursing	Up to 1.2 and at least 1 full time nurse per			
Nursing	team			
Medicine	0.1			

^{*}This reflects the time that a team member should be co-located within the MDT and could include additional skill mix, e.g. assistant psychologist.

The service should also include:

- Appropriate administration and management (including data management) support;
- Timely access to psychological and neuropsychological services (e.g. Improving Access
 to Psychological Therapies [IAPT] and community mental health services with strokespecific training and appropriate supervision, psychology or neuropsychology
 departments), return to work and vocational rehabilitation services, dietetics,
 pharmacy, orthotics, orthoptics, spasticity services, specialist seating, assistive
 technology and information, pain management, advice and support for people with
 stroke and their family/carers. [2023]
- G Early supported discharge and community stroke rehabilitation services should include:

- a co-ordinated multidisciplinary team that meets at least once a week for the exchange of information about people with stroke in their care;
- provision of needs-based stroke rehabilitation, support and any appropriate management plans, with the option for re-referral after discharge if stroke rehabilitation needs and goals are defined, and with access to support services on discharge;
- information (aphasia-friendly), advice, and support for people with stroke and their family/carers;
- management protocols for common problems, based upon the best available evidence;
- collaboration, close links and protocols for the transfer of care with inpatient stroke services, primary care, community services and the voluntary sector;
- training for healthcare professionals in the specialty of stroke. [2023]
- H People with stroke and their family/carers should be involved in decisions about the transfer of their care out of hospital, and the care that will be provided. [2023]
- I Members of the early supported discharge and community stroke rehabilitation services should be involved in hospital discharge planning and decision making by attending stroke unit multidisciplinary team meetings. [2023]
- J Before the transfer of care for a person with stroke from hospital to home (including a care home) occurs:
 - the person and their family/carers should be prepared, and have been involved in planning their transfer of care if they are able;
 - primary healthcare teams and social services should be informed before or at the time of the transfer of care;
 - all equipment and support services necessary for a safe transfer of care should be in place;
 - any continuing treatment the person requires should be provided without delay by a co-ordinated, specialist multidisciplinary service;
 - the person and their family/carers should be given information and offered contact with relevant statutory and voluntary agencies (e.g. stroke key worker). [2023]
- K Before the transfer home of a person with stroke who is dependent in any activities, the person's home environment should be assessed by a visit with an occupational therapist. If a home visit is not considered appropriate, they should be offered an access visit or an interview about the home environment including viewing photographs or videos taken by family/carers. [2023]
- L People with stroke who are dependent in personal activities (e.g., dressing, toileting) should be offered a transition package before being transferred home that includes:
 - visits or leave at home prior to the final transfer of care;
 - training and education for their carers specific to their needs;
 - telephone advice and support for three months. [2023]
- M Before the transfer of care for a person with stroke from hospital to home (including a care home) they should be provided with:
 - a named point of contact for information and advice;
 - personalised written information in an appropriate format about their diagnosis, medication and management plan. [2023]
- N People with stroke, including those living in care homes, should continue to have access to specialist services after leaving hospital, and should be provided with information about how to contact them, and supported to do so if necessary. [2023]

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O Early supported discharge and community stroke rehabilitation services should participate in national and local audit, multicentre research, and quality improvement programmes.

[2023]

2.8 Sources

- A-I Fisher et al, 2011, 2013, 2016, 2020, 2021; Langhorne et al, 2017; NHS England, 2022
- J Guideline Development Group consensus
- K Drummond et al, 2013; Guideline Development Group consensus
- L Grasel et al, 2006; Lannin et al, 2007a; Barras et al, 2010
- M, N Guideline Development Group consensus
- O Obligations under the NHS Standard Contract; Guideline Development Group consensus

2.8 Evidence to recommendations

Consensus studies and national policy guidance recommend that services are available to provide early supported discharge and community stroke rehabilitation in a timely way following hospital discharge. They also recommend that the duration and intensity of stroke rehabilitation provided needs to be based on clinical need and tailored to the person's goals and outcomes (Fisher et al, 2011; Fisher et al, 2013; NHS England, 2022). [2023]

There is strong evidence for the effectiveness of stroke specialist early supported discharge for those who experience mild to moderate disability after stroke. Trials and observational studies have demonstrated that early supported discharge can reduce long-term dependency and admission to institutional care and clinical trials demonstrated a reduction in length of hospital stay (Fisher et al, 2016; Langhorne et al, 2017). However, more recent evidence has found that the impact of early supported discharge on length of hospital stay in practice is less than was previously reported in clinical trials, likely due to the fact that the length of hospital stay for all inpatients with stroke is much shorter than when many of the trials were conducted (Fisher et al, 2021). It should be noted that evidence suggests that early supported discharge is only appropriate for a proportion of the stroke population (those with mild to moderate disability - up to 40% of patients) and is usually offered as a time-limited intervention (Fisher et al, 2011). [2023]

Consensus-based recommendations state that people with more severe disability following a stroke, those with rehabilitation needs beyond early supported discharge or those going into residential or nursing homes need access to community stroke rehabilitation. This should be available following discharge from hospital, immediately following early supported discharge, or at a later point if needs are identified within the community (Fisher et al, 2013; NHS England, 2022). People with complex stroke-related needs are likely to require rehabilitation in hospital and should be transferred into the community only when they can be supported in their place of residence, including care homes, by a community stroke rehabilitation service (Fisher et al, 2013; NHS England, 2022). [2023]

The greatest benefits of rehabilitation are associated with co-ordinated, multidisciplinary stroke specialist community services (Langhorne et al, 2017; Fisher et al, 2020). Stroke specialist care is defined as that provided by healthcare professionals with the necessary knowledge, skills and experience in managing stroke, evidenced by a suitable qualification and training. A stroke specialist team or service is defined as a group of specialists who work together regularly to manage people with stroke, and who between them have the specific knowledge and skills to assess and manage most stroke-related problems (Fisher et al, 2013; Fisher et al, 2020; NHS England, 2022). While in some instances it may be appropriate for stroke and neurological rehabilitation to be delivered by the same integrated team, the service must be able to deliver all the relevant recommendations made in this guideline. [2023]

The importance of in-reach from the community and collaborative working across the stroke care pathway has also been emphasised. Members of early supported discharge and community stroke rehabilitation services should be involved in hospital discharge planning and decision making by attending stroke unit multidisciplinary team meetings (Fisher et al, 2013; Fisher et al, 2020). [2023]

Evidence also supports the need for at least a minimum multidisciplinary core team structure defined by recommended ratios of WTE staff per 100 patients treated annually. These ratios should be viewed as the minimum core team requirements and will require local review and modelling to ensure that services meet patients' needs and deliver the required intensity of therapy, recognising that appropriate resources will be required to support people with stroke with more complex disability and needs. To achieve this, existing services including early supported discharge teams and community stroke rehabilitation could be brought together into one integrated seamless service e.g. an Integrated Community Stroke Service (Fisher et al, 2011; Fisher et al, 2020; NHS England, 2022). A regular review of the number of patients seen and monitoring of the patients' characteristics and needs should be an integral process undertaken by community rehabilitation services. [2023]

Stroke services should routinely use standardised measures to monitor the person's recovery (Fisher et al, 2011; Fisher et al, 2013). Consensus and observational studies suggest that the carer's needs should also be assessed and appropriate training in care provided (Fisher et al, 2013; Fisher et al, 2016; NHS England, 2022) although a large cluster RCT of a structured training programme for caregivers of inpatients after stroke showed no benefit of the intervention over usual care (Forster et al, 2013), and further research is needed in this area. [2023]

2.8 Implications

All of the recommendations about transfers of care require close collaboration between those who commission/sanction and provide care in hospital and in the community. Service redesign based around the needs of the person with stroke often requires a willingness to shift resources from one sector to another if that is where care is more appropriately and effectively provided. Service redesign or extra resources may be required to ensure equity of access for people living in care homes. [2016]

2.9 Remotely delivered therapy and telerehabilitation

Remotely delivered therapy is rehabilitation delivered using technology, with a remote therapist personalising a programme or tasks to specifically address identified impairments and goals. Technological innovations such as telerehabilitation may help address barriers to face-to-face rehabilitation, such as time and resource limitations, geographical isolation, and compliance with rehabilitation (Appleby et al, 2019). Remotely delivered therapy is discussed in more detail in Section 4.5 Remotely delivered therapy and telerehabilitation. [2023]

2.10 Measuring rehabilitation outcomes

The measurement of function is central to the rehabilitation process. A review of the literature relating to assessment and measurement is beyond the scope of this guideline, and the Working Party does not specify which measures should be used beyond a small number of specific circumstances and examples. Many valid tools exist and it is important when considering the use of an assessment measure to understand which domain of the WHO ICF framework the instrument is measuring, and to ensure that the instrument is appropriate to the intervention in question (Wade, 1992). Clinicians should be trained in the use of measurement scales to ensure consistent use within the team and to provide an understanding of their properties and limitations. This section therefore only considers the general principles of measurement in stroke rehabilitation. [2016]

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2.10 Recommendations

- A Assessment measures used in stroke rehabilitation should meet the following criteria as far as possible:
 - they should collect relevant data across the required range (i.e. they are valid and fulfil a need);
 - they should have sufficient sensitivity to detect change within a person and differences between people;
 - their reliability should be known when used by different people on different occasions and in different settings;
 - they should be simple to use under a variety of circumstances;
 - they should provide scores that are easily understood. [2016]
- B A stroke service should agree on a standard set of assessment measures that should be collected and recorded routinely. [2016]
- C A stroke service should have protocols for determining the routine collection and use of data that:
 - specify the reason for and proposed use of each assessment measure;
 - provide individual clinicians with a choice of assessment measures where no measure is obviously superior;
 - review the utility of each assessment measure regularly. [2016]
- D A stroke service should have protocols for the use of more complex assessment measures, describing:
 - when it is appropriate or necessary to consider their use;
 - which assessment measure(s) should be used;
 - what specific training or experience is needed to use the assessment measure(s).
 [2016]

2.10 Sources

A–D Wade, 1992; Wikander et al, 1998; Working Party consensus

2.10 Implications

Services should consider the assessment measures that best serve their patients with stroke. These are likely to vary according to where they are in their treatment and recovery, but the preference should always be towards assessment measures that describe activities and participation, as opposed to impairments (see the WHO ICF framework in <u>Section 1.3 Models underpinning guideline development</u>). **[2016]**

2.11 Psychological care – organisation and delivery

Psychological care should be provided by stroke services across acute and community settings. National audits continue to highlight inadequate service provision, and surveys of the long term needs of people with stroke echo the need for service improvement. This section covers issues of service organisation and delivery, with recommendations for the rehabilitation of specific cognitive and mood difficulties contained in Chapter 4. [2016]

The three main models (collaborative care, matched care and stepped care) are summarised in NICE Clinical Guideline 91: Depression in adults with a chronic physical health problem (NICE, 2010b). Stepped care involves starting all people at the lowest level intervention and stepping up to the next level if they do not adequately respond. Matched (or stratified) care includes an initial triage so that people start on the most appropriate step, which may be the highest level. Stepped or matched care

can be part of collaborative care, a model for the management of chronic disease. Collaborative care has four components: collaborative identification of problems; goal-planning; self-management training and support to facilitate intervention plans, behaviour change and emotional coping; and active monitoring and follow-up. [2016]

A key feature of these models is to highlight the complementary roles played by specialists in neuropsychological provision (clinical neuropsychologist/clinical psychologist and assistants) and by other members of the stroke team. In these models the latter provide psychological support at the first and second levels whilst the clinical neuropsychologist/clinical psychologist's role is principally at level three/high-intensity provision and in training other service providers. [2016]

One further model of psychological care is comprehensive neuropsychological rehabilitation, based on a biopsychosocial model of illness. Comprehensive programmes integrate evaluation of cognition, behaviour and emotional needs to formulate the individual's difficulties. They assist in developing alternative or compensatory expectations and behaviours, leading towards independent self-management (see Section 4.4 Self-management). They acknowledge that people with stroke may have limited awareness of impairments or their impact, and that many therapies require motivation for engagement. [2016]

2.11 Recommendations

- A Services for people with stroke should have a comprehensive approach to delivering psychological care that includes specialist clinical psychology/neuropsychology input within the multidisciplinary team. [2016]
- B Services for people with stroke should offer psychological support to all patients regardless of whether they exhibit specific mental health or cognitive difficulties, and use a matched care model to select the level of support appropriate to the person's needs.

 [2016]
- C Services for people with stroke should provide training to ensure that clinical staff have an awareness of psychological problems following stroke and the skills to manage them.

 [2016]
- D Services for people with stroke should ensure that the psychological screening and assessment methods used are appropriate for use with people with aphasia and cognitive impairments. [2016]
- E Services for people with stroke should provide screening for mood and cognitive disturbance within six weeks of stroke (in the acute phase of rehabilitation and at the transfer of care into post-acute services) and at six and 12 months using validated tools and observations over time. [2016]
- F Services for people with stroke should include specialist clinical psychology/neuropsychology provision for severe or persistent symptoms of emotional disturbance, mood or cognition. [2016]
- G Services for people with stroke should consider a collaborative care model for the management of people with moderate to severe neuropsychological problems who have not responded to high-intensity psychological interventions or pharmacological treatments. This care model should involve collaboration between the GP, primary and secondary physical health services and case management, with supervision from a senior mental health professional and should include long-term follow-up. [2016]

2.11 Sources

A Salazar et al, 2000; Cicerone et al, 2008; NICE, 2016d; Working Party consensus

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- B, C Gillham and Clark, 2011; NICE, 2010b; Working Party consensus
- D Working Party consensus
- E NICE, 2016d; Working Party consensus
- F, G Working Party consensus

2.11 Evidence to recommendations

Both NICE (2011) and the former NHS Stroke Improvement Programme (Gillham & Clark, 2011) advocate a stepped-care model based on an initial awareness of need and which places individuals on an appropriate step, or quickly identifies those who need to be immediately stepped up. Essentially, this is matched care. No stroke-specific evidence was found for stepped care. The literature from general mental health includes one systematic review including non-controlled trials (Firth et al, 2015) and one meta-analysis (van Straten et al, 2015). These focused on stepped care for depression and there were no trials in anxiety. They conclude that stepped care is as effective as usual care, with some results favouring stepped care. Both papers noted that the evidence for stepped care was limited and further research was required comparing stepped care with other models such as matched care and collaborative care, both in terms of efficacy and cost-effectiveness. Additionally, what is considered to be stepped care is highly variable, including the quality of services provided and the use of mixed models of service delivery (Firth et al, 2015; van Straten et al, 2015). A Cochrane review (Archer et al, 2012) of the effectiveness of collaborative care for the treatment of depression and anxiety in mental health concluded that collaborative care is associated with greater improvement in depression and anxiety outcomes compared with usual care. [2016]

Most of the evidence for comprehensive and holistic rehabilitation programmes after acquired brain injury, including stroke, comes from case series or cohort studies. Two RCTs in acquired brain injury support the integration of cognitive, interpersonal and functional skills (Salazar et al, 2000; Cicerone et al, 2008). Evidence for long-term improvement is mixed. Methodological concerns were reported in two reviews of traumatic brain injury (Cicerone et al, 2009; Cattelani et al, 2010) suggesting a need for more well-designed trials. [2016]

2.11 Implications

Stroke services need to consider how to develop and maintain the knowledge and skills in all clinical staff to provide appropriate psychological support to people with stroke, and how to provide the high-intensity support needed by a minority of people with cognitive and mental health issues. Compared to historical levels of provision, this will require considerable investment which is likely to prove cost-effective in the longer term. Commissioners/planners of therapy services for people with stroke should bear in mind that many current arrangements do not include psychological provision, or it may be separately commissioned often from another provider. For instance the 2016 NICE Quality Standard QS2 is clear that a clinical psychologist/neuropsychologist with expertise in stroke rehabilitation should be a core member of the multidisciplinary team. Those responsible for planning and providing stroke services should also provide for the long-term management of psychological difficulties of delayed onset (e.g. anxiety, depression). [2016]

2.12 Vocational rehabilitation

Returning to work is an important goal for many people after stroke, and comprehensive stroke services should include vocational rehabilitation provision to support people with stroke to return to work. Vocational rehabilitation is summarised as 'a co-ordinated plan supported by all those working with the employee to optimise their work capability' (British Society of Rehabilitation Medicine, 2021). The organisation and delivery of vocational rehabilitation is discussed in more detail in Section 4.15 Return to work. [2023]

2.13 Follow-up review and longer term support

The course of recovery after stroke in any individual may fall outside expected time frames. The consensus of the Guideline Development Group is that a comprehensive, structured needs reassessment should be undertaken at 6 months and annually thereafter, depending on the individual's needs. This review should consider physical, psychological and social needs (including relationships and work, where applicable) related to adjusting to life after stroke. Whilst limited, there is evidence to suggest that for some people improvements in communication, arm function, walking, physical fitness and ADL can be achieved with interventions more than 6 months after stroke (Palmer & Enderby, 2007; Duncan et al, 2011; Ferrarello et al, 2011; Lohse et al, 2014; Veerbeek et al, 2014b; Ward et al, 2019). The provision and timing of appropriate, person-centred follow-up rehabilitation, holistic structured reviews and long-term support after stroke are discussed in more detail in Sections 5.27 Further rehabilitation, and 5.28 Social integration and participation. [2023]

2.14 Stroke services for younger adults

Stroke occurs at all ages and about a quarter of people with stroke are aged under 65 years. Some younger adults feel that general stroke services, of which the majority of users are older adults, do not meet their needs. For example, younger adults are more likely to have an unusual cause for their stroke, rehabilitation may require specific attention to work and bringing up children, and social needs and expectations may be different. Thus, although all stroke services should respond to the particular needs of each individual regardless of age or other factors, it is appropriate to draw attention to this group of younger people with stroke. Guideline users should also refer to Section 4.15 Return to work. A separate guideline covering stroke in children has been produced (Royal College of Paediatrics and Child Health, 2017). [2023]

2.14 Recommendations

- A All stroke care, including (hyper-) acute care for younger adults with stroke, should be based on an assessment of the person's individual needs and priorities. [2023]
- B Acute stroke services should:
 - recognise and manage the particular physical, psychological and social needs of younger people with stroke (e.g. vocational rehabilitation, childcare);
 - liaise with the most appropriate specialist neurorehabilitation service. [2023]
- C People who have had a stroke in childhood and require ongoing healthcare into adulthood should have their care transferred in a planned manner to appropriate adult services.

 [2023]

2.14 Sources

- A, B Guideline Development Group consensus
- C Department of Health (UK), 2005; Guideline Development Group consensus

2.14 Implications

These recommendations can most readily be met by a specialist neurological rehabilitation service as such services generally, though not exclusively, focus on people of working age. Each locality (health economy) should have a specialist neurological rehabilitation service to comply with the National Service Framework for Long-term (Neurological) Conditions (Department of Health (UK), 2005). There also needs to be a close link between neurological and stroke rehabilitation services and a system in place to ensure that there is a seamless transition for younger people with stroke from paediatric to adult neurological services. [2016]

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2.15 End-of-life (palliative) care

About one in 20 people with acute stroke will be receiving end-of-life care within 72 hours of onset, and one in seven people with acute stroke will die in hospital (Intercollegiate Stroke Working Party, 2016), making stroke one of the most lethal acute conditions in modern medicine. This means that providing high quality end-of-life care is a core activity for any multidisciplinary stroke team. Predicting the prognosis after acute stroke can be challenging and may account for the low proportion of people with stroke identified for end-of-life care in hospital and community settings. Stroke may cause a range of problems including pain and distress, depression, cognitive problems, confusion and agitation, and problems with nutrition and hydration. When these issues are appropriately and holistically managed, distress associated with the end of life for both the person and the family/carers can be alleviated. In particular, while there is the risk of aspiration and choking, rigid adherence to recommendations elsewhere in this guideline on access to oral food or fluids could, in palliative care, result in burdensome restrictions that may exacerbate suffering. The decision-making process to support people to eat and drink with acknowledged risks should be person-centred and involve the person and their family/carers, and other members of the multidisciplinary team and include a swallowing assessment and steps to minimise risk (Royal College of Physicians, 2021; Royal College of Speech and Language Therapists, 2021). The process can be supported by material such as the clinically-assisted nutrition and hydration guidance from the RCP (London)/BMA (2018) at https://www.bma.org.uk/advice-andsupport/ethics/adults-who-lack-capacity/clinically-assisted-nutrition-and-hydration. [2023]

Advance care planning should take place for those people who may survive the acute stroke with limited life expectancy, to facilitate the timely involvement of specialist palliative care services. [2023]

2.15 Recommendations

- A Services providing acute and long-term care for people with stroke should provide high quality end-of-life care for those who need it. [2016]
- B Staff caring for people dying of stroke should be trained in the principles and practice of end-of-life care, including the recognition of people who are approaching the end of life. [2016]
- C Decisions to withhold or withdraw life-prolonging treatments after stroke including artificial nutrition and hydration should, whenever possible, take the person's prior expressed wishes and preferences into account and should be taken in the best interests of that person. When withdrawing artificial nutrition and hydration, a recognised nutrition and hydration decision-making process should be considered. [2023]
- D End-of-life (palliative) care for people with stroke should include an explicit decision not to have burdensome restrictions that may exacerbate suffering. In particular, following assessment this may involve a decision, taken together with the person with stroke, their family/carers, and the multidisciplinary team, to allow oral food or fluids despite risks including aspiration and choking. [2023]
- People with stroke with limited life expectancy, and their family where appropriate, should be offered advance care planning, with access to specialist inpatient and community palliative care services when needed. The multidisciplinary team should establish whether there is any existing documentation of the patient's wishes regarding management of risks associated with continued eating and drinking and whether it remains relevant, and agree with the patient and/or family/carers an advanced care plan where appropriate. [2023]
- F People dying of stroke should have access to specialist palliative care, including the timely transfer of care to their home or to a hospice or care home according to the wishes of the person and their family/carers. This should also include timely communication and

involvement of the primary care team. [2016]

2.15 Sources

- A, B NICE, 2015a; Working Party consensus
- C-E Royal College of Physicians, 2021; Royal College of Speech and Language Therapists, 2021; Guideline Development Group consensus
- F Payne et al, 2010; NICE, 2015a; Working Party consensus

2.15 Evidence to recommendations

Much of the research in end-of-life care has come from the field of cancer, and there are few good quality end-of-life studies in stroke. A Cochrane review by Good et al (2014) reviewed medically assisted hydration in adults receiving palliative care, and concluded there was no clear evidence of benefit with assisted hydration as problems from side effects can be as distressing as symptoms associated with withholding fluids. Gardiner et al (2013) conducted a small qualitative study of focus groups and interviews with the multidisciplinary team, and concluded that more people with stroke should benefit from end-of-life care, and collaboration between palliative care and stroke teams at an earlier stage could improve patient care. [2016]

2.15 Implications

The main implication of these recommendations is that staff in stroke teams will need to increase their awareness and expertise in end-of-life/palliative care and recognise that this is a core part of the work of a comprehensive stroke service. This includes high quality liaison with palliative care and primary care teams. A systematic mortality audit can identify and encourage good practice in this important area of clinical care. [2016]

2.16 Carers

The term 'carers' can refer both to formal, paid carers (people with professional training) and to informal and unpaid carers such as family and friends who undertake care. This section is relevant to informal, unpaid carers: their role and involvement with the person with stroke is central from the outset and is likely to be a constant and continuing relationship with the person, long after other services have ended. [2016]

In the UK, the 2014 Care Act enshrines the legal duty of a Local Authority to assess any carer who requests an assessment or who appears to need support. The authority can use the assessment to identify support needs, and to discuss how these could be met. This might mean providing help or putting the carer in touch with other organisations, such as local charities. There is no Irish equivalent of this Act but the Carer's Leave Act 2001 and the provision for a dedicated carer's allowance support carers in their role in Ireland. [2016]

2.16 Recommendations

- A The views of the person with stroke should be sought, to establish the extent to which they wish family/carers and others to be involved in the planning and delivery of their care. [2016]
- B If the person with stroke agrees, family/carers should be involved in significant decisions as an additional source of information about the person both clinically and socially. [2016]
- C The primary carer(s) of a person with stroke should be offered an educational programme which:
 - explains the nature, consequences and prognosis of stroke and what to do in the event of a further stroke or other problems e.g. post-stroke epilepsy;

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- teaches them how to provide care and support;
- gives them opportunities to practise giving care;
- provides advice on secondary prevention, including lifestyle changes. [2016]
- D When care is transferred out of hospital to the home or care home setting, the carer of a person with stroke should be offered:
 - an assessment of their own needs, separate to those of the person with stroke;
 - the practical or emotional support identified as necessary;
 - guidance on how to seek help if problems develop. [2016]
- E The primary carer(s) of a person with stroke should be provided with the contact details of a named healthcare professional (e.g. a stroke co-ordinator or key worker) who can provide further information and advice. [2016]
- F After a person with stroke has returned to the home or care home setting, their carer should:
 - have their need for information and support reassessed whenever there is a significant change in circumstances (e.g. if the health of the carer or the person with stroke changes);
 - be shown how to seek further help and support. [2016]

2.16 Sources

- A, B Working Party consensus
- C Patel et al, 2004; Legg et al, 2011; Forster et al, 2012
- D Obligations under the 2014 Care Act; Working Party consensus
- E NICE, 2016d; Working Party consensus
- F Obligations under the 2014 Care Act; Working Party consensus

2.16 Evidence to recommendations

Two Cochrane reviews have addressed this issue: Legg et al (2011) and Forster et al (2012). Research into interventions that prepare carers for the role have focused on three main areas; support and information, procedural knowledge, and psycho-educational training (Legg et al, 2011). Whilst these systematic reviews are of high quality and support the provision of information and training for caregivers, information on implementation is lacking. With regard to long-term follow-up, only one Dutch trial (Fens et al, 2014) provided 18-month follow-up data but this was non-randomised and thus subject to bias. An earlier, single-site RCT found that a structured caregiver training programme, delivered in an inpatient setting by stroke unit staff significantly reduced carer burden, anxiety and depression (Patel et al, 2004). However a much larger cluster RCT and economic evaluation did not reproduce these benefits when using a cascade training model i.e. training some staff to train all staff and then to train carers (Forster et al, 2013). A nested process evaluation indicated that many carers had not been trained to the necessary competency level (Clarke et al, 2013) and so the efficacy and generalizability of the cascade model for delivering caregiver training is still unproven, and recommendations remain largely based on consensus regarding best practice. [2016]

2.17 People with stroke in care homes

One in twelve people with stroke have to move into a care home because of their stroke (Intercollegiate Stroke Working Party, 2016). Conversely, about a quarter of care home residents have had a stroke, often in association with other significant co-morbidities. At present people in care homes in both the UK and Ireland rarely receive any ongoing rehabilitation or equipment provision by statutory stroke services despite this being their main domicile. Reducing dependency as far as possible and improving

quality of life for people with stroke whatever their place of residence is an important and compassionate objective of community provision for people with stroke. [2016]

2.17 Recommendations

- A People with stroke living in care homes should be offered assessment and treatment from community stroke rehabilitation services to identify activities and adaptations that might improve quality of life. [2016]
- B Staff caring for people with stroke in care homes should have training in the physical, cognitive, communication, psychological and social effects of stroke and the management of common activity limitations. [2016]
- C People with stroke living in care homes with limited life expectancy, and their family where appropriate, should be offered advance care planning, with access to community palliative care services when needed. [2016]

2.17 Sources

- A Crocker et al, 2013; Working Party consensus
- B, C Working Party consensus

2.17 Evidence to recommendations

A Cochrane review (Crocker et al, 2013) examined the evidence for physical rehabilitation for older people in care homes with a range of co-morbidities that included stroke. The review identified small reductions in disability that may not be applicable to all residents, without adverse effects, and called for further trials. In a large cluster RCT of people with stroke living in care homes (1,042 participants in 228 care homes), Sackley et al (2015) found no benefits in disability, mood or quality of life from a 3-month person-centred goal setting intervention for residents and staff delivered by occupational therapists and assistants. This may be because the functional limitations in this group of people were so severe, and a third of all participants died over the course of the trial. On the strength of current evidence, the best means to reduce dependency and improve quality of life for people with stroke living in care homes is not known. [2016]

2.17 Implications

The extent of unmet need in people living in care homes is unknown, but resource implications are likely. The level of need may be considerable and not easily met within existing resources or with existing interventions. Presently, it will usually be more appropriate for staff from the stroke service to visit the care home which has implications for travel and use of time. Furthermore in practice it would be difficult within a single home, both morally and practically, to restrict input to people with stroke when many other residents may also need and benefit from specialist rehabilitation assessment, advice and interventions. [2016]

2.18 Service governance and quality improvement

Stroke services should develop a culture of continuous quality improvement, and attention to good governance is mandatory. The obligation to seek and respond to information regarding service quality, safety and patient experience is another of the principal implications of the 2013 Francis report into the failings in hospital care at Mid-Staffordshire NHS Foundation Trust (Francis, 2013). The process of clinical governance should be embedded within all healthcare organisations, and this section only considers the stroke-specific aspects. People's perceptions of the quality of care they receive do not always match the clinicians' views of the care that they have delivered and these views need to be separately audited, in a manner that enables the participation of those with significant disabilities. The

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process of quality improvement includes collecting appropriate data in a timely manner, analysing the data and acting upon the findings. [2016]

2.18 Recommendations

- A Clinicians providing care for people with stroke should participate in national stroke audit to enable comparison of the clinical and organisational quality of their services, and use the findings to plan and deliver service improvements. [2016]
- B Services for people with stroke should take responsibility for all aspects of service quality by:
 - keeping a quality register of all people admitted to their organisation with a stroke;
 - regularly reviewing service provision against the evidence-based standards set out in relevant national clinical guidelines;
 - providing practical support and multidisciplinary leadership to the process of clinical audit;
 - encouraging patients to participate in research whenever possible;
 - participating actively in regional and national quality improvement initiatives such as Clinical Networks. [2016]
- C General practitioners should regularly audit the primary and secondary prevention of stroke within their practice, and maintain a register of people with stroke or TIA. [2016]
- D The views of people with stroke and their family/carers should be actively sought when evaluating service quality and safety, and when planning service developments. [2016]
- People with stroke and their family/carers should be offered any practical support necessary to enable participation in service user consultations. [2016]

2.18 Sources

- A, B Obligations under the NHS Standard Contract; Working Party consensus
- C-E Working Party consensus

2.18 Implications

Data collection and quality control procedures require specific resources, including staff time and unfortunately these are often not made available, particularly for continuous audit. It also requires commitment to the process by the whole multidisciplinary team. Regulators and other organisations that monitor performance should use data that are collected routinely or through national audit, rather than demanding data that require additional resources to deliver. [2016]

Some resources need to be allocated to facilitate the involvement of service users who have limitations with mobility or communication. These recommendations require organisations to be supportive and listening in their attitude to the opinions of service users. [2016]

3 Acute care

3.0 Introduction

This chapter covers the acute presentation and treatment of people with stroke and TIA. The recommendations relate to the diagnosis and management of the underlying condition (at the WHO-ICF framework level of pathology) over the course of the first few days while clinical stability is being achieved, complications prevented, and rehabilitation can begin in earnest. A detailed examination of the evidence for rehabilitation is contained in Chapter 4. [2023]

3.1 Pre-hospital care

Most people with acute stroke (95%) have their first symptoms outside hospital. It is vital that members of the public and healthcare professionals (e.g. primary care team members, telephone advice line staff, paramedics, accident and emergency (A&E) personnel) can recognise stroke as early and accurately as possible to facilitate an appropriate emergency response. Measures taken by clinicians outside hospital (such as reduced time at the scene) can reduce the overall time to treatment, and thereby improve the prospects for the patient to respond to time-critical treatments. [2016]

3.1 Recommendations

- A People seen by ambulance clinicians outside hospital with sudden onset of focal neurological symptoms should be screened for hypoglycaemia with a capillary blood glucose, and for stroke or TIA using a validated tool. Those people with persisting neurological symptoms who screen positive using a validated tool should be transferred to a hyperacute stroke service as soon as possible. [2016]
- B People who are negative when screened with a validated tool but in whom stroke is still suspected should be treated as if they have stroke until the diagnosis has been excluded by a specialist stroke clinician. [2016]
- C The pre-hospital care of people with suspected stroke should minimise time from call to arrival at hospital and should include a hospital pre-alert to expedite specialist assessment and treatment. [2016]
- D Patients with suspected stroke whose airway is considered at risk should be managed appropriately with suction, positioning and airway adjuncts. [2016]
- E Patients with residual neurological symptoms or signs should remain nil by mouth until screened for dysphagia by a specifically trained healthcare professional. [2016]
- Patients with suspected TIA should be given 300 mg of aspirin immediately and assessed urgently within 24 hours by a specialist physician in a neurovascular clinic or an acute stroke unit. [2016]
- G Patients with suspected stroke or TIA should be monitored for atrial fibrillation and other arrhythmias. [2016]

3.1 Sources

- A Harbison et al, 2003; Working Party consensus
- B-E Working Party consensus
- F Rothwell, 2007; Lavallee et al, 2007; Giles and Rothwell, 2007; Rothwell et al, 2016
- G Working Party consensus

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3.1 Evidence to recommendations

A number of pre-hospital screening tools have been developed that are sensitive in detecting the majority of people with acute stroke that present with facial weakness, speech disturbance or unilateral limb weakness. The FAST test is accepted as the screening tool of choice for clinicians and the general public (Harbison et al, 2003). However, some people with symptoms of stroke will not be identified by the FAST test (e.g. sudden onset visual disturbance, lateralising cerebellar dysfunction) and thus stroke may not be suspected. The Working Party considers that community-based clinicians should continue to treat a person as having a suspected stroke if they are suspicious of the diagnosis despite a negative FAST test. Further evidence is required before the Working Party could recommend the use of other screening tools, e.g. forms of the National Institutes of Health Stroke Scale (NIHSS), Recognition of Stroke in the Emergency Room (ROSIER) that screen for non-FAST symptoms in the pre-hospital phase. [2016]

Community-based clinicians are likely to assess people whose neurological symptoms have already resolved before reaching hospital, suggesting a diagnosis of TIA rather than stroke. These people should be given antiplatelet treatment with aspirin immediately (Rothwell et al, 2016) and referred for urgent investigation in a specialist neurovascular clinic since the risk of subsequent stroke is substantial in the first few days. There was insufficient precision in the current evidence for the Working Party to make recommendations concerning risk stratification by community-based clinicians. When considering the diagnosis of TIA and making a direct referral, clinicians need to be aware that a person may have ongoing focal neurological deficits despite a negative FAST test – such people should be managed along the acute stroke pathway rather than a TIA pathway. [2016]

There is a general paucity of research evidence on the management of the person with suspected stroke before arrival at the hospital. The majority of recommendations are based on consensus and widely accepted practice in the pre-hospital management of people with suspected stroke or TIA. Pre-hospital brain imaging in other healthcare settings may reduce onset-to-treatment time (Ebinger et al, 2014), but cost-effectiveness and clinical outcomes have not been tested in UK/Ireland settings. [2016]

3.1 Implications

The training of primary care teams, other healthcare personnel and the general public in the recognition of the signs of possible stroke using the FAST involves an ongoing public health commitment requiring multiple approaches (Section 2.1 Public awareness of stroke). Patients in groups at high risk of stroke (e.g. older people with diabetes, hypertension or atrial fibrillation) and their family and/or carers should have training in the FAST test as part of their disease education. [2016]

3.2 Management of TIA and minor stroke – assessment and diagnosis

Any person with a fully resolved acute onset neurological syndrome that might be due to cerebrovascular disease needs urgent specialist assessment to establish the diagnosis and to determine whether the cause is vascular, given that about half have an alternative diagnosis. [2023]

3.2 Recommendations

- A Patients with acute focal neurological symptoms that resolve completely within 24 hours of onset (i.e. suspected TIA) should be given aspirin 300 mg immediately unless contraindicated and assessed urgently within 24 hours by a stroke specialist clinician in a neurovascular clinic or an acute stroke unit. [2023]
- B Healthcare professionals should not use assessment tools such as the ABCD2 score to stratify risk of TIA, inform urgency of referral or subsequent treatment options. [2023]

- C Patients with suspected TIA that occurred more than a week previously should be assessed by a stroke specialist clinician as soon as possible within 7 days. [2016]
- D Patients with suspected TIA and their family/carers should receive information about the recognition of stroke symptoms and the action to be taken if they occur. [2016]
- Patients with suspected TIA should be assessed by a stroke specialist clinician before a decision on brain imaging is made, except when haemorrhage requires exclusion in patients taking an anticoagulant or with a bleeding disorder when unenhanced CT should be performed urgently. [2023]
- For patients with suspected TIA, MRI should be the principal brain imaging modality for detecting the presence and/or distribution of brain ischaemia. [2023]
- G For patients with suspected TIA in whom brain imaging cannot be undertaken within 7 days of symptoms, MRI (using a blood-sensitive sequence, e.g. SWI or T2*-weighted imaging) should be the preferred means of excluding haemorrhage. [2023]

3.2 Sources

- A Lavallee et al, 2007; Rothwell et al, 2016; Guideline Development Group consensus
- B Amarenco et al, 2012; Ildstad et al, 2021
- C Giles and Rothwell, 2007
- D Working Party consensus
- E-G Wardlaw et al, 2014; NICE, 2022e

3.2 Evidence to recommendations

A systematic review of observational studies of the risk of stroke within 7 days of confirmed TIA (Giles & Rothwell, 2007) showed a risk of stroke at 2 days of between 2.0 and 4.1%, and at 7 days of between 3.9 and 6.5%. The risk of completed stroke was much lower in studies of emergency treatment in specialist stroke services compared to non-urgent settings (0.9% v. 11.0%). Patients with suspected TIA should therefore have a full diagnostic assessment urgently without further risk stratification (Lavallee et al, 2007; Wardlaw et al, 2014). Risk predictive clinical tools such as ABCD2, ABCD2-I and ABCD3-I scores did not discriminate sufficiently between low- and high-risk patients in both the short-term and long-term follow-up (Ildstad et al, 2021) either for determining the urgency of assessment or subsequent treatment options (Amarenco et al, 2012) and their use is no longer recommended. Secondary prevention measures which can reduce the risk of recurrence should be promptly initiated (Rothwell, 2007). Additional risk may be conferred by the presence of atrial fibrillation or anticoagulant therapy, or with recurrent attacks, while patients presenting with symptoms more than a week ago can be considered at lower risk. [2023]

There is little evidence to guide the use of brain imaging in suspected TIA. The consensus of the Guideline Development Group is that imaging all people referred to a neurovascular clinic is not always appropriate or cost-effective given the high rate of stroke mimics in most clinics. Patients with suspected TIA should normally be assessed by a specialist clinician before a decision on brain imaging is made, and imaging should be used in those patients where the results are likely to influence management such as reducing diagnostic uncertainty, confirming the territory of ischaemia prior to making a decision about carotid artery surgery and prior to commencing dual antiplatelet therapy. When the exclusion of haemorrhage is the objective of imaging, early unenhanced computed tomography (CT) remains the most sensitive investigation (Wardlaw et al, 2014). The greater sensitivity of magnetic resonance imaging (MRI) to detect ischaemic lesions using diffusion-weighted imaging (DWI) makes it the modality of choice if positive confirmation of the presence or location of a lesion is the objective (Whiteley et al, 2022), but the significant false-negative rate with DWI precludes

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its use as a diagnostic tool in isolation from clinical assessment, particularly in unselected patients (Wardlaw et al, 2014). [2023]

3.2 Implications

Additional training of healthcare professionals and other primary care staff may be required so that they are able to appreciate the immediate risk in people presenting with a suspected TIA or minor stroke, advise immediate aspirin use where appropriate and expedite the process of referral for diagnostic assessment. Referrers and neurovascular clinics should discontinue the practice of triaging patients with suspected TIA according to risk stratification tools, and ensure that all patients with suspected TIA are assessed and diagnosed urgently 7 days a week. [2023]

3.3 Management of TIA and minor stroke – treatment and vascular prevention

Patients who have short-lived symptoms due to cerebrovascular disease remain at high risk of further vascular events, and this risk is highest in the first few days. Consequently, their management is urgent. This section covers medical and surgical management following confirmation of the diagnosis. [2023]

3.3 Recommendations

- A Patients with minor ischaemic stroke or TIA should receive treatment for secondary prevention as soon as the diagnosis is confirmed, including:
 - support to modify lifestyle factors (smoking, alcohol consumption, diet, exercise);
 - antiplatelet or anticoagulant therapy;
 - high intensity statin therapy;
 - blood pressure-lowering therapy with a thiazide-like diuretic, long-acting calcium channel blocker or angiotensin-converting enzyme inhibitor. [2023]
- B Patients with TIA or minor ischaemic stroke should be given antiplatelet therapy provided there is neither a contraindication nor a high risk of bleeding. The following regimens should be considered as soon as possible:
 - For patients within 24 hours of onset of TIA or minor ischaemic stroke and with a low risk of bleeding, the following dual antiplatelet therapy should be given:
 Clopidogrel (initial dose 300 mg followed by 75 mg per day) plus aspirin (initial dose 300 mg followed by 75 mg per day for 21 days) followed by monotherapy with clopidogrel 75 mg once daily
 OR
 - Ticagrelor (initial dose 180 mg followed by 90 mg twice daily) plus aspirin (300 mg followed by 75 mg daily for 30 days) followed by antiplatelet monotherapy with ticagrelor 90 mg twice daily or clopidogrel 75 mg once daily at the discretion of the prescriber;
 - For patients with TIA or minor ischaemic stroke who are not appropriate for dual antiplatelet therapy, clopidogrel 300 mg loading dose followed by 75 mg daily should be given;
 - A proton pump inhibitor should be considered for concurrent use with dual antiplatelet therapy to reduce the risk of gastrointestinal haemorrhage;
 - For patients with recurrent TIA or stroke whilst taking clopidogrel, consideration should be given to clopidogrel resistance. [2023].
- C Patients with TIA or ischaemic stroke should receive high-intensity statin therapy (e.g. atorvastatin 20-80 mg daily) started immediately. [2023]

- D Patients with non-disabling ischaemic stroke or TIA in atrial fibrillation should be anticoagulated, as soon as intracranial bleeding has been excluded, with an anticoagulant that has rapid onset, provided there are no other contraindications. [2016]
- Patients with ischaemic stroke or TIA who after specialist assessment are considered candidates for carotid intervention should have carotid imaging performed within 24 hours of assessment. This includes carotid duplex ultrasound or either CT angiography or MR angiography. [2023]
- F The degree of carotid artery stenosis should be reported using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method. [2016]
- G Patients with TIA or acute non-disabling ischaemic stroke with stable neurological symptoms who have symptomatic severe carotid stenosis of 50–99% (NASCET method) should:
 - be assessed and referred for carotid endarterectomy to be performed as soon as possible within 7 days of the onset of symptoms in a vascular surgical centre routinely participating in national audit;
 - receive optimal medical treatment: control of blood pressure, antiplatelet treatment, cholesterol reduction through diet and medication, and lifestyle advice including smoking cessation. [2016]
- H Patients with TIA or acute non-disabling ischaemic stroke who have mild or moderate carotid stenosis of less than 50% (NASCET method) should:
 - not undergo carotid intervention;
 - receive optimal medical treatment: control of blood pressure, antiplatelet treatment, cholesterol reduction through diet and medication, and lifestyle advice including smoking cessation. [2016]
- Patients with recurrent attacks of transient focal neurological symptoms despite optimal medical treatment, in whom an embolic source has been excluded, should be reassessed for an alternative neurological diagnosis. [2016]
- J Patients who meet the criteria for carotid intervention but who are unsuitable for open surgery (e.g. inaccessible carotid bifurcation, re-stenosis following endarterectomy, radiotherapy-associated carotid stenosis) should be considered for carotid angioplasty and stenting. [2016]
- K Patients who have undergone carotid revascularisation should be reviewed postoperatively by a stroke clinician to optimise medical aspects of vascular secondary prevention. [2016]

3.3 Sources

- A PROGRESS Collaborative Group, 2001; Rothwell et al, 2007; NICE, 200b, 2022e, 2023a; Follows from the evidence concerning antiplatelet treatment and lipid modification (Section 5.5 Lipid modification, Section 5.6 Antiplatelet treatment)
- B Wang et al, 2013, 2021c; Johnston et al, 2018, 2020
- C Rothwell et al, 2007; NICE, 2010b, 2022e, 2023a
- D Working party consensus
- E Guideline Development Group consensus
- F Working Party consensus
- G, H Barnett et al, 1998; Rothwell et al, 2003b; NICE, 2022d, 2023a; Working Party consensus
- I Working Party consensus

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- J Economopoulos et al, 2011; International Carotid Stenting Study investigators, 2010; Bonati et al, 2012
- K Working Party consensus

3.3 Evidence to recommendations

Ischaemic stroke and TIA are similar manifestations of vascular disease and their treatment for the prevention of recurrent vascular events reflects this. Long-term risk factor management is reviewed in Chapter 5 on secondary prevention. In the acute setting, there is no evidence to support the use of anticoagulation for recurrent TIA for those in sinus rhythm. There are also no studies specifically addressing the clinical benefit of early anticoagulation for patients with cardioembolic TIA, but the consensus of the Working Party is that the balance of risk and benefit from the early secondary prevention of cardioembolism with a rapidly-acting anticoagulant is favourable in the majority of patients. [2016]

Recent evidence supports the early use of dual antiplatelet therapy in patients with TIA or minor ischaemic stroke. The CHANCE trial (Wang et al, 2013) showed in a Chinese population of patients with TIA or minor ischaemic stroke (NIHSS 0-3) that dual antiplatelet therapy started within 24 hours of onset for 21 days resulted in a significant reduction in ischaemic stroke from 11.7% (aspirin group) to 8.2 % (aspirin-clopidogrel group) with no significant difference in haemorrhagic stroke. A 300 mg loading dose of clopidogrel was used in this trial. The POINT trial (Johnston et al, 2018) showed in patients with TIA or minor ischaemic stroke (NIHSS 0-3) that dual antiplatelet therapy started within 12 hours of onset and continued for 90 days resulted in a significant reduction of ischaemic stroke from 6.5% (aspirin group) to 5.0% (aspirin-clopidogrel group). The trial was stopped early because of effectiveness and a significant increase in major haemorrhage in the dual antiplatelet group with an absolute risk increase of 0.5%. A 600 mg loading dose of clopidogrel was used in this trial. Pooled analysis of these trials demonstrated the benefit of dual antiplatelet therapy up to at least 21 days. The THALES trial (Johnston et al, 2020), showed in patients with a high-risk TIA or minor ischaemic stroke (NIHSS 0-5) that dual antiplatelet therapy with aspirin and ticagrelor started within 24 hours of onset resulted in a significant reduction in composite outcome of stroke or death from 6.6% (aspirin group) to 5.5% (aspirin-ticagrelor group) within 30 days. A 180 mg loading dose of ticagrelor was used. Severe bleeding was more frequent with ticagrelor with an absolute risk increase of 0.4%. In these three trials, high risk TIA was defined using an ABCD2 score of 4 or 6, despite evidence that the score performs poorly in successfully identifying TIAs previously identified as low risk which should be considered high risk (Amarenco et al, 2012). In these trials of TIA and minor stroke, patients underwent either CT or MRI to exclude the presence of cerebral haemorrhage or alternative explanations for their symptoms. [2023]

A substantial proportion of patients with TIA and stroke in some populations may be resistant to clopidogrel (Pan et al, 2017). Clopidogrel resistance and non-responsiveness is linked to a genetic polymorphism in the cytochrome *CYP2C19* loss-of-function allele. Ticagrelor is not affected. In a selected Chinese population with a genetic polymorphism in the *CYP2C19* loss-of-function allele, the CHANCE 2 trial (Wang et al, 2021c) showed that the risk of ischaemic stroke was significantly reduced from 7.6% in patients treated with clopidogrel (90 days) plus aspirin (21 days) to 6.0% in those randomised to ticagrelor (90 days) plus aspirin (21 days). These results are promising but not yet generalisable owing to the selected nature of the population. **[2023]**

Carotid imaging is essential for any patient, presenting with symptoms suggesting anterior circulation cerebral ischaemia, who might be suitable for intervention for carotid stenosis. There are two methods for reporting the degree of carotid stenosis that give differing results, derived from the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST). Both are valid but the Working Party considers that the NASCET method is preferred (Rothwell et al, 2003b). After carotid territory TIA or non-disabling stroke, the Working Party consensus was that carotid intervention should be performed as soon as possible. [2016]

A Cochrane review of carotid stenting for symptomatic carotid stenosis identified a higher risk of both short- and long-term stroke complications, especially in patients 70 years and older, but a lower risk of peri-procedural myocardial infarction and cranial nerve injury (Bonati et al, 2012). This section should be read in conjunction with Section 5.3 *Carotid artery stenosis*. [2016]

3.3 Implications

Local health economies and networks should establish clinical pathways designed to expedite referral of appropriate patients to vascular surgical centres, especially where reconfiguration has resulted in vascular services being at another site. [2016]

A protocol should be in place for the use of parenteral or direct oral anticoagulants (DOACs) in the setting of a neurovascular clinic, with a process to supervise the transition from acute to long-term anticoagulation. [2016]

3.4 Diagnosis and treatment of acute stroke – imaging

Stroke is a medical emergency and if outcomes are to be optimised there should be no time delays in diagnosis and treatment. Any person with the acute onset of a focal neurological syndrome with persisting symptoms and signs (i.e. suspected stroke) needs urgent diagnostic assessment to differentiate between acute stroke and other causes needing their own specific treatments. To maximise the potential benefit from revascularisation treatments and the acute management of intracerebral haemorrhage, a corresponding increase in the availability of advanced imaging techniques is required, and all hyperacute stroke services should have timely access to brain imaging including CT or MR angiography and perfusion (See Section 2.3 *Transfer to acute stroke services*). [2023]

Underlying causes of stroke such as heart disease, diabetes and hypertension need diagnosis and management in their own right, but these are outside the scope of this guideline. [2016]

3.4 Recommendations

- A Patients with suspected acute stroke should be admitted directly to a hyperacute stroke service and be assessed for emergency stroke treatments by a specialist clinician without delay. [2016]
- B Patients with suspected acute stroke should receive brain imaging as soon as possible (at most within 1 hour of arrival at hospital). [2023]
- C Interpretation of acute stroke imaging for decisions regarding reperfusion treatment should only be made by healthcare professionals who have received appropriate training.

 [2023]
- D Patients with ischaemic stroke who are potentially eligible for mechanical thrombectomy should have a CT angiogram from aortic arch to skull vertex immediately. This should not delay the administration of intravenous thrombolysis. [2023]
- Patients with stroke with a delayed presentation for whom reperfusion is potentially indicated should have CT or MR perfusion as soon as possible (at most within 1 hour of arrival at hospital). An alternative for patients who wake up with stroke is MRI measuring DWI-FLAIR mismatch. [2023]
- F MRI brain with stroke-specific sequences (DWI with SWI or T2*-weighted imaging) should be considered in patients with suspected acute stroke when there is diagnostic uncertainty. [2023]

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3.4 Sources

- A, B Follows from the evidence for emergency stroke treatments in <u>Section 3.5 Management</u> of ischaemic stroke, 3.6 Management of intracerebral haemorrhage
- C Spokoyny et al, 2014; Guideline Development Group consensus
- D, E Follows from the evidence for emergency stroke treatments in <u>Section 3.5 Management</u> of ischaemic stroke
- F Wardlaw et al, 2014

3.4 Evidence to recommendations

The evidence supporting stroke unit care from the Stroke Unit Trialists in the 1990s has been updated in a 2013 Cochrane review, which found that patients with stroke who receive organised inpatient care in a stroke unit are more likely to be alive, independent, and living at home one year after a stroke (Stroke Unit Trialists' Collaboration, 2013). [2016]

Imaging patients with suspected stroke immediately is cost-effective compared to other approaches because it enables emergency treatments directed at the pathology of stroke (Wardlaw et al, 2004), although MRI with DWI may be required when diagnostic uncertainty persists (Wardlaw et al, 2014). Interpretation of acute stroke imaging by trained non-radiologists is safe and effective (Spokoyny et al, 2014). Multi-modal imaging is becoming more widely available and quicker to undertake and interpret. It is recommended that if multi-modal imaging is required, all relevant imaging should be performed in the same session to avoid delays in decision making for acute treatments (National Optimal Stroke Imaging Pathway [NOSIP], NHS England, 2021). The recommendations regarding reperfusion treatments contained in Section 3.5 Management of ischaemic stroke require CT angiography (with or without CT perfusion) to be performed immediately in potentially eligible patients, but image processing and interpretation should not delay intravenous thrombolysis if this is indicated. [2023]

3.4 Implications

These recommendations align with the recommendations in Chapter 2 concerning the organisation of acute stroke care and <u>Sections 3.5 Management of ischaemic stroke</u> and <u>3.6 Management of intracerebral haemorrhage</u> regarding the management of acute stroke. Hyperacute stroke services will need to review their provision of specialist assessment and imaging policies for people with suspected acute stroke, which in many centres will involve a step-change in provision. [2023]

3.5 Management of ischaemic stroke

Thrombolysis with alteplase is now administered to between 10 and 11% of patients with acute stroke in the UK and Ireland (Scottish Stroke Care Audit, 2022; Sentinel Stroke National Audit Programme, 2022; National Office of Clinical Audit (Ireland), 2023) although higher rates should be readily achievable (Allen et al, 2022). Treatment with thrombolysis should only be given in units where staff are trained and experienced in the provision of stroke thrombolysis, and have a thorough knowledge of the contraindications to treatment and the management of complications such as neurological deterioration. [2023]

Reperfusion treatment for people with acute ischaemic stroke has evolved significantly since the 2016 edition and new guidance is provided in this section, including updates to the management of thrombolysis and thrombectomy. [2023]

3.5 Recommendations

A Patients with acute ischaemic stroke, regardless of age or stroke severity, in whom treatment can be started within 4.5 hours of known onset, should be considered for

- thrombolysis with alteplase or tenecteplase. [2023]
- B Patients with acute ischaemic stroke, regardless of age or stroke severity, who were last known to be well more than 4.5 hours earlier, should be considered for thrombolysis with alteplase if:
 - treatment can be started between 4.5 and 9 hours of known onset, or within 9 hours of the midpoint of sleep when they have woken with symptoms

AND

- they have evidence from CT/MR perfusion (core-perfusion mismatch) or MRI (DWI-FLAIR mismatch) of the potential to salvage brain tissue (see Table 3.5.1 below).

This should be irrespective of whether they have a large artery occlusion and require mechanical thrombectomy.

Table 3.5.1 Eligibility criteria for extending thrombolysis to 4.5-9 hours and wake-up stroke

	Time window	Imaging	Imaging criteria
Wake-up stroke	>4.5 hours from last seen well, no upper limit	MRI DWI-FLAIR mismatch	DWI lesion and no FLAIR lesion
Wake-up stroke or unknown onset time	>4.5 hours from last seen well, and within 9 hours of the midpoint of sleep. The midpoint of sleep is the time halfway between going to bed and waking up	CT or MRI core- perfusion mismatch	Suggested: mismatch ratio greater than 1.2, a mismatch volume greater than 10 mL, and an ischaemic core volume <70 mL
Known onset time	4.5-9 hours	CT or MRI core- perfusion mismatch	Suggested: mismatch ratio greater than 1.2, a mismatch volume greater than 10 mL, and an ischaemic core volume <70 mL

[2023]

- C Patients with acute ischaemic stroke otherwise eligible for treatment with thrombolysis should have their blood pressure reduced to below 185/110 mmHg before treatment.

 [2016]
- D Thrombolysis should only be administered within a well-organised stroke service with:
 - processes throughout the emergency pathway to minimise delays to treatment to ensure that thrombolysis is administered as soon as possible after stroke onset;
 - staff trained in the delivery of thrombolysis and monitoring for post-thrombolysis complications;
 - nurse staffing levels equivalent to those required in level 1 or level 2 nursing care with training in acute stroke and thrombolysis;
 - timely access to appropriate imaging and trained staff;
 - protocols in place for the management of post-thrombolysis complications. [2016]
- E Emergency medical staff, if appropriately trained and supported, should only administer thrombolysis for the treatment of acute ischaemic stroke provided that patients can be subsequently managed within a hyperacute stroke service with appropriate neuroradiological and stroke specialist support. [2016]
- Patients with acute ischaemic stroke eligible for mechanical thrombectomy should receive prior intravenous thrombolysis (unless contraindicated) irrespective of whether they have presented to an acute stroke centre or a thrombectomy centre. Every effort should be made to minimise process times throughout the treatment pathway and thrombolysis

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- should not delay urgent transfer to a thrombectomy centre. [2023]
- Patients with acute anterior circulation ischaemic stroke, who were previously independent (mRS 0-2), should be considered for combination intravenous thrombolysis and intra-arterial clot extraction (using a stent retriever and/or aspiration techniques) if they have a proximal intracranial large artery occlusion causing a disabling neurological deficit (NIHSS score of 6 or more) and the procedure can begin within 6 hours of known onset. [2023]
- H Patients with acute anterior circulation ischaemic stroke and a contraindication to intravenous thrombolysis but not to thrombectomy, who were previously independent (mRS 0-2), should be considered for intra-arterial clot extraction (using a stent retriever and/or aspiration techniques) if they have a proximal intracranial large artery occlusion causing a disabling neurological deficit (NIHSS score of 6 or more) and the procedure can begin within 6 hours of known onset. [2023]
- Patients with acute anterior circulation ischaemic stroke and a proximal intracranial large artery occlusion (ICA and/or M1) causing a disabling neurological deficit (NIHSS score of 6 or more) of onset between 6 and 24 hours ago, including wake-up stroke, and with no previous disability (mRS 0 or 1) should be considered for intra-arterial clot extraction (using a stent retriever and/or aspiration techniques, combined with thrombolysis if eligible) providing the following imaging criteria are met:
 - between 6 and 12 hours: an ASPECTS score of 3 or more, irrespective of the core infarct size;
 - between 12 and 24 hours: an ASPECTS score of 3 or more and CT or MRI perfusion mismatch of greater than 15 mL, irrespective of the core infarct size. [2023]
- Clinicians interpreting brain imaging for eligibility for mechanical thrombectomy should have the appropriate knowledge and skills and should consider all the available information (e.g. plain and angiographic images, colour maps, Al-derived figures for core/penumbra and mismatch overlays). [2023]
- Religibles in the posterior circulation within 12 hours of onset should be considered for mechanical thrombectomy (combined with thrombolysis if eligible) if they have a confirmed intracranial vertebral or basilar artery occlusion and their NIHSS score is 10 or more, combined with a favourable PC-ASPECTS score and Pons-Midbrain Index. Caution should be exercised when considering mechanical thrombectomy for patients presenting between 12 and 24 hours of onset and/or over the age of 80 owing to the paucity of data in these groups. [2023]
- The selection of anaesthetic technique for thrombectomy should be guided by local protocols for general anaesthesia, local anaesthesia and conscious sedation which include choice of anaesthetic agents, timeliness of induction, blood pressure parameters and postoperative care. Selection of anaesthesia should be based on an individualised assessment of patient risk factors, technical requirements of the procedure and other clinical characteristics such as conscious level and degree of agitation. General anaesthesia should be considered in the following circumstances:
 - patients with agitation or a reduced level of consciousness, or those judged to be at high risk of requiring conversion to general anaesthesia;
 - patients with airway compromise or who are already intubated, or at risk of aspiration due to nausea or vomiting;
 - patients in whom, due to technical or anatomical factors, thrombectomy is anticipated to be more complicated. [2023]
- M Hyperacute stroke services providing endovascular therapy should participate in national

stroke audit to enable comparison of the clinical and organisational quality of their services with national data, and use the findings to plan and deliver service improvements. **[2016]**

- N Patients with middle cerebral artery (MCA) infarction who meet the criteria below should be considered for decompressive hemicraniectomy. Patients should be referred to neurosurgery within 24 hours of stroke onset and treated within 48 hours of stroke onset:
 - pre-stroke mRS score of 0 or 1;
 - clinical deficits indicating infarction in the territory of the MCA;
 - NIHSS score of more than 15;
 - a decrease in the level of consciousness to a score of 1 or more on item 1a of the NIHSS;
 - signs on CT of an infarct of at least 50% of the MCA territory with or without additional infarction in the territory of the anterior or posterior cerebral artery on the same side, or infarct volume greater than 145 mL on MRI DWI. [2016]
- O Patients with acute ischaemic stroke treated with thrombolysis should be started on an antiplatelet agent after 24 hours unless contraindicated, once significant haemorrhage has been excluded. [2016]
- P Patients with disabling acute ischaemic stroke should be given aspirin 300 mg as soon as possible within 24 hours (unless contraindicated):
 - orally if they are not dysphagic;
 - rectally or by enteral tube if they are dysphagic.
 - Thereafter aspirin 300 mg daily should be continued until 2 weeks after the onset of stroke at which time long-term antithrombotic treatment should be initiated. Patients being transferred to care at home before 2 weeks should be started on long-term treatment earlier. [2016]
- Q Patients with acute ischaemic stroke reporting previous dyspepsia with an antiplatelet agent should be given a proton pump inhibitor in addition to aspirin. [2016]
- R Patients with acute ischaemic stroke who are allergic to or intolerant of aspirin should be given an alternative antiplatelet agent (e.g. clopidogrel). [2016]

3.5 Sources

- A Wardlaw et al, 2012; Emberson et al, 2014; Menon et al, 2022
- B Thomalla et al, 2018; Campbell et al, 2019
- C, D Wardlaw et al, 2012; Working Party consensus
- E Working Party consensus
- F Yang et al, 2020; LeCouffe et al, 2021; Suzuki et al, 2021; Zi et al, 2021; Fischer et al, 2022; Mitchell et al, 2022; Turc et al, 2022
- G, H Goyal et al, 2016
- I Sarraj et al, 2023; Huo et al, 2023
- J Jovin et al, 2022a, b
- K Liu et al, 2020; Langezaal et al, 2021; Tao et al, 2022; Jovin et al, 2022a
- L Mortimer et al, 2021; Maurice et al, 2022
- M Obligations under the NHS Standard Contract; Working Party consensus
- N Cruz-Flores et al, 2012; Jüttler et al, 2014
- O, P Sandercock et al, 2015; Working Party consensus

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Q, R NICE, 2010a; Working Party consensus

3.5 Evidence to recommendations

An updated Cochrane systematic review and an individual patient meta-analysis by the Stroke Thrombolysis Trialists' Collaboration guide the use of intravenous thrombolysis without advanced imaging (International Stroke Trial Collaborative Group, 2012; Wardlaw et al, 2012; Emberson et al, 2014). These analyses emphasise the importance of rapid treatment. Patients who are over 80 years old with mild or severe stroke and those with early signs of infarction on initial brain imaging all benefit from treatment. [2023]

The Enhanced Control of Hypertension and Thrombolysis Stroke Study (ENCHANTED) of lower (0.6 mg/kg) versus standard dose alteplase showed a lower risk of intracerebral haemorrhage and early mortality with the lower dose, without conclusively demonstrating that the doses were of equivalent efficacy (Anderson et al, 2016). These findings suggest that there may be circumstances in which the treating physician and/or the patient wish to forgo some of the potential disability benefit from standard dose alteplase in order to reduce the early risk of intracerebral haemorrhage through the use of the lower dose. A meta-analysis of risk factors for intracerebral haemorrhage with alteplase (Whiteley et al, 2012) suggested a greater risk in people with atrial fibrillation, congestive cardiac failure, renal impairment, prior antiplatelet treatment, leukoaraiosis and visible cerebral infarction on pretreatment brain imaging, but the extent to which any of these factors should influence dose selection for alteplase remains unknown. [2016]

Patients presenting with acute ischaemic stroke whilst taking a direct oral anticoagulant (DOAC) should be excluded from receiving thrombolysis unless, in the case of dabigatran, the prothrombin time and activated partial thromboplastin time are both normal. The use of reversal agents (idarucizumab or andexanet alfa) in order to then administer thrombolysis for an ischaemic stroke that has occurred during DOAC treatment is not recommended. [2016]

Patients more than 4.5 hours after stroke or with an unknown time of onset, and those with wake-up stroke, who have radiologically defined 'penumbra' benefit from alteplase. Participants in the WAKE-UP trial (Thomalla et al, 2018) were aged up to 80 years and had woken from sleep or could not report the time of stroke onset, were at least 4.5 hours from when last seen well, and had evidence of MRI DWI-FLAIR mismatch. Allocation to 0.9 mg/kg alteplase rather than placebo led to a higher proportion of patients (53.3% v. 41.8%) with an excellent functional outcome at 90 days. The THAWS trial (Koga et al, 2020) demonstrated no clear benefit from a lower dose of alteplase (0.6mg/kg). [2023]

In an individual participant data meta-analysis of EXTEND (Ma et al, 2019), ECASS-4 (Ringleb et al, 2019) and a subset of the EPITHET trial (Davis et al, 2008) patients with CT or MR perfusion imaging-defined penumbra between 4.5 and 9 hours after onset or with wake-up stroke (Campbell et al, 2019) gained benefit from intravenous alteplase (7% absolute increase in excellent outcome). No patients received mechanical thrombectomy in these trials. In a prespecified subset who had mismatch defined by a mismatch ratio greater than 1·2, a mismatch volume greater than 10 mL, and an ischaemic core volume less than 70 mL (EXTEND criteria), benefit with alteplase was also seen. Participants with and without a large artery occlusion appeared to benefit similarly. The TWIST trial (Roaldsen et al, 2023) comparing intravenous thrombolysis with tenecteplase given within 4.5 hours of awakening versus control (no thrombolysis) in patients with wake-up stroke, did not demonstrate benefit in patients selected with non-contrast CT imaging alone. [2023]

Tenecteplase is a single bolus thrombolytic agent with higher fibrin specificity and longer half-life than alteplase. Nine RCTs have compared tenecteplase with alteplase in people with acute ischaemic stroke (Haley et al, 2010; Parsons et al, 2012; Huang et al, 2015; Logallo et al, 2017; Campbell et al, 2018b;

Bivard et al, 2022; Kvistad et al, 2022; Menon et al, 2022; Wang et al, 2023). No single trial in unselected patients has demonstrated that tenecteplase leads to greater recovery than alteplase. A 2019 meta-analysis (Burgos & Saver, 2019) concluded that tenecteplase was non-inferior to alteplase but this was confounded by the significant contribution of the large NOR-TEST study which used a higher dose of 0.4 mg/kg and included a substantial proportion of people with stroke mimics (Logallo et al, 2017). A subsequent trial of 0.4 mg/kg tenecteplase in patients with moderate-severe ischaemic stroke showed this higher dose led to higher rates of intracerebral haemorrhage than alteplase (NOR-TEST 2, part A; (Kvistad et al, 2022)), and this dose is no longer recommended. Tenecteplase (0.25 mg/kg) delivered in an MSU setting (TASTE-A; (Bivard et al, 2022)) led to better measures of imaging reperfusion than alteplase but the study was inadequately powered to test any difference in outcomes. Two large randomised trials have demonstrated that tenecteplase 0.25 mg/kg is non-inferior to alteplase for excellent clinical outcome when delivered within 4.5 hours of stroke onset (Menon et al, 2022; Wang et al, 2023). In patients with proven large artery occlusion prior to planned thrombectomy tenecteplase (0.25 mg/kg) may be superior to alteplase when given within 4.5 hours of onset (Campbell et al, 2018b). [2023]

Since the 2012 edition of the guideline, five RCTs have been published evaluating the effects of endovascular treatment in addition to thrombolysis, compared with standard treatment (intravenous thrombolysis alone administered within 4.5 hours) in 'early-presenting' patients (typically within 6 hours) with proven large artery occlusion stroke (Berkhemer et al, 2015; Campbell et al, 2015; Goyal et al, 2015; Jovin et al, 2015; Saver et al, 2015). In an individual patient meta-analysis of these five trials involving 1,287 patients (Goyal et al, 2016) endovascular therapy showed significant improvements in functional outcomes at 90 days. The number needed to treat for one additional patient to have reduced disability of at least one point on the mRS was 3. The trials were heterogenous in their patient selection (age, NIHSS score) and only included patients with pre-stroke mRS of 2 or less. There was also variation in imaging criteria, in particular whether the identification of salvageable brain tissue on neuroimaging was a trial inclusion criterion (EXTEND-IA, ESCAPE, SWIFT-PRIME, and REVASCAT beyond 4.5 hours) or not (MR CLEAN). Three trials included some patients for whom intravenous thrombolysis was contraindicated. The trials varied in onset to endovascular treatment from a maximum of 6 up to 12 hours, and it is pertinent that all the trials with an extended time window required imaging identification of the potential to salvage brain tissue prior to randomisation (see below). The SWIFT-PRIME trial had the fastest process times with a median time from hospital arrival to groin puncture of 90 minutes, and the median procedure time in the five trials was just under 60 minutes. An NIHSS score of 6 or more was an inclusion criterion for several trials with clear positive subgroup effects for NIHSS 6-19 (ESCAPE) and 6-17 (SWIFT-PRIME). Not all trials reported a positive effect on mortality. The Working Party concludes that mechanical thrombectomy is an effective acute stroke treatment for selected patients with proximal large artery occlusions as an adjunct to intravenous thrombolysis, and for those patients with contraindications to intravenous thrombolysis but not to mechanical thrombectomy (e.g. recent surgery, anticoagulant use). Centres that provide endovascular treatment should meet the professional standards set out by the joint societies' working group (White et al, 2015; NICE, 2016a). There remain significant challenges to the full implementation of this treatment in the UK and Ireland. [2023]

Two RCTs have reported on patients with a large ischaemic core who have previously been ineligible for trials of thrombectomy beyond 6 hours. SELECT2 (N=352; Sarraj et al, 2023) demonstrated that patients aged 18-85 years with a pre-stroke mRS score of 0 or 1 presenting with a proximal large artery occlusion (ICA/M1) and an ASPECTS score of 3-5 or an infarct core of >50 mL benefitted from mechanical thrombectomy up to 24 hours after onset. Thrombectomy resulted in functional independence (mRS 0-2) in 20.3% of treated patients compared with 7% in the medical arm (NNT=8). ANGEL-ASPECT (N=456; Huo et al, 2023) also demonstrated significant benefit from mechanical thrombectomy in patients aged 18-80 years with a pre-stroke mRS score of 0 or 1 and an ICA/M1 occlusion and either ASPECTS 3-5 or an infarct core of 70-100 mL presenting within 24 hours of onset. Thrombectomy increased the proportion of patients with functional independence (mRS 0-2) to 30%

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compared with 11.6% in the medical arm (NNT=6). In both trials, perfusion imaging (almost all CT perfusion) was undertaken to confirm a large infarct core volume (median 80 mLs in SELECT2, 62 mLs in ANGEL-ASPECT) and benefits were observed despite a higher rate of intracranial haemorrhage with thrombectomy. It is noteworthy in these late-presenting groups that around two thirds of patients were still ineligible for treatment, and after thrombectomy the median mRS at 90 days was 4 and mortality ranged from 22-38%. Considering this evidence in conjunction with the results of DEFUSE-3 (Albers et al, 2018), in patients presenting between 12 and 24 hours after onset, there is robust evidence to select individuals for mechanical thrombectomy based on perfusion imaging (particularly perfusion mismatch > 15 mL). In patients presenting between 6 and 24 hours after onset with a pre-stroke modified Rankin score of 2 or more, or who are older than 85 years, there is still insufficient evidence, and the more selective DAWN/DEFUSE-3 radiological criteria should be considered as the primary means of selection for these groups. As yet there are no RCT data from patients with anterior circulation stroke presenting between 12 and 24 hours with non-proximal M1/intracranial ICA occlusion. It should also be noted that the perfusion criteria applied in these trials of late-presenting patients (core defined by rCBF below 30% and penumbra by T_{max} greater than 6 secs) were mostly based on the use of RAPID™ AI decision-support software from IschemaView (Stanford, USA) and direct extrapolation of these results to other AI systems should not be assumed as appropriate or equivalent to the referenced trials. [2023]

A recent meta-analysis (Turc et al, 2022b) of six RCTs (Yang et al, 2020; LeCouffe et al, 2021; Suzuki et al, 2021; Zi et al, 2021; Fischer et al, 2022; Mitchell et al, 2022) supports the administration of thrombolysis within 4.5 hours of onset in eligible patients prior to thrombectomy (bridging thrombolysis) given that no trial showed superiority and only two of the six trials, both judged at high or moderate risk of bias, showed non-inferiority for proceeding direct to thrombectomy (Yang et al, 2020; Zi et al, 2021). Furthermore, the meta-analysis indicated superior reperfusion rates, trends to improved clinical outcome and no statistical increase in adverse safety outcomes (mortality and symptomatic intracranial haemorrhage) with bridging thrombolysis. All the randomised trials recruited patients presenting directly to thrombectomy centres. No randomised trial has yet addressed the question of whether patients presenting initially to an acute stroke centre should proceed directly to mechanical thrombectomy without bridging thrombolysis. However, a meta-analysis of observational studies found better clinical outcomes for the bridging thrombolysis group, although direct mechanical thrombectomy was deemed safe (Turc et al, 2022b). There is now sufficient evidence to guide the selection of patients for both thrombolysis and thrombectomy presenting later than 4.5 hours after symptom onset or where the onset time is not known (Albers et al, 2018; Nogueira et al, 2018; Thomalla et al, 2018; Campbell et al, 2019; Albers et al, 2021; Jovin et al, 2022b; Tao et al, 2022). [2023]

Two RCTs (BASICS and BEST) were published in 2020 and 2021 addressing whether thrombectomy and best medical therapy was superior to best medical therapy alone in imaging-confirmed basilar artery occlusion (BAO)/vertebral artery (VA) occlusion (Liu et al, 2020; Langezaal et al, 2021). Neither trial had an NIHSS restriction on eligibility or systematic imaging exclusion criteria other than extensive bilateral brainstem ischaemia. Both trials were neutral on an intention-to-treat analysis for their primary endpoint of mRS of 0-3 at 90 days. Two further Chinese RCTs of the effectiveness of thrombectomy in BAO have been published (Jovin et al, 2022a; Tao et al, 2022). The ATTENTION trial randomised 340 patients in a 2:1 ratio to either thrombectomy and best medical therapy or best medical therapy alone, with additional eligibility criteria of an NIHSS of 10 or more, PC-ASPECTS of 6 or more and in a time window of up to 12 hours after stroke onset (Tao et al, 2022). Patients over 80 years of age additionally had to have PC-ASPECTS of 8 or more and a pre-stroke mRS of 0-1. The trial demonstrated superiority of thrombectomy with an absolute difference in mRS 0-3 of 23.2%. The BAOCHE trial randomised 218 patients aged 80 or younger between 6 and 24 hours after stroke onset in a 1:1 ratio if the NIHSS was 6 or more, PC-ASPECTS 6 or more and the Pons-Midbrain Index was 2 or more (Jovin et al, 2022a). It enrolled 82 patients (38%) in the 12-24 hour window and also showed superiority for thrombectomy with an absolute difference in mRS 0-3 of 22.1%. All three Chinese trials had much lower intravenous thrombolysis rates than was seen in BASICS. Despite the results from 4 RCTs, there are very limited data

for patients over the age of 80 years, those with a baseline NIHSS of 6-9 and those presenting beyond 12 hours. [2023]

A systematic review and meta-analysis of five small trials randomising 498 patients either to general anaesthesia or heavy conscious sedation concluded that general anaesthesia resulted in superior functional independent outcomes, with only one of the five small RCTs showing statistical superiority for general anaesthesia over conscious sedation (Bai et al, 2021). A subsequent meta-analysis including non-randomised data from eight studies including 7,797 patients demonstrated that local anaesthesia without sedation was not significantly superior to either conscious sedation or general anaesthesia in improving outcomes (Butt et al, 2021). A subsequent larger multi-centre trial (GASS; Maurice et al, 2022) which included standardised approaches to blood pressure management did not demonstrate differences in functional outcome with anaesthetic method, despite a higher recanalisation rate with general anaesthesia. These data contrast with larger volume real-world registries or individual patient data level RCT post-hoc analyses, which tend to favour non-general anaesthesia over general anaesthesia in terms of functional outcomes (Campbell et al, 2018a; Powers et al, 2019). There is a paucity of randomised evidence comparing general anaesthesia with local anaesthesia or minimal conscious sedation approaches, but trials are ongoing. [2023]

The DESTINY II trial of decompressive hemicraniectomy for older patients with severe space-occupying MCA territory infarction has shown a substantial survival benefit for patients over the age of 60 years (Jüttler et al, 2014) akin to that seen in young patients (Cruz-Flores et al, 2012). Decisions to undertake major life-saving surgery need to be carefully considered on an individual basis, but patients should not be excluded from treatment by age alone. [2016]

3.5 Implications

These recommendations underpin the earlier recommendations concerning the organisation of acute stroke care (Section 2.2 Definitions of specialist stroke services, Section 2.3 Transfer to acute stroke services, Section 2.4 Organisation of inpatient services), with significant implications for the organisation of acute stroke services and referrals to tertiary neurosurgical and interventional neuroradiology services. Provision of hyperacute stroke care should be organised to minimise time to treatment for the maximum number of people with stroke, and in some areas this will require reconfiguration of hyperacute stroke services with some hospitals stopping providing acute stroke services altogether. [2023]

A global shortage of tenecteplase will limit the initial extent to which Recommendation 3.5A can be implemented, at least until the end of 2024. Individual nations and clinicians will need to consider these supply implications when planning a managed transition from alteplase to tenecteplase – for example, in England, the NHS expects a planned transition (licence permitting) from April 2025. [2023]

3.6 Management of intracerebral haemorrhage

About 11% of all patients presenting to hospital in the UK and Ireland with acute stroke have intracerebral haemorrhage (ICH) as the cause (Kelly et al, 2012; Intercollegiate Stroke Working Party, 2016). Patients with ICH can deteriorate quickly and should be admitted directly to a hyperacute stroke unit for urgent specialist assessment and monitoring. [2023]

3.6 Recommendations

- A Patients with intracerebral haemorrhage in association with vitamin K antagonist treatment should have the anticoagulant urgently reversed with a combination of prothrombin complex concentrate and intravenous vitamin K. [2016]
- B Patients with intracerebral haemorrhage in association with direct oral anticoagulant

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- (DOAC) treatment should have the anticoagulant urgently reversed. For patients taking dabigatran, idarucizumab should be used. If idarucizumab is unavailable, 4-factor prothrombin complex concentrate may be considered. For those taking factor Xa inhibitors, 4-factor prothrombin complex concentrate should be considered and andexanet alfa may be considered in the context of a randomised controlled trial. [2023]
- C Patients with acute spontaneous intracerebral haemorrhage with a systolic BP of 150-220 mmHg should be considered for urgent treatment within 6 hours of symptom onset using a locally agreed protocol for BP lowering, aiming to achieve a systolic BP between 130-139 mmHg within one hour and sustained for at least 7 days, unless:
 - the Glasgow Coma Scale score is 5 or less;
 - the haematoma is very large and death is expected;
 - a macrovascular or structural cause for the haematoma is identified;
 - immediate surgery to evacuate the haematoma is planned, in which case BP should be managed according to a locally agreed protocol. [2023]
- D Patients with intracerebral haemorrhage should be admitted directly to a hyperacute stroke unit for monitoring of conscious level and referred immediately for repeat brain imaging if deterioration occurs. [2023]
- E Patients with intracranial haemorrhage who develop hydrocephalus should be considered for surgical intervention such as insertion of an external ventricular drain. [2016]
- Patients with intracerebral haemorrhage in whom the haemorrhage location or other imaging features suggest cerebral venous thrombosis should be investigated urgently with a CT or MR venogram. [2023]
- The DIAGRAM score (or its components: age; intracerebral haemorrhage location; CTA result where available; and the presence of white matter low attenuation [leukoaraiosis] on the admission non-contrast CT) should be considered to determine the likelihood of an underlying macrovascular cause and the potential benefit of intra-arterial cerebral angiography. [2023]
- Early non-invasive cerebral angiography (CTA/MRA within 48 hours of onset) should be considered for all patients with acute spontaneous intracerebral haemorrhage aged 18-70 years who were independent, without a history of cancer, and not taking an anticoagulant, except if they are aged more than 45 years with hypertension and the haemorrhage is in the basal ganglia, thalamus, or posterior fossa. If this early CTA/MRA is normal or inconclusive, MRI/MRA with susceptibility-weighted imaging (SWI) should be considered at 3 months. Early CTA/MRA and MRI/MRA at 3 months may also be considered in patients not meeting these criteria where the probability of a macrovascular cause is felt to justify further investigation. [2023]

3.6 Sources

- A Working Party consensus
- B Pollack et al, 2017
- C Anderson et al, 2013; Qureshi et al, 2016; NICE, 2022e; Guideline Development Group consensus
- D Guideline Development Group consensus
- E Working Party consensus
- F van Asch et al, 2015
- G van Asch et al, 2015; Hilkens et al, 2018
- H Guideline Development Group consensus

3.6 Evidence to recommendations

The effect of reducing blood pressure in the first few hours after the onset of ICH has been tested in two international RCTs. In INTERACT-2, the rapid lowering of systolic blood pressure (SBP) to a target below 140 mmHg within 1 hour in 2839 patients presenting within 6 hours of onset with mainly small, deep (thalamic or basal ganglia) ICH did not reduce haematoma expansion or improve the primary outcome of death or major disability (mRS 3-6), but secondary outcomes (ordinal shift analysis of the mRS and health-related quality of life measures) were improved. Death (12% at 3 months) and institutionalisation (9%) were not affected by intensive treatment (Anderson et al, 2013). In ATACH-2, pursuing a lower SBP target of 110-139 mmHg within 2 hours in 1,000 patients presenting within 4.5 hours of onset with small, deep ICH tended to reduce haematoma expansion but conferred no reduction in severe disability or death (mRS 4-6) compared to a target of 140-179 mmHg (Qureshi et al, 2016). Mortality (6.7%) was also not affected. More intensive SBP lowering was associated with more renal adverse events in the first 7 days. In comparing these two trials, it is noteworthy that a lower SBP was achieved in the acute phase in the standard treatment arm of ATACH-2 (all of whom received intravenous nicardipine) than in the intensive treatment arm of INTERACT2 (141 mmHg vs. 150 mmHg respectively). As the intensive arm of ATACH-2 led to a still greater SBP reduction, ATACH-2 can be interpreted as showing no additional benefit from a more aggressive blood pressure target than that tested in INTERACT2. More research is still needed to clarify the effect on clinical outcomes from hyperacute SBP reductions in people with acute ICH, including in large and/or lobar haemorrhages. [2016]

A systematic review and individual participant meta-analysis summarised the evidence regarding a much broader range of blood pressure-lowering strategies during the first 7 days after ICH (Moullaali et al, 2022). Active/intensive blood pressure-lowering interventions had no overall effect on mRS at the end of follow-up compared with placebo/standard (guideline-based) treatment but significantly reduced haematoma expansion. Subgroup analyses suggested that an intensive target should be preferred to a fixed dose of a specific agent and that other antihypertensive agents should be preferred over reninangiotensin system blockers, though all data on renin-angiotensin system blockers in the meta-analysis came from a single trial of candesartan (Sandset et al, 2011). Post-hoc secondary analyses of INTERACT2 and ATACH-2 used as observational cohorts (i.e. no longer providing randomised data on the effects of the intervention) found that achieving early and stable target blood pressure over the first 24 hours was associated with better outcomes (Moullaali et al, 2019). Although there is sufficient evidence to support the safety of intensive blood pressure lowering as delivered in the INTERACT2 trial, further evidence is required to establish the optimal strategy for intensive blood pressure lowering. There is limited RCT evidence regarding intensive blood pressure lowering in patients after ICH with baseline systolic blood pressure greater than 220 mmHg or beyond 6 hours from onset, so no specific recommendations can be made regarding these patient groups although more careful acute blood pressure lowering may need to be considered. [2023]

Abnormalities of clotting, especially in patients taking anticoagulants, should be urgently reversed, using 4-factor prothrombin complex concentrate (PCC) to reverse vitamin K antagonists. A trial of idarucizumab in patients taking the direct thrombin inhibitor dabigatran has shown the agent to be safe, rapid in action and effective in reversing the anticoagulant effect (Pollack et al, 2017). Multiple low to medium quality, non-randomised, observational studies suggest that 4-factor PCC demonstrates haemostatic efficacy in ICH in patients taking factor Xa inhibitors (Jaspers et al, 2021), but there is insufficient evidence to support a significant benefit in terms of haematoma expansion, mortality, or functional outcome. Andexanet alfa has been shown in normal volunteers to reverse the anticoagulant effect of the factor Xa inhibitors apixaban and rivaroxaban (Siegal et al, 2015) and this has been replicated in patients with ICH (Demchuk et al, 2021). However, the lack of comparative trials examining the effects of andexanet alfa in improving clinical outcome needs to be addressed to inform treatment of this patient group (NICE, 2021e). [2023]

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In contrast to the long-standing and clear role for neurosurgical intervention in posterior fossa haemorrhage, and following a neutral neurosurgical trial in lobar haemorrhage without intraventricular haemorrhage (Mendelow et al, 2013), the role of neurosurgery for supratentorial ICH remains unclear. Most patients with ICH do not require surgical intervention and should receive monitoring and initial medical treatment on an acute stroke unit. Such patients are those with small, deep haemorrhage; lobar haemorrhage without hydrocephalus, intraventricular haemorrhage or neurological deterioration; large haemorrhage and significant co-morbidities before the stroke; and those with supratentorial haemorrhage with a Glasgow Coma Scale score below 8 unless this is because of hydrocephalus. [2016]

The majority of spontaneous ICH is caused by cerebral small vessel disease, including arteriolosclerosis (also termed deep perforator arteriopathy or hypertensive arteriopathy) and cerebral amyloid angiopathy (CAA). In a minority of patients, bleeding is caused by a macrovascular abnormality such as an arteriovenous malformation, dural arteriovenous fistula, intracranial aneurysm or cavernous malformation or by cerebral venous thrombosis (CVT). Detection of these causes may be worthwhile because of the risk of ICH recurrence and progression, if preventative interventions are in the patient's best interests. Intra-arterial digital subtraction angiography is the reference standard investigation for detection of all macrovascular abnormalities other than cavernous malformations, which require MRI for diagnosis; the angiography procedure is associated with a very small (0.5-1%) but important risk of serious vascular and neurological complications. A 2015 Cochrane review found that studies of noninvasive angiography (CTA or MRA) of the entire cerebral vasculature (i.e. not limited to the Circle of Willis) had good diagnostic accuracy in comparison to acute intra-arterial angiography. However, studies were of varying quality, with partial verification bias and retrospective designs being common (Josephson et al, 2015). Subsequently, the use of CTA or MRI/MRA has been investigated in the high quality, prospective DIAGRAM study (van Asch et al, 2015). In a selected cohort (aged 18-70 years but excluding patients over 45 years of age with hypertension and ICH in the basal ganglia, thalamus or posterior fossa because of the low probability of finding an underlying macrovascular cause), DIAGRAM demonstrated early CTA (within 48 hours of onset) to have a positive predictive value of 72% (60 to 82%), detecting 51 of 69 (86%) macrovascular causes identified after a systematic investigation pathway in a total study sample of 298 patients. Subsequent MRI/MRA at 4-8 weeks in 214 patients with a negative CTA identified another two of 69 (3%) macrovascular causes. Delayed intra-arterial angiography then identified the remaining 15 of 69 (22%) macrovascular causes in 97 patients where the CTA and MRI/MRA were normal or inconclusive. [2023]

For patients not meeting the DIAGRAM study criteria, clinicians will need to estimate the probability of an underlying macrovascular cause to decide on whether to proceed to CTA, MRI/MRA, and/or intra-arterial angiography. The DIAGRAM score (which includes as predictors younger age, lobar or posterior fossa ICH location and absence of cerebral small vessel disease markers) has been derived from the original study cohort and externally validated, with moderate performance for detection of a macrovascular cause in the validation cohort (Hilkens et al, 2018). Including the CTA result in the DIAGRAM score resulted in good performance in the external cohort. The secondary ICH score uses age, sex, hypertension and imaging features and has good performance in validation cohorts. High probability imaging features included enlarged vessels or calcifications along margins of ICH suggesting an AVM or hyperattenuation within dural venous sinus or cortical vein along the path of drainage of the ICH suggesting cortical vein or venous sinus thrombosis. Low probability features were basal ganglia, thalamus or brainstem ICH location (van Asch et al, 2013). Where CTA/MRI/MRA is normal or inconclusive, it is important to consider a subsequent intra-arterial angiogram so as not to miss a macrovascular cause amenable to treatment. [2023]

3.6 Implications

Poor therapeutic outcomes affecting the management of patients with acute intracerebral haemorrhage have been partially reversed by the findings of INTERACT2. The resulting potential benefit of care associated with blood pressure reduction, in addition to the safety of blood pressure lowering,

was the rationale for the strength of the Guideline Development Group's recommendation being 'should be considered' despite the recent individual patient data meta-analysis showing no effect of blood pressure lowering on functional outcome. All hyperacute stroke units should consider developing processes to quickly identify patients presenting with intracerebral haemorrhage within 6 hours of onset and consider rapidly and safely lowering SBP for the majority of these patients. As in Section 2.3
Transfer to acute stroke services, referral protocols will need to be developed or refined to specify the role of neurosurgery in ICH. A systematic, multidisciplinary, evidence-based approach to investigation for a macrovascular cause of ICH will aid timely and equitable detection of underlying causes amenable to treatment aimed at reducing the risk of recurrence. In implementing these recommendations, efficient resource use should be considered, such as undertaking CTA immediately after diagnostic noncontrast CT. [2023]

3.7 Management of subarachnoid haemorrhage

The incidence of subarachnoid haemorrhage (SAH) has been declining in the UK and Ireland (Kelly et al, 2012) and mortality has improved significantly in recent years with improvements in diagnosis and management (Mukhtar et al, 2016). SAH still accounts for approximately 5% of all acute strokes. 10-15% of those affected die before reaching hospital and overall survival is about 70%, but amongst patients admitted to a neurosurgical unit with a confirmed aneurysm, 85% will survive (Society of British Neurosurgeons, 2006). Case fatality and unfavourable outcomes rise with age and are highest in the over 65 age group (Society of British Neurosurgeons, 2006), and in those patients of a 'poor clinical grade' (Hunt and Hess or World Federation of Neurological Surgeons grades 4 & 5). Recurrent haemorrhage from the culprit aneurysm is the most frequent cause of death after the initial presentation. Diagnosis, referral to a tertiary centre and treatment to prevent rebleeding are therefore urgent. CT scanning is the most sensitive method to detect subarachnoid blood but when CT is negative lumbar puncture for xanthochromia after 12 hours may still be required, particularly if there has been a delay in presentation, as the sensitivity of CT for SAH declines with time from ictus. Usually non-invasive angiography (CT or MR) is required prior to intra-arterial angiography undertaken in the referring or neurosciences centre. After SAH many patients will have residual disability requiring neurorehabilitation and most will experience long-term symptoms, especially fatigue and cognitive disability. [2016]

3.7 Recommendations

- A Any person presenting with sudden severe headache and an altered neurological state should have the diagnosis of subarachnoid haemorrhage investigated by:
 - immediate CT brain scan (also including CT angiography if a protocol is agreed with the neurosciences centre);
 - lumbar puncture 12 hours after ictus (or within 14 days if presentation is delayed) if the CT brain scan is negative and does not show any contraindication;
 - spectrophotometry of the cerebrospinal fluid for xanthochromia. [2016]
- B Patients with spontaneous subarachnoid haemorrhage should be referred immediately to a neurosciences centre and receive:
 - nimodipine 60 mg 4 hourly unless contraindicated;
 - frequent neurological observation for signs of deterioration. [2016]
- C Following transfer to the neurosciences centre, patients with spontaneous subarachnoid haemorrhage should receive:
 - CT or MR angiography (if this has not already been done by agreed protocol in the referring hospital) with or without intra-arterial angiography to identify the site of bleeding;
 - specific treatment of any aneurysm related to the haemorrhage by endovascular

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embolisation or surgical clipping if appropriate. Treatment to secure the aneurysm should be undertaken within 48 hours of ictus for patients of appropriate status (Hunt and Hess or World Federation of Neurological Sciences grades 1-3), or within a maximum of 48 hours of diagnosis if presentation was delayed. [2016]

- D After any immediate treatment, patients with subarachnoid haemorrhage should be monitored for the development of treatable complications, such as hydrocephalus and cerebral ischaemia. [2016]
- E After any immediate treatment, patients with subarachnoid haemorrhage should be assessed for hypertension treatment and smoking cessation. [2016]
- Patients with residual symptoms or disability after definitive treatment of subarachnoid haemorrhage should receive specialist neurological rehabilitation including appropriate clinical/neuropsychological support. [2016]
- People with two or more first-degree relatives affected by aneurysmal subarachnoid haemorrhage and/or polycystic kidney disease should be referred to a neurovascular and/or neurogenetics specialist for information and advice regarding the risks and benefits of screening for cerebral aneurysms. [2016]

3.7 Sources

- A Working Party consensus
- B Allen et al, 1983; Barker and Ogilvy, 1996; Pickard et al, 1989
- C Molyneux et al, 2005; Society of British Neurosurgeons, 2006
- D-F Working Party consensus
- G Bor et al, 2008

3.7 Evidence to recommendations

There have been a number of negative trials in SAH management. Statins (Liu & Chen, 2015), magnesium (Mees et al, 2012) and endothelin receptor antagonists (Guo et al, 2012) have all been shown not to improve clinical outcome after SAH. [2016]

3.8 Cervical artery dissection

A small proportion of patients with acute ischaemic stroke will have a dissection of a carotid or vertebral artery as the underlying cause of their stroke. As non-invasive carotid and vertebral imaging has become more accessible and of higher quality, the proportion of patients diagnosed with dissection has increased. This group of patients tends to be younger, and may have experienced preceding neck trauma. [2023]

3.8 Recommendations

- A Any patient suspected of cervical artery dissection should be investigated with CT or MR including angiography. [2016]
- B Patients with acute ischaemic stroke suspected to be due to cervical arterial dissection should receive thrombolysis if they are otherwise eligible. [2016]
- C Patients with acute ischaemic stroke suspected to be due to cervical arterial dissection should be treated with either an anticoagulant or an antiplatelet agent for at least 3 months. [2016]
- D For patients with cervical arterial dissection treated with an anticoagulant, either a DOAC or a Vitamin K antagonist may be used for three months. [2023]
- E For patients with acute ischaemic stroke or TIA secondary to cervical artery dissection,

dual antiplatelet therapy with aspirin and clopidogrel may be considered for the first 21 days, to be followed by antiplatelet monotherapy until at least three months after onset. [2023]

3.8 Sources

- A Working Party consensus
- B Zinkstok et al, 2011; Engelter et al, 2012
- C CADISS Trial Investigators, 2015
- D CADISS Trial Investigators, 2015; TREAT-CAD Trial Investigators, 2021; Debette et al, 2021; Guideline Development Group consensus
- E Guideline Development Group consensus

3.8 Evidence to recommendations

The CADISS RCT in people with symptomatic carotid and vertebral artery dissection showed no significant difference between anticoagulant and antiplatelet treatment in the prevention of recurrent stroke or death (CADISS Trial Investigators, 2015). The incidence of either outcome was low, with a 2% stroke rate within 3 months and no deaths. This low rate may reflect greater diagnostic yield in patients previously classified as 'cryptogenic'. The TREAT-CAD RCT did not show that aspirin was non-inferior to anticoagulation (Vitamin K antagonist) in the prevention of either new MRI lesions during follow-up, or clinical endpoints (acute ischaemic stroke, major intra- or extracranial haemorrhage, death) in a primary composite endpoint. The endpoint occurred in 21 (23%) patients in the aspirin group and in 12 (15%) in the VKA group (absolute difference 8% [95% CI, –4 to 21], non-inferiority p=0.55). There were no deaths in either group (TREAT-CAD Trial Investigators, 2021). [2023]

A meta-analysis combining the per-protocol results of CADISS and TREAT-CAD showed that at 3 months there was no significant difference between anticoagulant and antiplatelet treatment for the composite endpoint of ischaemic stroke or major haemorrhage (Debette et al, 2021). In patients randomised to anticoagulation, the odds of the composite endpoint was 0.35 (95% CI, 0.08-1.63), ischaemic stroke was 0.18 (95% CI, 0.03 to 1.10) and major bleeding was 3.28 (95% CI, 0.34 to 31.80). Overall, the two RCTs did not show a significant difference between the two treatment groups in the acute phase of symptomatic extracranial cervical artery dissection. [2023]

There is no evidence on which to base a recommendation regarding long-term antithrombotic treatment after cervical artery dissection as the intervention (anticoagulant or antiplatelet) in the two trials (CADISS and TREAT-CAD) was stopped at 3 months. [2023]

There is no evidence to suggest that thrombolysis carries any greater risk in patients with cervical artery dissection compared to stroke from other causes (Engelter et al, 2012). [2016]

3.9 Cerebral venous thrombosis

Cerebral venous thrombosis (CVT) is a rare cause of an acute stroke syndrome. Headache, seizures and focal (sometimes bilateral) neurological deficits are typical presenting features. CVT is more likely in patients with a prothrombotic tendency (e.g. around the time of pregnancy), or who have local infection, dehydration or malignancy, and it is important to investigate for a possible underlying cause. In the largest published registry series of 11,400 patients with CVT, 232 (2%) died in hospital due to the CVT (Nasr et al, 2013). Older patients and those with sepsis had the greatest risk of in-hospital mortality. Hydrocephalus, intracranial haemorrhage, and motor deficits were also associated with a worse outcome. [2016]

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3.9 Recommendations

- A Any patient suspected of cerebral venous thrombosis should be investigated with CT or MRI including venography. [2016]
- B Patients with cerebral venous thrombosis (including those with secondary cerebral haemorrhage) should receive full-dose anticoagulation (initially full-dose heparin and then warfarin with a target INR of 2–3) for at least three months unless there are comorbidities that preclude their use. [2016]

3.9 Sources

- A Working Party consensus
- B Coutinho et al, 2011; Working Party consensus

3.9 Evidence to recommendations

Case series suggest that anticoagulation is the treatment of choice for CVT, even when haemorrhage is seen on brain imaging, with a reduction in death and dependency (Stam et al, 2002). A Cochrane review (Coutinho et al, 2011) identified two small trials of anticoagulation after CVT. Although not reaching statistical significance, there was a trend toward a positive benefit from anticoagulation for at least three months. DOACs are licensed for venous thromboembolism but not for CVT. There is no evidence to support the use of corticosteroids in the management of CVT; what information is available is likely to be affected by selection bias and does not support their use, and may even suggest some circumstances where their use may be harmful (Canhao et al, 2008). [2016]

3.10 Acute stroke care

Many patients presenting with acute neurological deficits secondary to vascular disease will have other problems requiring attention during and after their initial diagnosis (Section 3.4 Diagnosis and treatment of acute stroke - imaging) and the pathology-specific treatments described in Sections 3.5 Management of ischaemic stroke and 3.6 Management of intracerebral haemorrhage. Three-quarters of patients with acute stroke admitted to hospital in the UK have at least one co-morbidity, and one in ten have at least three (Intercollegiate Stroke Working Party, 2016). Patients need specialist care on a stroke unit focused initially on preserving life, limiting brain damage and preventing complications before rehabilitation can begin in earnest. Patients with stroke often have significant disturbances of physiological homeostasis with raised temperature, raised blood glucose, hypoxia, etc. During the first week, 5% of patients with acute stroke develop urinary sepsis, and 9% require antibiotic treatment for pneumonia (Intercollegiate Stroke Working Party, 2016). [2016]

3.10 Recommendations

- A Patients with acute stroke should be admitted directly to a hyperacute stroke unit with protocols to maintain normal physiological status and staff trained in their use. [2016]
- B Patients with acute stroke should have their clinical status monitored closely, including:
 - level of consciousness;
 - blood glucose;
 - blood pressure;
 - oxygen saturation;
 - hydration and nutrition;
 - temperature;
 - cardiac rhythm and rate. [2016]
- C Patients with acute stroke should only receive supplemental oxygen if their oxygen saturation is below 95% and there is no contraindication. [2016]

- D Patients with acute stroke should have their hydration assessed using a standardised approach within four hours of arrival at hospital, and should be reviewed regularly and managed so that normal hydration is maintained. [2016]
- Patients with acute stroke should have their swallowing screened, using a validated screening tool, by a trained healthcare professional within four hours of arrival at hospital and before being given any oral food, fluid or medication. [2016]
- F Until a safe swallowing method is established, patients with dysphagia after acute stroke should:
 - be immediately considered for alternative fluids;
 - have a comprehensive specialist assessment of their swallowing;
 - be considered for nasogastric tube feeding within 24 hours;
 - be referred to a dietitian for specialist nutritional assessment, advice and monitoring;
 - receive adequate hydration, nutrition and medication by alternative means;
 - be referred to a pharmacist to review the formulation and administration of medication. [2023]
- G Patients with swallowing difficulties after acute stroke should only be given food, fluids and medications in a form that can be swallowed without aspiration. [2016]
- H Patients with acute stroke should be treated to maintain a blood glucose concentration between 5 and 15 mmol/L with close monitoring to avoid hypoglycaemia. [2016]
- Patients with acute ischaemic stroke should only receive blood pressure-lowering treatment if there is an indication for emergency treatment, such as:
 - systolic blood pressure above 185 mmHg or diastolic blood pressure above 110 mmHg when the patient is otherwise eligible for treatment with thrombolysis;
 - hypertensive encephalopathy;
 - hypertensive nephropathy;
 - hypertensive cardiac failure or myocardial infarction;
 - aortic dissection;
 - pre-eclampsia or eclampsia. [2016]
- J Patients with acute stroke admitted on antihypertensive medication should resume oral treatment once they are medically stable and as soon as they can swallow medication safely. [2016]
- K Patients with acute ischaemic stroke should receive high-intensity statin treatment with atorvastatin 20-80 mg daily as soon as they can swallow medication safely. [2016]
- L Patients with primary intracerebral haemorrhage should only be started on statin treatment based on their cardiovascular disease risk and not for secondary prevention of intracerebral haemorrhage. [2016]

3.10 Sources

- A, B Middleton et al, 2011
- C Working Party consensus; Roffe et al, 2011
- D Working Party consensus
- E NICE, 2016d; Kertscher et al, 2014; Martino et al, 2014; Bray et al, 2017
- F Geeganage et al, 2012; NICE, 2017b, 20023b
- G, H Working Party consensus
- I, J Bath and Krishnan, 2014; Working Party consensus
- K, L Amarenco and Labreuche, 2009; NICE, 2023a

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3.10 Evidence to recommendations

Patients with acute stroke are at high risk of dehydration, malnutrition, infection, hypoxia and hyperglycaemia. Middleton et al (2011) showed that training stroke unit staff in the use of standardised protocols to manage physiological status can significantly improve outcomes. The management of blood pressure after acute ischaemic stroke remains an area with little evidence to guide practice (see Section 3.6 Management of intracerebral haemorrhage for the recommendation regarding blood pressure management in acute intracerebral haemorrhage). There is no evidence for the use of hyperbaric oxygen therapy in stroke (Bennett et al, 2014) nor for the use of supplemental oxygen in normoxic patients (Roffe et al, 2011) and from the evidence available, the Working Party recommends that mannitol for the treatment of cerebral oedema should not be used outside of a clinical trial. [2016]

There is very little trial evidence on which to base the management of hydration in acute stroke. A Cochrane review of the signs and symptoms of impending and current water-loss dehydration in older people (Hooper et al, 2015) concluded that there is little evidence that any one symptom, sign or test, including many that clinicians customarily rely on, have any diagnostic utility for dehydration. [2016]

There is good evidence that a multi-item dysphagia screening protocol that includes at least a water intake test of 10 teaspoons and a lingual motor test was more accurate than screening protocols with only a single item (Martino et al, 2014). There is good evidence from a systematic review (Kertscher et al, 2014) that the investigation of dysphagia with instrumental assessments providing direct imaging for evaluation of swallowing physiology help to predict outcomes and improve treatment planning. [2016]

In contrast to acute myocardial infarction, tight glycaemic control has not been shown to improve outcome in stroke (Gray et al, 2007) and studies have warned against aggressive lowering with insulin infusions due to the risk of hypoglycaemia. This has led the Working Party to recommend a broadening of the target range for blood glucose in acute stroke from 4-11 mmol/L to 5-15 mmol/L. [2016]

Two recent studies showed no clinical benefit from the prophylactic use of antibiotics in dysphagic stroke patients and thus routine antibiotic prophylaxis is not recommended (Kalra et al, 2015; Westendorp et al, 2015). [2016]

3.11 Positioning

Following a stroke many patients are left with varying degrees of physical impairment which can reduce their ability to change position and posture. Therapeutic positioning, whether in bed, chair or wheelchair, aims to reduce skin damage, limb swelling, shoulder pain or subluxation, and discomfort, and maximise function and maintain soft tissue length. Good positioning may also help to reduce respiratory complications and avoid compromising hydration and nutrition. [2016]

3.11 Recommendations

- A Patients with acute stroke should have an initial specialist assessment for positioning as soon as possible and within 4 hours of arrival at hospital. [2016]
- B Patients admitted to hospital with acute stroke should be allowed to adopt either a sittingup or lying-flat head position in the first 24 hours, according to comfort. Stroke units should not have a policy or practice that favours either head position. [2023]
- C Healthcare professionals responsible for the initial assessment of patients with acute stroke should be trained in how to position patients appropriately, taking into account the degree of their physical impairment after stroke. [2016]
- D When lying or sitting, patients with acute stroke should be positioned to minimise the risk of aspiration and other respiratory complications, shoulder pain and subluxation, contractures and skin pressure ulceration. [2016]

3.11 Sources

- A Working Party consensus
- B Anderson et al, 2017
- C, D Working Party consensus

3.11 Evidence to recommendations

One systematic review (Olavarria et al, 2014) examined four small non-randomised trials of head position in acute patients with ischaemic stroke. The trials studied cerebral blood flow using transcranial Doppler but did not report on functional outcome. In the international multicentre cluster-randomised trial HeadPoST (Anderson et al, 2017) of 11,093 patients hospitalised with acute stroke, there was no significant difference between the lying-flat head position and the sitting-up position for the first 24 hours with respect to the primary outcome of disability at 90 days. There were also no significant differences in mortality or in the rates of serious adverse events, including pneumonia. [2023]

3.12 Early mobilisation

Immobility and/or bed rest are well-documented to have detrimental effects on hospital patients in general. Early mobilisation (e.g. activities such as sitting out of bed, transfers, standing and walking) aims to minimise the risk of the complications of immobility and improve functional recovery. [2016]

3.12 Recommendations

- A Patients with difficulty moving after stroke should be assessed as soon as possible within the first 24 hours of onset by an appropriately trained healthcare professional to determine the most appropriate and safe methods of transfer and mobilisation. [2016]
- B Patients with difficulty moving early after stroke who are medically stable should be offered frequent, short daily mobilisations (sitting out of bed, standing or walking) by appropriately trained staff with access to appropriate equipment, typically beginning between 24 and 48 hours of stroke onset. Mobilisation within 24 hours of onset should only be for patients who require little or no assistance to mobilise. [2016]

3.12 Sources

- A Working Party consensus
- B AVERT Trial Collaboration group, 2015; Bernhardt et al, 2016

3.12 Evidence to recommendations

Recommendations have been changed as a result of an international RCT of over 2000 people with acute stroke (AVERT Trial Collaboration group, 2015). Although two small RCTs previously showed that very early mobilisation (beginning within 24 hours) was feasible in an acute setting, the AVERT trial showed that very early, more frequent, higher dose mobilisation focused on out-of-bed activities in addition to usual care was worse than usual care alone. Very early mobilisation led to greater disability at three months with no effect on immobility-related complications or walking recovery. The trial included people with previous stroke, severe stroke, intracerebral haemorrhage and those who were thrombolysed, if they required help to mobilise and were expected to remain in hospital for at least three days. It excluded those who were medically unstable or with significant previous disability. [2016]

To implement this evidence into practice it is important to understand the nature of the usual care and the other factors within this complex intervention. In AVERT's very early intervention, 92% were mobilised within 24 hours of stroke onset (as opposed to admission) and 23% were mobilised within 12

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hours. This was carried out by nurses or therapists an average of six times per day, and included an average daily amount of 31 minutes of mobilisation by a physiotherapist measured over 14 days or until transfer of care if earlier. Given the trial outcomes, such very early mobilisation cannot be recommended. [2016]

The more beneficial usual care was still early but slightly later, less frequent and at a lower dose. Almost everyone (93%) was mobilised within 48 hours of onset, 59% within 24 hours and 14% within 12 hours, by nurses or therapists an average of three times per day, and including an average daily amount of 10 minutes of mobilisation by a physiotherapist. A subsequent exploration of dose hypothesised that early mobilisation might be best delivered in short, frequent amounts (Bernhardt et al, 2016) but this requires further research. [2016]

3.13 Deep vein thrombosis and pulmonary embolism

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are common complications of hemiplegic stroke with up to 50% of patients having thrombus in either the calf or thigh of the paretic limb (Kelly et al, 2004). [2016]

3.13 Recommendations

- A Patients with immobility after acute stroke should be offered intermittent pneumatic compression within 3 days of admission to hospital for the prevention of deep vein thrombosis. Treatment should be continuous for 30 days or until the patient is mobile or discharged, whichever is sooner. [2016]
- B Patients with immobility after acute stroke should not be routinely given low molecular weight heparin or graduated compression stockings (either full-length or below-knee) for the prevention of deep vein thrombosis. [2016]
- C Patients with ischaemic stroke and symptomatic deep vein thrombosis or pulmonary embolism should receive anticoagulant treatment provided there are no contraindications. [2016]
- D Patients with intracerebral haemorrhage and symptomatic deep vein thrombosis or pulmonary embolism should receive treatment with a vena caval filter. [2016]

3.13 Sources

- A CLOTS Trials Collaboration, 2014
- B Geeganage et al, 2013; CLOTS Trials Collaboration, 2013
- C, D Working Party consensus

3.13 Evidence to recommendations

The risk of symptomatic intracerebral haemorrhage outweighs the benefit from the prevention of venous thromboembolism (VTE) with routine anticoagulation with low-dose heparin (including low molecular weight heparin) following acute ischaemic stroke (Geeganage et al, 2013). It is also not possible to predict which patients with acute stroke may be at sufficiently high risk of VTE compared to haemorrhagic complications to inform the targeted use of heparin treatment in selected patients (Whiteley et al, 2013). The CLOTS 1 and 2 trials showed that graduated compression stockings were ineffective in preventing VTE or improving functional outcome in stroke (CLOTS Trials Collaboration, 2013). The CLOTS 3 trial showed that intermittent pneumatic compression (IPC) using sequential compression with venous refill technology in immobile patients in the first 30 days after stroke is an effective treatment for reducing proximal DVT and improves survival but not functional outcomes (CLOTS Trials Collaboration, 2014). In evaluating the cost-effectiveness of IPC in stroke, NICE



recommended that healthcare professionals explain to the patient or their family members or carers that IPC reduces the risk of DVT and may provide an increase in survival, but it will not help them recover from their stroke, and there may be an associated increased risk of surviving with severe disability (NICE, 2015a). [2016]

If proximal DVT does occur in a patient with ischaemic stroke, the risk of PE is high and such patients should receive treatment-dose anticoagulation. If DVT occurs in a patient with ICH there are no randomised trial data to support any particular treatment, but single-centre case series have reported that in such cases a vena caval filter is probably safe and effective for the prevention of PE (Somarouthu et al, 2011). There is no evidence to guide the management of patients with ICH and PE, and the decision to use or to avoid the use of anticoagulant treatment can only be made on the physician's individualised assessment of the balance of risk and benefit. [2016]

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4 Rehabilitation and recovery

Principles of rehabilitation

4.0 Introduction

This section addresses the core principles of rehabilitation and its delivery. All subsequent sections of this chapter should be read keeping these overarching principles and recommendations in mind. It is acknowledged that rehabilitation, recovery, and adjustment are different albeit linked concepts that may take place over differing time frames and require differing levels of support. Where necessary and appropriate, community rehabilitation may be delivered by combined stroke and neuro-therapy teams; however, these teams should have the skills and resources (including staffing) to be able to meet the standards within this guideline. Interventions and support provided by rehabilitation and life after stroke services should span these varying needs and timescales to fulfil the requirement of the United Nations Convention on the Rights of Persons with Disabilities (United Nations, 2022) to deliver "effective and appropriate measures, including through peer support, to enable persons with disabilities to attain and maintain maximum independence, full physical, mental, social and vocational ability, and full inclusion and participation in all aspects of life". [2023]

4.1 Rehabilitation potential

Decisions about rehabilitation potential have far-reaching consequences for individual patients, including the withdrawal of active rehabilitation. The term 'rehabilitation potential' is viewed negatively by stroke survivors and can be inappropriately used by clinicians as justification for rationing access to services. Access to rehabilitation should be driven by the presence of stroke-specific goals. These should not be limited to functional improvement and should include domains such as adjustment, psychological well-being, education regarding stroke, social participation, management of complications, and the management of care needs. All domains should be considered as aspects of rehabilitation and therefore the term 'no rehabilitation potential' is not appropriate and should not be used. [2023]

Given the dynamic nature of stroke recovery, fixed decisions around appropriateness of rehabilitation should not be made too early after stroke. Co-existent conditions such as dementia, sensory impairments, or other comorbidities can complicate delivery of rehabilitation, but they should not be the sole reason for not pursuing a rehabilitative approach. [2023]

Selection of an appropriate rehabilitation pathway (e.g. inpatient rehabilitation, early supported discharge) should be determined by the patient's goals coupled with an understanding of their impairments, abilities, prognosis and the evidence base, informing access to the right service at the right time, at an appropriate intensity. Information should be shared with the person with stroke and their carer(s), to ensure goals and expectations are informed and achievable. There are predictive tools (such as the Orpington Prediction Scale (Mohapatra & Jones, 2015), PREP2 (Stinear et al, 2017a), and TWIST (Smith et al, 2017)) that give useful information at a population level and can be used to inform such discussions. [2023]

Decisions regarding discharge from rehabilitation should be made with involvement of the person with stroke (shared decision making) when stroke-related goals have been met. This should never be an irrevocable decision, but should include the opportunity for review and access back into services at any time via self referral or professional referral. The decision should relate to the person's rehabilitation

needs at a single point in time. It should be understood that a person with stroke may have stroke-related needs or goals at any point following their stroke. Life after stroke services should be available to support and advise during, between, and following different phases of rehabilitation (Section 5.27 Further rehabilitation). [2023]

4.1 Recommendations

- A People with stroke should be considered to have the potential to benefit from rehabilitation at any point after their stroke. [2023]
- B People with stroke and their carers should be involved in a collaborative process with healthcare professionals to agree rehabilitation options, guided by the person's own needs, goals and preferences. [2023]
- C The multidisciplinary team should consider all available rehabilitation options and recommend the service that is most likely to enable the person with stroke to meet their goals and needs.
 - For those people for whom standard rehabilitation services (such as early supported discharge, or community stroke teams) may not be appropriate, collaborative local decision making should ensure that a stroke-skilled multidisciplinary team works with the person with stroke and their family towards achievable and meaningful goals, which may be in conjunction with other statutory or voluntary provision;
 - People with stroke involving the spinal cord should be referred to specialist spinal injuries service for advice and support and/or to provide rehabilitation. [2023]
- D Stroke rehabilitation should be needs-led and not time-limited, and available to those people with stroke for whom:
 - ongoing needs have been identified by the person with stroke, their carer(s) or the multidisciplinary team across all areas of stroke recovery, e.g. functional abilities, mental health, cognitive function, psychological well-being, education regarding stroke, social participation, management of complications and care needs;
 - and their needs remain related to the stroke and/or are best met by the skills of the stroke team. [2023]
- E Clinicians should facilitate shared decision making and communicate the likelihood of the individual achieving their goals in an informed, compassionate, and individualised manner. [2023]
- From an early stage in rehabilitation, clinicians should prepare people with stroke and their carer(s) that discharge from the service will occur and ensure an adequate transition plan is created collaboratively. Discharge information should include how to re-access services if required. [2023]
- G Statistically derived tools which predict future functional capacity should be considered to guide expectations of treatment or to predict risk:
 - Tools should only be applied in the population and phase of stroke within which the tool was developed;
 - Clinicians need to be trained to understand the limitations of tools, and how to use the tools effectively. [2023]
- H The multidisciplinary team should complete weekly reviews whilst providing rehabilitation in any setting, considering the needs, goals and progress of the person with stroke, and their treatment and discharge plans. The choice of rehabilitation pathway should be regularly reviewed to ensure rehabilitation continues to best meet the person's needs.
- For people with stroke who are no longer receiving stroke rehabilitation at 6 months, a primary focus of the 6 month review should be to identify and redirect those with ongoing needs and/or

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- goals back into stroke services. Reviews should be holistic in nature and be completed by a stroke specialist with appropriate skills and expertise. [2023]
- J People with stroke should receive a holistic annual review conducted by a professional with a broad range of skills and knowledge across physical, psychological and social domains. Those for whom new or ongoing stroke rehabilitation goals can be identified and agreed should be referred to stroke services for further rehabilitation. [2023]

4.1 Source

A-J Guideline Development Group consensus

4.1 Evidence to recommendations

This section has been written by an expert group reaching consensus on the topic of rehabilitation potential, its definition, appropriateness of use and implications for people with stroke and the stroke pathway. More research is needed to identify which people with stroke will gain the most from different approaches and intensities of rehabilitation, and how to reliably identify those people who will not benefit from such interventions. Provision of six month reviews is currently inequitable (Sentinel Stroke National Audit Programme, 2022) and continues to be a focus for improvement to ensure unmet need is identified and people are redirected back into stroke specialist services appropriately. [2023]

4.2 Rehabilitation approach – intensity of therapy (motor recovery and function)

Rehabilitation is an adaptive process, and the practice and repetition of functional tasks for months or years is a key component of optimal recovery. The evidence for intensity of therapy within this chapter mainly relates to physical and functional rehabilitation after stroke. Less is known about the intensity of therapy required for psychological, cognitive or sensory effects of stroke; however, some principles regarding practice and training may be relevant. [2023]

Greater amounts of physical therapy (i.e. dose) are associated with better recovery (Kwakkel et al, 1999; Kwakkel & Wagenaar, 2002; Bhogal et al, 2003a; Bhogal et al, 2003b; Kwakkel et al, 2004). The dose of therapy is multi-faceted, encompassing not only the number of treatment sessions, but also their duration and frequency. It is unclear whether therapy needs to be more intense (i.e. the same amount of therapy over a shorter time) but there is evidence that motor learning is best accomplished with challenging, motivating tasks and variable training schedules (Krakauer, 2006). In reality, stroke therapy is rarely delivered intensively or in high doses. Studies have shown that therapy sessions commonly feature low numbers of repetitions, low cardiovascular activity, and with the patient frequently inactive (Bernhardt et al, 2004; Lang et al, 2009; Scrivener et al, 2012; West & Bernhardt, 2012; Hayward & Brauer, 2015). This is a particular issue in the UK, where many services are unable to deliver guidelinerecommended levels of activity. In the year April 2021-22 the Sentinel Stroke National Audit Programme (SSNAP) reported that 16.8% of patients received more than 45 minutes of occupational therapy 7 days a week, 11.9% received more than 45 minutes of physiotherapy 7 days a week and 6.6% received at least 45 minutes of speech and language therapy 7 days a week in participating UK hospitals. In recent years other countries such as Australia (Stroke Foundation, 2022), Canada (Teasell et al, 2020) and the Netherlands (Veerbeek et al, 2014a) have significantly progressed this target to the expectation that patients receive at least three hours of therapy per day. [2023]

The content of therapy is also important. An ineffective therapy will not benefit patients whatever the dose or intensity. As detailed in this chapter, the most effective therapy for promoting motor recovery after stroke is based on exercise and practice of functional tasks augmented as necessary by technological and priming techniques (Veerbeek et al, 2014b; French et al, 2016a; Wattchow et al, 2018; Scrivener et al, 2020). The main points of post-stroke therapy aimed at motor recovery are

understanding the impairments, activity, and individualised goals, leading to a high number of repetitions of relevant exercise and functional tasks. The amount of activity that patients are able to undertake during rehabilitation is more important than how much time patients spend in face-to-face therapy with qualified therapists. These principles apply to inpatient, outpatient and community settings. Commissioners/service planners, service managers and clinicians must drive improvements in the culture and processes of rehabilitation to maximise both therapist-delivered therapy and opportunities and support for practice and activity outside formal therapy sessions, recognising that rehabilitation can be delivered in a number of ways including supervised practice, group work and self practice. Delivery methods should be considered to ensure both effective delivery for patients and efficient use of resources. [2023]

4.2 Recommendations

- A People with motor recovery goals undergoing rehabilitation after a stroke should receive a minimum of 3 hours of multidisciplinary therapy a day (delivered or supervised by a therapist or rehabilitation assistant focused on exercise, motor retraining and/or functional practice), at least 5 days out of 7, to enable the range of required interventions to be delivered at an effective dose.
 - Rehabilitation programmes should be individualised to account for comorbidities, baseline activity levels, post-stroke fatigue, tolerance, goals and preferences. Therapy can be paced throughout the day, to accumulate at least 3 hours of motor/functional therapy;
 - For people unable to tolerate 3 hours of therapy a day, the barriers to doing so should be fully assessed and actively managed with strategies to ensure they are able to participate in therapy and be active as far as possible;
 - People undergoing rehabilitation after a stroke should be supported to remain active for up to 6 hours a day (including therapist-delivered therapy), for example through the use of open gyms, self-practice, carer-assisted practice, engaging in activities of daily living, and activities promoting cardiovascular fitness. [2023]
- B Services delivering rehabilitation for people after stroke should:
 - deliver a range of individualised one-to-one therapies, structured semi-supervised practice and group work (including rehabilitation gym sessions and a range of exercise and activity groups relevant to the person's needs);
 - have access to adequate rehabilitation space such as a gym and areas for functional practice (e.g. kitchen and bathroom), appropriate space to accommodate group work, and quiet space for psychological assessment and sensitive discussions;
 - ensure that delivery of rehabilitation intensity includes education for both the person with stroke and their family/carers to better understand their difficulties, and their recovery and rehabilitation;
 - be organised to encourage and support people with stroke to remain active outside of therapist-delivered sessions. [2023]
- C In the first two weeks after stroke, therapy targeted at the recovery of mobility should consist of frequent, short interventions every day, typically beginning between 24 and 48 hours after stroke onset. [2016]
- D Multidisciplinary stroke teams should incorporate the practice of functional skills gained in therapy into the person's daily routine in a consistent manner, and the care environment should support people with stroke to practise their activities as much as possible.

 Functional activities should be individualised to the person's goals and interests. [2023]
- E Healthcare staff who support people with stroke to practise their activities should do so under the guidance of a qualified therapist. [2016]

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4.2 Sources

- A, B Veerbeek et al, 2014a; Stroke Foundation, 2022; Teasell et al, 2020; Guideline Development Group consensus
- C AVERT Trial Collaboration group, 2015; Bernhardt et al, 2016
- D Smith et al, 1981; Langhorne et al, 1996; Kwakkel et al, 1994, 2004; Lincoln et al, 1999; Kwakkel and Wagenaar, 2002
- E Working Party consensus

4.2 Evidence to recommendations

The large international AVERT trial (AVERT Trial Collaboration group, 2015; Bernhardt et al, 2016) suggested that in the first two weeks after stroke, therapy targeted at the recovery of mobility should be redesigned around frequent, short interventions, except for those people who require little or no assistance to mobilise (see Section 3.12 Early mobilisation). Therapy targeted at other activities of daily living should be task-specific, progressive and practised frequently. Practice should be incorporated into routine activities on the stroke unit by the entire healthcare team every day of the week, rather than confined to lengthy therapy sessions separated by long periods of inactivity. The objective is for rehabilitation to be a pervasive activity, combining time spent with therapists in assessment and treatment with time spent practising with other professional and/or support staff, or with family/carers or alone. Rehabilitation intensity in both acute and longer-term settings remains an area which requires more research. [2016]

The recommendation for people with stroke to receive 45 minutes of each therapy per day in previous editions of this guideline was set pragmatically as a minimum through consensus by the Working Party at the time. The Guideline Development Group has debated this further and has increased the recommended amount of therapy in this edition to stimulate much-needed transformation of rehabilitation to improve clinical outcomes. This is supported by evidence regarding the effects of greater amounts of therapy (dose) (Kwakkel et al, 1999; Kwakkel & Wagenaar, 2002; Bhogal et al, 2003a; Bhogal et al, 2003b; Kwakkel et al, 2004) and is reflected in other clinical guidelines around the world (Australia (Stroke Foundation, 2022), Canada (Teasell et al, 2020) and the Netherlands (Veerbeek et al, 2014a)). The revised recommendation is based on the cumulative evidence that the interventions recommended within this chapter need to be delivered in a significant dose to be effective, and this dose is rarely provided in clinical practice. Progress implementing the previous recommendation (at least 45 minutes/day) has been incomplete, not least because it is commonly considered a target rather than a minimum dose and many clinicians underestimate the dose of therapy that people with stroke can tolerate. Increasing time in therapist-delivered sessions allows effective delivery of these interventions, with the added focus on self-directed or semi-supervised practice aimed at shifting the culture of rehabilitation. [2023]

4.3 Rehabilitation approach – goal setting

Goal setting can be defined as a behavioural target that is central to rehabilitation, but is also effective in secondary risk factor reduction such as weight loss, smoking cessation or alcohol consumption reduction. Goal setting is the process by which the person with stroke (and their family or carers if they wish) and members of the stroke team identify individual treatment goals which are meaningful, challenging and have personal value. Goals are worked towards over a specified period of time, both short and long term. Traditionally goals have been therapy-led and orientated to specific therapy targets which are realistic and measurable. This method has proved to be an effective and efficient rehabilitation tool when used flexibly to reflect that the person's ability and motivation to participate may fluctuate over time. A balance should be made between practicality, working in a stepwise approach and supporting the aspirations of the person with stroke. Recently a move towards self-

management and self-efficacy has been promoted as a more person-centred approach to goal setting. **[2016]**

4.3 Recommendations

- A People with stroke should be actively involved in their rehabilitation through:
 - having their feelings, wishes and expectations for recovery understood and acknowledged;
 - participating in the process of goal setting unless they choose not to, or are unable to because of the severity of their cognitive or linguistic impairments;
 - being given help to understand the process of goal setting, and to define and articulate their personal goals. [2016]
- B People with stroke should be helped to identify goals that:
 - are meaningful and relevant to them;
 - are challenging but achievable;
 - aim to achieve both short-term (days/weeks) and long-term (weeks/months) objectives;
 - are documented, with specific, time-bound and measurable outcomes;
 - have achievement measured and evaluated in a consistent way;
 - include family/carers where this is appropriate;
 - are used to guide and inform therapy and treatment. [2016]
- C People with stroke should be supported and involved in a self-management approach to their rehabilitation goals. [2016]

4.3 Sources

- A, B Malec et al, 1991; Wressle et al, 2002; Stein et al, 2003; Hurn et al, 2006; Levack et al, 2006; Holliday et al, 2007a, b; Working Party Consensus
- C Rosewilliam et al, 2011; Sugavanam et al, 2013; Taylor et al, 2012

4.3 Evidence to recommendations

Recent literature includes one systematic review of qualitative and quantitative studies (Sugavanam et al, 2013) which examined 17 trials and concluded that no consistent approach was used and there were difficulties implementing a self-management approach. A qualitative paper by Jones et al. (2013) highlighted a lack of training and awareness of the self-management approach. A Cochrane review of 39 RCTs in 2846 subjects participating in rehabilitation with a variety of conditions including acquired brain injury (Levack et al, 2015) concluded there was low-quality evidence that goal setting may improve health-related quality of life and other psychosocial outcomes such as emotional status and self-efficacy. Goal setting should involve the person with stroke and their family/carers where appropriate, and be measured and evaluated in a consistent and standardised way. [2016]

4.4 Self-management

There is increasing evidence of psychological factors that influence confidence and adjustment to life after stroke. Self-efficacy has been defined as an 'individual's belief in their own capability' and has been found to be positively associated with mobility, activities of daily living, and quality of life and negatively associated with depression after stroke (Korpershoek et al, 2011). Self-efficacy is closely related to mood and self-esteem, and there are relations between self-efficacy and emotional states (depression, anxiety) and quality of life. [2016]

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Self-efficacy may mediate self-management skills such as problem solving and goal setting and is used as an outcome measure in some self-management programmes (Korpershoek et al, 2011; Lennon et al, 2013; Parke et al, 2015; Warner et al, 2015). There is emerging evidence on the utility of changing self-efficacy to influence independence and the promotion of self-management after stroke. Self-management has been defined in various ways but many programmes refer to the 'actions and confidence of individuals to manage the medical and emotional aspects of their condition in order to maintain or create new life roles' (Corbin, 1998; Parke et al, 2015). Programmes mainly focus on supporting the knowledge and skills required to self-manage, and range from educational approaches to interventions to support behaviour change. [2016]

4.4 Recommendations

- A People with stroke should be offered self-management support based on self-efficacy, aimed at the knowledge and skills needed to manage life after stroke, with particular attention given to this at reviews and transfers of care. [2016]
- B People with stroke whose motivation and engagement in rehabilitation appears reduced should be assessed for changes in self-esteem, self-efficacy or identity and mood. [2016]
- C People with significant changes in self-esteem, self-efficacy or identity after stroke should be offered information, support and advice and considered for one or more of the following psychological interventions:
 - increased social interaction;
 - increased exercise;
 - other psychosocial interventions, such as psychosocial education groups. [2016]

4.4 Sources

- A Lennon et al, 2013; Parke et al, 2015; Warner et al, 2015; Working Party consensus
- B Working Party consensus
- C Kendall et al, 2007; Watkins et al, 2007; De Man-van Ginkel et al, 2010; Jones et al, 2010

4.4 Evidence to recommendations

Evidence suggests that self-management programmes based on self-efficacy can influence functional capability and social participation. Recent systematic reviews support self-management interventions after stroke although meta-analysis was not possible because of heterogeneity in the methods of delivery, clinical outcomes and stroke severity (Lennon et al, 2013; Parke et al, 2015; Warner et al, 2015). Not all studies in these reviews used self-efficacy as a mediator nor explicitly used self-efficacy outcome measures. A recent feasibility cluster RCT showed it was feasible to integrate stroke self-management into community rehabilitation and provided data to design future definitive trials (Jones et al, 2016). More research is needed to understand the role of self-efficacy in rehabilitation, the skills required by professionals, and how participants perceive the impact of self-management interventions on their self-efficacy. [2016]

4.4 Implications

These recommendations serve to emphasise the important interaction between newly-recognised psychosocial concepts of self-efficacy and self-management, and functional outcomes and social participation after recovery from stroke. Stroke services need to consider how to develop the knowledge and skills in rehabilitation staff to support self-management, and how to provide psychological interventions as an adjunct to more familiar physical treatments, including in community stroke services. [2016]

4.5 Remotely delivered therapy and telerehabilitation

Remotely delivered therapy is rehabilitation delivered using technology, with a remote therapist personalising a programme or tasks to specifically address identified impairments or goals. This may take place with a therapist present during the session remotely to adapt and give feedback in real time, or asynchronous practice, when the therapist gives and receives feedback offline. Therapy can be delivered via videoconferencing, and can be individual or in a group. The term is used synonymously with telerehabilitation, which has been defined as "the use of telecommunication, by either direct video or audio, to deliver rehabilitative interventions" (Appleby et al, 2019). Telehealth or telemedicine often uses similar technologies but focuses on risk factors, secondary prevention, behaviour or lifestyle modifications (Bashshur, 1995). [2023]

Telerehabilitation saw significant advances during the COVID-19 pandemic, with programmes such as N-ROL (Neuro Rehab On-Line) and the Bridges community of practice (www.bridgesselfmanagement.org.uk) providing examples and guidance to assist patients and therapists to engage in remotely delivered rehabilitation. [2023]

A range of technologies can be used for communication between the patient and therapist, such as telephone, videoconferencing, apps, sensors (e.g. pedometers, wearable devices) and virtual reality (Laver et al, 2020). Technological innovations such as telerehabilitation may help address barriers to accessing face-to-face rehabilitation, such as time and resource limitations, geographical isolation and compliance with rehabilitation (Appleby et al, 2019). There are potential advantages of remotely delivered therapy in terms of patient satisfaction (although studies are affected by selection bias), motivation, agency, the patient and therapist not needing to travel, and efficiency for multidisciplinary teams. Barriers to use by patients and therapists can include difficulties with equipment set up, connectivity and problems with the interface (Tyagi et al, 2018) and lack of privacy in the home setting. Additional barriers may impact on ability to engage with telerehabilitation for those with reduced comprehension, cognitive processing difficulties, or visual deficits. [2023]

Local systems should consider digital inequities and digital literacy, as well as socio economic impact on availability of equipment. Careful consideration should be taken as to whether remotely delivered therapy is best placed to meet the needs of individuals (particularly those with cognitive or language deficits), and which programs and equipment may be most accessible. For those unable to access remotely delivered therapy, a face-to-face alternative should be available. Support such as volunteers or peer support should be considered for those who are keen to trial technology-based options. [2023]

4.5 Recommendations

- A People undergoing rehabilitation after stroke should be considered for remotely delivered rehabilitation to augment conventional face-to-face rehabilitation. Telerehabilitation programmes should:
 - be personalised to the individual's goals and preferences;
 - be used when it is considered to be the most beneficial option to promote recovery and should not be used as a substitute for essential in-person rehabilitation;
 - be monitored and adapted by the therapist according to progress towards goals;
 - be supplemented with face-to-face reviews and include the facility for contact with the therapist as required. [2023]
- B People receiving rehabilitation after stroke should have an assessment of their ability to use assistive technology and programmes and equipment should be adapted accordingly.

 [2023]
- C Stroke services should ensure adequate technology is available to enable access to telerehabilitation for people with stroke (this could be resourced via grants, community

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- health services, library loan services etc.). [2023]
- D People with stroke receiving telerehabilitation should be trained and supported in the use of the appropriate technology. [2023]
- E Stroke rehabilitation staff who are recommending the use of telerehabilitation devices should be trained in their use, technological specification and limitations. This should include the review of technologies for appropriateness, safety and information governance (storage of personal data). [2023]
- F Therapists should promote engagement and adherence to telerehabilitation through a coaching style relationship with the person with stroke. [2023]

4.5 Source

A-F Guideline Development Group consensus

4.5 Evidence to recommendations

The evidence base for remotely delivered therapy is new and developing. The evidence reviewed was heterogeneous in terms of the types of remote therapy, location (hospital versus home), comparison group and the selection of patients, which makes synthesis challenging. A systematic review of 31 studies showed high levels of adherence to telerehabilitation, interventions observed were comparable to in-person rehabilitation and no safety concerns related to the delivery of telerehabilitation interventions were reported. A systematic review and meta-analysis of 13 studies of technology-based distant physical rehabilitation interventions found comparable effects to traditional treatments on ADL but not walking, although there was heterogeneity in the interventions and people with cognitive impairments were often excluded (Rintala et al, 2019). A Cochrane review of 22 RCTs of telerehabilitation in stroke found evidence of variable quality from heterogeneous studies suggesting no difference between telerehabilitation and conventional rehabilitation (Laver et al, 2020). Limited data were reported on safety and economic analyses. Many studies were small, pilot and/or nonrandomised and did not account for attrition from the intervention. Few studies had long-term followup and there was variability in the level of detail provided about the intervention, including personalisation and adherence. The evidence base is therefore of insufficient quality to strongly recommend specific remotely delivered therapy approaches. Therefore, the Guideline Development Group has made consensus recommendations for this topic. [2023]

Consideration needs to be given to the person with stroke being cognitively able to manage the approach being used, being motivated to participate, having appropriate privacy and physical space where required, and their technological proficiency. [2023]

Telehealth has the potential to decrease the burden of treatment for patients with long-term and multiple conditions. It also has the ability to introduce inequities (Eddison et al, 2022). [2023]

4.6 Self-directed therapy

Self-directed rehabilitation (or self-practice) refers to approaches for promoting independent therapeutic activity away from a clinical setting (Da-Silva et al, 2018). Self-directed rehabilitation can be considered as an option alongside other rehabilitation approaches to increase overall therapy time and dose. Personalising programmes to the individual's health beliefs, situation, preferences and needs is important for facilitating adherence to self-practice (Vadas et al, 2021). Self-directed rehabilitation is often part of a comprehensive rehabilitation approach rather than a separate entity. [2023]

4.6 Recommendations

A People with stroke should be offered training and resources to support them to carry out

- appropriately targeted self-directed therapy practice in addition to their standard rehabilitation, in accordance with the individual's goals and preferences. Self directed therapy should be monitored and reviewed regularly. [2023]
- People with stroke who are able to follow regimes independently or with the support of a carer should be considered for self-directed rehabilitation to increase practice in addition to standard rehabilitation; for example, patients undergoing constraint-induced movement therapy, electrical stimulation or computerised speech and language therapy.

 [2023]
- C For people undergoing rehabilitation after stroke, the use of competition (with self or others) may be considered to give people motivation to practise self-directed rehabilitation. [2023]

4.6 Sources

- A Guideline Development Group consensus
- B Da-Silva et al, 2018; Palmer et al, 2019; Working Party consensus
- C Guideline Development Group consensus

4.6 Evidence to recommendations

Self-directed rehabilitation is a new topic for this edition of the guideline. There is limited high quality evidence available on the particular groups of people with stroke who may benefit most from self-directed rehabilitation and the optimal timing for these interventions. It is also important that further research identifies those who may not benefit from this approach. [2023]

A systematic review of 40 studies evaluated the effectiveness of self-directed interventions for arm rehabilitation after stroke (Da-Silva et al, 2018). Self-directed interventions using constraint-induced movement therapy and electrical stimulation were found to have a beneficial effect on arm function, although studies had a risk of bias and used different types of stimulation, dose, timing and outcome measures. Constraint-induced movement therapy and therapy programmes which increase practice without using additional technology improved independence in activities of daily living assessed on a self-perceived outcome measure. [2023]

Results of a proof-of-concept study (Studer et al, 2016) suggest that experimental or perceived competition may be beneficial in enhancing self-directed cognitive training but more robust evidence is required to guide practice. [2023]

Activity and participation

4.7 Introduction

This section covers difficulties that can occur after stroke affecting personal, domestic and extended activities of daily living (e.g. work and driving), and recommendations to help the person with stroke to engage in independent living and social participation. These activities can be affected by a range of difficulties (e.g. cognition (Sections 4.28 Psychological effects of stroke – general, 4.29 Cognitive screening, 4.30 Cognitive assessment), Section 4.18 Arm function, Section 4.25 Fatigue and the guideline user should refer to all relevant sections. [2016]

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4.8 Independence in daily living

Personal activities of daily living (PADL) refer to a range of basic activities such as washing, dressing, bathing, going to the toilet, eating and drinking; these activities usually depend on the ability to transfer and the use of at least one hand. After a stroke PADL can be difficult due to both physical and cognitive impairments. The resultant loss of function can have implications on a person's ability to live independently at home and is therefore a key part of stroke rehabilitation. [2016]

4.8 Recommendations

- A People with stroke should be formally assessed for their safety and independence in all relevant personal activities of daily living by a clinician with the appropriate expertise, and the findings should be recorded using a standardised assessment tool. [2016]
- B People with limitations of personal activities of daily living after stroke should:
 - be referred to an occupational therapist with knowledge and skills in neurological rehabilitation. Assessment should include consideration of the impact of hidden deficits affecting function including neglect, executive dysfunction and visual impairments;
 - be assessed by an occupational therapist within 24 hours of admission to a stroke unit;
 - be offered treatment for identified problems (e.g. feeding, work) by the occupational therapist, in discussion with other members of the specialist multidisciplinary team.
 [2023]
- C People with stroke should be offered, as needed, specific treatments that include:
 - dressing practice for people with residual problems with dressing;
 - as many opportunities as appropriate to practise self-care as possible;
 - assessment, provision and training in the use of equipment and adaptations that increase safe independence;
 - training their family/carers in how to help them. [2016]

4.8 Sources

- A Working Party consensus
- B Legg et al, 2006; Guideline Development Group consensus
- C Walker et al, 2011; Working Party consensus

4.8 Evidence to recommendations

There is limited new research in this area since the 2012 edition of this guideline. The main evidence is summarised in a Cochrane systematic review (Legg et al, 2006) which found that people with stroke who received occupational therapy targeting PADL performed better and had a reduced risk of a poor outcome (dependency in PADL, deterioration or death) compared to those without occupational therapy input. [2016]

However, there was limited information on the content of the therapy and research investigating the specific interventions that improve PADL is still required. A feasibility RCT has shown potential benefits of a systematic neuropsychological approach to dressing therapy after stroke (Walker et al, 2011) but more robust evidence is required to guide practice. A recent Cochrane review (Elsner et al, 2016) found low to moderate quality evidence that transcranial direct current stimulation (tDCS) was effective in eliciting short-term improvements in ADL, but it is unclear whether these effects are lasting and benefits were not seen in an analysis confined to high quality RCTs. There are ongoing trials of tDCS which may improve the quality of the evidence. Informal carers often provide support with PADL but, as described elsewhere (Section 2.16 Carers), how and when to train informal carers remains unclear despite a large RCT (Forster et al, 2012). [2016]

4.9 Hydration and nutrition

This section should be considered in conjunction with Section 4.26 Swallowing. [2023]

Dehydration and malnutrition are common in hospital inpatients with stroke and associated with poor outcomes (Foley et al, 2008; Rowat et al, 2012). Malnutrition is associated with increased mortality and complications, as well as poorer functional and clinical outcomes (Davalos et al, 1996; Yoo et al, 2008). Up to one quarter of patients become more malnourished in the first weeks following stroke, and the risk of malnutrition increases with increasing hospital stay (Davalos et al, 1996; Yoo et al, 2008). [2016]

Poor nutritional intake, weight loss, and feeding and swallowing problems can persist for many months (Finestone et al, 2002; Perry, 2004; Jonsson et al, 2008). Multiple factors may contribute to a high risk of dehydration and malnutrition after stroke including physical, social and psychological issues. These include swallowing problems (Section 4.26 Swallowing), reduced ability to self-feed, cognitive impairment (Section 4.28 Psychological effects of stroke - general), anxiety or depression (Section 4.39 Anxiety, depression and psychological distress), fatigue (Section 4.25 Fatigue), and unfamiliar foods.

[2016]

The assessment of dehydration is complex, and when used in isolation many common assessment methods are inaccurate (Hooper et al, 2015). Structured screening tools for malnutrition (e.g. the Malnutrition Universal Screening Tool [MUST]) have been validated in stroke (Gomes et al, 2016). [2016]

All measures considered should be in line with the Restraint Reduction Network training standards (Ridley & Leitch, 2021) and the relevant mental capacity legislation. [2023]

4.9 Recommendations

- A Patients with acute stroke should have their hydration assessed using a standardised approach within four hours of arrival at hospital, and should be reviewed regularly and managed so that hydration is maintained. [2023]
- B Patients with acute stroke should be screened for the risk of malnutrition on admission and at least weekly thereafter. Screening should be conducted by trained staff using a structured, standardised, validated tool. [2023]
- C Patients with acute stroke who are at low risk of malnutrition on admission, and are able to meet their nutritional needs orally, should not routinely receive oral nutritional supplements. [2023]
- D Patients with acute stroke who are at risk of malnutrition or who require tube feeding or dietary modification should be referred to a dietitian for specialist nutritional assessment, advice and monitoring. [2023]
- Patients with stroke who are at risk of malnutrition should be offered nutritional support. This may include oral nutritional supplements, specialist dietary advice and/or tube feeding in accordance with their expressed wishes or, if the patient lacks mental capacity, in their best interests. [2023]
- F Patients with stroke who are unable to maintain adequate nutrition and hydration orally should be:
 - referred to a dietitian for specialist nutritional assessment, advice and monitoring;
 - be assessed for nasogastric tube feeding within 24 hours of admission;
 - assessed for a nasal bridle if the nasogastric tube needs frequent replacement, using locally agreed protocols;
 - assessed for gastrostomy feeding if they are unable to tolerate a nasogastric tube with

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nasal bridle. [2023]

- G People with stroke who require food or fluid of a modified consistency should:
 - be referred to a dietitian for specialist nutritional assessment, advice and monitoring;
 - have the texture of modified food or fluids prescribed using internationally agreed descriptors;
 - be referred to a pharmacist to review the formulation and administration of medication. [2023]
- H People with stroke should be considered for gastrostomy feeding if they:
 - need but are unable to tolerate nasogastric tube feeding, including a trial with a nasal bridle if appropriate and other measures such as taping the tube or increased supervision;
 - are unable to swallow adequate food and fluids orally by four weeks from the onset of stroke and gastrostomy feeding is considered to be required long-term;
 - reach the point where shared decision making by the person with stroke, their family/carers, and the multidisciplinary team has agreed that artificial nutrition is appropriate due to the high long-term risk of malnutrition. [2023]
- People with difficulties self-feeding after stroke should be assessed and provided with the appropriate equipment and assistance including physical help and encouragement, environmental considerations, and postural support to promote independent and safe feeding. [2023]
- People with stroke discharged from stroke services with continuing problems meeting their nutritional needs should have a documented care plan to ensure their dietary intake and nutritional status are monitored at a frequency appropriate to their needs and which identifies who will be responsible for ongoing monitoring (such as district nurses or family/carers). [2023]
- K People with stroke receiving end-of-life (palliative) care should not have burdensome restrictions on oral food and fluid intake, if those restrictions would exacerbate suffering.
 [2023]
- L The carers and family of those with a gastrostomy tube should receive training, equipment and ongoing support from a specialist team, e.g. a home enteral feeding team. [2023]

4.9 Sources

- A, B Guideline Development Group consensus
- C, D NICE, 2017b, 2022e; Geeganage et al, 2012
- E Geeganage et al, 2012; Guideline Development Group consensus
- F NICE, 2023b; Beavan et al, 2010; Guideline Development Group consensus
- G British Dietetic Association, 2009; Carnaby et al, 2006; National Patient Safety Agency et al, 2011
- H Dennis et al, 2005; NICE, 2017b
- I Guideline Development Group consensus
- J NICE, 2017b
- Royal College of Physicians, 2021 Royal College of Speech and Language Therapists, 2021;
 Guideline Development Group consensus
- L Guideline Development Group consensus

4.9 Evidence to recommendations

There is little RCT evidence to guide the management of hydration in people with acute stroke. A Cochrane review by Hooper et al (2015) of the signs and symptoms of impending and current dehydration in older people concluded that there is little evidence that any one symptom, sign or test, including many that clinicians customarily rely on, has any diagnostic utility for dehydration. [2016]

A Cochrane review (Geeganage et al, 2012) included eight trials of the effectiveness of nutritional support in people with acute and subacute stroke (less than six months) who were non-dysphagic. Although nutritional supplementation resulted in significantly reduced pressure sores, increased energy intake and increased protein intake, this did not affect length of hospital stay, dependency or mortality. Studies included people with variable baseline nutritional status, not just those who were malnourished or at risk of malnutrition. The effects of the nutritional composition of nutritional support warrants further study, including the role of leucine supplementation (Yoshimura et al, 2019). [2023]

Since the 2012 edition of this guideline, two Cochrane reviews have compared routes of enteral tube feeding. One reviewed 11 RCTs comparing gastrostomy versus nasogastric tubes in adults with swallowing difficulties (Gomes Jr et al, 2015), including four trials in people after stroke (Norton et al, 1996; Bath et al, 2000; Dennis et al, 2005; Hamidon et al, 2006). Although gastrostomy reduced intervention failure, there was no difference between the interventions in weight change, pneumonia or mortality. Most studies were small with considerable heterogeneity and methodological limitations. Geeganage et al (2012) reviewed five RCTs comparing gastrostomy with nasogastric tube feeding in people with acute and subacute stroke. Although gastrostomy feeding was associated with fewer feeding failures, less gastrointestinal bleeding and fewer pressure sores, there was no significant difference in length of hospital stay, dependency or mortality. [2016]

Beavan et al. (2010) conducted a multicentre RCT in people with stroke who required nasogastric tube feeding due to dysphagia (Section 4.26 Swallowing). In a sample of 104 people, those who had a nasogastric tube secured using a nasal bridle received a higher proportion of prescribed feed and fluid compared to the control group who had tubes secured using standard practice. Mahoney et al (2015) identified the need for training and protocols in confirming the placement and securing of nasogastric tubes. [2016]

There is insufficient evidence to determine the effectiveness and acceptability of hand mittens or other measures used to prevent nasogastric tube dislodgement. The impact of practical strategies and environmental modifications to support people after stroke who are at risk of malnutrition are recommended areas for future research. [2023]

4.10 Mouth care

Mouth care (also referred to as oral care) refers to the promotion and maintenance of a clean oral cavity including the teeth, gums, cheeks, tongue and palate. A clean mouth requires the removal of traces of food and debris and dental plaque. A clean mouth is pleasant for the person with stroke and maintains the health of the mouth, teeth and gums. Poor oral hygiene can lead to dental caries, periodontal gum disease, the development of ulceration, soreness, cracked lips and fungal infections, and is associated with increased bacteria in the mouth and in saliva. In people with dysphagia (Section 4.26 Swallowing) this may increase the risk of aspiration pneumonia. People with problems chewing and swallowing and soreness of the mouth report a decrease in the range of food they are able to eat. A clean and healthy mouth can prevent discomfort and help to achieve good nutrition (Section 4.9 Hydration and nutrition). Maintaining good oral hygiene can be difficult following a stroke because of cognitive impairment, dysphagia or arm weakness, and can be made worse by inadequate control of saliva and medication side effects such as xerostomia (dry mouth). Members of the multidisciplinary team should be trained to ensure provision of adequate mouth care. [2023]

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4.10 Recommendations

- A People with stroke, especially those who have difficulty swallowing or who are tube fed, should have mouth care at least three times a day (particularly after mealtimes), which includes removal of food debris and excess secretions, and application of lip balm. [2023]
- B People with stroke, including those who have full or partial dentition and/or wear dentures and especially those who have difficulty swallowing or who are tube fed, should have mechanical removal of plaque at least twice a day by the brushing of teeth and cleaning of gums and tongue with a low foaming, fluoride-containing toothpaste.

 Chlorhexidine dental gel may be prescribed short term and requires regular review. A powered toothbrush should be considered. [2023]
- C People with stroke who have dentures should have their dentures:
 - put in during the day, using a fixative if required;
 - cleaned regularly using a denture cleansing agent or soap and water;
 - checked, and the individual referred to a dental professional if ill-fitting or replacement is required.

Any remaining teeth should be cleaned with a toothbrush and fluoride-containing toothpaste. [2023]

- D Staff delivering mouth care in hospital or in a care home or domiciliary setting should receive training on mouth care, which should include:
 - assessment of oral hygiene;
 - selection and use of appropriate oral hygiene equipment and cleaning agents;
 - provision of mouth care routines;
 - awareness and recognition of swallowing difficulties. [2023]
- People with stroke and their family/carers should receive information and training in mouth care and maintaining good oral hygiene before transfer of their care from hospital. This information should be clearly communicated within and across care settings, e.g. within a care plan which includes regular dental reviews. [2023]

4.10 Sources

- A Guideline Development Group consensus
- B, D Campbell et al, 2020; Guideline Development Group Consensus
- C, E Brady et al, 2006; Guideline Development Group Consensus

4.10 Evidence to recommendations

A Cochrane systematic review (Campbell et al, 2020) compared the effectiveness of oral health care interventions with usual care or other treatment options. There was low quality evidence suggesting oral health care interventions can improve the cleanliness of patient's dentures. There was very low quality evidence that such interventions can improve the knowledge and attitudes of people after a stroke and healthcare providers. The review acknowledged that maintenance of oral health care after a stroke should be a priority in clinical care and research. It also noted that co-ordination of future research is required to address the wide range of outcome measures and associated measurement tools. [2023]

Establishing locally agreed roles and responsibilities for oral health care is regarded as important to enable the delivery of high quality oral health care, the efficacy of which should be evaluated to improve practice. A care plan for oral health, including for people with stroke in care homes, would support information sharing and emphasise the importance of oral health care. [2023]

4.11 Continence

Loss of bladder and bowel control is common in the acute phase of stroke and may persist. Incontinence of urine greatly increases the risk of skin breakdown and pressure ulceration. Incontinence of faeces is associated with more severe stroke and is more difficult to manage. Constipation is common, occurring in 55% of people within the first month of stroke, and can compound urinary and faecal incontinence. Incontinence has a detrimental effect on mood, confidence, self-image and participation in rehabilitation and is associated with carer stress. Incontinence is an area of stroke that has received little research interest, despite its substantial negative impact. It needs to be managed proactively to allow people with stroke to fully participate in their own care and recovery both in the acute phase and beyond, for example people with mental capacity (Section 4.35 Mental capacity) should be involved in decisions around the use of catheters and sheaths. [2016]

4.11 Recommendations

- A Stroke unit staff should be trained in the use of standardised assessment and management protocols for urinary and faecal incontinence and constipation in people with stroke. [2016]
- B People with stroke should not have an indwelling (urethral) catheter inserted unless indicated to relieve urinary retention or when fluid balance is critical. [2016]
- C People with stroke who have continued loss of bladder and/or bowel control 2 weeks after onset should be reassessed to identify the cause of incontinence, and be involved in deriving a treatment plan (with their family/carers if appropriate). The treatment plan should include:
 - treatment of any identified cause of incontinence;
 - training for the person with stroke and/or their family/carers in the management of incontinence;
 - referral for specialist treatments and behavioural adaptations if the person is able to participate;
 - adequate arrangements for the continued supply of continence aids and services.
 [2016]
- D People with stroke with continued loss of urinary continence should be offered behavioural interventions and adaptations prior to considering pharmaceutical and long-term catheter options, such as:
 - timed toileting;
 - prompted voiding;
 - review of caffeine intake;
 - bladder retraining;
 - pelvic floor exercises;
 - external equipment. [2016]
- E People with stroke with constipation should be offered:
 - advice on diet, fluid intake and exercise;
 - a regulated routine of toileting;
 - a prescribed medication review to minimise use of constipating medication;
 - oral laxatives;
 - a structured bowel management programme which includes nurse-led bowel care interventions:
 - education and information for the person with stroke and their family/carers;
 - rectal laxatives if severe problems persist. [2016]
- F People with continued continence problems on transfer of care from hospital should

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receive follow-up with specialist continence services in the community. [2016]

4.11 Sources

- A, B Working Party consensus
- C Thomas et al, 2008; Working Party consensus
- D NICE, 2013, NICE, 2015
- E NICE, 2007; Coggrave et al, 2006; Working Party consensus
- F Working Party consensus

4.11 Evidence to recommendations

A 2013 review of bowel management strategies (Lim & Childs, 2013) identified three small studies of varying quality, and concluded that the evidence was limited but a structured nurse-led approach may be effective. In a review of therapeutic education for people with stroke, Daviet et al (2012) concluded from small non-randomised studies that a nurse-targeted education programme may improve longer-term continence. A small RCT by Moon et al (2012) provided no evidence for bladder reconditioning with intermittent clamping. A small study by Guo et al (2014) examined the use of transcutaneous electrical nerve stimulation for the treatment of urinary incontinence over six months and found an improvement in nocturia, urgency and frequency. Thomas et al (2015) demonstrated the feasibility of a systematic voiding programme for urinary incontinence in a cluster RCT and proposed a definitive trial. Recommendations are therefore largely based on NICE guidance and Working Party consensus. [2016]

4.12 Extended activities of daily living

Extended activities of daily living (EADL) encompass both domestic and community activities such as shopping, cooking and housework that allow complete or virtually complete independence. These activities also enable community and social participation. See <u>Section 4.14 Driving</u>, and <u>Section 4.15 Return to work</u>. [2016]

4.12 Recommendations

- A People whose activities have been limited by stroke should be:
 - assessed by an occupational therapist with expertise in neurological disability;
 - trained in how to achieve activities safely and given as many opportunities to practise as reasonable under supervision, provided that the activities are potentially achievable;
 - provided with and trained in how to use any adaptations or equipment needed to perform activities safely. [2016]
- B People with stroke who cannot undertake a necessary activity safely should be offered alternative means of achieving the goal to ensure safety and well-being. [2016]

4.12 Sources

- A Legg et al, 2004
- B Working Party consensus

4.12 Evidence to recommendations

New evidence in this area is problematic and has not changed the recommendations since a systematic review (Legg et al, 2004) found that therapy improved EADL. Although several studies have included EADL as a secondary outcome, the interventions did not plausibly target EADL. For example, a systematic review of transcranial direct current stimulation found only limited evidence of any effect on

EADL (Elsner et al, 2016). The Working Party excluded for methodological reasons one small, non-randomised trial of community-dwelling people with stroke which substituted a portion of physiotherapy time with virtual reality games (Singh et al, 2013). [2016]

One large multi-centre RCT included people with stroke who wanted to get out of the house more often. It compared an intervention to increase outdoor mobility (e.g. exercise, activities and confidence-building, provided by a therapist over an average of seven sessions) with a single session of personalised advice and leaflets on transport and mobility (Logan et al, 2014). This increased the number of journeys made and had a lasting effect, but practical limitations in collecting the data on the number of journeys may have limited the reliability of the outcome measure. The intervention did not affect the primary (quality of life) or any other outcome, and was not cost-effective. More appropriate and reliable outcome measures are needed in future trials. [2016]

4.13 Sex

The physical and psychological impact of stroke can affect role identity and relationships with sexual partners, and sexual dysfunction can amplify these problems. Sexual dysfunction is common after stroke, affecting both the person with stroke and their partner (Korpelainen et al, 1999; Thompson & Ryan, 2009; Rosenbaum et al, 2014). It is typically multifactorial including other vascular disease, altered sensation, limited mobility, the effects of medication, mood changes and fear of precipitating further strokes. Regaining intimacy with partners can have a positive effect on self-esteem and quality of life and help to strengthen relationships. Discussion of sex and sexual dysfunction after stroke can be overlooked - healthcare professionals are often reluctant to raise the issue, and people with stroke are unlikely to raise the subject without encouragement (Rosenbaum et al, 2014). [2016]

4.13 Recommendations

- A People with stroke should be asked, soon after discharge and at their 6-month and annual reviews, whether they have any concerns about sex. Partners should also have an opportunity to raise any problems. [2016]
- B People with sexual dysfunction after stroke who want further help should be:
 - assessed for treatable causes including a medication review;
 - reassured that sexual activity is not contraindicated after stroke and is extremely unlikely to precipitate a further stroke;
 - assessed for erectile dysfunction and the use of a phosphodiesterase type 5 inhibitor (e.g. sildenafil);
 - advised against the use of a phosphodiesterase type 5 inhibitor for 3 months after stroke and/or until blood pressure is controlled;
 - referred to a professional with expertise in psychosexual problems if sexual dysfunction persists. [2016]

4.13 Sources

- A Thompson and Ryan, 2009; Schmitz and Finkelstein, 2010; Rosenbaum et al, 2014; Working Party consensus
- B Cheitlin et al, 1999; Melnik et al, 2007; Lorberboym et al, et al, 2010; Song et al, 2007

4.13 Evidence to recommendations

The Working Party found no new evidence that could inform a recommendation. A narrative literature review (Rosenbaum et al, 2014) identified the need for staff training and a structured approach to assessment. There is little evidence of the risks and benefits of phosphodiesterase type 5 inhibitors

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after stroke (e.g. sildenafil), as people within 6 months of stroke or with ischaemic heart disease were excluded from the original trials. There is no reason to suspect that people are at increased risk of side effects after stroke but the consensus of the Working Party is to wait for 3 months after stroke before prescribing sildenafil, once blood pressure is controlled. [2016]

4.14 Driving

Being able to drive is important to people with stroke for practical reasons and because it influences self- esteem and mood. However, there are potential risks associated with driving after stroke. Healthcare professionals therefore need to discuss and give advice on fitness to drive. The current UK regulations regarding driving are available online at https://www.gov.uk/guidance/general-information-assessing-fitness-to-drive and for the Republic of Ireland at https://www.ndls.ie/images/PDF Documents/Slainte agus Tiomaint Medical Fitness to Drive Guidel ines.pdf. [2016]

4.14 Recommendations

- A People who have had an acute stroke or TIA should be asked about driving before they leave the hospital or specialist outpatient clinic. [2016]
- B People with stroke who wish to drive should:
 - be advised of the exclusion period from driving and their responsibility to notify the DVLA, DVA or NDLS if they have any persisting disability which may affect their eligibility;
 - be asked about or examined for any absolute bars to driving e.g. epileptic seizure (excluding seizure within 24 hours of stroke onset), significant visual field defects, reduced visual acuity or double vision;
 - be offered an assessment of the impairments that may affect their eligibility, including their cognitive, visual and physical abilities;
 - receive a written record of the findings and conclusions, copied to their general practitioner. [2016]
- C People with persisting cognitive, language or motor disability after stroke who wish to return to driving should be referred for on-road screening and evaluation. [2016]
- D People who wish to drive after a stroke should be informed about eligibility for disabled concessions (e.g. Motability, the Blue Badge scheme). [2016]

4.14 Sources

- A, B Working Party consensus
- C Devos et al, 2011; Working Party consensus
- D Working Party consensus

4.14 Evidence to recommendations

A Cochrane review of four small trials of interventions to improve on-road driving skills after stroke concluded there was insufficient evidence to guide practice (George et al, 2014). No trials evaluated on-road driving lessons, and one study investigated simulator training. This showed promise but is not sufficient to recommend routine use in rehabilitation after stroke. [2016]

Observational studies of the predictive value of neuropsychological tests and screening tools for on-road driving performance suggest several that may support decision making when referring people with stroke for on-road driving tests (Korner-Bitensky et al, 2011; Aslaksen et al, 2013; Devos et al, 2014). A systematic review suggested that the Road Sign Recognition and Compass subtests of the Stroke Drivers

Screening Assessment, together with Trail Making Test B, may be indicators of those at risk of failing an on-road assessment (Devos et al, 2011). Many cognitive tests are not valid for people with aphasia (Section 4.43 Aphasia) for whom on-road assessment may be needed. Studies investigating fitness to drive often exclude people with visual impairments and therefore clinicians should ensure that they assess all relevant impairments including vision (Section 4.48 Vision) and cognition (Sections 4.28 Psychological effects of stroke – general, 4.29 Cognitive screening, 4.30 Cognitive assessment). [2016]

4.15 Return to work

Returning to work is an important goal for many people after a stroke, and people should be asked about their work at the earliest opportunity to enable staff to better understand their role in society. 'Work' comprises different forms of occupation, including paid employment, vocational training, sheltered, therapeutic or voluntary work, and adult education (Tyerman, 2012). The UN Convention on the Rights of Persons with Disabilities (United Nations, 2022) discusses the importance of work and education and recreation in equal measure. Specifically, Article 27 identifies "the right of persons with disabilities to work, on an equal basis with others". The average rate of return to work after stroke is 56% at 1 year (Duong et al, 2019). Not being in work after stroke is associated with health risks (Waddel & Aylward, 2005) reduced quality of life and poorer psychosocial outcomes (Busch et al, 2009; Robison et al, 2009). Benefits of returning to work include improvements in quality of life (Matérne et al, 2018), better perceived general health, reduced pain and depression, and higher perceived participation and autonomy compared to those not returning to work (Westerlind et al, 2020). [2023]

Returning to work is often complex and depends on a range of interacting factors and the engagement of different stakeholders (Schwarz et al, 2018). Barriers and facilitators after stroke include personal factors, workplace factors and factors related to rehabilitation services (Brannigan et al, 2017; Schwarz et al, 2018). Given the complexity of returning to work after stroke, many people require co-ordinated action involving trained staff with the required competencies and knowledge of the relevant legislation (Scott & Bondoc, 2018), involving all stakeholders. [2023]

Vocational rehabilitation (VR) is summarised as "a co-ordinated plan supported by all those working with the employee to optimise their work capability" (British Society of Rehabilitation Medicine, 2021). VR is a neglected area within statutory health services, and returning to work remains a largely unmet need (BSRM, 2021). The BSRM (2021) and the National Stroke Service Model for England (2021) outline three levels of VR services, ranging from routine guidance to specialist VR for people with complex problems. VR services need to be aware of recommendations based on the experiences of people who have had a stroke, their colleagues and managers (Hellman et al, 2016; Brannigan et al, 2017; Öst Nilsson et al, 2020). [2023]

4.15 Recommendations

- A People with stroke should be asked about their work at the earliest opportunity, irrespective of whether they plan to return. This will enable staff to have a better understanding of their role before having a stroke, and offer the person an opportunity to discuss their thoughts and feelings. [2023]
- B People who need or wish to return to any type of work after stroke should:
 - be provided with information regarding rights, financial support and vocational rehabilitation. This should include information regarding driving, where appropriate (e.g. in the work role or travelling to work);
 - be supported to understand the consequences of their stroke in relation to work;
 - be supported by an appropriate professional with an understanding of the person's work-related needs to discuss with their employer their return to work, at a time that is appropriate, taking account of their job role and the support available. Timing

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- should be mutually agreed between the person with stroke, the employer and the professional delivering vocational rehabilitation. This should include human resources where appropriate;
- be supported to identify their work requirements with their employer, with input from occupational health, where available;
- be assessed on relevant work-related skills and competencies to establish their potential for return;
- participate in discussions and decision making regarding the most suitable time and way to return to work, including the nature and amount of work;
- be referred to statutory employment support (e.g. Jobcentre Plus, Intreo) or vocational rehabilitation (VR), as appropriate to their needs. VR may be provided by publicly funded organisations (such as the NHS), the independent sector (including services funded through the UK's Department for Work and Pensions such as Access to Work) or the voluntary sector (including support from stroke key workers);
- signposted if required to seek advice from their employer's human resources department (or equivalent), trade union and/or seek specific legal advice. [2023]
- C Services supporting people with stroke to return to work should ensure that:
 - there is a co-ordinator (or co-ordinating team or joint cross-agency working)
 responsible for liaison and support with planning and negotiating return to work with all those involved (including co-workers and managers, where applicable) and who ensures all involved are aware of their roles, responsibilities, and relevant legislation;
 - employers are provided with information and education regarding the individual needs of the person following stroke such as communication needs or fatigue;
 - workplaces offer flexibility (e.g. workplace accommodation) to enable people with stroke to adapt their return to work, in line with the requirements of the Equality Act (2010) in the UK and Employment Equality Acts (1998-2015) in Ireland. [2023]
- D Vocational rehabilitation programmes for people returning to work after stroke should include:
 - assessment of potential barriers and facilitators to returning to work, based on the work role and demands from both the employee's and employer's perspectives;
 - an action plan for how barriers may be overcome;
 - interventions as required by the individual, which may include vocational counselling and coaching, emotional support, adaptation of the working environment, strategies to compensate for functional limitations (e.g. communication, cognition, mobility and arm function), and fatigue management;
 - collaboration between the person with stroke, their employer and healthcare professional in planning, facilitating and monitoring their return to work. [2023]
- E Healthcare professionals who work with people following stroke should have knowledge and skills about supporting them to return to work, appropriate to the nature and level of service they provide. [2023]
- F Authorised healthcare professionals should provide a statement of fitness to work (e.g. 'fit note') to support people to return to work, including recommended alterations to work patterns, tasks undertaken or environment. [2023]

4.15 Sources

- A Guideline Development Group consensus
- B Ntsiea et al, 2015, Guideline Development Group consensus



- C Öst Nilsson et al, 2017, 2020; Guideline Development Group consensus
- D Guideline Development Group consensus
- E Scott and Bondoc, 2018; Guideline Development Group consensus
- F Guideline Development Group consensus

4.15 Evidence to recommendations

There is a paucity of evidence to inform recommendations on returning to work after a stroke. In countries where usual care includes a statutory programme of vocational rehabilitation (VR), it may not be possible to conduct RCTs where the control group is denied VR. An RCT by Ntsiea (2015) involving 80 participants (N=40 each in the intervention and control group) reported benefits from a workplace intervention versus usual care in improving return to work rates after stroke (60% versus 20%, odds ratio (OR) 5.2, 95% CI 1.8 to 15.0 at 6 months). The 6-week person-centred intervention included a multiprofessional, multiphase intervention involving collaboration between the person with stroke, healthcare professionals and their employer. Participants were mainly better-educated, in higher paid jobs, and were independent in ADL after their stroke. The intervention was based in each person's workplace. This was a small study, undertaken in South Africa, where policies, employment circumstances and services for people with stroke will differ from those in the UK and Ireland. [2023]

Key factors for a successful return to work include having an understanding of the consequences of stroke, clear communication and active participation in planning the process (Öst Nilsson et al, 2017). This study also identified the important role of a co-ordinator, acting as a liaison by providing information and support for planning and negotiating return to work. Continuing communication and support were considered important, as well as flexibility to ensure work can be adapted to the individual (Öst Nilsson et al, 2017). [2023]

In addition to the person with stroke, successfully returning to work may also require consideration of their colleagues. Returning to work is likely to be stressful, as relationships need to be re-established and increased responsibility and workload for colleagues need to be managed (Öst Nilsson et al, 2020). This study identified the need for co-ordination to ensure the person with stroke, their co-workers and managers are aware of roles, responsibilities, and relevant legislation, along with commitment and support from the employer (Öst Nilsson et al, 2020). [2023]

A RCT is underway in the UK (RETAKE, ISRCTN12464275) which will help identify the key ingredients of effective VR and guide the future model of clinical delivery. [2023]

Motor recovery and physical effects of stroke

4.16 Introduction

This section focuses on the physical effects of stroke which are common in the majority of people following stroke, and often lead to activity limitations. This section reviews the evidence associated with the various physical effects of stroke with a particular focus on intensive rehabilitation approaches to promote motor recovery. [2023]

Various therapeutic options may be appropriate for a person during their rehabilitation after a stroke. It is important that interventions are selected in collaboration with the person, considering their goals, preferences and other impairments. Whatever the intervention chosen, it must be delivered at the appropriate intensity and dose to achieve optimal outcomes, and at the right point in the person's recovery. Multidisciplinary planning and collaboration are essential in the delivery of rehabilitation programmes, and all interventions should be regularly monitored and evaluated using appropriate

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outcome measures to guide ongoing rehabilitation plans. Exercise should be commenced early after stroke (see <u>Section 3.12 Early mobilisation</u>) and to a level appropriate to the medical status of the individual. **[2023]**

4.17 Motor Impairment

Muscle Weakness

Weakness of the limbs and face are amongst the most common impairments after stroke, giving rise to a hemiplegia. Weakness is the strongest factor influencing dexterity and upper limb function, activities of daily living, balance and walking (Jørgensen et al, 1995; Tyson et al, 2006b; Harris & Eng, 2007; Veerbeek et al, 2011; Preston et al, 2021). This is reflected in tools to predict recovery of upper limb function and walking after stroke, in which the degree of weakness is the main predictive factor (Smith et al, 2017; Stinear et al, 2017b; Selles et al, 2021). Weakness should therefore be the main focus of treatment to improve movement and subsequently physical function and activity. [2023]

Weakness is defined as an inability to generate muscle forces. It is caused by loss of facilitatory drive to anterior horn motor neurones from higher centres, primarily the motor cortex via the corticospinal tract. This primary impairment is exacerbated by further weakness and stiffness secondary to inactivity and disuse (Gracies, 2005; Kamper et al, 2006; Gray et al, 2007; Hoffmann et al, 2016). Limited force generation is seen in all types of muscle contraction (isometric, concentric and eccentric), speed of contractions (power), sustained and repeated contractions (endurance) and integration within and between muscle groups (co-ordination; Kristensen et al, 2017). In most cases, the degree of weakness is similar between the upper and lower limbs, and in all muscle groups within a limb. The degree of weakness is mainly determined by stroke severity, location and pre-morbid strength; age, sex and side or type of stroke are not factors (Tyson et al, 2006a). Strengthening interventions increase strength, improve activity, and do not increase spasticity (Ada et al, 2006); however, selection of appropriate exercises for an individual is important. [2023]

Cardiorespiratory fitness

Cardiorespiratory or aerobic fitness is defined as the ability to transport and use oxygen (Saunders et al, 2020), which confers some degree of endurance. Many people with stroke have low cardiorespiratory fitness pre-morbidly (Kurl et al, 2003) which is exacerbated by the increased energy costs of moving, and by inactivity after stroke (Ivey et al, 2005; Smith et al, 2012; Tieges et al, 2015; Kramer et al, 2016). Low cardiorespiratory fitness is seen in all stages of recovery and can make it difficult for people with stroke to engage in rehabilitation and maintain basic mobility and daily activities (Kunkel et al, 2015). In turn, this feeds into further inactivity, limits participation and increases the risk of recurrent stroke (Mayo et al, 1999; Billinger et al, 2015) making cardiorespiratory fitness an important target for rehabilitation to both maximise recovery and to reduce the risk of recurrence. [2023]

The principal approach to treat both weakness and cardiorespiratory fitness after a stroke is exercise, which is defined as "physical activity that is planned, structured and repetitive to condition any part of the body" (Saunders et al, 2020). There is overlap between exercise and repetitive task practice (where functional tasks or activities are practised intensively) and physical activity in which exercise is often set in a recreational context. These terms are sometimes used interchangeably. There are many different ways of exercising, often classified as:

- cardiorespiratory training generally walking (often on a treadmill) or cycling (stationary or recumbent) at sufficient intensity to produce a cardiorespiratory training effect;
- resistance or strength training using body weight or equipment to resist muscle contractions with a primary aim of improving muscle strength, power and endurance;
- mixed training a combination of cardiorespiratory and resistance training e.g. circuit training classes. [2023]

Treadmills with and without bodyweight support (including underwater and robot-assisted treadmills) and other equipment (such as arm ergometers, seated steppers and static bicycles) are all ways of delivering aerobic and strength training and have been recommended as training methods. Exercise in any form can be delivered individually or in groups, supervised, semi-supervised or independently in health-related or community venues (Mahmood et al, 2022a; Mahmood et al, 2022b). People with stroke report that they value exercise activity and are willing to exercise intensively, even early after stroke. As well as the physical benefits, exercise helps to build confidence, reduce boredom and fosters autonomy. Many also appreciate the camaraderie and peer support experienced in group exercise, preferably in non-healthcare community settings. However, patients also often lack confidence and the self-efficacy to exercise, needing information and the support of professionals and family to overcome the difficulties caused by the stroke and other health conditions (Luker et al, 2015; Poltawski et al, 2015; Young et al, 2021). Health care professionals also face barriers to implementing exercise after stroke. Many feel they lack the knowledge and skills to prescribe exercise effectively, are concerned about safety and have misconceptions about the capabilities and motivation of people with stroke. Lack of resources in terms of staffing, resources, knowledge and training are also an issue (Gaskins et al, 2021; Moncion et al, 2022). [2023]

4.17 Recommendations

- A People with stroke should be assessed for weakness and cardiovascular fitness using a standardised approach, and have the impairment explained to them and their family/carers. Assessment and outcome measures used should encompass the range of effects of exercise including weakness, cardiovascular fitness and activities. [2023]
- B People with weakness after stroke sufficient to limit their activities should be assessed within 24 hours of admission by a therapist with knowledge and skills in neurological rehabilitation. [2023]
- C Clinicians should screen for, prescribe and monitor exercise programmes for people with stroke, e.g. using a 6 minute walk test or shuttle test. Programmes should be individualised to the person's goals and preferences. Screening equipment (such as treadmills, ECG and blood pressure monitors) should be available, and clinicians should liaise with other services that offer exercise-based rehabilitation (e.g. cardiac or pulmonary rehabilitation) with regard to integrating screening and exercise resources.

 [2023]
- People with weakness after stroke should be taught task-specific, repetitive, intensive exercises or activities to increase their strength. Exercise and repetitive task practice should be the principal rehabilitation approaches, in preference to other therapy approaches including Bobath. [2023]
- E People with stroke should be offered cardiorespiratory training or mixed training once they are medically stable, regardless of age, time since stroke and severity of impairment.
 - Facilities and equipment to support high-intensity (greater than 70% peak heart rate) cardiorespiratory fitness training (such as bodyweight support treadmills and/or static/recumbent cycles) should be available;
 - The dose of training should be at least 30-40 minutes, 3 to 5 times a week for 10-20 weeks:
 - Programmes of mixed training (medium intensity cardiorespiratory [40%-60% of heart rate reserve] and strength training [50-70% of one-repetition maximum]) such as circuit training classes should also be available at least 3 days per week for 20 weeks;
 - Exercise aimed at increasing heart rate should be used for those with more severe weakness, such as using arm cycles or seated exercise groups;

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- The choice of programme should be guided by patients' goals and preferences and delivery of the programme individualised to their level of impairment and goals.
 [2023]
- F People with respiratory impairment and at risk of pneumonia after stroke should be considered for respiratory muscle training using a threshold resistance trainer or flow-oriented resistance trainer.
 - Training should be carried out for at least 20 minutes per day, 3 days per week for 3 weeks;
 - The relevant clinicians (nurses, speech and language therapists, physiotherapists and support staff) should be trained in how to use the training equipment. [2023]
- G People with stroke who are unable to exercise against gravity independently should be considered for adjuncts to exercise (such as neuromuscular or functional electrical stimulation), to support participation in exercise training. [2023]
- H People with stroke should be supported with measures to maximise exercise adherence such as:
 - measures to build confidence and self-efficacy (such as the use of social networking apps or physical activity platforms);
 - ensuring patients and family/carers know the benefits of exercise and why they are doing it, including how the exercises given relate to their individual needs;
 - incorporation of exercise into documented goal setting;
 - individualisation of exercise programme to suit their abilities and goals;
 - use of technology (e.g. apps, videos, phone check-ins);
 - ongoing coaching to support written exercise instructions;
 - the involvement of family and carers with exercise. [2023]
- Clinicians should not use risk assessment protocols that limit training for fear of cardiovascular or other adverse events except where screening has identified intensive exercise is contraindicated for an individual. [2023]

4.17 Sources

- A, B Guideline Development Group consensus
- C MacKay-Lyons et al, 2020
- D Pollock et al, 2014a, c; Veerbeek et al, 2014b; Scrivener et al, 2020; Dorsch et al, 2020, 2023
- E Guideline Development Group consensus
- F Zheng et al, 2020; Zhang et al, 2022; Guideline Development Group consensus
- G MacKay-Lyons et al, 2020; Guideline Development Group consensus
- H Miller et al, 2017; Gunnes et al, 2019; García-Cabo and López-Cancio, 2020; Mahmood et al, 2022; Guideline Development Group consensus
- I Guideline Development Group consensus

4.17 Evidence to recommendations

Seven high quality systematic reviews including one Cochrane review that assessed the effect of exercise on motor impairments (weakness and/or cardio-respiratory fitness) (Lloyd et al, 2018; Lee & Stone, 2020; Luo et al, 2020; MacKay-Lyons et al, 2020; Saunders et al, 2020; Anjos et al, 2022; Machado et al, 2022). These reviews provided a moderate to high level of evidence that all types of exercise are safe and feasible for all stages of stroke recovery in people with all severities of stroke, even those with severe impairments who are unable to walk (English et al, 2017; Lloyd et al, 2018; Luo et al, 2020;

MacKay-Lyons et al, 2020; Pogrebnoy & Dennett, 2020; Saunders et al, 2020; Anjos et al, 2022). A high quality review (albeit with a small number of trials) indicated improvements in cardiorespiratory fitness can be maintained over six months after training (Machado et al, 2022). Exercise did not negatively affect spasticity, muscle tone, quality of movement, pain, falls, fatigue, or cardiac events (Ada et al, 2006; Kuys et al, 2011; Mead et al, 2012; Billinger et al, 2014). However, it should be noted that safety was rarely a focus in the selected trials and safety reporting often lacked detail. One high quality trial of aerobic training in people with subacute stroke that specifically completed a safety assessment as a planned secondary analysis (Rackoll et al, 2022) reported a higher incidence of serious adverse events in the aerobic training group than the control group. However, these were not, or were highly unlikely to be, related to the training. Regression analyses indicated that risk was greater in people with diabetes or atrial fibrillation, unmodified by age or stroke severity. The trial was not powered for this analysis so any interpretation needs to be treated with caution. However, it does highlight that more research is needed to fully understand the safety aspects of aerobic training, particularly in those with stroke-related co-morbidities. [2023]

Cardiorespiratory training, especially when involving walking, appears to be the most effective (with a moderate effect size) for cardiorespiratory fitness, and walking and balance. Mixed training has a slightly lesser effect. Resistance training is most effective in improving muscle strength and endurance (Saunders et al, 2020). The type of exercise prescribed depends, therefore, on the patient's treatment goals. However, cardiorespiratory training involving walking has the greatest overall benefit, which can persist into the long term (Saunders et al, 2020). [2023]

Although the optimal way to deliver exercise after stroke is still not clear, there is an indication from high quality meta-analyses (albeit of a small number of trials) that treadmill gait training may be more effective than cycle ergometry (Luo et al, 2020), and that high intensity interval training (HIIT, in which periods of maximal intensity exercise are interspersed with low activity or rest) may be more effective than continuous aerobic training in terms of cardiorespiratory fitness, strength and function (Anjos et al, 2022). The optimal dose of exercise is unclear and there have been no dose-response studies of sufficient quality to inform practice. Nonetheless, several high quality meta-analyses have made recommendations for the minimum dose of exercise needed to be effective:

- Cardiorespiratory training: High-intensity exercise (70-85% heart rate reserve / VO₂ peak) for 30-40 minutes, 3 to 5 times a week for about 12 weeks. High-intensity exercise can also be defined as 'achieving greater than 70% peak heart rate' or 'a score of more than 14/20 on the Borg Rating of Perceived Exertion (RPE) scale' (Luo et al, 2020; Anjos et al, 2022).
- Mixed training: Moderate intensity aerobic training (40%-60% of heart rate reserve) plus moderate
 intensity resistance training (50%-70% of one-repetition maximum) 3 days per week for at least 20
 weeks. Longer training sessions promote greater cardiorespiratory fitness; moderate frequency
 and lower volume exercise (number of repetitions) benefit muscle strength; and moderate
 frequency and longer duration benefit walking capacity (Lee & Stone, 2020).
- Non-ambulant individuals are able to take part in cardiorespiratory training using bodyweight-supported treadmill training (increasing the treadmill incline as well as speed to achieve the required heart rate), electromechanical gait training or static or recumbent cycle ergometry. A high quality meta-analysis found insufficient evidence to make specific recommendations but the dose of cardiorespiratory training that improved fitness and mobility was similar to that above (Lloyd et al, 2018; Shen et al, 2018; MacKay-Lyons et al, 2020). [2023]

A key issue when prescribing exercise is that the effects of exercise are specific to the movements or tasks trained. Two high quality systematic reviews with meta-analysis have also concluded that respiratory muscle training using a threshold resistance trainer or flow-oriented resistance trainer can reduce the risk of post-stroke respiratory complications (i.e. pneumonia RR 0.11-0.51) with a number needed to treat of 15 (Zheng et al, 2020; Zhang et al, 2022). However, the nature or extent of the respiratory impairment and proportion of participants who had dysphagia were unclear. The most

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effective training protocol was more than 20 minutes per day, three times per week for three weeks (Zhang et al, 2022). [2023]

Exercise is only effective if people do it. Although adherence to supervised exercise in a treatment setting is often good, the rates tend to fall when people are not directly supervised, whether outside therapy sessions whilst an inpatient, or when exercising at home. Clinicians need to take measures to support adherence, such as ensuring people and their family/carers know the benefits of exercise and why they are doing it, incorporating exercise into goal setting, individualising the exercise programme to suit patients' abilities and goals, using technology (e.g. apps, videos, phone check-ins), providing ongoing supervision and coaching to support written exercise instructions, and involving family and carers (Miller et al, 2017; Gunnes et al, 2019; García-Cabo & López-Cancio, 2020; Mahmood et al, 2022a). [2023]

4.18 Arm function

Approximately 70% of people experience loss of arm function after a stroke, and this persists for about 40%. This section includes interventions intended to deliver repetitive and functionally relevant practice to improve arm function. Guideline users should also refer to other relevant sections that cover the following: weakness (Section 4.17 Motor impairment), sensation (Section 4.47 Sensation), shoulder subluxation and pain (Section 4.23.3 Shoulder subluxation and pain), activities of daily living (Section 4.8 Independence in daily living). [2023]

Patterns of arm recovery are varied and are largely dependent on the initial degree of weakness and patency of the corticospinal tract (Stinear et al, 2017a), particularly preservation or return of finger extension and shoulder abduction. This has led to the development of tools to predict arm recovery in clinical practice: for example the SAFE and PREP2 tools (Nijland et al, 2010; Stinear et al, 2017b) and the Viatherapy app, an app to guide evidence-based rehabilitation (Wolf et al, 2016). Prognostic tools may be useful to help identify who is most likely to benefit from intensive upper limb interventions and who requires a compensatory approach focusing on reduction of secondary complications such as shoulder subluxation, pain and spasticity. [2023]

Whilst research regarding interventions to promote motor recovery has progressed, continued focus is required to ensure these are implemented into practice. Intensity of practice of movements and tasks during therapy must be coupled with efforts to translate movements into everyday activities. Current practice in the UK indicates too few rehabilitation sessions are dedicated to the upper limb and within sessions too few repetitions are achieved (Stockley et al, 2019). A co-ordinated multidisciplinary approach should be taken to maximise upper limb rehabilitation as well as ensuring that people are supported to practise outside of therapist-delivered sessions. [2023]

Management and recovery of the hemiplegic upper limb often takes place over months or years and must be considered in the context of other impairments including sensation, sensory or visual neglect, learnt non-use, spasticity and balance. Whilst promoting motor recovery (particularly early after stroke) is of the utmost importance, enabling the person to be independent in daily life activities, such as eating and drinking, is essential, and compensatory strategies should be used where appropriate. [2023]

Repetitive task practice

Recovery of the upper limb is best achieved through training that involves repetition of functional tasks and targeted exercises that follow motor learning principles. Components of functional tasks may be practised but should then be incorporated into practice of the whole functional task. Training should be supplemented with aids and equipment as necessary to enable safe, intensive and functionally relevant practice. [2023]

Electrical stimulation

Electrical stimulation has been used as an adjunctive treatment for the upper limb for many years. The most common form is therapeutic or cyclical electrical stimulation (also known as neuromuscular electrical stimulation [NMES]) to the wrist and finger extensors, which stimulates the muscles to contract in order to improve weakness and reduce motor impairment. [2023]

Vagus nerve stimulation

Vagus nerve stimulation (VNS) aims to enhance the effects of repetitive task training by stimulating the vagus nerve during the movement(s) being practised. It is therefore limited to use in people with mild-moderate upper limb weakness (typically, a Fugl-Meyer Upper limb Assessment score of 20-50/100). The stimulation is applied either by an implanted device directly attached to the vagus nerve, or indirectly by transcutaneous nerve stimulation over the vagus nerve in the left side of the neck or the sensory area of the nerve on the external part of the ear. The exact mechanism of action is unknown but it is associated with increased neuroplasticity (Hays et al, 2013; Engineer et al, 2019). [2023]

Constraint-induced movement therapy

The original constraint-induced movement therapy (CIMT) protocol incorporates three components of rehabilitation consisting of (1) intensive graded practice of the paretic arm for 6 hours a day for 2 weeks (shaping), (2) constraining the non-paretic arm with a mitt to promote use of the weak arm for 90% of waking hours, (3) a transfer training package to learn to use the paretic arm in a real-world environment completing functional tasks (Wolf et al, 2006; Taub et al, 2013). Original protocols for CIMT were found to be effective in improving arm function for people following a subacute stroke but only when all three components were used, and 'forced use' is not effective alone (Kwakkel et al, 2015). The time resource needed for CIMT has made this approach challenging to adopt in clinical practice. [2023]

In subsequent years various protocols have been developed aiming for 3-4 hours of CIMT, core components of which are consistent with the original intervention. These are now more commonly adopted in clinical practice, delivered by a combination of qualified therapists, rehabilitation assistants and self-practice, supported remotely as appropriate. Using the paretic arm in functional daily tasks remains a key feature of all modified CIMT (mCIMT) programmes and should be aligned to individualised goals. [2023]

Mental practice

Mental practice is a training method that involves repetitive cognitive rehearsal of physical movements in the absence of physical, voluntary attempts. From a practical perspective, mental practice constitutes a feasible alternative to other rehabilitation approaches to produce the movement because it does not require physical movement, can be performed without direct supervision, and requires minimal expense and equipment (Page & Peters, 2014). Mental practice may promote neuroplasticity, as neuroimaging studies have shown that similar overlapping brain areas are activated in mental practice and with physical movement (Di Rienzo et al., 2014). [2023]

Mirror therapy

Mirror therapy involves performing movements of the non-affected arm, whilst watching its mirror reflection hiding the affected arm. This creates a visual illusion of enhanced movement capability of the affected arm (Yang et al, 2018). The precise mechanisms of mirror therapy are not fully understood, but it is proposed that it promotes motor function of the upper limb via activation of the primary motor cortex or mirror neurones (Garry et al, 2005; Cattaneo & Rizzolatti, 2009). [2023]

Robotics

A robot is defined as a reprogrammable, multifunctional manipulator designed to move material, parts, or specialised devices through variable programmed motions to accomplish a task (Chang & Kim, 2013). Robot-mediated treatment uses devices to provide passive, active-assisted or resistive limb movement,

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and has the potential to offer extended periods of treatment and an opportunity to increase intensity through repetition. Some robots may be able to adapt treatment in response to performance. [2023]

4.18 Recommendations

- A People with some upper limb movement at any time after stroke should be offered repetitive task practice as the principal rehabilitation approach, in preference to other therapy approaches including Bobath. Practice should be characterised by a high number of repetitions of movements that are task-specific and functional, both within and outside of therapy sessions (self-directed). Repetitive task practice:
 - may be bilateral or unilateral depending on the task and level of impairment;
 - should be employed regardless of the presence of cognitive impairment such as neglect or inattention;
 - may be enhanced by using trunk restraint and priming techniques. [2023]
- B People with stroke who have at least 20 degrees of active wrist extension and 10 degrees of active finger extension in the affected hand should be considered for constraint-induced movement therapy. [2023]
- People with wrist and finger weakness which limits function after stroke should be considered for functional electrical stimulation applied to the wrist and finger extensors, as an adjunct to conventional therapy. Stimulation protocols should be individualised to the person's presentation and tolerance, and the person with stroke, their family/carers and clinicians in all settings should be trained in the safe application and use of electrical stimulation devices. [2023]
- D People with stroke without movement in the affected arm or hand (and clinicians, families and carers) should be trained in how to care for the limb in order to avoid complications (e.g. loss of joint range, pain). They should be monitored for any change and repetitive task practice should be offered if active movement is detected. [2023]
- People with stroke may be considered for mirror therapy to improve arm function following stroke as an adjunct to usual therapy. [2023]
- F People with stroke who are able and motivated to participate in the mental practice of an activity should be offered training and encouraged to use it to improve arm function, as an adjunct to usual therapy. [2023]
- People with arm weakness after stroke, who are able and motivated to follow regimes independently or with the support of a carer, should be considered for self-directed upper limb rehabilitation to increase practice in addition to usual therapy, e.g. patients undergoing constraint-induced movement therapy or functional electrical stimulation.

 [2023]
- H People with mild-moderate arm weakness after stroke may be considered for transcutaneous vagus nerve stimulation in addition to usual therapy. Implanted vagus nerve stimulation should only be used in the context of a clinical trial. [2023]
- People with reduced arm function after a stroke may be considered for robot-assisted movement therapy to improve motor recovery of the arm as an adjunct to usual therapy, preferably in the context of a clinical trial. [2023]

4.18 Sources

- A Veerbeek et al, 2014b; French et al, 2016; Grattan et al, 2016; Wattchow et al, 2018; Chen et al, 2019; Zhang et al, 2021; da Silva et al,2020
- B Kwakkel et al, 2015; Corbetta et al, 2015; Barzel et al, 2015; Yadav et al, 2016; Liu et al, 2017; Abdullahi, 2018

- C, D Guideline Development Group Consensus
- E Thieme et al, 2018; Yang et al, 2018; Zeng et al, 2018; Zhang et al, 2021
- F Page and Peters, 2014; Di Rienzo et al, 2014; Barclay et al, 2020; Stockley et al, 2021; Poveda-Garcia et al, 2021
- G Da-Silva et al, 2018; Guideline Development Group consensus
- H Dawson et al, 2021; Ahmed et al, 2022; Guideline Development Group consensus
- I Mehrholz et al, 2018; Takebayashi et al, 2020

4.18 Evidence to recommendations

Repetitive task practice

There is good quality evidence for interventions involving intensive, repetitive, task-oriented and task-specific training including constraint-induced movement therapy, mental practice, virtual reality and interactive video games (Pollock et al, 2014b). It remains unclear whether practising unilateral functional activities is more beneficial than bilateral practice, but this is likely to depend on a person's level of impairment. The evidence base for virtual reality and interactive video gaming-based interventions for the arm (as an adjunct to usual care to increase overall therapy time) is developing, though studies are often of low quality and further research is needed before recommendations can be made regarding their use. [2023]

The ideal dose of repetitive task practice required to be beneficial remains unclear (Lang et al, 2009; French et al, 2016a) but is likely to be substantially higher than is currently being delivered (Schneider et al, 2016; Clark et al, 2021) and in the order of several hundred repetitions per day (McCabe et al, 2015; Daly et al, 2019; Ward et al, 2019; Hayward et al, 2021). This can lead to both short-term and sustained improvements in arm and hand function in people with both subacute and chronic stroke (French et al, 2016a; Wattchow et al, 2018) even in those with cognitive impairments such as neglect or inattention (Grattan et al, 2016). [2023]

Adding trunk restraint to task-oriented arm and hand training can further improve impairments and activity within the first six months after stroke by limiting compensatory movements (Zhang et al, 2022). There is some evidence that priming activities can enhance training effects, with moderate quality evidence for brain stimulation or sensory priming, and low quality evidence for motor priming to enhance improvements in impairments and activity (da Silva et al, 2020). Brain stimulation usually involves transcranial magnetic or direct current stimulation, sensory priming involves electrical or sensory stimulation and motor priming involves aerobic activity or bilateral activities (da Silva et al, 2020) but there is little information on the appropriate dose, timing or type of priming activity. [2023]

High quality systematic reviews and meta-analyses provide sufficient evidence to discourage routine use of Bobath therapy in place of repetitive training or practice of functional tasks (Veerbeek et al, 2014b; Wattchow et al, 2018). [2023]

Electrical stimulation

Four good quality systematic reviews with meta-analysis have shown that electrical stimulation to the wrist and hand can improve motor impairments and function (Yang et al, 2019; Tang et al, 2021; Kristensen et al, 2022; Loh et al, 2022). Tang et al (2021) included a network meta-analysis which indicated that functional electrical stimulation to the wrist and finger extensors during practice of functional tasks was more effective at improving upper limb function than passive neuromuscular electrical stimulation, especially when used to enable repetitive task practice (Yang et al, 2019). A suggested way to do this is by coupling stimulation of the weak arm with movements of the unaffected arm (referred to as contralaterally controlled functional electrical stimulation; Loh et al, 2022). The optimal dose and stimulation protocol are still unclear so clinical decisions should be made according to an individual person's needs, goals and preferences. [2023]

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Vagus nerve stimulation

High quality evidence from systematic reviews of six RCTs of vagus nerve stimulation (VNS, n=237, (Xie et al, 2021; Zhao et al, 2021; Ahmed et al, 2022)) including a phase III trial of implanted VNS in 108 people with chronic stroke (Dawson et al, 2021), showed VNS can enhance the effect of repetitive task practice on upper limb impairment, with a moderate effect size. All trials which reported on safety found VNS to be safe. However, many factors remain unclear, such as the optimal dose and stimulation parameters, integration of stimulation with repetitive task practice and identifying those who benefit most. Further research is needed to understand these factors, and the relative merits of implanted or transcutaneous stimulation. Furthermore, the dose of repetitive task training is likely to be important; it is unlikely that VNS would be effective without a high dose of repetitive task practice, which is currently rarely achieved in practice. VNS may be considered, when it can be provided without reducing the amount of practice completed, alongside other priming techniques according to patients' presentation, goals and preferences. [2023]

Intensive upper limb programmes

Whilst findings from single-centre studies of specialist intensive upper limb programmes for selected patients appear promising (Daly et al, 2019; Ward et al, 2019), there was insufficient high quality evidence to make general recommendations regarding provision of such programmes. Providing the evidence-based, intensive upper limb treatments contained in the recommendations in this section at a sufficient dose should remain the priority, along with delivering generalisable RCTs of intensive upper limb programmes in chronic stroke. Providers and commissioners/service planners should ensure access for all people with stroke who could benefit from rehabilitation at the intensities recommended, including measures to ensure therapy can be replicated and maintained over the longer term at home. [2023]

Constraint-induced movement therapy

Constraint-induced movement therapy (CIMT) includes an extended daily period of constraint of the non-paretic arm, repetitive task training for the paretic arm (shaping and task practice) and a 'transfer package' to support implementation into everyday life. Evidence suggests the transfer package is of particular importance, ensuring that motor gains translate into functional tasks and improve outcomes. Outcomes generally relate to arm function and effects are mostly confined to the trained activities (Pollock et al, 2014a; Pollock et al, 2014b; Veerbeek et al, 2014b). Challenges in clinical delivery and adherence to original CIMT protocols have resulted in modified CIMT (mCIMT) being adopted, where the time during which the non-paretic arm is constrained is reduced and the training hours spread over a longer period of time. Other mCIMT protocols have explored different methods and locations of delivery, for example home, clinic or remote delivery. Both CIMT and mCIMT improve arm function and activities of daily living in people with mild-moderate weakness (that is at least 20 degrees of active wrist extension and 10 degrees of active finger extension in the affected hand) in people with acute and subacute stroke (Corbetta et al, 2015; Kwakkel et al, 2015; Liu et al, 2016). However, mCIMT protocols vary and the optimal way to modify CIMT is unclear (Barzel et al, 2015; Yadav et al, 2016; Abdullahi, 2018). [2023]

Future research should aim to identify the most effective mCIMT protocols to use in clinical practice for people with different degrees of weakness and disability (e.g. the duration and frequency of constraint). Research should also consider the acceptability of CIMT and mCIMT for people with stroke and consider the support required for its use. There is emerging evidence of successful alternative ways to administer CIMT/mCIMT for example through video games or telehealth (Smith & Tomita, 2020; Taub et al, 2021; Gauthier et al, 2022) that merit further investigation. [2023]

Mental practice

Mental practice is an adjunct to conventional therapy, which can lead to significant improvement in upper limb function in the acute, subacute and chronic phases after stroke (Barclay et al, 2020). There is

some evidence that mental practice may be more effective in the first three months after stroke in people with the most severe arm weakness, but the required dose is unclear and further research is warranted (Barclay et al, 2020; Stockley et al, 2021). A small observational study has indicated that the ability to mentally visualise (i.e. imagine) movements should be assessed before prescribing mental practice (Poveda-Garcia et al, 2021). [2023]

Mirror therapy

Systematic reviews and meta-analyses provide moderate evidence that mirror therapy can improve arm function and activities of daily living for people after a stroke (Thieme et al, 2018; Yang et al, 2018; Zeng et al, 2018; Zhang et al, 2021). [2023]

Mirror therapy is only effective for improving arm function as an adjunct to therapy or compared to a placebo (Thieme et al, 2018). Mirror therapy is not superior to dose-matched, conventional rehabilitation that involves upper limb action observation, movement or functional training (Lin et al, 2019). More robust research is required, and future research should focus on defining the most effective treatment protocols and the patients for whom it is most beneficial (Morkisch et al, 2019). Systematic reviews also suggest that mirror therapy may be effective in the treatment of pain and neglect, but this was not a focus of the 2023 update. [2023]

Robotics

A Cochrane review (Mehrholz et al, 2018) concluded that electromechanical and robot-assisted arm training resulted in a slight improvement in activities of daily living, muscle strength and arm function. However, a variety of types of robot were used and the dose of training was under-reported making it unclear how robotics could be routinely adopted in practice. Further uncertainty comes from suggestions from other trials that the effects of robotic therapy on arm function are confined to secondary outcomes in people with subacute stroke when combined with conventional therapy (Takebayashi et al, 2022) or only if enhanced by the addition of functional electrical stimulation (Straudi et al, 2020). A further systematic review suggested robotic therapy maybe slightly superior to therapistled training (Chen et al, 2020) while other studies indicate that including robotic therapy in a conventional therapy session could achieve similar improvements to conventional therapist-led treatment but with less staffing resource (Aprile et al, 2020; Budhota et al, 2021). Further research is needed to find ways to translate the improvements in upper limb impairment seen with robot-assisted training into meaningful benefits in upper limb function and activities of daily living (Rodgers et al, 2019a). In the meantime, teams may consider or continue supplementing face-to-face therapy with robot-assisted arm training and be reassured regarding its safety, and seek opportunities for their patients to participate in research studies. Future research should include non-inferiority or equivalence trials, as it may be that equivalent clinical outcomes can be achieved using less resource. The target population should be people with severe arm weakness and less potential for spontaneous recovery (Wu et al, 2021). An economic evaluation concluded that robot-assisted therapy was not cost-effective, and also recommended further research (Fernandez-Garcia et al, 2021). [2023]

4.19 Ataxia

Ataxia occurs in around 3% of people with ischaemic strokes, principally in cases involving the cerebellum or its connections (Tohgi et al, 1993). It is characterised by four cardinal signs; gait and limb ataxia, dysarthria and nystagmus (Deluca et al., 2011). It may also occur as a consequence of severe sensory dysfunction (known as sensory ataxia). Balance problems and falls are also common, as is the presence of dysphagia. Examples of standardised measures of motor impairment include the Motricity Index and the Scale for the Assessment and Rating of Ataxia (SARA). Ataxia UK published a guideline in 2016 on management of various types of ataxia (Ataxia UK, 2016); however there is little high quality evidence in stroke populations to support specific interventions. [2023]

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4.19 Recommendations

- A People with posterior circulation stroke should be assessed for ataxia using a standardised approach, and have the impairment explained to them, their family/carers and the multidisciplinary team. [2023]
- B People with ataxia after stroke sufficient to limit their activities should be assessed by a therapist with knowledge and skills in neurological rehabilitation. [2023]
- C People with ataxia after stroke should be taught task-specific, repetitive, intensive exercises or activities to increase strength and function. [2023]
- D People with ataxia after stroke should be considered for compensatory techniques to aid functional independence and safety, such as proximal stabilisation, and provision of equipment (small aids). [2023]

4.19 Sources

- A, B Guideline Development Group consensus
- C Pollock et al, 2014a, c; Veerbeek et al, 2014c
- D Guideline Development Group consensus

4.19 Evidence to recommendations

The Scale for Assessment and Rating of Ataxia (SARA) is a standardised measures of ataxia which has been validated for stroke-related ataxia (Kim et al, 2011b; Choi et al, 2018). [2023]

There is little research evidence specific to stroke to guide the management of ataxia. Therefore our recommendations are informed by those for the inherited ataxias and multiple sclerosis (NICE, 2022a) and a systematic review of 19 studies of ataxia included a small proportion of people with stroke (Marquer et al, 2014). These provide low quality evidence that intensive rehabilitation programmes involving balance, walking (including treadmill training) and co-ordination training, and strengthening exercises were effective. No specific recommendations about the type or dose of training could be made. Virtual reality and visual or auditory feedback may be useful adjuncts to exercise and task-specific training. [2023]

4.20 Balance

Many people experience difficulty with balance after a stroke. This is primarily because of lower limb weakness, but limited trunk control, altered sensation, difficulties with dual tasking and perception of verticality can also be factors. Whatever its cause, impaired balance reduces confidence and increases the risk of falls (Section 4.21 Falls and fear of falling). See also Section 4.22 Walking and Section 4.48 Vision. [2023]

4.20 Recommendations

- A People with impaired balance after a stroke should receive a structured multi-factorial assessment including investigation of other causes such as medication, and issues with vision, weakness, dual tasking and the peripheral vestibular system. The assessment should include impacts on daily activities, safety and independence. Onward specialist referral for vestibular rehabilitation should be considered for those people with peripheral vestibular problems. [2023]
- B People with impaired balance at any level (sitting, standing, stepping, walking) at any time after stroke should receive repetitive task practice in the form of progressive balance training such as trunk control exercises, treadmill training, circuit and functional training, fitness training, and strengthening exercises. [2023]

- C People with impaired balance after stroke should be offered repetitive task practice and balance training as the principal rehabilitation approach, in preference to other therapy approaches including Bobath. [2023]
- D People with limitations of dorsiflexion or ankle instability causing balance limitations after stroke should be considered for ankle-foot orthoses and/or functional electrical stimulation. The person with stroke, their family/carers and clinicians in all settings should be trained in the safe use and application of orthoses and electrical stimulation devices.

 [2023]
- E People with limitations of their standing balance or confidence after stroke should be offered walking aids to improve their stability. [2023]
- People with difficulties with sitting balance after stroke should receive an assessment of postural and seating needs. Equipment should be available and provided for patients with identified seating and postural needs regardless of setting. [2023]

4.20 Sources

- A Guideline Development Group consensus
- B van Duijnhoven et al, 2016; Tally et al, 2017; Arienti et al, 2019; Hugues et al, 2019; Nindorera et al, 2021
- C Scrivener et al, 2020 C Scrivener et al, 2020
- D Hong et al, 2018; Nascimento et al, 2020; Johnston et al, 2021; Guideline Development Group consensus
- E, F Guideline Development Group consensus

4.20 Evidence to recommendations

Evidence from Cochrane (Pollock et al, 2014a; French et al, 2016b; English et al, 2017; Mehrholz et al, 2017; Laver et al, 2020; Saunders et al, 2020) and other good quality reviews (Veerbeek et al, 2014b; Tally et al, 2017b; Hugues et al, 2019; Van Criekinge et al, 2019; Nindorera et al, 2021) indicate that the basis of balance rehabilitation after stroke should be repetitive task practice and exercise, supplemented by aids such as ankle foot orthoses and functional electrical stimulation as necessary to enable safe intensive and functionally relevant practice and function in everyday life (Tyson & Kent, 2013; Hong et al, 2018; Johnston et al, 2021). Several methods for delivering repetitive task practice and exercise have been found to improve balance including treadmill training (Mehrholz et al, 2017; Tally et al, 2017a; Nindorera et al, 2021), circuit and functional training classes (English et al, 2017), fitness training (Saunders et al, 2020), practising functional tasks including trunk control (Veerbeek et al, 2014b; Van Criekinge et al, 2019; Moreno-Segura et al, 2022) and exercise (van Duijnhoven et al, 2016). These effects are seen at any time after stroke including the chronic stages (French et al, 2016a; Hugues et al, 2019) and included all aspects of balance (sitting, standing, stepping, standing up and sitting down). However, the optimal type of training for people with stroke at different stages and levels of ability remains unclear, but it is likely to be substantially higher than is currently delivered. For example, Nindorera et al. (2021) found at least 30 minutes of treadmill training, 3 times per week for 8 weeks was needed to have an effect, while Hugues et al. (2019) reported that in trials with a positive effect, patients received on average an additional 300 minutes of treadmill training in 12 sessions over 3 weeks. There was insufficient evidence to reach conclusions about the effect on balance of virtual reality and interactive video gaming (Laver et al, 2017). [2023]

A high quality systematic review and meta-analysis has shown that repetitive task practice is more effective than Bobath therapy for the recovery of lower limb activities including balance (Scrivener et al, 2020), and thus Bobath therapy (or other approaches which prioritise normal movement and tone or

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inhibition of reflex activity rather than maximising practice and patient activity) should not be used in preference to repetitive task training. [2023]

Several systematic reviews with meta-analysis (Hong et al, 2018; Johnston et al, 2021; Nascimento et al, 2021) have found strong evidence that functional electrical stimulation of dorsiflexion can improve balance. One meta-analysis (Johnston et al, 2021) found no difference in benefit between an ankle-foot orthosis or functional electrical stimulation, so either could be used depending on the person's needs, goals and preferences. An ankle-foot orthosis is less expensive than functional electrical stimulation but practical considerations such as comfort, ability to apply and remove, and ability to accommodate the device with the person's footwear and clothing need to be considered. [2023]

4.21 Falls and fear of falling

People with stroke are at high risk of falls at all stages in their recovery (Verheyden et al, 2013). Falls are associated with balance and mobility problems, assisted self-care, sedative or psychotropic medications, cognitive impairment, depression, history of falling (Xu et al, 2018) and circumstances involving dual tasking and the planning and execution of tasks (Baetens et al, 2013). Falls may have serious physical and psychological consequences, including an increased risk of hip fracture (usually on the weaker side), reduced physical activity, and greater morbidity and mortality (Ramnemark et al, 2000; Pouwels et al, 2009). Support for the sensory, physical and psychological difficulties contributing to fear of falling should be available. [2023]

4.21 Recommendations

- A People with stroke should be offered a falls risk assessment and management as part of their stroke rehabilitation, including training for them and their family/carers in how to get up after a fall. Assessment should include physical, sensory, psychological, pharmacological and environmental factors. [2023]
- B People with stroke should be offered an assessment of fear of falling as part of their falls risk assessment and receive psychological support if identified. [2016]
- C People at high risk of falls after stroke should be offered a standardised assessment of fragility fracture risk as part of their stroke rehabilitation. [2016]
- D People with stroke with symptoms of vitamin D deficiency, or those who are considered to be at high risk (e.g. housebound) should be offered calcium and vitamin D supplements.

 [2016]
- People at high risk of falls after stroke should be advised to participate in physical activity/exercise which incorporates balance and co-ordination at least twice perweek. [2016]
- People with stroke and limitations of dorsiflexion or ankle instability causing impaired balance and risk or fear of falling should be considered for referral to orthotics for an ankle-foot orthosis and/or functional electrical stimulation. The person with stroke, their family/carers and clinicians in all settings should be trained in the safe use and application of orthoses and electrical stimulation devices. [2023]

4.21 Sources

- A NICE, 2013b; Guideline Development Group consensus
- B Working Party consensus
- C, D NICE, 2017a; SIGN, 2021; Working Party consensus
- D NICE, 2019b, Working Party consensus
- E Department of Health (UK), 2019; Working Party consensus

F Hong et al, 2018; Johnston et al, 2021; Guideline Development Group consensus

4.21 Evidence to recommendations

Several studies have tried to identify people with stroke at risk of falls using composite and single tests, but none of these tools accurately predict falls (Nystrom & Hellstrom, 2013; Breisinger et al, 2014) and nearly all people with stroke can be presumed to be at high falls risk (as high as 73% in the first year after severe stroke (Sackley et al, 2008) and their care planned accordingly (NICE, 2013a). [2016]

Despite evidence for the effectiveness of progressive muscle strengthening and balance training to prevent falls among community-dwelling older people, a Cochrane review (Denissen et al, 2019) found insufficient evidence that exercise interventions were effective in people with stroke. Two trials suggested reduced falls with bone protection medication (vitamin D or alendronic acid), but low statistical power means that they cannot be routinely recommended. More research is needed to evaluate interventions to reduce falls, injuries and fear of falling in people with stroke. Future studies should evaluate multi-factorial interventions including education and adaptations, strength and balance training, bone protection and strategies that target specific stroke-related factors. [2023]

A clinical practice guideline has provided strong evidence that functional electrical stimulation to the dorsiflexor muscles or an ankle-foot orthosis can reduce falls and fear of falling (Johnston et al, 2021). An ankle-foot orthosis or functional electrical stimulation were equally effective, so selection should be based on the person's needs, goals and preferences. An ankle-foot orthosis is less expensive but practical considerations such as comfort, ability to apply and remove the orthosis, and the ability to accommodate the device with the person's footwear and clothing need to be considered. [2023]

4.22 Walking

Approximately half of people with stroke are unable or are limited in their ability to walk. Although most regain some mobility, few regain their previous level. Impaired speed, endurance and energy efficiency often limit activity and participation even in those who are independently mobile. Unsurprisingly, walking is a high priority for many people after a stroke and enables increased independence in functional tasks and participation. This section focuses on treatments and equipment to improve walking, the basis of which should be intensive practice of walking and exercise using aids and equipment as necessary to enable safe practice and mobility during usual activities (such as treadmills, electro-mechanical gait trainers, activity and heart rate monitors). Walking practice at a level that promotes cardiovascular training builds motor skills, strength and cardiovascular fitness which enables greater activity in everyday life. Real-world walking is an important aspect of rehabilitation and is often a goal identified by people with stroke who need to traverse uneven ground, walk dogs or manage inclines. [2023]

4.22 Recommendations

- A People with limited mobility after stroke should be assessed for, provided with and trained to use appropriate mobility aids, including a wheelchair, to enable safe independent mobility. [2023]
- B People with stroke, including those who use wheelchairs or have poor mobility, should be advised to participate in exercise with the aim of improving aerobic fitness and muscle strength unless there are contraindications. [2023]
- C People with impaired mobility after stroke should be offered repetitive task practice as the principal rehabilitation approach, in preference to other therapy approaches including Bobath. [2023]
- D People who cannot walk independently after stroke should be considered for electromechanical-assisted gait training including body weight support. [2023]

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- People with stroke who are able to walk (albeit with the assistance of other people or assistive devices) and who wish to improve their mobility at any stage after stroke should be offered access to equipment to enable intensive walking training such as treadmills or electromechanical gait trainers. To achieve this, training needs to be at 60-85% heart rate reserve (by adjustment of inclination or speed) for at least 40 minutes, three times a week for 10 weeks. [2023]
- People with stroke with limited ankle/foot stability or limited dorsiflexion ('foot drop') that impedes mobility or confidence should be offered an ankle-foot orthosis (using a lightweight, flexible orthosis in the first instance) or functional electrical stimulation to improve walking and balance, including referral to orthotics if required.
 - Any orthosis or electrical stimulation device should be evaluated and individually fitted before long-term use.
 - The person with stroke, their family/carers and clinicians in all settings should be trained in the safe application and use of orthoses and electrical stimulation devices.
 - People using an orthosis after stroke should be educated about the risk of pressure damage from their orthosis, especially if sensory loss is present in addition to weakness. Services should provide timely access for orthotic repairs and adaptations. [2023]
- G Stroke services should have local protocols and agreements in place to ensure specialist assessment, evaluation and follow-up is available for long-term functional electrical stimulation use. [2023]
- H People with stroke who are mobile should be assessed for real-world walking such as road crossing, walking on uneven ground, over distances and inclines. This should include assessment of the impact of dual tasking, neglect, vision and confidence in busy environments. [2023]
- Stroke services should consider building links with voluntary sector and recreational fitness facilities such as gyms or leisure centres or providing equipment in outpatient departments to enable community-dwelling people with stroke to access treadmills and other relevant fitness equipment. [2023]
- J Clinicians should not use risk assessment protocols that limit training for fear of cardiovascular or other adverse events, given the good safety record of repetitive gait training however it is delivered. [2023]

4.22 Sources

- A Guideline Development Group consensus
- B Meek et al, 2003; Saunders et al, 2004; Ada et al, 2006; Pang et al, 2006; Brazzelli et al, 2011
- C Scrivener et al, 2020; Veerbeek et al, 2014b
- D Mehrholz et al, 2013, 2020
- E Mehrholz et al, 2017, 2018; French et al, 2016; Nindorera et al, 2021; Nascimento et al, 2020; Luo et al, 2020; Balinski and Madhavan, 2021; Klassen et al, 2020
- F Johnston et al, 2021; Nascimento et al, 2020; Prenton et al, 2016; Tyson et al, 2018; Guideline Development Group consensus
- G-J Guideline Development Group consensus

4.22 Evidence to recommendations

Evidence from Cochrane (Pollock et al, 2014b; French et al, 2016a; Mehrholz et al, 2017) and other high quality systematic reviews with meta-analyses and network meta-analysis (Veerbeek et al, 2014b; Prenton et al, 2016; Mehrholz et al, 2018; Luo et al, 2020; Scrivener et al, 2020; Johnston et al, 2021; Nascimento et al, 2021; Nindorera et al, 2021; Balinski & Madhavan, 2022) was considered. [2023]

At any time after stroke, people benefit from intensive task-specific gait training in the short and long term. For those who are already able to walk (albeit with assistance) interventions that can achieve this effect should be considered, including treadmill training with or without body weight support (Mehrholz et al, 2017), electromechanical gait training using an end-effector device (Mehrholz et al, 2018), strengthening exercises for the leg, over-ground walking with activity and heart rate monitors (Klassen et al, 2020) and circuit classes (English et al, 2017). Regardless of the intervention, treatment should be 'intensive', and involve walking at a pace to generate a cardiovascular training effect i.e. heart rate of 60-85% of heart rate reserve (Luo et al, 2020). Walking speed (and inclination if using a treadmill) should be adjusted as necessary to achieve the required target heart rate. For more severely impaired individuals, the use of up to 40% body weight support may also be useful to enable the required training protocol to be achieved, but this should be reduced as the person progresses. [2023]

The evidence to date indicates that the amount of training is important, as greater amounts of training are associated with greater, more sustained improvements. Programmes which involved at least 30 training sessions within 10 weeks (i.e. three times per week) and at least 40 minutes per session appear necessary to reach a meaningful change in gait speed (of 0.1 m/s) and overall mobility (Mehrholz et al, 2017; Klassen et al, 2020; Luo et al, 2020; Nindorera et al, 2021; Balinski & Madhavan, 2022). It may be possible to achieve these training levels without using equipment if the cardiovascular training level is reached and around 4,000 steps per training session are achieved (Klassen et al, 2020). [2023]

It appears that treadmill training is at least as effective as over-ground training (Nascimento et al, 2021) and that training using an end-effector electro-mechanical gait trainer is more effective than treadmill training with or without bodyweight support (Mehrholz et al, 2018). [2023]

People who are not able to walk independently at the start of treatment do not appear to benefit from treadmill training (Mehrholz et al, 2017) but electromechanical-assisted gait training (in addition to standard physiotherapy) does enable more people to regain independent mobility, especially in the first three months after stroke (Mehrholz et al, 2020). [2023]

Several studies have included adverse events as an outcome and report that repetitive gait training, however delivered, is safe (French et al, 2016b; Mehrholz et al, 2017; Klassen et al, 2020; Luo et al, 2020; Mehrholz et al, 2020). [2023]

Intensive walking training can be supplemented by aids and equipment to enable safe walking both during treatment and in real life, including walking sticks/canes and an ankle-foot orthosis to support the hemiplegic foot and ankle. People with stroke sometimes choose to use a walking aid to help them practise walking earlier rather than waiting until they can walk without one (Tyson & Rogerson, 2009). A systematic review and meta-analysis of ankle-foot orthosis for people after stroke (Tyson & Kent, 2013) found improvements in walking activity in short-term studies. An alternative device is functional electrical stimulation, in which the peroneal nerve is stimulated electrically to produce a contraction of the ankle dorsiflexors. A foot switch is used to time the stimulation with the swing phase of gait and thus prevent foot drop. Several systematic reviews have shown strong evidence that functional electrical stimulation and ankle-foot orthoses improve mobility in terms of gait speed and endurance in both the short and long term (Prenton et al, 2016; Johnston et al, 2021; Nascimento et al, 2021) with no difference in efficacy between the devices. Thus the choice about which to use should be based on the person's goals, needs and preferences and other practical considerations, such as cost. [2023]

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A high quality systematic review and meta-analysis has shown that repetitive task practice is more effective than Bobath therapy for the recovery of walking and other lower limb activities (Scrivener et al, 2020), and Bobath therapy should not be used in preference to repetitive task practice. [2023]

A systematic review of nine studies of real world walking showed a small but significant effect, indicating that programmes that included behavioural change interventions appeared to be more effective at improving real world walking habits than exercise alone (Stretton et al, 2017). [2023]

4.23 Pain

Pain is a frequent problem after stroke and can be due to many causes including neuropathic pain, musculoskeletal pain including spasticity, and depression. It may also be due to a pre-existing problem which is not directly related to the stroke. This section includes musculoskeletal pain, neuropathic pain and shoulder pain, as well as shoulder subluxation. Guideline users may need to refer to separate sections on sensation (Section 4.47 Sensation) and spasticity (Section 4.24 Spasticity and contractures). Pain management includes non-pharmacological and medical approaches and may require collaboration with a specialist pain management team. [2016]

4.23.1 Neuropathic pain (central post-stroke pain)

Stroke is one cause of pain following damage to neural tissues (called neuropathic pain or central post-stroke pain [CPSP]). The incidence of CPSP is uncertain, with estimates varying between 5% and 20% of people with stroke, and it can often be overlooked. There may be some overlap with spasticity which can cause pain, and with sensory loss which can be associated with unpleasant sensory phenomena. It is separate from musculoskeletal pain, which is considered in Section 4.23.2 <u>Musculoskeletal pain</u>. [2016]

4.23.1 Recommendations

- A People with central post-stroke pain should be initially treated with amitriptyline, gabapentin or pregabalin:
 - amitriptyline starting at 10 mg per day, with gradual titration as tolerated, but no higher than 75 mg per day (higher doses could be considered in consultation with a specialist pain service);
 - gabapentin starting at 300 mg twice daily with titration as tolerated to a maximum of
 3.6 g per day;
 - pregabalin starting at 150 mg per day (in two divided doses; a lower starting dose may be appropriate for some people), with titration as tolerated but no higher than 600 mg per day in two divided doses. [2016]
- B People with central post-stroke pain who do not achieve satisfactory pain reduction with initial pharmacological treatment at the maximum tolerated dose should be considered for treatment with another medication of or in combination with the original medication:
 - if initial treatment was with amitriptyline switch to or combine with pregabalin;
 - if initial treatment was with gabapentin switch to pregabalin;
 - if initial treatment was with pregabalin switch to or combine with amitriptyline. [2016]
- C People with central post-stroke pain should be regularly reviewed including physical and psychological well-being, adverse effects, the impact on lifestyle, sleep, activities and participation, and the continued need for pharmacological treatment. If there is sufficient improvement, treatment should be continued and gradual reductions in the dose over time should be considered if improvement is sustained. [2016]



4.23.1 Sources

A-C NICE, 2020; Wiffen et al, 2013

4.23.1 Evidence to recommendations

There is very little trial evidence specific to the management of CPSP, and it may well be that CPSP is different from neuropathic pain resulting from other conditions such as peripheral neuropathy or spinal cord pathology. There is no evidence that simple or opioid analgesics have any role in the treatment of neuropathic pain, and many anticonvulsant and antidepressant medicines have a very poor quality evidence base despite their frequent use. The NICE guideline CG173 on neuropathic pain (NICE, 2020) recommends the initial use of amitriptyline, duloxetine (based purely on evidence of effectiveness in painful diabetic neuropathy), gabapentin or pregabalin for neuropathic pain, switching between them if the response is inadequate. [2016]

4.23.2 Musculoskeletal pain

Musculoskeletal pain is not uncommon in people with stroke. Prolonged immobility and abnormal posture can cause pain and exacerbate pre-existing musculoskeletal conditions such as osteoarthritis. The most specific musculoskeletal pain problem after stroke, shoulder pain, is considered in Section 4.23.3 Shoulder subluxation and pain. Pain management may be non-pharmacological (e.g. physiotherapy) as well as pharmacological. [2016]

4.23.2 Recommendations

- A People with musculoskeletal pain after stroke should be assessed to ensure that movement, posture and moving and handling techniques are optimised to reduce pain.

 [2016]
- B People who continue to experience musculoskeletal pain should be offered pharmacological treatment with simple analgesic medication. Paracetamol, topical non-steroidal anti-inflammatory drugs (NSAIDs) or transcutaneous electrical nerve stimulation (TENS) should be offered before considering the addition of opioid analgesics. [2016]

4.23.2 Sources

A, B NICE, 2022c; Working Party consensus

4.23.2 Evidence to recommendations

The Working Party did not find any research evidence on musculoskeletal pain specific to stroke. Recommendations are based on NICE guidance for osteoarthritis and the consensus of the Working Party. [2016]

4.23.3 Shoulder subluxation and pain

Hemiplegic shoulder pain affects 30-65% of people with stroke and is often associated with upper limb weakness, gleno-humeral subluxation and restricted range of shoulder movement (Kumar et al, 2022). Furthermore, shoulder pain and subluxation are associated with reduced function and recovery of the upper limb, interference with rehabilitation, higher rates of depression and poorer quality of life, so they are important targets for rehabilitation (Adey-Wakeling et al, 2016; Paolucci et al, 2016). The precise aetiology of shoulder pain is unknown, but it is often associated with subluxation of the joint and, in the later stages, spasticity. Shoulder subluxation is not always associated with pain and the two may have different causes. Addressing shoulder subluxation is a priority in order to optimise upper limb motor recovery, and manage spasticity and pain. [2023]

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Slings to support the upper limb should be used with caution, as they are often ineffective at reducing the subluxation and encourage the upper limb to rest in adduction, internal rotation and flexion at the elbow, which can result in muscle shortening. [2023]

4.23.3 Recommendations

- A People with functional loss in their arm after stroke should have the risk of shoulder pain reduced by:
 - careful positioning of the arm, with the weight of the limb supported, including the use of wheelchair arm rests;
 - ensuring that healthcare staff and family/carers handle the affected arm correctly, avoiding mechanical stress and excessive range of movement;
 - avoiding the use of overhead arm slings/ shoulder supports and pulleys. [2023]
- B People with arm weakness after stroke should be asked regularly about shoulder pain. [2016]
- C People who develop shoulder pain after stroke should:
 - be assessed for causes and these should be managed accordingly, including musculoskeletal issues, subluxation and spasticity;
 - have the severity monitored and recorded regularly, using a validated pain assessment tool:
 - have preventative measures put in place;
 - be offered regular simple analgesia. [2016]
- D People with shoulder pain after stroke should only be offered intra-articular steroid injections if they also have inflammatory arthritis. [2016]
- People with inferior shoulder subluxation within 6 months of hemiplegic stroke should be considered for neuromuscular electrical stimulation, unless contraindicated. The stimulation protocol should be individualised to the person's presentation and tolerance. The person with stroke, their family/carers and clinicians in all settings should be trained in the safe application and use of electrical stimulation devices. [2023]
- F People with persistent shoulder pain after stroke should be considered for other interventions such as orthotic provision, spasticity management, or suprascapular nerve block, including specialist referral if required. [2023]

4.23.3 Sources

- A Guideline Development Group consensus
- B, C Working Party consensus
- D Kalita et al, 2006; Lakse et al, 2009; Rah et al, 2012
- E Lee et al, 2017; Guideline Development Group consensus
- F Guideline Development Group consensus

4.23.3 Evidence to recommendations

The literature on hemiplegic shoulder pain and shoulder subluxation in stroke consists of small trials and systematic reviews that evaluate interventions such as electrical stimulation of the long head of biceps (Manigandan et al, 2014), subacromial injections of corticosteroid (Rah et al, 2012) or local injections of botulinum toxin (Singh & Fitzgerald, 2010). Botulinum toxin injections showed some positive benefits in reducing pain and improving shoulder function and range of motion. Low statistical power means that this intervention cannot be confidently recommended and larger high quality RCTs are required. There is little evidence to support shoulder strapping as a way of preventing or treating shoulder subluxation.

Strapping may have a preventative role by making it clear to carers that the shoulder is at risk of damage from incorrect handling or positioning. [2023]

A high quality systematic review and meta-analysis of 11 trials including 432 participants provided moderate to good evidence that neuromuscular stimulation can reduce shoulder subluxation for people when used in the acute or subacute stages of stroke (i.e. up to 6 months; Lee et al, 2017). The meta-analysis was underpowered to test the effects for people with chronic stroke and the impact on pain and function. Further research is needed to establish the optimal stimulation parameters and dose of stimulation. [2023]

4.24 Spasticity and contractures

There is considerable debate on the definition, physiological nature and importance of spasticity. Although spasticity is less common than assumed in the past, it represents a considerable burden for those who develop it, affecting up to 40% of people with severe weakness after stroke, and is considered severe and disabling in about 15% of people. It is associated with pain, contracture and other motor impairments (Wissel et al, 2013; Zorowitz et al, 2013; Glaess-Leistner et al, 2021). [2023]

Any joint that does not move frequently is at risk of developing shortening of surrounding tissues leading to restricted movement. This is referred to as a contracture, and is not uncommon in limbs affected by spasticity. Contractures can impede activities such as washing or dressing, and may also be uncomfortable or painful and limit the ability to sit in a wheelchair or mobilise. Splinting is the process of applying a prolonged stretch through an external device, most commonly splints or serial casts, historically believed to prevent or treat contractures. Standardised measures for ease of care and resistance to passive stretches include the Arm Activity measure and modified Ashworth Scale respectively. [2023]

4.24 Recommendations

- A People with motor weakness after stroke should be assessed for spasticity as a cause of pain, as a factor limiting activities or care, and as a risk factor for the development of contractures. [2016]
- B People with stroke should be supported to set and monitor specific goals for interventions for spasticity using appropriate clinical measures for ease of care, pain and/or range of movement. [2016]
- C People with spasticity after stroke should be monitored to determine the extent of the problem and the effect of simple measures to reduce spasticity e.g. positioning, passive movement, active movement (with monitoring of the range of movement and alteration in function) and/or pain control. [2016]
- People with persistent or progressive focal spasticity after stroke affecting one or two areas for whom a therapeutic goal can be identified (e.g. ease of care, pain) should be offered intramuscular botulinum toxin. This should be within a specialist multidisciplinary team and be accompanied by rehabilitation therapy and/or splinting or casting for up to 12 weeks after the injections. Goal attainment should be assessed 3-4 months after the injections and further treatment planned according to response. [2016]
- People with generalised or diffuse spasticity after stroke should be offered treatment with skeletal muscle relaxants (e.g. baclofen, tizanidine) and monitored for adverse effects, in particular sedation and increased weakness. Combinations of antispasticity medication should only be initiated by healthcare professionals with specific expertise in managing spasticity. [2016]
- F People with stroke should only receive intrathecal baclofen, intraneural phenol or similar

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G People with stroke with increased tone that is reducing passive or active movement around a joint should have the range of passive joint movement assessed. They should only be offered splinting or casting following individualised assessment and with monitoring by appropriately skilled staff. [2016]

interventions in the context of a specialist multidisciplinary spasticity service. [2016]

- H People with stroke should not be routinely offered splinting for the arm and hand. [2016]
- People with spasticity in the upper or lower limbs after stroke should not be treated with electrical stimulation to reduce spasticity. [2023]
- J People with spasticity in their wrist or fingers who have been treated with botulinum toxin may be considered for electrical stimulation (cyclical/neuromuscular electrical stimulation) after the injection to maintain range of movement and/or to provide regular stretching as an adjunct to splinting or when splinting is not tolerated. [2023]
- K People with stroke at high risk of contracture should be monitored to identify problematic spasticity and provided with interventions to prevent skin damage, or significant difficulties with hygiene, dressing, pain or positioning. [2023]

4.24 Sources

- A Working Party consensus
- B Turner-Stokes et al, 2013; Working Party consensus
- C Royal College of Physicians et al, 2018; Working Party consensus
- D Royal College of Physicians et al, 2018; Gracies et al, 2015
- E Montane et al, 2004; Working party consensus
- F Sampson et al, 2002; Royal College of Physicians et al, 2018
- G-H College of Occupational Therapists and Association of Chartered Physiotherapists in Neurology, 2015; Lannin et al, 2007b, Working party consensus
- Tang et al, 2021; Johnston et al, 2021; Guideline Development Group consensus
- J-K Guideline Development Group consensus

4.24 Evidence to recommendations

The evidence for spasticity management includes a clinical guideline (Royal College of Physicians et al, 2018) and several RCTs of botulinum toxin (McCrory et al, 2009; Shaw et al, 2011; Ward et al, 2014; Gracies et al, 2015). There are systematic reviews (Rosales & Chua, 2008; Elia et al, 2009; Rosales et al, 2012) and a Cochrane review (Katalinic et al, 2011) of splinting and stretching and two systematic reviews with meta-analyses of electrical stimulation (Johnston et al, 2021; Tang et al, 2021). [2023]

Botulinum toxin administration improves spasticity, range of movement and ease of care (i.e. passive function) and clinical goal attainment (Turner-Stokes et al, 2013) but not activity-level function (i.e. active function). This may partly reflect limitations in some of the measurement tools used. Improvements in activity for leg spasticity require further evaluation, but one study indicates improvements in goal attainment and ambulatory outcomes (Demetrios et al, 2014). [2016]

The evidence base for splinting remains limited and therapists must be circumspect in identifying who and when to splint and when not to splint. Splints should only be assessed, fitted and reviewed by appropriately skilled staff. NICE-accredited national guidance has been published to support best practice (College of Occupational Therapists & Association of Chartered Physiotherapists in Neurology, 2015). [2016]

High quality evidence from two meta-analyses showed that electrical stimulation does not affect spasticity after stroke and should not be used alone for the purpose of reducing spasticity (Johnston et al, 2021; Tang et al, 2021). [2023]

4.25 Fatigue

Post-stroke fatigue has been described by people with stroke as 'a fatigue like no other' (Thomas et al, 2019a). It is characterised by a disproportionate sense of tiredness, a lack of energy, and a need to rest that is greater than usual, although rest may not be effective in alleviating it (Lanctot et al, 2020). There is no consensus on how to define post-stroke fatigue, but case definitions have been proposed (Lynch et al, 2007). Post-stroke fatigue needs to be differentiated from post-stroke apathy (see Section 4.40 Apathy). [2023]

Post-stroke fatigue can profoundly impact the lives of people with stroke, particularly their return to work, mobility, physical activity, mood, cognitive function, functional ADL (e.g. shopping) and social activities (Worthington et al, 2017). Post-stroke fatigue can also impact on a person's ability to engage in rehabilitation, requiring therapists to adopt strategies to manage it during therapy (Riley, 2017). Post-stroke fatigue often affects the lives of families and carers, as it may limit their social life and result in increased loneliness and isolation (Ablewhite et al, 2022b). As family members or carers are often involved in overseeing the implementation of post-stroke fatigue management strategies, fatigue may add considerably to the burden of care. [2023]

Post-stroke fatigue is common and may be the sole residual problem in people who have made an otherwise good recovery (Stroke Association, 2022). Between 35 and 92% of people with stroke are estimated to have post-stroke fatigue (Duncan et al, 2012), with estimates varying by the type of measure, the point at which it is measured during recovery, and the type of stroke (Alghamdi et al, 2021). Post-stroke fatigue may present early or later after stroke, whilst early-onset fatigue persists in a proportion of cases (Wu et al, 2015). Persistent fatigue may continue to impact on functioning and participation several years after stroke (Elf et al, 2016). [2023]

The causes of post-stroke fatigue are not fully understood. It needs to be considered in a holistic manner (Thomas et al, 2019a) and a biopsychosocial model has been proposed (Wu et al, 2015). Post-stroke fatigue appears to be multi-factorial (Wu et al, 2015; Aarnes et al, 2020), and may fluctuate over the course of the day and vary in severity. It is commonly associated with pre-stroke fatigue (Wu et al, 2015), demographic (older age, female gender), clinical (stroke site, immune response characteristics, pain, sleep disturbance), physical (disability severity), emotional (depression, anxiety, avoidant or confrontational coping styles), cognitive (impaired information processing), and social factors (lack of social support) (Aarnes et al, 2020). It is plausible that different factors are associated with early compared to late-onset post-stroke fatigue, while psychological factors play a role in both (Wu et al, 2015; Chen & Marsh, 2018). There is overlap between post-stroke fatigue and depression, but post-stroke fatigue should be considered a condition in its own right (Aarnes et al, 2020). Potential triggers include physical or cognitive exertion, emotional experiences and sedentary behaviour, but in a proportion of cases there are no known triggers, rendering it unpredictable (Worthington et al, 2017). [2023]

The multifactorial nature of post-stroke fatigue should be captured in tools used to assess it, but a systematic review showed that the most commonly used outcome measures do not address potentially relevant aspects of post-stroke fatigue (Skogestad et al, 2021). Measures for post-stroke fatigue have been reviewed by Mead et al (2007) and Skogestad et al (2021). [2023]

People with stroke indicate that their fatigue is often not understood by healthcare professionals (Thomas et al, 2019a), that they are rarely provided with information or advice on how to manage it

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(Worthington et al, 2017; Thomas et al, 2019a; Drummond et al, 2021) and that recommended approaches may be conflicting (Thomas et al, 2019a). People with post-stroke fatigue indicate that this lack of awareness by healthcare professionals can cause anxiety (Drummond et al, 2021). Healthcare professionals' understanding of post-stroke fatigue varies widely (Thomas et al, 2019b), and in the absence of clear evidence, their management of it largely relies on their own clinical experience (Riley, 2017). [2023]

4.25 Recommendations

- A Healthcare professionals should anticipate post-stroke fatigue, and ask people with stroke (or their family/ carers) if they experience fatigue and how it impacts on their life. [2023]
- B Healthcare professionals should use a validated measure in their assessment of poststroke fatigue, with a clear rationale for its selection, and should also consider physical and psychological fatigue, personality style, context demands and coping styles. [2023]
- People with stroke should be assessed and periodically reviewed for post-stroke fatigue, including for factors that might precipitate or exacerbate fatigue (e.g. depression and anxiety, sleep disorders, pain) and these factors should be addressed accordingly. Appropriate time points for review are at discharge from hospital and then at regular intervals, including at 6 months and annually thereafter. [2023]
- D People with stroke should be provided with information and education regarding fatigue being a common post-stroke problem, and with reassurance and support as early as possible, including how to prevent and manage it, and signposting to peer support and voluntary sector organisations. Information should be provided in appropriate and accessible formats. [2023]
- People with post-stroke fatigue should be involved in decision making about strategies to prevent and manage it that are tailored to their individual needs, goals and circumstances.

 [2023]
- People with post-stroke fatigue should be referred to appropriately skilled and experienced clinicians as required, and should be considered for the following approaches, whilst being aware that no single measure will be effective for everyone:
 - building acceptance and adjustment to post-stroke fatigue and recognising the need to manage it;
 - education on post-stroke fatigue for the person with stroke, and their family/ and carers;
 - using a diary to record activities and fatigue;
 - predicting situations that may precipitate or exacerbate fatigue;
 - pacing and prioritising activities;
 - relaxation and meditation;
 - rest
 - setting small goals and gradually expanding activities;
 - changing diet and/or exercise (applied with caution and tailored to individual needs);
 - seeking peer support and/or professional advice;
 - coping methods including compensatory techniques, equipment and environmental adaptations. [2023]
- G Healthcare professionals working with people affected by post-stroke fatigue should be provided with education and training on post-stroke fatigue, including its multi-factorial nature and impact, potential causes and triggers, validated assessment tools and the importance of involving people affected by post-stroke fatigue in designing strategies to prevent and manage it. [2023]

- H Healthcare professionals working with people with post-stroke fatigue should consider the impact of fatigue on their day-to-day ability to engage with assessment and rehabilitation, and tailor the scheduling and length of such activities accordingly. [2023]
- Service planners and managers should consider people with stroke whose ability to engage in rehabilitation is affected by post-stroke fatigue, and provide access to alternative solutions to ensure that they are still able to benefit from personalised rehabilitation input as required. [2023]

4.25 Sources

- A Lanctot et al, 2020; Drummond et al, 2022a; Guideline Development Group consensus
- B Drummond et al, 2021; Ablewhite et al, 2022b
- C Hinkle et al, 2017; Lanctot et al, 2020; Guideline Development Group consensus
- D Lanctot et al, 2020; Drummond et al, 2021; Ablewhite et al, 2022a, 2022b; Guideline Development Group consensus
- E Thomas 2019b; Drummond et al, 2021; Ablewhite et al, 2022a, 2022b; Guideline Development Group consensus
- F Drummond et al, 2021; Ablewhite et al, 2022a, 2022b; Guideline Development Group consensus
- G Thomas et al, 2019b; Drummond et al, 2021; Ablewhite et al, 2022a
- H, I Guideline Development Group consensus

4.25 Evidence to recommendations

Recommendations are based on one Cochrane systematic review (Legg et al, 2019), three other systematic reviews (Mead et al, 2019; Pacheco et al, 2019; Chen et al, 2022); four randomised controlled trials (Bivard et al, 2017; Dennis et al, 2020; Hankey et al, 2020; Dong et al, 2021) and one follow-up study (Hankey et al, 2021), one survey (Ablewhite et al, 2022a), two qualitative studies (Drummond et al, 2021; Ablewhite et al, 2022b), one scientific statement (Hinkle et al, 2017), and best practice recommendations (Lanctot et al, 2020) together with the consensus of the Guideline Development Group. [2023]

Two high quality systematic reviews (Legg et al, 2019; Mead et al, 2019) and two large, high quality RCTs including a follow-up study (Dennis et al, 2020; Hankey et al, 2020; Hankey et al, 2021) provide clear evidence that fluoxetine should not be used to prevent post-stroke fatigue as it is not effective, but increases the likelihood of falls, fractures and epileptic seizures. [2023]

One high quality but small RCT (Bivard et al, 2017) of modafinil found a significant reduction in post-stroke fatigue without any serious adverse events. However, a large RCT is ongoing and until its findings have been published, modafinil for people with post-stroke fatigue should only be provided in the context of a clinical trial. [2023]

A systematic review of acupuncture of acceptable quality (Chen & Marsh, 2018) found a statistically significant reduction in post-stroke fatigue, but only one of the studies included had received ethical approval. All studies were small and at risk of bias, and only one study reported adverse events (which were absent). Until more rigorous evidence has been published, acupuncture for people with post-stroke fatigue should only be provided in the context of a clinical trial. [2023]

One small RCT of transcranial direct current stimulation (tDCS) of acceptable quality (Dong et al, 2021) reported a significant reduction in post-stroke fatigue without any serious adverse events, but until

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more rigorous evidence has been published, tDCS for post-stroke fatigue should only be provided in the context of a clinical trial. [2023]

In the absence of clear evidence, healthcare professionals and people affected rely on their own expertise and experience to prevent and manage post-stroke fatigue (Drummond et al, 2021; Ablewhite et al, 2022b). A UK survey of clinical approaches to post-stroke fatigue found variations in the type, amount and duration of support, including access to follow-up, and that a proportion of healthcare professionals lack confidence in managing post-stroke fatigue (Ablewhite et al, 2022a). This survey also found that assessment of post-stroke fatigue lacks standardisation, both in terms of the tools used and in the timing of assessment (Ablewhite et al, 2022a). [2023]

A qualitative study of healthcare professionals in the UK found that fatigue management approaches commonly used include: diaries to record activities and fatigue; pacing and prioritising; education on post-stroke fatigue for the person with stroke, their family, friends and carers; coping methods including compensatory techniques, equipment and environmental adaptations; and exercise applied with caution and tailored to individual needs (Drummond et al, 2021). A qualitative study of people with stroke and their carers indicated that raising the topic of post-stroke fatigue and receiving support from professionals and peers can be helpful (Ablewhite et al, 2022b). The following measures were used to self-manage fatigue: learning to accept post-stroke fatigue and recognise the need to manage it, predicting situations that may precipitate fatigue, pacing, using a diary, relaxation or meditation, rest, setting small goals and gradually expanding activities, optimising diet and exercise, seeking peer support and professional advice, and educating family and friends about their fatigue and its management (Ablewhite et al, 2022b). However, the findings also showed that no single approach was effective for everyone, and any measure should be tailored to the individual and their personal circumstances (Ablewhite et al, 2022b). [2023]

4.26 Swallowing

Dysphagia (swallowing difficulty associated with foods, fluids and saliva) is common after acute stroke with an incidence between 40 and 78%. There is an association between dysphagia and poor outcomes including a higher risk of longer hospital stay, chest infection, disability and death (Martino et al, 2005). Evidence from national audit shows that delays in the screening and assessment of dysphagia are associated with an increased risk of stroke-associated pneumonia (Bray et al, 2017). Prompt detection of dysphagia in patients with acute stroke is therefore essential. In patients with dysphagia on initial screening, a specialist swallowing assessment is indicated that includes consideration of function and cognition and a broader range of food and fluids of varying texture. [2016]

The majority of people with dysphagia after stroke will recover, in part due to bilateral cortical representation of neurological pathways (Hamdy et al, 1998). A proportion will have persistent abnormal swallow and continued aspiration at 6 months (Mann et al, 1999) and a small proportion, particularly those with brainstem lesions, will have chronic and severe swallowing difficulty. People with persistent swallowing problems may avoid eating in social settings and thus lose the physical and social pleasures connected with food and drink. [2016]

This section should be read in conjunction with the sections on hydration and nutrition (Section 4.9 Hydration and nutrition), mental capacity (Section 4.35 Mental capacity) and end-of-life (palliative) care (Section 2.15 End-of-life (palliative) care). In particular, these recommendations are not intended as burdensome restrictions on oral food and fluid intake for people with stroke receiving holistic palliative care. The decision-making process to support people to eat and drink with acknowledged risks should be person-centred and involve the person and/or family/carers, and other members of the multidisciplinary team, and include a swallowing assessment and steps to minimise risk (Royal College of Physicians, 2021). [2023]

4.26 Recommendations

- A Patients with acute stroke should have their swallowing screened, using a validated screening tool, by a trained healthcare professional within four hours of arrival at hospital and before being given any oral food, fluid or medication. [2023]
- B Until a safe swallowing method is established, patients with swallowing difficulty after acute stroke should:
 - be immediately considered for alternative fluids;
 - have a comprehensive specialist assessment of their swallowing completed by a specialist in dysphagia management within 24 hours of admission;
 - be considered for nasogastric tube feeding within 24 hours;
 - be referred to a dietitian for specialist nutritional assessment, advice and ongoing monitoring;
 - receive adequate hydration, nutrition and medication by alternative means;
 - be referred to a pharmacist to review medication formulation. [2023]
- C Patients with swallowing difficulty in the acute phase of stroke should only be given food, fluids and medications in a form that minimizes the risk of aspiration. [2023]
- D People with stroke who require modified food or fluid consistency should have these provided in line with internationally agreed descriptors e.g. International Dysphagia Diet Standardisation Initiative (IDDSI). [2023]
- Patients with stroke with suspected aspiration or who require tube feeding or dietary modification should be considered for instrumental assessment (videofluoroscopy or fibre-optic endoscopic evaluation of swallowing [FEES]). [2023]
- F Patients with stroke who require instrumental assessment of swallowing (videofluoroscopy or fibre-optic endoscopic evaluation of swallowing [FEES]) should only receive this:
 - in conjunction with a specialist in dysphagia management;
 - in order to investigate the nature and causes of swallowing difficulties;
 - to facilitate shared decision making and direct an active treatment/rehabilitation programme for swallowing difficulties. [2023]
- Patients with swallowing difficulty after stroke should be considered for compensatory measures and adaptations to oral intake aimed at reducing the risks of aspiration and choking, improving swallowing efficiency and optimising nutrition and hydration. This should be based on a thorough assessment of dysphagia and may include:
 - texture modification of food and fluids;
 - sensory modification, such as altering the volume, taste and temperature of foods or carbonation of fluids;
 - compensatory measures such as postural changes (e.g. chin tuck) or swallowing manoeuvres (e.g. supraglottic swallow). [2023]
- H People with swallowing difficulty after stroke should be considered for swallowing rehabilitation by a specialist in dysphagia management. This should be based on a thorough assessment of dysphagia, such as by a speech and language therapist, to decide on the most appropriate behavioural intervention, and may include a variety of muscle strengthening and/or skill training exercises. [2023]
- People with dysphagia after stroke may be considered for neuromuscular electrical stimulation as an adjunct to behavioural rehabilitation where the device is available and it can be delivered by a trained healthcare professional. [2023]
- J Patients with tracheostomy and severe dysphagia after stroke may be considered for pharyngeal electrical stimulation to aid decannulation where the device is available and it

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- can be delivered by a trained healthcare professional. [2023]
- K People with difficulties feeding themselves after stroke should be assessed and provided with the appropriate equipment and assistance (including physical help and verbal encouragement) to promote independent and safe feeding. [2023]
- L People with swallowing difficulty after stroke should be provided with written guidance for all staff and carers to follow when feeding them or providing fluids. [2023]
- M People with stroke should be considered for gastrostomy feeding if they:
 - need, but are unable to tolerate, nasogastric tube feeding, even after a trial with a
 nasal bridle if appropriate and other measures such as taping the tube or increased
 supervision;
 - are unable to swallow adequate food and fluids orally by four weeks from the onset of stroke and gastrostomy feeding is considered to be required long-term;
 - reach the point where shared decision making by the person with stroke, their family/carers, and the multidisciplinary team has agreed that artificial nutrition is appropriate due to the high long-term risk of malnutrition. [2023]
- N For people with dysphagia after stroke the option to eat and drink orally despite acknowledged risks should be considered. This decision-making process should be person-centred and taken together with the person with stroke, their family/carers and the multidisciplinary team. It should include a swallowing assessment and steps to minimise risk. [2023]
- O People with stroke who are discharged from specialist treatment with continuing problems with swallowing food or fluids safely should be trained, or have family/carers trained, in the management of their swallowing and be regularly reassessed. [2023]
- People with stroke receiving end-of-life (palliative) care should not have burdensome restrictions on oral food or fluids if those restrictions would exacerbate suffering. In particular, following assessment this may involve a decision, taken together with the person with stroke, their family/carers and the multidisciplinary team, to allow oral food or fluids despite risks including aspiration and choking. [2023]

4.26 Sources

- A Kertscher et al, 2014; Martino et al, 2014; Bray et al, 2017
- B Geeganage et al, 2012; NICE, 2017c, 2022e
- C Guideline Development Group consensus
- D Cichero et al, 2017
- E Wilson and Howe, 2012; Bax et al, 2014; Kertscher et al, 2014
- F Martino et al, 2005; Carnaby et al, 2006; Royal College of Speech and Language Therapists, 2007, 2008; Terre and Mearin, 2012
- G Bath et al, 2018; Dziewas et al, 2021
- H Bath et al, 2018; Dziewas et al, 2021; Zhang et al, 2022
- Bath et al, 2018; Dziewas et al, 2021; Wang et al, 2021a; Li et al, 2021; Zhao et al, 2022; Hsiao et al, 2022; He et al, 2022
- J Dziewas et al, 2018
- K, L Guideline Development Group consensus
- M Dennis et al, 2005; Geeganage et al, 2012; NICE, 2017c
- N Royal College of Physicians, 2021; Royal College of Speech and Language Therapists, 2021;



- Guideline Development Group consensus
- O Heckert et al, 2009; Drury et al, 2014; NICE, 2017c, Guideline Development Group consensus
- P Royal College of Physicians, 2021; Royal College of Speech and Language Therapists, 2021; Guideline Development Group consensus

4.26 Evidence to recommendations

There is good evidence that a multi-item dysphagia screening protocol that includes at least a water intake test of 10 teaspoons and a lingual motor test is more accurate than screening protocols with only a single item (Martino et al, 2014). Additionally a systematic review (Kertscher et al, 2014) and cost-effectiveness analysis (Wilson & Howe, 2012) suggest that the investigation of dysphagia with instrumental assessments (providing direct imaging for evaluation of swallowing physiology) helps to predict outcomes and improve treatment planning (Bax et al, 2014). [2016]

A number of treatments for dysphagia after stroke have been studied, including swallowing exercises, acupuncture, medicines, neuromuscular electrical stimulation (NMES), pharyngeal electrical stimulation (PES), thermal stimulation, transcranial direct current (tDCS), transcranial magnetic stimulation (TMS) and expiratory muscle strength training (EMST). The aim of treatment in these studies is to improve swallowing and to reduce the risk of the person developing aspiration pneumonia. A Cochrane review of swallowing therapy, which included acupuncture, behavioural interventions, medication, NMES, PES, physical stimulation, tDCS, and TMS concluded that as a whole, swallowing therapy did not change outcomes of death or dependency/disability, case fatality or penetration aspiration score, but may have reduced length of hospital stay, dysphagia, chest infections, and improved swallowing ability (Bath et al, 2018). However, the results were based on studies of variable quality and did not distinguish between specific interventions. The review concluded that additional high quality trials in the field are required to investigate the effectiveness of individual swallowing therapies. [2023]

Two systematic reviews investigating non-invasive neurostimulation therapies reported some positive effects on swallowing function and quality of life for NMES, tDCS, TMS (Li et al, 2021a; Wang et al, 2021a) but not PES (Wang, 2021). Similar findings were also reported in recent European Stroke Organisation and European Society for Swallowing Disorders guidelines, although there is a lack of evidence of improvements in other outcomes such as mortality, pneumonia, length of stay or feeding tube removal (Dziewas et al, 2018). [2023]

More high quality research is required on NMES treatment regimens, including a comparison with a sham intervention (Wang et al, 2021a). Similarly, treating dysphagia with tDCS, repetitive transcranial magnetic stimulation (rTMS) or PES appeared to be safe, but the interventions require further investigation in larger, high quality trials (Bath et al, 2018; Dziewas et al, 2021; Li et al, 2021a; Wang et al, 2021a; He et al, 2022; Hsiao et al, 2022; Zhao et al, 2022). Currently tDCS and rTMS are only carried out as part of a clinical trial. [2023]

Two systematic reviews have suggested that respiratory muscle training may reduce the occurrence of respiratory complications and reduce laryngeal penetration in patients with dysphagia after stroke (Zheng et al, 2020; Zhang et al, 2022). However, the time since stroke and the proportion of participants who had dysphagia were unclear, and the authors recommended that further research was needed (Zhang et al, 2022). [2023]

PES to aid decannulation in patients with a tracheostomy and dysphagia after stroke was shown to be effective in a single blind RCT (Dziewas et al, 2018). In this trial, PES significantly increased the number of patients who were ready to be decannulated compared to sham stimulation. [2023]

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In the presence of dysphagia, eating and drinking with acknowledged risks should be considered. This is recognised as a complex and personalised decision. Whilst there is a need for more research on this topic, recent multiprofessional guidance describes the characteristics of shared decision making. These include that decisions should be person-centred and involve the person and/or family/carers and other members of the multidisciplinary team, and include a swallowing assessment and steps to minimise risk, principally of aspiration and choking (Royal College of Physicians, 2021). [2023]

Psychological effects of stroke

4.27 Introduction

Neuropsychological sequelae are common following stroke and include a range of cognitive and mood disorders, as well as difficulties with adjustment, body image and confidence. Cognitive difficulties (changes in thinking skills as a direct effect of brain injury) are different from changes in mood or emotion which could be a direct effect of brain injury, but also as psychosocial consequences of adjusting to stroke. People with stroke report that psychological problems are often under-recognised, with high levels of unmet need. Psychological effects of stroke can have a significant and long-lasting impact on people with stroke and their carers and are associated with poorer rehabilitation outcomes. It is important that any pre-stroke psychological conditions are understood and considered in the assessment and treatment of any further psychological consequences of stroke. [2023]

National policymakers have identified the importance of improvements in psychological care after stroke in the NHS England National Stroke Service Model (2021) and Integrated Community Stroke Service Model (2022). Clinical psychologists/neuropsychologists are an essential member of the multidisciplinary stroke team along the pathway of care and have an important role in supporting the delivery of psychological care by the broader team. [2023]

These sections on cognition covers the range of cognitive problems that can occur after stroke with recommendations to help the person with stroke to reduce the impact of these problems on social participation. General issues are covered (Section 4.28 Psychological effects of stroke – general) followed by recommendations for specific cognitive domains (Sections 4.29-4.34) and mental capacity (Section 4.35 Mental capacity) and should be read together with recommendations for the organisation of psychological care (Section 2.11 Psychological care – organisation and delivery). [2023]

4.28 Psychological effects of stroke – general

Awareness, identification and management of both cognitive and mood impairment can be viewed through the lens of the stepped care (Gillham & Clark, 2011) and matched care models more commonly associated with mood disorders (see Section 2.11 Psychological care – organisation and delivery). Knowledge and skills required by the multidisciplinary team must be maintained across all levels of the model, with all members being able to support those with mild impairment (level 1), those with specialist skills and competencies such as occupational therapists working with those with moderate impairment affecting activities of daily living or engagement in rehabilitation (level 2), and access to clinical psychology/neuropsychology for those with severe or persistent impairment or where psychological issues are significantly impacting on safety or decision making (level 3). Adequate provision of clinical psychology/neuropsychology is required along the pathway to assist in training and supporting the stroke team as well as providing specialist clinical management for those requiring it, particularly those with level 3 needs. [2023]

Mood disorders are associated with poor outcomes after stroke and increased mortality (House, et al, 2001). Some patient groups have higher prevalence, such as those with aphasia being twice as likely to

develop depression after stroke, than those without aphasia. Assessment of mood requires use of validated tools for people with stroke, being mindful of cognitive and communication difficulties. Gillham & Clark (2011) suggest a screening pathway which includes those with aphasia. It is important that pre-existing mental health conditions are well understood by the team, including management and previously used strategies. [2023]

There are some shared features across domains which can make it challenging to identify where to start with screening and assessment. For example, someone may present as 'flat' and not initiating activities for a variety of reasons, including mood disorder, apathy, fatigue, or cognitive lack of initiation (due to memory, or executive dysfunction). These features can present similarly and can co-exist. Working with clinical psychology/neuropsychology colleagues assists the multidisciplinary team to understand the contribution and impact of these various factors in interpreting findings and informs treatment planning. [2023]

Cognitive impairment is associated with poor outcomes after stroke, such as increased length of hospital stay and reduced independence. Cognitive deficits are probably present in the early period after stroke for the majority of people, even those without limb weakness. Each cognitive domain (e.g. perception, attention, memory, executive functioning) should not be considered in isolation because most everyday activities draw on a range of abilities. Assessment and treatment need to take this overlap into account, particularly where changes to communication skills or mood exist. People should not be excluded from rehabilitation by an existing diagnosis of dementia. [2023]

4.28 Recommendations

- A Healthcare professionals should select screening tools and assessments for psychological problems appropriate to the needs of the person with stroke, with a clear rationale regarding which tools are to be used in which circumstances. These tools and assessments should:
 - be validated for use in people with stroke;
 - include freely available training in their use for staff;
 - cover the full range of potential impairments including attention, visual perception, memory, and executive functioning;
 - be applied consistently along local stroke pathways;
 - be completed with a speech and language therapist if the person with stroke has language difficulties;
 - be conducted in the patient's first language, using an interpreter if required;
 - be conducted in a quiet environment where distractions are minimised, at a time of day appropriate for the individual (particularly those with fatigue). [2023]
- B All members of the stroke multidisciplinary team should be trained and engaged in supporting those with psychological problems following stroke. The team should have the stroke-specific knowledge and skills to support people with cognitive impairment after stroke in daily activities and reduce the impact on participation, including making any necessary adjustments to the rehabilitation approach. [2023]
- C Stroke-skilled clinical psychology/neuropsychology should be available to multidisciplinary team members involved in the assessment and formulation of psychological problems people may have after stroke to provide training, clinical supervision, advice and support. [2023]
- D Stroke-skilled clinical psychology/neuropsychology should be available for people with stroke who have complex or atypical psychological presentations, or specific issues affecting risk or safety. [2023]
- E Following any screening or cognitive assessment, people with cognitive impairment after

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stroke and their family/carers should receive appropriate supporting information and education regarding the findings, implications, and recommended approach to their cognitive problems. [2023]

People with cognitive impairment after stroke should be considered for moderateintensity cardiorespiratory training programmes to improve cognitive function according to the person's needs, goals and preferences, as part of an overall treatment approach that also includes neuropsychological assessment and intervention. Cognitive impairment should not be considered a barrier to engaging with repetitive task training. [2023]

4.28 Sources

A-E Guideline Development Group consensus

F Lin et al, 2022; Guideline Development Group consensus

4.28 Evidence to recommendations

Cognitive research usually focuses on a specific impairment meaning there is little high quality evidence regarding general cognitive rehabilitation. Two RCTs were identified. Schmidt et al (2013) evaluated a self-awareness intervention based on a meal preparation activity, comparing three groups: video with verbal feedback, verbal feedback alone and no feedback. Video with verbal feedback was superior to the other methods but the type of brain injury was unspecified and the relevance to stroke is unclear. Alvarez-Sabin et al (2013) evaluated citicoline and cautiously concluded that citicoline showed promise in a composite score derived from multiple cognitive tests, but larger trials with functional outcomes are needed. A high quality systematic review and meta-analysis indicated that physical exercise can significantly improve overall cognition, executive function and working memory in people with chronic cerebrovascular disease, particularly if there was a cognitive impairment at the start of the intervention. Moderate-intensity aerobic training was the most effective form of delivery (Lin et al, 2022). [2023]

4.29 Cognitive screening

Cognitive screening uses a brief multidomain test to identify cognitive problems after stroke. Screening makes a distinction between those with and without likely problems, and identifies a group who may need more detailed or bespoke assessment. Initial screening (in the first few days after stroke) is expected to offer value in care planning and is applicable for most patients with exceptions where conscious level is reduced, delirium or severe cognitive impairment would confound the interpretation. Decision-making about if/when to proceed with cognitive screening should be based on clinical judgement and an understanding of the purpose of screening. Where cognitive screening is judged to be impractical or inappropriate, consideration must nevertheless be given to the potential influence of cognitive impairment on immediate support and care needs of the patient e.g. awareness of risk, initiating taking drinks, making meal choices, managing visitors. [2023]

Cognitive screening is not diagnostic, and the screening test result is only a part of the initial multidisciplinary assessment process. The MDT approach and treatment plan should be informed by a holistic understanding of the patient's and (if relevant) family's perception of current cognitive status, ongoing clinical interpretation of patient's presentation, cultural factors and their screening performance. [2023]

Common uses of cognitive screening will include: to establish the presence or absence of a deficit; to provide preliminary information regarding strengths and weaknesses; to give an indication of immediate support needs and long-term care and rehabilitation planning considerations (along with wider clinical information available to the MDT); to optimise the design of individual rehabilitation programmes; to consider assessment needs regarding mental capacity; and to plan further detailed and specific

assessments. Screening alone should not be used to inform any rehabilitation outcomes (especially long term). It is widely accepted that screening tools have limitations, such as a 'ceiling effect', therefore there will be some people with stroke who do experience cognitive impairments but perform well during screening. It is therefore important that screening performance is considered along with patient-reported difficulties and functional performance. Cognitive assessment should be considered for any person reporting or demonstrating a change in cognition, irrespective of their screening score. [2023]

The timing of cognitive screening is influenced by several variables, including the ability of the patient to engage in the process and the intended purpose of screening. Impaired performance on a screening test is common in the first days following stroke and the natural history is usually a degree of spontaneous improvement over time. It is important that screening results are considered in the context of pre-morbid ability, function and age, rather than solely on cut-off scores. The key consideration in timing must be the identification of cognitive factors required for planning necessary support and rehabilitation. Direct cognitive assessment may not be feasible or useful early after stroke, but screening for delirium and pre-stroke cognitive issues can begin immediately (SIGN, 2019; NICE, 2023b). [2023]

Re-screening is not routinely required at each transition along the pathway, but should be undertaken when clinically indicated. Re-screening is part of the ongoing pathway of care and is indicated when knowledge of cognitive function is not sufficient (due to the passage of time or change of patient status over time); or when the conclusions from previous cognitive screening or assessment cannot be accessed. [2023]

Screening should only be administered and interpreted by staff trained in the use of the selected tool, and who are familiar with its limitations. Advice from colleagues with appropriate expertise should be sought to aid test interpretation where needed. [2023]

4.29 Recommendations

- A Healthcare professionals screening people for cognitive problems after stroke should establish a baseline of their cognitive abilities prior to the stroke by taking a collateral history from family/carers and clinical records. [2023]
- B People with stroke should be routinely screened for delirium. Multidisciplinary teams should be aware of delirium throughout the person's inpatient stay, and an unexpected change in cognition should prompt a further assessment for delirium. [2023]
- C People with stroke should be screened for cognitive problems as soon as it is medically appropriate and they are able to participate in a brief interaction, usually within the initial days after onset of stroke. [2023]
- D Registered healthcare professionals who undertake cognitive screening of people with stroke should have the necessary knowledge and skills to appropriately select a screening tool for the identified purpose; to appropriately administer cognitive screening tools; and to interpret the findings taking account of the person's pre-stroke cognition, perception of cognition, functional abilities and other relevant factors such as mood. [2023]
- People with cognitive impairment after stroke, identified by screening, should have further assessment, including functional assessment and cognitive or neuropsychological assessment where indicated, to inform treatment planning, patient and family education and discharge planning. [2023]

4.29 Sources

A-E Guideline Development Group consensus

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4.30 Cognitive assessment

In this context assessment means undertaking a detailed or focused investigation and evaluation, that may be both diagnostic and prognostic. This can be achieved by combining assessment of functional performance, standardised cognitive assessments and the person's perception of their cognitive skills and difficulties. Assessment is required to determine the nature and extent of the impairment, to detect more subtle cognitive changes and to provide a detailed cognitive profile. However, assessment is an ongoing process that should continue along the stroke pathway, with assessments undertaken as required to inform a rehabilitation approach relevant to the person's needs at that time. [2023]

Assessment requires a trained assessor such as an occupational therapist, clinical psychologist, or clinical neuropsychologist. The assessor requires the knowledge and skills to undertake and interpret the assessment, and to evaluate the clinical presentation in the context of other variables such as educational attainment and the clinical context. Access to or supervision by a clinical psychologist/clinical neuropsychologist is required for members of the multidisciplinary team administering neuropsychological assessments. Standardised assessments can be multi-domain but are more likely to be limited to a specific aspect of cognition under investigation. [2023]

4.30 Recommendations

- A People with cognitive problems after stroke should receive an in-depth cognitive assessment, including functional performance, using standardised and validated tools to determine the nature of their cognitive difficulties and to detect uncommon or subtle changes for which screening tests may lack sensitivity. [2023]
- B Community stroke teams (including clinical psychology/neuropsychology) should be available to accept referrals for further cognitive assessment, identification of rehabilitation goals and assessment and management of risk, including when it is inappropriate for this to be conducted in the acute hospital setting. This should include contributing to mental capacity or safeguarding decisions and the assessment and management of people returning to cognitively demanding roles such as work or driving. [2023]
- C Standardised cognitive assessments should be carried out by a specialised assessors (e.g. occupational therapists with relevant knowledge and skills, or stroke clinical psychologists/neuropsychologists) with appropriate training and awareness of the properties and limitations of the various tests. [2023]
- D People with stroke returning to cognitively demanding roles such as managing instrumental activities of daily living (e.g. finances, driving or work) should have detailed cognitive assessments performed by an appropriately skilled assessor. [2023]
- E People with stroke who are unable to tolerate or adequately engage in standardised cognitive assessment should be assessed using appropriate functional tasks within a structured approach. [2023]

4.30 Sources

A-E Guideline Development Group consensus

4.31 Apraxia

Apraxia is the difficulty performing purposeful actions due to disturbance of the conceptual ability to organise actions to achieve a goal. People with apraxia often have problems carrying out everyday activities such as dressing or making a hot drink despite adequate strength and sensation. They may also have difficulties in selecting the right object at the right time or in using everyday objects correctly.

Apraxia can be detected using standardised tools (e.g. Test of Upper Limb Apraxia [TULIA]) and is usually associated with damage to the left cerebral hemisphere. [2016]

4.31 Recommendations

- A People with difficulty executing tasks after stroke despite adequate limb movement should be assessed for the presence of apraxia using standardised measures. [2016]
- B People with apraxia after stroke should:
 - have their profile of impaired and preserved abilities determined using a standardised approach;
 - have the impairment and the impact on function explained to them, their family/carers, and the multidisciplinary team;
 - be offered therapy and trained in compensatory techniques specific to the deficits identified, ideally in the context of a clinical trial. [2016]

4.31 Sources

- A Working Party consensus
- B West et al, 2008; Vanbellingen et al, 2010, 2011

4.31 Evidence to recommendations

One Cochrane review found insufficient evidence for the effectiveness of strategy training, transfer of training or gesture training (West et al, 2008). Case series research suggests that the types of observed action errors are important clues for the type of retraining needed (Sunderland et al, 2006). Future research needs to provide detailed descriptions of the interventions and measure the impact on everyday function. [2016]

4.32 Attention and concentration

Attention is a prerequisite for almost all cognitive functions and everyday activities. Disturbed alertness is common after stroke especially in the first few days and weeks, and more so in non-dominant hemisphere stroke. Attention impairments may persist in the longer term and may be specific (e.g. focusing, dividing or sustaining attention) or more generalised, affecting alertness and speed of processing and be evident in poor engagement or general slowness. Attention problems may lead to fatigue, low mood and difficulty with independent living. [2016]

4.32 Recommendations

- A People who appear easily distracted or unable to concentrate after stroke should have their attentional abilities assessed using standardised measures. [2016]
- B People with impaired attention after stroke should have cognitive demands reduced by:
 - having shorter treatment sessions;
 - taking planned rests;
 - reducing background distractions;
 - avoiding activities when tired. [2016]
- C People with impaired attention after stroke should:
 - have the impairment explained to them, their family/carers and the multidisciplinary team;
 - be offered an attentional intervention (e.g. time pressure management, attention process training, environmental manipulation), ideally in the context of a clinical trial;
 - be given as many opportunities to practise their activities as reasonable under supervision. [2016]

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4.32 Sources

A-B Working Party consensus

C Loetscher and Lincoln, 2013; Working Party consensus

4.32 Evidence to recommendations

One Cochrane review of six small studies (Loetscher & Lincoln, 2013) found limited evidence that cognitive rehabilitation interventions (attention process training, time pressure management and/or computer-based training packages) improved some aspects of attention in the short term, but insufficient evidence for any persisting effects. [2016]

4.33 Memory

Subjective problems with memory are very common after stroke, and memory deficits are often revealed on formal testing with standardised measures (e.g. the Rivermead Behavioural Memory Test [RBMT]). Memory deficits can lead to longer hospital stay, poorer outcomes, risks to personal safety, and cause distress to people with stroke and their family. Memory loss is a characteristic feature of dementia, which affects about 20% of people after stroke, but this section is not directly concerned with the impairments associated with diffuse cerebrovascular disease. It should also be noted that subjective memory problems can result from attentional or executive difficulties. [2016]

4.33 Recommendations

- A People with stroke who report memory problems and those considered to have problems with learning and remembering should have their memory assessed using standardised measures. [2016]
- B People with memory impairment after stroke causing difficulties with rehabilitation should:
 - have the impairment explained to them, their family/carers and the multidisciplinary team;
 - be assessed for treatable or contributing factors (e.g. delirium, hypothyroidism);
 - have their profile of impaired and preserved memory abilities determined, including the impact of other cognitive deficits e.g. attention;
 - have nursing and therapy sessions altered to capitalise on preserved abilities;
 - be trained in approaches that help them to encode, store and retrieve new information e.g. spaced retrieval (increasing time intervals between review of information) or deep encoding of material (emphasising semantic features);
 - be trained in compensatory techniques to reduce their prospective memory problems (e.g. use of electronic reminders or written checklists);
 - receive therapy in an environment as similar as possible to their usual environment.
 [2016]

4.33 Sources

- A Working Party consensus
- B Fish et al, 2008; Das Nair and Lincoln, 2012; Working Party consensus

4.33 Evidence to recommendations

Previous editions of this guideline identified one Cochrane review of two small trials (Das Nair & Lincoln, 2007), one RCT of mostly younger people with subarachnoid haemorrhage suggesting temporary benefits from electronic paging reminder systems, and two inconclusive studies of the impact of active music listening (Fish et al, 2008; Winkens et al, 2009; Sarkamo et al, 2010). For this guideline the

Working Party included one small RCT of sufficient quality (Das Nair & Lincoln, 2012). The ReMiND trial compared two memory rehabilitation strategies (compensation and restitution) against a control condition ('self-help'). People with stroke were in the minority in this mixed neurological sample. The compensation and restitution groups used more internal memory strategies than the control group but there was no difference in outcomes. Further research is needed to establish the clinical effectiveness (at the level of activities or participation) and acceptability of memory rehabilitation approaches, recruiting larger, more representative, groups of people with stroke. [2016]

4.34 Executive function

Executive function refers to the ability to plan and execute a series of tasks, inhibit inappropriate automatic impulses, regulate emotional responses, foresee the consequences of actions and make judgements about risk. The 'dysexecutive syndrome' encompasses various impairments, including difficulties with problem solving, planning, organising, initiating, inhibiting and monitoring behaviour. It also includes impairments in cognitive flexibility, which is the ability to change cognitive or behavioural strategies to adapt to novel or evolving task demands. These can be detected using standardised tools (e.g. the Behavioural Assessment of the Dysexecutive Syndrome [BADS]). Executive functions rely heavily upon attention (Section 4.32 Attention and concentration) and are associated with deficits in everyday function and independence. [2016]

4.34 Recommendations

- A People with stroke who appear to have adequate skills to perform complex activities but fail to initiate, organise or inhibit behaviour should be assessed for the dysexecutive syndrome using standardised measures. [2016]
- B People with an impairment of executive function and activity limitation after stroke should be trained in compensatory techniques, including internal strategies (e.g. self-awareness and goal setting), structured feedback on performance of functional tasks and external strategies (e.g. use of electronic reminders or written checklists). [2016]
- C People with an executive disorder after stroke should have the impairment and the impact on function explained to them, their family/carers, and the multidisciplinary team. [2016]

4.34 Sources

- A Working Party consensus
- B Chung et al, 2013; Working Party consensus
- C Working Party consensus

4.34 Evidence to recommendations

For this guideline, the Working Party evaluated a Cochrane review (Chung et al, 2013), another systematic review (Poulin et al, 2012) and two RCTs (Levine et al, 2011; Schmidt et al, 2013). The Cochrane review identified 19 trials (and selected 13 for meta-analysis) but concluded that there was insufficient high quality evidence to guide practice. Further high quality research is needed. [2016]

4.35 Mental capacity

Assessment of mental capacity and subsequent actions are an important feature of stroke care because of the prevalence of cognitive and communication impairments after stroke. The law is clear that these are not reasons to assume that a person lacks capacity. [2023]

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Mental capacity is assessed by whether a person has an impairment of mind or brain that affects their ability to understand, retain and weigh up information relating to a particular decision and to express their opinions, desires and feelings about the decision. A capacity assessment is decision-specific and often requires the skills of the multidisciplinary team to enable the person with stroke to demonstrate their ability to make a decision for themselves. Every opportunity should be taken to support the individual to demonstrate capacity, which may involve preparatory sessions introducing resources, orientation to the decision, and establishing the most reliable means of communication. The capacity interview should be undertaken by someone with the appropriate skills, relationship with the person, and knowledge of the relevant information, including, for example, speech and language therapists for those with aphasia or complex feeding decisions. The interview should be augmented according to the person's individual needs, such as time of day, environment, means of communication and the length of interview. Information gathered at the capacity interview should be presented alongside information gathered regarding functional abilities, previously expressed wishes and consistently held preferences. [2023]

Where a person with stroke lacks capacity regarding a specific decision, decision making should be made in line with the best interest process, considering foremost the decision the individual would have made had they had capacity and the least restrictive option available. The use of best interest balance charts may help in ensuring all aspects of the decision are included, such as medical, social, ethical, and safety issues. [2023]

4.35 Recommendations

- A When making decisions with and on behalf of people with stroke, healthcare professionals should adhere to the principles defined in the relevant legislation (England and Wales: Mental Capacity Act 2005; Scotland: Adults with Incapacity (Scotland) Act 2000; Northern Ireland: Mental Capacity Act (Northern Ireland) 2016; Ireland: Assisted Decision-Making (Capacity) Act 2015), especially with regard to determining mental capacity and making decisions in the best interests of a person who lacks mental capacity. [2016]
- B The specialist multidisciplinary team should be involved in making decisions about mental capacity, and should provide information and advice to the person with stroke (when appropriate) and their family/carers. [2016]

4.35 Sources

A http://www.legislation.gov.uk/ukpga/2005/9/contents;

http://www.legislation.gov.uk/asp/2000/4/contents;

https://www.legislation.gov.uk/nia/2016/18/contents/enacted;

https://www.gov.ie/en/publication/5830f-assisted-decision-making-capacity-act-2015/

B Working party consensus

4.35 Evidence to recommendations

This section covers the ability of people with stroke to make decisions about their health, with reference to the specific and legally-defined framework described in the relevant legislation (England and Wales: Mental Capacity Act 2005; Scotland: Adults with Incapacity (Scotland) Act 2000; Northern Ireland: Mental Capacity Act (Northern Ireland) 2016; Ireland: Assisted Decision-Making (Capacity) Act 2015). For instance, the Mental Capacity Act 2005 lays out statutory principles underpinning practice including that 'a person must be assumed to have capacity unless it is established that they lack capacity'. The Act states that 'a person is not to be treated as unable to make a decision unless all practicable steps to help them to do so have been taken without success' and 'the fact that a person is able to retain the information relevant to a decision for a short period only does not prevent them from being regarded as able to make the decision'. This is of particular relevance to people with communication (e.g. Section

<u>4.43 Aphasia</u>) and cognitive impairments (<u>Sections 4.28-4.30</u>) after stroke. The Act obliges those taking a decision on behalf of an adult who lacks mental capacity to decide in their best interests and 'must consider so far as is reasonably ascertainable...the person's past and present wishes and feelings and, in particular, any relevant written statement made by them when they had capacity'. **[2016]**

4.36 Perception

Perception involves the processing and interpretation of incoming sensations, which is essential to everyday activities. Perceptual functions include awareness, recognition, discrimination and orientation. Disorders of perception are common after stroke and may affect any sensory modality. However, visual perception has been the most widely studied, particularly visual agnosia (impaired object recognition). Perceptual disorders can be detected using standardised assessment tools (e.g. the Visual Object and Space Perception battery [VOSP]). It is important to distinguish between deficits affecting the whole perceptual field (covered in this section) and unilateral neglect (Section 4.37 Sensation) or damage to the visual pathway or eye movements (Section 4.48 Vision). [2016]

4.36 Recommendations

- A People who appear to have perceptual difficulties after stroke should have a perceptual assessment using standardised measures. [2016]
- B People with agnosia after stroke should:
 - have the impairment explained to them, their family/carers and the multidisciplinary team;
 - have their environment assessed and adapted to reduce potential risks and promote independence;
 - be offered a perceptual intervention, such as functional training, sensory stimulation, strategy training and/or task repetition, ideally in the context of a clinical trial. [2016]

4.36 Sources

- A Working Party consensus
- B Bowen et al, 2011; Working Party consensus

4.36 Evidence to recommendations

A Cochrane review (Bowen et al, 2011) examined the evidence for the four main intervention approaches that are used, often in combination, in clinical practice: functional training, sensory stimulation, strategy training and task repetition. There is uncertainty over the merits of any one approach over any other. [2016]

4.37 Neglect

Neglect refers to a neuropsychological condition common after stroke whereby a person has reduced and impaired ability to process spatial information. This has consequences for further neuropsychological processing including reasoning, memory encoding and retrieval, as well as the frequently observed impaired interaction with the environment whereby people overlook or appear to be unaware of items or their contextual field. [2023]

Problems with spatial awareness (also referred to as visuospatial inattention) refer to a reduced awareness of some part/s of the person's body or their environment. Visual neglect can be allocentric (relating to interpreting environmental stimuli) or egocentric (relating to the person's own point of view). It is more common in people with non-dominant hemisphere stroke (typically causing left-sided

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neglect) and those with hemianopia. Behavioural symptoms include bumping into objects on the affected side or only reading one side of pages in newspapers or books. Patients are usually unaware of the impairment, and therefore the treatment approach differs from that used in hemianopia where patients are more readily able to compensate. [2023]

Neglect can be detected using standardised assessments (e.g. the Catherine Bergago Scale) and should be reviewed across personal, reaching and locomotor space. Neglect can be severe, with a person demonstrating features of the neglect syndrome (such as being unable to turn their head beyond the midline), or very subtle, affecting people moving through locomotor space, which may only be evident during a more cognitively demanding task. It is particularly important to ensure those who are using electric wheelchairs, crossing roads or returning to driving (see Section 4.14 Driving) or work (see Section 4.15 Return to work) are fully assessed. Neglect is linked with the attentional systems of the brain, thus occurs in people with difficulties maintaining and dividing attention, and impacts on activities of daily living, motor recovery (through learnt non-use) and safety. [2023]

Sensory neglect is also a feature post stroke, with people lacking awareness of the sense of touch, proprioception or movement in a limb, despite sensation being present. In those with severe neglect, both sensory and visual neglect are often present. [2023]

4.37 Recommendations

- A People with stroke affecting the non-dominant cerebral hemisphere should be considered at risk of impaired awareness on the contralateral side and should be assessed for this using standardised measures. [2016]
- B When assessing problems with spatial awareness in people with stroke, clinicians should use a standardised test battery in preference to a single subtest, and the effect on functional tasks such as dressing and mobility should be included. [2016]
- C People with impaired awareness to one side after stroke should:
 - have the impairment explained to them, their family/carers and the multidisciplinary team;
 - be trained in compensatory strategies to reduce the impact on their activities;
 - be given cues to draw attention to the affected side during therapy and nursing activities;
 - be monitored to ensure that they do not eat too little through missing food on one side of the plate;
 - be offered interventions aimed at reducing the functional impact of the reduced awareness (e.g. visual scanning training, limb activation, sensory stimulation, eye patching, prism wearing, prism adaptation training, mirror therapy, galvanic vestibular stimulation, transcranial magnetic stimulation), ideally in the context of a clinical trial.
 [2016]

4.37 Sources

- A Working Party consensus
- B Jehkonen et al, 2006
- C Bowen et al, 2013; Working Party consensus

4.37 Evidence to recommendations

Current evidence consists of a Cochrane review of 23 RCTs (Bowen et al, 2013) and three further recent RCTs which investigated mirror therapy (Pandian et al, 2014), galvanic vestibular stimulation (Wilkinson et al, 2014) and sensory cueing (Fong et al, 2013). Transcranial magnetic stimulation (TMS) was outside

the scope of the review. There is insufficient high quality evidence to recommend any specific interventions to increase independence. However, there is some very limited evidence that cognitive rehabilitation may have an immediate beneficial effect on tests of neglect (Bowen et al, 2013). The trials of mirror therapy, galvanic vestibular stimulation, sensory cueing and TMS showed promise, but these require evaluation in larger trials with higher quality research design and reporting. [2016]

4.38 Mood and well-being

The following sections cover a range of emotional problems that can occur after a stroke, with recommendations to help the person with stroke to achieve improved well-being and quality of life. The recommendations should be implemented in the context of a psychological needs assessment and care planning and in relation to the organisation of psychological care <u>Section 2.11 Psychological care – organisation and delivery</u>). See also the section on self-management (<u>Section 4.4 Self-management</u>). [2023]

4.39 Anxiety, depression and psychological distress

Mood disturbance is very common after stroke. It may present as low mood, depression or anxiety, or with increased levels of emotional agitation, instability or emotionalism, limiting functional recovery and often associated with risk assessment needs and increased mortality (Morris et al, 1993; House et al, 2001). Many people with stroke are troubled by psychological distress that does not meet diagnostic criteria for depression and anxiety but which nevertheless disrupts and impedes their lives and relationships. A stroke is a significant life event and in this context some emotional distress is normal and part of adjustment to a substantial change in circumstances. Healthcare professionals working with people with stroke should be aware that mood disturbance after stroke can arise because of psychosocial factors (e.g. disability, loss, trauma), or as a result of neurochemical changes in the brain, or both. [2023]

Depression affects about one third of people with stroke and frequently persists long-term (Hackett et al, 2009; Ayerbe et al, 2014). Anxiety is also common, affecting around one-quarter of people with stroke, and, like depression, may only become evident after several months (Knapp et al, 2020). Depression and anxiety are closely linked and may be part of a single emotional response to stroke, commonly alongside additional psychological effects such as hopelessness, frustration or anger. [2023]

In a UK survey, three-quarters of people with stroke reported experiencing at least one mental health problem after a stroke, with 44% of people reporting experiencing anxiety or depression, 42% experiencing mood swings, 47% experiencing reduced self-confidence and 16% reporting suicidal thoughts (Stroke Association, 2020). A survey of long-term needs found that nearly three-quarters of people with emotional difficulties felt their needs had not been fully met (McKevitt et al, 2011). [2023]

Psychological disturbances also commonly follow on from neuropsychological consequences of stroke, whether such underlying effects are recognised or hidden. This highlights the need for sufficient and adequate assessment to correctly identify what may underpin and explain emotional changes after stroke and thereby guide appropriate rehabilitation approaches. Additionally, mood disturbance or other mental health issues may frequently exist for people prior to a stroke, which will affect their post-stroke experience (Taylor-Rowan et al, 2019), and need to be considered and understood for their clinical management and rehabilitation planning. [2023]

As far as is possible, approaches and assessment measures should be adapted for use with people with mild aphasia, and several have been designed specifically for people with more severe aphasia (e.g. the Stroke Aphasic Depression Questionnaire [SADQ], the Depression Intensity Scale Circles [DISCs] or the Behavioural Outcomes of Anxiety [BOA] scale). [2016]

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4.39 Recommendations

- A Healthcare professionals should be aware of the psychological needs of people with stroke and their family/carers, and routinely provide education, advice, and emotional support for them. Multidisciplinary teams should embed measures that promote physical and mental well-being within the wider rehabilitation package, and collaborate with other statutory and voluntary services to deliver them, such as:
 - increased social interaction;
 - meaningful activities to support rebuilding of self-confidence and self-esteem;
 - increased exercise;
 - mind-body interventions such as relaxation, mindfulness, Tai Chi and yoga;
 - other psychosocial interventions such as psychological education groups. [2023]
- B People with stroke should be routinely screened for anxiety and depression using standardised tools, the results of which should be used alongside other sources of information to inform clinical formulation of treatment and support needs. [2023]
- C People with stroke with one mood disorder (e.g. depression) should be assessed for others (e.g. anxiety). [2023]
- D When assessing, diagnosing or treating people with mood disorders after stroke, clinicians should take account of other relevant factors such as prior psychological history, type of stroke and other features such as cognitive or language deficits and fatigue. [2023]
- People with mood disorders after stroke who are assessed to have suicidal ideas or intent, or who have a previous history of suicidal ideas or intent, should be referred for assessment and risk management by a psychiatric team and have a risk management plan put in place immediately. [2023]
- F People with depression or anxiety after stroke, and those assessed to be at risk, should be considered by the multidisciplinary team for non-pharmacological approaches, education and a reasonable period of watchful waiting where appropriate. [2023]
- G People with stroke should be offered one-to-one motivational interviewing or problemsolving therapy, adapted as necessary for people with aphasia or cognitive impairment, as part of a multidisciplinary rehabilitation approach to prevent depression. [2023]
- H People with stroke at significant risk of anxiety or depression should be offered psychological therapies (motivational interviewing, cognitive behavioural therapy, problem-solving therapy or acceptance and commitment therapy) provided they have sufficient cognitive and language skills to engage with the therapy. [2023]
- People with stroke should not be routinely offered SSRIs for the prevention of depression, but SSRIs may be considered when other preventative approaches are not appropriate (e.g. in people with severe cognitive or language impairment) or when the risk of depression is high (e.g. in people with a previous history of depression). The balance of risk and benefit from SSRIs should take account of the potential for increased adverse effects (seizures and hip fracture). [2023]
- J People with depression after stroke should be offered psychological interventions (motivational interviewing, cognitive behavioural therapy or problem-solving therapy) adapted as necessary for use with people with aphasia or cognitive impairment and/or an SSRI. [2023]
- K People with depression after stroke may be considered for non-invasive brain stimulation in the context of a clinical trial. [2023]
- L People with aphasia and low mood after stroke should be considered for individual behavioural therapy. [2023]
- M People with anxiety after stroke may be considered for medication therapy, after

- discussion between clinician and the person about adverse events and alternative treatment approaches including psychological interventions. [2023]
- N People with depression or anxiety after stroke who are treated with antidepressant medication should be monitored for effectiveness and adverse effects within the first 6 weeks. If there has been a benefit people should be treated for at least four months beyond initial recovery. If the person's mood has not improved after 6 weeks, medication adherence should be checked before considering a dose increase, a change to another antidepressant or an alternative non-pharmacological treatment. [2023]
- O People with persistent moderate to severe emotional disturbance after stroke who have not responded to high-intensity psychological intervention or pharmacological treatment should receive collaborative care, which should include long-term follow-up and involve liaison between the GP, stroke team and secondary care mental health services with supervision from a senior mental health professional. [2023]
- P Where people with depression or anxiety after stroke are being treated within primary care mental health services (such as Improving Access to Psychological Therapies [IAPT]) or secondary care mental health services, advice, consultation and training should be available from the stroke service. Guidance for the management of people with significant language and cognitive impairment should be agreed between services and joint working offered where appropriate. [2023]
- Q People with severe, persistent, or atypical symptoms of emotional disturbance after stroke, and those with complex presentations where emotional disturbance, cognitive and language deficits co-exist, should receive specialist assessment and treatment from a clinical psychologist/neuropsychologist to facilitate formulation and treatment planning within the multidisciplinary team. [2023]
- R Healthcare professionals who undertake mood assessment of people with stroke should have the knowledge and skills to select a screening tool appropriate for the purpose; to administer assessment tools appropriately; and to interpret the findings taking into account the person's pre-stroke psychological history, perception of mood, and other relevant contextual factors such as medical state, fatigue, and sleep. [2023]
- Stroke-skilled clinical psychology/neuropsychology should be available to multidisciplinary team members involved in the assessment and formulation of psychological problems after stroke, to help facilitate an understanding of these problems for people with stroke, to facilitate appropriate treatment approaches, and to provide training, clinical supervision, advice and support. [2023]

4.39 Sources

- A-F Guideline Development Group consensus
- G Allida et al, 2020a
- H Guideline Development Group consensus
- I-K Allida et al, 2020a, b; Guideline Development Group consensus
- L Thomas et al, 2013
- M Knapp et al, 2017; Guideline Development Group consensus
- N NICE, 2022d
- O-S Guideline Development Group consensus

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4.39 Evidence to recommendations

The evidence reviewed for the current edition of the guideline was largely based on three Cochrane systematic reviews: treating anxiety (Campbell Burton et al, 2011), and preventing and treating depression (Allida et al, 2020a & b). For anxiety, the Cochrane review of three studies indicated that psychological interventions and medication treatments appear useful (Campbell Burton et al, 2011) but the studies were of low quality. SSRIs reduce anxiety but no single SSRI is superior to any other (Mead et al, 2012). The Guideline Development Group considered a small RCT of a self-help relaxation recording which showed promise (Golding et al, 2015) but a larger sample would be needed to confirm recommendations. More research is needed into psychological interventions for anxiety after stroke. [2023]

A Cochrane review of 19 RCTs with 1,771 patients found that there was low quality evidence that selective serotonin reuptake inhibitors (SSRIs) can prevent depression in some people at risk of depression after stroke but there remains uncertainty over the balance of benefits and risk of adverse events (Hackett et al, 2009; Tsai et al, 2011; Allida et al, 2020a). Another systematic review and meta-analysis (Kalbouneh et al, 2022) found SSRIs had a significant effect in preventing and treating depression but with an increased risk of seizures. Similarly, low quality evidence showed that psychological interventions, such as motivational interviewing or problem-solving therapy, may help prevent depression (NICE, 2022d). [2023]

There have been three large scale RCTs of the SSRI fluoxetine in the first days following stroke (Dennis et al, 2020; Lundström et al, 2020; Almeida et al, 2021), one of which is cited in the Cochrane review of SSRIs for stroke recovery (Legg et al, 2019) and in two meta-analyses of fluoxetine for stroke recovery (Mead et al, 2019; Elsnhory et al, 2022). The trials were designed to assess functional recovery but collected information on the incidence of depression. Two of the studies suggested that medication therapy could reduce depression but at the cost of more serious adverse events, principally seizures and hip fracture. [2023]

A Cochrane review (Allida et al, 2020b) of 49 trials and over 3,000 patients synthesised low quality (high risk of bias) evidence that non-invasive brain stimulation and psychological interventions may be of benefit in the treatment of depression, in addition to pharmacological treatment with SSRIs. Of interest, psychological interventions were evaluated as a stand-alone treatment and were found to be as effective as combined therapy (SSRI and psychological therapy). For people with aphasia after stroke, individual behavioural therapy from an assistant psychologist was found to be more effective than usual care at improving mood (Thomas et al, 2013). [2023]

Acceptance and commitment therapy following stroke is a promising new area (Majumdar & Morris, 2019; Niu et al, 2022) that has received interest from clinicians and where further research is required. Further work is also needed to explore the adaptations required to cognitive behavioural therapy for use in people with stroke. All psychological therapies should be underpinned by a neuropsychological understanding of the effects of stroke and should only be practised by members of the team with adequate training and clinical supervision. [2023]

4.40 Apathy

Apathy is described as a reduction in goal-directed activity in behavioural, cognitive or social dimensions of a person's life in comparison to their previous level of functioning (Robert et al, 2018). It can be characterised by both subjective motivational changes and reduced observable behaviour, and by decreased emotional responsiveness. Apathy occurs in about one third of people with stroke and has a negative impact on functional outcomes, and is under-recognised and poorly understood (Tay et al, 2021). In clinical practice, recognition of apathy is in its infancy. Increased understanding and training is required by stroke healthcare professionals to identify apathy alongside other cognitive or mood-related

changes. Training should be provided by those with appropriate knowledge and skills such as clinical psychologists/neuropsychologists. [2023]

4.40 Recommendations

- A For people with stroke who show diminished motivation, reduced goal-directed behaviour or decreased emotional responsiveness that is persistent and affects engagement with rehabilitation or functional recovery, apathy should be considered alongside other cognitive and mood disorders. [2023]
- B People with apathy after stroke should have a review of rehabilitation goals to ensure they reflect the person's values, preferences and priorities. The person's confidence to complete rehabilitation activities and plans should also be considered as an additional need requiring support. [2023]
- People with apathy after stroke should be managed by a multidisciplinary approach in line with the stepped care and matched care models of psychological care. Assessment and treatment from a clinical psychologist/neuropsychologist should be available, particularly when the presentation is complex, persistent or is resistant to approaches trialled by the multidisciplinary team, to support assessment, clinical formulation and rehabilitation planning. [2023]
- D People with apathy after stroke should have the impairment and the impact on function explained to them, their family/carers, and the multidisciplinary team. [2023]
- Members of the stroke multidisciplinary team should receive training in psychological care including apathy, at levels appropriate to the stepped care and matched care models.[2023]

4.40 Sources

A-E Guideline Development Group consensus

4.40 Evidence to recommendations

Systematic reviews and meta-analyses have reported apathy in people after stroke is associated with high levels of disability, depression and cognitive impairment (Caeiro et al, 2013; van Dalen et al, 2013). Recognition of apathy after stroke is important for informing rehabilitation approaches and outcomes, but there is a lack of high quality evidence to guide recommendations on assessment and management. Recent studies have included an underpowered RCT (n=13) of the pharmacological treatment nefiracetam (Brockman et al, 2016), a pilot trial (n=13) of repetitive transcranial magnetic stimulation (Sasaki et al, 2017) and a RCT (n=30) of strategy training (Skidmore et al, 2015). Earlier trials have examined antidepressants, modafinil and cholinesterase inhibitors, but no agent has shown a convincing treatment effect. [2023]

4.41 Emotionalism

Emotionalism is an increase in emotional behaviour (crying or, less commonly, laughing) following minimal provoking stimuli. Around 20% of people with stroke are affected in the first six months and although frequency decreases by 12 months, more than 10% remain affected (Hackett et al, 2010). Emotionalism can be distressing for people with stroke and their families and can interfere with rehabilitation. [2016]

4.41 Recommendations

A People with stroke who persistently cry or laugh in unexpected situations or are upset by their fluctuating emotional state should be assessed by a specialist member of the

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- multidisciplinary team trained in the assessment of emotionalism. [2016]
- B People diagnosed with emotionalism after stroke should be appropriately distracted from the provoking stimulus when they show increased emotional behaviour. [2016]
- People with severe or persistent emotionalism after stroke should be given antidepressant medication, monitoring effectiveness by the frequency of crying. They should be monitored for adverse effects and treated for at least four months beyond initial recovery. If the person's emotionalism has not improved after 2-4 weeks, medication adherence should be checked before considering a dose increase or a change to another antidepressant. [2016]

4.41 Sources

- A, B Working Party consensus
- C Hackett et al, 2010

4.41 Evidence to recommendations

Recommendations have not changed since the 2012 edition of the guideline when they were based on one Cochrane review (Hackett et al, 2010) and the consensus of the Working Party, as there have been no subsequent high quality research studies. There is no evidence regarding the choice of antidepressant or length of treatment, and well designed longer-term studies are needed. [2016]

Communication and language

4.42 Introduction

This section covers the range of speech and language problems that can occur after stroke with recommendations to help the person with stroke to communicate and increase social participation. Swallowing impairment (dysphagia) is covered in <u>Section 4.26 Swallowing</u>. [2023]

4.43 Aphasia

Aphasia refers to an impairment of language function affecting all aspects of communication including speaking, understanding, reading (separately called alexia) and writing (agraphia). Aphasia affects about a third of people with stroke, and can have a significant impact on the lives of individuals and their family/carers. Aphasia has wide-ranging effects on mood, self-image, well-being, relationships, employment, leisure and social opportunities. Problems with communication can also occur following damage to the non-dominant hemisphere. [2023]

Delivery of speech and language interventions can be described under two main approaches: interventions delivered by trained professionals (e.g. speech and language therapists), which are currently the majority and address many aspects of language use, and digital therapies delivered on computers, mobile devices or as apps, which tend to target a specific aspect of language function e.g. the ability to retrieve and produce specific spoken words. Some studies have investigated a blend of the two approaches and use mainstream and specialist software to augment therapist-delivered speech and language therapy. In order to evaluate complex interventions such as speech and language therapy a broad range of studies are required (Skivington et al, 2021). [2023]

4.43 Recommendations

A People should be assessed early after stroke for communication difficulties by a speech and language therapist to diagnose the problem, devise and implement a treatment programme and explain the nature and implications to the person, their family/carers and

- the multidisciplinary team. [2023]
- B People with aphasia after stroke should be given the opportunity to improve their language and communication abilities as frequently and for as long as they continue to make meaningful gains, under supervision from a speech and language therapist. [2023]
- C People with aphasia after stroke should be offered access to appropriate practice-based digital therapies. Adherence to and engagement with these digital therapies will likely be improved if supported by a carer or healthcare professional. Telerehabilitation programmes should:
 - be personalised to the individual's goals and preferences;
 - be used when it is considered to be a beneficial option to promote recovery and should not be used as an alternative to in-person rehabilitation;
 - be monitored and adapted by the therapist according to progress towards goals;
 - be supplemented with face-to-face reviews and include the facility for contact with the therapist as required. [2023]
- D People with communication difficulties after stroke should:
 - be assessed and offered access to a range of communication aids, prescribed according to the person's needs, goals, and preferences;
 - be assessed for their ability to use assistive technology and have programmes and equipment adjusted accordingly;
 - be trained and supported in the use of the appropriate technology. [2023]
- People with communication difficulties after stroke should be offered access to social and participatory activities such as conversation partners, peer support groups, and return to work programmes as appropriate. [2023]
- People with aphasia after stroke whose first language is not English should be assessed and provided with information about aphasia and offered therapy and communication practice in their preferred language. Referral to appropriate services such as interpreters should be made promptly to facilitate early assessment and treatment. [2023]
- G Intensive speech and language therapy such as comprehensive aphasia programmes may be considered from 3 months after stroke for those who can tolerate high-intensity therapy. [2023]
- H People with aphasia after stroke should be monitored and assessed for depression and other mood disorders using validated tools. Accessible information should be provided and psychological interventions tailored to the person's needs. [2023]
- The carers and family of a person with communication difficulties after stroke, and health and social care staff, should receive information and training from a speech and language therapist to improve their communication skills and enable them to optimise engagement in the person's rehabilitation, and promote autonomy and social participation. [2023]
- J People with persistent communication difficulties after stroke, that limit their social activities, should be offered information about local or national groups for people with aphasia and referred as appropriate. [2023]

4.43 Sources

- A, B Brady et al, 2016; RELEASE Collaborators, 2021, 2022a, 2022b; Guideline Development Group consensus
- C Lavoie et al, 2017; Palmer et al, 2019; Harrison et al, 2021; Braley et al, 2021; Guideline Development Group consensus
- D-F Guideline Development Group consensus

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- G Hoover et al, 2017; Leff et al, 2021
- H Guideline Development Group consensus
- I Kagan et al, 2001; Simmons-Mackie et al, 2016
- J Guideline Development Group consensus

4.43 Evidence to recommendations

A high quality meta-analysis carried out by the RELEASE Collaborators (2022b) re-examined data from 25 published trials involving 959 people with aphasia across 10 different languages. This meta-analysis demonstrated a clear dose effect (total hours of therapy); that is, people with aphasia who received more hours of therapy (more than 20 to 50 hours) made large and clinically meaningful gains in language abilities and function, compared with those who received fewer hours. No functional communication gains were observed for people with aphasia receiving less than 5 hours of therapy nor comprehension gains for those receiving less than 20 hours. There was a weaker effect of frequency (number of days per week that therapy was delivered) with 3-5 days being best. The data on intensity (hours of therapy per week) were less clear (Dignam et al, 2015; RELEASE Collaborators, 2022a). [2023]

The majority of evidence derives from people with aphasia in the chronic phase (more than 6 months after stroke but often much longer than this). There is no evidence to support a set time limit after stroke when therapy should be stopped. People with aphasia should be offered therapy for as long as they continue to make meaningful gains in their language and communication abilities (RELEASE Collaborators, 2021). [2023]

The greatest overall gains in language outcomes for people with aphasia after stroke are seen when therapy starts in the acute/subacute stage, within 1 month of stroke (RELEASE Collaborators, 2021). There is less evidence regarding the intensity and dose for people with aphasia when treatment starts within one month of stroke. A high quality RCT of people with acute stroke showed no difference between 10 hours (control group) and 23 hours (active group) of speech and language therapy delivered over a month (Godecke et al, 2021). [2023]

For people with aphasia in the chronic phase (more than 3 months after stroke) the greatest gains were associated with moderate-intensity/high-dose therapy (3-4 hours/week; more than 50 hours of treatment in total; (RELEASE Collaborators, 2022b)). One way of delivering higher doses of therapy is through comprehensive aphasia programmes, with positive results seen in one non-randomised trial (Hoover et al, 2017) and one observational study (Leff et al, 2021). However, not all people with aphasia can manage the high-intensity treatment mandated by these programmes. These studies suffer from selection bias and their results cannot be generalised to all people with aphasia, and more high quality research is needed. [2023]

There has been a lot of interest in digital therapies for people with aphasia, with several RCTs demonstrating large gains in naming in particular (Palmer et al, 2019; Braley et al, 2021). It should be noted that the majority of digital therapies are not designed to replicate the interventions delivered by a speech and language therapist - rather, they automate the repetitive and often impairment-based aspects of therapy. As such, their effects are often only seen on the aspects of language, or items, that the person with aphasia practices. There is good evidence that both clinician and self-administered digital therapies can be effective (Lavoie et al, 2017), but those with more support from carers or therapists tend to engage more and make larger language gains (Harrison et al, 2020). [2023]

4.43 Implications

Stroke services should consider all the ways that the dose of speech and language therapy can be increased to the levels recommended here, as they are considerably higher than currently delivered. Holistic aspects of rehabilitation such as peer support, social and singing groups may have

communication benefits as they provide opportunity for social communication practice. Groups or programmes (such as return to work) should be facilitated and adapted to ensure accessibility for those with aphasia. Aphasia-specific participation activities, such as with communication partners from the statutory or voluntary sectors, should be available, together with equipment and training for supervised telerehabilitation. [2023]

4.44 Dysarthria

Dysarthria is a neurological motor speech impairment that is characterised by slow, weak, imprecise and/or uncoordinated movements of the speech musculature and may involve respiration, phonation, resonance, and/or oral articulation. Impaired muscular control affects speech intelligibility, which is usually described as slurred or blurred. Dysarthria is common in the early stages of stroke, and is often associated with dysphagia (see Section 4.26 Swallowing). [2016]

4.44 Recommendations

- A People with unclear or unintelligible speech after stroke should be assessed by a speech and language therapist to diagnose the problem and to explain the nature and implications to the person, their family/carers and the multidisciplinary team. [2016]
- B People with dysarthria after stroke which limits communication should:
 - be trained in techniques to improve the clarity of their speech;
 - be assessed for compensatory and augmentative communication techniques (e.g. letter board, communication aids) if speech remains unintelligible. [2016]
- C The communication partners (e.g. family/carers, staff) of a person with severe dysarthria after stroke should be trained in how to assist the person in their communication. [2016]

4.44 Sources

- A Working Party consensus
- B King and Gallegos-Santillan, 1999; Mackenzie and Lowit, 2007; Palmer and Enderby, 2007
- C King and Gallegos-Santillan, 1999

4.44 Evidence to recommendations

There are only two small RCTs on this topic, neither of which provides definitive evidence regarding treatment. Bowen et al (2012) included a planned subgroup of 66 people with dysarthria and Mackenzie et al (2014) was a feasibility study of 39 people. In the former, there was no significant difference between speech and language therapy and an attention control in the first few months after stroke, but a nested, qualitative study found that early, regular and frequent contact from a therapist or trained visitor was positively rated by people with stroke and their family/carers (Young et al, 2013). Mackenzie et al (2014) involved people with chronic dysarthria, and there was no difference in outcomes between individuals who received only speech practice and those who received speech practice and oro-motor exercises, although both groups improved over time. Participants were compliant with both interventions and many completed daily independent practice and reported an increase in confidence with treatment. There is little evidence to support the interventions in common use but there is some evidence of qualitative benefits (Palmer & Enderby, 2007). [2016]

4.45 Apraxia of speech

A few people with stroke have specific and relatively isolated impairment of the ability to plan and execute the multiple skilled oral motor tasks that underlie successful talking — this is apraxia of speech. It is usually associated with damage to the non-dominant hemisphere, and requires careful separation

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from aphasia and dysarthria. Interventions such as syllable level therapy and metrical pacing have been studied and the use of computers to increase intensity of practice has been suggested. [2016]

4.45 Recommendations

- A People with marked difficulty articulating words after stroke should be assessed for apraxia of speech and treated to maximise articulation of key words to improve speech intelligibility. [2016]
- People with severe communication difficulties but good cognitive and language function after stroke should be assessed and provided with alternative or augmentative communication techniques or aids to supplement or compensate for limited speech.

 [2016]

4.45 Sources

- A Stolk-Hornsveld et al, 2006; Connell et al, 2008; Working Party consensus
- B Working Party consensus

4.45 Evidence to recommendations

Studies in apraxia of speech are often small a Cochrane review (West et al, 2005) found no trials. There has been one subsequent crossover trial (Varley et al, 2016) which compared self-administered computerised communication therapy with a sham computerised treatment for people with chronic speech apraxia. Improvements in spoken word production (naming and repetition) were greater for the intervention group after the six week treatment but limited to trained single words. [2016]

Sensory effects of stroke

4.46 Introduction

A stroke can result in changes to any of the senses, including touch, vision, hearing, taste and smell. Little trial evidence exists regarding taste and smell, but evidence for changes to hearing after stroke is reported (Bamiou, 2015). Changes to vision or touch senses after stroke often lead to concerns regarding safety; visual impairment can significantly limit independence; and most sensory changes impact on aspects of social engagement. Hypersensitivity is also described across the senses, and may contribute to processing or attentional limitations. [2023]

4.47 Sensation

Sensory loss after stroke is a recognised impairment. Reported prevalence rates vary, with some estimating that up to 80% of people have loss or alteration in various somatic sensations – touch, position sense, temperature, pain, etc. (Doyle et al, 2010). The severity of sensory loss is associated with the extent of motor loss, and so the independent importance of sensory loss is difficult to quantify but one example of a standardised assessment tool is the Nottingham Sensory Assessment. Sensory retraining can be passive using electrical stimulation, or active involving repeated exposure to varying stimuli such as texture, temperature, joint position sense or shape. [2016]

4.47 Recommendations

- A People with stroke should be screened for altered sensation and if present, assessed for sensory impairments using standardised measures. [2016]
- B People with sensory loss after stroke should be trained in how to avoid injury to the affected body parts. [2016]

4.47 Sources

- A Stolk-Hornsveld et al, 2006; Connell et al, 2008; Working Party consensus
- B Working Party consensus

4.47 Evidence to recommendations

There is no good evidence to support any particular passive or active intervention for sensory impairment after stroke. Studies evaluating mirror therapy (Thieme et al, 2012) and electrical stimulation (Veerbeek et al, 2014b) show promising results but further research is needed into specific interventions as part of goal-directed rehabilitation (Pollock et al, 2014b). [2016]

4.48 Vision

Visual problems after stroke are common. In a multicentre prospective cohort study, 58% of people with stroke were found to have visual problems and about half of them, regardless of the visual impairment type, were visually asymptomatic (Rowe, 2017; Rowe et al, 2020). Visual problems include altered acuity, field loss such as hemianopia and disruption of eye movements causing diplopia, nystagmus, blurred vision and loss of depth perception (NICE, 2013b; Hepworth et al, 2015). Ocular stroke can cause visual loss due to central or branch retinal artery occlusion, but central visual loss can be due to coexistent ocular conditions. Perceptual disorders such as visual agnosia (Section 4.36 Perception) and neglect (Section 4.37 Neglect) should be distinguished from visual impairments. Visual disturbance has a significant impact on confidence, safety and independence and should therefore remain a focus for all members of the multidisciplinary team to support with identification, adjustment and adaptation. People with visual changes following stroke who were previously driving should be advised of the requirements and restrictions (see Section 4.14 Driving). [2023]

4.48 Recommendations

- A People with stroke should be screened for visual changes by a professional with appropriate knowledge and skills, using a standardised approach. [2023]
- B People with stroke should be:
 - assessed for visual acuity whilst wearing their usual glasses or contact lenses to check their ability to read newspaper text and see distant objects clearly;
 - examined for the presence of visual field deficit (e.g. hemianopia) and eye movement disorders (e.g. strabismus and motility deficit);
 - assessed using adapted visual tests for those with communication impairment. [2023]
- C People with altered vision, visual field defects or eye movement disorders after stroke should receive information, support and advice from an orthoptist and/or an ophthalmologist. [2023]
- D People reporting visual disturbance following stroke should be assessed by an occupational therapist to assess its impact on their ability to carry out functional tasks independently, their confidence and safety. [2023]
- People with visual loss due to retinal artery occlusion should be jointly managed by an ophthalmologist and a stroke physician. [2023]
- Multidisciplinary treatment programmes should be developed with an orthoptist and should include restorative and compensatory approaches to maximise safety and independence, in accordance with the person's presentation, goals and preferences. For people with visual field loss due to stroke, compensation training such as visual scanning or visual search training should be considered. [2023]
- G People with visual deficits following stroke should be advised about driving restrictions and receive accessible written information regarding the process of assessment and

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decision making. [2023]

4.48 Sources

- A-D Working Party consensus
- E-G Hanna and Rowe, 2017; Howard and Rowe, 2018, Liu et al, 2019, Pollock et al, 2019; Guideline Development Group consensus

4.48 Evidence to recommendations

All patients with stroke should be screened for visual impairment early after their stroke. Given that visual impairment is frequently asymptomatic, screening should be carried out by those with the appropriate knowledge and skills, such as an occupational therapist, or with specialist skills in visual assessment, such as an orthoptist or optometrist. These specialists can carry out further assessment and targeted treatment specific to the type of visual impairment (Rowe, 2017). One study found that it is feasible to undertake a visual screen for most patients within the first 3 days after stroke and a full visual assessment within 4 days (Rowe et al, 2019). Therefore, a visual screen could be completed in the same 72-hour time frame as other therapy assessments, given that visual problems can impact on delivery of other rehabilitation interventions. [2023]

An agreed visual care pathway is required to ensure appropriate access to a range of specialists, including orthoptists, ophthalmologists, optometrists and low vision rehabilitation workers.

Recommendations for orthoptist staffing levels in hyperacute and acute stroke units are set out in a British and Irish Orthoptists Society consensus document (British and Irish Orthoptic Society, 2021) which advises orthoptic staffing for hyperacute units as 0.4 WTE/10 beds, and for acute units as 0.2 WTE/10 beds. Specialists are required for identification of post-stroke visual impairment, diagnosis of eye movement disorders and the assessment of functional and driving implications (also see Section 4.14 Driving). [2023]

With regard to visual impairment of central vision and eye movement deficits, management may include interventions such as compensatory (e.g. head scanning training to adjust for poor eye movements), substitutive (e.g. magnifiers to increase print size) and restitutive (e.g. botulinum toxin/eye muscle surgery to correct strabismus) approaches, which require referral to specialist eye services. [2023]

For people with visual field loss after stroke, interventions are proposed to work by either compensating for the visual field defect by changing their behaviour or activity, substituting for the defect by using devices such as prisms to shift the field of view from the affected side, or restoring the visual field through repetitive stimulation of the affected field of vision. Compensatory training includes both visual scanning training, which involves repetitive symmetrical movements to each (right/left) side and visual search training, which involves repeatedly looking for (searching) for objects on each side. A Cochrane review found that there is limited, low quality evidence that compensatory training, and in particular visual scanning and search training, may be more beneficial than placebo, sham or control at improving quality of life, but not other outcomes (Hanna & Rowe, 2017; Howard & Rowe, 2018; Liu et al, 2019; Pollock et al, 2019). There is insufficient evidence to reach any generalised conclusions about the effect of substitutive interventions (prisms) or restitutive interventions as compared to placebo, control, or no treatment. There is low-quality evidence that prisms may cause minor adverse events (Pollock et al, 2019). All these areas warrant further research. [2023]

5 Long-term management and secondary prevention

5.0 Introduction

From the moment a person has a stroke or TIA they are at substantial increased risk of further events; 26% within 5 years of a first stroke and 39% by 10 years (Mohan et al, 2011). There are additional risks of about the same magnitude for other vascular events such as acute coronary syndrome. Stroke is not a single disease entity and in some cases (e.g. arterial dissection) the underlying pathology is associated with a relatively low risk of recurrence. Clinicians should seek to identify and reduce the risks that are specific to each individual. [2016]

The greatest risk of a vascular event is early after stroke or TIA and may be as high as 25% within three months, half of which is within the first four days (Johnston et al, 2000). Secondary prevention should therefore be commenced as soon as possible, and recent registry evidence suggests these measures can substantially reduce the risk of recurrent events (Amarenco & Steering Committee Investigators of the TIAregistry.org, 2016). Some of the recommendations for management in the acute phase, such as starting aspirin immediately after ischaemic stroke, are part of secondary prevention. This chapter assumes that all the recommendations made in Chapter 3 have been implemented, and the recommendations concerning early risk reduction are not repeated here. However, it is important that attention to secondary prevention is continued throughout the rehabilitation and recovery phase, as persistence with treatment is vital to long-term risk reduction. [2016]

Diet and lifestyle issues such as smoking, exercise and alcohol intake contribute significantly to cardiovascular risk, including the risk of first and recurrent stroke; their modification provides an important mechanism for influencing recurrent events. Much of the evidence here comes from primary prevention studies or from patients with coronary artery disease, with the presumption that the evidence translates to the secondary prevention of stroke based on the two conditions often sharing the same underlying pathology. Given the different causes of stroke, this will not always be the case. [2016]

People with stroke and their family/carers often face substantial challenges returning to life in the home, community and workplace. The huge variety of individual circumstances and the complex nature of the outcomes concerned complicate the design, conduct and interpretation of research into living with the long-term effects of stroke. As a consequence, the evidence to guide recommendations here is more difficult to interpret; this does not diminish the importance of the topics under consideration nor the need for expert guidance on best practice. [2016]

5.1 A comprehensive and personalised approach

Ensuring the identification and modification of all risk factors, including lifestyle issues, should lead to more effective secondary prevention of stroke and other vascular events. This section covers advice and general principles of management – specific interventions are covered in subsequent sections. The clinician's approach to the modification of risk factors through lifestyle changes or medication should observe the principles of shared decision making recommended in NICE guidance (NICE, 2021c) and these principles apply to all the following sections. [2023]

5.1 Recommendations

A People with stroke or TIA should receive a comprehensive and personalised strategy for

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- vascular prevention including medication and lifestyle factors, which should be implemented as soon as possible and should continue long-term. [2016]
- B People with stroke or TIA should receive information, advice and treatment for stroke, TIA and vascular risk factors which is:
 - given first in the hospital or clinic setting;
 - reinforced by all health professionals involved in their care;
 - provided in an appropriate format. [2016]
- C People with stroke or TIA should have their risk factors and secondary prevention reviewed and monitored at least once a year in primary care. [2016]
- D People with stroke or TIA who are receiving medication for secondary prevention should:
 - receive information about the reason for the medication, how and when to take it and common side effects;
 - receive verbal and written information about their medicines in an appropriate format;
 - be offered compliance aids such as large-print labels, non-childproof tops and dosette boxes according to their level of manual dexterity, cognitive impairment, personal preference and compatibility with safety in the home;
 - be aware of how to obtain further supplies of medication;
 - have their medication regularly reviewed;
 - have their capacity to take full responsibility for self-medication assessed (including cognition, manual dexterity and ability to swallow) by the multidisciplinary team as part of their rehabilitation prior to the transfer of their care out of hospital. [2016]

5.1 Sources

- A Working Party consensus
- B Ovbiagele et al, 2004; Maasland et al, 2007; Sit et al, 2007
- C, D Working Party consensus

5.2 Identifying risk factors

The risk of recurrent vascular events may vary significantly between individuals according to underlying pathology, co-morbidities and lifestyle factors. This guideline applies to the vast majority of people with TIA and stroke, including those not admitted to hospital; some of the recommendations may not be appropriate for the small minority of people with unusual stroke pathologies. [2016]

5.2 Recommendations

- A People with stroke or TIA for whom secondary prevention is appropriate should be investigated for risk factors as soon as possible within 1 week of onset. [2016]
- B Provided they are eligible for any resultant intervention, people with stroke or TIA should be investigated for the following risk factors:
 - ipsilateral carotid artery stenosis;
 - atrial fibrillation;
 - structural cardiac disease. [2016]
- C People with evidence of non-symptomatic cerebral infarction on brain imaging (silent cerebral ischaemia) should have an individualised assessment of their vascular risk and secondary prevention. [2016]

5.2 Source

A-C Working Party consensus

5.2 Implications

The identification of risk factors for stroke and TIA should be part of the assessment during the acute phase. Regular review of risk factors and secondary prevention in primary care may require additional resources. [2016]

5.3 Carotid artery stenosis

Atheroma and stenosis of the carotid arteries is commonly associated with stroke and TIA, and surgical or radiological interventions (endarterectomy or stenting) have been used to reduce the risk of recurrent ipsilateral stroke. [2016]

5.3 Recommendations

- A Following stroke or TIA, the degree of carotid artery stenosis should be reported using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method. [2016]
- B People with non-disabling carotid artery territory stroke or TIA should be considered for carotid revascularisation, and if they agree with intervention:
 - they should have carotid imaging (duplex ultrasound, MR or CT angiography)
 performed urgently to assess the degree of stenosis;
 - if the initial test identifies a relevant severe stenosis (greater than or equal to 50%), a second or repeat non-invasive imaging investigation should be performed to confirm the degree of stenosis. This confirmatory test should be carried out urgently to avoid delaying any intervention. [2016]
- C People with non-disabling carotid artery territory stroke or TIA should be considered for carotid revascularisation if the symptomatic internal carotid artery has a stenosis of greater than or equal to 50%. The decision to offer carotid revascularisation should be:
 - based on individualised risk estimates taking account of factors such as the time from the event, gender, age and the type of qualifying event;
 - supported by risk tables or web-based risk calculators (e.g. the Oxford University Stroke Prevention Research Unit calculator, https://www.ndcn.ox.ac.uk/divisions/cpsd/carotid-stenosis-tool-1). [2016]
- D People with non-disabling carotid artery territory stroke or TIA and a carotid stenosis of less than 50% should not be offered revascularisation of the carotid artery. [2016]
- E Carotid endarterectomy for people with symptomatic carotid stenosis should be:
 - the treatment of choice, particularly for people who are 70 years of age and over or for whom the intervention is planned within seven days of stroke or TIA;
 - performed in people who are neurologically stable and who are fit for surgery using either local or general anaesthetic according to the person's preference;
 - performed as soon as possible and within 1 week of first presentation;
 - deferred for 72 hours in people treated with intravenous thrombolysis;
 - only undertaken by a specialist surgeon in a vascular centre where the outcomes of carotid surgery are routinely audited. [2016]
- F Carotid angioplasty and stenting should be considered for people with symptomatic carotid stenosis who are:
 - unsuitable for open surgery (e.g. high carotid bifurcation, symptomatic re-stenosis

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following endarterectomy, radiotherapy-associated carotid stenosis);

or

- less than 70 years of age and who have a preference for carotid artery stenting.
 The procedure should only be undertaken by an experienced operator in a vascular centre where the outcomes of carotid stenting are routinely audited. [2016]
- G People who have undergone carotid revascularisation should be reviewed postoperatively by a stroke physician to optimise medical aspects of vascular secondary prevention. [2016]
- H Patients with atrial fibrillation and symptomatic internal carotid artery stenosis should be managed for both conditions unless there are contraindications. [2016]

5.3 Sources

- A Working Party consensus
- B Wardlaw et al, 2006
- C, D Rothwell et al, 2004, 2005; Rerkasem and Rothwell, 2011
- E Rerkasem and Rothwell, 2011; Bonati et al, 2012; Vaniyapong et al, 2013; Rantner et al, 2013; Working Party consensus
- F Economopoulos et al, 2011; Bonati et al, 2015; Working Party consensus
- G, H Working Party consensus

5.3 Evidence to recommendations

The principal evidence for carotid endarterectomy for people with recent symptoms is from the European Carotid Surgery Trial (ECST) and the North American Symptomatic Carotid Endarterectomy Trial (NASCET) (Rothwell et al, 2003b). Only people with non-disabling stroke or TIA were included in these trials and the benefits of surgery cannot be assumed to apply to those with more disabling strokes. People with possible cardioembolism were also excluded. When allowance is made for the different methods used to measure stenosis from angiograms, the two trials report consistent findings. To avoid confusion regarding the degree of stenosis the technique used in NASCET should be used (the ratio of the diameter of the residual lumen at the point of maximum narrowing to that of the more distal internal carotid artery, expressed as a percentage). In a pooled analysis of the individual data from 6,092 patients, carotid endarterectomy reduced the 5-year absolute risk of ipsilateral ischaemic stroke by 16.0% in patients with 70–99% stenosis, and by 4.6% in patients with 50–69%. There was no benefit for patients with 30–49% stenosis and surgery increased the risk in patients with less than 30% stenosis. There was no evidence of benefit for patients with a near-occlusion. In these trials conducted in the 1980s the operative risk of stroke (ocular or cerebral) and death within 30 days of endarterectomy was 7%. [2016]

There is evidence of considerable heterogeneity in individual risk according to age, gender, degree of stenosis, presenting symptom, time from presenting symptom and presence of plaque ulceration (Rothwell et al, 2004). Prognostic models based on these characteristics have been derived which may be useful in the decision making process (Rothwell et al, 2005). These models are based on trial data which are now over 20 years old and with improvements in other treatments these models are likely to overestimate the absolute risk of stroke. Modified prognostic models incorporating corrections to allow for improvements in 'best medical therapy' have been developed (e.g. the Carotid Artery Risk score - www.ecst2.com/), but await validation. [2016]

In a systematic review of operative risks in relation to timing of surgery, no statistically significant difference for early versus late surgery was identified for patients with stable stroke (Rerkasem & Rothwell, 2009). In patients undergoing emergency surgery the pooled absolute risk of stroke and death

was 20.2% for those with 'stroke-in-evolution' (fluctuating or progressive deficit) and 11.4% for those with crescendo TIA (more than 2 episodes in a week), significantly higher than for those undergoing non-emergency surgery (odds ratio [OR] 4.6). Such patients are likely to be at increased risk if surgery is not performed, but given these risks and the effectiveness of medical management it cannot be assumed that emergency surgery is beneficial in neurologically unstable patients. The outcome from carotid endarterectomy is not significantly influenced by whether the procedure is carried out under local or general anaesthesia (Vaniyapong et al, 2013), and if the person has a particular preference, this should be taken into account. [2016]

Compared to surgical endarterectomy, endovascular therapy involving carotid angioplasty and stenting is associated with an increased risk of stroke of any severity or death (Bonati et al, 2012). This increased risk is modified by age, with no difference in stroke or death when the comparison is confined to those below 70 years of age (International Carotid Stenting Study investigators, 2010). Long-term follow-up identifies an excess of procedure-related and non-disabling strokes with endovascular therapy (Bonati et al, 2015). By contrast, carotid endarterectomy is associated with an excess of cranial nerve palsy and myocardial infarction (Bonati et al, 2012). For endovascular procedures undertaken within the first few days after symptom onset there is an excess of disabling and fatal, as well as non-disabling strokes in comparison to carotid endarterectomy (Rantner et al, 2013). [Rantner et al, 2013). [2016]

There is no high quality evidence to guide decision making regarding the timing and indications for carotid revascularisation in patients presenting with ischaemic stroke who have been treated with intravenous thrombolysis. A number of case series have been reported with small numbers and few outcome events (Naylor, 2015). Activation of the coagulation system and fibrin formation occurs following alteplase therapy with changes peaking at 1 to 3 hours but detectable for up to 72 hours (Fassbender et al, 1999). It is not clear what impact if any these changes in the coagulation system may have on the balance of risks and benefits, but in the absence of high quality data it would seem reasonable to advise caution if considering surgery within 72 hours of intravenous thrombolysis. [2016]

5.3 Implications

Vascular surgery services should offer the option to perform carotid endarterectomy surgery under local or general anaesthetic. Multidisciplinary teams should include a carotid interventionist able to advise on and deliver carotid artery angioplasty and stenting. [2016]

5.4 Blood pressure

Blood pressure (BP) is the pre-eminent treatable risk factor for first and recurrent stroke. It is estimated to cause about 50% of ischaemic strokes and is the principal risk factor for intracerebral haemorrhage. The relationship to cerebral perfusion pressure means that changes in BP in people with hyperacute stroke may influence the extent of brain damage. Treatment recommendations therefore differ when comparing hyperacute management (Section 3.5 Management of ischaemic stroke and Section 3.6 Management of intracerebral haemorrhage) with long-term secondary prevention, with this section concentrating on the latter. [2016]

5.4 Recommendations

A People with stroke or TIA should have their blood pressure checked, and treatment should be initiated or increased as tolerated to consistently achieve a clinic systolic blood pressure below 130 mmHg, equivalent to a home systolic blood pressure below 125 mmHg. The exception is for people with severe bilateral carotid artery stenosis, for whom a systolic blood pressure target of 140–150 mmHg is appropriate. Concern about potential adverse effects should not impede the initiation of treatment that prevents stroke, major cardiovascular events or mortality. [2023]

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- B For people with stroke or TIA aged 55 or over, or of African or Caribbean origin at any age, antihypertensive treatment should be initiated with a long-acting dihydropyridine calcium-channel blocker or a thiazide-like diuretic. If target blood pressure is not achieved, an angiotensin converting enzyme inhibitor or angiotensin II receptor blocker should be added. [2016]
- C For people with stroke or TIA not of African or Caribbean origin and younger than 55 years, antihypertensive treatment should be initiated with an angiotensin converting enzyme inhibitor or an angiotensin II receptor blocker. [2016]
- D People with stroke or TIA should have blood pressure-lowering treatment initiated prior to the transfer of care out of hospital or at 2 weeks, whichever is the soonest, or at the first clinic visit for people not admitted. [2016]
- People with stroke or TIA should have their blood pressure-lowering treatment monitored frequently in primary care and increased to achieve target blood pressure as quickly and safely as tolerated. People whose blood pressure remains above target despite treatment should be checked for medication adherence at each visit before escalation of treatment, and people who do not achieve their target blood pressure despite escalated treatment should be referred for a specialist opinion. Once blood pressure is controlled to target, people taking antihypertensive treatment should be reviewed at least annually. [2023]
- F In people with stroke being treated with antihypertensive agents to reduce recurrent stroke risk, management guided by home or ambulatory BP monitoring should be considered, in order to improve treatment compliance and BP control. [2023]
- People with stroke using home BP monitoring should use a validated device with an appropriate measurement cuff and a standardised method. They (or where appropriate, their family/carer) should receive education on how to use the device, the implications of readings for management, and be provided with ongoing support, particularly if they have anxiety or cognitive and physical disability after stroke. [2023]

5.4 Sources

- A Rothwell et al, 2003a; Ettehad et al, 2016
- B PROGRESS Collaborative Group, 2001; NICE, 2022a
- C NICE, 2022a
- D Rothwell et al, 2007; NICE, 2022a; Working Party consensus
- E Rothwell et al, 2007; NICE, 2022a; Guideline Development Group consensus
- F Ovaisi et al, 2011; Kerry et al, 2013; Hanley et al, 2015; Guideline Development Group consensus
- G Kerry et al, 2013; Breaux-Shropshire et al, 2015

5.4 Evidence to recommendations

There is high quality evidence that BP reduction after stroke or TIA prevents further vascular events including recurrent ischaemic and haemorrhagic stroke (PROGRESS Collaborative Group, 2001). In PROGRESS, giving two more BP-lowering medicines to people after stroke or TIA, 52% of whom were classified as normotensive, reduced BP by 12/5 mmHg and resulted in a 42% reduction in recurrent stroke and 35% fewer major coronary events. A net benefit was seen for those with baseline BP levels as low as 115/75 with the lowest risk of recurrent stroke seen in those achieving the lowest follow-up BP levels. There was no evidence of increased stroke risk at lower BP (Arima et al, 2006). A meta-analysis of 123 studies and 613,815 participants found BP-lowering treatment significantly reduced cardiovascular events and death in proportion to the magnitude of BP reduction achieved, with no

differences in the proportional benefits between trials with lower (below 130 mmHg) or higher systolic BP at baseline (Ettehad et al, 2016). There was also no difference in the proportional risk reductions for major cardiovascular events by baseline medical conditions, but calcium-channel blockers were found to be superior to other medication classes in the prevention of stroke. Overall, a 10 mmHg reduction in systolic BP reduced the risk of cardiovascular disease by 20% and stroke by 27%. [2016]

In the Secondary Prevention of Small Subcortical Strokes (SPS3) trial targeting a systolic BP of below 130 mmHg in patients with recent lacunar stroke, reductions in the rate of all stroke, disabling or fatal stroke and the composite outcome of myocardial infarction or vascular death were not significant, but the rate of cerebral haemorrhage was reduced and the lower target was well tolerated (SPS Study Group, 2013). In addition to the PROGRESS trial (2001), further evidence to support the benefit of a SBP target of below 130/80 mmHg in reducing recurrent stroke was observed in a clinical trial and as a secondary outcome in another study (Mant et al, 2016; Kitagawa et al, 2019). Accompanying meta-analyses (Thomopoulos et al, 2015, 2016), have shown that lowering BP to below 130/80 mmHg, if tolerated, is beneficial in preventing stroke and major cardiovascular events. Two analyses with greater statistical power that included the Systolic Blood pressure Intervention trial (SPRINT research group, 2015) have shown that intensive treatment even to below 120 mmHg may be beneficial (Bangalore et al, 2017; Bundy et al, 2017). However, in SPRINT, patients with a history of stroke were excluded and the trial was not powered to assess a difference in stroke incidence (a secondary outcome). A U-shaped BPcardiovascular risk relationship was observed both in the intensive and standard treatment groups in SPRINT, but randomised comparisons found a significant cardiovascular and mortality benefit for more versus less intensive treatment at each level of baseline BP (Beddhu et al, 2018). [2023]

There is uncertainty regarding the best time to start antihypertensive therapy following ischaemic stroke. Whilst BP can be successfully and safely reduced in the acute phase, there is no evidence that such early intervention results in long-term benefits (Bath & Krishnan, 2014). For patients admitted with stroke who are already taking antihypertensive medication, treatment can be safely withheld until patients are medically and neurologically stable and have suitable oral or enteral access (Bath et al, 2015). Unless there is severe hypertension or treatment is required for acute intracerebral haemorrhage (Section 3.6 Management of intracerebral haemorrhage) or to facilitate intravenous thrombolysis treatment (Section 3.5 Management of ischaemic stroke) antihypertensive medication should generally be initiated prior to the transfer of care out of hospital or at 2 weeks, whichever is the soonest, or at the first clinic visit for people not admitted. [2016]

Home BP monitoring may usefully contribute to hypertension management, but there are few trials of home BP monitoring in stroke. Kerry et al (2013) conducted a randomised trial of home BP monitoring with nurse-led support versus standard care in people with hypertension and a history of stroke. More changes to antihypertensive treatment were made in the intervention group than controls (60% v. 47%; p=0.02), but the fall in systolic BP from baseline did not differ significantly between the two groups. A post-hoc analysis showed a reduction of 6 mm Hg in systolic BP at 12 months in the intervention group (Kerry et al, 2013). A prospective cohort study found that half of people with stroke offered a BP monitor without nurse support continued monthly use for up to 18 months, but around a quarter of participants reported a disability that made it difficult to measure their BP unaided (Ovaisi et al, 2011). [2023]

Studies suggest that treatment based on home BP monitoring may reduce vascular risk, principally through improving long term compliance (Ovaisi et al, 2011; Kerry et al, 2013; Hanley et al, 2015). Further evidence is required to determine which people with stroke benefit, and the type of equipment (semi-automated v. automated), timing of measurement, ideal target and duration. Systematic reviews emphasise that attention should be given to correct measurement and a clear management strategy for the patient (and carer as appropriate). It is also recommended that the pulse rhythm is recorded at each clinical contact to detect non-symptomatic atrial fibrillation (Cappuccio et al, 2004; Bray et al, 2010; Glynn et al, 2010; NICE, 2021a). [2023]

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5.4 Implications

There should be a move away from the concept of treating hypertension and towards the concept of modifying BP as a risk factor. It is appropriate to lower BP in patients who previously would have been considered normotensive. [2016]

5.5 Lipid modification

Raised lipid levels, especially hypercholesterolaemia, are an important modifiable risk factor for cardiovascular events, especially myocardial infarction. Lipid-lowering treatment is an effective intervention for primary and secondary prevention of vascular events, including stroke. [2016]

5.5 Recommendations

- A People with ischaemic stroke or TIA should be offered personalised advice and support on lifestyle factors to reduce cardiovascular risk, including diet, physical activity, weight reduction, alcohol moderation and smoking cessation. [2023]
- B People with ischaemic stroke or TIA should be offered treatment with a statin unless contraindicated or investigation of their stroke or TIA confirms no evidence of atherosclerosis. Treatment should:
 - begin with a high-intensity statin such as atorvastatin 80 mg daily. A lower dose should be used if there is the potential for medication interactions or a high risk of adverse effects:
 - be with an alternative statin at the maximum tolerated dose if a high-intensity statin is unsuitable or not tolerated. [2023]
- C Lipid-lowering treatment for people with ischaemic stroke or TIA and evidence of atherosclerosis should aim to reduce fasting LDL-cholesterol to below 1.8 mmol/L (equivalent to a non-HDL-cholesterol of below 2.5 mmol/L in a non-fasting sample). If this is not achieved at first review at 4-6 weeks, the prescriber should:
 - discuss adherence and tolerability;
 - optimise dietary and lifestyle measures through personalised advice and support;
 - consider increasing to a higher dose of statin if this was not prescribed from the outset;
 - consider adding ezetimibe 10 mg daily;
 - consider the use of additional agents such as injectables (inclisiran or monoclonal antibodies to PCSK9) or bempedoic acid (for statin-intolerant people taking ezetimibe monotherapy);
 - continue to escalate lipid-lowering therapy (in combination if necessary) at regular intervals in order to reduce LDL-cholesterol to below 1.8 mmol/L. [2023]
- D People with ischaemic stroke or TIA in whom investigation confirms no evidence of atherosclerosis should be assessed for lipid-lowering therapy on the basis of their overall cardiovascular risk. [2023]
- People with intracerebral haemorrhage should be assessed for lipid-lowering therapy on the basis of their overall cardiovascular risk and the underlying cause of the haemorrhage.

 [2023]
- In people with ischaemic stroke or TIA below 60 years of age with very high cholesterol (below 30 years with total cholesterol above 7.5 mmol/L or 30 years or older with total cholesterol concentration above 9.0 mmol/L) consider a diagnosis of familial hypercholesterolaemia. [2023]
- G In people with ischaemic stroke or TIA of presumed atherosclerotic cause below 60 years

of age, consider the measurement of lipoprotein(a) and specialist referral if raised above 200 nmol/L. [2023]

5.5 Sources

- A-D NICE, 2016a, b; 2021b, d; 2023a; Amarenco et al, 2020; NHS England Accelerated Access Collaborative, 2021; Lee et al, 2022
- E Vergouwen et al, 2008; Guideline Development Group consensus
- F NICE, 2023b
- G HEART UK Medical Scientific and Research Committee, 2019

5.5 Evidence to recommendations

The benefit of lipid-lowering therapy with statins in reducing cardiovascular events and mortality has been confirmed in RCTs and meta-analyses both for individuals with cardiovascular disease and specifically those with cerebrovascular disease. The Cholesterol Treatment Trialists' Collaboration (Baigent et al, 2005) showed that for each 1.0 mmol/L reduction in LDL-cholesterol with statin therapy there was a relative risk reduction of 12% in all-cause mortality and a 21% reduction in major cardiovascular events, including a 17% reduction in fatal or non-fatal stroke (Baigent et al, 2005). The SPARCL trial investigated the effect of atorvastatin 80 mg daily in patients with TIA or stroke in the preceding 6 months and demonstrated a relative risk reduction of 15% in stroke and 35% in major coronary events with treatment (Amarenco et al, 2006). More recently, the Treat Stroke to Target Trial (TSTT) demonstrated that patients with ischaemic stroke or TIA in whom investigation confirmed evidence of atherosclerosis had a lower risk of subsequent cardiovascular events with a target LDLcholesterol of below 1.8 mmol/L than those with a higher target of 2.3-2.8 mmol/L (Amarenco et al, 2020). 'Evidence of atherosclerosis' in TSTT included intracranial or extracranial artery stenosis, aortic atheroma or known coronary artery disease. A meta-analysis (11 RCTs of 20,163 people with stroke, including TSTT) compared intensive versus less intensive LDL-cholesterol lowering for secondary prevention (Lee et al, 2022). Intensive lowering over 4 years reduced the absolute risk of stroke (of any type) by 1.2%, and major cardiovascular events by 2.8%, but increased haemorrhagic stroke by 0.4%. Although small numerical increases were seen in both intracranial haemorrhage and newly diagnosed diabetes in the lower-target group in TSTT, these were not statistically significant and were more than outweighed by the benefits in prevention of major cardiovascular events. [2023]

In primary and secondary prevention studies, lowering LDL-cholesterol by 1.0 mmol/L leads to a relative risk reduction of 21% in major cardiovascular events, 9% in total mortality, and 15% in stroke (of any type) irrespective of baseline cholesterol and gender (Fulcher et al, 2015). Thus the decision to initiate treatment should be determined by a person's absolute cardiovascular risk rather than their cholesterol level. NICE clinical guideline CG181 for lipid modification (2021d) provides recommendations consistent with the findings from SPARCL and TSTT, and recommends high-intensity statin therapy with atorvastatin 80 mg daily with a lower starting dose for people at high risk of adverse events or medication interactions, with subsequent guidance identifying the role of newer agents (NICE, 2016c, d; NHS England Accelerated Access Collaborative, 2021; NICE, 2021b, d, 2022c). The Guideline Development Group emphasizes the importance of characterising the finding of atherosclerosis in communications to primary care about long-term risk factor management so the correct treatment strategy can be followed. The recommendations also reiterate NICE and specialist society guidance on when to suspect familial hypercholesterolaemia, or lipoprotein abnormalities requiring specialist lipid clinic referral. [2023]

One randomised trial of icosapent ethyl in people with elevated triglycerides on optimal statin therapy (Bhatt et al, 2019) showed a significant reduction in major cardiovascular events that was greater than accounted for by the observed reduction in triglycerides (NICE, 2022c). For cardiovascular prevention after ischaemic stroke the emphasis remains on achieving LDL-cholesterol reduction to target, but

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people with raised triglycerides should be reviewed for lifestyle interventions such as alcohol reduction, weight reduction and diabetes control, and those with persistent severe hypertriglyceridaemia (greater than 10 mmol/L) should be referred to a lipid clinic to consider treatment to reduce the risk of pancreatitis. [2023]

5.6 Antiplatelet treatment

Antiplatelet treatment is one of the most important interventions for reducing the risk of recurrent vascular events including stroke. Most long-term evidence relates to aspirin, although combination antiplatelet therapy may offer the prospect of greater efficacy, tempered by an increased risk of bleeding. [2016]

5.6 Recommendations

- A For long-term prevention of vascular events in people with ischaemic stroke or TIA without paroxysmal or permanent atrial fibrillation:
 - clopidogrel 75 mg daily should be the standard antithrombotic treatment;
 - aspirin 75 mg daily should be used for those who are unable to tolerate clopidogrel;

if a patient has a recurrent cardiovascular event on clopidogrel, clopidogrel resistance may be considered.

The combination of aspirin and clopidogrel is not recommended for long-term prevention of vascular events unless there is another indication e.g. acute coronary syndrome, recent coronary stent. [2023]

- B People with ischaemic stroke with acute haemorrhagic transformation should be treated with long-term antiplatelet or anticoagulant therapy unless the prescriber considers that the risks outweigh the benefits. [2023]
- Patients who have a spontaneous (non-traumatic) intracerebral haemorrhage (ICH) whilst taking an antithrombotic (antiplatelet or anticoagulant) medication for the prevention of occlusive vascular events may be considered for restarting antiplatelet treatment beyond 24 hours after ICH symptom onset. [2023]
- D Clinicians should consider the baseline risks of recurrent ICH and occlusive vascular events when making a decision about antiplatelet use after ICH outside randomised controlled trials. [2023]
- E Wherever possible, patients with spontaneous (non-traumatic) ICH and a co-existent indication for antithrombotic medication treatment should be encouraged to participate in randomised controlled trials of antithrombotic therapy. [2023]

5.6 Sources

- A NICE, 2010a; Guideline Development Group consensus
- B Guideline Development Group consensus
- C Al-Shahi Salman et al, 2019, 2021; Guideline Development Group consensus
- D Charidimou et al, 2017; Li et al, 2021
- E Guideline Development Group consensus

5.6 Evidence to recommendations

The Antithrombotic Trialists' Collaboration (2002) demonstrated a 22% reduction in the odds of a vascular event (myocardial infarction, stroke or vascular death) in patients with a previous stroke or TIA treated with antiplatelet medication. Comparative trials such as CAPRIE (CAPRIE Steering Committee, 1996), ESPRIT (ESPIRIT Study Group, 2006) and PROFESS (Sacco et al, 2008) show that aspirin plus

modified-release dipyridamole and clopidogrel monotherapy are equally effective, with both options superior to aspirin monotherapy. **[2016]**

The combination of aspirin and clopidogrel has been compared to clopidogrel monotherapy in patients with recent TIA or stroke (Diener et al, 2004). The combination was not superior to clopidogrel alone, with evidence of increased adverse effects particularly bleeding. There is evidence that even in short-term use the combination carries an increased risk of bleeding, particularly in aspirin-naive individuals (Geraghty et al, 2010). The use of combination antiplatelet treatment within the first few weeks after stroke or TIA is addressed in Section 3.3 Management of TIA and minor stroke – treatment and vascular prevention and Section 3.5 Management of ischaemic stroke. [2016]

RESTART was a UK multicentre open label pilot phase RCT (RESTART Collaboration, 2019) that included 537 participants in the UK with spontaneous (non-traumatic) intracerebral haemorrhage (ICH) who were taking an antithrombotic medication (antiplatelet or anticoagulant) for the prevention of occlusive vascular events. Participants were allocated at random to either start or avoid antiplatelet treatment, with a median time from ICH symptom onset to randomisation of 76 days (IQR 29-146). The primary outcome was recurrent ICH. Over a median follow-up period of two years, 4% of those allocated to antiplatelet therapy had recurrent ICH compared with 9% of those allocated to avoid antiplatelet therapy [adjusted hazard ratio 0.51, 95% CI 0.25 to 1.03; p=0.06]. There was no difference in major occlusive vascular events, but a reduction in all serious vascular events, as defined by the Antithrombotic Trialists' Collaboration, was reported. The results were consistent across subgroups including ICH location, time since symptom onset, type of antiplatelet medication, participant age, and history of atrial fibrillation, although the Guideline Development Group noted the lack of statistical power to test for these interactions. [2023]

After extended follow-up to five years (Al-Shahi Salman et al, 2021), ICH affected 22 of 268 participants (8.2%) allocated to antiplatelet therapy compared with 25 of 268 participants (9.3%) allocated to avoid antiplatelet therapy (adjusted hazard ratio, 0.87; 95%CI 0.49 to 1.55; p=0.64). A major vascular event affected 72 participants (26.8%) allocated to antiplatelet therapy compared with 87 participants (32.5%) allocated to avoid antiplatelet therapy (hazard ratio, 0.79; 95%CI 0.58 to 1.08; p=0.14). A brain imaging substudy of the RESTART trial (n=254 with MRI; Al-Shahi Salman et al, 2019) found no evidence of more frequent recurrent ICH in patients with two or more cerebral microbleeds compared to one or no cerebral microbleeds (adjusted hazard ratio 0.30 [95% CI 0.08 to 1.13] v. 0.77 [0.13 to 4.61]; p-interaction=0.41), nor in subgroups according to cerebral microbleed burden or strictly lobar location (that might indicate cerebral amyloid angiopathy [CAA]). [2023]

The Guideline Development Group considered the RESTART trial to be well conducted and of high quality although the small sample size limited statistical power and precision. There were also concerns regarding possible selection bias (average ICH volume of 4 mL smaller than most ICH seen in clinical practice) which might limit generalisability. There were few participants with probable CAA, a subgroup which appears to be at highest risk of ICH (Charidimou et al, 2017). The group also noted that the evidence from RESTART cannot be applied to patients very soon after ICH symptom onset (only 21 participants (4%) were randomised in the first week after ICH while most (74%) were randomised at or beyond 30 days), although RESTART appears to give some reassurance that restarting antiplatelet therapy after ICH may be safe with regard to recurrent ICH, the consensus was that the evidence was insufficient to provide a strong recommendation. The group also identified some observational cohort studies, but due to methodological limitations (including risks of selection bias and confounding by indication) none was judged to provide sufficiently strong evidence to inform a recommendation about antiplatelet therapy after ICH. Further randomised trials are ongoing or planned and clinicians and patients are strongly encouraged to participate in these wherever possible. [2023]

In practice clinicians will continue to make case-by-case decisions based on their understanding of the baseline risk of future events including recurrent ICH and vaso-occlusive events. For example, in

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observational studies the recurrence risk for lobar ICH is consistently higher than for deep ICH (Li et al, 2021b) while the risk of ICH recurrence in patients with probable CAA is substantially higher than in those without probable CAA (Charidimou et al, 2017). Haemorrhagic MRI biomarkers of CAA, including cerebral microbleeds and cortical superficial siderosis, are also associated with an increased risk of ICH recurrence. Clinicians are recommended to take these prognostic factors into account when deciding whether to recommend antiplatelet medication after ICH. [2023]

5.7 Anticoagulation

Treatment with anticoagulation after TIA or ischaemic stroke is now usually restricted to long-term secondary prevention of cardioembolic stroke due to atrial fibrillation (AF), intracardiac thrombus, valvular heart disease or mechanical heart valve replacement. [2023]

For over 50 years, the oral anticoagulant of choice has been a vitamin K antagonist (VKA) such as warfarin. Direct oral anticoagulants (DOACs; also known as non-vitamin K oral anticoagulants [NOACs]) which directly inhibit thrombin or factor Xa offer a number of practical advantages for both patient and prescriber and their use has been recommended as first-line treatment for stroke prevention in various European guidelines for the management of AF and stroke prevention (Klijn et al, 2019; Hindricks et al, 2021; Steffel et al, 2021). [2023]

5.7 Recommendations

- A For people with ischaemic stroke or TIA and paroxysmal, persistent or permanent atrial fibrillation (AF: valvular or non-valvular) or atrial flutter, oral anticoagulation should be the standard long-term treatment for stroke prevention. Anticoagulant treatment:
 - should not be given if brain imaging has identified significant haemorrhage;
 - should not be commenced in people with severe hypertension (clinic blood pressure of 180/120 or higher), which should be treated first;
 - may be considered for patients with moderate-to-severe stroke from 5-14 days after onset. Wherever possible these patients should be offered participation in a trial of the timing of initiation of anticoagulation after stroke. Aspirin 300 mg daily should be used in the meantime;
 - should be considered for patients with mild stroke earlier than 5 days if the prescriber considers the benefits to outweigh the risk of early intracranial haemorrhage. Aspirin 300 mg daily should be used in the meantime;
 - should be initiated within 14 days of onset of stroke in all those considered appropriate for secondary prevention;
 - should be initiated immediately after a TIA once brain imaging has excluded haemorrhage, using an agent with a rapid onset (e.g. DOAC in non-valvular AF or subcutaneous low molecular weight heparin while initiating a VKA for those with valvular AF);
 - should include measures to reduce bleeding risk, using a validated tool to identify modifiable risk factors. [2023]
- B First-line treatment for people with ischaemic stroke or TIA due to non valvular AF should be anticoagulation with a DOAC. [2023]
- C People with ischaemic stroke or TIA in sinus rhythm should not receive anticoagulation unless there is another indication. [2023]
- D People with ischaemic stroke or TIA due to valvular/rheumatic AF or with mechanical heart valve replacement, and those with contraindications or intolerance to DOAC

- treatment, should receive anticoagulation with adjusted-dose warfarin (target INR 2.5, range 2.0 to 3.0) with a target time in the therapeutic range of greater than 72%. [2023]

 For people with cardioembolic TIA or stroke for whom treatment with anticoagulation is considered inappropriate because of a high risk of bleeding:
 - antiplatelet treatment should not be used as an alternative when there are absolute contraindications to anticoagulation (e.g. undiagnosed bleeding);
 - measures should be taken to reduce bleeding risk, using a validated tool to identify modifiable risk factors. If after intervention for relevant risk factors the bleeding risk is considered too high for anticoagulation, antiplatelet treatment should not be routinely used as an alternative;
 - a left atrial appendage occlusion device may be considered as an alternative,
 provided the short-term peri-procedural use of antiplatelet therapy is an acceptable risk. [2023]
- F People with cardioembolic TIA or stroke for whom treatment with anticoagulation is considered inappropriate for reasons other than the risk of bleeding may be considered for antiplatelet treatment to reduce the risk of recurrent vaso-occlusive disease. [2023]
- People who initially present with recurrent TIA or stroke should receive the same antithrombotic treatment as those who have had a single event. More intensive antiplatelet therapy or anticoagulation treatment should only be given as part of a clinical trial or in exceptional clinical circumstances. [2023]

5.7 Sources

- A EAFT Study Group, 1993; Miller et al, 2012; Paciaroni et al, 2015; Gioia et al, 2016; Klijn et al, 2019; Hindricks et al, 2020; Labovitz et al, 2021; Steffel et al, 2021; De Marchis et al, 2022; Guideline Development Group consensus
- B Guideline Development Group consensus
- C De Schryver et al, 2012; Guideline Development Group consensus
- D EAFT Study Group, 1993; Miller et al, 2012; Eikelboom et al, 2013; Ruff et al, 2014; Graham et al, 2015; Makam et al, 2018; Hirschl and Kundi, 2019; Hindricks et al, 2020; Shen et al, 2020; Steffel et al, 2021; Xu et al, 2021; Connolly et al, 2022
- E Reddy et al, 2013; NICE, 2021a; Guideline Development Group consensus
- F Benz et al, 2022
- G Guideline Development Group consensus

5.7 Evidence to recommendations

Anticoagulant treatment is not more effective than antiplatelet therapy in people with non-cardioembolic ischaemic stroke or TIA and carries a greater risk of bleeding (Mohr et al, 2001; Sandercock et al, 2009). Neither is there evidence of greater efficacy for anticoagulation in embolic stroke of uncertain source (ESUS; Hart et al, 2018; Diener et al, 2019). A Cochrane review found no evidence that early initiation of anticoagulation (within 2 weeks) in unselected patients with (all cause) ischaemic stroke reduced death or disability at or beyond 1 month. There was moderate grade evidence of large reductions in recurrent ischaemic stroke and pulmonary embolism with moderate increased rates of intracranial and extracranial bleeding (Wang et al, 2021b). [2023]

Intracranial haemorrhage (including haemorrhagic transformation of the acute infarct) should be assessed by brain imaging and taken into account when deciding whether and when to commence anticoagulation. Less severe degrees of haemorrhagic transformation may not necessarily be a contraindication to anticoagulation, an issue that will be clarified by ongoing randomised trials. In the

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case of patients with moderate-large volume infarction such as occurs often with cardioembolic stroke, there is concern that anticoagulation may increase the risk of haemorrhagic transformation of the infarct, and a delay of an arbitrary 2-week period has been recommended in previous editions of this guideline. Observational data have suggested a lower rate of the composite outcome of recurrent stroke, bleeding or symptomatic ICH when anticoagulation is started between days 4 and 14 compared to within 4 days of AF-associated stroke (Paciaroni et al, 2015). Cohort studies suggest that commencing anticoagulation with a DOAC may be safe between days 4 and 14 in patients with small- or mediumsized infarcts, at least (Gioia et al, 2016; Labovitz et al, 2021). Pooled data analysis of over 2,500 patients in European and Japanese prospective cohort studies showed no increase in ICH when a DOAC was started earlier (within 5 days) rather than later in people with AF-associated stroke (De Marchis et al, 2022). Such observational studies are vulnerable to selection bias and confounding by indication, but they suggest that for patients with minor stroke (e.g. NIHSS 0-3) and a lower risk of haemorrhagic transformation it may be appropriate to commence treatment sooner, at the discretion of the treating clinician. Recent evidence from the TIMING randomised trial showed early initiation of anticoagulation with a DOAC in people with AF-related stroke was non-inferior to delayed initiation, with no ICH in either group (Oldgren et al, 2022), although the majority of strokes in both groups were mild (median NIHSS of 4 in both groups). Definitive guidance, particularly in relation to moderate-severe stroke, must await the findings from RCTs addressing the issue of early versus late initiation in people with AF-related stroke that have either recently completed (e.g. ELAN: NCT03148457) or are ongoing (e.g. OPTIMAS: NCT03759938), and a planned individual participant data meta-analysis. [2023]

There is strong evidence for the use of anticoagulation for long-term secondary prevention of stroke in people with permanent AF (Saxena & Koudstaal, 2004), and the 12% risk of recurrent stroke per year (EAFT Study Group, 1993) substantially alters the balance of risk and benefit in favour of anticoagulation in almost every instance. In people with relative contraindications to anticoagulation identified through the use of a validated tool (e.g. HAS-BLED; (Pisters et al, 2010) or MICON-ICH; Best et al., 2021) it may be possible to intervene to reduce the bleeding risk through control of blood pressure, medication review, treatment of other conditions and multidisciplinary input to reduce risk of falls and improve medication adherence. Falls are associated with higher risk of injury and bleeding but the risk is very unlikely to outweigh the benefits of anticoagulation for stroke prevention (Man-Son-Hing et al, 1999) The safety and benefit of DOACs over VKA is maintained in people with a history of falls in the available RCT evidence (Steffel et al, 2016; Rao et al, 2018). Single-centre data also suggest a reduced risk of traumatic brain injury in people with a history of falls on DOACs compared with VKA (Scotti et al. 2019). Other imaging biomarkers that may influence the balance of risk and benefit from anticoagulation in individual patients are considered in Section 5.21 Cerebral microbleeds. [2023]

DOACs are rapidly replacing VKAs for secondary stroke prevention in people with non-valvular AF. These medications have a rapid onset of action, have fewer interactions with other medications and foodstuffs, do not require coagulation monitoring and are more patient-friendly. Meta-analysis of the four primary DOAC trials, RE-LY (Connolly et al, 2009), ROCKET AF (Patel et al, 2011), ARISTOTLE (Granger et al, 2011) and ENGAGE AF-TIMI 48 (Giugliano et al, 2013) involving over 70,000 patients, has shown significantly greater stroke and thromboembolic prevention (RR 0.81, 95% CI 0.73 to 0.91; p<0.0001), with a substantially reduced risk of intracranial bleeding compared to warfarin (Ruff et al, 2014). No age interaction was observed for efficacy or safety with any DOAC with the exception of standard dose dabigatran and excess GI bleeding (Eikelboom et al, 2011; Graham et al, 2015). Subsequent meta-analyses with almost three million patient-years of observation have shown consistently better safety with DOACs compared to VKA (Hirschl & Kundi, 2019; Xu et al, 2021) and possibly better efficacy overall (Makam et al, 2018; Shen et al, 2020). [2023]

Given the high attributable risk of recurrent stroke in people with AF, unmodifiable relative contraindications (e.g. age, history of stroke) should not dissuade prescribers from the use of anticoagulation, as these patients are also at greatest of recurrent stroke (Olesen et al, 2011). Older people (aged 65 years or older) with AF have a reduced risk of stroke and thromboembolism on

anticoagulant treatment compared to no treatment (relative risk 0.59, 95% CI 0.51 to 0.76, I² = 12.3%), and with a DOAC rather than a VKA (Bai et al, 2018). If, despite addressing modifiable risk factors for bleeding, the bleeding risk is still considered to be too high to use an anticoagulant safely, then aspirin cannot be regarded as a safer alternative, particularly among older patients (Mant et al, 2007). A current NICE guideline does not recommend the routine use of aspirin in these circumstances aside from when there are other indications unrelated to AF (NICE, 2021a). However, a recent systematic review and meta-analysis of antiplatelet use in patients with AF not treated with anticoagulation (Benz et al, 2022) identified an increased risk of major bleeding and intracerebral haemorrhage, and a reduced risk of myocardial infarction compared to no treatment, suggesting that in selected patients with a low or normal risk of bleeding and a higher risk of vaso-occlusive disease (such as in secondary vascular prevention), antiplatelet treatment may still be appropriate. There may be an emerging role for very low dose edoxaban in achieving an acceptable balance of overall benefit and risk in such patients (Okumura et al, 2020). [2023]

Bearing in mind that participants in all the original comparative trials of DOACs with warfarin had to be eligible for both treatments, the trials do not provide evidence regarding the safety or efficacy of DOACs in people for whom the bleeding risk is considered to be too high to safely use warfarin. However, such patients were included in the AVERROES trial comparing apixaban with aspirin (Connolly et al, 2011), and very low dose edoxaban (15 mg OD) in a high-risk elderly Japanese population appears to be effective and relatively safe (Okumura et al, 2020). [2023]

For selected patients with AF who cannot be treated with anticoagulation, it may be appropriate to consider a left atrial appendage occlusion device if the short-term use of antiplatelets/anticoagulation required following the procedure can be tolerated. In the PROTECT AF trial percutaneous left atrial appendage occlusion with a filter device (Watchman) was non-inferior to warfarin for stroke prevention in people with non-valvular AF (Holmes et al, 2009; Reddy et al, 2013). Device implantation was accompanied by warfarin anticoagulation for the first 45 days. No trials have compared left atrial appendage occlusion with DOAC treatment. [2023]

For people with mechanical heart valves or rheumatic heart disease-associated AF, VKA remains the anticoagulant of choice as DOACs have been shown to be inferior in these situations (Eikelboom et al, 2013; Connolly et al, 2022). There is evidence that combining antiplatelet medication with warfarin reduces the risk of thromboembolic complications, but with an increased risk of bleeding (Little & Massel, 2003; Dentali et al, 2007). Apart from some high-risk patients with mechanical heart valves and patients in AF requiring antiplatelet therapy after coronary stenting, there is no evidence that combining antiplatelet medication with warfarin is beneficial, but there is clear evidence of harm (Hart et al, 2005). [2023]

5.7 Implications

This guideline is likely to lead to an increase in the prescribing of DOACs, which are expensive but considered cost-effective by NICE and SMC, particularly when used for secondary prevention where the attributable risk of stroke is several times higher than in primary prevention. Management of patients with TIA or ischaemic stroke in association with AF requires an interdisciplinary team approach to stroke prevention with close collaboration between stroke physicians/neurologists, cardiologists, general practitioners, pharmacists, specialist nurses. [2023]

5.8 Other risk factors

In about a quarter of people with stroke, and more commonly in younger age groups, no cause is evident on initial investigation. Other causes that should be considered include paroxysmal or occult atrial fibrillation (PAF), intracranial arterial disease, cervical artery dissection, antiphospholipid syndrome and other prothrombotic conditions, and patent foramen ovale (PFO). In younger people in

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whom no cause is identified with a history of venous or arterial thrombosis or early miscarriage, a thrombophilia screen should be performed. [2016]

5.9 Paroxysmal atrial fibrillation

All forms of atrial fibrillation (AF) represent a potentially significant risk for stroke. AF may be intermittent and not immediately evident. It can be classified as paroxysmal (PAF) if self-limiting, or persistent if not terminating spontaneously or lasting more than a week. There is no consensus concerning the shortest duration of PAF that constitutes a risk of cardioembolism. Secondary prevention with anticoagulation is the recommended intervention after ischaemic stroke or TIA in patients with AF or PAF. [2023]

5.9 Recommendations

- A Patients with ischaemic stroke or TIA not already diagnosed with atrial fibrillation or flutter should undergo an initial period of cardiac monitoring for a minimum of 24 hours if they are appropriate for anticoagulation. [2023]
- Patients with ischaemic stroke or TIA, in whom no other cause of stroke has been found after comprehensive neurovascular investigation (stroke of undetermined aetiology or 'cryptogenic' stroke) and in whom a cardioembolic cause is suspected, should be considered for more prolonged sequential or continuous cardiac rhythm monitoring with an external patch, wearable recorder or implantable loop recorder if they are appropriate for anticoagulation. [2023]

5.9 Sources

- A Kishore et al, 2014; Guideline Development Group consensus
- B Kang et al, 2003; Grond et al, 2013, Higgins et al, 2013; Gladstone et al, 2014; Sanna et al, 2014; Sposato et al, 2015; Edwards et al, 2020; Buck et al, 2021; Noubiap et al, 2021; Rubiera et al, 2022; Guideline Development Group consensus

5.9 Evidence to recommendations

AF may not be detected by a standard 12-lead ECG and may require more prolonged monitoring. In a systematic review involving 5038 participants with recent stroke or TIA who had at least 12 hours of monitoring, the detection rate for new AF was 11.5% (Kishore et al, 2014). Rates of detection were higher in selected patients (e.g. by age, stroke pattern, pre-screening risk scores). In general, the more prolonged the period of ECG monitoring the greater the likelihood of detection (Grond et al, 2013; Higgins et al, 2013; Gladstone et al, 2014; Sanna et al, 2014). A sequential approach to investigation, involving four incrementally more prolonged phases of monitoring, provided detection rates of AF ranging from 7.7% to 16.9%; the overall AF detection rate was 23.7% after all phases (Sposato et al, 2015). [2023]

Implantable loop recorders (ILRs) have been shown to be superior to short-term external monitoring in detecting AF and could lead to better stroke reduction through the greater uptake of anticoagulation following a stroke or TIA. The use of ILRs seems superior to external monitoring strategies to detect AF in stroke of unknown aetiology or 'cryptogenic' stroke - 15.3 vs 4.7% at 12 months (Buck et al, 2021), with AF detected in 22.8% at 12 months with ILRs in another study (Noubiap et al, 2021). In a meta-analysis of three trials using ILRs compared to conventional monitoring, the 12-month detection rate for AF was 13% v. 2.4% and stroke or TIA occurred in 7% of participants with an ILR-based strategy v. 9% with usual care (odds ratio 0.8, 95% CI 0.5 to 1.2; Ko et al, 2022). ILR-monitored patients were also observed to have a reduced relative risk of stroke or TIA (0.49, 95% CI, 0.30 to 0.81) in one meta-analysis (Tsivgoulis et al, 2019), but a subsequent larger meta-analysis of eight studies (five RCTs, three observational; 2,994 participants) by the same group showed that while patients with an ILR were more

likely to receive anticoagulation, a reduction in stroke was not seen in the RCTs (Tsivgoulis et al, 2022). It therefore remains uncertain whether an ILR-based investigation strategy reduces stroke in an unselected population of patients after stroke or TIA. [2023]

The rate of detection of AF with ILRs at 12 months varies widely in reported studies (range 12-25%) and compared to conventional strategies it may be more cost-effective in patients with cryptogenic stroke with no AF detected after 24 hours of external monitoring (Edwards et al, 2020). Monitoring using smart digital technologies such as wearables and smartphone recording may be superior to traditional 'holter' monitoring and may be an alternative method where an ILR is not feasible or desired by patients (Koh et al, 2021). [2023]

In selecting patients for prolonged cardiac monitoring and/or ILR insertion those with stroke of undetermined aetiology ('cryptogenic') are more likely to have PAF (Kishore et al, 2014). Likewise, certain patterns of ischaemic change seen on brain imaging increase the likelihood of an underlying cardioembolic source such as cortical/subcortical infarcts or multiple lesions in anterior and posterior circulations and/or both cerebral hemispheres (Kang et al, 2003). [2016]

5.9 Implications

These recommendations are likely to increase the number of patients requiring prolonged cardiac rhythm monitoring and ILR insertion with implications for cardiac procedural and monitoring resources. Paroxysmal AF after stroke or TIA warrants treatment with anticoagulation or consideration for left atrial appendage occlusion where anticoagulation is contraindicated. Close collaboration between stroke physicians/neurologists and cardiologists, through a cardiology-stroke multidisciplinary meeting, can facilitate decision making in challenging cases, and agreement on local protocols for ILR implantation and explantation, and monitoring and alert-response procedures. [2023]

5.10 Patent foramen ovale

A patent foramen ovale (PFO) may predispose people to a TIA or stroke by acting as a conduit for paradoxical embolism of thrombus, fat or air from the venous into the arterial circulation, or by clot formation in the PFO channel itself. A PFO may be found in at least a quarter of the general population, but can be identified on contrast echocardiography in 40-56% of patients under 55 years old with ischaemic stroke of otherwise undetermined aetiology (Mesa et al, 2003; McCabe & Rakhit, 2007). A PFO is probably more relevant to the aetiology of stroke in younger patients (under 55 years), especially if there is a clear history of the symptoms occurring during or shortly after a Valsalva manoeuvre, in the setting of a deep venous thrombosis, or where there are recurrent strokes in different arterial territories of otherwise undetermined aetiology. However, a PFO may also be relevant to the aetiology of ischaemic stroke in older patients, with a higher prevalence of PFO observed in patients older than 55 years of age with ischaemic stroke of undetermined aetiology (28.3%) than in patients with stroke of known aetiology (12%; Handke et al, 2007). [2023]

5.10 Recommendations

- A People with ischaemic stroke or TIA and a PFO should receive optimal secondary prevention treatment, including antiplatelet therapy, treatment for high blood pressure, lipid-lowering therapy and lifestyle modification. Anticoagulation is not recommended unless there is another recognised indication. [2023]
- B Selected people below the age of 60 with ischaemic stroke or TIA of otherwise undetermined aetiology, in association with a PFO and a right-to-left shunt or an atrial septal aneurysm, should be considered for endovascular PFO device closure within six months of the index event to prevent recurrent stroke. This decision should be made after careful consideration of the benefits and risks by a multidisciplinary team including

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- the patient's physician and the cardiologist performing the procedure. The balance of risk and benefit from the procedure, including the risk of atrial fibrillation and other recognised peri-procedural complications should be fully considered and explained to the person with stroke. [2023]
- C People older than 60 years with ischaemic stroke or TIA of otherwise undetermined aetiology and a PFO should preferably be offered closure in the context of a clinical trial or prospective registry. [2023]

5.10 Sources

- A Homma et al, 2002; Guideline Development Group consensus
- B, C Furlan et al, 2012; Meier at al, 2013; Søndergaard et al, 2017; Saver et al, 2017; Mas et al, 2017; Lee at al, 2018; Guideline Development Group consensus

5.10 Evidence to recommendations

In some people with stroke or TIA, a PFO will be an incidental finding and optimal medical therapy and secondary prevention strategies alone should be used. There is no evidence that anticoagulation is superior to antiplatelet therapy in patients with stroke of undetermined aetiology in association with a PFO (Homma et al, 2002). Three multicentre RCTs did not show a significant benefit of PFO closure over medical therapy alone, based on an intention-to-treat analysis (Furlan et al, 2012; Carroll et al, 2013; Meier et al, 2013). However, three subsequent RCTs (Mas et al, 2017; Søndergaard et al, 2017; Lee et al, 2018), and extended follow-up data from the RESPECT trial (Saver et al, 2017) showed a significant reduction in recurrent stroke risk in patients allocated to endovascular PFO closure compared with medical therapy alone, most of whom were older than 60 years of age. It is important to note that these more recent trials which showed a benefit of PFO closure over medical therapy alone only included patients with a PFO and a large right-to-left shunt or an atrial septal aneurysm (Mas et al, 2017) or a PFO with a right-to-left shunt (Søndergaard et al, 2017; Lee et al, 2018). [2023]

Most of the RCTs described above excluded patients over the age of 60 years, so it is not known whether the observed benefit from PFO closure is applicable to older patients with ischaemic stroke of otherwise undetermined aetiology. Furthermore, there is insufficient evidence to address whether oral anticoagulation alone (either with a VKA or DOAC) is inferior, equivalent or superior to PFO closure, and more research is needed in this area. [2023]

PFO closure is associated with an approximately five-fold increase in the risk of developing AF (5-6.6% following closure), although the duration and nature of the resultant AF is not fully understood. Implantation is also associated with other peri-procedural risks, including inadequate PFO closure, implantation failure, pericardial effusion, and pseudoaneurysm formation. [2023]

5.10 Implications

These recommendations are likely to increase the number of patients referred for further investigation and treatment, and stroke services should establish regular multidisciplinary meetings with their colleagues in cardiology to consider and appropriately select patients for further investigation and consideration of endovascular device closure. Further research is needed to clarify optimal secondary preventative strategies in patients with a PFO and a co-existent thrombophilia as such patients were excluded from the definitive trials of PFO closure. [2023]

5.11 Other cardioembolism

Between 20-30% of ischaemic strokes can be attributed to cardioembolism (Sandercock et al, 1989; Kolominsky-Rabas et al, 2001), with the majority of these accounted for by AF. A variety of other cardiac pathologies have been implicated, often categorised as high risk (myocardial infarction, mitral stenosis, left ventricular aneurysm or thrombus, mechanical valve prosthesis) and low/uncertain risk (atrial septal aneurysm, mitral annular calcification, aortic stenosis). The value of echocardiography in people with TIA and stroke depends upon the assumption that the risk of recurrent stroke can be modified by treatment which would otherwise not have been considered, should one of these pathologies be detected. Identifying a putative cardioembolic source does not prove a cardioembolic mechanism, particularly in individuals with competing risk factors. With the notable exception of AF, it is unclear for the majority of potential cardioembolic pathologies what risk of stroke recurrence they pose, whether or not intervention genuinely lessens this risk and if so, whether the benefit outweighs the risk associated with intervention. [2023]

5.11 Recommendation

- A People with stroke or TIA should be investigated with transthoracic echocardiography if the detection of a structural cardiac abnormality would prompt a change of management and if they have:
 - clinical or ECG findings suggestive of structural cardiac disease that would require assessment in its own right, or
 - unexplained stroke or TIA, especially if other brain imaging features suggestive of cardioembolism are present. [2016]

5.11 Sources

A Holmes et al, 2014; Working Party consensus

5.11 Evidence to recommendations

A systematic review and economic evaluation sought to evaluate the cost-effectiveness of routine echocardiography in the assessment of individuals presenting with first-ever ischaemic stroke or TIA (Holmes et al, 2014). Clinically identifiable cardiac pathologies were excluded. Across a range of cardiac pathologies, transthoracic echocardiography (TTE) was found to be less sensitive compared with transoesophageal (TOE), with both demonstrating high specificity. In consultation with an expert panel it was determined that only the identification of left atrial and left ventricular thrombus by echocardiography would alter patient management. A median prevalence of 0.8% was reported for left ventricular thrombus and of 1.4% for left atrial thrombus. Considerable variability was found for the reported prevalence of atrial septal aneurysm (median 9.3%, range 0.4-28%) and PFO (median 17%, range 0.25-73%). Economic analysis in the UK concluded that TTE is a cost-effective use of healthcare resources compared with TOE, when clinicians deem it the most appropriate test, and might be applied primarily to people with stroke of undetermined aetiology if they are also candidates for oral anticoagulation. Certain patterns of ischaemic change seen on brain imaging increase the suspicion of a cardioembolic source such as cortico-subcortical infarcts or multiple lesions in anterior and posterior circulations and/or both cerebral hemispheres (Kang et al, 2003). [2016]

5.12 Vertebral artery disease

Stroke in the vertebrobasilar territory accounts for 20% of all strokes and is more often associated with corresponding large artery stenosis than is the case for carotid territory stroke (Marquardt et al, 2009). Pooled individual patient data from two prospective studies found a 90-day risk of stroke after vertebrobasilar stroke or TIA of 9.6% in those with vertebrobasilar stenosis and 2.8% in those without, with the highest risk (13.9%) if the stenosis was intracranial (Gulli et al, 2013). [2016]

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5.12 Recommendation

A People with ischaemic stroke or TIA and symptomatic vertebral artery stenosis should receive optimal secondary prevention including antithrombotic therapy, blood pressure treatment, lipid-lowering therapy and lifestyle modification. Angioplasty and stenting of the vertebral artery should only be offered in the context of a clinical trial. [2016]

5.12 Sources

A Compter et al, 2015; Working Party consensus

5.12 Evidence to recommendations

The open randomised phase 2 study VAST compared stenting with medical management in patients with recently symptomatic vertebral artery stenosis of more than 50% (Compter et al, 2015). The study was terminated early, after enrolment of 115 patients. There were no significant differences between the two groups, and based on the low stroke recurrence rate seen in the trial, a conclusive phase 3 trial would need to include 9,500 patients. A subsequent pre-planned individual participant data meta-analysis of three randomised trials including 354 patients did not show a significant benefit from extracranial or intracranial vertebral artery stenting (Markus et al, 2019). There is therefore no evidence to suggest that revascularisation for people with vertebral artery stenosis (stenting, endarterectomy or reconstruction/transposition) is superior to best medical therapy. [2016]

5.13 Intracranial artery stenosis

In Western populations, atherosclerotic stenosis of the large intracranial arteries is found in about 40% of patients with ischaemic stroke and is likely to be causative in about 7% (Sacco et al, 1995; Mazighi et al, 2008). Significantly higher rates are seen in African-Americans, and in Asian populations it is the dominant pathology. [2016]

5.13 Recommendation

A People with ischaemic stroke or TIA due to severe symptomatic intracranial stenosis should be offered dual antiplatelet therapy with aspirin and clopidogrel for the first three months in addition to optimal secondary prevention including blood pressure treatment, lipid-lowering therapy and lifestyle modification. Endovascular or surgical intervention should only be offered in the context of a clinical trial. [2016]

5.13 Sources

A Chimowitz et al 2005, 2011; Working Party consensus

5.13 Evidence to recommendations

The recurrent stroke rate in people with intracranial artery stenosis is high; in the WASID RCT comparing aspirin with warfarin in people with greater than 50% stenosis of intracranial arteries, those on aspirin had a 22% risk of stroke or death during a mean follow-up of 1.8 years (Chimowitz et al, 2005). This trial confirmed an association between increasing degree of intracranial stenosis and stroke risk and showed that the development of an effective collateral circulation is protective (Liebeskind et al, 2011). Warfarin anticoagulation was no more effective than aspirin for stroke prevention in WASID, including for the subgroup enrolled with stroke whilst on antithrombotic therapy, but was associated with significantly more adverse events. [2016]

The SAMMPRIS trial (Chimowitz et al, 2011) compared angioplasty and stenting of intracranial stenosis of greater than 70% with medical management, including an initial 90 days of dual antiplatelet therapy with clopidogrel plus aspirin. The 30-day rate of stroke or death in the SAMMPRIS control group was

lower than in WASID (5.8% v. 10.7%) suggesting dual antiplatelet therapy may be superior to aspirin alone. Targeted risk factor modification, particularly BP and LDL-cholesterol reduction, was also more frequently achieved in SAMMPRIS, and the trial found that medical management was superior to angioplasty and stenting with the difference maintained over a median follow-up of 32 months (Derdeyn et al, 2014). The VISSIT trial exploring the effect of balloon-expandable stents in people with symptomatic intracranial stenosis was halted following the results of SAMMPRIS, with analysis also demonstrating an increased risk of recurrent stroke with endovascular intervention (Zaidat et al, 2015). No comparison of dual antiplatelet therapy with clopidogrel monotherapy in this setting has yet been conducted. [2016]

5.14 Oral contraception and hormone replacement therapy

The observation that stroke tends to affect women at a later age than men raises the possibility that female sex hormones, and specifically oestrogens, might protect against vascular disease. This was initially supported by observational studies suggesting hormone replacement therapy (HRT) might reduce the risk of stroke in postmenopausal women. There is now evidence that oestrogen actually increases the risk of cardiovascular events including ischaemic stroke both when used by younger women as the combined oral contraceptive (COC) and by postmenopausal women as HRT. [2016]

5.14.1 Oral contraception

5.14.1 Recommendation

A Premenopausal women with stroke and TIA should not be offered the combined oral contraceptive pill. Alternative hormonal (progestogen-only) and non-hormonal contraceptive methods should be considered instead. [2016]

5.14.1 Source

A Working Party consensus

5.14.1 Evidence to recommendations

No studies have assessed how the COC modifies the risk of recurrent stroke or TIA. Studies in women with no history of stroke or TIA indicate that there may be an approximate doubling of the relative risk of ischaemic stroke associated with use of combined (low-dose) oestrogen oral contraception. A Cochrane review of one cohort study and 23 case-control studies compared the risk of myocardial infarction or ischaemic stroke in users and non-users of COC (Roach et al, 2015). The relative risk of ischaemic stroke was 1.7 for COC users and the risk increased according to the dose of oestrogen. The risk was not influenced by the progestogen used. It has been estimated that for 10,000 women using a 20 μ g oestrogen COC for 1 year, 2 will have an arterial thrombosis (Lidegaard et al, 2012). Pregnancy is associated with a risk of stroke of about 3 per 10,000 deliveries (James et al, 2005). [2016]

A meta-analysis of six case-control studies comprising 3,091 cases and 11,385 controls found no association between progestogen-only contraceptive (POC) use and stroke risk (Chakhtoura et al, 2009). The analysis provides limited support for use of the POC in situations where hormonal contraception is necessary, but the full range of contraceptive methods (hormonal and non-hormonal) should be considered. [2016]

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5.14.2 Hormone replacement therapy

5.14.2 Recommendations

- A Post-menopausal women with ischaemic stroke or TIA who wish to start or continue hormone replacement therapy should receive advice based on the overall balance of risk and benefit, taking account of the woman's preferences. [2016]
- B Post-menopausal women with ischaemic stroke or TIA should not be offered hormone replacement therapy for secondary vascular prevention. [2016]

5.14.2 Sources

- A Working Party consensus
- B Boardman et al, 2015

5.14.2 Evidence to recommendations

Treatment decisions concerning HRT must balance clinical need (treatment of premature menopause or relief of menopausal symptoms) against a number of different risks. A Cochrane review of 19 RCTs (40,410 participants) comparing hormonal therapy with placebo or no treatment found no benefit in all-cause mortality, cardiovascular death, non-fatal myocardial infarction, angina or revascularisation (Boardman et al, 2015). An increased risk of stroke was found in primary prevention studies, but the effect was not significant in secondary prevention studies (5,172 participants in five studies). For the subgroup of women starting HRT within a mean of 10 years after the menopause or who were less than 60 years of age, treatment was associated with a significant all cause mortality benefit and coronary heart disease benefit compared with placebo, although with a persisting risk of venous thromboembolism and a trend towards increased risk of stroke (9,838 participants in three studies). In a nested case-control study of 15,710 cases of stroke matched to 59,958 controls from the UK General Practice Research Database, the risk of stroke was not increased with use of low-dose oestrogen patches (alone or with progestogen) when compared with no use in post-menopausal women (Renoux et al, 2010). The stroke rate was increased with use of high-dose patches. [2016]

5.15 Obstructive sleep apnoea

There is a prevalence of obstructive sleep apnoea (OSA) of between 30 and 70% in people with ischaemic or haemorrhagic stroke, depending upon the diagnostic criteria used (Johnson & Johnson, 2010). Not only are typical cardiovascular risk factors such as hypertension, hyperlipidaemia, diabetes, smoking, AF and obesity more prevalent in people with OSA, but OSA itself is an independent risk factor for stroke (Loke et al, 2012). [2016]

5.15 Recommendation

A People with stroke or TIA should be screened for obstructive sleep apnoea with a valid clinical screening tool. People who screen positive who are suspected of having sleep apnoea should be referred for specialist respiratory/sleep medicine assessment. [2016]

5.15 Source

A Working Party consensus

5.15 Evidence to recommendations

People with stroke and OSA have been shown to have worse functional outcomes, longer hospitalisation and an increased risk of stroke recurrence (Kaneko et al, 2003; Rola et al, 2008). Treatment with continuous positive airways pressure (CPAP) has been shown to favourably modify cardiovascular risk

factors such as hypertension (Marin et al, 2012) and in a prospective observational study to reduce the risk of recurrent cardiovascular events (Martinez-Garcia et al, 2012). Several small RCTs have failed to confirm a reduction in cardiovascular events with CPAP (Sandberg et al, 2001; Hsu et al, 2006; Bravata et al, 2011; Parra et al, 2011; Ryan et al, 2011; Parra et al, 2015). Whilst uncertainty remains concerning stroke recurrence, there are other benefits from recognising and treating OSA and given the high reported prevalence, presentation with stroke provides an opportunity to screen patients for OSA. As in the general population, patients with stroke and OSA may not declare a classical history of severe snoring and subjective daytime sleepiness. The use of a simple clinical screening tool (such as the 'STOP-BANG' questionnaire) in people with stroke or TIA will identify those who are likely to benefit from further specialist assessment (Silva et al, 2011). [2016]

5.15 Implications

There will be resource implications for sleep services from an increased awareness of OSA among people with stroke or TIA. [2016]

5.16 Antiphospholipid syndrome

Antiphospholipid syndrome (APS) is an autoimmune disorder which may occur with or without associated rheumatic disease, particularly systemic lupus erythematosus. Patients with APS are at increased risk of venous and arterial thrombotic events, including ischaemic stroke. Pregnancies in women with APS have an increased risk of miscarriage, intrauterine growth retardation and premature birth (Cervera et al, 2015). The condition is diagnosed in individuals with a history of venous or arterial thrombosis and/or pregnancy-related morbidity in the presence of persistent antiphospholipid antibodies. A finding of antiphospholipid antibodies is more likely to be of relevance in people younger than 50 years in whom other risk factors for stroke have been excluded. [2016]

5.16 Recommendations

- A People with ischaemic stroke or TIA in whom other conditions such as atrial fibrillation and large or small vessel atherosclerotic disease have been excluded should be investigated for antiphospholipid syndrome (with IgG and IgM anticardiolipin ELISA and lupus anticoagulant), particularly if the person:
 - is under 50 years of age;
 - has any autoimmune rheumatic disease, particularly systemic lupus erythematosus;
 - has a history of one or more venous thromboses;
 - has a history of recurrent first trimester pregnancy loss or at least one late pregnancy loss (second or third trimester). [2016]
- B People with antiphospholipid syndrome who have an ischaemic stroke or TIA:
 - should be managed acutely in the same way as people without antiphospholipid syndrome;
 - should have decisions on long-term secondary prevention made on an individual basis in conjunction with appropriate specialists including haematology and/or rheumatology. [2016]

5.16 Source

A, B Working Party consensus

5.16 Evidence to recommendations

There is uncertainty concerning the most effective strategy to prevent arterial thrombotic events in people with APS. Recommendations include long-term low-dose aspirin, low-, medium- and high-

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intensity warfarin and the combination of aspirin and warfarin. There is little RCT evidence and those RCTs that are available have either not shown an advantage for any particular strategy (Crowther et al, 2003; Levine et al, 2004; Finazzi et al, 2005) or have included only very small numbers (Okuma et al, 2010). Until better evidence becomes available, the Working Party recommends that treatment decisions should be made on an individual basis, ideally involving multispecialty input. [2016]

5.17 Insulin resistance

Insulin resistance is a component of the metabolic syndrome in which a diminished target cell response to insulin results in a compensatory increase in insulin secretion to maintain normoglycaemia. The resulting hyperinsulinaemia leads to complex metabolic changes and the development of hypertension, central obesity, glucose intolerance, elevated triglyceride levels and reduced HDL-cholesterol. Genetic predisposition, ageing, oversupply of dietary lipid, sedentary lifestyle and central obesity are associated with the development of insulin resistance. It is estimated that about half of non-diabetic people with stroke or TIA have insulin resistance (Kernan et al, 2003), an independent risk factor for ischaemic stroke (Rundek et al, 2010; Thacker et al, 2011). Insulin resistance may be a modifiable target for secondary stroke prevention. Insulin-sensitising thiazolidinedione ('glitazone') medication have been developed to treat diabetes, with pioglitazone the only medicine in this class currently licensed in the UK and Ireland. [2016]

5.17 Recommendation

A People with stroke or TIA should not receive pioglitazone for secondary vascular prevention. [2016]

5.17 Source

A Kernan et al, 2016

5.17 Evidence to recommendations

The PROactive study (Dormandy et al, 2005) assessed secondary prevention with pioglitazone in people with diabetes and prior vascular disease and was neutral in terms of the primary outcome of major vascular events, but did show a reduction in a secondary outcome that included stroke. A subsequent Cochrane review (Liu & Wang, 2015) found that glitazones might reduce recurrent stroke in people with stroke or TIA. The IRIS trial (Kernan et al, 2016) compared pioglitazone with placebo in 3876 nondiabetic participants with insulin resistance and a history of stroke or TIA, excluding those with diabetes, structural heart disease or congestive cardiac failure. The primary outcome (first fatal/non-fatal stroke or non-fatal MI) occurred in 9% with pioglitazone and 11.8% with control over 4.8 years of follow-up. Progression to diabetes was also reduced, but weight gain, oedema and bone fractures were all significantly increased with pioglitazone. Based on these results, for every 100 patients treated with pioglitazone for about 5 years, 3 fewer would suffer stroke or MI; 4 fewer would develop diabetes mellitus; 2 more would suffer bone fracture requiring hospitalisation; 18 more would gain >4.5 kg in weight, and 11 more would have new or worsening peripheral oedema. The study did not report quality of life outcomes and more evidence would be required before glitazone treatment can be recommended routinely for patients with insulin resistance. Targeting lifestyle modification, particularly exercise and diet, appears to be a safe and effective approach for reducing insulin resistance and progression to diabetes (Knowler et al, 2002; Lindstrom et al, 2006; Ivey et al, 2007). [2016]

5.18 Fabry disease

Fabry disease is a multi-system disorder in which reduced activity of the enzyme α -galactosidase leads to the accumulation of glycolipid in various organs damaging tissues, particularly the skin, eye, kidney, heart, brain, and peripheral nervous system. The disorder is X-linked, affecting 1 in 40,000-60,000

males; females can also be affected. Onset is usually in childhood or adolescence, typical symptoms and signs including episodes of severe pain in the extremities (acroparesthesias), cutaneous vascular lesions typically more pronounced in the bathing-trunk distribution (angiokeratomas), decreased sweating, corneal opacities, tinnitus, hearing loss and proteinuria. Premature cardiovascular disease occurs as well as progressive deterioration in renal function leading to end-stage renal disease. Cerebrovascular manifestations primarily relate to small vessel disease and may be ischaemic or haemorrhagic. [2016]

5.18 Recommendations

- A Young people with stroke or TIA should be investigated for Fabry disease if they have suggestive clinical features such as acroparesthesias, angiokeratomas, sweating abnormalities, corneal opacities, unexplained renal insufficiency or a family history suggesting the condition. [2016]
- B People with stroke or TIA and a diagnosis of Fabry disease should receive optimal secondary prevention and be referred to specialist genetic and metabolic services for advice on other aspects of care including the provision of enzyme replacement therapy. [2016]

5.18 Source

A, B Working Party consensus

5.18 Evidence to recommendations

Early diagnosis allows timely screening for secondary complications, treatment to delay renal and cardiovascular effects, lifestyle advice particularly in relation to smoking cessation, and genetic counselling. The diagnosis should be considered in people with any of the clinical features above, and can be confirmed by tests measuring α -galactosidase activity and/or with molecular genetic testing for mutations of the GLA gene. Treatment with α -galactosidase A enzyme replacement therapy has been available for some years, but long-term effectiveness in preventing cerebrovascular complications has not so far been demonstrated (Rombach et al, 2013; Anderson et al, 2014; Germain et al, 2015). [2016]

5.19 Cerebral amyloid angiopathy

Sporadic cerebral amyloid angiopathy (CAA), a common age-related cerebral small vessel disease, is an important cause of lobar intracerebral haemorrhage (ICH), particularly in older people. It is caused by the deposition of amyloid-beta peptide in small cortical and leptomeningeal vessels. CAA can be diagnosed as a probable cause of lobar ICH with good accuracy using brain imaging as described in the MRI-based Boston criteria (Linn et al, 2010); more recently CT-based Edinburgh criteria have also been proposed (Rodrigues et al, 2018). The risk of recurrent ICH in patients with CAA is approximately 7% per year (Charidimou et al, 2017) in comparison to about 1% for ICH associated with arteriolosclerosis. However, patients with ICH are also at risk of vaso-occlusive cardiovascular diseases including ischaemic stroke, which is associated with AF in people with ICH (Li et al, 2021b). [2023]

5.19 Recommendations

- A Patients with lobar ICH associated with probable CAA should be considered for blood pressure lowering to below a long-term target of 130/80 mmHg. Wherever possible patients should be offered participation in a randomised trial of blood pressure-lowering treatment. [2023]
- B Patients with lobar ICH associated with probable CAA may be considered for antiplatelet therapy for the secondary prevention of vaso-occlusive events, but wherever possible patients should be offered participation in a randomised trial. If participation in a randomised trial is not possible then clinicians should make an individualised decision

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- based on estimates of the future risks of recurrent ICH and vaso-occlusive events. [2023]

 Patients with lobar ICH associated with probable CAA and AF may be considered for oral anticoagulation for stroke prevention, but wherever possible patients should be offered participation in a randomised trial. If participation in a randomised trial is not possible then clinicians should make an individualised decision based on estimates of the future risks of recurrent ICH and vaso-occlusive events. [2023]
- D Patients with lobar ICH associated with probable CAA and AF may be considered for a left atrial appendage occlusion (LAAO) device, but wherever possible patients should be offered participation in a randomised trial. If participation in a randomised trial is not possible then LAAO may be considered based on an estimation of the future risks of recurrent ICH and vaso-occlusive events. [2023]

5.19 Sources

- A Rodrigues et al, 2018; Charidimou et al, 2017
- B Arima et al, 2010; Linn et al, 2010
- C Linn et al, 2010; SoSTART Collaboration, 2021; Schreuder et al, 2021
- D Linn et al, 2010; Biffi et al, 2015

5.19 Evidence to recommendations

There are few directly relevant randomised trials relating to secondary prevention of recurrent ICH, and none specifically in people with CAA. In the PROGRESS trial (2001) which included 6,105 people with ischaemic stroke or ICH, treatment with 2-4 mg perindopril for all participants (plus 2-2.5 mg indapamide for those with neither an indication for nor a contraindication to a diuretic) reduced blood pressure (BP) by an average of 12 mmHg systolic and 5 mmHg diastolic, lowering the risks of first and recurrent ICH (adjusted HR 0.44 [95% CI 0.28 to 0.69] and 0.37 [95% CI 0.10 to 1.38] respectively; PROGRESS Collaborative Group, 2001). Patients with prior ICH derived the greatest benefit, and the risk of stroke decreased with lower follow-up BP without evidence of a lower threshold for hazard. In a PROGRESS subgroup analysis, intensive BP treatment reduced the relative risk of probable CAA-related ICH by 77% (95% CI 19 to 93%), that of probable hypertension-related ICH by 46% (95% CI 4 to 69%), and that of unclassified ICH by 43% (95% CI -5 to 69%) There are few directly relevant randomised trials relating to secondary prevention of recurrent ICH, and none specifically in people with CAA. In the PROGRESS trial (2001) which included 6,105 people with ischaemic stroke or ICH, treatment with 2-4 mg perindopril for all participants (plus 2-2.5 mg indapamide for those with neither an indication for nor a contraindication to a diuretic) reduced blood pressure (BP) by an average of 12 mmHg systolic and 5 mmHg diastolic, lowering the risks of first and recurrent ICH (adjusted HR 0.44 [95% CI 0.28 to0.69] and 0.37 [95% CI 0.10 to 1.38] respectively; PROGRESS Collaborative Group, 2001). Patients with prior ICH derived the greatest benefit, and the risk of stroke decreased with lower follow-up BP without evidence of a lower threshold for hazard. In a PROGRESS subgroup analysis, intensive BP treatment reduced the relative risk of probable CAA-related ICH by 77% (95% CI 19 to 93%), that of probable hypertensionrelated ICH by 46% (95% CI 4 to 69%), and that of unclassified ICH by 43% (95% CI -5 to 69%) (Arima et al, 2010). An observational cohort study in 1,145 people after ICH found that higher BP during follow-up was associated with increased risk of lobar ICH recurrence (HR 1.33 per 10 mmHg increase [95% CI 1.02 to 1.76]) and that the risk of recurrent ICH increased with systolic BP above 120 mmHg and diastolic above 80 mmHg (Biffi et al, 2015). However, such observational studies are subject to selection and severity bias and confounding by indication. Further RCTs of intensive BP reduction after lobar ICH probably or possibly due to CAA are required. [2023]

The RESTART trial in people after ICH associated with antithrombotic medication use did not find evidence for hazard of antiplatelet treatment in the small subgroup of participants with lobar ICH probably due to CAA, defined by the Edinburgh CT-based or Boston MRI-based criteria (Rodrigues et al,

2018; Al-Shahi Salman et al, 2019), but estimates in this subgroup were imprecise due to the limited sample size. In an observational study, resumption of oral anticoagulation (OAC) after lobar ICH attributed to CAA was associated with decreased mortality and a more favourable functional outcome, but such observational studies are subject to selection and severity bias and confounding by indication (Biffi et al, 2017). Two pilot-phase randomised trials (APACHE-AF and SoSTART) of OAC for AF after ICH (Schreuder et al, 2021; SoSTART Collaboration, 2021) did not find evidence of benefit or harm from OAC, but their sample sizes were insufficient to investigate the effect of OAC in the subgroup of patients with lobar ICH probably due to CAA, so further RCTs are ongoing (e.g. ENRICH-AF NCT03950076 and PRESTIGE-AF NCT03996772). Left atrial appendage occlusion with short duration antithrombotic therapy might be an alternative to OAC in ICH associated with CAA, and this is being investigated in an RCT (e.g. STROKECLOSE NCT02830152). [2023]

There are no proven disease modifying therapies for CAA. In a small RCT the monoclonal antibody ponezumab did not show benefit on vascular reactivity in patients with probable CAA (Leurent et al, 2019). [2023]

5.20 CADASIL

CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy) is caused by mutations in the *NOTCH3* gene, and is the most common single gene disorder causing stroke. Since it was first clinically and genetically characterised in the early 1990s, increasing numbers of cases are being recognised and diagnosed. It should be considered in younger patients with lacunar stroke or TIA, particularly in the presence of one or more of the following features: a family history of stroke or dementia, characteristic MRI changes particularly MRI white matter hyperintensities in the anterior temporal pole, and other features such as mood disorders or migraine with aura (Mancuso et al, 2020). [2023]

5.20 Recommendations

- A People with clinical and radiological features that are suggestive of CADASIL should only be offered genetic testing after appropriate counselling and discussion. Predictive testing in other family members should be performed by a specialist clinical genetics service after appropriate counselling. [2023]
- People with CADASIL should be considered for intensive cardiovascular risk factor management, particularly with respect to blood pressure management (target to below 130/80 mmHg) and smoking cessation advice. They should also be considered for active management of other risk factors including lipid lowering treatment (including with statins), and diabetes mellitus, and offered lifestyle advice (including regarding obesity and exercise). [2023]
- C People with CADASIL and ischaemic stroke or TIA may be considered for antiplatelet therapy; cerebral microbleeds are not a contraindication. [2023]

5.20 Sources

- A Mancuso et al, 2020; Guideline Development Group consensus
- B Peters et al, 2006; Adib-Samii et al, 2010; Mancuso et al, 2020
- C Puy et al, 2017

5.20 Evidence to recommendations

There are no RCTs examining secondary prevention approaches in people with CADASIL. Observational studies have shown that both smoking and hypertension are associated with an increased risk of stroke in this group (Peters et al, 2006; Adib-Samii et al, 2010). For this reason most clinicians, and the

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European Academy of Neurology (EAN) guidelines (Mancuso et al, 2020) recommend tight control of cardiovascular risk factors, particularly BP reduction and smoking cessation. Evidence is not available on other risk factors including exercise, obesity, and cholesterol, but most clinicians also actively treat these risk factors. These should be treated from the time of diagnosis, rather than waiting until the person has had a stroke. [2023]

There is no research to guide clinicians on whether antiplatelet agents should be given to patients with CADASIL. Most practitioners, and the EAN guidelines (Mancuso et al, 2020) recommend avoiding antiplatelet agents prior to the onset of clinical stroke, but treating with a single antiplatelet agent (aspirin or clopidogrel) rather than dual antiplatelet agents after a stroke or TIA. The presence of cerebral microbleeds is associated with an increased risk of ischaemic stroke and should not prevent administration of antiplatelets after a stroke or TIA (Puy et al, 2017). [2023]

5.21 Cerebral microbleeds

Cerebral microbleeds are small haemosiderin deposits detected by blood-sensitive MRI scans including T2-weighted gradient recalled echo and susceptibility-weighted imaging (SWI), Their identification has generated clinical concern as a potential marker of increased intracranial bleeding risk in people treated with antithrombotic medication, leading some clinicians to avoid giving antithrombotic medication if they are present (Wilson & Werring, 2017). [2023]

5.21 Recommendations

- A In patients with ischaemic stroke or TIA requiring antiplatelet or anticoagulant treatment, the presence of cerebral microbleeds (regardless of number or distribution) need not preclude antithrombotic medication use. [2023]
- In patients with recent ischaemic stroke or TIA treated with antithrombotic (i.e. antiplatelet or anticoagulant) medication, the use of a validated risk score (such as the MICON-ICH score) may be considered for predicting the risk of symptomatic intracranial haemorrhage to allow the mitigation of bleeding risk, including assertive management of modifiable factors (e.g. hypertension, alcohol intake and review of concurrent medication). [2023]

5.21 Source

A, B Guideline Development Group consensus

5.21 Evidence to recommendations

In patients prescribed oral anticoagulants after cardioembolic stroke or TIA in the CROMIS-2 (Wilson et al, 2018) and HERO (Martí-Fàbregas et al, 2019) prospective multicentre cohort studies the presence of cerebral microbleeds was independently associated with an approximate three-fold increase in the risk of symptomatic ICH, but the absolute risk of ischaemic stroke was consistently higher than that of symptomatic ICH independent of the presence of cerebral microbleeds. The Microbleeds International Collaborative Network [MICON]) included 20,322 patients taking any antithrombotic medication(s) (Wilson et al, 2019) and found that the absolute risk of ischaemic stroke exceeded that of ICH even in patients with 10 or more microbleeds (annual rates: ICH: 2.7%; ischaemic stroke: 6.4%), or microbleeds in a strictly lobar distribution suggesting CAA (annual rates: ICH: 1.3%; ischaemic stroke: 4.8%). The MICON-ICH collaborative group also demonstrated that a cerebral microbleed-based risk score (MICON-ICH) improves the prediction of intracranial haemorrhage during follow-up for patients with ischaemic stroke or TIA taking antiplatelets, anticoagulants, or both compared to widely used clinical prediction instruments like HAS-BLED, ATRIA, or ORBIT (Best et al, 2021). A high predicted risk of ICH might lead clinicians to pursue assertive management of modifiable bleeding risk factors such as BP and alcohol

intake, and review concurrent medication. A secondary analysis of the NAVIGATE-ESUS trial (Shoamanesh et al, 2021) did not find evidence that microbleeds modify the net benefit or harm of anticoagulant versus antiplatelet therapy. However, in the PICASSO trial, which enrolled Asian participants with previous ischaemic stroke and previous intracranial bleeding (symptomatic or radiological intracerebral bleeding or at least two cerebral microbleeds), in those with microbleeds only at baseline, cilostazol was associated with a lower risk of intracranial bleeding than aspirin (Park et al, 2021). More data are needed regarding the prognostic significance of cerebral microbleeds in patients taking direct oral anticoagulants (DOACs); moreover, the balance of risk and benefit is uncertain for patients with cerebral microbleeds taking combined antiplatelet and anticoagulant therapy and for patients with a large number of cerebral microbleeds beyond five years. [2023]

5.22 Lifestyle measures

The evidence for lifestyle interventions relates mainly to the primary prevention of vascular events; little high quality research has studied the secondary prevention of stroke or TIA. It would seem that changes in lifestyle are as important in secondary prevention as they are in primary prevention. Effective lifestyle interventions require changes in behaviour such as smoking, exercise, diet and alcohol consumption. Although it is the responsibility of the individual to change his or her own behaviour, healthcare practitioners have a responsibility to give accurate information, advice and support to help people to make and maintain lifestyle changes. In theory, the combination of lifestyle changes and other secondary prevention measures could deliver a greater than 80% risk reduction in vascular events for people with stroke or TIA (Hackam & Spence, 2007). In practice, the paucity of data makes it difficult to confirm the expected benefits (Lennon et al, 2014). [2016]

5.23 Physical activity

People who have sustained a stroke often become physically deconditioned, with low cardiorespiratory fitness, muscle strength and muscle power (Smith et al, 2012; Saunders et al, 2013). This low physical fitness is associated with functional limitation and disability (Saunders et al, 2013). Physical activity programmes to improve fitness and muscle strength have been implemented without adverse effects in people with stroke screened for contraindications (Billinger et al, 2014). A systematic review (Ammann et al, 2014) identified the need for better reporting of exercise prescription to improve the delivery of physical activity programmes, and the importance of peer support. [2016]

5.23 Recommendations

- A People with stroke or TIA should participate in physical activity for fitness unless there are contraindications. Exercise prescription should be individualised, and reflect treatment goals and activity recommendations. [2016]
- B People with stroke or TIA should aim to be active every day and minimise the amount of time spent sitting for long periods. **[2016]**
- C People with stroke should be offered cardiorespiratory training or mixed training regardless of age, time since having the stroke, and severity of impairment.
 - Facilities and equipment to support high-intensity (greater than 70% peak heart rate) cardiorespiratory fitness training (such as bodyweight support treadmills, or static or recumbent cycles) should be available;
 - The dose of training should be at least 30-40 minutes, 3 to 5 times a week for 10-20 weeks;
 - Programmes of mixed training (medium intensity cardiorespiratory [40%-60% of heart rate reserve] and strength training [50-70% of one-repetition maximum]) such as circuit training classes should also be available at least 3 days per week for 20 weeks;

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- The choice of programme should be guided by patients' goals and preferences and delivery of the programme individualised to their level of impairment and goals.
 [2023]
- D People with stroke or TIA who are at risk of falls should engage in additional physical activity which incorporates balance and co-ordination, at least twice per week. [2016]
- Physical activity programmes for people with stroke or TIA should be tailored to the individual after appropriate assessment, starting with low-intensity physical activity and gradually increasing to moderate levels. [2016]
- Physical activity programmes for people with stroke or TIA may be delivered by therapists, fitness instructors or other appropriately trained people, supported by interagency working where possible. When delivered outside statutory health services, physical fitness training should be delivered by professionals with appropriate education and training in stroke and exercise (e.g. Chartered Institute for the Management of Sport and Physical Activity [CIMSPA]-endorsed exercise professionals or clinical exercise physiologists). [2023]
- G Stroke rehabilitation services should build links with community-based exercise facilities (such as support groups, gyms, leisure centres or exercise referral schemes) to support people with stroke to transition to ongoing physical activity on completion of an exercise programme. [2023]
- H Stroke services should consider working with other established rehabilitation services, such cardiac or pulmonary rehabilitation, to develop exercise-based programmes and ensure access to equipment and screening protocols. [2023]

5.23 Sources

- A Ada et al, 2006; English and Hillier, 2010; Marsden et al, 2013; Saunders et al, 2013; Kendall and Gothe, 2015
- B Department of Health (UK), 2019
- C English and Hillier, 2010; Marsden et al, 2013; Saunders et al, et al, 2013; Kendall and Gothe, 2015; MacKay-Lyons et al, 2020
- D, E Department of Health (UK), 2019; Working Party consensus
- F-H Guideline Development Group consensus

5.23 Evidence to recommendations

There are Cochrane reviews (English & Hillier, 2010; Saunders et al, 2013), other systematic reviews (Ada et al, 2006; van de Port et al, 2007; Veerbeek et al, 2014b) and one high quality, moderate-sized RCT, other systematic reviews (Ada et al, 2006; van de Port et al, 2007; Veerbeek et al, 2014b) and one high quality, moderate-sized RCT (English et al, 2015) on physical activity after stroke. Overall, the evidence shows that activity programmes have a positive effect on global disability, albeit in the predominantly ambulant stroke population (Saunders et al, 2013). Treatment benefits physical function and supports the use of aerobic exercise and mixed training programmes to improve gait (English & Hillier, 2010; Marsden et al, 2013; Saunders et al, 2013; Kendall & Gothe, 2015). Other studies also suggest positive effects on outcomes such as vascular function (Moore et al, 2015) and psychosocial benefits (Faulkner et al, 2015). [2016]

Cardiorespiratory training, especially when involving walking, appears to be the most effective for cardiorespiratory fitness (with a moderate effect size) but also for walking and balance. Mixed training has a slightly lesser effect. Resistance training is most effective to improve muscle strength and endurance (Saunders et al, 2020). Thus the type of exercise prescribed depends on the patient's own

goals and preferences. However, cardio-respiratory training involving walking has the greatest overall benefit which can persist into the long-term (Saunders et al, 2020). [2023]

5.24 Smoking cessation

About 1 in 5 adults in the UK and Ireland are smokers (Department of Health (Ireland), 2021; Office of National Statistics, 2022). Each year, an estimated 454,700 hospital admissions in England can be attributed to smoking including around 1 in 4 strokes. Smokers have up to three times the risk of stroke and double the risk of recurrent stroke compared to non-smokers, but if they are able to stop, the risk decreases significantly and is at the level of non-smokers after about five years. The health benefits of reducing rather than stopping smoking are not clear. About two-thirds of smokers express the desire to stop but long-term success rates are low at 2-3%. [2016]

5.24 Recommendation

A People with stroke or TIA who smoke should be advised to stop immediately. Smoking cessation should be promoted in an individualised prevention plan using interventions which may include pharmacotherapy, psychosocial support and referral to statutory stop smoking services. [2016]

5.24 Sources

A NICE, 2023a; Working Party consensus

5.24 Evidence to recommendations

There have been a large number of Cochrane reviews assessing a variety of interventions to promote smoking cessation in the general population (for the individual reviews, see https://www.cochranelibrary.com/). A beneficial effect has been demonstrated for nicotine replacement therapy, nicotinic receptor partial agonists (varenicline, cytisine), antidepressant medication (bupropion, nortriptyline), combined pharmacotherapy and behavioural interventions, financial incentives, motivational interviewing, e-cigarettes, exercise, print-based self-help, telephone counselling and brief physician and nurse interventions. The evidence for interventions to increase smoking cessation in people with stroke is limited. A systematic review identified only four studies involving a total of 354 patients (Edjoc et al, 2012). Meta-analysis was not possible and a simple summed cessation rate of 24% for those receiving an intervention compared with 21% for controls was reported. [2016]

NICE public health guidelines (NICE guideline [NG209] Tobacco: preventing uptake, promoting quitting and treating dependence; NICE, 2023) provide guidance on smoking cessation services for all smokers. Stopping in one step is recommended as the approach must be likely to provide lasting success. Recommended interventions include behavioural counselling, group therapy, pharmacotherapy (licensed nicotine containing products, varenicline or bupropion) and referral to statutory stop smoking services, alone or in combination. [2016]

5.25 Nutrition (secondary prevention)

Long-term adherence to cardioprotective diets, when combined with other lifestyle modifications, may reduce stroke recurrence (Appel et al, 1997; Appel et al, 2003; Fung et al, 2008). While there is evidence that tailored dietary modifications can favourably modify cardiovascular risk factors, there is limited evidence that this translates into a reduction in stroke recurrence and mortality (Rees et al, 2013; Adler et al, 2014). [2016]

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5.25 Recommendations

- A People with stroke or TIA should be advised to eat an optimum diet that includes:
 - five or more portions of fruit and vegetables per day from a variety of sources;
 - two portions of oily fish per week (salmon, trout, herring, pilchards, sardines, fresh tuna). [2016]
- B People with stroke or TIA should be advised to reduce and replace saturated fats in their diet with polyunsaturated or monounsaturated fats by:
 - using low-fat dairy products;
 - replacing butter, ghee and lard with products based on vegetable and plant oils;
 - limiting red meat intake, especially fatty cuts and processed meat. [2016]
- C People with stroke or TIA who are overweight or obese should be offered advice and support to aid weight loss including adopting a healthy diet, limiting alcohol intake to 2 units a day or less and taking regular exercise. Targeting weight reduction in isolation is not recommended. [2016]
- D People with stroke or TIA should be advised to reduce their salt intake by:
 - not adding salt to food at the table;
 - using little or no salt in cooking;
 - avoiding high-salt foods, e.g. processed meat such as ham and salami, cheese, stock cubes, pre-prepared soups and savoury snacks such as crisps and salted nuts. [2016]
- E People with stroke or TIA who drink alcohol should be advised to limit their intake to 14 units a week, spread over at least three days. [2016]
- F Unless advised to do so for other medical conditions, people with stroke or TIA should not routinely supplement their diet with:
 - B vitamins or folate;
 - vitamins A, C, E or selenium;
 - calcium with or without vitamin D. [2016]

5.25 Sources

- A He et al, 2006; NICE, 2007; Chowdhury et al, 2012; Rees et al, 2003
- B Marik and Varon, 2009; Galan et al, 2010; Hooper et al, 2011
- C NICE, 2007c; Working Party consensus
- D Adler et al, 2014
- E Zhang et al, 2014; Department of Health (UK), 2016
- F Bazzano et al, 2006; Galan et al, 2010; Bin et al, 2011; Bolland et al, 2010, 2014; Marti-Carvajal et al, 2015

5.25 Evidence to recommendations

Cardioprotective diet

A Cochrane review of the Mediterranean diet for the primary prevention of cardiovascular disease found very small reductions in total and LDL-cholesterol (Rees et al, 2013). Three of five RCTs showed a positive effect on BP, with reductions of 0.7-7.8 mmHg in systolic and 0.7-3.7 mmHg in diastolic BP. The Dietary Approaches to Stop Hypertension (DASH) diet lowered systolic and diastolic BP when followed for 8 weeks (Appel et al, 1997). Long-term follow-up for up to 24 years (Fung et al., 2008) demonstrated that adherence to a DASH-style diet is associated with a lower risk of coronary heart disease and stroke among middle-aged women. Effects on stroke recurrence and mortality are not known. A Cochrane review (Adler et al, 2014) of dietary salt reduction for the prevention of cardiovascular disease confirms

that small reductions in BP can be achieved in normotensive individuals, and greater reductions in hypertensive individuals. Many of the component trials lacked sufficient detail to assess bias; any benefits in terms of cardiovascular mortality and morbidity were modest or non-significant and confined to hypertensive groups. [2016]

Weight-reducing diet

Overweight and obesity is a significant risk factor for the development of cardiovascular disease and is associated with an increase in all-cause mortality (Adams et al, 2006; Bazzano et al, 2006). Both overweight (body mass index [BMI] greater than 25 kg/m²) and obesity (BMI greater than 30 kg/m²) are associated with an increased risk of ischaemic stroke (Strazzullo et al, 2010). Customary advice has targeted a healthy BMI to reduce risk of stroke but high quality intervention studies to support this approach are lacking. Some observational studies have reported a paradoxical inverse relationship between BMI and mortality following stroke (Kim et al, 2011a; Vemmos et al, 2011) with overweight and obese people having reduced mortality, but how this observation might translate into an intervention to reduce recurrent stroke is unclear. [2016]

Alcohol

A meta-analysis of 27 prospective studies with 1,425,513 participants reviewed the dose-response relation between alcohol and risk of stroke (Zhang et al, 2014). In the majority of the component studies, alcohol intake was self-reported. Low alcohol intake (below 15 g/day) was associated with a reduced risk of total stroke, ischaemic stroke and stroke mortality with no significant effect on haemorrhagic stroke (one UK unit = 8 g of alcohol). Moderate alcohol intake (15-30 g/day) had little or no effect on risk of total stroke, haemorrhagic stroke, ischaemic stroke or stroke mortality. Heavy alcohol intake (above 30 g/day) was associated with an increased risk of total stroke. It is not known if a similar relationship would apply to people who have already experienced stroke. [2016]

Micronutrient supplementation

A Cochrane review (Marti-Carvajal et al, 2015) examined the use of B-vitamin supplementation to prevent cardiac events. No benefit was found for homocysteine-lowering interventions in the form of supplements of vitamins B6, B9 or B12 given alone or in combination, at any dosage. Two meta-analyses (Alkhenizan & Al-Omran, 2004; Bin et al, 2011) and one systematic review (Eidelman et al, 2004) examined the effects of vitamin E supplementation on stroke recurrence and mortality, with no benefit seen. Dietary calcium and/or vitamin D supplementation has not been shown to reduce cardiovascular risk (Elamin et al, 2011; Bolland et al, 2014) and in one systematic review it was associated with a modest increased risk (Bolland et al, 2010). Confining the analysis to people with vitamin D deficiency likewise showed no benefit. The impact of other nutrients, including plant stanols/sterols, antioxidants such as vitamins A and C or selenium in stroke prevention is unknown (Hookway et al, 2015). [2016]

5.26 Life after stroke

Stroke research has tended to concentrate on the acute and early phases of recovery yet for about half of those who survive, life after stroke involves some permanent impairment and restriction of their activities. As well as coping with the physical consequences, many people with stroke and their family/carers have long-term psychological and emotional needs. Defining these needs is challenging, and researchers and healthcare professionals may not prioritise the same outcomes as people with stroke. In a UK survey of patients between 1 and 5 years after stroke, about half reported having one or more (median three) unmet needs (McKevitt et al, 2011). Communication problems, worsening disability and ethnicity were associated with a greater number of reported unmet needs, as was living in a more deprived area. Self-reported outcomes after stroke included 52% with a negative change in work activity, 67% a change for the worse in relation to leisure activities or interests, 18% a loss of income, 31% an increase in expenses, and 42% a negative impact on the relationship with their partner.

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Over half of respondents reported needing more information about stroke, including diet, applying for benefits, aids and adaptations to the home and driving. Of those who reported emotional problems (over a third), the great majority felt they did not receive the support they needed. No relationship between unmet need and time since stroke was identified, indicating that these needs are persistent and long-term. [2016]

5.27 Further rehabilitation

Following discharge from rehabilitation, many people with stroke experience a discontinuity in their care (Hartford et al, 2019) whilst still adjusting to life after stroke. In addition to ongoing needs, the discharge process is likely to give rise to new needs because of changes in physical, psychological, social and environmental circumstances (Pringle et al, 2013; Hodson et al, 2016) for which people with stroke and their families often feel inadequately prepared, leaving them feeling unsupported (Tholin & Forsberg, 2014) or even abandoned (Pindus et al, 2018). The needs of people with stroke and their families are likely to change over time, as adjusting to life after stroke is an evolving, long-term challenge for many (Pallesen, 2014; Hall et al, 2022). [2023]

A systematic review of unmet needs after stroke identified that, on average, each person with stroke experiences between two and five unmet needs (Chen et al, 2019). Common unmet needs related to body function include fatigue, cognitive problems, neuropsychological and emotional needs and pain; those related to activity and participation include secondary prevention, mobility, work, leisure and hobbies, while those related to the environment include information, transport, therapy and home support or personal care. [2023]

In order to address these needs, many people with stroke seek to continue rehabilitation in the longer term, either continuously or on an intermittent basis. As well as facilitating recovery, rehabilitation (including exercise) delivered later after stroke may prevent regression of physical or cognitive gains achieved in the earlier stages of recovery, and prevent deconditioning. Furthermore, people affected by stroke often seek sources of support outside of the health and social care system (Forster et al, 2021). These may include advice lines and patient advocacy organisations, communication support groups, exercise groups and other informal gatherings to provide social, emotional and psychological support. [2023]

The provision of appropriate, person-centred follow-up rehabilitation and long-term support after stroke is advocated by several key organisations, including the British Society of Rehabilitation Medicine in their Specialist Standards for Community Rehabilitation (British Society of Rehabilitation Medicine, 2021), the Community Rehabilitation Alliance in their Manifesto (Community Rehabilitation Alliance, 2021), NHS England in their National Stroke Service Model for England (NHS England, 2021), the Scottish Government in their Programme for Government (Scottish Government, 2022), and the National Stroke Strategy (Ireland) (Health Service Executive, 2022). Inter-agency partnership working is highlighted in particular to ensure people are able to access the right service at the right time, preventing gaps in service transitions. [2023]

Healthcare professionals should facilitate timely access to services that are necessary to enable people with stroke and their families to address their evolving needs over time. Follow-up health and social care may be warranted, but a wide range of other support services may also be sought from the third sector (e.g. the Stroke Association, Chest Heart & Stroke Scotland, Different Strokes, the Irish Heart Foundation). Furthermore, healthcare professionals play a pivotal role in supporting people with stroke and their families in designing self-management plans and reviewing these (see also Section 4.4 Self-management). [2023]

As this guideline does not include a section dedicated to support services outside of health or social care, recommendations in this section include signposting to such services, to ensure that people affected by stroke are referred to the appropriate services to address their needs. [2023]

5.27 Recommendations

- A People with stroke, including those living in a care home, should be offered a structured, holistic review of their individual needs by a healthcare professional with appropriate knowledge and skills, using an appropriate mode of communication (e.g. face-to-face, by telephone or online).
 - This review should cover physical, neuropsychological and social needs, seek to identify what matters most to the person, and be undertaken at 6 months after stroke, or earlier if requested by the person with stroke.
 - At this 6-month review, the reviewer should discuss with the person with stroke who
 would be best placed to undertake the next review at 1 year post-stroke (or at
 another point in time, depending on the person's needs), as well as the agreed mode
 of communication.
 - This review should be offered annually thereafter (or at another point in time, if requested by the person with stroke), for as long as a need for ongoing review continues and on request thereafter. [2023]
- B People with stroke who have further needs identified at a 6-month or subsequent review should be considered for intervention or referral for health or social care assessment if:
 - new health or social care needs are identified;
 - existing health or social care needs have escalated;
 - further rehabilitation goals related to specific physical, psychological, vocational, family or social needs can be identified and agreed;
 - risk factors or co-morbidities are identified that would lead to deterioration if no action were taken. [2023]
- People with stroke who have further needs identified at a 6-month or subsequent review that do not require health or social care input should be provided with information about or referred to other appropriate services to address their needs (e.g. community-based support groups provided by voluntary or statutory services). Healthcare professionals should discuss with the person if they could facilitate the transition with their agreement (e.g. by providing relevant information to the service, or by a scheduling a joint session). [2023]
- D Healthcare professionals providing 6-month or subsequent reviews of people with stroke should maintain an up-to-date overview of appropriate health and social care services, and other service providers (e.g. community support groups and local councils) to facilitate transitions to other services as required. [2023]
- People with stroke should be provided with the contact details of a named healthcare professional (e.g. a stroke co-ordinator or key worker) who can provide further information, support and advice, as and when needed. [2023]
- People with stroke should be supported to develop their own self-management plan, based on their individual needs, goals, preferences and circumstances. [2023]
- G People with stroke who are unable to undertake their own self-management should be referred in a timely manner to appropriate health, social care, or other voluntary or statutory services depending on their needs. [2023]

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5.27 Sources

- A Guideline Development Group consensus
- B Rodgers et al, 2019b; Shaw et al, 2020
- C-G Guideline Development Group consensus

5.27 Evidence to recommendations

The literature related to follow-up after the end of formal rehabilitation is diverse; it includes specific rehabilitation interventions already described in Chapter 4 and overlaps with other areas, including secondary stroke prevention (Chapter 5), Vocational rehabilitation (Section 4.15 Return to work), and Supported self-management (Section 4.4 Self-management). [2023]

An intervention aimed at maintaining motor function using individual coaching was compared with usual care in a Norwegian RCT of moderate quality (Askim et al, 2018; Døhl et al, 2020). This intervention was provided once a month for 18 months, initially delivered mostly face-face, gradually introducing telephone contact. Individual goals were set and monthly schedules were agreed, which comprised 45 to 60 minutes of exercise (including 2 to 3 periods of vigorous activity) once a week plus physical activity for 30 minutes daily. Participants were given various options to join groups in different settings to match their requirements. Findings showed that this coaching intervention was safe but it had no additional effect on any aspect of motor function, ADL, fatigue, mood, quality of life, or caregiver strain. The cost analysis (Døhl et al, 2020) indicated that the intervention added costs to usual care. [2023]

An extended stroke rehabilitation service (Rodgers et al, 2019b; Shaw et al, 2020), which aimed to maximise recovery and adjustment to residual disability in the context of everyday activities, was compared with usual care in a high quality, UK-wide RCT. It comprised five extra telephone reviews (including goal setting and action planning) with senior therapists over 18 months after the end of early supported discharge. Compared with usual care, this intervention did not improve extended ADL but it did improve health-related quality of life, anxiety and depression, and patient satisfaction (including whether needs had been met, and whether sufficient treatment had been received to improve mobility). The intervention may also be cost-effective due to the quality of life advantages and a tendency towards lower overall costs in primary care. Participants with stroke felt that the reviews were reassuring, thorough and comprehensive, and that the goal setting had motivated them, but they were unclear if actual outcomes had been improved. Therapists thought that the intervention addressed the unmet need for ongoing support for people living with stroke and that reviews were comprehensive, but they disapproved of having to deliver the intervention by telephone only. They also thought that the reviews were useful, primarily around emotional and social issues, and they valued being able to connect people with stroke to services, although they felt uncomfortable if they were unable to provide the necessary support or onward referral for an identified rehabilitation need. [2023]

An intervention which aimed to identify physical, cognitive and emotional problems in daily life, provide support and psycho-education and refer to further specialised healthcare as required, was compared with usual care in a Dutch study (Verberne et al, 2021; Verberne et al, 2022). It comprised face-to-face sessions of up to 45 minutes each in a primary care centre at 6 months after hospital discharge, with the number of sessions depending on the nurse's judgement. This intervention did not result in any improvements in mood or social participation compared to usual care, whilst other outcomes were not reported. The authors concluded that the intervention was cost-effective (Verberne et al, 2021), but due to the low quality of the study design and differences in healthcare systems, no conclusions can be drawn to support a recommendation. [2023]

The Improving Longer Term Stroke Care (LoTS2Care) programme (Forster et al, 2021) was designed to develop and test a longer-term integrated stroke care intervention to improve quality of life for people

with stroke and their family/carers by addressing unmet needs and enhancing participation in life situations. Based on service user experiences, systematic literature reviews, and an evaluation of existing service models, a novel intervention (New Start) was designed, refined and tested in a feasibility cluster RCT involving 10 stroke services across England and Wales, recruiting 269 participants. Further development work will be undertaken before a full trial evaluation, and findings will inform subsequent editions of this guideline. [2023]

Some people start or continue to improve many months or years after the event, and these people may benefit from further rehabilitation or other support at a later stage. Whilst limited, there is evidence to suggest that for some people improvements in communication, arm function, walking, physical fitness and ADL can be achieved with interventions more than 6 months after stroke (Palmer & Enderby, 2007; Duncan et al, 2011; Ferrarello et al, 2011; Lohse et al, 2014; Veerbeek et al, 2014b; Ward et al, 2019). To provide personalised care to this group and to identify other unmet needs, the consensus of the Guideline Development Group is that a comprehensive, structured needs reassessment should be undertaken at 6 months – or earlier, depending on the individual's needs. Structured, planned follow-up may reduce some of the health inequalities between those with higher and lower levels of education (Irewall et al, 2019). [2023]

This review should consider physical, psychological and social needs (including relationships and work, where applicable) related to adjusting to life after stroke. The review should identify what matters most to the person with stroke, ensuring that any referrals are appropriately targeted. The role of the professional is to support the person with stroke to identify and prioritise their needs and goals and act as a facilitator, initiating timely referrals or providing guidance to appropriate service providers within health and social care or beyond, as and when required. Referrers should consider health and social care services, and services offered by other organisations, including stroke support groups (e.g. communication support provided by the Stroke Association, Chest Heart and Stroke Scotland, the Irish Heart Foundation or Different Strokes) and local councils (e.g. exercise referral schemes). [2023]

There is no 'one size fits all' with regard to onward referral; instead, given the diversity in recovery profiles, needs and timing, as well as the cultural contexts in which people with stroke lead their lives, a personalised approach is required. This is to ensure that the aims, content, mode of delivery (e.g. faceface, online) and timing of any services are aligned with the priorities, needs, goals and circumstances of the person with stroke and their family/carers where appropriate. [2023]

5.27 Implications

Primary care teams, in collaboration with hospital-based or community stroke teams, specialist community neurorehabilitation or brain injury rehabilitation teams, will need to consider the resource implications of implementing follow-up and annual review for people with stroke living in the community and make appropriate provision. [2023]

5.28 Social integration and participation

Helping people with stroke to integrate back into the community in the way that they want is a key goal of healthcare; engagement in community activity is associated with improved quality of life. Most healthcare focuses on improving a person's capacity to undertake activities. The wider task of achieving social and community integration depends upon factors such as the person with stroke and their family/carers having information about local opportunities and being aware of the physical and mental health benefits of activity and engagement, the availability of accessible social settings and transport and the appropriate training of community providers of leisure and social activities. Stroke voluntary sector services and peer support groups can play an important role in helping community integration. Lack of accessible transport is often a significant barrier to participation for disabled people. [2016]

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Other aspects of stroke and stroke recovery of relevance to integration and participation are covered in other parts of this guideline and include Section 2.7 Transfers of care – general principles, Section 2.11

Psychological care – organisation and delivery, Section 4.8 Extended activities of daily living, Section 4.14

Driving, Section 4.15 Return to work, Section 4.25 Fatigue, Section 4.38 Mood and well-being, Section 4.13 Sex. [2016]

5.28 Recommendations

- A As part of their self-management plan, people with stroke should be supported to identify social and leisure activities that they wish to participate in, taking into account their cognitive and practical skills. Healthcare professionals should:
 - advise the person with stroke and their family/carers about the benefits of participating in social and leisure activities;
 - identify and help them to overcome any barriers to participation (e.g. low self-confidence or lack of transport). [2016]
- B People with stroke should be provided with information and referral to statutory and voluntary community organisations that can support the person in social participation. [2016]
- C People with stroke whose social behaviour is causing distress to themselves or others should be assessed by an appropriately trained healthcare professional to determine the underlying cause and advise on management. Following the assessment:
 - the nature of the problem and its cause should be explained to family/carers, other people in social contact and the rehabilitation team;
 - the person should be helped to learn the best way to interact without causing distress;
 - those involved in social interactions should be trained in how to respond to inappropriate or distressing behaviour;
 - psychosocial management approaches should be considered;
 - antipsychotic medicines may be indicated if other causes have been excluded and the person is at risk of harm to themselves or others. The balance of risk and benefit from antipsychotic medication should be carefully considered. Treatment should be started with a low dose and increased slowly according to symptoms, and should be shortterm (e.g. one week) or intermittent and withdrawn slowly. [2016]

5.28 Sources

- A Langstaff et al, 2014; Dorstyn et al, 2014; Obembe and Eng, 2015
- B Working Party consensus
- C NICE, 2010b, 2019a; Obembe and Eng, 2015; Working Party consensus

5.28 Evidence to recommendations

A metasynthesis of qualitative research identified several themes which, from the perspective of people with stroke, acted as barriers or facilitators to community reintegration (Walsh et al, 2015). As well as the primary effects of the stroke (impairments and fatigue), these comprised personal factors (perseverance, adaptability, emotional challenges, relevance of activities), social factors (sense of belonging versus stigmatisation, levels of support, environmental limitations) and interactions with professionals (levels of support, joint decision-making, relevance of rehabilitation to real world requirements). Anger, frustration and more challenging behavioural problems may present barriers to social and community integration but other than generic principles, there is limited evidence to guide management for people or families/carers with these problems. [2016]



A systematic review of leisure therapy including eight studies and 615 participants identified methodological shortcomings but nonetheless some evidence of short-term improvements in quality of life and mood as well as increased participation and satisfaction with leisure activities (Dorstyn et al, 2014). In a review of 24 studies (including 2042 people with stroke) that included measures of social participation as an outcome, a small beneficial effect was identified for interventions utilising exercise (Obembe & Eng, 2015). A community walking training programme in which people with stroke undertook walking therapy in a real-world environment resulted in greater improvements in walking function and social participation (Kim et al, 2014), but a Cochrane review found the available evidence insufficient to establish effectiveness (Barclay-Goddard et al, 2015). [2016]

6 Implementation of this guideline

6.0 Introduction

Clinical guidelines usually focus on how an individual patient should be treated, and draw upon evidence concerning the efficacy, effectiveness and costs of interventions. This chapter brings together key recommendations to guide those responsible for the funding, planning and delivery of services along the entire pathway of stroke care, other than primary prevention. Clinical teams can only provide services that are appropriately planned, staffed and paid for. The recommendations in the 2023 National Clinical Guideline for Stroke will not provide the anticipated benefits for people with stroke unless organisations that plan and deliver health and social care fully support their implementation. [2023]

The recommendations for policy makers and service providers in this chapter are derived directly from the clinical and organisational recommendations made elsewhere in the guideline. Service design for stroke care should be planned in collaboration between commissioners/service planners, health and social care providers, healthcare professionals and patients and carers. Service planners/commissioners therefore have a critical part to play in the wider implementation of this guideline and the achievement of its aim to improve the care of all people with stroke. [2023]

Partnership working may also be required across geographical boundaries, for example in providing hyperacute stroke care and tertiary neuroscience services. Clinical Networks with an understanding of the complexity of the stroke pathway have brought service planners/commissioners and providers together, and have proved to be successful in quality improvement and service redesign. There needs to be an acknowledgement that investment of resources in one particular part of the pathway, e.g. acute stroke care by health services, may lead to a reduction in demand for services in another part of the pathway, e.g. long-term social care. Service planners/commissioners and health and social care providers need to work closely together to ensure that financial issues do not act as barriers to the provision of seamless, evidence-based care or to achieving better outcomes for people with stroke. [2023]

Service specifications will need to take full account of all the recommendations outlined in the preceding chapters 2-5 of this guideline. Individual contracts should be monitored against the service specification, which should include meaningful process and person-centred outcome measures. All services in all settings should be required to scrutinise their services through national comparative audit, and undertake periodic patient and carer surveys. [2023]

6.1 Overall structure of stroke services

The provision of a well-led, appropriately trained and skilled workforce providing holistic and compassionate care to patients and their families is one of the principal implications of the landmark 2013 report into the failings in hospital care at Mid-Staffordshire NHS Foundation Trust produced by Robert Francis (Francis, 2013), and this needs to be reflected in the services provided to people with stroke in both NHS/HSE and non-NHS/HSE settings. People with stroke present to health services with a broad range of problems, covering all illness domains over a prolonged period of time. Consequently, it is vital to have a service that is organised to respond in a timely and effective way to each person's unique needs as they arise. [2023]

6.1 Recommendations

A Comprehensive stroke services should include the whole stroke pathway from prevention (including neurovascular services) through pre-hospital and acute care, early rehabilitation, secondary prevention, early supported discharge, community

- rehabilitation, systematic follow-up, palliative care and long-term support. [2023]
- B Comprehensive stroke services should be provided based on an estimate of the needs of the population served, and derived from the best available evidence locally and nationally. [2016]
- C Comprehensive stroke services should ensure that:
 - people with suspected stroke or TIA are diagnosed and treated urgently, using evidence-based treatments;
 - sufficient provision is made for people with stroke with long-term disability covering the full range of their needs (e.g. nursing, therapy, emotional support, practical support, family/carer support);
 - people with stroke who live in care homes or are unable to leave their own home have equivalent access to specialist stroke services;
 - people with stroke can re-access specialist stroke services when necessary;
 - people dying with stroke receive end-of-life (palliative) care from the acute stroke service and whenever possible in their own homes. [2023]
- D A public education and professional training strategy should be developed and implemented to ensure that the public and emergency personnel (e.g. staff in emergency call centres) can recognise when a person has a suspected stroke or TIA and respond appropriately. This should be implemented in such a way that it can be formally evaluated. [2016]
- All those caring for people with stroke should have the knowledge, skills and attitudes to provide safe, compassionate and effective care, especially for vulnerable people with restricted mobility, sensory loss, impaired communication and cognition and neuropsychological problems. [2016]
- People with stroke and their family/carers should be provided with sufficient information about which services are available and how to access them at all stages of the pathway of care. All information should be provided in a format accessible to those with communication disability. [2016]
- G Along the pathway of stroke care, there should be:
 - protocols between healthcare providers and social services that enable seamless and safe transfers of care without delay;
 - protocols in place that enable rapid assessment and provision of all equipment, aids (including communication aids) and structural adaptations needed by people with disabilities after stroke. [2016]
- H The process of care, the patient experience and person-centred outcomes of hospital and community-based stroke services should be monitored and evaluated regularly through participation in national comparative audit. [2023]
- I All stroke services should regularly seek the views of those who use their services, and use the findings to design services around the needs of the person with stroke. [2016]

6.1 Implications

These recommendations should result in a comprehensive stroke service that is more coherent, responsive and cost-efficient. In some instances there will be costs associated with start-up or with changes in practice, but the evidence indicates that well-organised services deliver better outcomes at approximately the same cost. Early supported discharge services are a good example of this, with costs being transferred out of the hospital sector into community provision. Achieving change consistent with these recommendations will require considerable initial effort and commitment, involving negotiations

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with many stakeholders including health services, local government, voluntary and community groups, patient and carer groups and private providers. [2023]

6.2 Acute stroke services

This section covers aspects of the implementation of high quality acute care that will be of particular relevance to service planners/commissioners for acute hospital services. [2016]

6.2 Recommendations

- A Ambulance services, including call handlers, should respond to every person with a suspected acute stroke as a medical emergency. [2016]
- B Acute stroke services should provide:
 - urgent brain imaging for patients with suspected acute stroke, including the 24/7 provision of CT angiography and perfusion;
 - treatment with thrombolysis for eligible patients with acute ischaemic stroke;
 - an endovascular service for eligible patients with acute ischaemic stroke;
 - a neuroscience service to admit, investigate and manage patients referred with subarachnoid haemorrhage, both surgically and with interventional radiology;
 - a neuroscience service delivering neurosurgical interventions for patients with intracerebral haemorrhage, malignant cerebral oedema, and hydrocephalus;
 - direct admission of patients with acute stroke to a hyperacute stroke unit providing active management of physiological status and homeostasis within 4 hours of arrival at hospital;
 - an acute neurovascular service for the diagnosis and treatment of people with suspected TIA and minor stroke;
 - an acute vascular surgical service to investigate and manage patients with TIA and stroke due to carotid artery stenosis. [2023]
- C Acute stroke services should involve the active participation of people with stroke and their family/carers in the planning and evaluation of their services. [2016]

6.2 Implications

The provision of comprehensive acute stroke services may require the development of hub-and-spoke models of care (where a few hospitals in a region are designated to provide the hyperacute care for all patients), or telemedicine networks and other forms of cross-site working. The optimal disposition of acute stroke services will depend on the geography of the area served, with the objective of delivering the maximum number of time-critical treatments to the greatest number of people with stroke. Substantial service change will create obligations for service planners/commissioners to consult with people with stroke and the public in accordance with their statutory responsibilities. [2023]

6.3 Secondary prevention services

At least one quarter of all strokes are recurrences, and people who have already suffered a stroke or TIA have a 5-year risk of a further vascular event as high as 22.4%, even with modern multiple risk factor treatments (Amarenco et al, 2006; Mohan et al, 2011). Improving risk factor management in this group therefore offers the potential to deliver large reductions in cardiovascular events (Rothwell, 2007), but the incomplete implementation of the evidence for secondary vascular prevention described in this guideline leaves many people at high risk of recurrence and fails to deliver the anticipated benefits for patients and health services (Johnson et al, 2007). It is vital that secondary prevention services are

effective and prompt, and support people with stroke and TIA in maintaining their treatments in the long-term. [2016]

6.3 Recommendations

- A Healthcare providers should enact all the secondary stroke prevention measures recommended in this guideline. Effective secondary prevention should be assured through a process of regular audit and monitoring. [2016]
- B Comprehensive stroke services should:
 - identify and treat people's modifiable vascular risk factors, including symptomatic carotid artery stenosis, as soon as possible;
 - provide all people with stroke or TIA and their family/carers with information and support for treatments and lifestyle changes to reduce their risk of stroke, tailored to their individual needs;
 - liaise with and support general practitioners in the long-term management of risk factors in people with stroke or TIA. [2023]
- C The lifestyle recommendations for stroke prevention made in this guideline should be implemented through:
 - promoting increased physical activity and a reduction in sedentary behaviour;
 - providing smoking cessation services;
 - working with other organisations to make it easier for people with disabilities to participate in exercise;
 - promoting healthy eating;
 - supporting people who drink alcohol in excess to abstain or maintain their intake within recommended limits. [2023]

6.3 Implications

Service planners/commissioners should play an active role in promoting secondary vascular prevention, which is a public health issue as well as being relevant to the individual person with stroke. Addressing medical risk factors and making lifestyle changes are effective in reducing the risk of recurrent stroke, but clinical practice in primary and secondary care needs to support people with stroke to persist with their treatments long-term, something that could be done through annual review of people with stroke or TIA (NICE, 2016b) see also Section 5.1 A comprehensive and personalised approach). [2016]

6.4 Stroke rehabilitation services

Stroke rehabilitation services should be provided to reduce limitation in activities, increase participation and improve the quality of life of people with stroke using therapeutic and adaptive strategies. With stroke being the third largest cause of disability in the UK (Newton et al, 2015), providing effective rehabilitation is cost-effective in reducing long-term disability and the costs of domiciliary and institutional care. [2016]

6.4 Recommendations

- A Stroke rehabilitation services should provide:
 - an inpatient stroke unit capable of providing stroke rehabilitation for all people with stroke admitted to hospital;
 - community-based specialist rehabilitation services capable of meeting the specific health, social and vocational needs of people with stroke of all ages, including provision of early supported discharge to enable people with stroke to receive

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intensive rehabilitation within 24 hours of returning home or moving into a care home;

- services capable of delivering specialist rehabilitation, which best meets the person's needs in a variety of community settings including their own home, gyms or community centres, or outpatient clinics;
- for the ongoing information needs of people with stroke, including those with aphasia and other communication disabilities.

Such services should be integrated to provide seamless specialist care that is not time-limited. [2023]

- B Stroke rehabilitation services should be capable (from within the service or by referral if the need is particularly complex) of meeting all the needs of people with stroke (e.g. orthotics, specialist seating, equipment provision, management of physical effects such as continence and spasticity, vocational rehabilitation, emotional/psychological support, social care, assistance with benefits). [2023]
- C People with stroke whose mental capacity is impaired should have access to independent specialist advice and support in relation to advocacy. [2016]
- D Stroke rehabilitation services should ensure they have adequate equipment, including the technology requirements for providing telerehabilitation, to enable provision of all the treatments recommended within this guideline. [2023]
- E Stroke rehabilitation services should regularly review their skill mix and methods of delivering rehabilitation to ensure optimisation of resources and clinical effectiveness. [2023]

6.4 Implications

Service planners/commissioners will need to ensure that they procure specialist services in relation to the overall population need that are capable of meeting the specific and multiple needs of people with stroke, and that they meet their obligations under the Mental Capacity Act 2005 / Adults with Incapacity (Scotland) Act 2000 / Assisted Decision Making (Capacity) Act 2015 (Ireland) as they relate to people with acquired brain injury including stroke. [2023]

6.5 Long-term support services

Stroke is only one of many causes of long-term neurological disability including other conditions such as head injury, dementia and multiple sclerosis. Furthermore, many of the needs of a person with stroke will relate to other co-morbidities such as frailty, osteoarthritis, cognitive impairment or other vascular disease, or other social issues such as loneliness and isolation from mainstream society. These recommendations will inevitably be more general and overlap with other long-term disabling conditions, but emphasise the specific needs of stroke patients. [2023]

6.5 Recommendations

- A Long-term support services should provide:
 - routine follow-up of people with stroke six months after hospital discharge and annually thereafter;
 - reassessment and further treatment of people with stroke who are no longer receiving rehabilitation. Services should be accessible from primary or secondary care, social services or by self-referral. [2016]
- B Between health and social services and other agencies, people with stroke should be able to:
 - receive the practical and emotional support they need to live with long-term disability

- (e.g. housing, employment);
- access suitable social and leisure activities outside their homes;
- receive maintenance interventions (e.g. provision of exercise programmes and peer support) to enhance and maintain health and well-being. [2016]
- C Long-term support services should ensure that the family/carers of people with stroke:
 - are aware that their needs can be assessed separately;
 - are able to access the advice, support and help they need;
 - are provided with information, equipment and appropriate training (e.g. manual handling) to enable them to care for a person with stroke;
 - have their need for information and support reassessed whenever there is a significant change in circumstances (e.g. if the health of the family member/carer or the person with stroke changes). [2016]
- D Advance care planning and community palliative care services should be available for people with stroke with limited life expectancy, and their family/carers, where appropriate. [2016]

6.5 Implications

Integrated care from health, social and voluntary sectors can do much to alleviate the personal and social impact of dependency for the person living with the long-term consequences of stroke and their family. The high mortality from severe stroke dictates that access to palliative care services is an important means of relieving suffering for people with stroke and their families, who tend not to view stroke in the same way as other life-threatening or 'terminal' conditions. These needs and the interventions to mitigate them should be considered as part of a whole-system approach to physical and cognitive disability in the community, and include the obligations to carers placed upon health and social services under relevant legislation. [2023]

Glossary

Activities of daily living Refers to activities that people normally undertake (e.g. bathing, dressing,

feeding themselves).

Acupuncture A complementary medicine that involves inserting thin needles into the skin.

Acute stroke service Consists of: a) a comprehensive stroke centre (CSC) providing hyperacute,

acute and inpatient rehabilitation including thrombectomy (thrombectomy centre) and neurosurgery; or b) an acute stroke centre (ASC) providing hyperacute, acute and inpatient rehabilitation. All components of a specialist acute stroke service should be based in a hospital that can investigate and manage people with acute stroke and their medical and neurological

complications.

Aerobic exercise Low- to moderate-intensity exercise that can be sustained for long periods of

time (e.g. cycling, swimming or walking).

Agnosia The inability for a patient to recognise or make proper sense of sensory

information.

Alteplase A drug used for thrombolysis.

Aneurysm A bulge in the wall of a blood vessel that is filled with blood. This can burst

and cause a haemorrhage.

Angiography A technique that uses X-ray technology to image blood vessels.

Anticoagulants A group of drugs used to reduce the risk of clots by thinning the blood.

Antiphospholipid Sometimes called 'sticky blood syndrome' because blood clots form too quickly; this is due to antibodies against the body's phospholipid part of

every cell in the body.

Antiplatelets A group of drugs used to prevent the formation of clots by stopping platelets

in the blood sticking together.

Antithrombotics The generic name for all drugs that prevent the formation of blood clots. This

includes antiplatelets and anticoagulants.

Aphasia Communication difficulties after a stroke which can affect a person's speech,

processing, reading and writing.

Arterial dissection This is caused as a result of a small tear forming in the lining of the arterial

wall

Atherosclerosis Fatty deposits that harden on the inner wall of the arteries (atheroma) and

roughen its surface; this makes the artery susceptible to blockage either by

narrowing or by formation of a blood clot.

Atrial fibrillation A heart condition that causes an irregular heartbeat, often faster than the

normal heart rate.

Audit (clinical) A method of evaluating the performance of a clinical service against a set of

standards/criteria.

Bobath therapy Treatment which aims to use facilitative handling which prioritises normal

movement and muscle tone or inhibition of reflex activity rather than maximising practice and patient activity. Also known as neurophysiological

or neurodevelopmental treatment.

Body mass index (BMI) An index of body weight corrected for height.

Botulinum toxin A toxin which when injected can relax muscles to reduce spasticity.

Cardiovascular disease Disease of the heart and/or blood vessels.

Care pathway A tool used by healthcare professionals to define the sequence and timings of

a set of tasks or interventions that should be performed for a patient who

enters a healthcare setting (e.g. a hospital) with a specific problem.

Carotid angioplasty A surgical procedure that widens the internal diameter of the carotid artery,

after it has been narrowed by atherosclerosis.

Carotid arteries Main blood vessels in the neck, which supply oxygenated blood to the brain.

Carotid A surgical procedure used to clear the inside of the carotid artery of

endarterectomy (CEA) atheroma. Carotid stenosis The narrowing of the carotid arteries in the neck.

Carotid stenting Insertion of a tube into the carotid artery in order to prop the artery open

and reduce narrowing.

Caval filter A device that is inserted into the veins to prevent a blood clot entering the

Cerebral venous thrombosis

A blood clot that forms within a vein inside the brain.

Clinician A registered healthcare professional such as a doctor, nurse or therapist.

Cochrane review A systematic review of research in health care and health policy that is

published in the Cochrane Database of Systematic Reviews.

Commissioner (health

services) Community stroke

team, community stroke rehabilitation

team

Person or organisation in some parts of the UK National Health Service (NHS) that decides how to allocate the health budget for a service.

A stroke specialist multidisciplinary team that provides stroke rehabilitation for patients in their own home or other community setting (including care homes and nursing homes). This may be following hospital discharge, after a patient has been discharged from an early supported discharge team or at any point post stroke where rehabilitation needs are identified. The intensity

and duration of this service should be determined by patient need.

Compensatory strategies

Learning an alternative way of completing a task.

Computed

tomography (CT)

An X-ray technique used to examine the brain.

Confidence interval (CI)

Constraint-induced movement therapy When analysing a research study, this is the range ('interval') of possible results that statisticians are 95% confident the actual result lies between.

Therapy that involves preventing the use of the unaffected side of the body thus forcing the use of the affected side.

Cost-effectiveness The extent to which the benefits of a treatment outweigh the costs.

Decompressive hemicraniectomy

A surgical procedure for the treatment of raised pressure inside the brain from fluid, blood or swelling. A piece of skull is removed to allow the brain to

swell.

Deep vein thrombosis

(DVT)

A blood clot that develops in the large veins, usually in the legs.

Diabetes, diabetes

mellitus

A metabolic disease in which a person has high blood sugar.

Diagnostic accuracy

The degree to which a diagnostic (or screening) tool or procedure is able to distinguish between cases and non-cases. See also 'sensitivity' or 'specificity'.

Doppler ultrasound

An imaging technique that measures blood flow and velocity through blood

vessels.

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Dysarthria Difficulty producing clear speech, caused by muscle weakness.

Dyspepsia Indigestion.

Dysphagia Difficulty in swallowing.

Early supported

discharge

An intervention delivered by a co-ordinated, stroke specialist,

multidisciplinary team that facilitates the earlier transfer of care from hospital into the community and provides responsive (within 24 hours) and

intensive stroke rehabilitation in the patient's place of residence (usually over a time-limited period).

Endarterectomy The surgical removal of plaque from a blocked artery to restore blood flow.

Face Arms Speech Time (FAST) test

A test used to screen for the possibility of a stroke or a TIA.

Fatigue Physical or mental exhaustion that does not get better through normal

periods of rest.

Foot-drop A condition in which the foot hangs limply whilst walking.

Gastrointestinal Bleeding anywhere between the throat and the rectum.

bleeding

Gastrostomy A surgical opening into the stomach to enable feeding.

Gastrostomy feeding (also tube feeding)

Provision of nutrition and fluids via a tube directly into the gastrointestinal

tract.

Goal attainment Rehabilitation goals for particular tasks are set by the patient and therapists

together.

Haemorrhage Bleeding caused by blood escaping into the tissues.

Haemorrhagic stroke A stroke that happens when a blood vessel bursts, leading to bleeding in the

brain (also called a 'brain haemorrhage').

Healthcare A professional involved in stroke care, such as a doctor, nurse, therapist, or

professional care staff.

HEART UK A cholesterol charity.

Hemianopia Blindness or some loss of vision in one part of the visual field.

Homeostasis Regulation of internal environment (e.g. body temperature regulated at

37°C).

Hydrocephalus A build up of fluid within the skull.

Hyperacute stroke unit/centre/service

A stroke unit, centre or service that treats patients in the first 72 hours of

symptom onset.

Hyperlipidaemia Raised levels of lipids (cholesterol, triglycerides or both) in the blood serum.

Hypertension Raised blood pressure.

Hypertensive Brain damage caused by raised blood pressure.

encephalopathy

Hypoglycaemia Blood sugar levels lower than the normal range.

Hypoxia Blood oxygen levels outside the normal range, e.g. below 95% saturation.

Incontinence Inability to control passing of urine and/or faeces.

Infarct An area of cell death due to a deprived blood supply.

Integrated community An inte

stroke service

An integrated service that provides early supported discharge and

community stroke rehabilitation.

International A classification of health used as a framework by the World Health

Classification of Organization (WHO) to measure health and disability.

Functioning, Disability and Health (ICF)

Ischaemic stroke A stroke that happens when a blood clot blocks an artery that is carrying

blood to the brain.

A diagnostic or therapeutic procedure that involves collection of fluid from Lumbar puncture

the base of the spine.

Magnetic resonance

imaging (MRI)

A non-invasive imaging technique that allows for detailed examination of the

brain.

Malnutrition Universal

Screening Tool (MUST)

A screening tool consisting of five steps to help identify which adults are

malnourished or at risk of malnourishment.

Meta-analysis A statistical technique for combining the results of a number of studies that

address the same question and report on the same outcomes to produce a

summary result.

Mouth care Also referred to as oral health care. Refers to the promotion and

> maintenance of a clean oral cavity including the teeth, gums, cheeks, tongue and palate. A clean mouth requires the removal of traces of food and debris

and dental plaque.

MRI with diffusionweighted imaging

This type of scan shows areas of recent ischaemic brain damage.

Musculoskeletal pain Pain of the muscles and/or joints.

National Institute for Health and Care Excellence (NICE)

A special health authority set up within the NHS to develop appropriate and consistent advice on healthcare technologies, and to commission evidencebased guidelines. Its remit extends in most cases to England, Wales and

Northern Ireland.

National Institute of Health Stroke Scale (NIHSS)

A score to assess the severity of a stroke.

Neuropathic pain

Pain caused by damage to nerves.

Orthosis An appliance used to support or align an area of the body to facilitate

movement, or prevent or correct damage.

Palliative care Care that relieves rather than treats symptoms.

Pneumonia An inflammatory condition of the lungs usually caused by infection.

Pulmonary embolism A blood clot in the lungs.

Quality of life Refers to the level of comfort, enjoyment, and ability to pursue daily

activities.

Quality standard A standard set (e.g. by NICE) that is used to define whether the quality of

care is of a high standard.

Randomised controlled trial (RCT) (often

'randomised trial')

A trial in which people are randomly assigned to two (or more) groups: one (the experimental group) receiving the treatment that is being tested, and the other (the comparison or control group) receiving an alternative

treatment, a placebo (dummy treatment) or no treatment. The two groups are followed up to compare differences in outcomes to see how effective the experimental treatment was. Such trial designs help minimise experimental

bias.

Recognition of stroke in the emergency room (ROSIER)

A tool used to establish the diagnosis of stroke or TIA.

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Rehabilitation A set of treatments and activities to promote recovery and reduce

disability. Rehabilitation treatments are provided by therapists and therapy

assistants.

Saturated fat A type of fat that is commonly found in meat and dairy products as opposed

to fats found in plants and fish, which may be unsaturated.

Self-efficacy A person's belief in their own competency.

Self-management Actions and confidence of individuals to manage the medical and emotional

aspects of their condition in order to maintain or create new life roles.

Sensitivity The ability of a test to detect a problem.

Service planners Those responsible for planning and sanctioning health services in Ireland.

Side effect An adverse event that occurs because of a therapeutic intervention.

SIGN Scottish Intercollegiate Guidelines Network, an organisation set up to

develop evidence-based guidelines. It is part of Healthcare Improvement

Scotland and its remit covers Scotland.

Spasticity Increased stiffness of the muscles that occurs in the paralysed limbs after

stroke.

Specialist A healthcare professional with the necessary knowledge and skills in

managing people with stroke and conditions that mimic stroke, usually by having a relevant further qualification and keeping up to date through continuing professional development. This does not require the healthcare professional exclusively to manage people with stroke, but does require them to have specific knowledge and practical experience of stroke.

Specialist team A group of specialists who work together regularly managing people with

stroke and conditions that mimic stroke, and who between them have the knowledge and skills to assess and resolve the majority of problems. At a minimum, any specialist unit, team or service must be able to deliver all the relevant recommendations made in this guideline. This does not require the team exclusively to manage people with stroke, but the team should have

specific knowledge and practical experience of stroke.

Specificity The ability of a test to detect the right problem.

Splint A custom or ready-made external device to support a joint or limb in a

certain position.

Stenosis Abnormal narrowing of a blood vessel.

Stenting A metal mesh tube is placed in an artery or blood vessel to increase blood

flow to an area blocked by stenosis.

Stroke A clinical syndrome, of presumed vascular origin, typified by rapidly

developing signs of focal or global disturbance of cerebral functions lasting

more than 24 hours or leading to death.

Subarachnoid A haemorrhage from a cerebral blood vessel, aneurysm or vascular

haemorrhage (SAH) malformation into the subarachnoid space (the space surrounding the brain

where blood vessels lie between the arachnoid and pia mater).

Subluxation An incomplete or partial dislocation of a joint.

Systematic review A way of combining the findings from a variety of different research studies

to better analyse whether the studies have provided a convincing answer to a

research question.

Telemedicine The use of telecommunication and information technologies in order to

provide clinical healthcare at a distance.

Tenecteplase A drug used for thrombolysis.

Therapist In the context of the guideline this includes the allied health professionals

(UK) and health and social care professionals (Ireland) involved in stroke care.

The main ones are dietitians, occupational therapists, orthoptists, orthotists,

physiotherapists, and speech and language therapists.

Thrombectomy The excision of a blood clot from a blood vessel.

Thrombectomy centre A centre providing thrombectomies without providing acute stroke care.

Thrombolysis The use of drugs to break up a blood clot. An example of a thrombolysis drug

is alteplase, also sometimes called tPA.

Thrombosis A formation of a blood clot.

Transient ischaemic

attack (TIA)

An acute loss of focal cerebral or ocular function with symptoms lasting less than 24 hours and which is thought to be due to inadequate cerebral or ocular blood supply as a result of low blood flow, thrombosis or embolism

associated with diseases of the blood vessels, heart, or blood.

Tube feeding (also gastrostomy feeding)

Provision of nutrition and fluids via a tube directly into the gastrointestinal tract.

Venography An X-ray test that provides an image of the leg veins after a contrast dye is

injected into a vein in the patient's foot.

Videofluoroscopy A test for assessing the integrity of the oral and pharyngeal stages of the

swallowing process. It involves videotaping X-ray images as the patient

swallows a bolus of barium.

Vocational A co-ordinated plan to optimise a person's ability to participate in paid or

rehabilitation voluntary work.

Work Different forms of occupation, including paid employment, vocational

training, sheltered, therapeutic or voluntary work, and adult education.

Xanthochromia The yellowish appearance of cerebrospinal fluid that occurs after bleeding

into the fluid, usually after subarachnoid haemorrhage.

Abbreviations and acronyms

ABCD2 Age, blood pressure, clinical features, duration of TIA, and presence of diabetes

ADL Activities of daily living

AF Atrial fibrillation

APS Antiphospholipid syndrome

ASC Acute stroke centre

ASPECTS Alberta Stroke Program Early Computed Tomography Score

ASA Atrial septal aneurysm

BADS Behavioural Assessment of the Dysexecutive Syndrome

BMI Body mass index

BOA Behavioural Outcomes of Anxiety

BP Blood pressure

BPPV Benign paroxysmal positional vertigo

CAA Cerebral amyloid angiopathy

CADASIL Cerebral autosomal dominant arteriopathy with subcortical infarcts and

leucoencephalopathy

CI Confidence interval

CIMT Constraint-induced movement therapy

COC Combined oral contraceptive

COVID-19 Coronavirus disease

CPAP Continuous positive airways pressure

CPSP Central post-stroke pain
CSC Comprehensive stroke centre

CT Computed tomography

CTA Computed tomography angiography

CVT Cerebral venous thrombosis

DISCs Depression Intensity Scale Circles

DOAC Direct oral anticoagulant

DVA Driver and Vehicle Agency (Northern Ireland)

DVLA Driver and Vehicle Licencing Agency (England, Scotland, Wales)

DVT Deep vein thrombosis

DWI Diffusion-weighted imaging

EADL Extended activities of daily living

ECG Electrocardiogram

ELISA Enzyme-linked immunosorbent assay

EMA European Medicines Agency FAST test Face Arm Speech Time test

FEES Fibre-optic endoscopic evaluation of swallowing

FLAIR Fluid attenuated inversion recovery
GDG Guideline Development Group

GP General practitioner

HAS-BLED Hypertension, Abnormal score renal and liver function, Stroke, Bleeding, Labile

INRs, Elderly, Drugs or alcohol score

HDL High density lipoprotein

HIIT High intensity interval training

HR Hazard ratio

HRT Hormone replacement therapy
HSE Health Service Executive (Ireland)

IAPT Improving Access to Psychological Therapies

ICF International Classification of Functioning, Disability and Health

ICH Intracerebral haemorrhage ILR Implantable loop recorder

INR International normalised ratio (for blood clotting time)

IQR Interquartile range
LDL Low density lipoprotein
MCA Middle cerebral artery

mCIMT Modified constraint-induced movement therapy

MDT Multidisciplinary team

MHRA Medicines and Healthcare Products Regulatory Agency

MI Myocardial infarction

MICON Microbleeds International Collaborative Network

MR Magnetic resonance

MRA Magnetic resonance angiography
MRI Magnetic resonance imaging
mRS Modified Rankin Scale score

MSU Mobile stroke unit

MUST Malnutrition Universal Screening Tool

NASCET North American Symptomatic Carotid Endarterectomy Trial

NDLS National Driver Licence Service (Ireland)

NHS National Health Service (UK)

NICE National Institute for Health and Care Excellence

NIHSS National Institutes of Health Stroke Scale

NIMAST Northern Ireland Multidisciplinary Association of Stroke Teams

NMES Neuromuscular electrical stimulation

NNT Number needed to treat
NOAC Non-vitamin K anticoagulant

NSAID Non-steroidal anti-inflammatory drug

OR Odds ratio

OSA Obstructive sleep apnoea
PADL Personal activities of daily living
PAF Paroxysmal atrial fibrillation

PC-ASPECTS Posterior circulation – Alberta Stroke Program Early Computed Tomography Score

PCC Prothrombin complex concentrate

PE Pulmonary embolism

PES Pharyngeal electrical stimulation

PFO Patent foramen ovale

POC Progestin only contraceptive

RBMT Rivermead Behavioural Memory Test
RCP Royal College of Physicians of London

RCT Randomised controlled trial

ROSIER Recognition of Stroke in the Emergency Room

RR Relative risk

SAH Sub arachnoid haemorrhage

SARA Scale for the Assessment and Rating of Ataxia

SBP Systolic blood pressure

SIGN Scottish Intercollegiate Guidelines Network

SLT Speech and language therapy
SMC Scottish Medicines Consortium
SRU Stroke rehabilitation unit

SSNAP Sentinel Stroke National Audit Programme

NATIONAL CLINICAL GUIDELINE FOR STROKE

for the United Kingdom and Ireland

SSRI Selective serotonin reuptake inhibitor
SWI Susceptibility-weighted imaging
tDCS Transcranial direct current stimulation

TENS Transcutaneous electrical nerve stimulation
TIA Transient ischaemic attack

TMS Transcranial magnetic stimulation
TOE Transoesophageal echocardiogram
TTE Transthoracic echocardiogram
TULIA Test of Upper Limb Apraxia

VA Vertebral artery
VKA Vitamin K antagonist
VNS Vagus nerve stimulation

VOSP Visual Object and Space Perception battery

VR Vocational rehabilitation
VTE Venous thromboembolism
WHO World Health Organization
WTE Whole time equivalent

Bibliography

- Aarnes, R., Stubberud, J., & Lerdal, A. (2020). A literature review of factors associated with fatigue after stroke and a proposal for a framework for clinical utility *Neuropsychological Rehabilitation*, 30(8), 1449-1476.
- Abdullahi, A. (2018). Effects of Number of Repetitions and Number of Hours of Shaping Practice during Constraint-Induced Movement Therapy: A Randomized Controlled Trial *Neurology research international*, 2018, 5496408.
- Ablewhite, J., Condon, L., Nair, R. d., Jones, A., Jones, F., Nouri, F., et al. (2022a). UK clinical approaches to address post-stroke fatigue: findings from The Nottingham Fatigue after Stroke study *International Journal of Therapy and Rehabilitation*, *29*(5), 1-12.
- Ablewhite, J., Nouri, F., Whisker, A., Thomas, S., Jones, F., das Nair, R., et al. (2022b). How do stroke survivors and their caregivers manage post-stroke fatigue? A qualitative study *Clinical Rehabilitation*, 36(10), 1400-1410.
- Ada, L., Dorsch, S., & Canning, C. G. (2006). Strengthening interventions increase strength and improve activity after stroke: a systematic review *Australian Journal of Physiotherapy*, *52*(4), 241-248.
- Adams, K. F., Schatzkin, A., Harris, T. B., Kipnis, V., Mouw, T., Ballard-Barbash, R., et al. (2006).

 Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old New England Journal of Medicine, 355(8), 763-778.
- Adey-Wakeling, Z., Liu, E., Crotty, M., Leyden, J., Kleinig, T., Anderson, C. S., et al. (2016). Hemiplegic Shoulder Pain Reduces Quality of Life After Acute Stroke: A Prospective Population-Based Study *Am J Phys Med Rehabil*, *95*(10), 758-763.
- Adib-Samii, P., Brice, G., Martin, R. J., & Markus, H. S. (2010). Clinical spectrum of CADASIL and the effect of cardiovascular risk factors on phenotype: study in 200 consecutively recruited individuals *Stroke*, *41*(4), 630-634.
- Adler, A. J., Taylor, F., Martin, N., Gottlieb, S., Taylor, R. S., & Ebrahim, S. (2014). Reduced dietary salt for the prevention of cardiovascular disease *Cochrane Database of Systematic Reviews*, *12*, CD009217.
- Ahmed, I., Yeldan, I., & Mustafaoglu, R. (2022). The Adjunct of Electric Neurostimulation to Rehabilitation Approaches in Upper Limb Stroke Rehabilitation: A Systematic Review With Network Meta-Analysis of Randomized Controlled Trials *Neuromodulation*, 25(8), 1197-1214.
- Al-Shahi Salman, R., Minks, D. P., Mitra, D., Rodrigues, M. A., Bhatnagar, P., du Plessis, J. C., et al. (2019). Effects of antiplatelet therapy on stroke risk by brain imaging features of intracerebral haemorrhage and cerebral small vessel diseases: subgroup analyses of the RESTART randomised, open-label trial *The Lancet Neurology*, *18*(7), 643-652.
- Al-Shahi Salman, R., Dennis, M. S., Sandercock, P. A. G., Sudlow, C. L. M., Wardlaw, J. M., Whiteley, W. N., et al. (2021). Effects of Antiplatelet Therapy After Stroke Caused by Intracerebral Hemorrhage: Extended Follow-up of the RESTART Randomized Clinical Trial *JAMA Neurology*, 78(10), 1179-1186.
- Albers, G. W., Marks, M. P., Kemp, S., Christensen, S., Tsai, J. P., Ortega-Gutierrez, S., et al. (2018). Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging *New England Journal of Medicine*, *378*(8), 708-718.
- Albers, G. W., Lansberg, M. G., Brown, S., Jadhav, A. P., Haussen, D. C., Martins, S. O., et al. (2021).

 Assessment of Optimal Patient Selection for Endovascular Thrombectomy Beyond 6 Hours After Symptom Onset: A Pooled Analysis of the AURORA Database *JAMA Neurol*, 78(9), 1064-1071.
- Alghamdi, I., Ariti, C., Williams, A., Wood, E., & Hewitt, J. (2021). Prevalence of fatigue after stroke: A systematic review and meta-analysis *Eur Stroke J*, 6(4), 319-332.
- Alkhenizan, A. H., & Al-Omran, M. A. (2004). The role of vitamin E in the prevention of coronary events and stroke Meta-analysis of randomized controlled trials *Saudi Medical Journal*, *25*(12), 1808-1814.

- Allen, G. S., Ahn, H. S., Preziosi, T. J., Battye, R., Boone, S. C., Boone, S. C., et al. (1983). Cerebral arterial spasm--a controlled trial of nimodipine in patients with subarachnoid hemorrhage *New England Journal of Medicine*, 308(11), 619-624.
- Allen, M., James, C., Frost, J., Liabo, K., Pearn, K., Monks, T., et al. (2022). Using simulation and machine learning to maximise the benefit of intravenous thrombolysis in acute stroke in England and Wales: the SAMueL modelling and qualitative study *Health and Social Care Delivery Research*, *No. 10.*(31).
- Allida, S., Cox, K. L., Hsieh, C. F., House, A., & Hackett, M. L. (2020a). Pharmacological, psychological and non-invasive brain stimulation interventions for preventing depression after stroke *Cochrane Database Syst Rev*, *5*(5), Cd003689.
- Allida, S., Cox, K. L., Hsieh, C. F., Lang, H., House, A., & Hackett, M. L. (2020b). Pharmacological, psychological, and non-invasive brain stimulation interventions for treating depression after stroke *Cochrane Database of Systematic Reviews*, 2020(1), CD003437.
- Almeida, O. P., Hankey, G. J., Ford, A., Etherton-Beer, C., Flicker, L., & Hackett, M. (2021). Depression Outcomes among Patients Treated with Fluoxetine for Stroke Recovery: The AFFINITY Randomized Clinical Trial *JAMA Neurology*, 78(9), 1072-1079.
- Alvarez-Sabin, J., Ortega, G., Jacas, C., Santamarina, E., Maisterra, O., Ribo, M., et al. (2013). Long-term treatment with citicoline may improve poststroke vascular cognitive impairment *Cerebrovascular Diseases*, *35*(2), 146-154.
- Amarenco, P., Bogousslavsky, J., Callahan, A., 3rd, Goldstein, L. B., Hennerici, M., Rudolph, A. E., et al. (2006). High-dose atorvastatin after stroke or transient ischemic attack *New England Journal of Medicine*, *355*(6), 549-559.
- Amarenco, P., & Labreuche, J. (2009). Lipid management in the prevention of stroke: review and updated meta-analysis of statins for stroke prevention *Lancet Neurology*, 8(5), 453-463.
- Amarenco, P., Labreuche, J., & Lavallée, P. C. (2012). Patients with transient ischemic attack with ABCD2 <4 can have similar 90-day stroke risk as patients with transient ischemic attack with ABCD2 ≥4 Stroke, 43(3), 863-865.
- Amarenco, P., & Steering Committee Investigators of the TIAregistry.org. (2016). Risk of Stroke after Transient Ischemic Attack or Minor Stroke *New England Journal of Medicine*, *375*(4), 386-387.
- Amarenco, P., Kim, J. S., Labreuche, J., Charles, H., Abtan, J., Béjot, Y., et al. (2020). A Comparison of Two LDL Cholesterol Targets after Ischemic Stroke *N Engl J Med*, *382*(1), 9.
- Ammann, B. C., Knols, R. H., Baschung, P., de Bie, R. A., & de Bruin, E. D. (2014). Application of principles of exercise training in sub-acute and chronic stroke survivors: a systematic review *BMC*Neurology, 14(167), 1471-2377.
- Anderson, C. S., Heeley, E., Huang, Y., Wang, J., Stapf, C., Delcourt, C., et al. (2013). Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage *New England Journal of Medicine*, *368*(25), 2355-2365.
- Anderson, C. S., Robinson, T., Lindley, R. I., Arima, H., Lavados, P. M., Lee, T. H., et al. (2016). Low-Dose versus Standard-Dose Intravenous Alteplase in Acute Ischemic Stroke *New England Journal of Medicine*, *374*(24), 2313-2323.
- Anderson, C. S., Arima, H., Lavados, P., Billot, L., Hackett, M. L., Olavarría, V. V., et al. (2017). Cluster-Randomized, Crossover Trial of Head Positioning in Acute Stroke *New England Journal of Medicine*, *376*(25), 2437-2447.
- Anderson, L. J., Wyatt, K. M., Henley, W., Nikolaou, V., Waldek, S., Hughes, D. A., et al. (2014). Long-term effectiveness of enzyme replacement therapy in Fabry disease: results from the NCS-LSD cohort study *Journal of Inherited Metabolic Disease*, *37*(6), 969-978.
- Anjos, J. M., Neto, M. G., Dos Santos, F. S., Almeida, K. O., Bocchi, E. A., Lima Bitar, Y. S., et al. (2022). The impact Of high-intensity interval training On functioning And health-related quality Of life In post-stroke patients: A systematic review With meta-analysis *Clinical Rehabilitation*, *36*(6), 726-739.
- Antithrombotic Trialists Collaboration. (2002). Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients *BMJ*, 324(7329), 71-86.

- Appel, L. J., Moore, T. J., Obarzanek, E., Vollmer, W. M., Svetkey, L. P., Sacks, F. M., et al. (1997). A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group *New England Journal of Medicine*, *336*(16), 1117-1124.
- Appel, L. J., Champagne, C. M., Harsha, D. W., Cooper, L. S., Obarzanek, E., Elmer, P. J., et al. (2003). Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial *JAMA*, *289*(16), 2083-2093.
- Appleby, E., Gill, S. T., Hayes, L. K., Walker, T. L., Walsh, M., & Kumar, S. (2019). Effectiveness of telerehabilitation in the management of adults with stroke: A systematic review *PLoS One*, 14(11). e0225150.
- Aprile, I., Germanotta, M., Cruciani, A., Loreti, S., Pecchioli, C., Cecchi, F., et al. (2020). Upper Limb Robotic Rehabilitation After Stroke: A Multicenter, Randomized Clinical Trial *Journal of neurologic physical therapy : JNPT, 44*(1), 3-14.
- Archer, J., Bower, P., Gilbody, S., Lovell, K., Richards, D., Gask, L., et al. (2012). Collaborative care for depression and anxiety problems *The Cochrane Database of Systematic Reviews*, *10*, CD006525.
- Arienti, C., Lazzarini, S. G., Pollock, A., & Negrini, S. (2019). Rehabilitation interventions for improving balance following stroke: An overview of systematic reviews *PLoS One*, *14*(7), e0219781.
- Arima, H., Chalmers, J., Woodward, M., Anderson, C., Rodgers, A., Davis, S., et al. (2006). Lower target blood pressures are safe and effective for the prevention of recurrent stroke: the PROGRESS trial *Journal of Hypertension*, *24*(6), 1201-1208.
- Arima, H., Tzourio, C., Anderson, C., Woodward, M., Bousser, M. G., MacMahon, S., et al. (2010). Effects of perindopril-based lowering of blood pressure on intracerebral hemorrhage related to amyloid angiopathy: the PROGRESS trial *Stroke*, *41*(2), 394-396.
- Askim, T., Langhammer, B., Ihle-Hansen, H., Gunnes, M., Lydersen, S., & Indredavik, B. (2018). Efficacy and Safety of Individualized Coaching After Stroke: the LAST Study (Life After Stroke): A Pragmatic Randomized Controlled Trial *Stroke*, *49*(2), 426-432.
- Aslaksen, P. M., Orbo, M., Elvestad, R., Schafer, C., & Anke, A. (2013). Prediction of on-road driving ability after traumatic brain injury and stroke *European Journal of Neurology*, 20(9), 1227-1233.
- Asplund, K., Jonsson, F., Eriksson, M., Stegmayr, B., Appelros, P., Norrving, B., et al. (2009). Patient dissatisfaction with acute stroke care *Stroke*, *40*(12), 3851-3856.
- Ataxia UK. (2016). Management of the ataxias towards best clinical practice.

 https://www.ataxia.org.uk/wp-content/uploads/2020/11/Ataxia UK Medical Guidelines. Third Edition. v3m Dec 2016 updated Sep 2019.pdf
- AVERT Trial Collaboration group. (2015). Efficacy and safety of very early mobilisation within 24 hours of stroke onset (AVERT): a randomised controlled trial *Lancet*, *386*(9988), 46-55.
- Ayerbe, L., Ayis, S., Crichton, S., Wolfe, C. D., & Rudd, A. G. (2014). The long-term outcomes of depression up to 10 years after stroke; the South London Stroke Register *Journal of Neurology, Neurosurgery & Psychiatry*, 85(5), 514-521.
- Baetens, T., De Kegel, A., Palmans, T., Oostra, K., Vanderstraeten, G., & Cambier, D. (2013). Gait analysis with cognitive-motor dual tasks to distinguish fallers from nonfallers among rehabilitating stroke patients *Archives of Physical Medicine & Rehabilitation*, *94*(4), 680-686.
- Bai, X., Zhang, X., Wang, T., Feng, Y., Ma, Y., Wang, Y., et al. (2021). General anesthesia versus conscious sedation for endovascular therapy in acute ischemic stroke: A systematic review and meta-analysis *Journal of Clinical Neuroscience*, 86, 10-17.
- Bai, Y., Guo, S. D., Deng, H., Shantsila, A., Fauchier, L., Ma, C. S., et al. (2018). Effectiveness and safety of oral anticoagulants in older patients with atrial fibrillation: a systematic review and meta-regression analysis *Age Ageing*, *47*(1), 9-17.
- Baigent, C., Keech, A., Kearney, P. M., Blackwell, L., Buck, G., Pollicino, C., et al. (2005). Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins *Lancet*, *366*(9493), 1267-1278.
- Balinski, M., & Madhavan, S. (2022). 'Magic' number of treadmill sessions needed to achieve meaningful change in gait speed post stroke: a systematic review *American Journal of Physical Medicine & Rehabilitation*, 101(9), 826-835.

- Bamiou, D. E. (2015). Chapter 35 Hearing disorders in stroke. In M. J. Aminoff, F. Boller, & D. F. Swaab (Eds.), *Handbook of Clinical Neurology* (Vol. 129, pp. 633-647). Elsevier.
- Bangalore, S., Toklu, B., Gianos, E., Schwartzbard, A., Weintraub, H., Ogedegbe, G., et al. (2017). Optimal Systolic Blood Pressure Target After SPRINT: Insights from a Network Meta-Analysis of Randomized Trials *American Journal of Medicine*, 130(6), 707-719.
- Barclay-Goddard, R. E., Stevenson Ted, J., Poluha, W., Ripat, J., Nett, C., & Srikesavan Cynthia, S. (2015). Interventions for improving community ambulation in individuals with stroke *Cochrane Database of Systematic Reviews*, *3*, CD010200.
- Barclay, R. E., Stevenson, T. J., Poluha, W., Semenko, B., & Schubert, J. (2020). Mental practice for treating upper extremity deficits in individuals with hemiparesis after stroke *Cochrane Database of Systematic Reviews*, 2020(5), CD005950.
- Barker, F. G., & Ogilvy, C. S. (1996). Efficacy of prophylactic nimodipine for delayed ischemic deficit after subarachnoid hemorrhage: a metaanalysis *Journal of Neurosurgery*, *84*(3), 405-414.
- Barnett, H. J., Taylor, D. W., Eliasziw, M., Fox, A. J., Ferguson, G. G., Haynes, R. B., et al. (1998). Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators *New England Journal of Medicine*, 339(20), 1415-1425.
- Barras, S., Grimmer-Somers, K., & May, E. (2010). Consensus on 'core/essential' and 'ideal world' criteria of a pre-discharge occupational therapy home assessment *Journal of Evaluation in Clinical Practice*, *16*(6), 1295-1300.
- Barzel, A., Stark, A., Tetzlaff, B., van den Bussche, H., Scherer, M., Ketels, G., et al. (2015). Home-based constraint-induced movement therapy for patients with upper limb dysfunction after stroke (HOMECIMT): A cluster-randomised, controlled trial *The Lancet Neurology*, *14*(9), 893-902.
- Bashshur, R. L. (1995). On the definition and evaluation of telemedicine Telemed J, 1(1), 19-30.
- Bath, P. M., Bath, F. J., & Smithard, D. G. (2000). Interventions for dysphagia in acute stroke *Cochrane Database of Systematic Reviews*(2), CD000323.
- Bath, P. M., & Krishnan, K. (2014). Interventions for deliberately altering blood pressure in acute stroke *Cochrane Database of Systematic Reviews*, *10*, CD000039.
- Bath, P. M., Woodhouse, L., Scutt, P., Krishnan, K., Wardlaw, J. M., Bereczki, D., et al. (2015). Efficacy of nitric oxide, with or without continuing antihypertensive treatment, for management of high blood pressure in acute stroke (ENOS): a partial-factorial randomised controlled trial *Lancet*, 385(9968), 617-628.
- Bath, P. M., Lee, H. S., & Everton, L. F. (2018). Swallowing therapy for dysphagia in acute and subacute stroke *Cochrane Database of Systematic Reviews*, 2018(10), CD000323.
- Bax, L., McFarlane, M., Green, E., & Miles, A. (2014). Speech-language pathologist-led fiberoptic endoscopic evaluation of swallowing: Functional outcomes for patients after stroke *Journal of Stroke and Cerebrovascular Diseases*, 23(3), e195-e200.
- Bazzano, L. A., Reynolds, K., Holder, K. N., & He, J. (2006). Effect of folic acid supplementation on risk of cardiovascular diseases A meta-analysis of randomized controlled trials *JAMA*, *296*(22), 2720-2726.
- Beavan, J., Conroy, S. P., Harwood, R., Gladman, J. R., Leonardi, B. J., Sach, T., et al. (2010). Does looped nasogastric tube feeding improve nutritional delivery for patients with dysphagia after acute stroke? A randomised controlled trial *Age & Ageing*, *39*(5), 624-630.
- Beddhu, S., Chertow, G. M., Cheung, A. K., Cushman, W. C., Rahman, M., Greene, T., et al. (2018).
 Influence of Baseline Diastolic Blood Pressure on Effects of Intensive Compared With Standard Blood Pressure Control *Circulation*, 137(2), 134-143.
- Bennett, M. H., Weibel, S., Wasiak, J., Schnabel, A., French, C., & Kranke, P. (2014). Hyperbaric oxygen therapy for acute ischaemic stroke *Cochrane Database of Systematic Reviews*, *11*, CD004954.
- Benz, A. P., Johansson, I., Dewilde, W. J. M., Lopes, R. D., Mehran, R., Sartori, S., et al. (2022).

 Antiplatelet therapy in patients with atrial fibrillation: a systematic review and meta-analysis of randomized trials *Eur Heart J Cardiovasc Pharmacother*, 8(7), 648-659.

- Berkhemer, O. A., Fransen, P. S., Beumer, D., van den Berg, L. A., Lingsma, H. F., Yoo, A. J., et al. (2015). A randomized trial of intraarterial treatment for acute ischemic stroke.[Erratum appears in N Engl J Med. 2015 Jan 22;372(4):394] *New England Journal of Medicine*, 372(1), 11-20.
- Bernhardt, J., Dewey, H., Thrift, A., & Donnan, G. (2004). Inactive and alone: physical activity within the first 14 days of acute stroke unit care *Stroke*, *35*(4), 1005-1009.
- Bernhardt, J., Churilov, L., Ellery, F., Collier, J., Chamberlain, J., Langhorne, P., et al. (2016). Prespecified dose-response analysis for A Very Early Rehabilitation Trial (AVERT) *Neurology*, *86*(23), 2138-2145.
- Best, J. G., Ambler, G., Wilson, D., Lee, K. J., Lim, J. S., Shiozawa, M., et al. (2021). Development of imaging-based risk scores for prediction of intracranial haemorrhage and ischaemic stroke in patients taking antithrombotic therapy after ischaemic stroke or transient ischaemic attack: a pooled analysis of individual patient data from cohort studies *Lancet Neurol*, 20(4), 294-303.
- Bhatt, D. L., Steg, P. G., Miller, M., Brinton, E. A., Jacobson, T. A., Ketchum, S. B., et al. (2019). Effects of Icosapent Ethyl on Total Ischemic Events: From REDUCE-IT *J Am Coll Cardiol*, 73(22), 2791-2802.
- Bhogal, S. K., Teasell, R., & Speechley, M. (2003a). Intensity of aphasia therapy, impact on recovery *Stroke*, *34*(4), 987-993.
- Bhogal, S. K., Teasell, R. W., Foley, N. C., & Speechley, M. R. (2003b). Rehabilitation of aphasia: more is better *Top Stroke Rehabil*, *10*(2), 66-76.
- Biffi, A., Anderson, C. D., Battey, T. W., Ayres, A. M., Greenberg, S. M., Viswanathan, A., et al. (2015).

 Association Between Blood Pressure Control and Risk of Recurrent Intracerebral Hemorrhage *JAMA*, 314(9), 904-912.
- Biffi, A., Kuramatsu, J. B., Leasure, A., Kamel, H., Kourkoulis, C., Schwab, K., et al. (2017). Oral Anticoagulation and Functional Outcome after Intracerebral Hemorrhage *Ann Neurol*, 82(5), 755-765.
- Billinger, S. A., Arena, R., Bernhardt, J., Eng, J. J., Franklin, B. A., Johnson, C. M., et al. (2014). Physical activity and exercise recommendations for stroke survivors: a statement for healthcare professionals from the American Heart Association/American Stroke Association *Stroke*, *45*(8), 2532-2553.
- Billinger, S. A., Boyne, P., Coughenour, E., Dunning, K., & Mattlage, A. (2015). Does aerobic exercise and the FITT principle fit into stroke recovery? *Curr Neurol Neurosci Rep*, *15*(2), 519.
- Bin, Q., Hu, X., Cao, Y., & Gao, F. (2011). The role of vitamin E (tocopherol) supplementation in the prevention of stroke. A meta-analysis of 13 randomised controlled trials *Thrombosis & Haemostasis*, 105(4), 579-585.
- Bivard, A., Lillicrap, T., Krishnamurthy, V., Holliday, E., Attia, J., Pagram, H., et al. (2017). MIDAS (Modafinil in Debilitating Fatigue After Stroke): A Randomized, Double-Blind, Placebo-Controlled, Cross-Over Trial *Stroke*, *48*(5), 1293-1298.
- Bivard, A., Zhao, H., Churilov, L., Campbell, B. C. V., Coote, S., Yassi, N., et al. (2022). Comparison of tenecteplase with alteplase for the early treatment of ischaemic stroke in the Melbourne Mobile Stroke Unit (TASTE-A): a phase 2, randomised, open-label trial *The Lancet Neurology*, *21*(6), 520-527.
- Boardman, H. M., Hartley, L., Eisinga, A., Main, C., Roque i Figuls, M., Bonfill Cosp, X., et al. (2015).

 Hormone therapy for preventing cardiovascular disease in post-menopausal women *Cochrane Database of Systematic Reviews*, *3*, CD002229.
- Bolland, M. J., Avenell, A., Baron, J. A., Grey, A., MacLennan, G. S., Gamble, G. D., et al. (2010). Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis *BMJ*, 341, c3691.
- Bolland, M. J., Grey, A., Gamble, G. D., & Reid, I. R. (2014). The effect of vitamin D supplementation on skeletal, vascular, or cancer outcomes: A trial sequential meta-analysis *Lancet Diabetes & Endocrinology*, 2(4), 307-320.
- Bonati, L. H., Lyrer, P., Ederle, J., Featherstone, R., & Brown, M. M. (2012). Percutaneous transluminal balloon angioplasty and stenting for carotid artery stenosis *Cochrane Database of Systematic Reviews*, *9*, CD000515.

- Bonati, L. H., Dobson, J., Featherstone, R. L., Ederle, J., van der Worp, H. B., de Borst, G. J., et al. (2015). Long-term outcomes after stenting versus endarterectomy for treatment of symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomised trial *Lancet*, 385(9967), 529-538.
- Bor, A. S., Rinkel, G. J. E., Adami, J., Koffijberg, H., Ekbon, A., Buskens, E., et al. (2008). Risk of Subarachnoid haemorrhage according to number of affected relatives; a population based case —control study *Brain*, *131*(10), 2662-2665.
- Bowen, A., Knapp, P., Gillespie, D., Nicolson, D. J., & Vail, A. (2011). Non-pharmacological interventions for perceptual disorders following stroke and other adult-acquired, non-progressive brain injury *The Cochrane Database of Systematic Reviews*(4), CD007039.
- Bowen, A., Hesketh, A., Patchick, E., Young, A., Davies, L., Vail, A., et al. (2012). Effectiveness of enhanced communication therapy in the first four months after stroke for aphasia and dysarthria: a randomised controlled trial *BMJ*, *345*, e4407.
- Bowen, A., Hazelton, C., Pollock, A., & Lincoln, N. B. (2013). Cognitive rehabilitation for spatial neglect following stroke *Cochrane Database of Systematic Reviews*, *7*, CD003586.
- Brady, M., Furlanetto, D., Hunter, R. V., Lewis, S., & Milne, V. (2006). Staff-led interventions for improving oral hygiene in patients following stroke *Cochrane Database of Systematic Reviews*(4), CD003864.
- Braley, M., Pierce, J. S., Saxena, S., De Oliveira, E., Taraboanta, L., Anantha, V., et al. (2021). A Virtual, Randomized, Control Trial of a Digital Therapeutic for Speech, Language, and Cognitive Intervention in Post-stroke Persons With Aphasia *Frontiers in Neurology*, *12*, Article 626780.
- Brannigan, C., Galvin, R., Walsh, M. E., Loughnane, C., Morrissey, E. J., Macey, C., et al. (2017). Barriers and facilitators associated with return to work after stroke: a qualitative meta-synthesis *Disability and Rehabilitation*, 39(3), 211-222.
- Bravata, D. M., Concato, J., Fried, T., Ranjbar, N., Sadarangani, T., McClain, V., et al. (2011). Continuous positive airway pressure: evaluation of a novel therapy for patients with acute ischemic stroke *Sleep*, *34*(9), 1271-1277.
- Bray, B. D., Campbell, J., Cloud, G. C., Hoffman, A., Tyrrell, P. J., Wolfe, C. D., et al. (2013). Bigger, faster? Associations between hospital thrombolysis volume and speed of thrombolysis administration in acute ischemic stroke *Stroke*, *44*(11), 3129-3135.
- Bray, B. D., Ayis, S., Campbell, J., Cloud, G. C., James, M., Hoffman, A., et al. (2014). Associations between Stroke Mortality and Weekend Working by Stroke Specialist Physicians and Registered Nurses: Prospective Multicentre Cohort Study *PLOS Medicine*, *11*(8), e1001705.
- Bray, B. D., Smith, C. J., Cloud, G. C., Enderby, P., James, M., Paley, L., et al. (2017). The association between delays in screening for and assessing dysphagia after acute stroke, and the risk of stroke-associated pneumonia *Journal of Neurology, Neurosurgery & Psychiatry*, 88(1), 25-30.
- Bray, E. P., Holder, R., Mant, J., & McManus, R. J. (2010). Does self-monitoring reduce blood pressure? Meta-analysis with meta-regression of randomized controlled trials *Ann Med*, *42*(5), 371-386.
- Brazzelli, M., Saunders, D. H., Greig, C. A., & Mead, G. E. (2011). Physical fitness training for stroke patients *Cochrane Database of Systematic Reviews* (11), CD003316.
- Breaux-Shropshire, T. L., Judd, E., Vucovich, L. A., Shropshire, T. S., & Singh, S. (2015). Does home blood pressure monitoring improve patient outcomes? A systematic review comparing home and ambulatory blood pressure monitoring on blood pressure control and patient outcomes *Integr Blood Press Control*, *8*, 43-49.
- Breisinger, T. P., Skidmore, E. R., Niyonkuru, C., Terhorst, L., & Campbell, G. B. (2014). The Stroke Assessment of Fall Risk (SAFR): predictive validity in inpatient stroke rehabilitation *Clinical Rehabilitation*, 28(12), 1218-1224.
- British and Irish Orthoptic Society. (2021). *The British and Irish Orthoptic Society (BIOS) Position Statement for Vision Services in Stroke Practice*. https://www.orthoptics.org.uk/wp-content/uploads/2021/07/BIOS-Stroke-Neuro-Rehab-Consensus-Statement-2021.pdf
- British Dietetic Association. (2009). *National descriptors for texture modification in adults*. https://www.acquiredbraininjury-education.scot.nhs.uk/wp-content/uploads/National-Descriptors-Texture-Modification-Adults-2009.pdf

- British Society of Rehabilitation Medicine. (2021). *Specialist Standards for Community Rehabilitation*https://www.bsrm.org.uk/downloads/2021-v9.3-22-3-21-speccommunitystandards-summary-fortheweb-clean.pdf
- Brockman, S., Almeida, O. P., Hatch, K. K., Bruce, D. G., Davis, W. A., Robinson, R. G., et al. (2016). A Randomized, Placebo-Controlled, Double-Blind Efficacy Study of Nefiracetam to Treat Poststroke Apathy *Journal of Stroke and Cerebrovascular Diseases*, 25(5), 1119-1127.
- Buck, B. H., Hill, M. D., Quinn, F. R., Butcher, K. S., Menon, B. K., Gulamhusein, S., et al. (2021). Effect of Implantable vs Prolonged External Electrocardiographic Monitoring on Atrial Fibrillation Detection in Patients With Ischemic Stroke: The PER DIEM Randomized Clinical Trial JAMA, 325(21), 2160-2168.
- Budhota, A., Chua, K. S. G., Hussain, A., Kager, S., Cherpin, A., Contu, S., et al. (2021). Robotic Assisted Upper Limb Training Post Stroke: A Randomized Control Trial Using Combinatory Approach Toward Reducing Workforce Demands *Frontiers in Neurology*, *12*, Article 622014.
- Bundy, J. D., Li, C., Stuchlik, P., Bu, X., Kelly, T. N., Mills, K. T., et al. (2017). Systolic Blood Pressure Reduction and Risk of Cardiovascular Disease and Mortality: A Systematic Review and Network Meta-analysis *JAMA Cardiol*, 2(7), 775-781.
- Burgos, A. M., & Saver, J. L. (2019). Evidence that Tenecteplase Is Noninferior to Alteplase for Acute Ischemic Stroke: Meta-Analysis of 5 Randomized Trials *Stroke*, *50*(8), 2156-2162.
- Busch, M. A., Coshall, C., Heuschmann, P. U., McKevitt, C., & Wolfe, C. D. (2009). Sociodemographic differences in return to work after stroke: the South London Stroke Register (SLSR) *J Neurol Neurosurg Psychiatry*, 80(8), 888-893.
- Butt, W., Malik, L., Nair, S., Lenthall, R., McConachie, N., Dhillon, P. S., et al. (2021). Local anesthesia as a distinct comparator versus conscious sedation and general anesthesia in endovascular stroke treatment: A systematic review and meta-analysis *Journal of NeuroInterventional Surgery*, *14*(3), 221-226.
- CADISS Trial Investigators. (2015). Antiplatelet treatment compared with anticoagulation treatment for cervical artery dissection (CADISS): a randomised trial *Lancet Neurology*, *14*(4), 361-367.
- Caeiro, L., Ferro, J. M., Pinho, E. M. T., Canhão, P., & Figueira, M. L. (2013). Post-stroke apathy: an exploratory longitudinal study *Cerebrovasc Dis*, *35*(6), 507-513.
- Campbell, B. C., Mitchell, P. J., Kleinig, T. J., Dewey, H. M., Churilov, L., Yassi, N., et al. (2015).

 Endovascular therapy for ischemic stroke with perfusion-imaging selection *New England Journal of Medicine*, 372(11), 1009-1018.
- Campbell, B. C. V., Davis, S. M., Mitchell, P. J., Donnan, G. A., van Zwam, W. H., van Oostenbrugge, R. J., et al. (2018a). Effect of general anaesthesia on functional outcome in patients with anterior circulation ischaemic stroke having endovascular thrombectomy versus standard care: a meta-analysis of individual patient data *The Lancet Neurology*, *17*(1), 47-53.
- Campbell, B. C. V., Mitchell, P. J., Churilov, L., Yassi, N., Kleinig, T. J., Yan, B., et al. (2018b). Tenecteplase versus alteplase before endovascular thrombectomy (EXTEND-IA TNK): A multicenter, randomized, controlled study *International Journal of Stroke*, 13(3), 328-334.
- Campbell, B. C. V., Ma, H., Ringleb, P. A., Parsons, M. W., Churilov, L., Bendszus, M., et al. (2019). Extending thrombolysis to 4·5-9 h and wake-up stroke using perfusion imaging: a systematic review and meta-analysis of individual patient data *Lancet*, 394(10193), 139-147.
- Campbell Burton, C. A., Holmes, J., Murray, J., Gillespie, D., Lightbody, C. E., Watkins, C. L., et al. (2011). Interventions for treating anxiety after stroke *Cochrane Database of Systematic Reviews* (12), CD008860.
- Campbell, P., Bain, B., Furlanetto, D. L. C., & Brady, M. C. (2020). Interventions for improving oral health in people after stroke *Cochrane Database of Systematic Reviews*, 2020(12), CD003864.
- Canhao, P., Cortesao, A., Cabral, M., Ferro, J. M., Stam, J., Bousser, M. G., et al. (2008). Are steroids useful to treat cerebral venous thrombosis? *Stroke*, *39*(1), 105-110.
- Cappuccio, F. P., Kerry, S. M., Forbes, L., & Donald, A. (2004). Blood pressure control by home monitoring: meta-analysis of randomised trials *BMJ*, *329*(7458), 145-151.
- CAPRIE Steering Committee. (1996). A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE) *Lancet*, *348*(9038), 1329-1339.

- Carnaby, G., Hankey, G. J., & Pizzi, J. (2006). Behavioural intervention for dysphagia in acute stroke: a randomised controlled trial *Lancet Neurology*, *5*(1), 31-37.
- Carroll, J. D., Saver, J. L., Thaler, D. E., Smalling, R. W., Berry, S., MacDonald, L. A., et al. (2013). Closure of patent foramen ovale versus medical therapy after cryptogenic stroke *New England Journal of Medicine*, 368(12), 1092-1100.
- Cattaneo, L., & Rizzolatti, G. (2009). The Mirror Neuron System Archives of Neurology, 66(5), 557-560.
- Cattelani, R., Zettin, M., & Zoccolotti, P. (2010). Rehabilitation Treatments for Adults with Behavioral and Psychosocial Disorders Following Acquired Brain Injury: A Systematic Review.

 Neuropsychological Reviews, 20(1), 52-85.
- Cervera, R., Serrano, R., Pons-Estel, G. J., Ceberio-Hualde, L., Shoenfeld, Y., de Ramon, E., et al. (2015). Morbidity and mortality in the antiphospholipid syndrome during a 10-year period: a multicentre prospective study of 1000 patients *Annals of the Rheumatic Diseases*, 74(6), 1011-1018.
- Chakhtoura, Z., Canonico, M., Gompel, A., Thalabard, J. C., Scarabin, P. Y., & PluBureau, G. (2009). Progestogen-only contraceptives and the risk of stroke: A meta-analysis *Stroke*, *40*(4), 1059-1062.
- Chang, W. H., & Kim, Y. H. (2013). Robot-assisted Therapy in Stroke Rehabilitation *J Stroke*, *15*(3), 174-181.
- Charidimou, A., Imaizumi, T., Moulin, S., Biffi, A., Samarasekera, N., Yakushiji, Y., et al. (2017). Brain hemorrhage recurrence, small vessel disease type, and cerebral microbleeds: A meta-analysis *Neurology*, *89*(8), 820-829.
- Cheitlin, M. D., Hutter, A. M., Jr., Brindis, R. G., Ganz, P., Kaul, S., Russell, R. O., Jr., et al. (1999). Use of sildenafil (Viagra) in patients with cardiovascular disease. Technology and Practice Executive Committee *Circulation*, *99*(1), 168-177.
- Chen, J., Lin, X., Cai, Y., Huang, R., Yang, S., & Zhang, G. (2022). A Systematic Review of Mobile Stroke Unit Among Acute Stroke Patients: Time Metrics, Adverse Events, Functional Result and Cost-Effectiveness *Frontiers in Neurology*, *13*, Article 803162.
- Chen, K., & Marsh, E. B. (2018). Chronic post-stroke fatigue: It may no longer be about the stroke itself *Clinical Neurology and Neurosurgery*, *174*, 192-197.
- Chen, T., Zhang, B., Deng, Y., Fan, J.-C., Zhang, L., & Song, F. (2019). Long-term unmet needs after stroke: systematic review of evidence from survey studies *BMJ Open*, *9*(5), e028137.
- Chen, Z., Wang, C., Fan, W., Gu, M., Yasin, G., Xiao, S., et al. (2020). Robot-Assisted Arm Training versus Therapist-Mediated Training after Stroke: A systematic review and meta-analysis *Journal of Healthcare Engineering*, 2020, Article 8810867.
- Chimowitz, M. I., Lynn, M. J., Howlett-Smith, H., Stern, B. J., Hertzberg, V. S., Frankel, M. R., et al. (2005). Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis *New England Journal of Medicine*, *352*(13), 1305-1316.
- Chimowitz, M. I., Lynn, M. J., Derdeyn, C. P., Turan, T. N., Fiorella, D., Lane, B. F., et al. (2011). Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis *New England Journal of Medicine*, *365*, 993-1003.
- Choi, S. W., Han, N., Jung, S. H., Kim, H. D., Eom, M. J., & Bae, H. W. (2018). Evaluation of Ataxia in Mild Ischemic Stroke Patients Using the Scale for the Assessment and Rating of Ataxia (SARA) *Ann Rehabil Med*, 42(3), 375-383.
- Chowdhury, R., Stevens, S., Gorman, D., Pan, A., Warnakula, S., Chowdhury, S., et al. (2012). Association between fish consumption, long chain omega 3 fatty acids, and risk of cerebrovascular disease: systematic review and meta-analysis *BMJ*, *345*, e6698.
- Chung, C. S., Pollock, A., Campbell, T., Durward, B. R., & Hagen, S. (2013). Cognitive rehabilitation for executive dysfunction in adults with stroke or other adult non-progressive acquired brain damage *Cochrane Database of Systematic Reviews*, *4*, CD008391.
- Cicerone, K., Mott, T., Azulay, J., Sharlow-Galella, M. A., Ellmo, W. J., Paradise, S., et al. (2008). A Randomized Controlled Trial of Holistic Neuropsychologic Rehabilitation After Traumatic Brain Injury Archives of Physical Medicine and Rehabilitation, 89(12), 2239-2249.

- Cicerone, K., Azulay, J., & Trott, C. (2009). Methodological Quality of Research on Cognitive Rehabilitation After Traumatic Brain Injury *Medical Rehabilitation*, *90*, S52-S59.
- Clark, B., Whitall, J., Kwakkel, G., Mehrholz, J., Ewings, S., & Burridge, J. (2021). The effect of time spent in rehabilitation on activity limitation and impairment after stroke *Cochrane Database Syst Rev*, 10(10), Cd012612.
- Clarke, D. J., Godfrey, M., Hawkins, R., Sadler, E., Harding, G., Forster, A., et al. (2013). Implementing a training intervention to support caregivers after stroke: a process evaluation examining the initiation and embedding of programme change *Implementation Science* 8(96).
- CLOTS Trials Collaboration. (2013). The effect of graduated compression stockings on long-term outcomes after stroke: the CLOTS trials 1 and 2 *Stroke*, *44*(4), 1075-1079.
- CLOTS Trials Collaboration. (2014). Effect of intermittent pneumatic compression on disability, living circumstances, quality of life, and hospital costs after stroke: secondary analyses from CLOTS 3, a randomised trial *Lancet Neurology*, *13*(12), 1186-1192.
- Coggrave, M., Wiesel, P. H., & Norton, C. (2006). Management of faecal incontinence and constipation in adults with central neurological diseases *Cochrane Database of Systematic Reviews*(2), CD002115.
- College of Occupational Therapists, & Association of Chartered Physiotherapists in Neurology. (2015). Splinting for the prevention and correction of contractures in adults with neurological dysfunction. https://www.acpin.net/pdfs/Splinting_Guidelines.pdf
- Community Rehabilitation Alliance. (2021). Community Rehabilitation Alliance Manifesto
 https://www.csp.org.uk/system/files/documents/2021-11/001669 cr manifesto 2021 roll fold 3.pdf?utm content=bufferfc968&utm medium=socia
 l&utm_source=twitter.com&utm_campaign=buffer
- Compter, A., van der Worp, H. B., Schonewille, W. J., Vos, J. A., Boiten, J., Nederkoorn, P. J., et al. (2015). Stenting versus medical treatment in patients with symptomatic vertebral artery stenosis: a randomised open-label phase 2 trial *Lancet Neurology*, *14*(6), 606-614.
- Connell, L. A., Lincoln, N. B., & Radford, K. A. (2008). Somatosensory impairment after stroke: frequency of different deficits and their recovery *Clinical Rehabilitation*, *22*(8), 758-767.
- Connolly, S. J., Ezekowitz, M. D., Yusuf, S., Eikelboom, J., Oldgren, J., Parekh, A., et al. (2009). Dabigatran versus warfarin in patients with atrial fibrillation *New England Journal of Medicine*, *361*(12), 1139-1151.
- Connolly, S. J., Eikelboom, J., Joyner, C., Diener, H.-C., Hart, R., Golitsyn, S., et al. (2011). Apixaban in Patients with Atrial Fibrillation *New England Journal of Medicine*, *364*(9), 806-817.
- Connolly, S. J., Karthikeyan, G., Ntsekhe, M., Haileamlak, A., El Sayed, A., El Ghamrawy, A., et al. (2022). Rivaroxaban in Rheumatic Heart Disease-Associated Atrial Fibrillation *N Engl J Med*, *387*(11), 978-988.
- Corbetta, D., Sirtori, V., Castellini, G., Moja, L., & Gatti, R. (2015). Constraint-induced movement therapy for upper extremities in people with stroke *Cochrane Database Syst Rev*, *2015*(10), Cd004433.
- Corbin, J., Strauss, A. (1998). *Unending work and care: managing chronic illness at home*. Jossey-Bass.San Francisco.
- Coughlan, D., McMeekin, P., Flynn, D., Ford, G. A., Lumley, H., Burgess, D., et al. (2021). Secondary transfer of emergency stroke patients eligible for mechanical thrombectomy by air in rural England: economic evaluation and considerations *Emerg Med J*, *38*(1), 33-39.
- Coutinho, J., de Bruijn, S. F., Deveber, G., & Stam, J. (2011). Anticoagulation for cerebral venous sinus thrombosis *Cochrane Database of Systematic Reviews*, *8*, CD002005.
- Crocker, T., Forster, A., Young, J., Brown, L., Ozer, S., Smith, J., et al. (2013). Physical rehabilitation for older people in long-term care *Cochrane Database of Systematic Reviews*(2), CD004294.
- Crowther, M. A., Ginsberg, J. S., Julian, J., Denburg, J., Hirsh, J., Douketis, J., et al. (2003). A comparison of two intensities of warfarin for the prevention of recurrent thrombosis in patients with the antiphospholipid antibody syndrome *New England Journal of Medicine*, *349*(12), 1133-1138.
- Cruz-Flores, S., Berge, E., & Whittle, I. R. (2012). Surgical decompression for cerebral oedema in acute ischaemic stroke *The Cochrane Database of Systematic Reviews*, *1*, CD003435.

- Da-Silva, R. H., Moore, S. A., & Price, C. I. (2018). Self-directed therapy programmes for arm rehabilitation after stroke: a systematic review *Clin Rehabil*, *32*(8), 1022-1036.
- da Silva, E. S. M., Ocamoto, G. N., Santos-Maia, G. L. D., de Fátima Carreira Moreira Padovez, R., Trevisan, C., de Noronha, M. A., et al. (2020). The Effect of Priming on Outcomes of Task-Oriented Training for the Upper Extremity in Chronic Stroke: A Systematic Review and Meta-analysis *Neurorehabil Neural Repair*, 34(6), 479-504.
- Daly, J. J., McCabe, J. P., Holcomb, J., Monkiewicz, M., Gansen, J., & Pundik, S. (2019). Long-Dose Intensive Therapy Is Necessary for Strong, Clinically Significant, Upper Limb Functional Gains and Retained Gains in Severe/Moderate Chronic Stroke *Neurorehabilitation and Neural Repair*, 33(7), 523-537.
- Das Nair, R., & Lincoln, N. B. (2007). Cognitive rehabilitation for memory deficits following stroke Cochrane Database of Systematic Reviews(3), CD002293.
- Das Nair, R., & Lincoln, N. B. (2012). Evaluation of Rehabilitation of Memory in Neurological Disabilities (ReMiND): A randomized controlled trial *Clinical Rehabilitation*, *26*(10), 894-903.
- Davalos, A., Ricart, W., Gonzalez-Huix, F., Soler, S., Marrugat, J., Molins, A., et al. (1996). Effect of malnutrition after acute stroke on clinical outcome *Stroke*, *27*(6), 1028-1032.
- Daviet, J. C., Bonan, I., Caire, J. M., Colle, F., Damamme, L., Froger, J., et al. (2012). Therapeutic patient education for stroke survivors: Non-pharmacological management. A literature review *Annals of Physical & Rehabilitation Medicine*, *55*(9-10), 641-656.
- Davis, S. M., Donnan, G. A., Parsons, M. W., Levi, C., Butcher, K. S., Peeters, A., et al. (2008). Effects of alteplase beyond 3 h after stroke in the Echoplanar Imaging Thrombolytic Evaluation Trial (EPITHET): a placebo-controlled randomised trial *Lancet Neurol*, 7(4), 299-309.
- Dawson, J., Liu, C. Y., Francisco, G. E., Cramer, S. C., Wolf, S. L., Dixit, A., et al. (2021). Vagus nerve stimulation paired with rehabilitation for upper limb motor function after ischaemic stroke (VNS-REHAB): a randomised, blinded, pivotal, device trial *The Lancet*, *397*(10284), 1545-1553.
- De Man-van Ginkel, J., Gooskens, F., Schuurmans, M. J., Lindeman, E., Hafsteinsdottir, T. r. B., & Group, o. B. o. t. R. G. S. W. (2010). A systematic review of therapeutic interventions for poststroke depression and the role of nurses *Journal of Clinical Nursing*, *19*(23-24), 3274-3290.
- De Marchis, G. M., Seiffge, D. J., Schaedelin, S., Wilson, D., Caso, V., Acciarresi, M., et al. (2022). Early versus late start of direct oral anticoagulants after acute ischaemic stroke linked to atrial fibrillation: an observational study and individual patient data pooled analysis *Journal of Neurology, Neurosurgery & Psychiatry*, 93(2), 119.
- De Schryver, E. L., Algra, A., Kappelle, L. J., van Gijn, J., & Koudstaal, P. J. (2012). Vitamin K antagonists versus antiplatelet therapy after transient ischaemic attack or minor ischaemic stroke of presumed arterial origin *The Cochrane Database of Systematic Reviews*, *9*, CD001342.
- Debette, S., Mazighi, M., Bijlenga, P., Pezzini, A., Koga, M., Bersano, A., et al. (2021). ESO guideline for the management of extracranial and intracranial artery dissection *European Stroke Journal*, 6(3), XXXIX-LXXXVIII.
- Demchuk, A. M., Yue, P., Conley, P. B., Curnutte, J. T., Zotova, E., Nakamya, J., et al. (2021). Hemostatic Efficacy and Anti-FXa (Factor Xa) Reversal with Andexanet Alfa in Intracranial Hemorrhage: ANNEXA-4 Substudy *Stroke*, 2096-2105.
- Demetrios, M., Gorelik, A., Louie, J., Brand, C., Baguley, I. J., & Khan, F. (2014). Outcomes of ambulatory rehabilitation programmes following botulinum toxin for spasticity in adults with stroke *Journal of Rehabilitation Medicine*, 46(8), 730-737.
- Denissen, S., Staring, W., Kunkel, D., Pickering, R. M., Lennon, S., Geurts, A. C., et al. (2019). Interventions for preventing falls in people after stroke *Cochrane Database Syst Rev*, *10*(10), Cd008728.
- Dennis, M., Forbes, J., Graham, C., Hackett, M., Hankey, G. J., House, A., et al. (2020). Fluoxetine to improve functional outcomes in patients after acute stroke: The FOCUS RCT *Health Technology Assessment*, 24(22), 1-94.
- Dennis, M. S., Lewis, S. C., Warlow, C., & Collaboration, F. T. (2005). Effect of timing and method of enteral tube feeding for dysphagic stroke patients (FOOD): a multicentre randomised controlled trial *Lancet*, *365*(9461), 764-772.

- Dentali, F., Douketis, J. D., Lim, W., & Crowther, M. (2007). Combined aspirin-oral anticoagulant therapy compared with oral anticoagulant therapy alone among patients at risk for cardiovascular disease: a meta-analysis of randomized trials *Archives of Internal Medicine*, 167(2), 117-124.
- Department of Health (Ireland). (2021). *Healthy Ireland Survey 2021*. https://www.gov.ie/en/publication/9ef45-the-healthy-ireland-survey-2021/
- Department of Health (UK). (2005). *National service framework for long term conditions*. https://www.gov.uk/government/publications/quality-standards-for-supporting-people-with-long-term-conditions
- Department of Health (UK). (2016). *Alcohol Guidelines Review: Report from the Guidelines development group to the UK Chief Medical Officers*. https://www.gov.uk/government/consultations/health-risks-from-alcohol-new-guidelines
- Department of Health (UK). (2019). *UK Physical Activity Guidelines*. DH. https://www.gov.uk/government/collections/physical-activity-guidelines
- Derdeyn, C. P., Chimowitz, M. I., Lynn, M. J., Fiorella, D., Turan, T. N., Janis, L. S., et al. (2014). Aggressive medical treatment with or without stenting in high-risk patients with intracranial artery stenosis (SAMMPRIS): the final results of a randomised trial *Lancet*, 383(9914), 333-341.
- Devos, H., Akinwuntan, A. E., Nieuwboer, A., Truijen, S., Tant, M., & De Weerdt, W. (2011). Screening for fitness to drive after stroke: a systematic review and meta-analysis *Neurology*, *76*(8), 747-756.
- Devos, H., Tant, M., & Akinwuntan, A. E. (2014). On-road driving impairments and associated cognitive deficits after stroke *Cerebrovascular Diseases*, *38*(3), 226-232.
- Di Rienzo, F., Collet, C., Hoyek, N., & Guillot, A. (2014). Impact of neurologic deficits on motor imagery: a systematic review of clinical evaluations *Neuropsychol Rev*, 24(2), 116-147.
- Diener, H. C., Bogousslavsky, J., Brass, L. M., Cimminiello, C., Csiba, L., Kaste, M., et al. (2004). Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial *Lancet*, 364(9431), 331-337.
- Diener, H. C., Sacco, R. L., Easton, J. D., Granger, C. B., Bernstein, R. A., Uchiyama, S., et al. (2019).

 Dabigatran for Prevention of Stroke after Embolic Stroke of Undetermined Source *New England Journal of Medicine*, *380*(20), 1906-1917.
- Dignam, J., Copland, D., McKinnon, E., Burfein, P., O'Brien, K., Farrell, A., et al. (2015). Intensive Versus Distributed Aphasia Therapy: A Nonrandomized, Parallel-Group, Dosage-Controlled Study *Stroke; a journal of cerebral circulation*, *46*(8), 2206-2211.
- Døhl, Ø., Halsteinli, V., Askim, T., Gunnes, M., Ihle-Hansen, H., Indredavik, B., et al. (2020). Factors contributing to post-stroke health care utilization and costs, secondary results from the life after stroke (LAST) study *BMC Health Serv Res*, 20(1), 288-298.
- Donabedian, A. (1978). The quality of medical care Science, 200(4344), 856-864.
- Dong, X. L., Sun, X., Sun, W. M., Yuan, Q., Yu, G. H., Shuai, L., et al. (2021). A randomized controlled trial to explore the efficacy and safety of transcranial direct current stimulation on patients with post-stroke fatigue *Medicine*, 100(41), e27504.
- Dormandy, J. A., Charbonnel, B., Eckland, D. J., Erdmann, E., Massi-Benedetti, M., Moules, I. K., et al. (2005). Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomised controlled trial *Lancet*, *366*(9493), 1279-1289.
- Dorsch, S., Carling, C., Cao, Z., Fanayan, E., Graham, P. L., McCluskey, A., et al. (2023). Bobath therapy is inferior to task-specific training and not superior to other interventions in improving arm activity and arm strength outcomes after stroke: a systematic review *J Physiother*, 69(1), 15-22.
- Dorstyn, D., Roberts, R., Kneebone, I., Kennedy, P., & Lieu, C. (2014). Systematic review of leisure therapy and its effectiveness in managing functional outcomes in stroke rehabilitation *Topics in Stroke Rehabilitation*, 21(1), 40-51.
- Doyle, S., Bennett, S., Fasoli, S. E., & McKenna, K. T. (2010). Interventions for sensory impairment in the upper limb after stroke *Cochrane Database of Systematic Reviews*(6), CD006331.

- Drummond, A., Nouri, F., Ablewhite, J., Condon, L., das Nair, R., Jones, A., et al. (2021). Managing post-stroke fatigue: A qualitative study to explore multifaceted clinical perspectives *British Journal of Occupational Therapy*, 85(7), 505-512.
- Drummond, A. E., Whitehead, P., Fellows, K., Sprigg, N., Sampson, C. J., Edwards, C., et al. (2013).

 Occupational therapy predischarge home visits for patients with a stroke (HOVIS): results of a feasibility randomized controlled trial *Clinical Rehabilitation*, *27*(5), 387-397.
- Drury, P., Levi, C., D'Este, C., McElduff, P., McInnes, E., Hardy, J., et al. (2014). Quality in Acute Stroke Care (QASC): process evaluation of an intervention to improve the management of fever, hyperglycemia, and swallowing dysfunction following acute stroke *International Journal of Stroke*, *9*(6), 766-776.
- Duncan, F., Wu, S., & Mead, G. E. (2012). Frequency and natural history of fatigue after stroke: a systematic review of longitudinal studies *J Psychosom Res*, 73(1), 18-27.
- Duncan, P. W., Sullivan, K. J., Behrman, A. L., Azen, S. P., Wu, S. S., Nadeau, S. E., et al. (2011). Body-Weight Supported Treadmill Rehabilitation after Stroke *New England Journal of Medicine*, 364(21), 2026-2036.
- Duong, P., Sauvé-Schenk, K., Egan, M. Y., Meyer, M. J., & Morrison, T. (2019). Operational Definitions and Estimates of Return to Work Poststroke: A Systematic Review and Meta-Analysis *Arch Phys Med Rehabil*, 100(6), 1140-1152.
- Dutta, D., Kendall, J., Holmes, C., Murphy, P., Black, T., Whiting, R., et al. (2015). Evaluation of a telephone advice system for remote intravenous thrombolysis in ischemic stroke: data from a United Kingdom network *Stroke*, *46*(3), 867-869.
- Dziewas, R., Warnecke, T., Stellato, R., van der Tweel, I., Walther, E., Werner, C. J., et al. (2018).

 Pharyngeal electrical stimulation for early decannulation in tracheotomised patients with neurogenic dysphagia after stroke (PHAST-TRAC): a prospective, single-blinded, randomised trial *The Lancet Neurology*, *17*(10), 849-859.
- Dziewas, R., Michou, E., Hamdy, S., Trapl-Grundschober, M., Lal, A., Arsava, E. M., et al. (2021). European Stroke Organisation and European Society for Swallowing Disorders guideline for the diagnosis and treatment of post-stroke dysphagia *European Stroke Journal*, 6(3), LXXXIX-CXV.
- EAFT Study Group. (1993). Secondary prevention in non-rheumatic atrial fibrillation after transient ischaemic attack or minor stroke. EAFT (European Atrial Fibrillation Trial) Study Group *Lancet*, 342(8882), 1255-1262.
- Ebinger, M., Winter, B., Wendt, M., Weber, J. E., Waldschmidt, C., Rozanski, M., et al. (2014). Effect of the use of ambulance-based thrombolysis on time to thrombolysis in acute ischemic stroke: a randomized clinical trial *JAMA*, *311*(16), 1622-1631.
- Economopoulos, K. P., Sergentanis, T. N., Tsivgoulis, G., Mariolis, A. D., & Stefanadis, C. (2011). Carotid artery stenting versus carotid endarterectomy: a comprehensive meta-analysis of short-term and long-term outcomes *Stroke*, *42*(3), 687-692.
- Eddison, N., Leone, E., Healy, A., Royse, C., & Chockalingam, N. (2022). The potential impact of allied health professional telehealth consultations on health inequities and the burden of treatment *International Journal for Equity in Health*, *21*(1), Article number 91.
- Edjoc, R. K., Reid, R. D., & Sharma, M. (2012). The effectiveness of smoking cessation interventions in smokers with cerebrovascular disease: a systematic review *BMJ Open*, *2*(6), e002022-e002027.
- Edwards, S. J., Wakefield, V., Jhita, T., Kew, K., Cain, P., & Marceniuk, G. (2020). Implantable cardiac monitors to detect atrial fibrillation after cryptogenic stroke: a systematic review and economic evaluation, *24*(5), 1366-5278.
- Eidelman, R. S., Hollar, D., Hebert, P. R., Lamas, G. A., & Hennekens, C. H. (2004). Randomized trials of vitamin E in the treatment and prevention of cardiovascular disease *Archives of Internal Medicine*, *164*(14), 1552-1556.
- Eikelboom, J. W., Wallentin, L., Connolly, S. J., Ezekowitz, M., Healey, J. S., Oldgren, J., et al. (2011). Risk of bleeding with 2 doses of dabigatran compared with warfarin in older and younger patients with atrial fibrillation: an analysis of the randomized evaluation of long-term anticoagulant therapy (RE-LY) trial *Circulation*, 123(21), 2363-2372.

- Eikelboom, J. W., Connolly, S. J., Brueckmann, M., Granger, C. B., Kappetein, A. P., Mack, M. J., et al. (2013). Dabigatran versus Warfarin in Patients with Mechanical Heart Valves *New England Journal of Medicine*, *369*(13), 1206-1214.
- Elamin, M. B., Abu Elnour, N. O., Elamin, K. B., Fatourechi, M. M., Alkatib, A. A., Almandoz, J. P., et al. (2011). Vitamin D and cardiovascular outcomes: a systematic review and meta-analysis *Journal of Clinical Endocrinology and Metabolism*, *96*(7), 1931-1942.
- Elf, M., Eriksson, G., Johansson, S., von Koch, L., & Ytterberg, C. (2016). Self-Reported Fatigue and Associated Factors Six Years after Stroke *PLoS One*, *11*(8), e0161942.
- Elia, A. E., Filippini, G., Calandrella, D., & Albanese, A. (2009). Botulinum neurotoxins for post-stroke spasticity in adults: a systematic review *Movement Disorders*, 24(6), 801-812.
- Elsner, B., Kugler, J., Pohl, M., & Mehrholz, J. (2016). Transcranial direct current stimulation (tDCS) for improving activities of daily living, and physical and cognitive functioning, in people after stroke *Cochrane Database of Systematic Reviews*(3), CD009645.
- Elsnhory, A., Hasan, M. T., Hagrass, A. I., Hanbal, A., Fathy, A., Ahmed, E., et al. (2022). Recovery in Stroke Patients Treated With Fluoxetine Versus Placebo: A Pooled Analysis of 7165 Patients *The Neurologist*, [Epub ahead of print].
- Emberson, J., Lees, K. R., Lyden, P., Blackwell, L., Albers, G., Bluhmki, E., et al. (2014). Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: A meta-analysis of individual patient data from randomised trials *Lancet*, 384(9958), 1929-1935.
- Engelter, S. T., Dallongeville, J., Kloss, M., Metso, T. M., Leys, D., Brandt, T., et al. (2012). Thrombolysis in cervical artery dissection--data from the Cervical Artery Dissection and Ischaemic Stroke Patients (CADISP) database *European Journal of Neurology*, 19(9), 1199-1206.
- Engineer, N. D., Kimberley, T. J., Prudente, C. N., Dawson, J., Tarver, W. B., & Hays, S. A. (2019). Targeted Vagus Nerve Stimulation for Rehabilitation After Stroke *Front Neurosci*, *13*, 280-298.
- English, C., & Hillier, S. L. (2010). Circuit class therapy for improving mobility after stroke *Cochrane Database of Systematic Reviews*(7), CD007513.
- English, C., Bernhardt, J., Crotty, M., Esterman, A., Segal, L., & Hillier, S. (2015). Circuit class therapy or seven-day week therapy for increasing rehabilitation intensity of therapy after stroke (CIRCIT): a randomized controlled trial *International Journal of Stroke*, 10(4), 594-602.
- English, C., Hillier, S. L., & Lynch, E. A. (2017). Circuit class therapy for improving mobility after stroke *Cochrane Database of Systematic Reviews*, *2017*(6), CD007513.
- ESPIRIT Study Group. (2006). Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial *Lancet*, *367*(9523), 1665-1673.
- Ettehad, D., Emdin, C. A., Kiran, A., Anderson, S. G., Callender, T., Emberson, J., et al. (2016). Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis *Lancet*, *387*(10022), 957-967.
- Fassbender, K., Dempfle, C. E., Mielke, O., Schwartz, A., Daffertshofer, M., Eschenfelder, C., et al. (1999). Changes in coagulation and fibrinolysis markers in acute ischemic stroke treated with recombinant tissue plasminogen activator *Stroke*, *30*(10), 2101-2104.
- Faulkner, J., McGonigal, G., Woolley, B., Stoner, L., Wong, L., & Lambrick, D. (2015). A randomized controlled trial to assess the psychosocial effects of early exercise engagement in patients diagnosed with transient ischaemic attack and mild, non-disabling stroke *Clinical Rehabilitation*, 29(8), 783-794.
- Fens, M., van Heugten, C. M., Beusmans, G., Metsemakers, J., Kester, A., & Limburg, M. (2014). Effect of a stroke-specific follow-up care model on the quality of life of stroke patients and caregivers: A controlled trial *Journal of Rehabilitation Medicine*, 46(1), 7-15.
- Fernandez-Garcia, C., Ternent, L., Homer, T. M., Rodgers, H., Bosomworth, H., Shaw, L., et al. (2021). Economic evaluation of robot-assisted training versus an enhanced upper limb therapy programme or usual care for patients with moderate or severe upper limb functional limitation due to stroke: results from the RATULS randomised controlled trial *BMJ Open*, 11(5), e042081.

- Ferrarello, F., Baccini, M., Rinaldi, L. A., Cavallini, M. C., Mossello, E., Masotti, G., et al. (2011). Efficacy of physiotherapy interventions late after stroke: a meta-analysis *Journal of Neurology, Neurosurgery & Psychiatry*, 82(2), 136-143.
- Finazzi, G., Marchioli, R., Brancaccio, V., Schinco, P., Wisloff, F., Musial, J., et al. (2005). A randomized clinical trial of high-intensity warfarin vs. conventional antithrombotic therapy for the prevention of recurrent thrombosis in patients with the antiphospholipid syndrome (WAPS) *Journal of Thrombosis and Haemostasis*, *3*(5), 848-853.
- Finestone, H. M., Woodbury, M. G., Foley, N. C., Teasell, R. W., & Greene-Finestone, L. S. (2002). Tracking clinical improvement of swallowing disorders after stroke *Journal of Stroke & Cerebrovascular Diseases*, 11(1), 23-27.
- Firth, N., Barkham, M., & Kellett, S. (2015). The clinical effectiveness of stepped care systems for depression in working age adults: a systematic review *Journal of Affective Disorders*, *170*, 119-130.
- Fischer, U., Kaesmacher, J., Strbian, D., Eker, O., Cognard, C., Plattner, P. S., et al. (2022). Thrombectomy alone versus intravenous alteplase plus thrombectomy in patients with stroke: an open-label, blinded-outcome, randomised non-inferiority trial *Lancet*, *400*(10346), 104-115.
- Fish, J., Manly, T., Emslie, H., Evans, J. J., & Wilson, B. A. (2008). Compensatory strategies for acquired disorders of memory and planning: differential effects of a paging system for patients with brain injury of traumatic versus cerebrovascular aetiology *Journal of Neurology, Neurosurgery & Psychiatry*, 79(8), 930-935.
- Fisher, R. J., Gaynor, C., Kerr, M., Langhorne, P., Anderson, C., Bautz-Holter, E., et al. (2011). A consensus on stroke: early supported discharge *Stroke*, *42*(5), 1392-1397.
- Fisher, R. J., Walker, M. F., Golton, I., & Jenkinson, D. (2013). The implementation of evidence-based rehabilitation services for stroke survivors living in the community: the results of a Delphi consensus process *Clin Rehabil*, *27*(8), 741-749.
- Fisher, R. J., Cobley, C. S., Potgieter, I., Moody, A., Nouri, F., Gaynor, C., et al. (2016). Is Stroke Early Supported Discharge still effective in practice? A prospective comparative study *Clinical Rehabilitation*, 30(3), 268-276.
- Fisher, R. J., Byrne, A., Chouliara, N., Lewis, S., Paley, L., Hoffman, A., et al. (2020). Effectiveness of Stroke Early Supported Discharge *Circulation: Cardiovascular Quality and Outcomes*, *13*(8), e006395.
- Fisher, R. J., Byrne, A., Chouliara, N., Lewis, S., Paley, L., Hoffman, A., et al. (2021). Effect of stroke early supported discharge on length of hospital stay: Analysis from a national stroke registry *BMJ Open*, 11(1), e043480.
- Foley, N., Teasell, R., Salter, K., Kruger, E., & Martino, R. (2008). Dysphagia treatment post stroke: A systematic review of randomised controlled trials *Age and Ageing*, *37*(3), 258-264.
- Fong, K. N., Yang, N. Y., Chan, M. K., Chan, D. Y., Lau, A. F., Chan, D. Y., et al. (2013). Combined effects of sensory cueing and limb activation on unilateral neglect in subacute left hemiplegic stroke patients: a randomized controlled pilot study *Clinical Rehabilitation*, *27*(7), 628-637.
- Ford, G., James, M., & White, P. (2022). *Mechanical thrombectomy for acute ischaemic stroke: an implementation guide for the UK. Second Edition*. Oxford AHSN.

 https://www.oxfordahsn.org/our-work/our-programmes/adopting-innovation/cardiovascular-disease/mt-guide/
- Forster, A., Brown, L., Smith, J., House, A., Knapp, P., Wright, J. J., et al. (2012). Information provision for stroke patients and their caregivers *Cochrane Database of Systematic Reviews*, *11*, CD001919.
- Forster, A., Dickerson, J., Young, J., Patel, A., Kalra, L., Nixon, J., et al. (2013). A structured training programme for caregivers of inpatients after stroke (TRACS): a cluster randomised controlled trial and cost-effectiveness analysis *Lancet*, *382*(9910), 2069-2076.
- Forster, A., Ozer, S., Crocker, T. F., House, A., Hewison, J., Roberts, E., et al. (2021). Longer-term health and social care strategies for stroke survivors and their carers: the LoTS2Care research programme including cluster feasibility RCT *NIHR Journals Library*, *9*(2021), 3.
- Francis, R. (2013). In *Report of the Mid Staffordshire NHS Foundation Trust Public Inquiry*. The Stationery Office.

- French, B., Thomas, L. H., Coupe, J., McMahon, N. E., Connell, L., Harrison, J., et al. (2016a). Repetitive task training for improving functional ability after stroke *Cochrane Database Syst Rev*, 11(11), Cd006073.
- French, B., Thomas, L. H., Coupe, J., McMahon, N. E., Connell, L., Harrison, J., et al. (2016b). Repetitive task training for improving functional ability after stroke *The Cochrane Database of Systematic Reviews*, *11*, CD006073.
- Fulcher, J., O'Connell, R., Voysey, M., Emberson, J., Blackwell, L., Mihaylova, B., et al. (2015). Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials *Lancet*, 385(9976), 1397-1405.
- Fung, T. T., Chiuve, S. E., McCullough, M. L., Rexrode, K. M., Logroscino, G., & Hu, F. B. (2008). Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women *Archives of Internal Medicine*, *168*(7), 713-720.
- Furlan, A. J., Reisman, M., Massaro, J., Mauri, L., Adams, H., Albers, G. W., et al. (2012). Closure or medical therapy for cryptogenic stroke with patent foramen ovale *New England Journal of Medicine*, 366(11), 991-999.
- Galan, P., Kesse-Guyot, E., Czernichow, S., Briancon, S., Blacher, J., & Hercberg, S. (2010). Effects of B vitamins and omega 3 fatty acids on cardiovascular diseases: a randomised placebo controlled trial *BMJ*, *341*, c6273.
- García-Cabo, C., & López-Cancio, E. (2020). Exercise and Stroke Adv Exp Med Biol, 1228, 195-203.
- Gardiner, C., Harrison, M., Ryan, T., & Jones, A. (2013). Provision of palliative and end-of-life care in stroke units: a qualitative study *Palliative Medicine*, *27*(9), 855-860.
- Garry, M. I., Loftus, A., & Summers, J. J. (2005). Mirror, mirror on the wall: viewing a mirror reflection of unilateral hand movements facilitates ipsilateral M1 excitability *Experimental Brain Research*, 163(1), 118-122.
- Gaskins, N. J., Bray, E., Hill, J. E., Doherty, P. J., Harrison, A., & Connell, L. A. (2021). Factors influencing implementation of aerobic exercise after stroke: a systematic review *Disability and Rehabilitation*, 43(17), 2382-2396.
- Gauthier, L. V., Nichols-Larsen, D. S., Uswatte, G., Strahl, N., Simeo, M., Proffitt, R., et al. (2022). Video game rehabilitation for outpatient stroke (VIGoROUS): A multi-site randomized controlled trial of in-home, self-managed, upper-extremity therapy *eClinicalMedicine*, 43.
- Geeganage, C., Beavan, J., Ellender, S., & Bath Philip, M. W. (2012). Interventions for dysphagia and nutritional support in acute and subacute stroke *Cochrane Database of Systematic Reviews*, 10, CD000323.
- Geeganage, C. M., Sprigg, N., Bath, M. W., & Bath, P. M. (2013). Balance of symptomatic pulmonary embolism and symptomatic intracerebral hemorrhage with low-dose anticoagulation in recent ischemic stroke: a systematic review and meta-analysis of randomized controlled trials *Journal of Stroke & Cerebrovascular Diseases*, 22(7), 1018-1027.
- George, S., Crotty, M., Gelinas, I., & Devos, H. (2014). Rehabilitation for improving automobile driving after stroke *Cochrane Database of Systematic Reviews*, *2*, CD008357.
- Geraghty, O. C., Kennedy, J., Chandratheva, A., Marquardt, L., Buchan, A. M., & Rothwell, P. M. (2010). Preliminary evidence of a high risk of bleeding on aspirin plus clopidogrel in aspirin-naive patients in the acute phase after TIA or minor ischaemic stroke *Cerebrovascular Diseases*, 29(5), 460-467.
- Germain, D. P., Charrow, J., Desnick, R. J., Guffon, N., Kempf, J., Lachmann, R. H., et al. (2015). Ten-year outcome of enzyme replacement therapy with agalsidase beta in patients with Fabry disease *Journal of medical genetics*, *52*(5), 353-358.
- Getting it Right First Time. (2022). *Stroke GIRFT Report*. https://future.nhs.uk/GIRFTNational/view?objectId=130558949
- Giles, M. F., & Rothwell, P. M. (2007). Risk of stroke early after transient ischaemic attack: a systematic review and meta-analysis *Lancet Neurol*, *6*(12), 1063-1072.
- Gillham, S., & Clark, L. (2011). Psychological care after stroke Improving stroke services for people with cognitive and mood disorders, NHS Improvement Stroke.

- Gioia, L. C., Kate, M., Sivakumar, L., Hussain, D., Kalashyan, H., Buck, B., et al. (2016). Early Rivaroxaban Use After Cardioembolic Stroke May Not Result in Hemorrhagic Transformation: A Prospective Magnetic Resonance Imaging Study *Stroke*, *47*(7), 1917-1919.
- Giugliano, R. P., Ruff, C. T., Braunwald, E., Murphy, S. A., Wiviott, S. D., Halperin, J. L., et al. (2013). Edoxaban versus Warfarin in Patients with Atrial Fibrillation *New England Journal of Medicine*, 369(22), 2093-2104.
- Gladstone, D. J., Spring, M., Dorian, P., Panzov, V., Thorpe, K. E., Hall, J., et al. (2014). Atrial fibrillation in patients with cryptogenic stroke *New England Journal of Medicine*, *370*(26), 2467-2477.
- Glaess-Leistner, S., Ri, S. J., Audebert, H. J., & Wissel, J. (2021). Early clinical predictors of post stroke spasticity *Top Stroke Rehabil*, *28*(7), 508-518.
- Glynn, L. G., Murphy, A. W., Smith, S. M., Schroeder, K., & Fahey, T. (2010). Interventions used to improve control of blood pressure in patients with hypertension *Cochrane Database Syst Rev*(3), Cd005182.
- Godecke, E., Armstrong, E., Rai, T., Ciccone, N., Rose, M. L., Middleton, S., et al. (2021). A randomized control trial of intensive aphasia therapy after acute stroke: The Very Early Rehabilitation for SpEech (VERSE) study *International Journal of Stroke*, *16*(5), 556-572.
- Golding, K., Kneebone, I., & Fife-Schaw, C. (2015). Self-help relaxation for post-stroke anxiety: A randomised, controlled pilot study *Clinical Rehabilitation*, *30*, 174-180.
- Gomes, F., Emery, P. W., & Weekes, C. E. (2016). Risk of Malnutrition Is an Independent Predictor of Mortality, Length of Hospital Stay, and Hospitalization Costs in Stroke Patients *Journal of Stroke & Cerebrovascular Diseases*, 25(4), 799-806.
- Good, P., Richard, R., Syrmis, W., Jenkins-Marsh, S., & Stephens, J. (2014). Medically assisted hydration for adult palliative care patients *Cochrane Database of Systematic Reviews*(4), CD006273.
- Goyal, M., Demchuk, A. M., Menon, B. K., Eesa, M., Rempel, J. L., Thornton, J., et al. (2015). Randomized assessment of rapid endovascular treatment of ischemic stroke *New England Journal of Medicine*, *372*(11), 1019-1030.
- Goyal, M., Menon, B. K., van Zwam, W. H., Dippel, D. W., Mitchell, P. J., Demchuk, A. M., et al. (2016). Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials *Lancet*, *387*, 1723-1731.
- Gracies, J. M. (2005). Pathophysiology of spastic paresis. I: Paresis and soft tissue changes *Muscle Nerve*, 31(5), 535-551.
- Gracies, J. M., Brashear, A., Jech, R., McAllister, P., Banach, M., Valkovic, P., et al. (2015). Safety and efficacy of abobotulinumtoxina for hemiparesis in adults with upper limb spasticity after stroke or traumatic brain injury: a double-blind randomised controlled trial *Lancet Neurology*, *14*(10), 992-1001.
- Graham, D. J., Reichman, M. E., Wernecke, M., Zhang, R., Southworth, M. R., Levenson, M., et al. (2015). Cardiovascular, bleeding, and mortality risks in elderly Medicare patients treated with dabigatran or warfarin for nonvalvular atrial fibrillation *Circulation*, 131(2), 157-164.
- Granger, C. B., Alexander, J. H., McMurray, J. J., Lopes, R. D., Hylek, E. M., Hanna, M., et al. (2011). Apixaban versus warfarin in patients with atrial fibrillation *New England Journal of Medicine*, *365*(11), 981-992.
- Grasel, E., Schmidt, R., Biehler, J., & Schupp, W. (2006). Long-term effects of the intensification of the transition between inpatient neurological rehabilitation and home care of stroke patients *Clinical Rehabilitation*, 20(7), 577-583.
- Grattan, E. S., Lang, C. E., Birkenmeier, R., Holm, M., Rubinstein, E., Van Swearingen, J., et al. (2016). Examining the Feasibility, Tolerability, and Preliminary Efficacy of Repetitive Task-Specific Practice for People With Unilateral Spatial Neglect *Am J Occup Ther*, *70*(4), 21-28.
- Gray, C. S., Hildreth, A. J., Sandercock, P. A., O'Connell, J. E., Johnston, D. E., Cartlidge, N. E., et al. (2007). Glucose-potassium-insulin infusions in the management of post-stroke hyperglycaemia: the UK Glucose Insulin in Stroke Trial (GIST-UK) 16 *Lancet Neurology*, 6(5), 397-406.
- Grond, M., Jauss, M., Hamann, G., Stark, E., Veltkamp, R., Nabavi, D., et al. (2013). Improved detection of silent atrial fibrillation using 72-hour Holter ECG in patients with ischemic stroke: a prospective multicenter cohort study *Stroke*, *44*(12), 3357-3364.

- Gulli, G., Marquardt, L., Rothwell, P. M., & Markus, H. S. (2013). Stroke risk after posterior circulation stroke/transient ischemic attack and its relationship to site of vertebrobasilar stenosis: pooled data analysis from prospective studies *Stroke*, *44*(3), 598-604.
- Gunnes, M., Langhammer, B., Aamot, I.-L., Lydersen, S., Ihle-Hansen, H., Indredavik, B., et al. (2019). Adherence to a Long-Term Physical Activity and Exercise Program After Stroke Applied in a Randomized Controlled Trial *Physical Therapy*, *99*(1), 74-85.
- Guo, J., Shi, Z., Yang, K., Tian Jin, H., & Jiang, L. (2012). Endothelin receptor antagonists for subarachnoid hemorrhage *Cochrane Database of Systematic Reviews*, *9*, CD008354.
- Guo, Z. F., Liu, Y., Hu, G. H., Liu, H., & Xu, Y. F. (2014). Transcutaneous electrical nerve stimulation in the treatment of patients with poststroke urinary incontinence *Clinical Interventions In Aging*, *9*, 851-856.
- Hackam, D. G., & Spence, J. D. (2007). Combining multiple approaches for the secondary prevention of vascular events after stroke: a quantitative modeling study *Stroke*, *38*(6), 1881-1885.
- Hackett, M. L., Anderson, C. S., House, A. O., & Xia, J. (2009). Interventions for Treating Depression After Stroke *Cochrane Database of Systematic Reviews*(4), CD003437.
- Hackett, M. L., Yang, M., Anderson, C. S., Horrocks, J. A., & House, A. (2010). Pharmaceutical interventions for emotionalism after stroke *Cochrane Database of Systematic Reviews*(2), CD003690.
- Haley, E. C., Jr., Thompson, J. L., Grotta, J. C., Lyden, P. D., Hemmen, T. G., Brown, D. L., et al. (2010). Phase IIB/III trial of tenecteplase in acute ischemic stroke: results of a prematurely terminated randomized clinical trial *Stroke*, *41*(4), 707-711.
- Hall, J., Kroll, T., van Wijck, F., & Bassil-Morozow, H. (2022). Co-creating Digital Stories With UK-Based Stroke Survivors With the Aim of Synthesizing Collective Lessons From Individual Experiences of Interacting With Healthcare Professionals *Front Rehabil Sci*, *3*, 877442-877460.
- Hamdy, S., Aziz, Q., Rothwell, J. C., Power, M., Singh, K. D., Nicholson, D. A., et al. (1998). Recovery of swallowing after dysphagic stroke relates to functional reorganization in the intact motor cortex *Gastroenterology*, 115(5), 1104-1112.
- Hamidon, B. B., Abdullah, S. A., Zawawi, M. F., Sukumar, N., Aminuddin, A., & Raymond, A. A. (2006). A prospective comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding in patients with acute dysphagic stroke *Medical Journal of Malaysia*, *61*(1), 59-66.
- Handke, M., Harloff, A., Olschewski, M., Hetzel, A., & Geibel, A. (2007). Patent Foramen Ovale and Cryptogenic Stroke in Older Patients *New England Journal of Medicine*, *357*(22), 2262-2268.
- Hankey, G. J., Hackett, M. L., Almeida, O. P., Flicker, L., Mead, G. E., Dennis, M. S., et al. (2020). Safety and efficacy of fluoxetine on functional outcome after acute stroke (AFFINITY): a randomised, double-blind, placebo-controlled trial *The Lancet Neurology*, *19*(8), 651-660.
- Hankey, G. J., Hackett, M. L., Almeida, O. P., Flicker, L., Mead, G. E., Dennis, M. S., et al. (2021). Twelve-Month Outcomes of the AFFINITY Trial of Fluoxetine for Functional Recovery After Acute Stroke: AFFINITY Trial Steering Committee on Behalf of the AFFINITY Trial Collaboration *Stroke*, *52*(8), 2502-2509.
- Hanley, J., Fairbrother, P., McCloughan, L., Pagliari, C., Paterson, M., Pinnock, H., et al. (2015).

 Qualitative study of telemonitoring of blood glucose and blood pressure in type 2 diabetes *BMJ Open*, 5(12), e008896.
- Hanna, K. L., & Rowe, F. J. (2017). Health Inequalities Associated with Post-Stroke Visual Impairment in the United Kingdom and Ireland: A Systematic Review *Neuro-Ophthalmology*, *41*(3), 117-136.
- Harbison, J., Hossain, O., Jenkinson, D., Davis, J., Louw, S. J., & Ford, G. A. (2003). Diagnostic accuracy of stroke referrals from primary care, emergency room physicians, and ambulance staff using the face arm speech test *Stroke*, *34*(1), 71-76.
- Harris, J. E., & Eng, J. J. (2007). Paretic upper-limb strength best explains arm activity in people with stroke *Phys Ther*, *87*(1), 88-97.
- Harrison, M., Palmer, R., & Cooper, C. (2020). Factors Associated With Adherence to Self-Managed Aphasia Therapy Practice on a Computer-A Mixed Methods Study Alongside a Randomized Controlled Trial *Frontiers in Neurology*, *11*, 582328.

- Hart, R. G., Tonarelli, S. B., & Pearce, L. A. (2005). Avoiding central nervous system bleeding during antithrombotic therapy: recent data and ideas *Stroke*, *36*(7), 1588-1593.
- Hart, R. G., Sharma, M., Mundl, H., Kasner, S. E., Bangdiwala, S. I., Berkowitz, S. D., et al. (2018).
 Rivaroxaban for Stroke Prevention after Embolic Stroke of Undetermined Source *New England Journal of Medicine*, *378*(23), 2191-2201.
- Hartford, W., Lear, S., & Nimmon, L. (2019). Stroke survivors' experiences of team support along their recovery continuum *BMC Health Services Research*, *19*(1), 723-735.
- Hays, S. A., Rennaker, R. L., & Kilgard, M. P. (2013). Targeting plasticity with vagus nerve stimulation to treat neurological disease *Prog Brain Res*, 207, 275-299.
- Hayward, K. S., & Brauer, S. G. (2015). Dose of arm activity training during acute and subacute rehabilitation post stroke: a systematic review of the literature *Clin Rehabil*, *29*(12), 1234-1243.
- Hayward, K. S., Kramer, S. F., Dalton, E. J., Hughes, G. R., Brodtmann, A., Churilov, L., et al. (2021). Timing and Dose of Upper Limb Motor Intervention After Stroke: A Systematic Review *Stroke*, *52*(11), 3706-3717.
- He, F. J., Nowson, C. A., & MacGregor, G. A. (2006). Fruit and vegetable consumption and stroke: meta-analysis of cohort studies *Lancet*, *367*(9507), 320-326.
- He, K., Wu, L., Huang, Y., Chen, Q., Qiu, B., Liang, K., et al. (2022). Efficacy and Safety of Transcranial Direct Current Stimulation on Post-Stroke Dysphagia: A Systematic Review and Meta-Analysis *Journal of Clinical Medicine*, *11*(9), 2297-2314.
- Health Service Executive. (2022). *National Stroke Strategy 2022-2027 (Ireland)*. https://www.hse.ie/eng/services/publications/clinical-strategy-and-programmes/national-stroke-strategy-2022-2027.pdf
- HEART UK Medical Scientific and Research Committee. (2019). HEART UK consensus statement on Lipoprotein(a): A call to action *Atherosclerosis*, 291, 62-70.
- Heckert, K. D., Komaroff, E., Adler, U., & Barrett, A. M. (2009). Postacute Reevaluation May Prevent Dysphagia-Associated Morbidity *Stroke*, *40*(4), 1381-1385.
- Heffner, D. L., Thirumala, P. D., Pokharna, P., Chang, Y. F., & Wechsler, L. (2015). Outcomes of Spoke-Retained Telestroke Patients Versus Hub-Treated Patients After Intravenous Thrombolysis: Telestroke Patient Outcomes After Thrombolysis *Stroke; a journal of cerebral circulation*, 46(11), 3161-3167.
- Hellman, T., Bergstrom, A., Eriksson, G., Hansen Falkdal, A., & Johansson, U. (2016). Return to work after stroke: Important aspects shared and contrasted by five stakeholder groups *Work (Reading, Mass.)*, 55(4), 901-911.
- Hepworth, L. R., Rowe F. J., Walker M. F., Rockliffe J., Noonan C., Howard C., et al. (2015). Post-stroke Visual Impairment: A Systematic Literature Review of Types and Recovery of Visual Conditions *Ophthalmology Research: An International Journal*, *5*(1), 1-43.
- Higgins, P., MacFarlane, P. W., Dawson, J., McInnes, G. T., Langhorne, P., & Lees, K. R. (2013).

 Noninvasive cardiac event monitoring to detect atrial fibrillation after ischemic stroke: A randomized, controlled trial *Stroke*, *44*(9), 2525-2531.
- Hilkens, N. A., Werring, D. J., Wilson, D., Algra, A., De Kort, G. A. P., Witkamp, T. D., et al. (2018). Predicting the presence of macrovascular causes in non-traumatic intracerebral haemorrhage: The DIAGRAM prediction score *Journal of Neurology, Neurosurgery and Psychiatry*, 89(7), 674-679.
- Hindricks, G., Potpara, T., Dagres, N., Arbelo, E., Bax, J. J., Blomström-Lundqvist, C., et al. (2021). 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC *European Heart Journal*, 42(5), 373-498.
- Hinkle, J. L., Becker, K. J., Kim, J. S., Choi-Kwon, S., Saban, K. L., McNair, N., et al. (2017). Poststroke Fatigue: Emerging Evidence and Approaches to Management: A Scientific Statement for Healthcare Professionals from the American Heart Association *Stroke*, *48*(7), e159-e170.

- Hirschl, M., & Kundi, M. (2019). Safety and efficacy of direct acting oral anticoagulants and vitamin K antagonists in nonvalvular atrial fibrillation a network meta-analysis of real-world data *Vasa*, 48(2), 134-147.
- Hodson, T., Aplin, T., & Gustafsson, L. (2016). Understanding the dimensions of home for people returning home post stroke rehabilitation *British Journal of Occupational Therapy*, *79*(7), 427-433.
- Hoffmann, G., Conrad, M. O., Qiu, D., & Kamper, D. G. (2016). Contributions of voluntary activation deficits to hand weakness after stroke *Top Stroke Rehabil*, *23*(6), 384-392.
- Holliday, R. C., Ballinger, C., & Playford, E. D. (2007). Goal setting in neurological rehabilitation: patients' perspectives *Disability and Rehabilitation*, *29*(5), 389-394.
- Holmes, D. R., Reddy, V. Y., Turi, Z. G., Doshi, S. K., Sievert, H., Buchbinder, M., et al. (2009).

 Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial *Lancet*, *374*(9689), 534-542.
- Holmes, M., Rathbone, J., Littlewood, C., Rawdin, A., Stevenson, M., Stevens, J., et al. (2014). Routine echocardiography in the management of stroke and transient ischaemic attack: A systematic review and economic evaluation *Health Technology Assessment*, 18(16), 1-176.
- Homma, S., Sacco, R. L., Di Tullio, M. R., Sciacca, R. R., Mohr, J. P., & Investigators, P. F. O. i. C. S. S. (2002). Effect of medical treatment in stroke patients with patent foramen ovale: patent foramen ovale in Cryptogenic Stroke Study *Circulation*, *105*(22), 2625-2631.
- Hong, Z., Sui, M., Zhuang, Z., Liu, H., Zheng, X., Cai, C., et al. (2018). Effectiveness of Neuromuscular Electrical Stimulation on Lower Limbs of Patients With Hemiplegia After Chronic Stroke: A Systematic Review *Arch Phys Med Rehabil*, *99*(5), 1011-1022.e1011.
- Hookway, C., Gomes, F., & Weekes, C. E. (2015). Royal College of Physicians Intercollegiate Stroke Working Party evidence-based guidelines for the secondary prevention of stroke through nutritional or dietary modification *Journal of Human Nutrition & Dietetics*, 28(2), 107-125.
- Hooper, L., Summerbell, C. D., Thompson, R., Sills, D., Roberts, F. G., Moore, H., et al. (2011). Reduced or modified dietary fat for preventing cardiovascular disease *Cochrane Database of Systematic Reviews*, 7, CD002137.
- Hooper, L., Abdelhamid, A., Attreed, N. J., Campbell, W. W., Channell, A. M., Chassagne, P., et al. (2015). Clinical symptoms, signs and tests for identification of impending and current water-loss dehydration in older people *Cochrane Database of Systematic Reviews*, 4, CD009647.
- Hoover, E. L., Caplan, D. N., Waters, G. S., & Carney, A. (2017). Communication and quality of life outcomes from an interprofessional intensive, comprehensive, aphasia program (ICAP) *Top Stroke Rehabil*, 24(2), 82-90.
- House, A., Knapp, P., Bamford, J., & Vail, A. (2001). Mortality at 12 and 24 months after stroke may be associated with depressive symptoms at 1 month *Stroke*, *32*(3), 696-701.
- Howard, C., & Rowe, F. J. (2018). Adaptation to poststroke visual field loss: A systematic review *Brain* and *Behavior*, 8(8), e01041.
- Hsiao, M. Y., Choo, Y. J., Liu, I. C., Boudier-Reveret, M., & Chang, M. C. (2022). Effect of Repetitive Transcranial Magnetic Stimulation on Post-stroke Dysphagia: A Meta-analysis of Stimulation Frequency, Stimulation Site, and Timing of Outcome Measurement *Dysphagia*, 435-445.
- Hsu, C. Y., Vennelle, M., Li, H. Y., Engleman, H. M., Dennis, M. S., & Douglas, N. J. (2006). Sleep-disordered breathing after stroke: A randomised controlled trial of continuous positive airway pressure *Journal of Neurology, Neurosurgery and Psychiatry*, 77(10), 1143-1149.
- Huang, X., Cheripelli, B. K., Lloyd, S. M., Kalladka, D., Moreton, F. C., Siddiqui, A., et al. (2015). Alteplase versus tenecteplase for thrombolysis after ischaemic stroke (ATTEST): A phase 2, randomised, open-label, blinded endpoint study *The Lancet Neurology*, *14*(4), 368-376.
- Hugues, A., Di Marco, J., Ribault, S., Ardaillon, H., Janiaud, P., Xue, Y., et al. (2019). Limited evidence of physical therapy on balance after stroke: A systematic review and meta-analysis *PLoS One*, *14*(8), e0221700.
- Huo, X., Ma, G., Tong, X., Zhang, X., Pan, Y., Nguyen, T. N., et al. (2023). Trial of Endovascular Therapy for Acute Ischemic Stroke with Large Infarct *New England Journal of Medicine*, Epub ahead of print.

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-AnnualResultsPortfolio.aspx

- Hurn, J., Kneebone, I., & Cropley, M. (2006). Goal setting as an outcome measure: A systematic review *Clinical Rehabilitation*, *20*(9), 756-772.
- Ildstad, F., Ellekjaer, H., Wethal, T., Lydersen, S., Fjaertoft, H., & Indredavik, B. (2021). ABCD3-I and ABCD2 Scores in a TIA Population with Low Stroke Risk *Stroke Research and Treatment*, 2021, 8845898.
- Intercollegiate Stroke Working Party. (2016). Sentinel Stroke National Audit Programme Annual Results
 Portfolio.
 https://www.strokeaudit.org/Documents/Results/National/Apr2015Mar2016/Apr2015Mar2016
- International Carotid Stenting Study investigators. (2010). Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomised controlled trial *Lancet*, *375*(9719), 985-997.
- International Stroke Trial Collaborative Group. (2012). The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): a randomised controlled trial *Lancet*, 379(9834), 2352-2363.
- Irewall, A. L., Ögren, J., Bergström, L., Laurell, K., Söderström, L., & Mooe, T. (2019). Nurse-led, telephone-based secondary preventive follow-up benefits stroke/TIA patients with low education: a randomized controlled trial sub-study *Trials*, 20(1), 52-62.
- Ivey, F. M., Macko, R. F., Ryan, A. S., & Hafer-Macko, C. E. (2005). Cardiovascular health and fitness after stroke *Top Stroke Rehabil*, *12*(1), 1-16.
- Ivey, F. M., Ryan, A. S., Hafer-Macko, C. E., Goldberg, A. P., & Macko, R. F. (2007). Treadmill aerobic training improves glucose tolerance and indices of insulin sensitivity in disabled stroke survivors: a preliminary report *Stroke*, *38*(10), 2752-2758.
- James, A. H., Bushnell, C. D., Jamison, M. G., & Myers, E. R. (2005). Incidence and risk factors for stroke in pregnancy and the puerperium *Obstetrics & Gynecology*, *106*(3), 509-516.
- Jaspers, T., Shudofsky, K., Huisman, M. V., Meijer, K., & Khorsand, N. (2021). A meta-analysis of andexanet alfa and prothrombin complex concentrate in the treatment of factor Xa inhibitor-related major bleeding *Research and Practice in Thrombosis and Haemostasis*, *5*(4), e12518.
- Jehkonen, M., Laihosalo, M., & Kettunen, J. E. (2006). Impact of neglect on functional outcome after stroke: a review of methodological issues and recent research findings *Restorative Neurology & Neuroscience*, 24(4-6), 209-215.
- Johnson, K. G., & Johnson, D. C. (2010). Frequency of sleep apnea in stroke and TIA patients: a metaanalysis *Journal of Clinical Sleep Medicine*, 6(2), 131-137.
- Johnson, P., Rosewell, M., & James, M. A. (2007). How good is the management of vascular risk after stroke, transient ischaemic attack or carotid endarterectomy? *Cerebrovascular Diseases*, *23*(2-3), 156-161.
- Johnston, S. C., Gress, D. R., Browner, W. S., & Sidney, S. (2000). Short-term prognosis after emergency department diagnosis of TIA *JAMA*, *284*(22), 2901-2906.
- Johnston, S. C., Easton, J. D., Farrant, M., Barsan, W., Conwit, R. A., Elm, J. J., et al. (2018). Clopidogrel and Aspirin in Acute Ischemic Stroke and High-Risk TIA *New England Journal of Medicine*, *379*(3), 215-225.
- Johnston, S. C., Amarenco, P., Denison, H., Evans, S. R., Himmelmann, A., James, S., et al. (2020).

 Ticagrelor and Aspirin or Aspirin Alone in Acute Ischemic Stroke or TIA *New England Journal of Medicine*, 383(3), 207-217.
- Johnston, T. E., Keller, S., Denzer-Weiler, C., & Brown, L. (2021). A Clinical Practice Guideline for the Use of Ankle-Foot Orthoses and Functional Electrical Stimulation Post-Stroke *Journal of neurologic physical therapy : JNPT*, 45(2), 112-196.
- Jones, F., Livingstone, E., & Hawkes, L. (2013). 'Getting the balance between encouragement and taking over': reflections on using a new stroke self-management programme *Physiotherapy Research International*, 18(2), 91-99.

- Jones, F., Gage, H., Drummond, A., Bhalla, A., Grant, R., Lennon, S., et al. (2016). Feasibility study of an integrated stroke self-management programme: a cluster-randomised controlled trial *BMJ Open*, *6*(1), e008900.
- Jones, S. P., Jenkinson, A. J., Leathley, M. J., & Watkins, C. L. (2010). Stroke knowledge and awareness: an integrative review of the evidence *Age & Ageing*, *39*(1), 11-22.
- Jonsson, A. C., Lindgren, I., Norrving, B., & Lindgren, A. (2008). Weight loss after stroke: a population-based study from the Lund Stroke Register *Stroke*, *39*(3), 918-923.
- Jørgensen, H. S., Nakayama, H., Raaschou, H. O., & Olsen, T. S. (1995). Recovery of walking function in stroke patients: the Copenhagen Stroke Study *Arch Phys Med Rehabil*, *76*(1), 27-32.
- Josephson, C. B., White, P. M., Krishan, A., & Al-Shahi Salman, R. (2015). Computed tomographic angiography or magnetic resonance angiography for detection of intracranial vascular malformations in patients with intracerebral hemorrhage *Stroke*, *46*(1), e2-e3.
- Jovin, T. G., Chamorro, A., Cobo, E., de Miquel, M. A., Molina, C. A., Rovira, A., et al. (2015).

 Thrombectomy within 8 hours after symptom onset in ischemic stroke *New England Journal of Medicine*, *372*(24), 2296-2306.
- Jovin, T. G., Li, C., Wu, L., Wu, C., Chen, J., Jiang, C., et al. (2022a). Trial of Thrombectomy 6 to 24 Hours after Stroke Due to Basilar-Artery Occlusion *New England Journal of Medicine*, *387*(15), 1373-1384.
- Jovin, T. G., Nogueira, R. G., Lansberg, M. G., Demchuk, A. M., Martins, S. O., Mocco, J., et al. (2022b). Thrombectomy for anterior circulation stroke beyond 6 h from time last known well (AURORA): a systematic review and individual patient data meta-analysis *The Lancet*, *399*(10321), 249-258.
- Jüttler, E., Unterberg, A., Woitzik, J., Bosel, J., Amiri, H., Sakowitz, O. W., et al. (2014). Hemicraniectomy in older patients with extensive middle-cerebral-artery stroke *New England Journal of Medicine*, 370(12), 1091-1100.
- Kagan, A., Black, S. E., Duchan, F. J., Simmons-Mackie, N., & Square, P. (2001). Training volunteers as conversation partners using "Supported Conversation for Adults with Aphasia" (SCA): a controlled trial *Journal of Speech Language and Hearing Research Impact*, 44(3), 624-638.
- Kalbouneh, H. M., Toubasi, A. A., Albustanji, F. H., Obaid, Y. Y., & Al-Harasis, L. M. (2022). Safety and Efficacy of SSRIs in Improving Poststroke Recovery: A Systematic Review and Meta-Analysis *Journal of the American Heart Association*, 11(13), e025868.
- Kalita, J., Vajpayee, A., & Misra, U. K. (2006). Comparison of prednisolone with piroxicam in complex regional pain syndrome following stroke: a randomized controlled trial *QJM*, *99*(2), 89-95.
- Kalra, L., Irshad, S., Hodsoll, J., Simpson, M., Gulliford, M., Smithard, D., et al. (2015). Prophylactic antibiotics after acute stroke for reducing pneumonia in patients with dysphagia (STROKE-INF): a prospective, cluster-randomised, open-label, masked endpoint, controlled clinical trial *Lancet*, 386, 1835-1844.
- Kamper, D. G., Fischer, H. C., Cruz, E. G., & Rymer, W. Z. (2006). Weakness is the primary contributor to finger impairment in chronic stroke *Arch Phys Med Rehabil*, *87*(9), 1262-1269.
- Kaneko, Y., Hajek, V. E., Zivanovic, V., Raboud, J., & Bradley, T. D. (2003). Relationship of sleep apnea to functional capacity and length of hospitalization following stroke *Sleep*, *26*(3), 293-297.
- Kang, D. W., Chalela, J. A., Ezzeddine, M. A., & Warach, S. (2003). Association of ischemic lesion patterns on early diffusion-weighted imaging with TOAST stroke subtypes *Archives of Neurology & Psychiatry*, 60(12), 1730-1734.
- Katalinic, O. M., Harvey, L. A., & Herbert, R. D. (2011). Effectiveness of stretch for the treatment and prevention of contractures in people with neurological conditions: a systematic review *Physical Therapy*, *91*(1), 11-24.
- Kelly, J., Rudd, A., Lewis, R. R., Coshall, C., Moody, A., & Hunt, B. J. (2004). Venous thromboembolism after acute ischemic stroke: a prospective study using magnetic resonance direct thrombus imaging *Stroke*, *35*(10), 2320-2325.
- Kelly, P. J., Crispino, G., Sheehan, O., Kelly, L., Marnane, M., Merwick, A., et al. (2012). Incidence, event rates, and early outcome of stroke in Dublin, Ireland: the North Dublin population stroke study *Stroke*, *43*(8), 2042-2047.

- Kendall, B. J., & Gothe, N. P. (2015). Effect of Aerobic Exercise Interventions on Mobility among Stroke Patients: A Systematic Review *American Journal of Physical Medicine & Rehabilitation*, 95(3), 214-224.
- Kendall, E., Catalano, T., Kuipers, P., Posner, N., Buys, N., & Charker, J. (2007). Recovery following stroke: the role of self-management education *Social Science & Medicine*, *64*(3), 735-746.
- Kernan, W. N., Inzucchi, S. E., Viscoli, C. M., Brass, L. M., Bravata, D. M., Shulman, G. I., et al. (2003). Impaired insulin sensitivity among nondiabetic patients with a recent TIA or ischemic stroke *Neurology*, *60*(9), 1447-1451.
- Kernan, W. N., Viscoli, C. M., Furie, K. L., Young, L. H., Inzucchi, S. E., Gorman, M., et al. (2016). Pioglitazone after Ischemic Stroke or Transient Ischemic Attack New England Journal of Medicine, 374(14), 1321-1331.
- Kerry, S. M., Markus, H. S., Khong, T. K., Cloud, G. C., Tulloch, J., Coster, D., et al. (2013). Home blood pressure monitoring with nurse-led telephone support among patients with hypertension and a history of stroke: a community-based randomized controlled trial *Cmaj*, 185(1), 23-31.
- Kertscher, B., Speyer, R., Palmieri, M., & Plant, C. (2014). Bedside screening to detect oropharyngeal dysphagia in patients with neurological disorders: an updated systematic review *Dysphagia*, 29(2), 204-212.
- Kim, B. J., Lee, S. H., Ryu, W. S., Kim, C. K., Lee, J., & Yoon, B. W. (2011a). Paradoxical longevity in obese patients with intracerebral hemorrhage *Neurology*, *76*(6), 567-573.
- Kim, B. R., Lim, J. H., Lee, S. A., Park, S., Koh, S. E., Lee, I. S., et al. (2011b). Usefulness of the Scale for the Assessment and Rating of Ataxia (SARA) in Ataxic Stroke Patients *Ann Rehabil Med*, *35*(6), 772-780.
- Kim, M., Cho, K., & Lee, W. (2014). Community walking training program improves walking function and social participation in chronic stroke patients *Tohoku Journal of Experimental Medicine*, 234(4), 281-286.
- King, J. M., & Gallegos-Santillan, P. (1999). Strategy use by speakers with dysarthria and both familiar and unfamiliar conversational partners *Journal of Medical Speech-Language Pathology*, 7(2), 113-116.
- Kishore, A., Vail, A., Majid, A., Dawson, J., Lees, K. R., Tyrrell, P. J., et al. (2014). Detection of atrial fibrillation after ischemic stroke or transient ischemic attack: a systematic review and meta-analysis *Stroke*, *45*(2), 520-526.
- Kitagawa, K., Yamamoto, Y., Arima, H., Maeda, T., Sunami, N., Kanzawa, T., et al. (2019). Effect of Standard vs Intensive Blood Pressure Control on the Risk of Recurrent Stroke: A Randomized Clinical Trial and Meta-analysis *JAMA Neurology*, *76*(11), 1309-1318.
- Klassen, T. D., Dukelow, S. P., Bayley, M. T., Benavente, O., Hill, M. D., Krassioukov, A., et al. (2020). Higher Doses Improve Walking Recovery During Stroke Inpatient Rehabilitation *Stroke*, *51*(9), 2639-2648.
- Klijn, C. J., Paciaroni, M., Berge, E., Korompoki, E., Kõrv, J., Lal, A., et al. (2019). Antithrombotic treatment for secondary prevention of stroke and other thromboembolic events in patients with stroke or transient ischemic attack and non-valvular atrial fibrillation: A European Stroke Organisation guideline *Eur Stroke J*, 4(3), 198-223.
- Knapp, P., Campbell Burton, C. A., Holmes, J., Murray, J., Gillespie, D., Lightbody, C. E., et al. (2017). Interventions for treating anxiety after stroke *Cochrane Database Syst Rev*, *5*(5), Cd008860.
- Knapp, P., Dunn-Roberts, A., Sahib, N., Cook, L., Astin, F., Kontou, E., et al. (2020). Frequency of anxiety after stroke: An updated systematic review and meta-analysis of observational studies *Int J Stroke*, *15*(3), 244-255.
- Knowler, W. C., Barrett-Connor, E., Fowler, S. E., Hamman, R. F., Lachin, J. M., Walker, E. A., et al. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin *New England Journal of Medicine*, *346*(6), 393-403.
- Ko, D., Dai, Q., Flynn, D. B., Bosch, N. A., Helm, R. H., Monahan, K. M., et al. (2022). Meta-Analysis of Randomized Clinical Trials Comparing the Impact of Implantable Loop Recorder Versus Usual Care After Ischemic Stroke for Detection of Atrial Fibrillation and Stroke Risk Am J Cardiol, 162, 100-104.

- Koga, M., Inoue, M., Yoshimura, S., Miwa, K., Toyoda, K., Yamamoto, H., et al. (2020). Thrombolysis with Alteplase at 0.6 mg/kg for Stroke with Unknown Time of Onset: A Randomized Controlled Trial *Stroke*, *51*(5), 1530-1538.
- Koh, K. T., Law, W. C., Zaw, W. M., Foo, D. H. P., Tan, C. T., Steven, A., et al. (2021). Smartphone electrocardiogram for detecting atrial fibrillation after a cerebral ischaemic event: a multicentre randomized controlled trial *EP Europace*, *23*(7), 1016-1023.
- Kolominsky-Rabas, P. L., Weber, M., Gefeller, O., Neundoerfer, B., & Heuschmann, P. U. (2001). Epidemiology of ischemic stroke subtypes according to TOAST criteria: incidence, recurrence, and long-term survival in ischemic stroke subtypes: a population-based study *Stroke*, *32*(12), 2735-2740.
- Korner-Bitensky, N., Audet, T., Man-Son-Hing, M., Benoit, D., Kaizer, F., & Gelinas, I. (2011). Test-retest reliability of the preroad DriveABLE competence screen *Physical and Occupational Therapy in Geriatrics*, 29(3), 202-212.
- Korpelainen, J. T., Nieminen, P., & Myllyla, V. V. (1999). Sexual functioning among stroke patients and their spouses *Stroke*, *30*(4), 715-719.
- Korpershoek, C., van der Bijl, J., & Hafsteinsdottir, T. B. (2011). Self-efficacy and its influence on recovery of patients with stroke: a systematic review *Journal of Advanced Nursing*, *67*(9), 1876-1894.
- Krakauer, J. W. (2006). Motor learning: its relevance to stroke recovery and neurorehabilitation *Curr Opin Neurol*, 19(1), 84-90.
- Kramer, S., Johnson, L., Bernhardt, J., & Cumming, T. (2016). Energy Expenditure and Cost During Walking After Stroke: A Systematic Review *Arch Phys Med Rehabil*, *97*(4), 619-632.e611.
- Kristensen, M. G. H., Busk, H., & Wienecke, T. (2022). Neuromuscular Electrical Stimulation Improves Activities of Daily Living Post Stroke: A Systematic Review and Meta-analysis *Arch Rehabil Res Clin Transl*, 4(1), 42-57.
- Kristensen, O. H., Stenager, E., & Dalgas, U. (2017). Muscle Strength and Poststroke Hemiplegia: A Systematic Review of Muscle Strength Assessment and Muscle Strength Impairment *Arch Phys Med Rehabil*, *98*(2), 368-380.
- Kumar, P., Fernando, C., Mendoza, D., & Shah, R. (2022). Risk and associated factors for hemiplegic shoulder pain in people with stroke: a systematic literature review *Physical Therapy Reviews*, 27(3), 191-204.
- Kunkel, D., Fitton, C., Burnett, M., & Ashburn, A. (2015). Physical inactivity post-stroke: a 3-year longitudinal study *Disabil Rehabil*, *37*(4), 304-310.
- Kurl, S., Laukkanen, J. A., Rauramaa, R., Lakka, T. A., Sivenius, J., & Salonen, J. T. (2003). Cardiorespiratory fitness and the risk for stroke in men *Arch Intern Med*, *163*(14), 1682-1688.
- Kuys, S. S., Brauer, S. G., & Ada, L. (2011). Higher-intensity treadmill walking during rehabilitation after stroke in feasible and not detrimental to walking pattern or quality: a pilot randomized trial *Clin Rehabil*, 25(4), 316-326.
- Kvistad, C. E., Naess, H., Helleberg, B. H., Idicula, T., Hagberg, G., Nordby, L. M., et al. (2022).

 Tenecteplase versus alteplase for the management of acute ischaemic stroke in Norway (NORTEST 2, part A): a phase 3, randomised, open-label, blinded endpoint, non-inferiority trial *The Lancet Neurology*, 21(6), 511-519.
- Kwakkel, G., Wagenaar, R. C., Twisk, J. W., Lankhorst, G. J., & Koetsier, J. C. (1999). Intensity of leg and arm training after primary middle-cerebral-artery stroke: a randomised trial *Lancet*, *354*(9174), 191-196.
- Kwakkel, G., & Wagenaar, R. C. (2002). Effect of duration of upper and lower-extremity rehabilitation sessions and walking speed on recovery of interlimb coordination in hemiplegic gait *Physical Therapy Journal*, 82(5), 432-448.
- Kwakkel, G., van Peppen, R., Wagenaar, R. C., Wood Dauphinee, S., Richards, C., Ashburn, A., et al. (2004). Effects of augmented exercise therapy time after stroke: a meta-analysis *Stroke*, *35*(11), 2529-2539.
- Kwakkel, G., Veerbeek, J. M., van Wegen, E. E., & Wolf, S. L. (2015). Constraint-induced movement therapy after stroke *Lancet Neurol*, *14*(2), 224-234.

- Labovitz, A. J., Rose, D. Z., Fradley, M. G., Meriwether, J. N., Renati, S., Martin, R., et al. (2021). Early Apixaban Use Following Stroke in Patients With Atrial Fibrillation: Results of the AREST Trial *Stroke*, *52*(4), 1164-1171.
- Lakse, E., Gunduz, B., Erhan, B., & Celik, E. C. (2009). The effect of local injections in hemiplegic shoulder pain: a prospective, randomized, controlled study *American Journal of Physical Medicine & Rehabilitation*, 88(10), 805-811.
- Lanctot, K. L., Lindsay, M. P., Smith, E. E., Sahlas, D. J., Foley, N., Gubitz, G., et al. (2020). Canadian Stroke Best Practice Recommendations: Mood, Cognition and Fatigue following Stroke, 6th edition update 2019 *International Journal of Stroke*, 15(6), 668-688.
- Lang, C. E., Macdonald, J. R., Reisman, D. S., Boyd, L., Jacobson Kimberley, T., Schindler-Ivens, S. M., et al. (2009). Observation of amounts of movement practice provided during stroke rehabilitation *Arch Phys Med Rehabil*, *90*(10), 1692-1698.
- Langezaal, L. C. M., Van Der Hoeven, E. J. R. J., Mont'Alverne, F. J. A., De Carvalho, J. J. F., Lima, F. O., Dippel, D. W. J., et al. (2021). Endovascular therapy for stroke due to basilar-artery occlusion *New England Journal of Medicine*, *384*(20), 1910-1920.
- Langhorne, P., Wagenaar, R., & Partridge, C. (1996). Physiotherapy after stroke: more is better? *Physiotherapy Research International*, 1(2), 75-88.
- Langhorne, P., Baylan, S., & Trialists, E. S. D. (2017). Early supported discharge services for people with acute stroke *Cochrane Database of Systematic Reviews*, 2017(7), CD000443.
- Langstaff, C., Martin, C., Brown, G., McGuinness, D., Mather, J., Loshaw, J., et al. (2014). Enhancing community-based rehabilitation for stroke survivors: Creating a discharge link *Topics in Stroke Rehabilitation*, 21(6), 510-519.
- Lannin, N. A., Novak, I., & Cusick, A. (2007). A systematic review of upper extremity casting for children and adults with central nervous system motor disorders *Clinical Rehabilitation*, *21*(11), 963-976.
- Lavallee, P. C., Meseguer, E., Abboud, H., Cabrejo, L., Olivot, J. M., Simon, O., et al. (2007). A transient ischaemic attack clinic with round-the-clock access (SOS-TIA): feasibility and effects *Lancet Neurology*, *6*(11), 953-960.
- Laver, K. E., Lange, B., George, S., Deutsch, J. E., Saposnik, G., & Crotty, M. (2017). Virtual reality for stroke rehabilitation *Cochrane Database of Systematic Reviews*, *11*(11), CD008349.
- Laver, K. E., Adey-Wakeling, Z., Crotty, M., Lannin, N. A., George, S., & Sherrington, C. (2020). Telerehabilitation services for stroke *Cochrane Database of Systematic Reviews*, 2020(1), CD010255.
- Lavoie, M., Macoir, J., & Bier, N. (2017). Effectiveness of technologies in the treatment of post-stroke anomia: A systematic review *Journal of Communication Disorders*, 65, 43-53.
- LeCouffe, N. E., Kappelhof, M., Treurniet, K. M., Rinkel, L. A., Bruggeman, A. E., Berkhemer, O. A., et al. (2021). A Randomized Trial of Intravenous Alteplase before Endovascular Treatment for Stroke *N Engl J Med*, *385*(20), 1833-1844.
- Lecouturier, J., Murtagh, M. J., Thomson, R. G., Ford, G., White, M., & Rodgers, H. (2010a). Response to symptoms of stroke in the UK: a systematic review *BMC Health Services Research*, 10(157).
- Lecouturier, J., Rodgers, H., Murtagh, M. J., White, M., Ford, G., & Thomson, R. G. (2010b). Systematic review of mass media interventions designed to improve public recognition of stroke symptoms, emergency response and early treatment *BMC Public Health*, *10*(784).
- Lee, J., & Stone, A. J. (2020). Combined Aerobic and Resistance Training for Cardiorespiratory Fitness, Muscle Strength, and Walking Capacity after Stroke: A Systematic Review and Meta-Analysis *Journal of Stroke and Cerebrovascular Diseases*, 29(1), 104498.
- Lee, J. H., Baker, L. L., Johnson, R. E., & Tilson, J. K. (2017). Effectiveness of neuromuscular electrical stimulation for management of shoulder subluxation post-stroke: a systematic review with meta-analysis *Clin Rehabil*, *31*(11), 1431-1444.
- Lee, M., Cheng, C. Y., Wu, Y. L., Lee, J. D., Hsu, C. Y., & Ovbiagele, B. (2022). Association Between Intensity of Low-Density Lipoprotein Cholesterol Reduction With Statin-Based Therapies and Secondary Stroke Prevention: A Meta-analysis of Randomized Clinical Trials *JAMA Neurol*, 79(4), 349-358.

- Lee, P. H., Song, J. K., Kim, J. S., Heo, R., Lee, S., Kim, D. H., et al. (2018). Cryptogenic Stroke and High-Risk Patent Foramen Ovale: The DEFENSE-PFO Trial *J Am Coll Cardiol*, *71*(20), 2335-2342.
- Leff, A. P., Nightingale, S., Gooding, B., Rutter, J., Craven, N., Peart, M., et al. (2021). Clinical Effectiveness of the Queen Square Intensive Comprehensive Aphasia Service for Patients with Poststroke Aphasia Stroke, 504-598.
- Legg, L., Langhorne, P., & Outpatient Service, T. (2004). Rehabilitation therapy services for stroke patients living at home: systematic review of randomised trials *Lancet*, *363*(9406), 352-356.
- Legg, L. A., Drummond, A. E., & Langhorne, P. (2006). Occupational therapy for patients with problems in activities of daily living after stroke *Cochrane Database of Systematic Reviews*(4), CD003585.
- Legg, L. A., Quinn, T. J., Mahmood, F., Weir, C. J., Tierney, J., Stott, D. J., et al. (2011). Non-pharmacological interventions for caregivers of stroke survivors *Cochrane Database of Systematic Reviews*(10), CD008179.
- Legg, L. A., Tilney, R., Hsieh, C. F., Wu, S., Lundström, E., Rudberg, A. S., et al. (2019). Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery *Cochrane Database Syst Rev*, *2019*(11).
- Lennon, O., Galvin, R., Smith, K., Doody, C., & Blake, C. (2014). Lifestyle interventions for secondary disease prevention in stroke and transient ischaemic attack: a systematic review *European Journal of Preventative Cardiology*, *21*(8), 1026-1039.
- Lennon, S., McKenna, S., & Jones, F. (2013). Self-management programmes for people post stroke: a systematic review *Clinical Rehabilitation*, *27*(10), 867-878.
- Leurent, C., Goodman, J. A., Zhang, Y., He, P., Lindsay, M., Frattura, L., et al. (2019). Immunotherapy with ponezumab for probable cerebral amyloid angiopathy *Annals of Clinical and Translational Neurology*, *6*(4), 795-806.
- Levack, W. M., Taylor, K., Siegert, R. J., Dean, S. G., McPherson, K. M., & Weatherall, M. (2006). Is goal planning in rehabilitation effective? A systematic review *Clinical Rehabilitation*, 20(9), 739-755.
- Levack, W. M., Weatherall, M., Hay-Smith, E. J., Dean, S. G., McPherson, K., & Siegert, R. J. (2015). Goal setting and strategies to enhance goal pursuit for adults with acquired disability participating in rehabilitation *Cochrane Database of Systematic Reviews*(7), CD009727.
- Levine, B., Schweizer, T. A., O'Connor, C., Turner, G., Gillingham, S., Stuss, D. T., et al. (2011).

 Rehabilitation of executive functioning in patients with frontal lobe brain damage with goal management training *Frontiers in Human Neuroscience*, *17*(5), 1-9.
- Levine, S. R., Brey, R. L., Tilley, B. C., Thompson, J. L., Sacco, R. L., Sciacca, R. R., et al. (2004).

 Antiphospholipid antibodies and subsequent thrombo-occlusive events in patients with ischemic stroke *JAMA*, *291*(5), 576-584.
- Li, L., Huang, H., Jia, Y., Liu, Z., Shi, X., Wang, F., et al. (2021a). Systematic review and network metaanalysis of noninvasive brain stimulation on dysphagia after stroke *Neural Plasticity*, 2021, 3831472.
- Li, L., Poon, M. T. C., Samarasekera, N. E., Perry, L. A., Moullaali, T. J., Rodrigues, M. A., et al. (2021b). Risks of recurrent stroke and all serious vascular events after spontaneous intracerebral haemorrhage: pooled analyses of two population-based studies *The Lancet Neurology*, 20(6), 437-447.
- Lidegaard, O., Lokkegaard, E., Jensen, A., Skovlund, C. W., & Keiding, N. (2012). Thrombotic stroke and myocardial infarction with hormonal contraception *New England Journal of Medicine*, *366*(24), 2257-2266.
- Liebeskind, D. S., Cotsonis, G. A., Saver, J. L., Lynn, M. J., Turan, T. N., Cloft, H. J., et al. (2011). Collaterals dramatically alter stroke risk in intracranial atherosclerosis *Annals of Neurology*, *69*(6), 963-974.
- Lim, S. F., & Childs, C. (2013). A systematic review of the effectiveness of bowel management strategies for constipation in adults with stroke *International Journal of Nursing Studies*, *50*(7), 1004-1010.
- Lin, H., Liu, H., Dai, Y., Yin, X., Li, Z., Yang, L., et al. (2022). Effect of Physical Activity on Cognitive Impairment in Patients With Cerebrovascular Diseases: A Systematic Review and Meta-Analysis *Frontiers in Neurology*, *13*, Article number 854158.
- Lin, I. H., Tsai, H.-T., Wang, C.-Y., Hsu, C.-Y., Liou, T.-H., & Lin, Y.-N. (2019). Effectiveness and Superiority of Rehabilitative Treatments in Enhancing Motor Recovery Within 6 Months Poststroke: A Systemic Review *Archives of Physical Medicine and Rehabilitation*, 100(2), 366-378.

- Lincoln, N. B., Parry, R. H., & Vass, C. D. (1999). Randomized, controlled trial to evaluate increased intensity of physiotherapy treatment of arm function after stroke *Stroke*, *30*(3), 573-579.
- Lindstrom, J., Ilanne-Parikka, P., Peltonen, M., Aunola, S., Eriksson, J. G., Hemio, K., et al. (2006).

 Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study *Lancet*, *368*(9548), 1673-1679.
- Linn, J., Halpin, A., Demaerel, P., Ruhland, J., Giese, A. D., Dichgans, M., et al. (2010). Prevalence of superficial siderosis in patients with cerebral amyloid angiopathy *Neurology*, *74*(17), 1346-1350.
- Little, S. H., & Massel, D. R. (2003). Antiplatelet and anticoagulation for patients with prosthetic heart valves *Cochrane Database of Systematic Reviews*(4), CD003464.
- Liu, J., & Chen, Q. (2015). Effect of statins treatment for patients with aneurysmalsubarachnoid hemorrhage: A systematic review andmeta-analysis of observational studies and randomized controlled trials *International Journal of Clinical and Experimental Medicine*, 8(5), 7198-7208.
- Liu, J., & Wang, L. N. (2015). Peroxisome proliferator-activated receptor gamma agonists for preventing recurrent stroke and other vascular events in patients with stroke or transient ischaemic attack *Cochrane Database of Systematic Reviews*, *10*, CD010693.
- Liu, K. P. Y., Balderi, K., Leung, T. L. F., Yue, A. S. Y., Lam, N. C. W., Cheung, J. T. Y., et al. (2016). A randomized controlled trial of self-regulated modified constraint-induced movement therapy in sub-acute stroke patients *European Journal of Neurology*, *23*(8), 1351-1360.
- Liu, K. P. Y., Hanly, J., Fahey, P., Fong, S. S. M., & Bye, R. (2019). A Systematic Review and Meta-Analysis of Rehabilitative Interventions for Unilateral Spatial Neglect and Hemianopia Poststroke From 2006 Through 2016 Archives of Physical Medicine and Rehabilitation, 100(5), 956-979.
- Liu, X., Dai, Q., Ye, R., Zi, W., Liu, Y., Wang, H., et al. (2020). Endovascular treatment versus standard medical treatment for vertebrobasilar artery occlusion (BEST): an open-label, randomised controlled trial *Lancet Neurol*, *19*(2), 115-122.
- Lloyd, M., Skelton, D. A., Mead, G. E., Williams, B., & van Wijck, F. (2018). Physical fitness interventions for nonambulatory stroke survivors: A mixed-methods systematic review and meta-analysis *Brain and Behavior*, 8(7), e01000.
- Loetscher, T., & Lincoln, N. B. (2013). Cognitive rehabilitation for attention deficits following stroke *The Cochrane Database of Systematic Reviews*, *5*, CD002842.
- Logallo, N., Novotny, V., Assmus, J., Kvistad, C. E., Alteheld, L., Ronning, O. M., et al. (2017).

 Tenecteplase versus alteplase for management of acute ischaemic stroke (NOR-TEST): a phase 3, randomised, open-label, blinded endpoint trial *The Lancet Neurology*, *16*(10), 781-788.
- Logan, P. A., Armstrong, S., Avery, T. J., Barer, D., Barton, G. R., Darby, J., et al. (2014). Rehabilitation aimed at improving outdoor mobility for people after stroke: a multicentre randomised controlled study (the Getting out of the House Study) *Health Technology Assessment*, 18(29), viiviii, 1-113.
- Loh, M. S., Kuan, Y. C., Wu, C. W., Liao, C. D., Hong, J. P., & Chen, H. C. (2022). Upper Extremity Contralaterally Controlled Functional Electrical Stimulation Versus Neuromuscular Electrical Stimulation in Post-Stroke Individuals: A Meta-Analysis of Randomized Controlled Trials Neurorehabil Neural Repair, 36(7), 472-482.
- Lohse, K. R., Lang, C. E., & Boyd, L. A. (2014). Is more better? Using metadata to explore dose-response relationships in stroke rehabilitation *Stroke*, *45*(7), 2053-2058.
- Loke, Y. K., Brown, J. W., Kwok, C. S., Niruban, A., & Myint, P. K. (2012). Association of obstructive sleep apnea with risk of serious cardiovascular events: a systematic review and meta-analysis *Circulation*, *5*(5), 720-728.
- Lorberboym, M., Mena, I., Wainstein, J., Boaz, M., & Lampl, Y. (2010). The effect of sildenafil citrate (Viagra) on cerebral blood flow in patients with cerebrovascular risk factors *Acta Neurologica Scandinavica*, 121(6), 370-376.
- Luker, J., Lynch, E., Bernhardsson, S., Bennett, L., & Bernhardt, J. (2015). Stroke Survivors' Experiences of Physical Rehabilitation: A Systematic Review of Qualitative Studies *Arch Phys Med Rehabil*, *96*(9), 1698-1708.e1610.

- Lundström, E., Isaksson, E., Näsman, P., Wester, P., Mårtensson, B., Norrving, B., et al. (2020). Safety and efficacy of fluoxetine on functional recovery after acute stroke (EFFECTS): a randomised, double-blind, placebo-controlled trial *The Lancet Neurology*, 19(8), 661-669.
- Luo, L., Meng, H., Wang, Z., Zhu, S., Yuan, S., Wang, Y., et al. (2020). Effect of high-intensity exercise on cardiorespiratory fitness in stroke survivors: A systematic review and meta-analysis *Annals of Physical and Rehabilitation Medicine*, *63*(1), 59-68.
- Lynch, J., Mead, G., Greig, C., Young, A., Lewis, S., & Sharpe, M. (2007). Fatigue after stroke: the development and evaluation of a case definition *J Psychosom Res*, *63*(5), 539-544.
- Ma, H., Campbell, B. C. V., Parsons, M. W., Churilov, L., Levi, C. R., Hsu, C., et al. (2019). Thrombolysis Guided by Perfusion Imaging up to 9 Hours after Onset of Stroke *New England Journal of Medicine*, *380*(19), 1795-1803.
- Maasland, L., Koudstaal, P. J., Habbema, J. D., & Dippel, D. W. (2007). Knowledge and understanding of disease process, risk factors and treatment modalities in patients with a recent TIA or minor ischemic stroke *Cerebrovascular Diseases*, *23*(5-6), 435-440.
- Machado, N., Wingfield, M., Kramer, S., Olver, J., Williams, G., & Johnson, L. (2022). Maintenance of Cardiorespiratory Fitness in People With Stroke: A Systematic Review and Meta-analysis *Arch Phys Med Rehabil*, 103(7), 1410-1421.e1416.
- MacKay-Lyons, M., Billinger, S. A., Eng, J. J., Dromerick, A., Giacomantonio, N., Hafer-Macko, C., et al. (2020). Aerobic Exercise Recommendations to Optimize Best Practices in Care After Stroke: AEROBICS 2019 Update *Physical Therapy*, 100(1), 149-156.
- Mackenzie, C., & Lowit, A. (2007). Behavioural intervention effects in dysarthria following stroke: communication effectiveness, intelligibility and dysarthria impact *International Journal of Language & Communication Disorders*, 42(2), 131-153.
- Mackenzie, C., Muir, M., Allen, C., & Jensen, A. (2014). Non-speech oro-motor exercises in post-stroke dysarthria intervention: a randomized feasibility trial *International Journal of Language & Communication Disorders*, 49(5), 602-617.
- Mahmood, A., Deshmukh, A., Natarajan, M., Marsden, D., Vyslysel, G., Padickaparambil, S., et al. (2022a). Development of strategies to support home-based exercise adherence after stroke: a Delphi consensus *BMJ Open*, *12*(1), e055946.
- Mahmood, A., Nayak, P., English, C., Deshmukh, A., U, S., N, M., et al. (2022b). Adherence to home exercises and rehabilitation (ADHERE) after stroke in low-to-middle-income countries: A randomized controlled trial *Topics in Stroke Rehabilitation*, 29(6), 438-448.
- Mahoney, C., Rowat, A., Macmillan, M., & Dennis, M. (2015). Nasogastric feeding for stroke patients: practice and education *British Journal of Nursing*, *24*(6), 319-320, 322-315.
- Majumdar, S., & Morris, R. (2019). Brief group-based acceptance and commitment therapy for stroke survivors *The British journal of clinical psychology*, *58*(1), 70-90.
- Makam, R. C. P., Hoaglin, D. C., McManus, D. D., Wang, V., Gore, J. M., Spencer, F. A., et al. (2018). Efficacy and safety of direct oral anticoagulants approved for cardiovascular indications: Systematic review and meta-analysis *PLoS One*, *13*(5), e0197583.
- Malec, J. F., Smigielski, J. S., & DePompolo, R. W. (1991). Goal attainment scaling and outcome measurement in postacute brain injury rehabilitation *Archives of Physical Medicine and Rehabilitation*, 72(2), 138-143.
- Man-Son-Hing, M., Nichol, G., Lau, A., & Laupacis, A. (1999). Choosing antithrombotic therapy for elderly patients with atrial fibrillation who are at risk for falls *Archives of Internal Medicine*, *159*(7), 677-685.
- Mancuso, M., Arnold, M., Bersano, A., Burlina, A., Chabriat, H., Debette, S., et al. (2020). Monogenic cerebral small-vessel diseases: diagnosis and therapy. Consensus recommendations of the European Academy of Neurology *Eur J Neurol*, *27*(6), 909-927.
- Manigandan, J. B., Ganesh, G. S., Pattnaik, M., & Mohanty, P. (2014). Effect of electrical stimulation to long head of biceps in reducing gleno humeral subluxation after stroke *NeuroRehabilitation*, 34(2), 245-252.
- Mann, G., Hankey, G. J., & Cameron, D. (1999). Swallowing function after stroke: prognosis and prognostic factors at 6 months *Stroke*, *30*(4), 744-748.

- Mant, J., Hobbs, F. D., Fletcher, K., Roalfe, A., Fitzmaurice, D., Lip, G. Y., et al. (2007). Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial *Lancet*, *370*(9586), 493-503.
- Mant, J., McManus, R. J., Roalfe, A., Fletcher, K., Taylor, C. J., Martin, U., et al. (2016). Different systolic blood pressure targets for people with history of stroke or transient ischaemic attack: PAST-BP (Prevention After Stroke--Blood Pressure) randomised controlled trial *BMJ*, 352, i708.
- Marik, P. E., & Varon, J. (2009). Omega-3 dietary supplements and the risk of cardiovascular events: a systematic review *Clin Cardiol*, *32*(7), 365-372.
- Marin, J. M., Agusti, A., Villar, I., Forner, M., Nieto, D., Carrizo, S. J., et al. (2012). Association between treated and untreated obstructive sleep apnea and risk of hypertension *JAMA*, *307*(20), 2169-2176.
- Markus, H. S., Harshfield, E. L., Compter, A., Kuker, W., Kappelle, L. J., Clifton, A., et al. (2019). Stenting for symptomatic vertebral artery stenosis: a preplanned pooled individual patient data analysis *Lancet Neurol*, *18*(7), 666-673.
- Marquardt, L., Kuker, W., Chandratheva, A., Geraghty, O., & Rothwell, P. M. (2009). Incidence and prognosis of > or = 50% symptomatic vertebral or basilar artery stenosis: prospective population-based study *Brain*, *132*(Pt 4), 982-988.
- Marquer, A., Barbieri, G., & Perennou, D. (2014). The assessment and treatment of postural disorders in cerebellar ataxia: A systematic review *Annals of Physical and Rehabilitation Medicine*, *57*(2), 67-78
- Marsden, D. L., Dunn, A., Callister, R., Levi, C. R., & Spratt, N. J. (2013). Characteristics of exercise training interventions to improve cardiorespiratory fitness after stroke: a systematic review with meta-analysis *Neurorehabilitation & Neural Repair*, 27(9), 775-788.
- Marti-Carvajal, A. J., Sola, I., & Lathyris, D. (2015). Homocysteine-lowering interventions for preventing cardiovascular events *Cochrane Database of Systematic Reviews*, *1*, CD006612.
- Martí-Fàbregas, J., Medrano-Martorell, S., Merino, E., Prats-Sánchez, L., Marín, R., Delgado-Mederos, R., et al. (2019). MRI predicts intracranial hemorrhage in patients who receive long-term oral anticoagulation *Neurology*, *92*(21), e2432-e2443.
- Martinez-Garcia, M. A., Campos-Rodriguez, F., Soler-Cataluna, J. J., Catalan-Serra, P., Roman-Sanchez, P., & Montserrat, J. M. (2012). Increased incidence of nonfatal cardiovascular events in stroke patients with sleep apnoea: effect of CPAP treatment *European Respiratory Journal*, *39*(4), 906-912.
- Martino, R., Foley, N., Bhogal, S., Diamant, N., Speechley, M., & Teasell, R. (2005). Dysphagia after stroke: incidence, diagnosis, and pulmonary complications *Stroke*, *36*(12), 2756-2763.
- Martino, R., Maki, E., & Diamant, N. (2014). Identification of dysphagia using the Toronto Bedside Swallowing Screening Test (TOR-BSST©): are 10 teaspoons of water necessary? *International Journal of Speech-Language Pathology*, 16(3), 193-198.
- Mas, J.-L., Derumeaux, G., Guillon, B., Massardier, E., Hosseini, H., Mechtouff, L., et al. (2017). Patent Foramen Ovale Closure or Anticoagulation vs. Antiplatelets after Stroke *New England Journal of Medicine*, 377(11), 1011-1021.
- Matérne, M., Strandberg, T., & Lundqvist, L.-O. (2018). Change in quality of life in relation to returning to work after acquired brain injury: a population-based register study *Brain Injury*, *32*, 1-9.
- Maurice, A., Eugene, F., Ronziere, T., Devys, J.-M., Taylor, G., Subileau, A., et al. (2022). General Anesthesia versus Sedation, Both with Hemodynamic Control, during Intraarterial Treatment for Stroke: The GASS Randomized Trial *Anesthesiology*, *136*(4), 567-576.
- Mayo, N. E., Wood-Dauphinee, S., Ahmed, S., Gordon, C., Higgins, J., McEwen, S., et al. (1999). Disablement following stroke *Disabil Rehabil*, *21*(5-6), 258-268.
- Mazighi, M., Labreuche, J., Gongora-Rivera, F., Duyckaerts, C., Hauw, J. J., & Amarenco, P. (2008). Autopsy prevalence of intracranial atherosclerosis in patients with fatal stroke *Stroke*, *39*(4), 1142-1147.

- McCabe, D. J., & Rakhit, R. D. (2007). Antithrombotic and interventional treatment options in cardioembolic transient ischaemic attack and ischaemic stroke *J Neurol Neurosurg Psychiatry*, 78(1), 14-24.
- McCabe, J., Monkiewicz, M., Holcomb, J., Pundik, S., & Daly, J. J. (2015). Comparison of robotics, functional electrical stimulation, and motor learning methods for treatment of persistent upper extremity dysfunction after stroke: a randomized controlled trial *Arch Phys Med Rehabil*, *96*(6), 981-990.
- McCrory, P., Turner, S. L., Baguley, I. J., De, G. S., Katrak, P., Sandanam, J., et al. (2009). Botulinum toxin A for treatment of upper limb spasticity following stroke: a multi-centre randomized placebocontrolled study of the effects on quality of life and other person-centred outcomes *Journal of Rehabilitation Medicine*, *41*(7), 536-544.
- McKevitt, C., Fudge, N., Redfern, J., Sheldenkar, A., Crichton, S., Rudd, A. R., et al. (2011). Self-reported long-term needs after stroke *Stroke*, *42*(5), 1398-1403.
- Mead, G., Lynch, J., Greig, C., Young, A., Lewis, S., & Sharpe, M. (2007). Evaluation of fatigue scales in stroke patients *Stroke*, *38*(7), 2090-2095.
- Mead, G. E., Hsieh, C. F., Lee, R., Kutlubaev, M. A., Claxton, A., Hankey, G. J., et al. (2012). Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery *Cochrane Database of Systematic Reviews*, *11*, CD009286.
- Mead, G. E., Legg, L., Tilney, R., Hsieh, C. F., Wu, S., Lundström, E., et al. (2019). Fluoxetine for stroke recovery: Meta-analysis of randomized controlled trials *International Journal of Stroke*, *15*(4), 365-376
- Meek, C., Pollock, A., Potter, J., & Langhorne, P. (2003). A systematic review of exercise trials post stroke *Clinical Rehabilitation*, *17*(1), 6-13.
- Mees, S. M. D., Algra, A., Vandertop, W. P., Van Kooten, F., Kuijsten, H. A. J. M., Boiten, J., et al. (2012). Magnesium for aneurysmal subarachnoid haemorrhage (MASH-2): A randomised placebocontrolled trial *Lancet*, *379*(9836), 44-49.
- Mehrholz, J., Thomas, S., & Elsner, B. (2017). Treadmill training and body weight support for walking after stroke *Cochrane Database of Systematic Reviews*, 8, CD002840.
- Mehrholz, J., Pohl, M., Platz, T., Kugler, J., & Elsner, B. (2018). Electromechanical and robot-assisted arm training for improving activities of daily living, arm function, and arm muscle strength after stroke *Cochrane Database of Systematic Reviews*, 2018(9), CD006876.
- Mehrholz, J., Thomas, S., Kugler, J., Pohl, M., & Elsner, B. (2020). Electromechanical-assisted training for walking after stroke *Cochrane Database Syst Rev*, *10*(10), Cd006185.
- Meier, B., Kalesan, B., Mattle, H. P., Khattab, A. A., Hildick-Smith, D., Dudek, D., et al. (2013).

 Percutaneous closure of patent foramen ovale in cryptogenic embolism *New England Journal of Medicine*, 368(12), 1083-1091.
- Melnik, T., Soares, B. G., & Nasselo, A. G. (2007). Psychosocial interventions for erectile dysfunction Cochrane Database of Systematic Reviews(3), CD004825.
- Mendelow, A. D., Gregson, B. A., Rowan, E. N., Murray, G. D., Gholkar, A., Mitchell, P. M., et al. (2013). Early surgery versus initial conservative treatment in patients with spontaneous supratentorial lobar intracerebral haematomas (STICH II): a randomised trial.[Erratum appears in Lancet. 2013 Aug 3;382(9890):396] *Lancet*, 382(9890), 397-408.
- Menon, B. K., Buck, B. H., Singh, N., Deschaintre, Y., Almekhlafi, M. A., Coutts, S. B., et al. (2022). Intravenous tenecteplase compared with alteplase for acute ischaemic stroke in Canada (AcT): a pragmatic, multicentre, open-label, registry-linked, randomised, controlled, non-inferiority trial *The Lancet*, 400(10347), 161-169.
- Mesa, D., Franco, M., Suarez de Lezo, J., Munoz, J., Rus, C., Delgado, M., et al. (2003). Prevalence of patent foramen ovale in young patients with cerebral ischemic accident of unknown origin *Revista Espanola de Cardiologia*, *56*(7), 662-668.
- Meyer, B. C., Raman, R., Hemmen, T., Obler, R., Zivin, J. A., Rao, R., et al. (2008). Efficacy of site-independent telemedicine in the STRokE DOC trial: a randomised, blinded, prospective study 13 *Lancet Neurology*, 7(9), 787-795.

- Middleton, S., McElduff, P., Ward, J., Grimshaw, J. M., Dale, S., D'Este, C., et al. (2011). Implementation of evidence-based treatment protocols to manage fever, hyperglycaemia, and swallowing dysfunction in acute stroke (QASC): a cluster randomised controlled trial *Lancet*, *378*(9804), 1699-1706.
- Miller, K. K., Porter, R. E., DeBaun-Sprague, E., Van Puymbroeck, M., & Schmid, A. A. (2017). Exercise after Stroke: Patient Adherence and Beliefs after Discharge from Rehabilitation *Topics in Stroke Rehabilitation*, 24(2), 142-148.
- Mitchell, P. J., Yan, B., Churilov, L., Dowling, R. J., Bush, S., Nguyen, T., et al. (2022). DIRECT-SAFE: A Randomized Controlled Trial of DIRECT Endovascular Clot Retrieval versus Standard Bridging Therapy *J Stroke*, *24*(1), 57-64.
- Mohan, K. M., Wolfe, C. D., Rudd, A. G., Heuschmann, P. U., Kolominsky-Rabas, P. L., & Grieve, A. P. (2011). Risk and cumulative risk of stroke recurrence: a systematic review and meta-analysis *Stroke*, *42*(5), 1489-1494.
- Mohapatra, S., & Jones, A. (2015). The Orpington Prognostic Scale: A predictive tool for discharge destination and outcomes in stroke survivors admitted to a hyperacute stroke unit *International Journal of Therapy and Rehabilitation*, 22(11), 510-516.
- Mohr, J. P., Thompson, J. L. P., Lazar, R. M., Levin, B., Sacco, R. L., Furie, K. L., et al. (2001). A Comparison of Warfarin and Aspirin for the Prevention of Recurrent Ischemic Stroke *New England Journal of Medicine*, 345(20), 1444-1451.
- Molyneux, A. J., Kerr, R. S., Yu, L. M., Clarke, M., Sneade, M., Yarnold, J. A., et al. (2005). International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion *Lancet*, *366*(9488), 809-817.
- Moncion, K., Rodrigues, L., MacKay-Lyons, M., Eng, J. J., Billinger, S. A., Ploughman, M., et al. (2022). Exercise-Based Stroke Rehabilitation: Clinical Considerations Following the COVID-19 Pandemic *Neurorehabil Neural Repair*, *36*(1), 3-16.
- Montane, E., Vallano, A., & Laporte, J. R. (2004). Oral antispastic drugs in nonprogressive neurologic diseases: a systematic review *Neurology*, *63*(8), 1357-1363.
- Moon, H. J., Chun, M. H., Lee, S. J., & Kim, B. R. (2012). The usefulness of bladder reconditioning before indwelling urethral catheter removal from stroke patients *American Journal of Physical Medicine & Rehabilitation*, *91*(8), 681-688.
- Moore, S. A., Hallsworth, K., Jakovljevic, D. G., Blamire, A. M., He, J., Ford, G. A., et al. (2015). Effects of Community Exercise Therapy on Metabolic, Brain, Physical, and Cognitive Function Following Stroke: A Randomized Controlled Pilot Trial *Neurorehabilitation & Neural Repair*, 29(7), 623-635.
- Moreno-Segura, N., Martin-San Agustin, R., Garcia-Bafalluy, S., & Escriche-Escuder, A. (2022). Effects of core training on trunk function, balance, and gait in stroke patients: A systematic review and meta-analysis of randomised controlled trials *Clinical Rehabilitation*, *36*(12), 1635-1654
- Morkisch, N., Thieme, H., & Dohle, C. (2019). How to perform mirror therapy after stroke? Evidence from a meta-analysis *Restorative Neurology & Neuroscience*, *37*(5), 421-435.
- Morris, P. L., Robinson, R. G., Andrzejewski, P., Samuels, J., & Price, T. R. (1993). Association of depression with 10-year poststroke mortality *American Journal of Psychiatry*, 150(1), 124-129.
- Mortimer, A., Lenthall, R., Wiggam, I., Dharmasiri, M., Dinsmore, J., Doubal, F., et al. (2021). To support safe provision of mechanical thrombectomy services for patients with acute ischaemic stroke: 2021 consensus guidance from BASP, BSNR, ICSWP, NACCS, and UKNG *Clin Radiol*, *76*(11), 862.e861-862.e817.
- Moullaali, T. J., Wang, X., Martin, R. H., Shipes, V. B., Robinson, T. G., Chalmers, J., et al. (2019). Blood pressure control and clinical outcomes in acute intracerebral haemorrhage: a preplanned pooled analysis of individual participant data *Lancet Neurol*, *18*(9), 857-864.
- Moullaali, T. J., Wang, X., Sandset, E. C., Woodhouse, L. J., Law, Z. K., Arima, H., et al. (2022). Early lowering of blood pressure after acute intracerebral haemorrhage: a systematic review and meta-analysis of individual patient data *Journal of Neurology, Neurosurgery & Psychiatry*, 93(1), 6-13.

- Mukhtar, T. K., Molyneux, A. J., Hall, N., Yeates, D. R., Goldacre, R., Sneade, M., et al. (2016). The falling rates of hospital admission, case fatality, and population-based mortality for subarachnoid hemorrhage in England, 1999-2010 *Journal of Neurosurgery*, 125, 698-704.
- Nascimento, L. R., Boening, A., Galli, A., Polese, J. C., & Ada, L. (2021). Treadmill walking improves walking speed and distance in ambulatory people after stroke and is not inferior to overground walking: a systematic review *Journal of Physiotherapy*, *67*(2), 95-104.
- Nasr, D. M., Brinjikji, W., Cloft, H. J., Saposnik, G., & Rabinstein, A. A. (2013). Mortality in cerebral venous thrombosis: results from the national inpatient sample database *Cerebrovascular Diseases*, 35(1), 40-44.
- National Office of Clinical Audit (Ireland). (2023). *Irish National Audit of Stroke: A critical review of national stroke data for Ireland from 2013 to 2021*. https://www.noca.ie/publications
- National Patient Safety Agency, Royal College of Speech and Language Therapists, British Dietetic Association, National Nurses Nutrition Group, & Hospital Caterers Association. (2011). Dysphagia Diet Food Texture Descriptors.
 - http://www.hospitalcaterers.org/media/1160/dysphagia-descriptors.pdf

 A.R. (2015). Thrombolysis and expedited carotid revascularization *Journal of Cardio*
- Naylor, A. R. (2015). Thrombolysis and expedited carotid revascularization *Journal of Cardiovascular Surgery*, *56*(2), 159-164.
- Newton, J. N., Briggs, A. D., Murray, C. J., Dicker, D., Foreman, K. J., Wang, H., et al. (2015). Changes in health in England, with analysis by English regions and areas of deprivation, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013 *Lancet*, 386(10010), 2257-2274.
- NHS England. (2021). *National Stroke Service Model: Integrated Stroke Delivery Networks*. https://www.england.nhs.uk/publication/national-stroke-service-model-integrated-stroke-delivery-networks/
- NHS England. (2022). *National Service Model for an Integrated Community Stroke Service*. https://www.england.nhs.uk/wp-content/uploads/2022/02/stroke-integrated-community-service-february-2022.pdf
- NHS England Accelerated Access Collaborative. (2021). Summary of National Guidance for Lipid Management for Primary and Secondary Prevention of CVD.

 https://www.england.nhs.uk/aac/publication/summary-of-national-guidance-for-lipid-management/
- NICE. (2007). Clinical guideline [CG49] Faecal incontinence: the management of faecal incontinence in adults. https://www.nice.org.uk/CG49
- NICE. (2010a). *Technology appraisal guidance [TA210] Clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events*. NICE. https://www.nice.org.uk/guidance/TA210
- NICE. (2010b). Clinical guideline [CG91] Depression in Adults with a Chronic Physical Health Problem: Treatment and Management. https://www.nice.org.uk/guidance/cg91
- NICE. (2011). Clinical guideline [CG123] Common mental health problems: identification and pathways to care. https://www.nice.org.uk/guidance/cg123
- NICE. (2013a). Clinical Guideline [CG161] Falls in older people: assessing risk and prevention. https://www.nice.org.uk/guidance/cg161
- NICE. (2013b). *Clinical Guideline [CG162] Stroke rehabilitation in adults*. https://www.nice.org.uk/guidance/CG162
- NICE. (2015a). NICE guideline [NG31] Care of Dying Adults in the Last Days of Life. https://www.nice.org.uk/guidance/ng31
- NICE. (2015b). *Clinical Guideline [CG97] Lower urinary tract symptoms in men: management*. https://www.nice.org.uk/guidance/cg97
- NICE. (2016a). *Interventional procedures guidance [IPG548] Mechanical clot retrieval for treating acute ischaemic stroke*. NICE. https://www.nice.org.uk/guidance/ipg548
- NICE. (2016b). Quality Standard 2: Stroke in adults. https://www.nice.org.uk/guidance/QS2
- NICE. (2016c). *Technology appraisal guidance [TA393] Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia*. https://www.nice.org.uk/guidance/ta393
- NICE. (2016d). *Technology appraisal guidance [TA394] Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia*. https://www.nice.org.uk/guidance/ta394

NATIONAL CLINICAL GUIDELINE FOR STROKE

for the United Kingdom and Ireland

- NICE. (2017a). *Clinical Guideline [CG146] Osteoporosis: assessing the risk of fragility fracture*. https://www.nice.org.uk/guidance/cg146
- NICE. (2017b). Clinical Guideline [CG32] Nutrition support in adults: oral nutrition support, enteral tube feeding and parenteral nutrition. http://guidance.nice.org.uk/CG32
- NICE. (2017c). *Public health guideline [PH56] Vitamin D: supplement use in specific population groups*. https://www.nice.org.uk/guidance/ph56
- NICE. (2019a). *NICE guideline [NG123] Urinary incontinence and pelvic organ prolapse in women:* management. https://www.nice.org.uk/guidance/ng123
- NICE. (2019b). *NICE guideline [NG97] Dementia: assessment, management and support for people living with dementia and their carers*. https://www.nice.org.uk/guidance/ng97
- NICE. (2020). Clinical Guideline [CG173] Neuropathic pain pharmacological management: the pharmacological management of neuropathic pain in adults in non-specialist settings. http://guidance.nice.org.uk/CG173
- NICE. (2021a). *NICE guideline [NG196] Atrial fibrillation: diagnosis and management*. https://www.nice.org.uk/guidance/ng196
- NICE. (2021b). *Technology appraisal guidance [TA733] Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia*. https://www.nice.org.uk/guidance/TA733
- NICE. (2021c). *NICE guideline [NG197] Shared Decision Making*. https://www.nice.org.uk/guidance/ng197
- NICE. (2021d). Technology appraisal guidance [TA694] Bempedoic acid with ezetimibe for treating primary hypercholesterolaemia or mixed dyslipidaemia. https://www.nice.org.uk/guidance/TA694
- NICE. (2021e). *Technology appraisal guidance* [TA697] *Andexanet alfa for reversing anticoagulation from apixaban or rivaroxaban*. https://www.nice.org.uk/guidance/ta697
- NICE. (2022a). *NICE guideline [NG220] Multiple sclerosis in adults: management*. https://www.nice.org.uk/guidance/ng220
- NICE. (2022b). *NICE Guideline [NG136] Hypertension in adults: diagnosis and management*. https://www.nice.org.uk/guidance/ng136
- NICE. (2022c). Technology appraisal guidance [TA805] Icosapent ethyl with statin therapy for reducing the risk of cardiovascular events in people with raised triglycerides.

 https://www.nice.org.uk/guidance/ta805
- NICE. (2022d). *NICE guideline [NG222] Depression in adults: treatment and management*. https://www.nice.org.uk/guidance/ng222
- NICE. (2022e). NICE guideline [NG128] Stroke and transient ischaemic attack in over 16s: diagnosis and initial management. https://www.nice.org.uk/guidance/ng128
- NICE. (2023a). *NICE guideline [NG209] Tobacco: preventing uptake, promoting quitting and treating dependence*. https://www.nice.org.uk/guidance/ng209
- NICE. (2023b). *Clinical guideline* [CG103] *Delirium: diagnosis, prevention and management*. https://www.nice.org.uk/guidance/CG103
- NICE. (2023c). Clinical Guideline [CG181] Cardiovascular disease: risk assessment and reduction, including lipid modification. https://www.nice.org.uk/guidance/CG181
- Nijland, R. H. M., van Wegen, E. E. H., Harmeling-van der Wel, B. C., & Kwakkel, G. (2010). Presence of Finger Extension and Shoulder Abduction Within 72 Hours After Stroke Predicts Functional Recovery *Stroke*, *41*(4), 745-750.
- Nindorera, F., Nduwimana, I., Thonnard, J. L., & Kossi, O. (2021). Effectiveness of walking training on balance, motor functions, activity, participation and quality of life in people with chronic stroke: a systematic review with meta-analysis and meta-regression of recent randomized controlled trials *Disability & Rehabilitation*, *44*(15), 3760-3771.
- Niu, Y., Sheng, S., Chen, Y., Ding, J., Li, H., Shi, S., et al. (2022). The Efficacy of Group Acceptance and Commitment Therapy for Preventing Post-Stroke Depression: A Randomized Controlled Trial *Journal of Stroke and Cerebrovascular Diseases*, *31*(2), 106225.

- Nogueira, R. G., Jadhav, A. P., Haussen, D. C., Bonafe, A., Budzik, R. F., Bhuva, P., et al. (2018). Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct *New England Journal of Medicine*, *378*(1), 11-21.
- Norton, B., Homer-Ward, M., Donnelly, M. T., Long, R. G., & Holmes, G. K. (1996). A randomised prospective comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding after acute dysphagic stroke *BMJ*, *312*(7022), 13-16.
- Noubiap, J. J., Agbaedeng, T. A., Kamtchum-Tatuene, J., Fitzgerald, J. L., Middeldorp, M. E., Kleinig, T., et al. (2021). Rhythm monitoring strategies for atrial fibrillation detection in patients with cryptogenic stroke: A systematic review and meta-analysis *Int J Cardiol Heart Vasc*, *34*, 100780.
- Ntsiea, M., Van Aswegen, H., Lord, S., & Olorunju, S. S. (2015). The effect of a workplace intervention programme on return to work after stroke: A randomised controlled trial *Clinical Rehabilitation*, *29*, 663-673.
- Nystrom, A., & Hellstrom, K. (2013). Fall risk six weeks from onset of stroke and the ability of the Prediction of Falls in Rehabilitation Settings Tool and motor function to predict falls *Clinical Rehabilitation*, *27*(5), 473-479.
- Obembe, A. O., & Eng, J. J. (2015). Rehabilitation Interventions for Improving Social Participation After Stroke: A Systematic Review and Meta-analysis *Neurorehabilitation & Neural Repair*, 30(4), 384-392.
- Office of National Statistics. (2022). Adult smoking habits in the UK: 2021.

 https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthandlifeex-pectancies/bulletins/adultsmokinghabitsingreatbritain/2021
- Okuma, H., Kitagawa, Y., Yasuda, T., Tokuoka, K., & Takagi, S. (2010). Comparison between single antiplatelet therapy and combination of anti-platelet and anticoagulation therapy for secondary prevention in ischemic stroke patients with antiphospholipid syndrome *International Journal of Medical Sciences*, 7(1), 15-18.
- Okumura, K., Akao, M., Yoshida, T., Kawata, M., Okazaki, O., Akashi, S., et al. (2020). Low-Dose Edoxaban in Very Elderly Patients with Atrial Fibrillation *New England Journal of Medicine*, *383*(18), 1735-1745.
- Olavarria, V. V., Arima, H., Anderson, C. S., Brunser, A. M., Munoz-Venturelli, P., Heritier, S., et al. (2014). Head position and cerebral blood flow velocity in acute ischemic stroke: A systematic review and meta-analysis *Cerebrovascular Diseases*, *37*(6), 401-408.
- Oldgren, J., Åsberg, S., Hijazi, Z., Wester, P., Bertilsson, M., & Norrving, B. (2022). Early Versus Delayed Non-Vitamin K Antagonist Oral Anticoagulant Therapy After Acute Ischemic Stroke in Atrial Fibrillation (TIMING): A Registry-Based Randomized Controlled Noninferiority Study *Circulation*, 146(14), 1056-1066.
- Olesen, J. B., Lip, G. Y., Lindhardsen, J., Lane, D. A., Ahlehoff, O., Hansen, M. L., et al. (2011). Risks of thromboembolism and bleeding with thromboprophylaxis in patients with atrial fibrillation: A net clinical benefit analysis using a 'real world' nationwide cohort study *Thrombosis & Haemostasis*, 106(4), 739-749.
- Öst Nilsson, A., Eriksson, G., Johansson, U., & Hellman, T. (2017). Experiences of the return to work process after stroke while participating in a person-centred rehabilitation programme *Scandinavian journal of occupational therapy*, 24(5), 349-356.
- Öst Nilsson, A., Eriksson, G., Asaba, E., Johansson, U., & Hellman, T. (2020). Being a co-worker or a manager of a colleague returning to work after stroke: A challenge facilitated by cooperation and flexibility *Scandinavian journal of occupational therapy*, *27*(3), 213-222.
- Ovaisi, S., Ibison, J., Leontowitsch, M., Cloud, G., Oakeshott, P., & Kerry, S. (2011). Stroke patients' perceptions of home blood pressure monitoring: a qualitative study *Br J Gen Pract*, *61*(590), e604-610.
- Ovbiagele, B., Saver, J. L., Fredieu, A., Suzuki, S., Selco, S., Rajajee, V., et al. (2004). In-hospital initiation of secondary stroke prevention therapies yields high rates of adherence at follow-up *Stroke*, *35*(12), 2879-2883.

- Pacheco, R. L., Latorraca, C. D. O. C., da Silva, L. D. G. M., Ferreira, D. B. G. D. M., Fernandes, C. D. A. A., Hosni, N. D., et al. (2019). Modafinil for poststroke patients: A systematic review *International Journal of Clinical Practice*, 73(2), e13295.
- Paciaroni, M., Agnelli, G., Falocci, N., Caso, V., Becattini, C., Marcheselli, S., et al. (2015). Early Recurrence and Cerebral Bleeding in Patients With Acute Ischemic Stroke and Atrial Fibrillation: Effect of Anticoagulation and Its Timing: The RAF Study *Stroke*, *46*(8), 2175-2182.
- Page, S. J., & Peters, H. (2014). Mental practice: applying motor PRACTICE and neuroplasticity principles to increase upper extremity function *Stroke*, *45*(11), 3454-3460.
- Pallesen, H. (2014). Body, coping and self-identity. A qualitative 5-year follow-up study of stroke *Disabil Rehabil*, 36(3), 232-241.
- Palmer, R., & Enderby, P. (2007). Methods of speech therapy treatment for stable dysarthria: a review *Advances in Speech Language Pathology*, *9*(2), 140-153.
- Palmer, R., Dimairo, M., Cooper, C., Enderby, P., Brady, M., Bowen, A., et al. (2019). Self-managed, computerised speech and language therapy for patients with chronic aphasia post-stroke compared with usual care or attention control (Big CACTUS): a multicentre, single-blinded, randomised controlled trial *The Lancet Neurology*, 18(9), 821-833.
- Pan, Y., Chen, W., Xu, Y., Yi, X., Han, Y., Yang, Q., et al. (2017). Genetic Polymorphisms and Clopidogrel Efficacy for Acute Ischemic Stroke or Transient Ischemic Attack: A Systematic Review and Meta-Analysis *Circulation*, 135(1), 21-33.
- Pandian, J. D., Arora, R., Kaur, P., Sharma, D., Vishwambaran, D. K., & Arima, H. (2014). Mirror therapy in unilateral neglect after stroke (MUST trial): a randomized controlled trial *Neurology*, *83*(11), 1012-1017.
- Pang, M. Y., Harris, J. E., & Eng, J. J. (2006). A community-based upper-extremity group exercise program improves motor function and performance of functional activities in chronic stroke: a randomized controlled trial *Archives of Physical Medicine & Rehabilitation*, 87(1), 1-9.
- Paolucci, S., Iosa, M., Toni, D., Barbanti, P., Bovi, P., Cavallini, A., et al. (2016). Prevalence and Time Course of Post-Stroke Pain: A Multicenter Prospective Hospital-Based Study *Pain Med*, *17*(5), 924-930.
- Park, H. K., Lee, J. S., Kim, B. J., Park, J. H., Kim, Y. J., Yu, S., et al. (2021). Cilostazol versus aspirin in ischemic stroke with cerebral microbleeds versus prior intracerebral hemorrhage *International Journal of Stroke*, *16*(9), 1019-1030.
- Parke, H. L., Epiphaniou, E., Pearce, G., Taylor, S. J., Sheikh, A., Griffiths, C. J., et al. (2015). Self-Management Support Interventions for Stroke Survivors: A Systematic Meta-Review *PLoS One*, 10(7), e0131448.
- Parra, O., Sanchez, A. A., Bonnin, M., Arboix, A., Campos, R. F., Perez, R. J., et al. (2011). Early treatment of obstructive apnoea and stroke outcome: a randomised controlled trial *European Respiratory Journal*, *37*(5), 1128-1136.
- Parra, O., Sanchez-Armengol, A., Capote, F., Bonnin, M., Arboix, A., Campos-Rodriguez, F., et al. (2015). Efficacy of continuous positive airway pressure treatment on 5-year survival in patients with ischaemic stroke and obstructive sleep apnea: a randomized controlled trial *Journal of Sleep Research*, 24(1), 47-53.
- Parsons, M., Spratt, N., Bivard, A., Campbell, B., Chung, K., Miteff, F., et al. (2012). A Randomized Trial of Tenecteplase versus Alteplase for Acute Ischemic Stroke *New England Journal of Medicine*, 366(12), 1099-1107.
- Patel, A., Knapp, M., Evans, A., Perez, I., & Kalra, L. (2004). Training care givers of stroke patients: economic evaluation *BMJ*, *328*(7448), 1102.
- Patel, M. R., Mahaffey, K. W., Garg, J., Pan, G., Singer, D. E., Hacke, W., et al. (2011). Rivaroxaban versus warfarin in nonvalvular atrial fibrillation *New England Journal of Medicine*, *365*(10), 883-891.
- Payne, S., Burton, C., AddingtonHall, J., & Jones, A. (2010). End-of-life issues in acute stroke care: A qualitative study of the experiences and preferences of patients and families *Palliative Medicine*, 24(2), 146-153.
- Pérez de la Ossa, N., Abilleira, S., Jovin, T. G., García-Tornel, Á., Jimenez, X., Urra, X., et al. (2022). Effect of Direct Transportation to Thrombectomy-Capable Center vs Local Stroke Center on

- Neurological Outcomes in Patients With Suspected Large-Vessel Occlusion Stroke in Nonurban Areas: The RACECAT Randomized Clinical Trial *JAMA*, *327*(18), 1782-1794.
- Perry, L. (2004). Eating and dietary intake in communication-impaired stroke survivors: a cohort study from acute-stage hospital admission to 6 months post-stroke *Clinical Nutrition*, *23*(6), 1333-1343.
- Peters, N., Holtmannspötter, M., Opherk, C., Gschwendtner, A., Herzog, J., Sämann, P., et al. (2006). Brain volume changes in CADASIL: a serial MRI study in pure subcortical ischemic vascular disease *Neurology*, *66*(10), 1517-1522.
- Pickard, J. D., Murray, G. D., Illingworth, R., Shaw, M. D., Teasdale, G. M., Foy, P. M., et al. (1989). Effect of oral nimodipine on cerebral infarction and outcome after subarachnoid haemorrhage: British aneurysm nimodipine trial *BMJ*, *298*(6674), 636-642.
- Pindus, D. M., Mullis, R., Lim, L., Wellwood, I., Rundell, A. V., Abd Aziz, N. A., et al. (2018). Stroke survivors' and informal caregivers' experiences of primary care and community healthcare services A systematic review and meta-ethnography *PLoS One*, *13*(2), e0192533.
- Pisters, R., Lane, D. A., Nieuwlaat, R., de Vos, C. B., Crijns, H. J., & Lip, G. Y. (2010). A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey *Chest*, *138*(5), 1093-1100.
- Pogrebnoy, D., & Dennett, A. (2020). Exercise Programs Delivered According to Guidelines Improve Mobility in People With Stroke: A Systematic Review and Meta-analysis *Archives of Physical Medicine and Rehabilitation*, 101(1), 154-165.
- Pollack, C. V., Wang, B., Young, L., Weitz, J. I., Reilly, P. A., Dubiel, R., et al. (2017). Idarucizumab for dabigatran reversal -full cohort analysis *New England Journal of Medicine*, *377*(5), 431-441.
- Pollock, A., Baer, G., Campbell, P., Choo Pei, L., Forster, A., Morris, J., et al. (2014a). Physical rehabilitation approaches for the recovery of function and mobility following stroke *Cochrane Database of Systematic Reviews*(4), CD001920.
- Pollock, A., Farmer Sybil, E., Brady Marian, C., Langhorne, P., Mead Gillian, E., Mehrholz, J., et al. (2014b). Interventions for improving upper limb function after stroke *Cochrane Database of Systematic Reviews*(11), CD010820.
- Pollock, A., Gray, C., Culham, E., Durward Brian, R., & Langhorne, P. (2014c). Interventions for improving sit-to-stand ability following stroke *Cochrane Database of Systematic Reviews*(5), CD007232.
- Pollock, A., Hazelton, C., Rowe, F. J., Jonuscheit, S., Kernohan, A., Angilley, J., et al. (2019). Interventions for visual field defects in people with stroke *Cochrane Database of Systematic Reviews*(5), CD008388.
- Poltawski, L., Boddy, K., Forster, A., Goodwin, V. A., Pavey, A. C., & Dean, S. (2015). Motivators for uptake and maintenance of exercise: perceptions of long-term stroke survivors and implications for design of exercise programmes *Disabil Rehabil*, *37*(9), 795-801.
- Poulin, V., Korner-Bitensky, N., Dawson, D. R., & Bherer, L. (2012). Efficacy of executive function interventions after stroke: a systematic review *Topics in Stroke Rehabilitation*, 19(2), 158-171.
- Pouwels, S., Lalmohamed, A., Leufkens, B., de Boer, A., Cooper, C., van Staa, T., et al. (2009). Risk of hip/femur fracture after stroke: a population-based case-control study *Stroke*, *40*(10), 3281-3285
- Poveda-Garcia, A., Moret-Tatay, C., & Gomez-Martinez, M. (2021). The Association between Mental Motor Imagery and Real Movement in Stroke *Healthcare (Basel, Switzerland)*, *9*(11), 1568.
- Powers, C. J., Dornbos, D., Nimjee, S. M., Gulati, D., Mlynash, M., Lansberg, M. G., et al. (2019). Thrombectomy with conscious sedation compared with general anesthesia: A DEFUSE 3 analysis *American Journal of Neuroradiology*, 40(6), 1001-1005.
- Prenton, S., Hollands, K. L., & Kenney, L. P. (2016). Functional electrical stimulation versus ankle foot orthoses for foot-drop: A meta-analysis of orthotic effects *J Rehabil Med*, *48*(8), 646-656.
- Preston, E., Ada, L., Stanton, R., Mahendran, N., & Dean, C. M. (2021). Prediction of Independent Walking in People Who Are Nonambulatory Early After Stroke: A Systematic Review *Stroke*, 52(10), 3217-3224.

- Pringle, J., Drummond, J. S., & McLafferty, E. (2013). Revisioning, reconnecting and revisiting: the psychosocial transition of returning home from hospital following a stroke *Disability and Rehabilitation*, 35(23), 1991-1999.
- PROGRESS Collaborative Group. (2001). Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack *Lancet*, *358*(9287), 1033-1041.
- Puy, L., De Guio, F., Godin, O., Duering, M., Dichgans, M., Chabriat, H., et al. (2017). Cerebral microbleeds and the risk of incident ischemic stroke in CADASIL (Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) *Stroke*, *48*(10), 2699-2703.
- Qureshi, A. I., Palesch, Y. Y., Barsan, W. G., Hanley, D. F., Hsu, C. Y., Martin, R. L., et al. (2016). Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage *New England Journal of Medicine*, 375(11), 1033-1043.
- Rackoll, T., Nave, A. H., Ebinger, M., Endres, M., Grittner, U., & Flöel, A. (2022). Physical Fitness Training in Patients with Subacute Stroke (PHYS-STROKE): Safety analyses of a randomized clinical trial *Int J Stroke*, *17*(1), 93-100.
- Rah, U. W., Yoon, S. H., Moon, D. J., Kwack, K. S., Hong, J. Y., Lim, Y. C., et al. (2012). Subacromial corticosteroid injection on poststroke hemiplegic shoulder pain: A randomized, triple-blind, placebo-controlled trial *Archives of Physical Medicine and Rehabilitation*, *93*(6), 949-956.
- Ramnemark, A., Nilsson, M., Borssen, B., & Gustafson, Y. (2000). Stroke, a major and increasing risk factor for femoral neck fracture *Stroke*, *31*(7), 1572-1577.
- Ramsay, A. I., Morris, S., Hoffman, A., Hunter, R. M., Boaden, R., McKevitt, C., et al. (2015). Effects of Centralizing Acute Stroke Services on Stroke Care Provision in Two Large Metropolitan Areas in England *Stroke*, *46*(8), 2244-2251.
- Rantner, B., Goebel, G., Bonati, L. H., Ringleb, P. A., Mas, J. L., & Fraedrich, G. (2013). The risk of carotid artery stenting compared with carotid endarterectomy is greatest in patients treated within 7 days of symptoms *Journal of Vascular Surgery*, *57*(3), 619-626.
- Rao, M. P., Vinereanu, D., Wojdyla, D. M., Alexander, J. H., Atar, D., Hylek, E. M., et al. (2018). Clinical Outcomes and History of Fall in Patients with Atrial Fibrillation Treated with Oral Anticoagulation: Insights From the ARISTOTLE Trial *Am J Med*, *131*(3), 269-275.e262.
- Reddy, V. Y., Doshi, S. K., Sievert, H., Buchbinder, M., Neuzil, P., Huber, K., et al. (2013). Percutaneous left atrial appendage closure for stroke prophylaxis in patients with atrial fibrillation: 2.3-Year Follow-up of the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation) Trial *Circulation*, 127(6), 720-729.
- Rees, K., Hartley, L., Flowers, N., Clarke, A., Hooper, L., Thorogood, M., et al. (2013). 'Mediterranean' dietary pattern for the primary prevention of cardiovascular disease *Cochrane Database of Systematic Reviews*, 8, CD009825.
- RELEASE Collaborators. (2021). Predictors of Poststroke Aphasia Recovery: A Systematic Review-Informed Individual Participant Data Meta-Analysis *Stroke*, *52*(5), 1778-1787.
- RELEASE Collaborators. (2022a). Dosage, Intensity, and Frequency of Language Therapy for Aphasia: A Systematic Review–Based, Individual Participant Data Network Meta-Analysis *Stroke*, *53*(3), 956-967.
- RELEASE Collaborators. (2022b). Precision rehabilitation for aphasia by patient age, sex, aphasia severity, and time since stroke? A prespecified, systematic review-based, individual participant data, network, subgroup meta-analysis *Int J Stroke*, 1067-1077.
- Renoux, C., Dell'aniello, S., Garbe, E., & Suissa, S. (2010). Transdermal and oral hormone replacement therapy and the risk of stroke: a nested case-control study *BMJ*, *340*, 2519.
- Rerkasem, K., & Rothwell, P. M. (2009). Systematic Review of the Operative Risks of Carotid Endarterectomy for Recently Symptomatic Stenosis in Relation to the Timing of Surgery *Stroke*, 40(10), 564-572.
- Rerkasem, K., & Rothwell, P. M. (2011). Carotid endarterectomy for symptomatic carotid stenosis Cochrane Database Syst Rev(4), CD001081.
- RESTART Collaboration. (2019). Effects of antiplatelet therapy after stroke due to intracerebral haemorrhage (RESTART): a randomised, open-label trial *Lancet*, *393*(10191), 2613-2623.

- Ridley, J., & Leitch, S. (2021). Restraint Reduction Network (RRN) Training Standards.

 https://restraintreductionnetwork.org/wp-content/uploads/2022/11/RRN standards v9 accessible PDF updated.pdf
- Riley, E. A. (2017). Patient Fatigue during Aphasia Treatment: A Survey of Speech-Language Pathologists *Communication Disorders Quarterly*, *38*(3), 143-153.
- Ringleb, P., Bendszus, M., Bluhmki, E., Donnan, G., Eschenfelder, C., Fatar, M., et al. (2019). Extending the time window for intravenous thrombolysis in acute ischemic stroke using magnetic resonance imaging-based patient selection *Int J Stroke*, *14*(5), 483-490.
- Rintala, A., Paivarinne, V., Hakala, S., Paltamaa, J., Heinonen, A., Karvanen, J., et al. (2019). Effectiveness of Technology-Based Distance Physical Rehabilitation Interventions for Improving Physical Functioning in Stroke: A Systematic Review and Meta-analysis of Randomized Controlled Trials *Archives of Physical Medicine and Rehabilitation*, 100(7), 1339-1358.
- Roach, R. E., Helmerhorst, F. M., Lijfering, W. M., Stijnen, T., Algra, A., & Dekkers, O. M. (2015). Combined oral contraceptives: the risk of myocardial infarction and ischemic stroke *Cochrane Database of Systematic Reviews*, 8, CD011054.
- Roaldsen, M. B., Eltoft, A., Wilsgaard, T., Christensen, H., Engelter, S. T., Indredavik, B., et al. (2023).

 Safety and efficacy of tenecteplase in patients with wake-up stroke assessed by non-contrast CT (TWIST): a multicentre, open-label, randomised controlled trial *Lancet Neurol*, 22(2), 117-126.
- Robert, P., Lanctôt, K. L., Agüera-Ortiz, L., Aalten, P., Bremond, F., Defrancesco, M., et al. (2018). Is it time to revise the diagnostic criteria for apathy in brain disorders? The 2018 international consensus group *Eur Psychiatry*, *54*, 71-76.
- Robison, J., Wiles, R., Ellis-Hill, C., McPherson, K., Hyndman, D., & Ashburn, A. (2009). Resuming previously valued activities post-stroke: who or what helps? *Disabil Rehabil*, *31*(19), 1555-1566.
- Rodgers, H., Bosomworth, H., Krebs, H. I., van Wijck, F., Howel, D., Wilson, N., et al. (2019a). Robot assisted training for the upper limb after stroke (RATULS): a multicentre randomised controlled trial *The Lancet*, *394*(10192), 51-62.
- Rodgers, H., Howel, D., Bhattarai, N., Cant, R., Drummond, A., Ford, G. A., et al. (2019b). Evaluation of an Extended Stroke Rehabilitation Service (EXTRAS): A Randomized Controlled Trial and Economic Analysis *Stroke*, *50*(12), 3561-3568.
- Rodrigues, M. A., Samarasekera, N., Lerpiniere, C., Humphreys, C., McCarron, M. O., White, P. M., et al. (2018). The Edinburgh CT and genetic diagnostic criteria for lobar intracerebral haemorrhage associated with cerebral amyloid angiopathy: model development and diagnostic test accuracy study *Lancet Neurol*, *17*(3), 232-240.
- Roffe, C., Ali, K., Warusevitane, A., Sills, S., Pountain, S., Allen, M., et al. (2011). The SOS pilot study: a RCT of routine oxygen supplementation early after acute stroke-effect on recovery of neurological function at one week *PLoS One*, *6*(5), e19113.
- Rola, R., Jarosz, H., Wierzbicka, A., Wichniak, A., Richter, P., Ryglewicz, D., et al. (2008). Sleep disorderd breathing and recurrence of cerebrovascular events, case-fatality, and functional outcome in patients with ischemic stroke or transient ischemic attack *Journal of Physiology & Pharmacology*, 59 Suppl 6, 615-621.
- Rombach, S. M., Smid, B. E., Bouwman, M. G., Linthorst, G. E., Dijkgraaf, M. G., & Hollak, C. E. (2013). Long term enzyme replacement therapy for Fabry disease: effectiveness on kidney, heart and brain *Orphanet Journal of Rare Diseases*, 8(47), 1750-1172.
- Rosales, R. L., & Chua, Y. A. S. (2008). Evidence-based systematic review on the efficacy and safety of botulinum toxin-A therapy in post-stroke spasticity *Journal of Neural Transmission*, *115*(4), 617-623.
- Rosales, R. L., Kong, K. H., Goh, K. J., Kumthornthip, W., Mok, V. C., Delgado-De Los Santos, M. M., et al. (2012). Botulinum toxin injection for hypertonicity of the upper extremity within 12 weeks after stroke: a randomized controlled trial *Neurorehabilitation & Neural Repair*, 26(7), 812-821.
- Rosenbaum, T., Vadas, D., & Kalichman, L. (2014). Sexual function in post-stroke patients: considerations for rehabilitation *Journal of Sexual Medicine*, *11*(1), 15-21.

- Rosewilliam, S., Roskell, C. A., & Pandyan, A. D. (2011). A systematic review and synthesis of the quantitative and qualitative evidence behind patient-centred goal setting in stroke rehabilitation *Clinical Rehabilitation*, 25(6), 501-514.
- Rothwell, P. M., Eliasziw, M., Gutnikov, S. A., Fox, A. J., Taylor, D. W., Mayberg, M. R., et al. (2003a). Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis *Lancet*, *361*(9352), 107-116.
- Rothwell, P. M., Gutnikov, S. A., Warlow, C. P., & European Carotid Surgery Trialist's, C. (2003b). Reanalysis of the final results of the European Carotid Surgery Trial *Stroke*, *34*(2), 514-523.
- Rothwell, P. M., Eliasziw, M., Gutnikov, S. A., Warlow, C. P., Barnett, H. J., & Carotid Endarterectomy Trialists, C. (2004). Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery *Lancet*, *363*(9413), 915-924.
- Rothwell, P. M., Mehta, Z., Howard, S. C., Gutnikov, S. A., & Warlow, C. P. (2005). Treating individuals 3: from subgroups to individuals: general principles and the example of carotid endarterectomy *Lancet*, *365*(9455), 256-265.
- Rothwell, P. M. (2007). Making the most of secondary prevention Stroke, 38(6), 1726.
- Rothwell, P. M., Algra, A., Chen, Z., Diener, H. C., Norrving, B., & Mehta, Z. (2016). Effects of aspirin on risk and severity of early recurrent stroke after transient ischaemic attack and ischaemic stroke: time-course analysis of randomised trials *Lancet*, *388*(10042), 365-375.
- Rowat, A., Graham, C., & Dennis, M. (2012). Dehydration in hospital-admitted stroke patients: detection, frequency, and association *Stroke*, *43*(3), 857-859.
- Rowe, F., Hepworth, L., Howard, C., Hanna, K., & Currie, J. (2020). Impact of visual impairment following stroke (IVIS study): a prospective clinical profile of central and peripheral visual deficits, eye movement abnormalities and visual perceptual deficits *Disability and Rehabilitation*, 44, 1-15.
- Rowe, F. J. (2017). Vision In Stroke cohort: Profile overview of visual impairment *Brain Behav*, 7(11), e00771.
- Rowe, F. J., Hepworth, L. R., Howard, C., Hanna, K. L., Cheyne, C. P., & Currie, J. (2019). High incidence and prevalence of visual problems after acute stroke: An epidemiology study with implications for service delivery *PLoS One*, *14*(3), e0213035.
- Royal College of Paediatrics and Child Health. (2017). Stroke in Childhood: Clinical Guideline for Diagnosis, Management, and Rehabilitation. Royal College of Paediatrics and Child Health. https://www.rcpch.ac.uk/resources/stroke-in-childhood-clinical-guideline
- Royal College of Physicians, & British Medical Association. (2018). *Clinically-assisted nutrition and hydration (CANH) and adults who lack the capacity to consent. Guidance for decision-making in England and Wales*. RCP. https://www.bma.org.uk/media/1161/bma-clinically-assisted-nutrition-hydration-canh-full-guidance.pdf
- Royal College of Physicians, Chartered Society of Physiotherapy, British Society of Rehabilitation Medicine, & Association of Chartered Physiotherapists Interested in Neurology. (2018). Spasticity in adults: management using botulinum toxin. National Guidelines. Royal College of Physicians. https://www.rcplondon.ac.uk/guidelines-policy/spasticity-adults-management-using-botulinum-toxin
- Royal College of Physicians. (2021). Supporting people who have eating and drinking difficulties. https://www.rcplondon.ac.uk/projects/outputs/supporting-people-who-have-eating-and-drinking-difficulties
- Royal College of Speech and Language Therapists. (2021). *Eating and drinking with acknowledged risks:*Multidisciplinary team guidance for the shared decision-making process (adults)

 https://www.rcslt.org/members/clinical-guidance/eating-and-drinking-with-acknowledged-risks-risk-feeding/#section-2
- Rubiera, M., Aires, A., Antonenko, K., Lémeret, S., Nolte, C. H., Putaala, J., et al. (2022). European Stroke Organisation (ESO) guideline on screening for subclinical atrial fibrillation after stroke or transient ischaemic attack of undetermined origin *Eur Stroke J*, 7(3), Vi.
- Ruff, C. T., Giugliano, R. P., Braunwald, E., Hoffman, E. B., Deenadayalu, N., Ezekowitz, M. D., et al. (2014). Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials *Lancet*, 383(9921), 955-962.

- Rundek, T., Gardener, H., Xu, Q., Goldberg, R. B., Wright, C. B., Boden-Albala, B., et al. (2010). Insulin resistance and risk of ischemic stroke among nondiabetic individuals from the northern Manhattan study *Archives of Neurology*, *67*(10), 1195-1200.
- Ryan, C. M., Bayley, M., Green, R., Murray, B. J., & Bradley, T. D. (2011). Influence of continuous positive airway pressure on outcomes of rehabilitation in stroke patients with obstructive sleep apnea *Stroke*, *42*(4), 1062-1067.
- Sacco, R. L., Kargman, D. E., Gu, Q., & Zamanillo, M. C. (1995). Race-ethnicity and determinants of intracranial atherosclerotic cerebral infarction. The Northern Manhattan Stroke Study *Stroke*, *26*(1), 14-20.
- Sacco, R. L., Diener, H. C., Yusuf, S., Cotton, D., Ounpuu, S., Lawton, W. A., et al. (2008). Aspirin and extended-release dipyridamole versus clopidogrel for recurrent stroke *New England Journal of Medicine*, 359(12), 1238-1251.
- Sackley, C., Brittle, N., Patel, S., Ellins, J., Scott, M., Wright, C., et al. (2008). The prevalence of joint contractures, pressure sores, painful shoulder, other pain, falls, and depression in the year after a severely disabling stroke *Stroke*, *39*(12), 3329-3334.
- Sackley, C. M., Walker, M. F., Burton, C. R., Watkins, C. L., Mant, J., Roalfe, A. K., et al. (2015). An occupational therapy intervention for residents with stroke related disabilities in UK care homes (OTCH): cluster randomised controlled trial *BMJ*, *350*, h468.
- Salazar, A. M., Warden, D. L., Schwab, K., Spector, J., Braverman, S., Walter, J., et al. (2000). Cognitive Rehabilitation for Traumatic Brain Injury *JAMA*, *283*(23), 3075-3081.
- Sampson, F. C., Hayward, A., Evans, G., Morton, R., & Collett, B. (2002). Functional benefits and cost/benefit analysis of continuous intrathecal baclofen infusion for the management of severe spasticity *Journal of Neurosurgery*, *96*(6), 1052-1057.
- Sandberg, O., Franklin, K. A., Bucht, G., Eriksson, S., & Gustafson, Y. (2001). Nasal continuous positive airway pressure in stroke patients with sleep apnoea: a randomized treatment study *European Respiratory Journal*, 18(4), 630-634.
- Sandercock, A. G., Counsell, C., & Kane Edward, J. (2015). Anticoagulants for acute ischaemic stroke *Cochrane Database of Systematic Reviews*(3), CD000024.
- Sandercock, P. A., Warlow, C. P., Jones, L. N., & Starkey, I. R. (1989). Predisposing factors for cerebral infarction: the Oxfordshire community stroke project *BMJ*, 298(6666), 75-80.
- Sandercock, P. A., Gibson, L. M., & Liu, M. (2009). Anticoagulants for preventing recurrence following presumed non-cardioembolic ischaemic stroke or transient ischaemic attack *Cochrane Database of Systematic Reviews*(2), CD000248.
- Sandset, E. C., Bath, P. M. W., Boysen, G., Jatuzis, D., Kõrv, J., Lüders, S., et al. (2011). The angiotensin-receptor blocker candesartan for treatment of acute stroke (SCAST): a randomised, placebo-controlled, double-blind trial *The Lancet*, *377*(9767), 741-750.
- Sanna, T., Diener, H.-C., Passman, R. S., Di Lazzaro, V., Bernstein, R. A., Morillo, C. A., et al. (2014). Cryptogenic stroke and underlying atrial fibrillation *New England Journal of Medicine*, *370*(26), 2478-2486.
- Sarkamo, T., Pihko, E., Laitinen, S., Forsblom, A., Soinila, S., Mikkonen, M., et al. (2010). Music and speech listening enhance the recovery of early sensory processing after stroke *Journal of Cognitive Neuroscience*, 22(12), 2716-2727.
- Sarraj, A., Hassan, A. E., Abraham, M. G., Ortega-Gutierrez, S., Kasner, S. E., Hussain, M. S., et al. (2023). Trial of Endovascular Thrombectomy for Large Ischemic Strokes *New England Journal of Medicine*.
- Sasaki, N., Hara, T., Yamada, N., Abo, M., Niimi, M., & Kakuda, W. (2017). The efficacy of high-frequency repetitive transcranial magnetic stimulation for improving apathy in chronic stroke patients *European Neurology*, 78(1-2), 28-32.
- Saunders, D. H., Greig, C. A., Young, A., & Mead, G. E. (2004). Physical fitness training for stroke patients Cochrane Database Systematic of Reviews(1), CD003316.
- Saunders, D. H., Sanderson, M., Brazzelli, M., Greig, C. A., & Mead, G. E. (2013). Physical fitness training for stroke patients *Cochrane Database of Systematic Reviews*, *10*, CD003316.

- Saunders, D. H., Sanderson, M., Hayes, S., Johnson, L., Kramer, S., Carter, D. D., et al. (2020). Physical fitness training for stroke patients *Cochrane Database Syst Rev*, *3*(3), Cd003316.
- Saver, J. L., Goyal, M., Bonafe, A., Diener, H. C., Levy, E. I., Pereira, V. M., et al. (2015). Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke *New England Journal of Medicine*, 372(24), 2285-2295.
- Saver, J. L., Carroll, J. D., Thaler, D. E., Smalling, R. W., MacDonald, L. A., Marks, D. S., et al. (2017). Long-Term Outcomes of Patent Foramen Ovale Closure or Medical Therapy after Stroke *New England Journal of Medicine*, *377*(11), 1022-1032.
- Saxena, R., & Koudstaal, P. (2004). Anticoagulants versus antiplatelet therapy for preventing stroke in patients with nonrheumatic atrial fibrillation and a history of stroke or transient ischemic attack *Cochrane Database of Systematic Reviews*(4), CD000187.
- Schmidt, J., Fleming, J., Ownsworth, T., & Lannin, N. A. (2013). Video feedback on functional task performance improves self-awareness after traumatic brain injury: a randomized controlled trial *Neurorehabilitation and Neural Repair*, *27*(4), 316-324.
- Schmitz, M. A., & Finkelstein, M. (2010). Perspectives on poststroke sexual issues and rehabilitation needs *Topics in Stroke Rehabilitation*, *17*(3), 204-213.
- Schneider, E. J., Lannin, N. A., Ada, L., & Schmidt, J. (2016). Increasing the amount of usual rehabilitation improves activity after stroke: a systematic review *J Physiother*, *62*(4), 182-187.
- Schreuder, F., van Nieuwenhuizen, K. M., Hofmeijer, J., Vermeer, S. E., Kerkhoff, H., Zock, E., et al. (2021). Apixaban versus no anticoagulation after anticoagulation-associated intracerebral haemorrhage in patients with atrial fibrillation in the Netherlands (APACHE-AF): a randomised, open-label, phase 2 trial *Lancet Neurol*, 20(11), 907-916.
- Schwarz, B., Claros-Salinas, D., & Streibelt, M. (2018). Meta-Synthesis of Qualitative Research on Facilitators and Barriers of Return to Work After Stroke *Journal of occupational rehabilitation*, 28(1), 28-44.
- Scott, S. L., & Bondoc, S. (2018). Return to Work After Stroke: A Survey of Occupational Therapy Practice Patterns *Occupational Therapy in Health Care*, *32*(3), 195-215.
- Scottish Government. (2019). *Health and Care (Staffing) (Scotland) Act 2019*. https://www.legislation.gov.uk/asp/2019/6/enacted
- Scottish Government. (2022). *Programme for Government*https://www.gov.scot/publications/progressive-stroke-pathway/pages/3/
- Scottish Stroke Care Audit. (2022). Scottish stroke improvement programme 2022 national report.

 https://publichealthscotland.scot/publications/scottish-stroke-improvement-programme-2022-national-report/
- Scrivener, K., Sherrington, C., & Schurr, K. (2012). Exercise dose and mobility outcome in a comprehensive stroke unit: description and prediction from a prospective cohort study *J Rehabil Med*, 44(10), 824-829.
- Scrivener, K., Dorsch, S., McCluskey, A., Schurr, K., Graham, P. L., Cao, Z., et al. (2020). Bobath therapy is inferior to task-specific training and not superior to other interventions in improving lower limb activities after stroke: a systematic review *J Physiother*, 66(4), 225-235.
- Selles, R. W., Andrinopoulou, E. R., Nijland, R. H., van der Vliet, R., Slaman, J., van Wegen, E. E., et al. (2021). Computerised patient-specific prediction of the recovery profile of upper limb capacity within stroke services: the next step *J Neurol Neurosurg Psychiatry*, *92*(6), 574-581.
- Sentinel Stroke National Audit Programme. (2022). Sentinel Stroke National Audit Programme 9th

 Annual Report: Road to recovery.

 https://www.strokeaudit.org/Documents/National/Clinical/Apr2021Mar2022/Apr2021Mar2022

 -AnnualReport.aspx
- Shaw, L., Bhattarai, N., Cant, R., Drummond, A., Ford, G. A., Forster, A., et al. (2020). An extended stroke rehabilitation service for people who have had a stroke: the EXTRAS RCT, 24, 24.
- Shaw, L. C., Price, C. I., van Wijck, F. M., Shackley, P., Steen, N., Barnes, M. P., et al. (2011). Botulinum Toxin for the Upper Limb after Stroke (BoTULS) Trial: effect on impairment, activity limitation, and pain *Stroke*, *42*(5), 1371-1379.

- Shen, C., Liu, F., Yao, L., Li, Z., Qiu, L., & Fang, S. (2018). Effects of MOTOmed movement therapy on the mobility and activities of daily living of stroke patients with hemiplegia: a systematic review and meta-analysis *Clinical Rehabilitation*, *32*(12), 1569-1580.
- Shen, N. N., Wu, Y., Wang, N., Kong, L. C., Zhang, C., Wang, J. L., et al. (2020). Direct Oral Anticoagulants vs. Vitamin-K Antagonists in the Elderly With Atrial Fibrillation: A Systematic Review Comparing Benefits and Harms Between Observational Studies and Randomized Controlled Trials *Front Cardiovasc Med*, 7, 132.
- Shoamanesh, A., Hart, R. G., Connolly, S. J., Kasner, S. E., Smith, E. E., Marti-Fabregas, J., et al. (2021). Microbleeds and the Effect of Anticoagulation in Patients with Embolic Stroke of Undetermined Source: An Exploratory Analysis of the NAVIGATE ESUS Randomized Clinical Trial *JAMA Neurology*, 78(1), 11-20.
- Siegal, D. M., Curnutte, J. T., Connolly, S. J., Lu, G., Conley, P. B., Wiens, B. L., et al. (2015). Andexanet Alfa for the Reversal of Factor Xa Inhibitor Activity *New England Journal of Medicine*, *373*(25), 2413-2424.
- SIGN. (2019). SIGN 157 Risk reduction and management of delirium. https://www.sign.ac.uk/ourguidelines/risk-reduction-and-management-of-delirium/
- SIGN. (2021). SIGN 142 Management of osteoporosis and the prevention of fragility fractures.

 https://www.sign.ac.uk/our-guidelines/management-of-osteoporosis-and-the-prevention-of-fragility-fractures/
- Silva, G. E., Vana, K. D., Goodwin, J. L., Sherrill, D. L., & Quan, S. F. (2011). Identification of patients with sleep disordered breathing: comparing the four-variable screening tool, STOP, STOP-Bang, and Epworth Sleepiness Scales *Journal of Clinical Sleep Medicine*, 7(5), 467-472.
- Simmons-Mackie, N., Raymer, A., Armstrong, E., Holland, A., & Cherney, L. R. (2010). Communication partner training in aphasia: a systematic review *Archives of Physical Medicine & Rehabilitation*, 91(12), 1814-1837.
- Singh, D. K., Mohd Nordin, N. A., Abd Aziz, N. A., Lim, B. K., & Soh, L. C. (2013). Effects of substituting a portion of standard physiotherapy time with virtual reality games among community-dwelling stroke survivors *BMC Neurology*, *13*, 199.
- Singh, J. A., & Fitzgerald, P. M. (2010). Botulinum toxin for shoulder pain *Cochrane Database of Systematic Reviews*(9), CD008271.
- Sit, J. W., Yip, V. Y., Ko, S. K., Gun, A. P., & Lee, J. S. (2007). A quasi-experimental study on a community-based stroke prevention programme for clients with minor stroke *Journal of Clinical Nursing*, 16(2), 272-281.
- Skidmore, E. R., Whyte, E. M., Butters, M. A., Reynolds, C. F., & Terhorst, L. (2015). Strategy Training During Inpatient Rehabilitation May Prevent Apathy Symptoms After Acute Stroke *PM and R*, 7(6), 562-570.
- Skivington, K., Matthews, L., Simpson, S. A., Craig, P., Baird, J., Blazeby, J. M., et al. (2021). A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance *BMJ*, *374*, n2061.
- Skogestad, I. J., Kirkevold, M., Larsson, P., Borge, C. R., Indredavik, B., Gay, C. L., et al. (2021). Post-stroke fatigue: an exploratory study with patients and health professionals to develop a patient-reported outcome measure *J Patient Rep Outcomes*, *5*(1), 35.
- Smith, A. C., Saunders, D. H., & Mead, G. (2012). Cardiorespiratory fitness after stroke: a systematic review *International Journal of Stroke*, *7*(6), 499-510.
- Smith, D. S., Goldenberg, E., Ashburn, A., Kinsella, G., Sheikh, K., Brennan, P. J., et al. (1981). Remedial therapy after stroke: a randomised controlled trial *British Medical Journal*, 282(6263), 517.
- Smith, M. A., & Tomita, M. R. (2020). Combined effects of Telehealth and Modified Constraint-Induced Movement Therapy for Individuals with Chronic Hemiparesis *International journal of telerehabilitation*, *12*(1), 51-62.
- Smith, M. C., Barber, P. A., & Stinear, C. M. (2017). The TWIST Algorithm Predicts Time to Walking Independently After Stroke *Neurorehabil Neural Repair*, *31*(10-11), 955-964.
- Society of British Neurosurgeons. (2006). *National study of subarachnoid haemorrhage: final report of an audit carried out in 34 neurosurgical units in the UK and Ireland between 14 September 2001*

- to 13 September 2002. SBNS. https://www.sbns.org.uk/index.php/download_file/view/1677/757/
- Somarouthu, B., Yeddula, K., Wicky, S., Hirsch, J. A., & Kalva, S. P. (2011). Long-term safety and effectiveness of inferior vena cava filters in patients with stroke *Journal of NeuroInterventional Surgery*, *3*(2), 141-146.
- Søndergaard, L., Kasner, S. E., Rhodes, J. F., Andersen, G., Iversen, H. K., Nielsen-Kudsk, J. E., et al. (2017). Patent Foramen Ovale Closure or Antiplatelet Therapy for Cryptogenic Stroke *New England Journal of Medicine*, *377*(11), 1033-1042.
- Song, H., Oh, H., Kim, H., & Seo, W. (2011). Effects of a sexual rehabilitation intervention program on stroke patients and their spouses *NeuroRehabilitation*, *28*(2), 143-150.
- SoSTART Collaboration. (2021). Effects of oral anticoagulation for atrial fibrillation after spontaneous intracranial haemorrhage in the UK: a randomised, open-label, assessor-masked, pilot-phase, non-inferiority trial *Lancet Neurol*, 20(10), 842-853.
- Spokoyny, I., Raman, R., Ernstrom, K., Demaerschalk, B. M., Lyden, P. D., Hemmen, T. M., et al. (2014). Pooled assessment of computed tomography interpretation by vascular neurologists in the STRokE DOC telestroke network *Journal of Stroke & Cerebrovascular Diseases*, 23(3), 511-515.
- Sposato, L. A., Cipriano, L. E., Saposnik, G., Vargas, E. R., Riccio, P. M., & Hachinski, V. (2015). Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis *Lancet Neurology*.
- SPRINT research group. (2015). A Randomized Trial of Intensive versus Standard Blood-Pressure Control *New England Journal of Medicine*, *373*(22), 2103-2116.
- SPS Study Group. (2013). Blood-pressure targets in patients with recent lacunar stroke: the SPS3 randomised trial *Lancet*, *382*(9891), 507-515.
- Stam, J., De Bruijn, S. F., & DeVeber, G. (2002). Anticoagulation for cerebral sinus thrombosis *Cochrane Database of Systematic Reviews*(4), CD002005.
- Steffel, J., Giugliano, R. P., Braunwald, E., Murphy, S. A., Mercuri, M., Choi, Y., et al. (2016). Edoxaban Versus Warfarin in Atrial Fibrillation Patients at Risk of Falling: ENGAGE AF-TIMI 48 Analysis *J Am Coll Cardiol*, 68(11), 1169-1178.
- Steffel, J., Collins, R., Antz, M., Cornu, P., Desteghe, L., Haeusler, K. G., et al. (2021). 2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation *Europace*, 23(10), 1612-1676.
- Stein, J., Shafqat, S., Doherty, D., Frates, E. P., & Furie, K. L. (2003). Patient knowledge and expectations for functional recovery after stroke *American Journal of Physical Medicine & Rehabilitation*, 82(8), 591-596.
- Stinear, C. M., Byblow, W. D., Ackerley, S. J., Barber, P. A., & Smith, M. C. (2017a). Predicting Recovery Potential for Individual Stroke Patients Increases Rehabilitation Efficiency *Stroke*, *48*(4), 1011-1019.
- Stinear, C. M., Byblow, W. D., Ackerley, S. J., Smith, M. C., Borges, V. M., & Barber, P. A. (2017b). PREP2: A biomarker-based algorithm for predicting upper limb function after stroke *Ann Clin Transl Neurol*, *4*(11), 811-820.
- Stockley, R., Peel, R., Jarvis, K., & Connell, L. (2019). Current therapy for the upper limb after stroke: a cross-sectional survey of UK therapists *BMJ Open*, *9*(9), e030262.
- Stockley, R. C., Jarvis, K., Boland, P., & Clegg, A. J. (2021). Systematic Review and Meta-Analysis of the Effectiveness of Mental Practice for the Upper Limb After Stroke: Imagined or Real Benefit? Archives of Physical Medicine and Rehabilitation, 102(5), 1011-1027.
- Stolk-Hornsveld, F., Crow, J. L., Hendriks, E. P., van der Baan, R., & Harmeling-van der Wel, B. C. (2006). The Erasmus MC modifications to the (revised) Nottingham Sensory Assessment: a reliable somatosensory assessment measure for patients with intracranial disorders *Clinical Rehabilitation*, 20(2), 160-172.
- Straudi, S., Baroni, A., Mele, S., Craighero, L., Manfredini, F., Lamberti, N., et al. (2020). Effects of a Robot-Assisted Arm Training Plus Hand Functional Electrical Stimulation on Recovery After Stroke: A Randomized Clinical Trial *Archives of Physical Medicine and Rehabilitation*, 101(2), 309-316.

- Strazzullo, P., D'Elia, L., Cairella, G., Garbagnati, F., Cappuccio, F. P., & Scalfi, L. (2010). Excess body weight and incidence of stroke: meta-analysis of prospective studies with 2 million participants *Stroke*, *41*(5), e418-426.
- Stretton, C. M., Mudge, S., Kayes, N. M., & McPherson, K. M. (2017). Interventions to improve real-world walking after stroke: a systematic review and meta-analysis *Clin Rehabil*, *31*(3), 310-318.
- Stroke Association. (2015). *Struggling to recover*. https://www.stroke.org.uk/resources/struggling-recover
- Stroke Association. (2020). *Stroke Recoveries at Risk Report*. https://www.stroke.org.uk/stroke-recoveries-at-risk-report
- Stroke Association. (2022). Fatigue After Stroke.
 - https://www.stroke.org.uk/sites/default/files/publications/fatigue_after_stroke_guide.pdf
- Stroke Foundation. (2022). Australian and New Zealand Living Clinical Guidelines for Stroke

 Management Chapter 5 of 8: Rehabilitation. https://app.magicapp.org/#/guideline/Kj2R8j
- Stroke Unit Trialists' Collaboration. (2013). Organised inpatient (stroke unit) care for stroke *Cochrane Database of Systematic Reviews*, *9*, CD000197.
- Studer, B., Van Dijk, H., Handermann, R., & Knecht, S. (2016). Increasing self-directed training in neurorehabilitation patients through competition *Progress in Brain Research*, 229, 367-388.
- Sugavanam, T., Mead, G., Bulley, C., Donaghy, M., & van Wijck, F. (2013). The effects and experiences of goal setting in stroke rehabilitation a systematic review *Disability & Rehabilitation*, 35(3), 177-190.
- Sunderland, A., Walker, C. M., & Walker, M. F. (2006). Action errors and dressing disability after stroke: an ecological approach to neuropsychological assessment and intervention *Neuropsychological Rehabilitation*, *16*(6), 666-683.
- Suzuki, K., Aoki, J., Nishiyama, Y., Kimura, K., Matsumaru, Y., Hayakawa, M., et al. (2021). Effect of Mechanical Thrombectomy without vs with Intravenous Thrombolysis on Functional Outcome among Patients with Acute Ischemic Stroke: The SKIP Randomized Clinical Trial *JAMA Journal of the American Medical Association*, 325(3), 244-253.
- Sweeney, K. G., MacAuley, D., & Gray, D. P. (1998). Personal significance: the third dimension *Lancet*, 351(9096), 134-136.
- Takebayashi, T., Takahashi, K., Amano, S., Gosho, M., Sakai, M., Hashimoto, K., et al. (2022). Robot-Assisted Training as Self-Training for Upper-Limb Hemiplegia in Chronic Stroke: A Randomized Controlled Trial *Stroke*, *53*(7), 2182-2191.
- Tally, Z., Boetefuer, L., Kauk, C., Perez, G., Schrand, L., & Hoder, J. (2017a). The efficacy of treadmill training on balance dysfunction in individuals with chronic stroke: a systematic review *Topics in Stroke Rehabilitation*, 24(7), 539-546.
- Tally, Z., Boetefuer, L., Kauk, C., Perez, G., Schrand, L., & Hoder, J. (2017b). The efficacy of treadmill training on balance dysfunction in individuals with chronic stroke: a systematic review *Top Stroke Rehabil*, 24(7), 539-546.
- Tang, Y., Wang, L., He, J., Xu, Y., Huang, S., & Fang, Y. (2021). Optimal Method of Electrical Stimulation for the Treatment of Upper Limb Dysfunction After Stroke: A Systematic Review and Bayesian Network Meta-Analysis of Randomized Controlled Trials *Neuropsychiatr Dis Treat*, *17*, 2937-2954.
- Tao, C., Nogueira, R. G., Zhu, Y., Sun, J., Han, H., Yuan, G., et al. (2022). Trial of Endovascular Treatment of Acute Basilar-Artery Occlusion *New England Journal of Medicine*, *387*(15), 1361-1372.
- Taub, E., Uswatte, G., Bowman, M. H., Mark, V. W., Delgado, A., Bryson, C., et al. (2013). Constraint-induced movement therapy combined with conventional neurorehabilitation techniques in chronic stroke patients with plegic hands: a case series *Arch Phys Med Rehabil*, *94*(1), 86-94.
- Taub, E., Barman, J., Bowman, M. H., Taylor, A., McKay, S., Sloman, S. B., et al. (2021). Tele-rehabilitation of upper-extremity hemiparesis after stroke: Proof-of-concept randomized controlled trial of inhome Constraint-Induced Movement therapy *Restorative Neurology and Neuroscience*, *39*(4), 303-318.
- Tay, J., Morris, R. G., & Markus, H. S. (2021). Apathy after stroke: Diagnosis, mechanisms, consequences, and treatment *Int J Stroke*, *16*(5), 510-518.

- Taylor-Rowan, M., Momoh, O., Ayerbe, L., Evans, J. J., Stott, D. J., & Quinn, T. J. (2019). Prevalence of pre-stroke depression and its association with post-stroke depression: a systematic review and meta-analysis *Psychol Med*, *49*(4), 685-696.
- Taylor, W. J., Brown, M., William, L., McPherson, K. M., Reed, K., Dean, S. G., et al. (2012). A pilot cluster randomized controlled trial of structured goal-setting following stroke *Clinical Rehabilitation*, 26(4), 327-338.
- Teasell, R., Salbach, N. M., Foley, N., Mountain, A., Cameron, J. I., Jong, A. d., et al. (2020). Canadian Stroke Best Practice Recommendations: Rehabilitation, Recovery, and Community Participation following Stroke. Part One: Rehabilitation and Recovery Following Stroke; 6th Edition Update 2019 International Journal of Stroke, 15(7), 763-788.
- Thacker, E. L., Psaty, B. M., McKnight, B., Heckbert, S. R., Longstreth, W. T., Jr., Mukamal, K. J., et al. (2011). Fasting and post-glucose load measures of insulin resistance and risk of ischemic stroke in older adults *Stroke*, *42*(12), 3347-3351.
- Thieme, H., Mehrholz, J., Pohl, M., Behrens, J., & Dohle, C. (2012). Mirror therapy for improving motor function after stroke *Cochrane Database of Systematic Reviews*(3), CD008449.
- Thieme, H., Morkisch, N., Mehrholz, J., Pohl, M., Behrens, J., Borgetto, B., et al. (2018). Mirror therapy for improving motor function after stroke *Cochrane Database of Systematic Reviews*(7), CD008449.
- Tholin, H., & Forsberg, A. (2014). Satisfaction with care and rehabilitation among people with stroke, from hospital to community care *Scandinavian Journal of Caring Sciences*, 28(4), 822-829.
- Thomalla, G., Cheng, B., Gellissen, S., Golsari, A., Gerloff, C., Fiehler, J., et al. (2018). MRI-Guided thrombolysis for stroke with unknown time of onset *New England Journal of Medicine*, *379*(7), 611-622.
- Thomas, K., Gamlin, C., De Simoni, A., Mullis, R., & Mant, J. (2019a). How is poststroke fatigue understood by stroke survivors and carers? A thematic analysis of an online discussion forum *BMJ Open*, *9*(7), e028958.
- Thomas, K., Hjalmarsson, C., Mullis, R., & Mant, J. (2019b). Conceptualising post-stroke fatigue: a cross-sectional survey of UK-based physiotherapists and occupational therapists *BMJ Open*, *9*(12), e033066
- Thomas, L. H., Cross, S., Barrett, J., French, B., Leathley, M., Sutton, C. J., et al. (2008). Treatment of urinary incontinence after stroke in adults *Cochrane Database of Systematic Reviews*(1), CD004462.
- Thomas, L. H., French, B., Sutton, C. J., Forshaw, D., Leathley, M. J., Burton, C. R., et al. (2015).

 Programme Grants for Applied Research. In *Identifying Continence Options after Stroke (ICONS):*an evidence synthesis, case study and exploratory cluster randomised controlled trial of the introduction of a systematic voiding programme for patients with urinary incontinence after stroke in secondary care (Vol. 3, pp. 1). NIHR Journals Library.
- Thomas, S. A., Walker, M. F., Macniven, J. A., Haworth, H., & Lincoln, N. B. (2013). Communication and low mood (CALM): A randomized controlled trial of behavioural therapy for stroke patients with aphasia *Clinical Rehabilitation*, *27*(5), 398-408.
- Thomopoulos, C., Parati, G., & Zanchetti, A. (2015). Effects of blood pressure lowering on outcome incidence in hypertension: 4. Effects of various classes of antihypertensive drugs--overview and meta-analyses *J Hypertens*, *33*(2), 195-211.
- Thomopoulos, C., Parati, G., & Zanchetti, A. (2016). Effects of blood pressure lowering on outcome incidence in hypertension: 7. Effects of more vs. less intensive blood pressure lowering and different achieved blood pressure levels Updated overview and meta-analyses of randomized trials *Journal of Hypertension*, *34*(4), 613-622.
- Thompson, H. S., & Ryan, A. (2009). The impact of stroke consequences on spousal relationships from the perspective of the person with stroke *Journal of Clinical Nursing*, *18*(12), 1803-1811.
- Tieges, Z., Mead, G., Allerhand, M., Duncan, F., van Wijck, F., Fitzsimons, C., et al. (2015). Sedentary behavior in the first year after stroke: a longitudinal cohort study with objective measures *Arch Phys Med Rehabil*, *96*(1), 15-23.

- Tohgi, H., Takahashi, S., Chiba, K., & Hirata, Y. (1993). Cerebellar infarction. Clinical and neuroimaging analysis in 293 patients. The Tohoku Cerebellar Infarction Study Group *Stroke*, *24*(11), 1697-1701.
- TREAT-CAD Trial Investigators. (2021). Aspirin versus anticoagulation in cervical artery dissection (TREAT-CAD): an open-label, randomised, non-inferiority trial *The Lancet Neurology*, *20*(5), 341-350.
- Tsai, C.-S., Wu, C.-L., Chou, S.-Y., Tsang, H.-Y., Hung, T.-H., & Su, J.-A. (2011). Prevention of poststroke depression with milnacipran in patients with acute ischemic stroke: A double-blind randomized placebo-controlled trial *International Clinical Psychopharmacology*, *26*(5), 263-267.
- Tsivgoulis, G., Katsanos, A. H., Grory, B. M., Köhrmann, M., Ricci, B. A., Tsioufis, K., et al. (2019).

 Prolonged Cardiac Rhythm Monitoring and Secondary Stroke Prevention in Patients With Cryptogenic Cerebral Ischemia *Stroke*, *50*(8), 2175-2180.
- Tsivgoulis, G., Triantafyllou, S., Palaiodimou, L., Grory, B. M., Deftereos, S., Köhrmann, M., et al. (2022). Prolonged Cardiac Monitoring and Stroke Recurrence: A Meta-analysis *Neurology*, *98*(19), e1942-e1952.
- Turc, G., Hadziahmetovic, M., Walter, S., Churilov, L., Larsen, K., Grotta, J. C., et al. (2022a). Comparison of Mobile Stroke Unit With Usual Care for Acute Ischemic Stroke Management: A Systematic Review and Meta-analysis *JAMA Neurol*, *79*(3), 281-290.
- Turc, G., Tsivgoulis, G., Audebert, H. J., Boogaarts, H., Bhogal, P., De Marchis, G. M., et al. (2022b). European Stroke Organisation (ESO)-European Society for Minimally Invasive Neurological Therapy (ESMINT) expedited recommendation on indication for intravenous thrombolysis before mechanical thrombectomy in patients with acute ischemic stroke and anterior circulation large vessel occlusion *J Neurointery Surg*, *14*(3), 209.
- Turner-Stokes, L., Fheodoroff, K., Jacinto, J., & Maisonobe, P. (2013). Results from the Upper Limb International Spasticity Study-II (ULIS-II): A large, international, prospective cohort study investigating practice and goal attainment following treatment with botulinum toxin a in real-life clinical management *BMJ Open*, *3*(6), e002771.
- Turner, M., Barber, M., Dodds, H., Dennis, M., Langhorne, P., Macleod, M. J., et al. (2016). Stroke patients admitted within normal working hours are more likely to achieve process standards and to have better outcomes *Journal of Neurology, Neurosurgery & Psychiatry*, 87(2), 138-143.
- Tyagi, S., Lim, D. S. Y., Ho, W. H. H., Koh, Y. Q., Cai, V., Koh, G. C. H., et al. (2018). Acceptance of Tele-Rehabilitation by Stroke Patients: Perceived Barriers and Facilitators *Arch Phys Med Rehabil*, 99(12), 2472-2477.e2472.
- Tyerman, A. (2012). Vocational rehabilitation after traumatic brain injury: models and services *NeuroRehabilitation*, *31*(1), 51-62.
- Tyson, S. F., Chillala, J., Hanley, M., Selley, A. B., & Tallis, R. C. (2006a). Distribution of weakness in the upper and lower limbs post-stroke *Disabil Rehabil*, *28*(11), 715-719.
- Tyson, S. F., Hanley, M., Chillala, J., Selley, A., & Tallis, R. C. (2006b). Balance disability after stroke *Phys Ther*, 86(1), 30-38.
- Tyson, S. F., & Rogerson, L. (2009). Assistive walking devices in nonambulant patients undergoing rehabilitation after stroke: the effects on functional mobility, walking impairments, and patients' opinion *Archives of Physical Medicine & Rehabilitation*, *90*(3), 475-479.
- Tyson, S. F., & Kent, R. M. (2013). Effects of an ankle-foot orthosis on balance and walking after stroke: a systematic review and pooled meta-analysis *Archives of Physical Medicine & Rehabilitation*, 94(7), 1377-1385.
- Tyson, S. F., Vail, A., Thomas, N., Woodward-Nutt, K., Plant, S., & Tyrrell, P. J. (2018). Bespoke versus off-the-shelf ankle-foot orthosis for people with stroke: randomized controlled trial *Clin Rehabil*, 32(3), 367-376.
- United Nations. (2022). *United Nations Convention on Rights of Person's with Disabilities*https://www.un.org/development/desa/disabilities/convention-on-the-rights-of-persons-with-disabilities.html

- Vadas, D., Prest, K., Turk, A., & Tierney, S. (2021). Understanding the facilitators and barriers of stroke survivors' adherence to recovery-oriented self-practice: a thematic synthesis *Disability and Rehabilitation*, 1-12.
- van Asch, C. J., Velthuis, B. K., Rinkel, G. J., Algra, A., de Kort, G. A., Witkamp, T. D., et al. (2015). Diagnostic yield and accuracy of CT angiography, MR angiography, and digital subtraction angiography for detection of macrovascular causes of intracerebral haemorrhage: prospective, multicentre cohort study *BMJ*, *351*, h5762.
- van Asch, C. J. J., Velthuis, B. K., Greving, J. P., van Laar, P. J., Rinkel, G. J. E., Algra, A., et al. (2013). External Validation of the Secondary Intracerebral Hemorrhage Score in The Netherlands *Stroke*, *44*(10), 2904-2906.
- Van Criekinge, T., Truijen, S., Schröder, J., Maebe, Z., Blanckaert, K., van der Waal, C., et al. (2019). The effectiveness of trunk training on trunk control, sitting and standing balance and mobility post-stroke: a systematic review and meta-analysis *Clin Rehabil*, *33*(6), 992-1002.
- van Dalen, J. W., Moll van Charante, E. P., Nederkoorn, P. J., van Gool, W. A., & Richard, E. (2013). Poststroke apathy *Stroke*, *44*(3), 851-860.
- van de Port, I., Wood, D. S., Lindeman, E., & Kwakkel, G. (2007). Effects of exercise training programs on walking competency after stroke: a systematic review *American Journal of Physical Medicine & Rehabilitation*, 86(11), 935-951.
- van Duijnhoven, H. J., Heeren, A., Peters, M. A., Veerbeek, J. M., Kwakkel, G., Geurts, A. C., et al. (2016). Effects of Exercise Therapy on Balance Capacity in Chronic Stroke: Systematic Review and Meta-Analysis *Stroke*, *47*(10), 2603-2610.
- van Straten, A., Hill, J., Richards, D. A., & Cuijpers, P. (2015). Stepped care treatment delivery for depression: a systematic review and meta-analysis *Psychol Med*, *45*(2), 231-246.
- Vanbellingen, T., Kersten, B., Van Hemelrijk, B., Van de Winckel, A., Bertschi, M., Muri, R., et al. (2010). Comprehensive assessment of gesture production: a new test of upper limb apraxia (TULIA) *European Journal of Neurology*, *17*(1), 59-66.
- Vaniyapong, T., Chongruksut, W., & Rerkasem, K. (2013). Local versus general anaesthesia for carotid endarterectomy *Cochrane Database of Systematic Reviews*, *12*, CD000126.
- Varley, R. A., Cowell, P. E., Dyson, L., Inglis, L., Roper, A., & Whiteside, S. P. (2016). Self-administered computer therapy for apraxia of speech: a two-period randomized control trial with crossover *Stroke*, *47*(3), 822-828.
- Veerbeek, J., van Wegen, E., Peppen, R. P. S., Hendriks, E., Rietberg, M. B., Wees, P. J., et al. (2014a). Clinical Practice Guideline for Physical Therapy after Stroke (Dutch: KNGF-richtlijn Beroerte). https://www.dsnr.nl/wp-content/uploads/2012/03/stroke_practice_guidelines_2014.pdf
- Veerbeek, J. M., Kwakkel, G., van Wegen, E. E., Ket, J. C., & Heymans, M. W. (2011). Early prediction of outcome of activities of daily living after stroke: a systematic review *Stroke*, *42*(5), 1482-1488.
- Veerbeek, J. M., van Wegen, E., van Peppen, R., van der Wees, P. J., Hendriks, E., Rietberg, M., et al. (2014b). What is the evidence for physical therapy poststroke? A systematic review and meta-analysis *PLoS One*, *9*(2), e87987.
- Vemmos, K., Ntaios, G., Spengos, K., Savvari, P., Vemmou, A., Pappa, T., et al. (2011). Association between obesity and mortality after acute first-ever stroke: the obesity-stroke paradox *Stroke*, 42(1), 30-36.
- Verberne, D. P. J., van Mastrigt, G., Ponds, R., van Heugten, C. M., & Kroese, M. (2021). Economic evaluation of nurse-led stroke aftercare addressing long-term psychosocial outcome: a comparison to care-as-usual *BMJ Open*, *11*(2), e039201.
- Verberne, D. P. J., Kroese, M. E. A. L., Staals, J., Ponds, R. W. H. M., & van Heugten, C. M. (2022). Nurseled stroke aftercare addressing long-term psychosocial outcome: a comparison to care-as-usual *Disability and Rehabilitation*, *44*(12), 2849-2857.
- Vergouwen, M. D., de Haan, R. J., Vermeulen, M., & Roos, Y. B. (2008). Statin treatment and the occurrence of hemorrhagic stroke in patients with a history of cerebrovascular disease *Stroke*, 39(2), 497-502.

- Verheyden, S. A. F., Weerdesteyn, V., Pickering Ruth, M., Kunkel, D., Lennon, S., Geurts Alexander, C. H., et al. (2013). Interventions for preventing falls in people after stroke *Cochrane Database of Systematic Reviews*(5), CD008728.
- Waddel, G., & Aylward, M. (2005). *The Scientific and Conceptual Basis of Incapacity Benefits*. The Stationary Office.London.
- Wade, D. T. (1992). Measurement in neurological rehabilitation *Current Opinion in Neurology & Neurosurgery*, 5(5), 682-686.
- Wade, D. T., & Halligan, P. W. (2004). Do biomedical models of illness make for good healthcare systems? *BMJ*, *329*(7479), 1398-1401.
- Walker, M. F., Sunderland, A., Fletcher-Smith, J., Drummond, A., Logan, P., Edmans, J. A., et al. (2011). The DRESS trial: a feasibility randomized controlled trial of a neuropsychological approach to dressing therapy for stroke inpatients *Clinical Rehabilitation*, 26, 675-685.
- Walsh, M. E., Galvin, R., Loughnane, C., Macey, C., & Horgan, N. F. (2015). Factors associated with community reintegration in the first year after stroke: a qualitative meta-synthesis *Disability & Rehabilitation*, *37*(18), 1599-1608.
- Wang, T., Dong, L., Cong, X., Luo, H., Li, W., Meng, P., et al. (2021a). Comparative efficacy of non-invasive neurostimulation therapies for poststroke dysphagia: A systematic review and meta-analysis *Neurophysiologie Clinique*, *51*(6), 493-506.
- Wang, X., Ouyang, M., Yang, J., Song, L., Yang, M., & Anderson, C. S. (2021b). Anticoagulants for acute ischaemic stroke *Cochrane Database of Systematic Reviews*(10), CD000024.
- Wang, Y., Wang, Y., Zhao, X., Liu, L., Wang, D., Wang, C., et al. (2013). Clopidogrel with Aspirin in Acute Minor Stroke or Transient Ischemic Attack *New England Journal of Medicine*, *369*(1), 11-19.
- Wang, Y., Meng, X., Wang, A., Xie, X., Pan, Y., Johnston, S. C., et al. (2021c). Ticagrelor versus Clopidogrel in CYP2C19 Loss-of-Function Carriers with Stroke or TIA *New England Journal of Medicine*.
- Wang, Y., Li, S., Pan, Y., Li, H., Parsons, M. W., Campbell, B. C. V., et al. (2023). Tenecteplase versus alteplase in acute ischaemic cerebrovascular events (TRACE-2): a phase 3, multicentre, openlabel, randomised controlled, non-inferiority trial *Lancet*, *40*(10377), P618-619.
- Ward, A. B., Wissel, J., Borg, J., Ertzgaard, P., Herrmann, C., Kulkarni, J., et al. (2014). Functional goal achievement in post-stroke spasticity patients: the BOTOX Economic Spasticity Trial (BEST) *Journal of Rehabilitation Medicine*, *46*(6), 504-513.
- Ward, N. S., Brander, F., & Kelly, K. (2019). Intensive upper limb neurorehabilitation in chronic stroke: outcomes from the Queen Square programme *Journal of Neurology, Neurosurgery & Samp; amp; Psychiatry*, 90(5), 498.
- Wardlaw, J., Brazzelli, M., Miranda, H., Chappell, F., McNamee, P., Scotland, G., et al. (2014). An assessment of the cost-effectiveness of magnetic resonance, including diffusion-weighted imaging, in patients with transient ischaemic attack and minor stroke: a systematic review, meta-analysis and economic evaluation *Health technology assessment (Winchester, England)*, 18, 1-6.
- Wardlaw, J. M., Seymour, J., Cairns, J., Keir, S., Lewis, S., & Sandercock, P. (2004). Immediate computed tomography scanning of acute stroke is cost-effective and improves quality of life *Stroke*, *35*(11), 2477-2483.
- Wardlaw, J. M., Murray, V., Berge, E., del Zoppo, G., Sandercock, P., Lindley, R. L., et al. (2012).

 Recombinant tissue plasminogen activator for acute ischaemic stroke: an updated systematic review and meta-analysis *Lancet*, *379*(9834), 2364-2372.
- Warner, G., Packer, T., Villeneuve, M., Audulv, A., & Versnel, J. (2015). A systematic review of the effectiveness of stroke self-management programs for improving function and participation outcomes: self-management programs for stroke survivors *Disability & Rehabilitation*, 1-23.
- Watkins, C. L., Auton, M. F., Deans, C. F., Dickinson, H. A., Jack, C. I., Lightbody, C. E., et al. (2007). Motivational interviewing early after acute stroke: a randomized, controlled trial *Stroke*, *38*(3), 1004-1009.
- Wattchow, K. A., McDonnell, M. N., & Hillier, S. L. (2018). Rehabilitation Interventions for Upper Limb Function in the First Four Weeks Following Stroke: A Systematic Review and Meta-Analysis of the Evidence *Arch Phys Med Rehabil*, *99*(2), 367-382.

- West, C., Hesketh, A., Vail, A., & Bowen, A. (2005). Interventions for apraxia of speech following stroke *Cochrane Database of Systematic Reviews*(4), CD004298.
- West, C., Bowen, A., Hesketh, A., & Vail, A. (2008). Interventions for motor apraxia following stroke *Cochrane Database of Systematic Reviews*(1), CD004132.
- West, T., & Bernhardt, J. (2012). Physical activity in hospitalised stroke patients *Stroke Res Treat*, *2012*, 813765.
- Westendorp, W. F., Vermeij, J. D., Zock, E., Hooijenga, I. J., Kruyt, N. D., Bosboom, H. J., et al. (2015). The Preventive Antibiotics in Stroke Study (PASS): a pragmatic randomised open-label masked endpoint clinical trial *Lancet*, *385*(9977), 1519-1526.
- Westerlind, E., Persson, H. C., Tornbom, K., & Sunnerhagen, K. S. (2020). Return to work predicts perceived participation and autonomy by individuals with stroke *Disability and Rehabilitation*, 42(25), 3673-3678.
- White, P. M., Bhalla, A., Dinsmore, J., James, M., McConachie, N., Roffe, C., et al. (2015). Standards for providing safe acute ischaemic stroke thrombectomy (on behalf of the British Association of Stroke Physicians British Society of Neuroradiologists Intercollegiate Stroke Working Party Neuroanaesthesia and Neurocritical Care Society of GB and Ireland, UK Neurointerventional Group) Clin Radiol, 72(2), 175.e171-175.e179.
- Whiteley, W. N., Slot, K. B., Fernandes, P., Sandercock, P., & Wardlaw, J. (2012). Risk factors for intracranial hemorrhage in acute ischemic stroke patients treated with recombinant tissue plasminogen activator: a systematic review and meta-analysis of 55 studies *Stroke*, *43*(11), 2904-2909.
- Whiteley, W. N., Adams, H. P., Bath, P. M. W., Berge, E., Sandset, P. M., Dennis, M., et al. (2013). Targeted use of heparin, heparinoids, or low-molecular-weight heparin to improve outcome after acute ischaemic stroke: An individual patient data meta-analysis of randomised controlled trials *The Lancet Neurology*, *12*(6), 539-545.
- Whiteley, W. N., MacRaild, A., Wang, Y., Dennis, M., Al-Shahi Salman, R., Gray, A., et al. (2022). Clinical Diagnosis and Magnetic Resonance Imaging in Patients With Transient and Minor Neurological Symptoms: A Prospective Cohort Study *Stroke*, *53*(11), 3419-3428.
- Wiffen, P. J., Derry, S., Moore, R. A., Aldington, D., Cole, P., Rice, A. S., et al. (2013). Antiepileptic drugs for neuropathic pain and fibromyalgia an overview of Cochrane reviews *Cochrane Database of Systematic Reviews*, *11*, CD010567.
- Wikander, B., Ekelund, P., & Milsom, I. (1998). An evaluation of multidisciplinary intervention governed by functional independence measure (FIMSM) in incontinent stroke patients *Scandinavian Journal of Rehabilitation Medicine*, 30(1), 15-21.
- Wilkinson, D., Zubko, O., Sakel, M., Coulton, S., Higgins, T., & Pullicino, P. (2014). Galvanic vestibular stimulation in hemi-spatial neglect *Frontiers in Integrative Neuroscience*, 8(JAN), Article 4.
- Wilson, D., & Werring, D. J. (2017). Antithrombotic therapy in patients with cerebral microbleeds *Curr Opin Neurol*, *30*(1), 38-47.
- Wilson, D., Ambler, G., Shakeshaft, C., Brown, M. M., Charidimou, A., Al-Shahi Salman, R., et al. (2018). Cerebral microbleeds and intracranial haemorrhage risk in patients anticoagulated for atrial fibrillation after acute ischaemic stroke or transient ischaemic attack (CROMIS-2): a multicentre observational cohort study *The Lancet Neurology*, *17*(6), 539-547.
- Wilson, D., Ambler, G., Lee, K. J., Lim, J. S., Shiozawa, M., Koga, M., et al. (2019). Cerebral microbleeds and stroke risk after ischaemic stroke or transient ischaemic attack: a pooled analysis of individual patient data from cohort studies *The Lancet Neurology*, 18(7), 653-665.
- Wilson, R. D., & Howe, E. C. (2012). A cost-effectiveness analysis of screening methods for dysphagia after stroke *Pm* & *R*, *4*(4), 273-282.
- Winkens, I., Van Heugten, C. M., Wade, D. T., Habets, E. J., & Fasotti, L. (2009). Efficacy of time pressure management in stroke patients with slowed information processing: a randomized controlled trial *Archives of Physical Medicine & Rehabilitation*, *90*(10), 1672-1679.
- Wissel, J., Manack, A., & Brainin, M. (2013). Toward an epidemiology of poststroke spasticity *Neurology*, 80(3 Suppl 2), S13-19.

- Wolf, S. L., Winstein, C. J., Miller, J. P., Taub, E., Uswatte, G., Morris, D., et al. (2006). Effect of constraint-induced movement therapy on upper extremity function 3 to 9 months after stroke: the EXCITE randomized clinical trial *JAMA*, *296*(17), 2095-2104.
- Wolf, S. L., Kwakkel, G., Bayley, M., & McDonnell, M. N. (2016). Best practice for arm recovery post stroke: an international application *Physiotherapy*, 102(1), 1-4.
- World Health Organization. (1978). *Cerebrovascular diseases: a clinical and research classification*. https://apps.who.int/iris/bitstream/handle/10665/37194/WHO_OFFSET_43.pdf?sequence=1&isAllowed=y
- Worthington, E., Hawkins, L., Lincoln, N., & Drummond, A. (2017). The day-to-day experiences of people with fatigue after stroke: Results from the Nottingham Fatigue After Stroke study *International Journal of Therapy and Rehabilitation*, 24(10), 449-455.
- Wressle, E., Eeg-Olofsson, A. M., Marcusson, J., & Henriksson, C. (2002). Improved client participation in the rehabilitation process using a client-centred goal formulation structure *J Rehabil Med*, *34*(1), 5-11.
- Wu, J., Cheng, H., Zhang, J., Yang, S., & Cai, S. (2021). Robot-Assisted Therapy for Upper Extremity Motor Impairment After Stroke: A Systematic Review and Meta-Analysis *Physical Therapy*, 101(4).
- Wu, S., Mead, G., Macleod, M., & Chalder, T. (2015). Model of understanding fatigue after stroke *Stroke*, 46(3), 893-898.
- Xie, Y. L., Wang, S., Wu, Q., & Chen, X. (2021). Vagus nerve stimulation for upper limb motor impairment after ischemic stroke: A meta-analysis *Medicine*, *100*(46), e27871.
- Xu, T., Clemson, L., O'Loughlin, K., Lannin, N. A., Dean, C., & Koh, G. (2018). Risk Factors for Falls in Community Stroke Survivors: A Systematic Review and Meta-Analysis *Arch Phys Med Rehabil*, 99(3), 563-573.e565.
- Xu, W., Lv, M., Wu, S., Jiang, S., Zeng, Z., Fang, Z., et al. (2021). Severe Bleeding Risk of Direct Oral Anticoagulants Versus Vitamin K Antagonists for Stroke Prevention and Treatment in Patients with Atrial Fibrillation: A Systematic Review and Network Meta-Analysis *Cardiovasc Drugs Ther*.
- Yadav, R. K., Sharma, R., Borah, D., & Kothari, S. Y. (2016). Efficacy of Modified Constraint Induced Movement Therapy in the Treatment of Hemiparetic Upper Limb in Stroke Patients: A Randomized Controlled Trial *Journal of clinical and diagnostic research : JCDR*, 10(11), YC01-YC05.
- Yang, J. D., Liao, C. D., Huang, S. W., Tam, K. W., Liou, T. H., Lee, Y. H., et al. (2019). Effectiveness of electrical stimulation therapy in improving arm function after stroke: a systematic review and a meta-analysis of randomised controlled trials *Clin Rehabil*, *33*(8), 1286-1297.
- Yang, P., Zhang, Y., Zhang, L., Li, Z., Zhou, Y., Xu, Y., et al. (2020). Endovascular thrombectomy with or without intravenous alteplase in acute stroke *New England Journal of Medicine*, 382(21), 1981-1993.
- Yang, Y., Zhao, Q., Zhang, Y., Wu, Q., Jiang, X., & Cheng, G. (2018). Effect of Mirror Therapy on Recovery of Stroke Survivors: A Systematic Review and Network Meta-analysis *Neuroscience*, *390*, 318-336
- Yoo, S. H., Kim, J. S., Kwon, S. U., Yun, S. C., Koh, J. Y., & Kang, D. W. (2008). Undernutrition as a predictor of poor clinical outcomes in acute ischemic stroke patients *Arch Neurol*, *65*(1), 39-43.
- Yoshimura, Y., Bise, T., Shimazu, S., Tanoue, M., Tomioka, Y., Araki, M., et al. (2019). Effects of a leucineenriched amino acid supplement on muscle mass, muscle strength, and physical function in post-stroke patients with sarcopenia: A randomized controlled trial *Nutrition*, 58, 1-6.
- Young, A., Gomersall, T., & Bowen, A. (2013). Trial participants' experiences of early, enhanced speech and language therapy after stroke compared with employed visitor support *Clinical Rehabilitation*, *27*(2), 174-182.
- Young, R., Broom, D., O'Brien, R., Sage, K., & Smith, C. (2021). Users' experience of community-based power assisted exercise: a transition from NHS to third sector services *International Journal of Qualitative Studies on Health and Well-being*, *16*(1), 1949899.
- Zaidat, O. O., Fitzsimmons, B. F., Woodward, B. K., Wang, Z., Killer-Oberpfalzer, M., Wakhloo, A., et al. (2015). Effect of a balloon-expandable intracranial stent vs medical therapy on risk of stroke in

NATIONAL CLINICAL GUIDELINE FOR STROKE

for the United Kingdom and Ireland

- patients with symptomatic intracranial stenosis: the VISSIT randomized clinical trial *JAMA*, 313(12), 1240-1248.
- Zeng, W., Guo, Y., Wu, G., Liu, X., & Fang, Q. (2018). Mirror therapy for motor function of the upper extremity in patients with stroke: A meta-analysis *Journal of Rehabilitation Medicine*, *50*(1), 8-15.
- Zhang, C., Qin, Y. Y., Chen, Q., Jiang, H., Chen, X. Z., Xu, C. L., et al. (2014). Alcohol intake and risk of stroke: a dose-response meta-analysis of prospective studies *International Journal of Cardiology*, 174(3), 669-677.
- Zhang, W., Pan, H., Zong, Y., Wang, J., & Xie, Q. (2022). Respiratory Muscle Training Reduces Respiratory Complications and Improves Swallowing Function After Stroke: A Systematic Review and Meta-Analysis Archives of Physical Medicine and Rehabilitation, 103(1179-1191).
- Zhang, Y., Xing, Y., Li, C., Hua, Y., Hu, J., Wang, Y., et al. (2021). Mirror therapy for unilateral neglect after stroke: A systematic review *European Journal of Neurology*, 24, 24.
- Zhao, K., Yang, J., Huang, J., Zhao, Z., & Qu, Y. (2021). Effect of vagus nerve stimulation paired with rehabilitation for upper limb function improvement after stroke: a systematic review and meta-analysis of randomized controlled trials *International journal of rehabilitation research*. *Internationale Zeitschrift fur Rehabilitationsforschung. Revue internationale de recherches de readaptation*, 45(2), 99-108.
- Zhao, N., Sun, W., Xiao, Z., Fan, C., Zeng, B., Xu, K., et al. (2022). Effects of Transcranial Direct Current Stimulation on Poststroke Dysphagia: A Systematic Review and Meta-analysis of Randomized Controlled Trials *Archives of Physical Medicine and Rehabilitation*, 103(7), 1436-1447.
- Zheng, Y., Dang, Y., Wang, L., Cheng, Y., Zhang, X., Mao, M., et al. (2020). Can inspiratory muscle training benefit patients after stroke? A systematic review and meta-analysis of randomized controlled trials *Clinical Rehabilitation*, *34*(7), 866-876.
- Zi, W., Qiu, Z., Li, F., Sang, H., Wu, D., Luo, W., et al. (2021). Effect of Endovascular Treatment Alone vs Intravenous Alteplase Plus Endovascular Treatment on Functional Independence in Patients With Acute Ischemic Stroke: The DEVT Randomized Clinical Trial *JAMA*, 325(3), 234-243.
- Zinkstok, S. M., Vergouwen, M. D. I., Engelter, S. T., Lyrer, P. A., Bonati, L. H., Arnold, M., et al. (2011). Safety and functional outcome of thrombolysis in dissection-related ischemic stroke: A meta-analysis of individual patient data *Stroke*, *42*(9), 2515-2520.
- Zorowitz, R. D., Gillard, P. J., & Brainin, M. (2013). Poststroke spasticity: sequelae and burden on stroke survivors and caregivers *Neurology*, *80*(3 Suppl 2), S45-52.