An Roinn Sláinte
Department of Health

Diagnosis, staging and treatment of patients with rectal cancer

National Clinical Guideline No. 25

December 2020

National Patient Safety Office
Oifig Náisiúnta um Shábháilteacht Othar

NATIONAL CLINICAL EFFECTIVENESS COMMITTEE

This National Clinical Guideline has been developed by the National Cancer Control Programme Guideline Development Group, within the Health Service Executive (HSE).

Using this National Clinical Guideline

This National Clinical Guideline applies to adults (18 years or older) with newly diagnosed rectal cancer, or, those that have a suspected diagnosis of rectal cancer in a hospital setting.

This guideline is intended for all health professionals involved in the diagnosis, staging and treatment of patients with rectal cancer. While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

This guideline is also relevant to those involved in clinical governance, in both primary and secondary care, to help ensure that arrangements are in place to deliver appropriate care for the population covered by this guideline.

Whilst the guideline is focused on clinical care, it is expected to be of interest to patients with rectal cancer and their significant others. Effort has been made to make this document more user friendly. A list of medical abbreviations used throughout the guideline can be found in Appendix 9: Glossary of terms and abbreviations.

Disclaimer

NCEC National Clinical Guidelines do not replace professional judgment on particular cases, whereby the clinician or health professional decides that individual guideline recommendations are not appropriate in the circumstances presented by an individual patient, or whereby an individual patient declines a recommendation as a course of action in their care or treatment plan. In these circumstances the decision not to follow a recommendation should be appropriately recorded in the patient's healthcare record.

Users of NCEC National Clinical Guidelines must ensure they have the current version (hardcopy or softcopy) by checking the relevant section in the National Patient Safety Office on the Department of Health website: https://www.gov.ie/en/collection/c9fa9a-national-clinical-guidelines/

Whilst every care has been taken to ensure that all information contained in this publication is correct, the Department of Health cannot accept responsibility for any errors or omissions which may have occurred.

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Membership of the Guideline Development Group

The Guideline Development Group was chaired by Professor Deborah McNamara, Consultant Colorectal Surgeon, Beaumont Hospital. This National Clinical Guideline is supported by the National Cancer Control Programme (NCCP).

Membership nominations were sought from a variety of clinical and non-clinical backgrounds so as to be representative of all key stakeholders within the Health Service Executive. Guideline Development Group members included those involved in clinical practice, research and library services, and health economics.

The NCCP recognise the importance of patient input and their role as key stakeholders in informing quality improvements in our healthcare system. Patients were engaged via patients' support & advocacy groups and charities and invited to contribute to the development of the guideline from a patient's perspective. This approach assisted in capturing the patient experience which encompassed important quality of life issues and patients' values.

Name	Title/Position	Role on guideline group
Professor Deborah McNamara	Consultant Colorectal Surgeon, BH	Chair and Member
Radiology		
Professor Martina Morrin	Consultant Radiologist, BH	Member
Dr Marie Staunton	Consultant Radiologist, MUH	Member
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Dr David Ryan	Radiology Specialist Registrar, CUH	Member
Dr David Woodlock	Radiology Specialist Registrar, GUH	Member
Dr Aileen O'Shea	Radiology Specialist Registrar, BH	Member
Dr Damien O'Neill	Radiology Specialist Registrar, BH	Member
Pathology		
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Dr Cian Muldoon	Consultant Histopathologist, SJH	Member
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Name	Title/Position	Role on guideline group
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Mr Eddie Myers	Consultant Colorectal Surgeon, PH	Member
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Mr Paul McCormick	Consultant Colorectal Surgeon, SJH	Member (from October 2019)
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Professor Ronan O'Connell	Consultant Colorectal Surgeon, SVUH	Member (from October 2019)
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Project Management		
Ms Keira Doherty-McCullough	Project Manager, NCCP	Project manager and Member (from January 2017)
Ms Deirdre Love	Project Manager, NCCP	Project manager and Member (July 2014 – December 2016)
Ms Angela Clayton-Lea	Project Manager, NCCP	Project manager and Member (December 2012 – May 2014)
Evidence and Research		
Dr Eve O'Toole	Head of Evidence and Quality Hub, NCCP	Methodology Chair and Member
Ms Louise Murphy	Research Officer, NCCP	Research and Member
Dr Helena Gibbons	Senior Research Officer, NCCP	Research and Member (from September 2017)

Name	Title/Position	Role on guideline group
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Ms Maura Flynn	HSE Librarian, HSE Midlands	Information services
Ms Nicola Fay	HSE Librarian, HSE Midlands	Information services
Mr Gethin White	HSE Librarian, HSE East	Information services
Mr Brendan Leen	HSE Librarian, HSE South	Information services
Ms Marie Carrigan	HSE Librarian, SLRON	Information services
Ms Helen Clarke	HSE Librarian, SUH	Information services
Ms Anne Madden	HSE Librarian, SVUH	Information services
Health Economist		
Ms Rebecca Moore	Health Economist, TCD	Health Economist and Member
Patient Representative Groups		
Irish Cancer Society Colorectal Cancer Group		
Mayo Stoma Support Group		
Waterford Stoma Support Group		
Southeast Ostomates		

Key:

BH	Beaumont Hospital
CUH	Cork University Hospital
MMUH	The Mater Misericordiae University Hospital
MUH	Mercy University Hospital
NCCP	National Cancer Control Programme
OLOLH	Our Lady of Lourdes Hospital, Drogheda
PH	Portiuncula Hospital, Ballinasloe
SFH	St. Francis Hospice
SJH	St. James's Hospital
SLRON	St. Lukes Radiation Oncology Network
SUH	Sligo University Hospital
SVUH	St Vincents University Hospital
TCD	Trinity College Dublin
TUH	Tallaght University Hospital
GUH	Galway University Hospital
UHW	University Hospital Waterford
UL	University Hospital Limerick

Credits

The role of the NCEC is to prioritise, quality assure and recommend clinical guidelines to the Chief Medical Officer for endorsement by the Minister for Health. It is intended through Ministerial endorsement that full implementation of the guideline will occur through the relevant service plans.

The NCEC and the Department of Health acknowledge and recognise the Chair and members of the Guideline Development Group for development of the guideline. The NCEC and Department of Health wish to express thanks and sincere gratitude to all persons contributing to this National Clinical Guideline; especially those that give of their time on a voluntary basis.

Acknowledgments

The following credits and acknowledgements are made by the Chair of the Guideline Development Group. The Chair, Professor Deborah McNamara wishes to acknowledge all members of the Guideline Development Group as full contributors credited with having given substantial intellectual leadership to the National Clinical Guideline.

Ms Deirdre Love and Dr Eve O' Toole successfully submitted the guideline for NCEC prioritisation. The Guideline Development Group clinical members, methodology chair, research members and project manager agreed the scope and developed the clinical questions. The Guideline Development Group librarians and research members carried out the systematic searches for evidence. The Guideline Development Group research members reviewed the evidence, appraised the literature and performed the data extraction. The Guideline Development Group led by Professor Deborah McNamara and Dr Eve O'Toole carried out the evidence synthesis including formulation of the evidence summaries and recommendations. Ms Keira Doherty-McCullough, Dr Helena Gibbons and Ms Louise Murphy conducted the budget impact analysis. Professor Deborah McNamara, Ms Keira Doherty-McCullough and Dr Eve O'Toole successfully submitted the guideline for NCEC quality assurance. All Guideline Development Group writing members approved the final guideline. Ms Louise Murphy and Dr Helena Gibbons edited the document and prepared it for publication.

The external review was carried out by Professor Maria A. Hawkins (Professor of Radiation Oncology, University College London), Professor Paul Horgan (Professor of Surgery, University of Glasgow), Mr Fergal Fleming (Assistant Professor of Surgery and Oncology, University of Rochester Medical Center, Rochester, New York), Professor Brian Saunders (Professor of Endoscopy Practice, London North West Hospitals University Healthcare Trust), Dr David Burling (Consultant Radiologist, St. Mark's Hospital, Harrow, UK) and Dr Amitabh Srivastava, (Associate Professor of Pathology, Harvard Medical School).

A full list of members of the Guideline Development Group is available in the previous pages.

Signed by the Chair:
Professor Deborah McNamara 

Date: December, 2020

National Clinical Guidelines

Providing standardised clinical care to patients in healthcare is challenging. This is due to a number of factors, among them diversity in environments of care and complex patient presentations. It is self-evident that safe, effective care and treatment are important in ensuring that patients get the best outcomes from their care.

The Department of Health is of the view that supporting evidence-based practice, through the clinical effectiveness framework, is a critical element of the health service to deliver safe and high quality care. The National Clinical Effectiveness Committee (NCEC) is a Ministerial committee set up in 2010 as a key recommendation of the report of the Commission on Patient Safety and Quality Assurance (2008). The establishment of the Commission was prompted by an increasing awareness of patient safety issues in general and high profile health service system failures at home and abroad.

The NCEC on behalf of the Department of Health has embarked on a quality assured National Clinical Guideline development process linked to service delivery priorities. Furthermore, implementing National Clinical Guidelines sets a standard nationally, to enable healthcare professionals to deliver safe and effective care and treatment while monitoring their individual, team and organisation's performance.

The aim of these National Clinical Guidelines is to reduce unnecessary variations in practice and provide an evidence base for the most appropriate healthcare in particular circumstances. As a consequence of Ministerial mandate, it is expected that NCEC National Clinical Guidelines are implemented across all relevant services in the Irish healthcare setting.

The NCEC is a partnership between key stakeholders in patient safety. NCEC's mission is to provide a framework for national endorsement of clinical guidelines and clinical audit to optimise patient and service user care. The NCEC has a remit to establish and implement processes for the prioritisation and quality assurance of clinical guidelines and clinical audit so as to recommend them to the Minister for Health to become part of a suite of National Clinical Guidelines and National Clinical Audit. The aim of the suite of National Clinical Guidelines is to provide guidance and standards for improving the quality, safety and cost-effectiveness of healthcare in Ireland. The implementation of these National Clinical Guidelines will support the provision of evidence-based and consistent care across Irish healthcare services.

NCEC Terms of Reference

1. Provide strategic leadership for the national clinical effectiveness agenda.
2. Contribute to national patient safety and quality improvement agendas.
3. Publish standards for clinical practice guidance.
4. Publish guidance for National Clinical Guidelines and National Clinical Audit.
5. Prioritise and quality assure National Clinical Guidelines and National Clinical Audit.
6. Commission National Clinical Guidelines and National Clinical Audit.
7. Align National Clinical Guidelines and National Clinical Audit with implementation levers.
8. Report periodically on the implementation and impact of National Clinical Guidelines and the performance of National Clinical Audit.
9. Establish sub-committees for NCEC workstreams.
10. Publish an annual report.

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1 Background

1.1 Impact of rectal cancer in Ireland

Cancer is a major healthcare challenge. Each year in Ireland, approximately 24,793 people are diagnosed with invasive cancer (excluding non-melanoma skin cancer (NMSC)) (National Cancer Registry Ireland (NCRI), 2020). Cancer is the second leading cause of death in Ireland after diseases of the circulatory system. Deaths from cancer averaged about 9,063 deaths per year during 2015-2017 (NCRI, 2020).

Cancer incidence data from the NCRI and population projections from the Central Statistics Office (CSO) have been combined by the NCRI to estimate the number of new cancer cases expected in five year bands from 2020 to 2045. Assuming that average age-standardised rates during 2011-2015 continue to apply ('demographic' projection), annual numbers of cases of all cancers combined (excluding NMSC) are projected to increase in males from 11,460 in 2015 to 24,160 in 2045 (+111%) and in females from 10,240 in 2015 to 18,840 in 2045 (+84%) — a doubling of numbers overall (+98%) (NCRI, 2019b).

Colorectal cancer is the second most common newly diagnosed cancer among men and the third most common among women. Each year approximately 2,800 new cases of colorectal cancer are reported (2018-202) (NCRI, 2020). The incidence of rectal cancer (ICD-10, C19-21) in Ireland is projected to rise. By 2045 the incidence of rectal cancers is projected to increase by 97% in females and 93% in males (based on demographic changes alone) (NCRI, 2019b).

1.2 The National Cancer Control Programme, cancer centres and multidisciplinary teams

The National Cancer Control Programme (NCCP) was established in 2007 to implement the recommendations of the 2006 National Cancer Strategy (Department of Health and Children (DoHC), 2006). In Ireland, there are nine hospitals designated as cancer centres which includes one paediatric cancer centre.

Recommendation 13 of the National Cancer Strategy 2017-2026 (Department of Health, 2017) states "Patients diagnosed with cancer will have their case formally discussed at a multidisciplinary team meeting. The NCCP, working with the Hospital Groups, will oversee and support multidisciplinary team composition, processes and reporting of outcomes"

A multidisciplinary team consists of clinicians representative of the specialities required to diagnose and treat a specific disease. For the implementation of this guideline the multidisciplinary teams must have representation from diagnostic and treatment specialities with experience in rectal cancer.

1.3 Centralisation of services

Cancer patients should have access to high quality care staffed by appropriate specialists to ensure optimal treatment and improve patient outcomes. Recommendation 21 of The National Cancer Strategy 2017-2026 states "The NCCP will draw up a plan setting out which number/location of designated cancer centres in which surgery will take place for the various tumour types. Timescales for the implementation of the plan will be included for each tumour type" (Department of Health, 2017).

The National Cancer Strategy 2017-2026 has set a target that 95% of cancer surgeries performed in public hospitals will be conducted in approved centres by 2020. The NCCP is working together with the Department of Health and the HSE Acute Hospital Division to achieve this goal. It is acknowledged in the implementation plan for this guideline, that centralisation of rectal cancer services is required in order to implement a number of its recommendations. Funding for centralisation of cancer surgeries will be sought through normal service planning processes.

1.4 Colorectal Cancer National Clinical Leads Group

The purpose of the Colorectal Cancer National Clinical Leads Group is to advise on the governance arrangements for colon and rectal cancer services nationally, ensuring it operates as a cohesive national clinical network for the purpose of clinical audit, sharing of good practice and problem solving. Membership of this group includes; clinicians with expertise in colorectal surgery, radiation oncology and medical oncology. Importantly, there is cross over between those involved in the clinical leads group and membership of the rectal Guideline Development Group which is key for the implementation of this guideline.

1.5 Context and scope of this National Clinical Guideline

The National Cancer Strategy (Department of Health and Children (DoHC), 2006) recommended that national, tumour site-specific, multidisciplinary groups be convened to develop national evidence-based clinical guidelines for cancer care. The purpose of developing these guidelines is to improve the quality of care received by patients.

The National Cancer Strategy 2017-2026 (Department of Health, 2017) recommendation 37 states that "the NCCP will develop further guidelines for cancer care in line with National Clinical Effectiveness Committee (NCEC) standards".

A Guideline Development Group was established to develop evidence-based guidelines for the diagnosis, staging and treatment of patients with rectal cancer. The guideline development process is described in detail in Section 3: Development of this National Clinical Guideline. This National Clinical Guideline integrates the best current research evidence with clinical expertise and patient values.

This guideline includes recommendations on the diagnosis, staging, and treatment of patients with rectal cancer. It focuses on areas of clinical practice that are known to be controversial or uncertain, where there is variation in practice, where there is new or emerging evidence, and where there is potential for most impact for the patient and services. It does not include recommendations covering every aspect of diagnosis, staging, and treatment. The aims, objectives and the scope of the guideline are outlined Section 3.3 Aims and objectives.

2 National Clinical Guideline recommendations

2.1 Summary of clinical recommendations, practical considerations around patient care and summary of budget impact analysis

Here follows a list of all the recommendations in this guideline, along with the grade of that recommendation. The grade reflects the level of evidence upon which the recommendations were based, the clinical significance of the evidence, and whether further research is likely to change the recommendation. The levels of evidence and grading systems used are documented in Appendix 10: Levels of evidence & grading systems.

A list of practical considerations around patient care was generated through collaboration with patients and patient representative organisations. The NCCP recognises the importance of patient input and of their role as key stakeholders in informing quality improvements in our healthcare system. This approach assisted in capturing the patient experience and aided discussion on important quality of life issues and patient values.

Recommendation	Grade
Diagnosis and staging	
2.2.1.1 **Initial staging** Contrast enhanced CT-TAP should be employed for the initial staging of patients diagnosed with rectal cancer.	**C**
2.2.1.2 **Hepatic metastases** Hepatocyte specific contrast enhanced MRI of the liver is the best modality for evaluation of liver metastases in patients with rectal cancer.	**A**
2.2.1.3 **Extrahepatic metastases** Currently, PET-CT is not a first-line imaging modality for staging rectal cancer and can be used as a problem solving tool in patients with equivocal imaging findings following a discussion at a multidisciplinary team meeting.	**C**
2.2.2.1 **Imaging for further liver lesions** Hepatocyte specific contrast enhanced MRI of the liver is the imaging modality of choice in patients with rectal cancer with a potentially resectable liver lesion to detect further liver lesions.	**A**
2.2.2.2 **Imaging for further liver lesions** PET-CT can be considered in patients with potentially resectable liver lesion with equivocal imaging findings following discussion at a multidisciplinary team meeting.	**C**
2.2.3.1 Patients with rectal cancer should have an MRI for locoregional staging.	**C**
2.2.3.2 When local expertise (surgical, radiology or gastroenterology) is available, preoperative endorectal ultrasound in low early rectal lesions may be considered to allow for surgical planning following discussion at a multidisciplinary team meeting.	**D**
2.2.4.1 In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available	**D**

Recommendation	Grade
Diagnosis and staging	
2.2.5.1 In patients with rectal cancer, complete visualisation of the entire colon by colonoscopy or CT colonography is recommended prior to surgery. CT colonography should only be performed in centres experienced in the technique	**C**
2.2.5.2 In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available.	**D**
2.2.6.1 In patients undergoing surgery with rectal cancer, it is recommended to identify as many nodes as possible, all of which should be submitted for microscopic examination/ evaluation. Overall, the median for the laboratory should be at least 12.	**C**
2.2.7.1 In patients diagnosed with rectal cancer Haggitt and Kikuchi classification systems may be considered where deemed applicable but are not routinely recommended.	**D**
2.2.8.1 In patients diagnosed with rectal cancer receiving neoadjuvant chemoradiation, it is recommended to employ the modified Ryan tumour regression grading system.	**B**
2.2.9 Staging algorithm for patients with rectal cancer and suspecteced hepatic metastases	
Restaging	
2.3.1.1 In patients with primary rectal cancer, after chemoradiotherapy no radiological investigation to date reliably predicts a pathological complete response.	**C**
2.3.1.2 In patients with primary rectal cancer following chemoradiotherapy where a non-operative strategy is planned frequent multimodal assessment and surveillance including DRE, endoscopy and imaging should be undertaken.	**D**
Treatment: Emergency presentation	
2.4.1.1 **Curative intent** In select patients with obstructing upper rectal cancers stenting as a bridge to surgery may be considered.	**C**
2.4.1.2 **Palliative intent** Stenting can be considered for the palliation of patients with upper rectal cancer (i.e. in those who are not appropriate for immediate resection or in those with advanced disease)	**C**
Treatment: Patients with early rectal cancer	
2.5.1.1 For patients who present with predicted node negative T1 rectal cancer with favourable histopathological features, local excision may be considered.	**B**
2.5.1.2 For patients being treated with curative intent for T1 rectal cancer with unfavourable histopathological features or T2 cancers, TME is recommended.	**B**
2.5.2.1 In patients with rectal cancer who have undergone local excision radical surgery should be considered if adverse pathological features are present.	**B**

Recommendation	Grade
Treatment: Patients receiving neoadjuvant therapy	
2.6.1.1. In patients with stage III rectal cancer preoperative short-course radiotherapy or chemoradiotherapy should be considered.	**B**
2.6.1.2 In patients with rectal cancer, preoperative chemoradiotherapy is recommended for patients with a threatened or involved CRM.	**B**
2.6.2.1 In patients diagnosed with rectal cancer who have an apparent complete clinical response to chemoradiation radical surgery is the standard of care. However, a watch and wait approach should be discussed with the patient and may be considered following shared decision making.	**C**
2.6.3.1 In patients diagnosed with rectal cancer where preoperative therapy has been recommended and the CRM is not threatened or involved short-course radiotherapy or chemoradiotherapy may be considered.	**A**
2.6.3.2 In patients diagnosed with rectal cancer preoperative chemoradiotherapy is recommended for patients with a threatened or involved CRM.	**A**
2.6.4.1 In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiotherapy IMRT and 3D-CRT techniques can both be considered.	**C**
2.6.5.1 In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiation the routine use of a boost is not recommended.	**B**
2.6.5.2 In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiation boost can be considered in selected high risk patients.	**D**
Treatment: Surgical techniques	
2.7.1.1 In patients with rectal cancer high quality total mesorectal excision (TME) surgery should be performed.	**B**
2.7.2.1 There is no clear evidence of difference in postoperative genitourinary function between minimally invasive and open total mesorectal excision (TME)	**D**
Treatment: Patients receiving adjuvant therapy	
2.8.1.1 In patients diagnosed with rectal cancer who have had a resection with a positive margin and have not received preoperative radiotherapy then postoperative chemoradiotherapy is an acceptable salvage approach.	**C**
Treatment: Palliative care	
2.9.1.1 For patients with cancer, early provision of palliative care can improve patient outcomes.	**C**
2.9.1.2 Assessment of palliative care needs should be an ongoing process throughout the course of a patient's cancer illness and services provided on the basis of identified need.	**D**

Practical considerations around patient care
• Patients with rectal cancer should have access to a stoma care/clinical nurse specialist to co-ordinate patients' education and care requirements that impact on quality of life.
• Consider referral of patients with rectal cancer to psycho-oncology and/or a medical social worker for psychological support.
• Patients with rectal cancer should be made aware of voluntary cancer support groups, charities and organisations to contact for support inside and outside the hospital setting.
• Patients with rectal cancer should be fully informed of the side effects of different treatment types they may undergo.
• All healthcare professionals who provide care to patients with rectal cancer should use patient friendly language when communicating with patients about their diagnosis, staging and treatment.
• Patients should be referred for a prehabilitation and preoperative assessment to identify what supports the patient requires.

Summary of budget impact analysis†				
Cost	**2020**	**2021**	**2022**	**Total cost**
Total capital costs for implementing recommendations	€511,744	€511,744	€511,744	€1,535,232
Total revenue costs of implementing the recommendations	Await outcome of surgical centralisation and workforce planning			
Total cost of implementing the guideline				€1,535,232 + Total Revenue costs (TBC)

† See Table 17 Budget impact assessment of staff costs of implementing recommendations for more information.

2.2 Diagnosis and staging

The following are responsible for implementation of the recommendations regarding diagnosis and staging:
While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this National Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

Clinical question 2.2.1

In patients with newly diagnosed rectal cancer, is CT-TAP the best imaging modality for diagnosing:

i) Hepatic metastasis

ii) Extrahepatic metastasis

Evidence summary

Initial staging

An UpToDate review (Macrae and Bendell, 2020) and a clinical guideline (NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®), 2020) addressed the most suitable imaging modality for initial staging of patients with newly diagnosed rectal cancer.

The NCCN (2020) panel recommends that all patients with stage II, III, or IV colorectal cancer undergo chest, abdomen, and pelvic CT before resection. In general, it is preferable to obtain these scans prior to, rather than after surgery, as the scan results will occasionally change surgical planning. (Macrae and Bendell, 2020)

Preoperative imaging for rectal cancer includes chest/abdominal CT and pelvic MRI or chest CT and abdominal/pelvic MRI. (NCCN, 2020)

Hepatic metastases

Three meta-analyses (Niekel et al., 2010, Floriani et al., 2010, Maffione et al., 2015a), an UpToDate review (Macrae and Bendell, 2020) and a clinical guideline (NCCN, 2020) addressed the issue of the most suitable imaging modality for identifying hepatic metastases.

The best meta-analysis from a methodological point of view was deemed to be Niekel et al. (2010). They concluded that MRI is the preferred first-line imaging study for evaluating colorectal cancer liver metastases in patients who have not previously undergone therapy (Table 1) (Niekel et al., 2010).

Table 1 Mean sensitivity (on a per lesion basis) of MRI and CT in the detection of colorectal liver metastases based on lesion size and study year (Niekel et al., 2010)

	Mean sensitivity (%)	
Subgroup	**MRI**	**CT**
Lesion size		
<10mm	60.2 (54.4, 65.7) [n=8]	47.3 (40.1, 54.5) [n=5]
≥10mm	89.0 (81.7, 93.7) [n=8]	86.7 (77.6, 92.5) [n=5]
Study year		
Before January 2004	70.2 (63.2, 76.3) [n=34]	73.4 (61.0, 83.0) [n=20]
After January 2004	84.9 (79.3, 89.2) [n=27]	74.9 (69.1, 79.9) [n=18]
Numbers in parentheses are the 95% CIs, numbers in brackets are numbers of data sets		

In current practice, hepatocyte specific contrast enhanced liver MRI is generally reserved for patients who have suspicious but not definitive findings on CT scan, particularly if better definition of hepatic disease burden is needed in order to make decisions about potential hepatic resection (Macrae and Bendell, 2020).

The consensus of the NCCN panel is that a PET scan is not indicated for preoperative staging of rectal cancer. PET-CT, if done, does not supplant a contrast-enhanced diagnostic CT scan. PET-CT should only be used to evaluate an equivocal finding on a contrast-enhanced CT scan or in patients with a strong contraindication to IV contrast. (NCCN, 2020)

Extrahepatic metastases

An UpToDate review (Macrae and Bendell, 2020) addressed the most suitable imaging modality for identifying patients with extrahepatic metastasis.

The clinical benefit of routine clinical staging with chest CT is also controversial. At least in theory, imaging of the chest might be of more value for rectal cancer since venous drainage of the lower rectum is through the hemorrhoidal veins to the vena cava, bypassing the liver, and lung metastases might be more common (Kirke et al., 2007). (Macrae and Bendell, 2020)

Recommendation 2.2.1.1	Grade
Initial staging Contrast enhanced CT-TAP should be employed for the initial staging of patients diagnosed with rectal cancer.	**C**

Recommendation 2.2.1.2	Grade
Hepatic metastases Hepatocyte specific contrast enhanced MRI of the liver is the best modality for evaluation of liver metastases in patients with rectal cancer.	**A**

Recommendation 2.2.1.3	Grade
Extrahepatic metastases Currently, PET-CT is not a first-line imaging modality for staging rectal cancer and can be used as a problem solving tool in patients with equivocal imaging findings following a discussion at a multidisciplinary team meeting.	**C**

Good Practice Point
If CT with IV contrast is contraindicated, then a non-contrast CT thorax, abdomen and pelvis in addition to an MRI liver should be considered.

Clinical question 2.2.2

In patients diagnosed with rectal cancer with a potentially resectable liver lesion, is MRI of the liver superior to PET-CT in determining the presence of further liver lesions?

Evidence summary

Hepatic metastases

Three meta-analyses (Niekel et al., 2010, Floriani et al., 2010, Maffione et al., 2015a) an UpToDate review (Macrae and Bendell, 2020) and a clinical guideline (NCCN, 2020) addressed the issue of the imaging modality of choice for diagnosing hepatic metastases.

The best meta-analysis from a methodological point of view was deemed to be Niekel et al. (2010). The authors concluded that as there was a limited number of FDG PET/CT studies, no check for heterogeneity could be performed and the number of studies was small, MRI is the preferred first-line imaging study for evaluating colorectal cancer liver metastases in patients who have not previously undergone therapy (Table 2) (Niekel et al., 2010).

Table 2 Mean sensitivity (on a per patient basis) of MRI and FDG PET-CT in the detection of colorectal liver metastases (Niekel et al., 2010)

Modality	Mean sensitivity (%)	Mean specificity (%)
MRI (n=6)*	88.2 (64.8, 96.8) †	92.5 (89.5, 94.6) †
PET-CT (n=3)*	96.5 (94.2, 97.9) †	97.2 (92.8, 99.0) †
* Numbers in parentheses are numbers of data sets † Numbers in parentheses are 95% CIs		

In current practice, hepatocyte specific contrast enhanced liver MRI is generally reserved for patients who have suspicious but not definitive findings on CT scan, particularly if better definition of hepatic disease burden is needed in order to make decisions about potential hepatic resection (Macrae and Bendell, 2020).

The consensus of the NCCN panel is that a PET scan is not indicated for preoperative staging of rectal cancer. PET-CT, if done, does not supplant a contrast-enhanced diagnostic CT scan. PET-CT should only be used to evaluate an equivocal finding on a contrast-enhanced CT scan or in patients with a strong contraindication to IV contrast. (NCCN, 2020)

Recommendation 2.2.2.1	Grade
Imaging for further liver lesions Hepatocyte specific contrast enhanced MRI of the liver is the imaging modality of choice in patients with rectal cancer with a potentially resectable liver lesion to detect further liver lesions.	**A**

Recommendation 2.2.2.2	Grade
Imaging for further liver lesions PET-CT can be considered in patients with potentially resectable liver lesion with equivocal imaging findings following discussion at a multidisciplinary team meeting.	**C**

Good Practice Point

PET-CT scans should only be requested after discussion at a multidisciplinary team meeting.

Clinical question 2.2.3

In patients newly diagnosed with rectal cancer, is MRI superior to endorectal ultrasound in assessing the local extent of tumour?

Evidence summary

A prospective study (Fernández-Esparrach et al., 2011) and a clinical guideline (SIGN, 2016) addressed this clinical question.

Endorectal ultrasound and MRI are useful and comparable techniques for T and N staging of rectal cancer. Endorectal ultrasound performs better than MRI in early stage (T1, T2) cancers, whereas MRI has better results with T3 and T4 lesions (Fernández-Esparrach et al., 2011).

Endoluminal US and MRI have complementary roles in the assessment of tumour depth. In patients with early tumours who may benefit from local excision, endoluminal US can be used to assess the degree of tumour penetration in relation to rectal wall layers (Bipat et al., 2004, Skandarajah and Tjandra, 2006, Puli et al., 2010) (SIGN, 2016).

The consensus of the Guideline Development Group is that endorectal ultrasound outperforms MRI for local staging and sphincter involvement for low rectal cancers. Endorectal ultrasound is a complimentary modality to MRI and is extremely operator dependant. When local expertise (surgical, radiology or gastroenterology) is available, preoperative endorectal ultrasound in low early rectal lesions may be considered to allow for surgical planning following discussion at a multidisciplinary team meeting.

Recommendation 2.2.3.1	**Grade**
Patients with rectal cancer should have an MRI for locoregional staging.	**C**

Recommendation 2.2.3.2	**Grade**
When local expertise (surgical, radiology or gastroenterology) is available, preoperative endorectal ultrasound in low early rectal lesions may be considered to allow for surgical planning following discussion at a multidisciplinary team meeting.	**D**

Good Practice Point

Endorectal ultrasound is a complementary modality to MRI, it is extremely operator dependant and should only be performed in a cancer centre by appropriately trained professionals, following discussion at a multidisciplinary team meeting.

Clinical Question 2.2.4

In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed, is CT colonography necessary prior to surgery?

Evidence summary

One prospective study (Mulder et al., 2011) and two retrospective studies (Flor et al., 2020, Park et al., 2012) addressed this clinical question.

All newly diagnosed colorectal cancer patients (n=13,683) were obtained from the Rotterdam Cancer Registry, and studied for synchronous colorectal cancer between 1995 and 2006. There was a large sample size and the study sample was representative of both the study population and target population (Mulder et al., 2011).

Of 3,168 patients with primary rectal cancer 2.5% of patients were found to have a synchronous colorectal lesion (Table 3) (Mulder et al., 2011). Of those synchronous neoplasms, 39.2% were located in a different surgical segment therefore the detection of a synchronous lesion(s) may change management in a number of patients (Mulder et al., 2011).

Table 3 Tumour localisation and the prevalence of synchronous colorectal cancer (Mulder et al., 2011)

	Sample size (n)	Solitary cancer	Synchronous cancer
Rectum	**3,168 (23.1%)**	**3,088**	**80 (2.5%)**
Left colon	5,985 (43.7%)	5,724	261 (4.4%)
Right colon	4,530 (33.2%)	4,337	193 (4.3%)
Total	13,683	13,149	534 (3.9%)

In obstructing colorectal cancer, pre-operative CT colonography is technically feasible and allows detection of synchronous colonic neoplasms with a high sensitivity. Suboptimal bowel preparation can occur in approximately 3 to 3.6% (Park et al., 2012, Flor et al., 2020) of patients; however the CT colonography completion rate across studies has been greater than 95%.

Park et al. (2012) evaluated CT colonography examinations in 284 patients with stenosing colorectal cancer. The per-patient CT colonography sensitivity for detecting patients harbouring synchronous colorectal cancer and advanced neoplasia in the proximal colon was 100% (6/6 patients) and 88.6% (39/44 patients), respectively. The corresponding per-patient NPV was high, 100% (194/194 patients) for proximal synchronous colorectal cancers and 97.4% (189/194) for advanced neoplasia. Therefore, negative CT colonography findings in the proximal colon exclude the need for additional surgical procedures in the proximal colon with high confidence (Park et al., 2012).

Flor et al. (2020) showed that CT colonography is a highly accurate test for detecting synchronous colonic lesions in patients with occlusive colorectal cancer. The prevalence of advanced neoplasia in their patient cohort was high (23%). They evaluated 70 patients with stenosing colorectal cancer of whom 27 (39%) had at least one 6-mm or larger synchronous lesion, and four patients (6%) had a total of five synchronous colorectal cancers. The overall per-patient CT colonography sensitivity in detecting synchronous lesions 6 mm or larger was 0.93 (25/27); specificity, 0.98 (42/43); PPV, 0.96; and NPV, 0.95. Per-patient sensitivity in the diagnosis of synchronous colorectal cancer was 1.00 (4/4). Per-patient sensitivity for the diagnosis of synchronous advanced neoplasia (advanced adenoma and colorectal cancers) was 0.94 (15/16). Per-lesion CT colonography sensitivity for detecting synchronous lesions 6 mm or larger was 0.88 (37/42), all adenomatous lesions was 0.89 (55/62) and advanced neoplasia, 0.92 (22/24). Per-lesion sensitivity of CT colonography for detecting colorectal cancers was 100% (5/5) (Flor et al., 2020).

Recommendation 2.2.4.1	**Grade**
In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available.	**D**

Good Practice Point
In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed preoperative CT colonography is technically feasible and allows detection of synchronous colonic neoplasm with high sensitivity.

Good Practice Point
In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed preoperative CT colonography should only be perfomed and interpreted by appropriately trained individuals.

Good Practice Point
In patients diagnosed with rectal cancer who show symptoms of an obstruction, CT colonography should be avoided where risk of perforation outweighs potential benefit of identifying synchronous cancer and advanced neoplasia.

Clinical question 2.2.5

In patients diagnosed with rectal cancer, is complete colonoscopy always necessary prior to surgery?

Evidence summary

One meta-analysis (Pickhardt et al., 2011), three randomised control trials (Halligan et al., 2015, Atkin et al., 2013, von Wagner et al., 2012) and one prospective study (Mulder et al., 2011) addressed this clinical question.

An important aspect of preoperative staging is complete visualisation of the colon. When a cancer has been diagnosed a complete colonoscopy or CT colonography should be carried out prior to surgery, if possible, to detect synchronous tumours.

Synchronous colorectal lesions were found in 2.5 % of patients with primary a rectal cancer lesion (Mulder et al., 2011) (Table 4).

Table 4 Tumour localisation and the prevalence of synchronous colorectal cancer (Mulder et al., 2011)

	Sample size (n)	Solitary cancer (n)	Synchronous tumour prevalence (%)
Rectum	**3,168 (23.1%)**	**3,088**	**80 (2.5%)**
Left colon	5,985 (43.7%)	5,724	261 (4.4%)
Right colon	4,530 (33.2%)	4,337	193 (4.3%)
Total	13,683	13,149	534 (3.9%)

The detection of synchronous tumours is important because of the implications for change of surgical management.

CT colonography and colonoscopy detect a similar proportion of cancers (96.1 vs. 94.7%) (Pickhardt et al., 2011) and their costs are also similar according to Halligan et al. (2015). Colonoscopy has the facility to take a biopsy from any suspected lesion and also permits complete removal of most benign lesions during the same procedure. The presence or absence of an obstruction will determine the feasibility of colonoscopy.

Non-completion rates for diagnostic colonoscopy in symptomatic patients are approximately 11-12% (Atkin et al., 2013). Reasons for incompleteness include the inability of the colonoscope to reach the tumour or to visualise the mucosa proximal to the tumour for technical reasons (e.g., partially or completely obstructing cancer, tortuous colon, poor preparation) and patient intolerance of the examination.

In non-emergent obstructing lesions or in the presence of an impending obstruction, where a colonoscopy may not be possible, CT colonography provides a non-invasive alternative (see Clinical Question 2.2.4). CT colonography is more tolerable and acceptable to patients (von Wagner et al., 2012).

Recommendation 2.2.5.1	**Grade**
In patients with rectal cancer, complete visualisation of the entire colon by colonoscopy or CT colonography is recommended prior to surgery. CT colonography should only be performed in centres experienced in the technique.	**C**

Recommendation 2.2.5.2	**Grade**
In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available.	**D**

Clinical question 2.2.6

In patients diagnosed with rectal cancer, is there a minimum number of lymph nodes that need to be identified in a resection specimen and, if so, what is that number?

Evidence summary

Current guidelines (NCCN, 2020, Royal College of Pathologists (RCPath), 2018) addressed this clinical question.

It is very important to emphasise that all of the lymph nodes that can be found in a specimen are examined histologically as the number of lymph nodes identified in resection specimens from patients with stage II and stage III colon cancer has been positively correlated with survival (Chang et al., 2007). The setting of a standard of 12 for the median number of lymph nodes examined per specimen in no way means that pathologists should stop searching for lymph nodes once 12 have been identified. Placing the specimen in a fat-clearing agent for 24 hours, after initial dissection, may be used to help increase nodal yield. Other methods such as GEWF (glacial acetic acid, ethanol, distilled water, formaldehyde) fixation have also been used for this purpose. This approach is not routinely recommended but should be considered if the laboratory has low lymph node yields or in the context of preoperative therapy. Judgement of quality should be on the median number of lymph nodes found by an individual dissector interpreted in the light of the material reported by the individual pathologist. (RCPath, 2018)

Two studies confined only to rectal cancer have reported 14 and >10 lymph nodes as the minimal number to accurately identify stage II rectal cancer (Pocard et al., 1998, Tepper et al., 2001). The number of lymph nodes retrieved can vary with age of the patient, gender, tumour grade, and tumour site (Sarli et al., 2005). For stage II (pN0) colon cancer, if fewer than 12 lymph nodes are initially identified, it is recommended that the pathologist go back to the specimen and resubmit more tissue of potential lymph nodes. If 12 lymph nodes are still not identified, a comment in the report should indicate that an extensive search for lymph nodes was undertaken. The mean number of lymph nodes retrieved from rectal cancers treated with neoadjuvant therapy is significantly less than those treated by surgery alone (13 vs. 19, $p<.05$, 7 vs. 10, $p<.001$) (Wichmann et al., 2002, Baxter et al., 2005). If 12 lymph nodes is considered the number needed to accurately identify stage II tumours, then only 20% of cases treated with neoadjuvant therapy had adequate lymph node sampling (Baxter et al., 2005). To date, the number of lymph nodes needed to accurately stage neoadjuvant-treated cases is unknown. (NCCN, 2020)

A more recent analysis of patients with stage I or II rectal cancer in the SEER database found that OS improved with greater numbers of lymph nodes retrieved (Kidner et al., 2012). (NCCN, 2020)

Recommendation 2.2.6.1	Grade
In patients undergoing surgery with rectal cancer, it is recommended to identify as many nodes as possible, all of which should be submitted for microscopic examination/evaluation. Overall, the median for the laboratory should be at least 12.	**C**

Good Practice Point

Where fewer than 12 nodes are identified, additional effort should be made to identify further lymph nodes, particularly in the area adjacent to the tumour (primary nodal basin).

Good Practice Point

There are many factors which may reduce the number of nodes retrieved in individual cases, including neoadjuvant treatment, patient age and surgical technique.

Clinical question 2.2.7

In patients diagnosed with rectal cancer, are the Haggitt and Kikuchi classification systems sufficiently applicable to recommend their use?

Evidence summary

An International guideline (RCPath, 2018) addressed this clinical question.

Neither Kikuchi (for sessile tumours) nor Haggitt (for polypoid tumours) systems are always easy to use in practice, especially if there is fragmentation or suboptimal orientation of the tissue, and one study found lymph node metastatic disease in 6/24 Haggitt level 3 lesions (Ueno et al., 2004). Kikuchi level requires division of the submucosa into thirds and this is not possible to do accurately unless muscularis propria is included in the specimen, which is rare in most local excision specimens with the exception of some transanal resection specimens. (RCPath, 2018)

Given these difficulties, and resultant limitations on clinical utility of Haggitt and Kikuchi levels, they should be reported as applicable and where possible, in the absence of good evidence as yet to recommend alternative measures. (RCPath, 2018)

Recommendation 2.2.7.1	**Grade**
In patients diagnosed with rectal cancer Haggitt and Kikuchi classification systems may be considered where deemed applicable but are not routinely recommended.	**D**

Clinical question 2.2 8

In patients diagnosed with rectal cancer receiving neoadjuvant chemoradiation:
a) Should a tumour regression grading (TRG) system be employed
b) If so, which one?

a) Multiple grading systems have been shown to predict recurrence and survival outcome.

An International guideline (RCPath, 2018) and a prospective cohort study (Ryan et al., 2005) addressed this clinical question.

"Tumour regression grade is a useful method of scoring tumour response to chemoradiotherapy in rectal cancer" (Ryan et al., 2005).

b) The four tier system currently advocated by the AJCC is recommended, based on a modification of that described by Ryan et al., (2005) and should be applied when any form of preoperative therapy is administered (Amin et al., 2017, Ryan et al., 2005) (Table 5). (RCPath, 2018)

Table 5 Modified Ryan tumour regression grading system

Evaluation	Tumour regression score
No viable cancer cells (complete response)	0
Single cells or rare small groups of cancer cells (near-complete response)	1
Residual cancer with evident tumour regression, but more than single cells or rare small groups of cancer cells (partial response)	2
Extensive residual cancer with no evident tumour regression (poor or no response)	3

Tumour regression should be assessed only in the primary tumour; lymph node metastases should not be included in the grading assessment. A seperate comment may be considered in evaluating the response in lymph nodes.

Recommendation 2.2.8.1	Grade
In patients diagnosed with rectal cancer receiving neoadjuvant chemoradiation, it is recommended to employ the modified Ryan tumour regression grading system.	**B**

2.2.9 Staging algorithm for patients with rectal cancer and suspected hepatic metastases

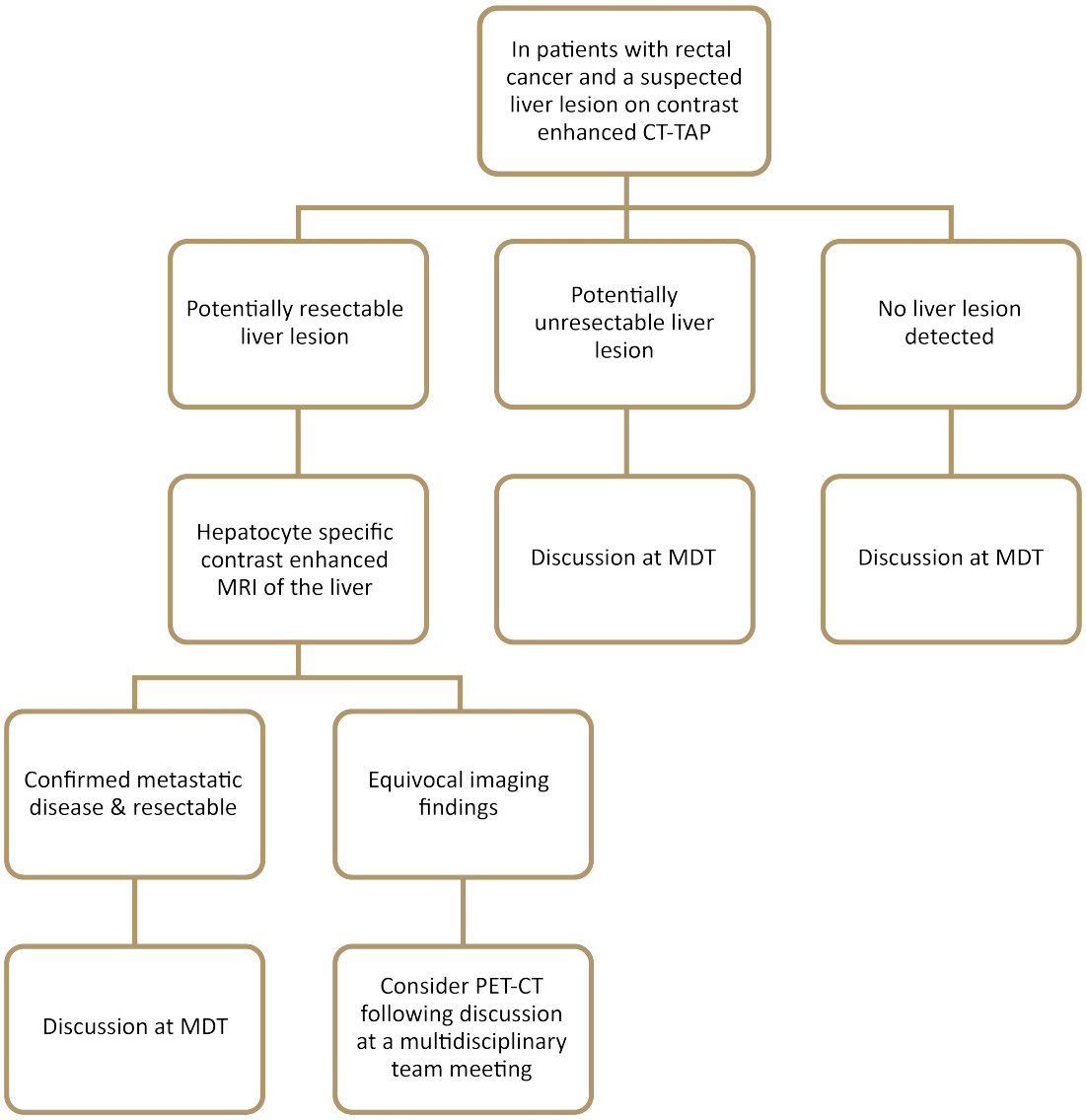


Figure 1 Staging algorithm recommended by the Guideline Development Group for patients with rectal cancer and suspected hepatic metastases

2.3 Restaging

Responsibility for the implementation of recommendations regarding restaging
While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this National Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

Clinical question 2.3.1

In patients diagnosed with rectal cancer who have an apparent complete clinical response to chemoradiation, which radiological investigation best determines if the patient is a complete pathological responder?

Evidence summary

A recent UpToDate review (Willett et al., 2020) has summarised the key findings.

The role of imaging for restaging for assessment of primary tumour and regional nodes after neoadjuvant chemoradiotherapy has been the subject of several studies, and all suggest that neither MRI, CT, transrectal EUS, or integrated PET-CT are sufficiently accurate for identifying the true complete responders (Patel et al., 2011, Kristiansen et al., 2008, Gollub et al., 2012, Perez et al., 2012, Zhang et al., 2012, Guillem et al., 2013, van der Paardt et al., 2013, Zhao et al., 2014, Hanly et al., 2014, Memon et al., 2014, Maffione et al., 2015b). (Willett et al., 2020)

- With MRI it is difficult to differentiate small areas of residual tumour from fibrosis, and readers tend to overestimate the presence of tumour (Zhao et al., 2014, Barbaro et al., 2009, Dresen et al., 2009, Jonas and Bähr, 2006).
- PET-CT findings that suggest a cCR are also associated with a low positive predictive value for a pCR (39% in one systematic review (Joye et al., 2014)). (Willett et al., 2020)

Ryan et al. (2016) stated that molecular profiling may hold the greatest potential to predict pCR but further research is required.

Recommendation 2.3.1.1	**Grade**
In patients with primary rectal cancer, after chemoradiotherapy no radiological investigation to date reliably predicts a pathological complete response.	**C**

Recommendation 2.3.1.2	**Grade**
In patients with primary rectal cancer following chemoradiotherapy where a non-operative strategy is planned frequent multimodal assessment and surveillance including DRE, endoscopy and imaging should be undertaken.	**D**

Good Practice Point

Patients on a watch and wait strategy following chemoradiotherapy should be enrolled on a clinical register.

2.4 Treatment: Emergency presentation

Responsibility for the implementation of recommendations regarding emergency presentation
While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this National Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

Clinical question 2.4.1

In patients diagnosed with obstructive rectal cancer, what is the role of stenting:

(i) When intention of treatment is curative?

(ii) When intention of treatment is palliative?

Evidence summary

Three meta-analyses (Allievi et al., 2017, Ceresoli et al., 2017, Ribeiro et al., 2018), an UpToDate review (Rodriguez-Bigas et al., 2020) and three clinical guidelines (van Hooft et al., 2014, NCCN, 2020, NICE, 2020) addressed this clinical question.

The majority of the evidence is based on left sided malignant colorectal obstruction. There are no specific data on obstructing rectal cancers.

In patients with colorectal cancer there are two major indications for colonic stenting:

- preoperative decompression in patients being treated with curative intent, and
- palliation in patients with advanced disease.

Curative intent

An updated meta-analysis, including seven randomised controlled trials, found no difference in the mortality rate between the stent group and the emergency surgery group (Allievi et al., 2017). The incidence of postoperative complications was significantly reduced in the stent group compared to the emergency surgery group (37.84% vs. 54.87%; RR 0.6, 95% CI 0.38-0.96, p=0.02). Primary anastomosis rate was not significantly different between the groups but stoma rate was significantly reduced in the stenting as a bridge to surgery group (28.8% vs. 46.02%, p<0.0001). Technical and clinical success rate was reported at 78.83% and 75.23% respectively and the perforation rate was 5.89%. (Allievi et al., 2017). Perforation of the tumour has led to two trials being closed prematurely (van Hooft et al., 2011, Pirlet et al., 2011). Stenting has no effect on mortality or recurrence (Ceresoli et al., 2017).

NICE (2020) recommend that either stenting or emergency surgery are offered to patients presenting with acute left-sided large bowel obstruction if potentially curative treatment is suitable. Patients need to be counselled regarding the risk of tumour perforation.

Palliative intent

Endoscopic or radiographic placement of self-expanding metal stent (SEMS) may achieve successful palliation of an obstructing or nearly obstructing tumour.

A meta-analysis including four randomised controlled trials (n=125 patients) in the palliative setting found no significant difference in 30-day mortality, mean survival days or adverse events between the emergency surgery and SEMS group (Ribeiro et al., 2018). Clinical success was higher in the emergency surgery group (96%) than in the SEMS group (84%) (Risk Difference (RD), −0.13, 95% CI −0.23 to −0.02, I^2: 51%). Permanent stoma rate was 84% in the emergency surgery group and 14.3% in the SEMS group (RR, 0.19, 95% CI 0.11-0.33], I^2: 28%).

Among the advantages of SEMS over palliative surgery are a faster recovery time (permitting earlier administration of chemotherapy) and a shorter hospital stay (Tilney et al., 2007, Karoui et al., 2007, Vemulapalli et al., 2010). (Rodriguez-Bigas et al., 2020)

A potential complication includes stent migration. According to the European Society of Gastrointestinal Endoscopy (ESGE) SEMS placement is strongly discouraged for patients who are being treated or considered for further treatment with antiangiogenic drugs (bevacizumab) due to the risk of perforation (van Hooft et al., 2014). The NCCN (2020) panel also cautions that the use of bevacizumab in patients with colon or rectal stents is associated with a possible increased risk of bowel perforation (Small et al., 2010, Cennamo et al., 2009).

Recommendation 2.4.1.1	Grade
Curative intent In select patients with obstructing upper rectal cancers stenting as a bridge to surgery may be considered.	**C**

Recommendation 2.4.1.2	Grade
Palliative intent Stenting can be considered for the palliation of patients with upper rectal cancer (i.e. in those who are not appropriate for immediate resection or in those with advanced disease).	**C**

Good Practice Point
Rectal stent insertion has the potential for significant morbidity and is only suitable in a minority of patients.

Good Practice Point
The risk of colonic perforation should be taken into account in every patient undergoing stenting.

2.5 Treatment: Patients with early rectal cancer

Responsibility for the implementation of recommendations regarding patients with early rectal cancer
While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this National Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

Clinical question 2.5.1

In predicted node negative patients diagnosed with T1 or T2 rectal cancer, what is the evidence for local resection without total mesorectal excision (TME)?

Evidence summary

Three clinical guidelines (SIGN, 2016, NCCN, 2020, ESMO, 2017), two meta-analyses (Rogers et al., 2016, Choi et al., 2015) and six retrospective studies (Saraste et al., 2013, Ozturk et al., 2015, Blumberg et al., 1999, Borschitz et al., 2008, Stornes et al., 2016, Junginger et al., 2016) addressed this clinical question.

The Guideline Development Group considered node negative T1 and T2 tumours exclusively.

The techniques of local excision include:
- transanal excision (TAE)
- transanal endoscopic microsurgery (TEM)
- transanal minimally invasive surgery (TAMIS)

International guidelines are consistent in recommending local excisional procedures as a single modality for node negative T1 early stage cancers without adverse features (NCCN, 2020, ESMO, 2017). More advanced tumours up to and including cT2c/T3a/b should be treated by radical TME surgery because of higher risks of recurrence and the higher risk of mesorectal lymph node involvement (Stornes et al., 2016). (ESMO, 2017)

T1 tumours (those with the smallest local spread) are often deemed suitable for local excision, but it must be stressed that extensive involvement of the submucosa is associated with a 17% rate of lymph node involvement (Kikuchi et al., 1995). Minimal involvement of the submucosa (T1 sm1 tumours) appears to be associated with minimal risk of lymph node involvement. Some rectal cancers may be excised locally and cohort studies indicate that such lesions do not require further surgery unless there is histopathological evidence of tumour at the margin (incomplete excision), lymphovascular invasion, or if the invasive tumour is poorly differentiated (Wolff et al., 1990, Chapman et al., 2000). (SIGN, 2016)

Factors which are known to influence lymph node status or prognosis in early rectal cancer include poor differentiation (Saraste et al., 2013, Choi et al., 2015), vascular invasion (Saraste et al., 2013, Choi et al., 2015), and tumour budding (Rogers et al., 2016, Choi et al., 2015), and should be accounted for when making treatment plans. As yet, perineural invasion and mucinous histology have not demonstrated prognostic potential in this specific subset, but they should be considered due to their association with negative outcomes in all stages of colorectal cancers (Ozturk et al., 2015, Blumberg et al., 1999, NCCN, 2020).

For patients undergoing a local excision, recurrences typically occur within the first three years after treatment. Local recurrences after five years have been reported (Junginger et al., 2016, Stornes et al., 2016).

Immediate reoperation for unfavourable histology is associated with better survival rates and lower rates of local recurrence compared with delayed salvage surgery (Borschitz et al., 2008).

Adjuvant radiotherapy and chemotherapy may reduce local recurrence rates, but a reliable and widely accepted regimen has not yet been developed (Breen and Bleday, 1997). (SIGN, 2016)

Recommendation 2.5.1.1	**Grade**
For patients who present with predicted node negative T1 rectal cancer with favourable histopathological features, local excision may be considered.	**B**

Recommendation 2.5.1.2	Grade
For patients being treated with curative intent for T1 rectal cancer with unfavourable histopathological features or T2 cancers, TME is recommended.	B

Good Practice Point
Every patient undergoing local resection for significant rectal lesion/polyps should be discussed at a multidisciplinary team meeting, ideally prior to the procedure.

Good Practice Point
All patients who have had local excision of rectal cancer should undergo serial clinical and radiological surveillance.

Good Practice Point
Consideration should be given to the potential impact of local excision if a further radical procedure might be required. The risk of compromising further surgery is particularly marked in lower third lesions.

Good Practice Point
TAMIS/TEMS should only be undertaken by someone with appropriately trained surgical expertise and outcomes should be audited.

Clinical question 2.5.2

In patients with early-stage rectal cancer treated with local excision what pathological features indicate that radical surgery is required?

Evidence summary

Three clinical guidelines (CAP, 2017, NCCN, 2020, RCPath, 2018), three meta-analyses (Rogers et al., 2016, Choi et al., 2015, Wada et al., 2015) and three retrospective studies (Saraste et al., 2013, Ozturk et al., 2015, Blumberg et al., 1999) addressed this clinical question.

Following the introduction of the National Bowel Screening Programme in Ireland, early rectal cancers are being diagnosed with increased frequency. Such cancers are expected to have a good prognosis. Local resection of early malignant lesions may be sufficient as the only management. There is a risk of local recurrence or metastatic spread, particularly to local lymph nodes, since the mesorectum, which contains the local lymph nodes, is usually not resected.

A number of meta-analyses have identified risk factors associated with recurrent malignancy or lymph node metastasis following local resections. Choi et al. (2015) revealed that submucosal invasion (≥ SM2 or ≥ 1,000 µm) (odds ratio [OR], 3.00, 95% CI, 1.36-6.62, p=0.007), vascular invasion (OR, 2.70, 95% CI, 1.95-3.74; p<0.001), lymphatic invasion (OR, 6.91, 95% CI, 5.40-8.85; p<0.001), poorly differentiated carcinomas (OR, 8.27; 95% CI, 4.67-14.66; p<0.001) and tumour budding (OR, 4.59; 95% CI, 3.44-6.13; p<0.001) were significantly associated with lymph node metastases. The authors concluded that a more extensive resection accompanied by a lymph node dissection is necessary. Similarly, Wada et al. (2015) revealed two factors significantly associated with T1 colorectal cancer lymph node metastasis: lymphatic vessel invasion identified by an anti-human podoplanin antibody [Mantel–Haenszel OR, 5.19, 95% CI 3.31–8.15; p=0.01] and tumour budding (OR 7.45, 95% CI 4.27–13.02; p=0.0077).

The completeness of the endoscopic excision appears to be the most reliable predictor of tumour recurrence and, although publications vary, it can be assumed that a distance of less than 1mm from the tumour to the margin of excision is associated with a high risk of cancer recurrence (CAP, 2017, RCPath, 2018).

Even when local excision margins are clear, a number of pathological features indicate a higher risk of recurrence or lymph node metastasis, and in such cases radical resection should be considered.

Factors which are known to influence lymph node status or prognosis in early rectal cancer include poor differentiation (Saraste et al., 2013, Choi et al., 2015) vascular invasion (Saraste et al., 2013, Choi et al., 2015), and tumour budding (Rogers et al., 2016, Choi et al., 2015), and should be accounted for when making treatment plans. As yet, perineural invasion and mucinous histology have not demonstrated prognostic potential in this specific subset, but they should be considered due to their association with negative outcomes in all stages of colorectal cancers (Ozturk et al., 2015, Blumberg et al., 1999, NCCN, 2020).

Local excision should only be performed in patients being treated with curative intent when a specimen of sufficient diagnostic quality can be obtained. The specimen should allow detailed pathologic examination including the criteria specified above, and should be discussed at a multidisciplinary team meeting.

Local excision has the potential to render a subsequent attempt at curative resection more technically challenging. In some cases it may compromise the patient's ability to have reconstructive surgery or may require a more radical procedure with adverse quality of life for patients. This risk is particularly marked for tumours of the middle and lower third of the rectum.

Recommendation 2.5.2.1	Grade
In patients with rectal cancer who have undergone local excision radical surgery should be considered if adverse pathological features are present.	B

Good Practice Point
Any suspicious lesions (histologically or endoscopically) should be discussed at a multidisciplinary team meeting involving a colorectal surgeon prior to treatment.

Good Practice Point
Local resection specimens should be of sufficient quality to enable pathological assessment and should be discussed at a multidisciplinary team meeting. A further local excision may be valuable in selected cases.

2.6 Treatment: Patients receiving neoadjuvant therapy

Responsibility for the implementation of recommendations regarding patients receiving neoadjuvant therapy

While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this National Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

Clinical question 2.6.1

In patients diagnosed with rectal cancer, what subgroups of patients would benefit from preoperative radiotherapy or chemoradiotherapy?

Evidence summary

A Cochrane meta-analysis (Abraha et al., 2018) addressed this clinical question.

The meta-analysis included four randomised controlled trials (van Gijn et al., 2011, Sebag-Montefiore et al., 2009, Marsh et al., 1994, Swedish RCT, 1997) that looked at the effect of preoperative radiotherapy on overall survival, disease specific survival and local recurrence. In total, they included 4663 patients with operable rectal cancer. All four included trials were of preoperative SCRT. One of these trials (van Gijn et al., 2011) allowed post operative radiotherapy for positive margins and Sebag-Montefiore et al. (2009) allowed post operative CRT in those with positive margins. TME was mandated in only one trial (van Gijn et al., 2011) and while not mandated occurred in 92% of patients in Sebag-Montefiore et al. (2009). On meta-analysis the mortality proportion was 42.5% in the preoperative radiotherapy group vs 45.4% in the control group, studies = 4; participants = 4,663; Peto odds ratio (OR) 0.90, 95% CI 0.83-0.98; p=0.02. Moderate quality evidence suggests an improvement in OS with preoperative radiotherapy. Two trials published disease specific mortality and meta-analysis shows a mortality proportion of 32.6% in the preoperative radiotherapy group and 31.9% in the control group. Low quality evidence suggests no difference in DSS (studies = 2, participants = 2145; Peto OR 0.89, 95% CI 0.77- 1.03; I^2 = 10%). As regards local recurrence this was mentioned in all 4 trials. LR was 6.7% in the preoperative radiotherapy group and 16.1% in the control group. Moderate quality evidence shows a reduction in pelvic recurrence (studies = 4; participants = 4663; Peto OR 0.48, 95% CI 0.40-0.57; I^2 = 51%, p=0.10).

The meta-analysis carried out various subgroup analyses. Subgroup analysis according to stage was attempted but unsuccessful. Some trials reported Duke's stage while others utilised TNM. Swedish RCT 2007 showed no difference in OS across all stage groups. Van Gijn et al. (2011) published 10 year follow-up data on OS for TNM stage I-III patients. When CRM status was not taken into account there was no survival benefit shown. When analysis was restricted to patients with a negative CRM, 10 year OS was superior in the preoperative radiotherapy group in stage III patients (45% vs 37%; Peto OR 0.76, 95% CI 0.59-0.98). The Swedish RCT (1997) reported LR according to stage, showing lower LR rates for both higher and lower stages. Three studies investigated the distance of the tumour from the anal verge in relation to effect of radiotherapy on local recurrence (van Gijn et al., 2011, Sebag-Montefiore et al., 2009, Swedish RCT, 1997). Due to the difference in the way data was reported between the trials it was not possible to perform meta-analysis. The Swedish RCT (1997) reported lower LR rates for tumour ≤ 5 cm and 6-10 cm from anal verge in those receiving preoperative radiotherapy but not for those at >10 cm. In Sebag-Montefiore et al. (2009) there was a significant reduction in LR at all tumour heights, with the effect of radiotherapy increasing with increasing distance from anal verge. Further supporting the importance of tumour height Van Gijn et al. (2011) reported that for all eligible patients, the effect of radiotherapy became stronger as the distance from the anal verge increased, with a significant distance by treatment interaction (p=0.03). However, when patients in this study with a negative CRM were excluded from the analysis, the relationship between distance from anal verge and effect of radiotherapy disappeared.

Quality of life/Benefit and Harm

Preoperative radiotherapy has been shown to reduce local recurrence and in some studies to improve overall survival. Among the characteristics to be considered when determining the need for preoperative radiotherapy are stage, tumour height, CRM status and distance from the anal verge. Caution is required in interpreting studies due to differences in surgical techniques; preoperative staging techniques; radiotherapy dose, fractionation and technique and reporting of disease stage between different trials.

Recommendation 2.6.1.1	Grade
In patients with stage III rectal cancer preoperative short-course radiotherapy or chemoradiotherapy should be considered.	**B**

Recommendation 2.6.1.2	Grade
In patients with rectal cancer, preoperative chemoradiotherapy is recommended for patients with a threatened or involved CRM.	**B**

Good Practice Point
The potential risks and benefits of preoperative radiotherapy should be considered at the preoperative multidisciplinary team meeting and subsequently discussed with every patient.

Good Practice Point
In patients with rectal cancer, tumour height, stage and CRM status need to be considered in decision making.

Clinical question 2.6.2

In patients diagnosed with rectal cancer who have an apparent complete clinical response to chemoradiotherapy, what is the evidence to support a watch and wait strategy?

Evidence summary

Five meta-analysis of retrospective studies (Chadi et al., 2018, Dattani et al., 2018, Sammour et al., 2017, Dossa et al., 2017, Kim et al., 2017) and a large retrospective study (van der Valk et al., 2018) addressed this clinical question.

The five meta-analysis studies were heterogeneous with different inclusion criteria, intervention, comparisons and outcomes used. They included retrospective studies with different baseline characteristics, neoadjuvant treatment, imaging modalities used and definition of what constitutes a cCR.

The Guideline Development Group agreed that the highest quality evidence currently available to address this clinical question was the individual participant meta-analysis carried out by Chadi et al. (2018) which included 11 studies (n=602 patients) and aimed to investigate factors affecting occurrence of local regrowth.

Chadi et al. sought to include a more uniform population and only included studies in which the definition of clinical complete response was judged to have used criteria equivalent to those of the So Paulo benchmarks described by Habr-Gama and colleagues (Habr-Gama et al., 2004, Habr-Gama et al., 2010). This is defined as absence of residual ulceration, stenosis, or mass within the rectum on clinical and endoscopic examination.

The summary two-year cumulative incidence of local regrowth was 21.4% however, there was a high level of between-study heterogeneity (I^2=61%). Two-year cumulative incidence of local regrowth increased in a stepwise manner from 31% (26–37) for cT3, to 37% (21–60) for cT4. Chadi et al. also reported that in 166 patients with local regrowth, 137 had salvage surgery (random-effects estimate 89% [95% CI 80–98]). R0 status was achieved in 131 of these patients (random-effects 98% [95–100]). The most common reason for no salvage surgery was synchronous distant metastases (12 patients). The three-year incidence of distant metastasis was 9.1% (random effects 95% CI 8.7–9.5) (Chadi et al., 2018).

The Guideline Development Group agrees that the benefit of a watch and wait approach is the potential to avoid radical surgery. The potential harms of a watch and wait approach includes an unsalvageable regrowth or the patient may develop otherwise avoidable metastatic disease.

Recommendation 2.6.2.1	Grade
In patients diagnosed with rectal cancer who have an apparent complete clinical response to chemoradiation radical surgery is the standard of care. However, a watch and wait approach should be discussed with the patient and may be considered following shared decision making.	**C**

Good Practice Point

In a subgroup of high risk patients the harms of surgery may outweigh the benefits and a watch and wait approach should be considered.

Clinical question 2.6.3

In patients diagnosed with rectal cancer, how does short-course preoperative radiotherapy (SCPRT) compare with chemoradiotherapy for survival, toxicity, down-staging (or sphincter preservation), local recurrence rates, and postoperative complications?

Evidence summary

Five randomised trials (Ngan et al., 2012, Bujko et al., 2005, Bujko et al., 2004, Bujko et al., 2006, Bujko et al., 2016, Ciseł et al., 2019, Latkauskas et al., 2016) addressed this clinical question.

Short-course radiotherapy alone with immediate surgery versus chemoradiotherapy

The Guideline Development Group define SCPRT as 5 x 5 Gy over five consecutive days to a total dose of 25 Gy followed by surgery within a week and CRT as 1.8-2.0 Gy per fraction to a total dose of 45-50.4 Gy with concomitant 5FU based chemotherapy, followed by surgery in 4-8 weeks.

Two trials were identified comparing short-course radiotherapy alone with chemoradiotherapy (Bujko et al., 2004, Bujko et al., 2005, Bujko et al., 2006, Ngan et al., 2012).

One randomised study of 312 patients in Poland directly compared conventional fractionation radiotherapy (50.4 Gy in 28 fractions of 1.8 Gy per fraction) in conjunction with bolus FU and LV during weeks 1 and 5 versus short-course radiotherapy (5 x 5 Gy fractions with surgery within seven days of the last RT dose) (Bujko et al., 2006). Early adverse effects were higher in the chemoradiation group (18.2% *vs* 3.2%; $p<0.001$) but there was no significant difference in the actuarial four-year overall survival (67.2% in the short-course group and 66.2% in the chemoradiation group), disease-free survival (58.4% in the short-course group *vs.* 55.6% in the chemoradiation group), crude incidence of local recurrence (9.0% short-course group *vs.* 14.2% in the chemoradiation group) and severe late toxicity (10.1% short-course group *vs.* 7.1% in the chemoradiation group) (Bujko et al., 2006). Despite significant downsizing, chemoradiation did not result in an increased sphincter preservation rate (Bujko et al., 2005). Furthermore there was no significant difference between arms in the numbers of patients with postoperative complications (Bujko et al., 2004).

In addition, an Australian/New Zealand trial (the Trans-Tasman Radiation Oncology Group [TROG] trial 01.04) randomly assigned 326 patients to short-course radiation or conventional fractionation chemoradiotherapy and found no differences in local recurrence and overall survival rates (Ngan et al., 2012). Rates of late toxicity, distant recurrence, and relapse-free survival were also not significantly different between the arms. Patients in the chemoradiotherapy arm were more likely to experience serious adverse events such as radiation dermatitis (0% vs. 5.6%; p=0.003), fatigue (0% vs 3.7%, p=0.016) and grade 3/4 diarrhoea (1.3% vs 14.2% p<0.001). In the short-course arm patients were more likely to have a permanent stoma (38.0% vs. 29.8%; p=0.13) (Ansari et al., 2017). However, no overall difference was seen in health-related quality of life between the groups in the first 12 months, after surgery (McLachlan et al., 2016).

Short-course radiotherapy alone with delayed surgery versus chemoradiotherapy

Studies have been published comparing SCPRT with delayed surgery to standard chemoradiotherapy.
A trial published by Latkauskas et al. (2016), included 150 patients with resectable stage II or III (T3 N0, T4 N0, Tx N+) rectal cancer randomly allocated to receive either SCRT or conventional chemoradiation with surgery 6-8 weeks following completion of radiotherapy. The median number of days from radiotherapy to surgery was 48 in the SCPRT arm and 47 in the CRT arm. The investigators report a pCR rate of 4.4% in the SCPRT arm and 11.1% in the CRT arm (p=0.112). Downstaging was achieved in 30.9% with SCPRT vs 37.5% with CRT (p=0.409). There was no difference in three-year overall survival (78% vs 82.4%; SCRT vs CRT; p=0.145), but an improvement in disease free survival (59% vs. 75.1%; SCPRT vs CRT; p=0.022) with CRT.

Short-course radiotherapy and consolidation neo adjuvant chemotherapy versus chemoradiotherapy

Cisel et al. (2019) published a RCT evaluating SCPRT with consolidation chemotherapy using FOLFOX followed by surgery as compared to neoadjuvant oxaliplatin based chemoradiotherapy. The early results of this study were previously published (Bujko et al., 2016), but are now presented with mature follow-up. 515

patients were included in the final analysis, randomised to SCPRT and chemotherapy, or chemoradiotherapy. The patients randomised to the SCPRT and chemotherapy arm received 5 x 5 Gy followed by three cycles of FOLFOX 4, cycle 1 beginning 1 week post radiotherapy. Oxaliplatin was administered in 70% in the SCPRT group and 66% in the CRT group. The median time from the start of radiotherapy to surgery was the same in both groups (12.4 weeks). Acute toxicity was higher in the CRT arm. Comparing the SCPRT and chemotherapy arm and the CRT arm, radical resection (defined in the trial as –ve CRM and –ve distal resection margin), was achieved in 77% vs 71% (p=0.07), and pCR was 16% vs 12% (p=0.17). There was no difference in post operative complications. There was no difference in overall survival (49% at eight years in both groups) or disease free survival. Late toxicity did not differ, late G3+ toxicity 11% for SCPRT and chemotherapy vs 9% for CRT (p=0.66).

Recommendation 2.6.3.1	**Grade**
In patients diagnosed with rectal cancer where preoperative therapy has been recommended and the CRM is not threatened or involved short-course radiotherapy or chemoradiotherapy may be considered.	**A**

Recommendation 2.6.3.2	**Grade**
In patients diagnosed with rectal cancer preoperative chemoradiotherapy is recommended for patients with a threatened or involved CRM.	**A**

Good Practice Point
In patients diagnosed with rectal cancer who are CRM threatened or involved but not fit for chemoradiotherapy short-course radiotherapy with a delay to surgery may be considered.

Clinical question 2.6.4

In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiotherapy, is IMRT (intensity-modulated radiotherapy) superior to 3D-CRT (three-dimensional conformal radiotherapy) with regard to toxicity and outcomes?

Evidence summary

A meta-analysis of retrospective studies (Wee et al., 2018) and a large retrospective study (Sun et al., 2017) addressed this clinical question.

The meta-analysis, which included six small retrospective studies demonstrated that IMRT resulted in less toxicity compared to 3D-CRT with reduced grade ≥ 2 acute overall GI toxicity and diarrhoea and reduced grade ≥ 2 and ≥ 3 proctitis ($p<0.05$) (Wee et al., 2018).

In a retrospective study of 7386 rectal cancer patients, IMRT significantly increased the rate of positive margins and sphincter loss surgery compared to 3D-CRT; however patient selection biases may have been present. At five years, unadjusted overall survival (follow up range: 1–102 months) was not different between patients who received IMRT vs. 3D-CRT (73 vs. 75 %, $p=0.131$) (Sun et al., 2017).

The potential benefit to the patient with IMRT is a reduction in toxicity, however we do not have randomised data to support this.

Recommendation 2.6.4.1	**Grade**
In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiotherapy IMRT and 3D-CRT techniques can both be considered.	**C**

Clinical question 2.6.5

In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiotherapy, does addition of boost (e.g. EBRT, brachytherapy, simultaneous integrated boost, endocavitary contact x-ray) improve oncological outcomes?

Evidence summary

Three randomised controlled trials (Gerard et al., 2004, Ortholan et al., 2012, Jakobsen et al., 2012, Appelt et al., 2014) addressed this clinical question.

Contact radiotherapy

In a study by Gerard et al. (2004), 88 patients with a rectal carcinoma located in the lower rectum, were randomly assigned to one of two groups: preoperative external-beam radiotherapy (EBRT; 39 Gy in 13 fractions over 17 days) versus the same EBRT with boost (85 Gy in three fractions) using endocavitary contact x-ray. A significant improvement was seen in favour of the contact x-ray boost for complete clinical response (24% *vs.* 2%) and for a complete or near-complete sterilisation of the operative specimen (57% *v* 34%). A significant increase in sphincter preservation was observed in the boost group (76% *vs.* 44%; *P*=.004). At a median follow-up of 35 months, there was no difference in morbidity, local relapse, and 2-year overall survival. Ortholan et al. (2012) reported the 10-year results of this trial and found that the 10-year cumulative colostomy rate was 29% in the EBRT+CXRT group vs. 63% in the EBRT alone group ($p < 0.001$). The 10-year cumulative rate of local recurrence was 15% in the EBRT group vs. 10% in the EBRT+CXRT group (p=0.69). The 10-year disease-free survival and overall survival was similar between the two groups (DFS; 54% vs. 53%, respectively, in the EBRT group vs. The EBRT+CXRT group; p=0.99) and (OS; 56% vs.55%, respectively (p=0.85)).

High dose rate brachytherapy

A prospective randomised trial of 248 patients with locally advanced rectal cancer comparing two radiation doses (arm A: 50.4 Gy in 28 fractions to the tumour and pelvic lymph nodes; arm B: the same treatment supplemented with an endorectal boost given as high-dose-rate brachytherapy [10 Gy in 2 fractions]) and concurrent chemotherapy was carried out by Jakobsen et al. (2012). The rate of R0 resection was different in T3 tumours (90% and 99%; p=.03). The same applied to the rate of major response (tumour regression grade, 1+2), 29% and 44%, respectively (p=.04), indicating that the higher dose increased the rate of major response by 50% in T3 tumours. There was however, no significant difference found in toxicity or surgical complications between the two groups and no significant difference was found in the pathological complete response rate between the two arms (18% and 18%).

Appelt et al. (2014) presented mature data on tumour control and overall survival for the 224 patients in the Danish part of the trial. 221 patients (111 control arm, 110 brachytherapy boost arm) had data available for analysis, with a median follow-up time of 5.4 years. Despite a significant increase in tumour response at the time of surgery, no differences in 5-year OS (70.6% vs 63.6%, HR=1.24, P=.34) or PFS (63.9% vs 52.0%, HR=1.22, p=.32) were observed. Freedom from locoregional failure at 5 years were 93.9% and 85.7% (HR=2.60, p=.06) in the standard and in the brachytherapy arms, respectively. There was no difference in the prevalence of stoma. Explorative analysis based on stratification for tumour regression grade and resection margin status indicated the presence of response migration. Despite increased pathologic tumour regression at the time of surgery, there was no benefit observed on late outcome and improved tumour regression does not necessarily lead to a relevant clinical benefit when the neoadjuvant treatment is followed by high quality surgery.

There is no clear evidence of a reduction in local recurrence however evidence is emerging that there is increased toxicity associated with boost (Couwenberg et al., 2019).

Recommendation 2.6.5.1	Grade
In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiation the routine use of a boost is not recommended.	B

Recommendation 2.6.5.2	Grade
In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiation boost can be considered in selected high risk patients.	D

2.7 Treatment: Surgical techniques

Responsibility for the implementation of recommendations regarding patients receiving specific surgical techniques

While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this National Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

Clinical question 2.7.1

In patients diagnosed with rectal cancer, what is the evidence for specific surgical techniques and the effectiveness of these techniques on patient outcomes?

Evidence summary

Laparoscopic versus open approach

Six randomised control trials COlorectal cancer Laparoscopic or Open Resection (COLOR II) (van der Pas et al., 2013, Bonjer et al., 2015), the COREAN trial (Kang et al., 2010, Jeong et al., 2014), the ACOSOG Z6051 trial (Fleshman et al., 2015, Fleshman et al., 2019), the Australian Laparoscopic Cancer of the Rectum Trial (ALaCaRT) (Stevenson et al., 2015, Stevenson et al., 2019), Robotic versus Laparoscopic Resection for Rectal Cancer (ROLARR) trial (Jayne et al., 2017), a prospective phase II randomised controlled trial (Kim et al., 2018) a Cochrane Review (Schwenk et al., 2005), a meta-analysis (Trastulli et al., 2012) a clinical guideline (SIGN, 2016) and a moratorium (Larsen et al., 2019) addressed this clinical question.

Curative resection of a rectal cancer was traditionally carried out with open techniques (i.e., low anterior resection [LAR] or abdominoperineal resection [APR]). Laparoscopic rectal cancer surgery has been compared with open surgery in four randomised trials with conflicting results (van der Pas et al., 2013, Bonjer et al., 2015, Kang et al., 2010, Jeong et al., 2014, Fleshman et al., 2015, Stevenson et al., 2015).

An international trial COLOR II compared laparoscopic and open resection of rectal cancer (van der Pas et al., 2013, Bonjer et al., 2015). The study randomised 1,044 patients with a solitary adenocarcinoma of the rectum within 15 cm from the anal verge without distant metastases (699 in the laparoscopic-surgery group and 345 in the open-surgery group). Van der pas et al. (2013) reported that completeness of resection was not different between the groups (589 [88%] of 666 vs 303 [92%] of 331; p=0.25), positive circumferential resection margins (<2 mm) were similar comparing laparoscopic and open groups (56 [10%] of 588 vs 30 [10%] of 300; p=0.85). In addition, median distal margin (3 cm [2.0-4.8] vs. 3 cm [1.8-5.0]; p=0.676), and mortality (8 [1%] of 699 vs. 6 [2%] of 345; p=0.409) were also similar. Bonjer et al. (2015) reported that at three years, the locoregional recurrence rate was 5.0% in the two groups (difference, 0 percentage points; 90% CI, −2.6 to 2.6). Disease-free survival rates were 74.8% in the laparoscopic-surgery group and 70.8% in the open-surgery group (95% CI, −1.9 to 9.9). Overall survival rates were 86.7% in the laparoscopic-surgery group and 83.6% in the open-surgery group (95% CI, −1.6 to 7.8).

The safety and short-term efficacy of laparoscopic surgery for rectal cancer after preoperative chemoradiotherapy was assessed in the COREAN trial (Kang et al., 2010, Jeong et al., 2014). The COREAN trial randomised 340 patients (cT3N0–2 mid or low rectal cancer without distant metastasis after preoperative chemoradiotherapy) to receive either open surgery (n=170) or laparoscopic surgery (n=170). Kang et al. (2010) found that involvement of the circumferential resection margin, macroscopic quality of the total mesorectal excision specimen, number of harvested lymph nodes, and perioperative morbidity did not differ between the two groups. Jeong et al. (2014) reported the three year disease-free survival was 72.5% (95% CI. 65.0–78.6) for the open surgery group and 79.2% (72.3–84.6) for the laparoscopic surgery group, with a difference that was lower than the pre-specified non-inferiority margin (–6.7%, 95% CI –15.8 to 2.4; p<0·0001).

The ACOSOG Z6051 randomised trial aimed to determine whether laparoscopic resection is non-inferior to open resection (Fleshman et al., 2015). 486 patients with clinical stage II or III rectal cancer within 12 cm of the anal verge were randomised after completion of neoadjuvant therapy to laparoscopic (n=243) or open resection (n=243). The primary endpoints were successful pathologic outcome, distal margin without tumour, and completeness of total mesorectal excision. A successful outcome (defined as a negative distal and circumferential radial margin) occurred in 81.7% of laparoscopic resections (95% CI, 76.8%-86.6%) and 86.9% of open resections (95% CI, 82.5%-91.4%), which did not support non-inferiority (p=0.41). A follow-up study reported no difference for two-year disease-free survival (laparoscopic 79.5 % vs. open 83.2 %), local and regional recurrence (laparoscopic 4.6 % vs. open 4.5 %), and distant recurrence (laparoscopic 14.6 % vs. open 16.7 %) (Fleshman et al., 2019). However it did not exclude the benefit of open over laparoscopic resection.

The Australian Laparoscopic Cancer of the Rectum Trial (ALaCaRT) aimed to determine whether laparoscopic resection is non-inferior to open rectal cancer resection for adequacy of cancer clearance (Stevenson et al., 2015). 475 patients with T1-T3 rectal adenocarcinoma less than 15 cm from the anal verge were randomised to laparoscopic resection (n=237) or open rectal cancer resection (n=238). The primary endpoint was successful resection, similar to the above study. Successful resection was achieved in 194 (82%) of 238 patients in the laparoscopic group vs. 208 (89%) of 237 patients in the open surgery group. Similarly, laparoscopic surgery failed to achieve the non-inferiority criteria (p=0.38). A follow-up study reported similar results for two-year disease-free survival (laparoscopic 80% vs. open 82%), overall survival (laparoscopic 94 % vs. open 93 %), and local and regional recurrence (laparoscopic 5.4% vs. open 3.1%) (Stevenson et al., 2019).

A Cochrane Review by Schwenk et al. (2005) analysed 25 randomised controlled trials for short-term (surgery to 3 months postoperative) benefits of laparoscopic colorectal resection. Operative time was longer in laparoscopic surgery, but intraoperative blood was less than in conventional surgery. Intensity of postoperative pain and duration of postoperative ileus was shorter after laparoscopic colorectal resection and pulmonary function was improved after a laparoscopic approach. Total morbidity and local (surgical) morbidity was decreased in the laparoscopic groups. General morbidity and mortality was not different between both groups. Until the 30th postoperative day, quality of life was better in laparoscopic patients. Postoperative hospital stay was less in laparoscopic patients.

The best surgical approach needs to be determined individually by tumour and patient characteristics, as well as surgeon experience. When performing laparoscopic rectal surgery for cancer, surgeons should have a low threshold for converting to open surgery when difficulties arise with dissection.

Benefits vs. Harms

Open surgery may be associated with a higher quality pathological specimen when compared to laparoscopy, which would be predicted to have an impact on local recurrence and survival.

Laparoscopic rectal cancer surgery is associated with short-term benefits such as less postoperative pain, shorter length of stay, less blood loss, lower wound morbidity. The issue of sexual and urinary dysfunction is addressed in clinical question 2.7.2.

Anastomotic leakage is one of the most significant complications after resection with anastomosis for rectal cancer. The rates are equivalent between open and laparoscopic (Kang et al., 2010, Stevenson et al., 2015). Leakage is increased with a low (<5 cm form anorectal junction) anastomosis (Rullier et al., 1998). (SIGN, 2016)

Robot-assisted laparoscopic vs conventional laparoscopic resection

A randomised controlled trial and a meta-analysis compared robot-assisted laparoscopic resection and conventional laparoscopic resection in patients with rectal cancer (Jayne et al., 2017, Trastulli et al., 2012).

In the ROLARR trial, 471 patients with rectal adenocarcinoma suitable for curative resection were randomly assigned to receive conventional laparoscopic surgery or robotic-assisted laparoscopic surgery (234 v 237) (Jayne et al., 2017). The short-term results to 6-month follow-up found that the overall rate of conversion to open laparotomy was 12.2% (28 of 230 patients) in the conventional laparoscopic group and 8.1% (19 of 236 patients) in the robotic assisted laparoscopic group (unadjusted difference in proportions, 4.1% [95% CI,1.4% to 9.6%]). There was no statistically significant difference between robotic-assisted and conventional laparoscopic surgery with respect to odds of conversion (adjusted OR=0.61 [95% CI, 0.31-1.21]; p=.16), circumferential resection margin positivity (adjusted OR = 0.78 [95% CI, 0.35-1.76]; p=.56) and intraoperative (adjusted OR=1.02 [95% CI, 0.60-1.74]; p=.94) and postoperative (adjusted OR 0.72 [95% CI, 0.41-1.26]; p=.25) complications. 30-day mortality was low at 0.9% and there was no significant difference in bladder and sexual dysfunction (Jayne et al., 2017).

Benefit vs Harms

Robot-assisted rectal surgery has demonstrated higher costs, longer intra-operative set-up times and longer procedure times (Jayne et al., 2017, Kim et al., 2018). In the ROLARR trial there was no difference in urogenital function between the conventional laparoscopic surgery or robotic-assisted laparoscopic surgery (Jayne et al., 2017). Rates of anastomotic leakage in robotic (6.7% [22/316]) and laparoscopic (7.5% [32/424]) resections have also been found to be similar OR = 0.91, 95% CI 0.52-1.61, p=0.76 (Trastulli et al., 2012).

TaTME

TaTME is a transanal technique, performed in conjunction with laparoscopic protectomy that may facilitate sphincter preservation in complex low rectal cancer. There is an international register of patients undergoing this novel technique and long-term outcomes remain to be determined but concern has been expressed about the risk of atypical local reccurrence related to this procedure (Larsen et al., 2019). As a result it is recommended that this should only be performed by surgeons formally trained in its use and that every patient undergoing this procedure should be included in a international registry.

Recommendation 2.7.1.1	Grade
In patients with rectal cancer high quality total mesorectal excision (TME) surgery should be performed.	**B**

Good Practice Point
Laparoscopic resection should only be performed by surgeons experienced in laparoscopic rectal cancer resection.

Good Practice Point
Laparoscopic resection should not be performed without HD laparoscopic equipment.

Good Practice Point
Patients should be informed that all minimally invasive procedures may require conversion to open surgery to ensure optimal oncological results.

Good Practice Point
New techniques are currently in evolution. These techniques should only be undertaken by surgeons trained in their use, patient outcomes should be audited.

Clinical question 2.7.2

In patients diagnosed with rectal cancer undergoing radical resection is minimally invasive or open total mesorectal excision (TME) more likely to preserve postoperative sexual and/or urinary function?

Evidence summary

A Cochrane review (Vennix et al., 2014), meta-analysis (Broholm et al., 2015), systematic review (Celentano et al., 2017) and two randomised trials (Jayne et al., 2017, Andersson et al., 2014) addressed this clinical question.

There is moderate quality evidence that laparoscopic TME leads to better short-term post-surgical outcomes in terms of recovery for non-locally advanced rectal cancer. There was no clear evidence of any differences in quality of life after laparoscopic or open TME regarding functional recovery, bladder and sexual function.

The reports on bladder and sexual functioning suffered from low response rates, varying from 71% overall response rate down to 10% on specific questions about sexual enjoyment and problems (Vennix et al., 2014).

Kang et al. (2010) showed that sexual function was better 3 months after surgery than at baseline (open group 92.5 *vs* 83.6, p<0.0001; laparoscopic group 90.9 *vs* 81.2 p<0.0001). In contrast, male sexual problems were worse three months after surgery but there was no difference between both groups. The laparoscopic TME group had significantly fewer micturition, gastrointestinal and defecation problems at three months after surgery. (Vennix et al., 2014)

MRC CLASICC (2005a; 2005b) both reported on participants in the CLASICC trial, but used different populations, questionnaires and time points. Jayne et al. (2005) showed worse sexual functioning after laparoscopic TME (overall function: difference −11.18 (95% CI −22.99 to 0.63), p=0.063; erectile function: difference −5.84 (95% CI −10.94 to −0.74), p=0.068) but none were statistically significant. No differences in sexual interest, activity and enjoyment were seen at any time point, although for women there was a significant decrease compared to the preoperative baseline for both groups. (Vennix et al., 2014) Similarly the Colorectal cancer Laparoscopic or Open Resection (COLOR II) randomised trial, comparing laparoscopic and open surgery found no significant differences regarding sexual dysfunction or micturition problems at any time point for patients (Andersson et al., 2014). The available data suggests that neither laparoscopic nor open surgery demonstrates superiority in preservation of sexual and bladder function (Celentano et al., 2017).

Long-term results for laparoscopic and open TME are consistent in showing a similar disease-free survival (OR 1.02; 95% CI 0.76-1.38, n=943) and overall survival (OR 1.15; 95% CI 0.87-1.52, n=957), and local recurrence (OR 0.89; 95% CI 0.57-1.39, n=1,538), although due to imprecision we cannot rule out superiority of either approach. We await long-term data from a number of ongoing and recently completed studies to contribute to a more robust analysis of long-term disease free, overall survival and local recurrence (Vennix et al., 2014).

A meta-analysis (Broholm et al., 2015) on urological and sexual dysfunction after robot-assisted rectal cancer surgery suggested improved function compared to laparoscopic surgery. International Prostate Symptom Scores (IPSS) at 3- and 12-month follow-up showed a small but significant difference in favour of robotic surgery (mean difference [MD] -1.58, 95% CI -3.1 to -0.05, p=0.04; MD -0.90, 95% CI -1.81 to 0.02, p=0.05, respectively). However, the quality of the evidence was low. Similarly International Index of Erectile Function (IIEF) scores at 3- and 6-month follow-up were also better after robot-assisted surgery (MD -2.59, 95% CI -4.25 to -0.94, p=0.002; MD -3.06, 95% CI -4.53 to -1.59, p=0.0001, respectively). However, the ROLARR trial found no significant difference in urogenital function from baseline to 6 months between conventional laparoscopic and robotic-assisted laparoscopic surgery (Jayne et al., 2017).

There is very little information in the literature to address genitourinary function in female patients and what was available in the Cochrane review (Vennix et al., 2014) was underpowered. There is no evidence to

date in favour of any surgical approach (open vs laparoscopic vs robotic) and further studies are needed with long-term follow-up (Celentano et al., 2017).

Recommendation 2.7.2.1	Grade
There is no clear evidence of difference in postoperative genitourinary function between minimally invasive and open total mesorectal excision (TME).	D

Good Practice Point
The risk of impaired genitourinary function following treatment for rectal cancer should be discussed with patients during the informed consent process. Supportive services and information should be made available to patients.

2.8 Treatment: Patients receiving adjuvant therapy

Responsibility for the implementation of radiation oncology recommendations
While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this National Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

Clinical question 2.8.1

In patients diagnosed with rectal cancer, does postoperative radiotherapy or chemoradiotherapy compensate for positive surgical margins?

Evidence summary

Several randomised controlled trials addressed this clinical question (Marijnen et al., 2003, Sebag-Montefiore et al., 2006, Sauer et al., 2004).

The use of short-course preoperative radiotherapy (SCPRT) did not influence the risk of local recurrence if the circumferential resection margin (CRM) was involved (1mm or less), 9.3% vs 16.4%; p=0.08 and 13.8% vs 20.7% (HR 0.64, 95% CI 0.25-1.64)) for the Dutch TME (Marijnen et al., 2003) and UK MRC CR07 (Sebag-Montefiore et al., 2009) trials, respectively. Postoperative radiotherapy or chemoradiotherapy (CRT) has not been shown to compensate adequately for an involved CRM in either trial.

Of 120 patients in the surgery-only group with a positive CRM, 47% received postoperative radiotherapy, in the Dutch trial. There was no difference in the local recurrence rate between the irradiated and non-irradiated patients (17.3% vs. 15.7%, p=0.98) (Marijnen et al., 2003).

In the German GAO/ARO/AIO-94 trial (Sauer et al., 2004), 402 patients were randomised to receive postoperative chemoradiotherapy. When compared to patients who were randomised to preoperative radiotherapy, the overall five-year survival rates were 76% and 74%, respectively (p=0.80). The five-year cumulative incidence of local relapse was 6% vs. 13% (p=0.006). Grade 3 or 4 acute toxic effects occurred in 27% of the patients in the preoperative-treatment group, as compared with 40% in the postoperative-treatment group (p=0.001); the corresponding rates of long-term toxic effects were 14% and 24%, respectively (p=0.01).

If a patient had a resection and has not received preoperative therapy then postoperative chemoradiotherapy is an acceptable salvage approach.

Recommendation 2.8.1.1	Grade
In patients diagnosed with rectal cancer who have had a resection with a positive margin and have not received preoperative radiotherapy then postoperative chemoradiotherapy is an acceptable salvage approach.	**C**

2.9 Treatment: Palliative Care

Responsibility for the implementation of palliative care recommendations
While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this National Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

Clinical question 2.9.1

When should palliative care be introduced for patients with cancer?

Evidence summary

Palliative care is an approach that improves the quality of life of people and their families facing the problems associated with life-limiting illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual (World Health Organization, 2014). It is a vital and integral part of all clinical practice.

When combined with standard cancer care or as the main focus of care, palliative care leads to better patient and caregiver outcomes. These include improvement in symptoms, quality of life (QOL), and patient satisfaction, with reduced caregiver burden. Earlier involvement of palliative care also leads to more appropriate referral to and use of hospice, and reduced use of futile intensive care (Smith et al., 2012). No trials to date have demonstrated harm to patients and caregivers from early involvement of palliative care (Smith et al., 2012).

A 2013 literature review on the cost and cost-effectiveness of palliative care found that despite wide variation in study type, characteristics and study quality, there are consistent patterns in the results. Palliative care is most frequently found to be less costly relative to comparator groups, and in most cases, the difference in cost is statistically significant. (Smith et al., 2014)

Good clinical practice dictates that assessment of palliative care needs should be an ongoing process throughout the course of a patient's illness; assessments should be carried out at key transition points in the patient pathway, for example:

- At diagnosis of a life-limiting condition
- At episodes of significant progression/exacerbation of disease
- A significant change in the patient's family/social support
- A significant change in functional status
- At patient or family request
- At end of life. (Health Service Executive (HSE), 2014)

Palliative care services should be structured in three levels of ascending specialisation according to the expertise of the staff providing the service (Department of Health, 2001):

- Level one (Palliative Care Approach): Palliative care prinicples should be appropriately applied by all healthcare professionals.
- Level two (General Palliative Care): At an intermediate level, a proportion of patients and families will benefit from the expertise of healthcare professionals who, although not engaged full time in palliative care, have had some additional training and experience in palliative care.
- Level three (Specialist Palliative Care): Specialist palliative care services are those services whose core activity is limited to the provision of palliative care.

All patients should be able to engage easily with the level of expertise most appropriate to their needs.

Recommendation 2.9.1.1	**Grade**
For patients with cancer, early provision of palliative care can improve patient outcomes.	**C**

Recommendation 2.9.1.2	**Grade**
Assessment of palliative care needs should be an ongoing process throughout the course of a patient's cancer illness and services provided on the basis of identified need.	**D**

Good Practice Point

Palliative care specialist services should be an integral part of the colorectal cancer multidisciplinary team meeting.

3 Development of this National Clinical Guideline

3.1 Epidemiology

3.1.1 Incidence

The estimated annual average incidence for colorectal cancer in Ireland between 2018 and 2020 was 2,818 cases per annum (Table 6), which represents 11.4% of invasive cancers (excluding non-melanoma skin cancer (National Cancer Registry Ireland (NCRI), 2020).

Table 6 Estimated annual average incidence for colorectal cancer in Ireland, 2018–2020 (NCRI, 2020)

Colorectal Cancer	Cases		
	Males	Females	Total
Colon C18*	1,038	853	1,891
Rectosigmoid junction C19*	108	79	187
Rectum C20*	487	253	740
Total	1,633	1,185	2,818

*C18 – malignant neoplasm of colon; C19 – malignant neoplasm of rectosigmoid junction; C20 – malignant neoplasm of rectum.

In 2020 the European Cancer Information System (ECIS) estimated age-standardised incidence rate of colorectal cancer in males in Ireland of 68.1 per 100,000 was 17.0% higher than the EU27 rate of 58.2 per 100,000, while the estimated age-standardised incidence rate in females in Ireland of 43.7 per 100,000 was 19.7% higher than the EU27 rate of 36.5 per 100,000 (ECIS, 2020).

Table 7 shows the annual average estimated percentages and rank of the most commonly diagnosed invasive cancers in Ireland from 2018 –2020. Excluding non-melanoma skin cancer, colorectal cancer was the 2nd most common cancer in males, making up 12.4% of all cancers (age-standardised rate per 100,000 was 58.3), and the 3rd most common cancer in females making up 10.1% of all cancers (age-standardised rate per 100,000 was 38.3) (NCRI, 2020).

Table 7 Estimated percentage and ranking among total cancer incidences of the most commonly diagnosed invasive cancers (excluding non-melanoma skin cancers) in Ireland, 2018 –2020 (NCRI, 2020)

Invasive Cancer	Males		Females	
	%	Rank	%	Rank
Prostate	29.6	1	-	-
Breast	-	-	31.5	1
Colorectal	12.4	2	10.1	3
Lung	11.4	3	10.7	2

3.1.2 Mortality

The annual average number of deaths from colorectal cancer in Ireland from 2015–2017 was 1,025 (605 males; 420 females), which represents 11.0% of all registered cancer deaths (Table 8) (NCRI, 2020).

Table 9 shows the average annual estimated percentages and rank of the most common causes of cancer death in Ireland from 2015-2017. Colorectal cancer was the second most common cancer death in males and the third most common cancer death in females (NCRI, 2020).

Table 8 Annual average mortality rate from colorectal cancer, 2015 –2017 (NCRI, 2020)

	Death		Rate/100,000*	
	Males	**Females**	**Males**	**Females**
Colorectal Cancer	605	420	23.5	13.4

*Rates are standardised to the 1976 European standard population

Table 9 Percentage and ranking of the most common cancer deaths in Ireland, 2015 –2017 (NCRI, 2020)

	Males		Females	
	%	Rank	%	Rank
Lung	22.1%	1	19.7%	1
Colorectal	12.3%	2	9.7%	3
Prostate	11.0%	3	-	-
Breast	-	-	16.9%	2

In 2020, the estimated age-standardised mortality rate of colorectal cancer in males in Ireland of 26.5 per 100,000 was 7.7% higher than the EU27 rate of 24.6 per 100,000, while the estimated age-standardised mortality rate in females in Ireland of 15.7 per 100,000 was 12.1 % higher than the EU27 rate of 14.0 per 100,000 (ECIS, 2020).

3.1.3 Survival

According to the latest NCRI statistics, the estimated complete prevalence of colorectal cancer at the end of December 2018 was 22,738 (12,427 males; 10,310 females) (Table 10). Overall, colorectal cancer is the third most common cancer in the prevalent cancer population (12% of all cancer survivors) after breast (23%) and prostate (21%) (NCRI, 2020).

The estimated five-year net survival (age-standardised for patients with colorectal cancer during the period 2012–2016 was 64% (NCRI, 2020).

Table 10 Estimated complete prevalence of colorectal cancer on 31st December 2018, by age and sex (NCRI, 2020)

	Males		Females		All	
Age	n	%	n	%	n	%
<50	677	5	894	9	1,570	7
50+	11,751	95	9,417	91	21,167	93
All	12,427	100.0	10,310	100.0	22,738	100.0

3.1.4 Cancer trends and projections 2020-2045

The annual numbers of cases of rectal and anal cancer (C19-21) are projected to increase. Based on the median of 5 model projection estimates and the demographic population increase (5+1), in females cases are projected to increase from 338 in 2015 to 656 in 2045 (+97%). In males, the projected increase is from 585 in 2015 to 1,126 in 2045 (+93%). Table 11 shows the projected numbers of incident cases of cancer of the rectum and anus up to the year 2045 (NCRI, 2019b).

Table 11 Projected numbers of incident cases 2020-2045 (with % increase compared to 2015): cancer of the rectum & anus (NCRI, 2019b)

Cancer of the Rectum & Anus (C19-20)				
	Projected numbers of incident cases 2020-2045 (based on median of 5 models and demographic projections)		% increase compared to 2015	
Year	Males	Females	Males	Females
2020	716	387	22%	18%
2025	810	440	39%	34%
2030	903	496	54%	51%
2035	986	553	69%	68%
2040	1,062	607	81%	83%
2045	1,126	656	93%	97%

3.2 Rationale for this National Clinical Guideline

The National Cancer Strategy (Department of Health and Children (DoHC), 2006) recommended that national tumour site-specific multidisciplinary groups be convened to develop national evidence-based clinical guidelines for cancer care.

The National Cancer Strategy 2017-2026 (DoH, 2017) recommends: *The NCCP will develop further guidelines for cancer care in line with National Clinical Effectiveness Committee (NCEC) standards.*

The purpose of developing this guideline is to improve the quality of care delivered to patients.

Rectal cancer is distinct from colon cancer, with different aetiologies and risk factors. The treatment for rectal cancer is highly specialised and can cause a number of cancer specific issues for patients which require expert management to provide the best outcomes. The diagnosis, staging, and treatment of patients with rectal cancer requires multidisciplinary care in an acute hospital setting. The majority of patients will require diagnostic tests (radiology, pathology) and depending on the treatment plan may require surgery, radiotherapy and chemotherapy. When centralisation of surgical services takes place, rectal cancer surgery will be performed in a number of designated cancer centres who will provide the multidisciplinary team expertise and possess the specialist facilities required to manage this type of cancer. As a result, the Guideline Development Group made the decision to develop an individual guideline which dealt specifically with rectal cancer.

3.3 Aims and objectives

The overall objectives of the NCCP's National Clinical Guideline 'Diagnosis, staging and treatment of patients with rectal cancer' are outlined below, along with the clinical question number that addresses the specific aim. The recommendations within this guideline relate to the clinical treatment of cancer and do not provide specific guidance on nutritional intervention, physical rehabilitation or full multidisciplinary management of patients with rectal cancer. The guideline is based on the best research evidence in conjunction with clinical expertise, and developed using a clear evidence-based internationally used methodology.

- Improvement in patient outcomes including potential for reduction in morbidity and mortality, improvement in quality of life (Clinical Questions 2.3.1, 2.4.1, 2.5.1, 2.5.2, 2.6.1, 2.6.2, 2.6.3, 2.6.4, 2.6.5, 2.7.1, 2.7.2, 2.8.1, 2.9.1),
- Promotion of interventions of proven benefit and discouragement of ineffective interventions, improvement in standard of care (Clinical Questions 2.2.1, 2.2.2, 2.2.3, 2.2.4, 2.2.5, 2.2.6, 2.2.7, 2.2.8),

- Improvement in consistency of care, and reduce variation in practice (Clinical Questions 2.2.1, 2.2.2, 2.2.3, 2.2.4, 2.2.5, 2.2.6, 2.2.7, 2.2.8, 2.5.2, 2.6.1, 2.6.3, 2.8.1),
- To address areas of clinical care with new and emerging evidence (Clinical Questions 2.6.2, 2.6.5, 2.7.2),
- Potential to have the most impact (on patients and resources) (Clinical Questions 2.7.2, 2.9.1).

3.4 Financial impact of rectal cancer

A population-based cost analysis (Luengo-Fernandez et al., 2013) illustrated the economic burden of cancer on the European Union (EU). In 2009, cancer is estimated to have cost the EU €126 billion, with healthcare costs accounting for €51 billion (40%). Across the EU, the cost of cancer healthcare was equivalent to €102 per person, but varied substantially from €33 per person in Lithuania to €171 per person in Germany.

In Ireland, in-patient care costs were estimated to account for €417 million of cancer-related healthcare costs out of a total of €619 million. Drug expenditure accounted for a further €127 million while primary, outpatient and emergency care were estimated at €32 million, €30 million and €13 million respectively (Luengo-Fernandez et al., 2013). Across the EU, healthcare costs per person were estimated to cost between €1 and €22 for colorectal cancer (€15 per person in Ireland) (Luengo-Fernandez et al., 2013). With rectal cancer incidence expected to increase by 93% in males and 97% in females by 2045 (NCRI, 2019b), there could be a significant increase seen in healthcare costs per person in Ireland.

The costs of colorectal cancer related informal care and productivity losses were estimated at €2.84 billion and €3.77 billion, respectively (Luengo-Fernandez et al., 2013).

A recent productivity loss analysis carried out in an Irish context (Pearce et al., 2016) projected that by 2030, premature death as a result of colorectal cancer will cost a value of €7 billion household production lost and an overall productivity loss of €1.3 billion.

The resource implications of implementing the recommendations within the guideline were identified by the clinicians during meetings to discuss and develop the recommendations (Appendix 6: Economic Assessment and Appendix 7: Implementation plan).

Healthcare investment of over €1.5 million over three years is required to implement the recommendations of this guideline. However, this estimate does not include the cost for centralisation of cancer surgical services and workforce planning. The NCCP in partnership with the Department of Health will be in a position to provide more accurate costing for this area once the project to centralise cancer services is complete in late 2020.

A number of the recommendations made within the surgical section can be implemented by centralising the service which would take into consideration staffing, expertise, infrastructure and equipment requirements. By adopting novel surgical techniques as recommended, length of hospital stay could be reduced resulting in a cost-saving, which is currently unknown.

Much of the budget is required to ensure adequate availability the different radiological modalities to appropriately diagnose stage and restage disease in patients with rectal cancer. €695,250 is required for contrast enhanced CT-TAP, €719,532 is required to adequately finance the use of MRI while CT colonography requires €120,450 in funding for this patient population.

Importantly, by implementing the recommendations of this guideline, the misuse of PET-CT as a first line staging modality for rectal cancer can be reduced, resulting in a potential cost-saving. The recommendations relating to pathology, gastroenterology, and radiation oncology are mostly current practice and do not require any further healthcare investment outside of what is already provided via normal service planning.

3.5 Guideline scope

3.5.1 Target population

Patients that are covered by this guideline are:

- Adults (18 years or older) that have a suspected diagnosis of rectal cancer.
- Adults with newly diagnosed early and locally advanced rectal cancer.

3.5.2 Target audience

This guideline is intended for all health professionals involved in the diagnosis, staging and treatment of patients with rectal cancer. While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

This guideline is also relevant to those involved in clinical governance, in both primary and secondary care, to help ensure that arrangements are in place to deliver appropriate care for the population covered by this guideline.

Whilst the guideline is focused on clinical care, it is expected to be of interest to patients diagnosed with rectal cancer and their significant others. A list of medical abbreviations used throughout the guideline can be found in Appendix 9: Glossary of terms and abbreviations.

3.6 Conflicts of interest statement

A conflict of interest form developed by the NCEC was signed by all Guideline Development Group members and reviewers. The Guideline Development Group was managed by the Chair to promote the highest professional standard in the development of this guideline.

Any member of the Guideline Development Group who declares a conflict of interest is not permitted to attend a recommendation meeting where their stated conflict is relevant to the evidence being reviewed or which may influence the recommendation being generated. All research evidence along with an assessment of its quality is presented to the Guideline Development Group by its research members. Membership of colleges or professional bodies do not represent a conflict of interest in this guideline. No specific pharmaceutical devices, products or equipment are specified in this guideline and no items were discussed which were relevant to any conflicts declared. Conflicts of interests declared by members of the Guideline Development Group are described in Table 12.

Table 12 Conflicts of interests declared by members of the Guideline Development Group

Guideline Development Group Member	Detail of conflict declared
Professor Debbie McNamara	RCSI Council member and Co-Lead National Clinical Programme for Surgery.
Professor Padraic MacMathuna	Member of Bowel Screen Clinical Advisory Group.
Dr Brian O' Neill	Principal investigator of an national rectal cancer trial TRILARC with cancer trials Ireland. This is a randomised trial comparing 3D-CRT with IMRT for locally advanced rectal cancer.
Professor Kieran Sheahan	Consultancy work for Roche Diagnostics, research sponsorship by Roche Diagnostics, research Sponsorship by Genomics Medicine Ireland.

3.6.1 Governance

Governance of the guideline development process was provided by a multidisciplinary Guideline Steering Group which was chaired by the Director of the NCCP. Details of Guideline Development Group members are provided at the beginning of the document and Guideline Steering Group members are available in Appendix 1: Guideline Development Group terms of reference

The Guideline Development Group was responsible for the development and delivery of the National Clinical Guideline and included representatives from relevant professional groups (radiology, pathology, gastroenterology, surgery and radiation oncology) with expertise in the diagnosis, staging and treatment of patients with rectal cancer, a project manager, a methodologist, a research officer, a health economist and a number of clinical librarians.

3.7 Sources of funding

The guideline was commissioned and funded by the NCCP; however, the guideline content was not influenced by the NCCP or any other funding body. This process is fully independent of lobbying powers. All recommendations were based on the best research evidence integrated with clinical expertise.

3.8 Guideline methodology

The methodology for the development of the guideline was designed by a research methodologist and is based on the principles of Evidence-Based Practice (EBP) (Sackett et al., 2000). The methodology is described in detail in the NCCP Methodology Manual for guideline development which is available on the NCCP website. This manual adheres to the standards outlined in the NCEC Guideline Development Manual. Figure 2 outlines the stages of guideline development.

3.8.1 Step 1: Formulate the clinical questions

Guideline Development Group members met and through clinician led experience identified areas of new and emerging evidence, areas with identifiable variation in practice, or areas with potential to impact on patients care. These questions then formed the basis for the types of evidence being gathered, the search strategy, and the inclusion and exclusion criteria.

To formulate the clinical questions they were broken down into their component parts using the PICO(T) framework:

- Participant/Population
- Intervention/Exposure
- Control/Comparison
- Outcome
- Time

This process was carried out by discipline specific subgroups. The Guideline Development Group signed off the entire list of clinical questions to ensure a comprehensive guideline. The resulting 20 clinical questions are listed in Appendix 2: Clinical and Economic Questions in PICO format.

3.8.2 Step 2: Search methodology

The clinical questions formulated in step one were used to conduct literature searches of the primary literature. The systematic literature review protocol was developed for the guideline development process by the HSE librarians in conjunction with the NCCP (Appendix 4: Systematic literature review protocol). The following bibliographic databases were searched in the order specified below using keywords implicit in the PICO(T) question and any identified subject headings:

- Cochrane Library
- Point-of-Care Reference Tools
- Medline
- Embase (where available)
- Other bibliographic databases such as PsycINFO, CINAHL, as appropriate.

The literature was searched based on the hierarchy of evidence. The search strategies for all clinical questions and the five economic questions in the budget impact assessment are available on request by contacting the NCCP at guidelines@cancercontrol.ie

3.8.3 Step 3: Screen and appraise the evidence

International guidelines were appraised using the international, validated tool the AGREE II instrument (Brouwers et al., 2010). Primary papers were appraised using validated checklists developed by the Scottish Intercollegiate Guideline Network (SIGN).

Economic papers included in the Budget Impact Assessment (Part A: Economic) were appraised by a health economist using validated economic checklists developed by SIGN.

There were three main points considered when appraising all the research evidence:

- Are the results valid? (internal validity)
- What are the results? (statistical and clinical significance)
- Are the results applicable/generalisable to the patient/population of this guideline? (external validity)

After literature appraisals were completed, the data selected for possible inclusion in the guideline were compiled in the data extraction tables by the research officers. The data extraction tables are available upon request.

3.8.4 Step 4: Formulation and grading of recommendations

The evidence which addressed each clinical question from international guidelines and primary literature was extracted into evidence tables. Recommendations were formulated through a formal structured process. A 'considered judgment form' (adapted from SIGN) was completed for each clinical question.

The following items were considered and documented:

- What evidence is available to answer the clinical question?
- What is the quality of the evidence?
  - Is the evidence consistent?
  - Is the evidence generalisable to the Irish population?
  - Is the evidence applicable in the Irish context?
- What is the potential impact on the health system?
- What is the potential benefit versus harm to the patient?
- Are there resource implications?

The evidence summaries and recommendations were then written. Each recommendation was assigned a grade by the Guideline Development Group. The grade reflected the level of evidence upon which the recommendations were based, the directness of the evidence, and whether further research is likely to change the recommendation. The levels of evidence tables and grading systems used are documented in Appendix 10: Levels of evidence & grading systems.

Good Practice Points are intended to assist guideline users by providing short pieces of advice which may not have an evidence base, but which are seen as essential to good clinical practice (SIGN, 2015). The Good Practice Points presented in this clinical guideline were based on the clinical expertise of the Guideline Development Group. For the economic literature, key messages are presented in boxes entitled 'relevance to the guideline recommendations'.

Practical considerations around patient care are statements developed through collaboration with patients and patient representative organisations on issues that were important to them with regards to their own experience of the diagnosis and staging of their cancer.

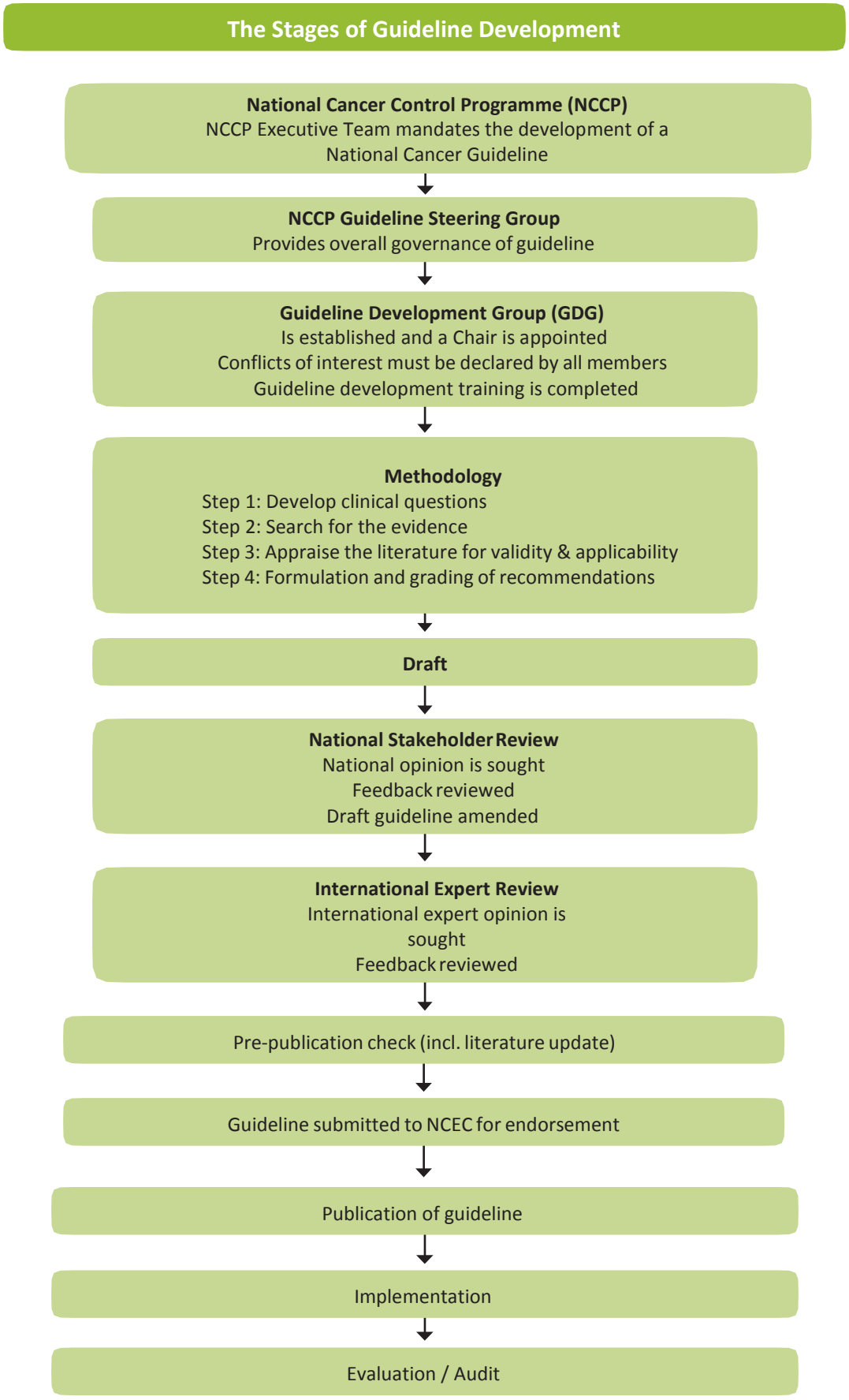


Figure 2 The stages of guideline development

3.9 Consultation process

The guideline was placed on the NCCP website and circulated for comment from the 17th of February 2020 to March 16th 2020. Stakeholders were asked to comment on the comprehensiveness of evidence used to form the recommendations. Stakeholders were required to submit feedback with supporting evidence on a form provided (see NCCP Methodology Manual) along with a completed conflict of interest form. A time-period of four weeks was allocated to submit comments. A list of the stakeholders including groups, organisations and committees can be found in Appendix 5: Details of consultation process.

All feedback received was reviewed by the project managers and research team. Suggested amendments and supporting evidence were reviewed by the discipline specific subgroup and consensus reached to accept or reject the amendments. Amendments were rejected following discussion between members of the relevant subgroup(s) and in instances where no superior evidence was provided or no conflict of interest form was provided. All modifications were documented and the report is available upon request.

3.9.1 Patient involvement

The views and preferences of the target population were sought by inviting patient advocacy groups (HSE Patient Forum, Irish Cancer Society, Cancer Care West, Marie Keating Foundation, Gary Kelly Cancer Support Centre Purple House Support Centre and a number of nationwide stoma support groups) to engage in the National Stakeholder Review process.

A number of cancer patients groups and charitable organisations were contacted and their patient representatives and family members were invited to engage with the NCCP and asked to provide feedback on issues important to them with regards to their own experiences of the diagnosis, staging and treatment of their rectal cancer.

Three patients from various patient cancer organisations and charities provided feedback which included issues around quality of life and patient dissatisfaction. A list of practical considerations from a patient perspective was developed and this can be found in Section 2.1 Summary of clinical recommendations, practical considerations around patient care and summary of budget impact analysis.

3.9.2 Patient advocacy

A collaborative approach is used in the development of the NCCP patient information, clinical guidelines and other national projects. All NCCP booklets are submitted to the National Adult Literacy Agency (NALA) (www.nala.ie) for the Plain English Award. This is to ensure comprehension and readability is in line with health literacy best practice standards. Service user testing is a key part of the process, and includes liaising with the HSE Patient Forum, online surveys, and engaging with other relevant patient groups e.g. Irish Cancer Society, Marie Keating Foundation.

The NCCP in partnership with the Irish Cancer Society has commenced a cancer survivorship programme. The main goal for the NCCP Survivorship Programme is to empower patients to achieve their best possible health while living with and beyond a diagnosis of cancer. This involves providing information, guidance and support to survivors and their families and healthcare professionals in relation to healthy lifestyle, disease prevention and control. It aims to promote a good quality of life and prolonged survival for people who experience cancer.

3.10 External review

The draft guideline was submitted for international expert review. The Guideline Development Group nominated six international reviewers to provide feedback on the draft guideline. These reviewers were chosen based on their in-depth knowledge of the subject area and guideline development processes. The review followed the same procedure as the National Stakeholder Review. The guideline was circulated for comment from 17th of February 2020 to March 16th 2020.

All feedback received was reviewed by the project managers and research team. Suggested amendments and supporting evidence were reviewed by the discipline specific subgroup and consensus reached to accept or reject the amendments. Amendments were rejected following discussion between members of the relevant subgroup(s) and in instances where no superior evidence was provided or no conflict of interest form was provided. All modifications were documented.

A log was recorded of all submissions and amendments from the national stakeholder review and international expert review process and is available on request from the Guideline Development Group.

3.11 Plan to update this National Clinical Guideline

This guideline published in December 2020 will be considered for review by the NCCP in three years. Surveillance of the literature base will be carried out periodically by the NCCP. Any updates to the guideline in the interim period or as a result of three year review will be subject to the NCEC approval process and noted in the guidelines section of the NCCP and NCEC websites.

3.12 Implementation

The implementation plan (Appendix 7: Implementation plan) was developed based on the NCEC implementation guide (Department of Health, 2018). The implementation plan outlines the actions required to implement the recommendations, who has lead responsibility for delivering the action, the timeframe for completion and the expected outcomes of implementation.

This National Clinical Guideline including the implementation plan should be reviewed by the multidisciplinary team and senior management in the hospital to plan the implementation of the recommendations.

The CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the National Clinical Guideline and to ensure that all relevant staff are appropriately supported to implement the guideline.

The Colorectal Cancer Clinical Leads group will also have an important role in implementation of the recommendations contained in this guideline with regards to local clinical arrangements, clinical audit, sharing of good practice and problem solving.

All medical staff with responsibility for the care of patients with rectal cancer are required to:

- Comply with this National Clinical Guideline and any related procedures or protocols.
- Adhere to their code of conduct and professional scope of practice guidelines as appropriate to their role and responsibilities.
- Maintain their competency for the management and treatment of patients with rectal cancer.

The National Clinical Guideline will be circulated and disseminated through the professional networks who participated in developing and reviewing this document. The guideline will also be available on the NCEC and NCCP websites.

A summary of tools to assist in the implementation of this National Clinical Guideline are available in Appendix 3: Supporting tools.

3.12.1 Dissemination and communication plan

The National Clinical Guideline will be circulated and disseminated through the professional networks who participated in developing and reviewing this guideline (HSE Clinical Programmes in Surgery, Radiology, and Palliative Care, RCSI, HSE Patient Forum, Irish Cancer Society, Cancer Care West etc.). The guideline will also be available via the NCEC and NCCP websites.

The NCCP will co-ordinate with HSE Communications to distribute, share and disseminate through the media (HSE Broadcast, Health Matters, and Twitter). The guideline will be officially launched and circulated to all relevant faculties and colleges for dissemination to their members. The implementation of the guideline will also be supported by communication, training and education.

Potential dissemination and communication strategies:

- Create slide for inclusion in presentations by clinical leads, subgroup chairs, NCCP Director around published guidelines.
- Included link to guidelines in NCCP email signatures.
- Liaise with cancer voluntary support groups, organisations and charities to ensure guidelines are represented in their patient and public information.
- Promote through NCCP website and social media.
- Direct communication from NCCP Director/CCO/Acute Operations to hospital managers raising awareness and setting out expectations/actions.
- Include discussion on implementation at launch.

3.13 Monitoring and audit

The NCCP engages regularly with the individual cancer centres and with Hospital Group structures. Discussion of performance data, improvement plans, resources including manpower, service planning and development takes place at regular review meetings between the NCCP and senior management at cancer centre and Hospital Group level.

It is important that both the implementation of the guideline and patient outcomes are audited to ensure that this guideline positively impacts on patient care. For audit criteria see Appendix 8: Monitoring and audit.

3.14 Recommendations for research

The following areas have been identified by the Guideline Development Group that require further research:

Recommendation 2.2.6.1
In patients undergoing surgery with rectal cancer, it is recommended to identify as many nodes as possible, all of which should be submitted for microscopic examination/evaluation. Overall, the median for the laboratory should be at least 12.

Recommendation 2.6.2.1
In patients diagnosed with rectal cancer who have an apparent complete clinical response to chemoradiation radical surgery is the standard of care. However, a watch and wait approach should be discussed with the patient and may be considered following shared decision making.

Recommendation 2.6.5.1
In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiation the routine use of a boost is not recommended.

Recommendation 2.7.2.1
There is no clear evidence of difference in postoperative genitourinary function between minimally invasive and open total mesorectal excision (TME)**.**

4 Appendices

Appendix 1: Guideline Development Group terms of reference and logic model

Membership of the Guideline Development Group is outlined at the beginning of this document.

Terms of Reference: To develop a national evidence-based clinical guideline for the diagnosis, staging, and treatment of patients with rectal cancer. Full terms of reference are available in the NCCP Methodology Manual for guideline development.

Table 13 Membership of the NCCP Guideline Steering Group

Name	Title/Position	Role on guideline group
Professor Risteárd Ó Laoide	National Director, NCCP	Chair
Ms Fiona Bonas	Interim Deputy Director, NCCP	Member
Dr Eve O'Toole	Head of Evidence and Quality Hub, NCCP	Member
Dr Deirdre Murray	Health Intelligence, NCCP	Member
Ms Patricia Heckmann	Assistant National Director, NCCP	Member
Professor Arnold Hill	NCCP Surgical Advisor & BH	Member
Dr Aileen Flavin	NCCP Radiation Oncology Advisor & CUH	Member
Professor Maccon Keane	NCCP Medical Oncology Advisor & GUH	Member
Mr Brendan Leen	Regional Librarian, HSE South-East	Member
Mr David Galvin	Chair Prostate GDG, SVUH	Member
Dr Marcus Kennedy	Chair Lung GDG, CUH	Member
Professor John Reynolds	Chair Gastrointestinal GDG, SJH	Member
Professor Deborah McNamara	Chair Lower GI GDG, BH	Member
Mr Justin Geoghegan	Chair Hepatobiliary GI GDG, SVUH	Member
Dr Josephine Barry	Co-chair Ovarian GDG, CUH	Member
Dr Ciarán Ó Riain	Co-chair Ovarian GDG, SJH	Member
Mr Martin O Sullivan	Chair Breast GP GDG, CUH	Member
Mr John Coulter	Chair Gestational trophoblastic disease GDG, CUH	Member
Dr Brian Creedon	Clinical Lead Clinical Programme for Palliative Care, UHW	Member

Table 14 Guideline contributors

Name	Title/Position	Role
Mr Rory Kennelly	Consultant Colorectal Surgeon, SVUH	Contributor
Dr Ciara Lyons	Consultant Radiation Oncologist, CUH	Contributor
Dr Moya Cunnigham	Consultant Radiation Oncologist, SLRON	Contributor
Dr Aoife McErlean	Consultant Radiologist, BH	Contributor
Ms Michelle O'Neill	Senior Health Economist, HIQA	Contributor
Dr Paul Patrick Healy	Clinical Lecturer, RCSI	Contributor
Ms Laura Currie-Murphy	Postdoctoral Research Fellow, SJH	Contributor
Ms Elaine Scanlon	Library Assistant, Dr Steevens' Library	Contributor
Professor Mike Clarke	Director of MRC Methodology Hub, QUB	Methodology advisor
Mr Robin Harbour	Lead Methodological, SIGN	Contributor
Dr Sandra Deady	Data Analyst, NCRI	Contributor

Name	Title/Position	Role
Dr Francis Delaney	Radiology Specialist Registrar, MMUH	Contributor
Dr Austin Donnelly	Radiology Specialist Registrar, NI ST2	Contributor
Dr Padraic Kennedy	Radiology Specialist Registrar, CUH	Contributor
Dr David Ryan	Radiology Specialist Registrar, SVUH	Contributor
Dr Joseph Morrow	Radiology Specialist Registrar, SVUH	Contributor
Dr Niamh Kilgallen	Senior Research Officer, NCCP	Contributor

Monitoring and Evaluation
Audit on compliance of implementation of guideline recommendations, identification of key performance indicators and NCRI data monitoring on rectal cancer incidence

Situation Analysis

- Approximately 2,818 new cases of colorectal cancer diagnosed yearly
- 1,025 deaths from colorectal cancer yearly contributing to 11% of all cancer deaths
- Ranked Ireland's 2nd and 3rd most common mortality-causing cancer in males and females respectively
- The incidence rate of colorectal cancer in males in Ireland is 68.1 per 100,000 (7 % higher than the EU27 rate of 58.2 per 100,000) and in females 43.7 per 100,000 (19.7 % higher than the EU27 rate of 36.5 per 100,000)
- By 2045 cancer of the rectum and anus is expected to increase by 93% in males and 97% in females
- Variation in practice regarding how rectal cancer is diagnosed, staged and treated in Ireland
- There is new and emerging evidence to suggest changes to practice
- All rectal cancer patients should be provided with the best opportunity at survival
- Emphasis on QOL
- Rectal cancer patient treatment specific to specialist centres
- Need for national guidance

Inputs

- Department of Health- NCEC
- Rectal cancer Guideline Development Group (GDG)
- Patient representatives
- Non GDG clinical expert input
- Guideline Steering Group
- NCCP colorectal clinical leads group
- National and international reviewers
- HSE
  - NPSO
  - QID
- Local implementation teams
- Colorectal Clinical Nurse Specialists
- Hospital management
- Medical & nursing specialists in every hospital
- Allied healthcare professionals
- Guideline champions
- Undergraduate colleges – nursing and medical
- Hospital pricing unit
- Service planning
- NCRI

Activities/Outputs

- Communication & engagement with key stakeholders
- Dissemination and communication of guideline recommendations
- Accessibility of guideline recommendations to frontline staff
- Delivery of appropriate diagnosis, staging and treatment
- Staff training
- Staff support
- Resources to provide education at local level
- Development of audit tools and schedule of audit
- National audits
- Guideline Steering Group meetings
- Monitoring of rectal cancer KPIs

Short-Term Outcomes

Implementation Outcome

- Acceptance of the rectal cancer guideline by clinicians
- Rectal cancer guideline widely disseminated & used in the care of rectal cancer patients
- All relevant staff have understanding and awareness of new rectal cancer guideline and its recommendations
- Pathways of care are feasible
- Programme of education established for undergraduate and qualified staff incorporating current practice
- Increase clinician satisfaction with care provided

Service Outcomes

- Use of rectal cancer guideline for diagnosis, staging and treatment of rectal cancer
- Guideline widely available in all clinical areas to aid diagnosis, staging and treatment
- Recommendations widely used and documented by all staff
- Better communication across all healthcare teams & professionals
- Funding from the DOH

Client Outcomes

- Decreased mortality and morbidity associated with rectal cancer
- Evidence-based treatment for patients in all clinical settings
- Reduction of adverse outcomes
- Increased QOL

Long-Term Outcomes

Implementation Outcome

- National adoption of guideline with fidelity
- Use of the national guidelines is embedded across all service areas

Service Outcomes

- Cost-effective implementation of recommendations
- Recommendations fully resourced
- Reduction in variation in practice
- Standardised practices across Ireland

Client Outcomes

- Decreased mortality/morbidity associated with rectal cancer
- Improved quality of life for patients
- Improved patient and family satisfaction with care received
- Measurable patients outcomes via regular audit
- Minimal deviation from recommendations- patient dependent
- Sustainable improvements in care provided to rectal cancer patients

Evidence
Systematic review of literature; international guidelines; expert national and international review; budget impact analysis

Appendix 2: Clinical and Economic Questions in PICO format

Diagnosis and staging

Clinical question 2.2.1 In patients with newly diagnosed rectal cancer, is CT-TAP the best imaging modality for diagnosing: i) Hepatic metastasis ii) Extrahepatic metastasis	
Population:	Patients diagnosed with rectal cancer
Intervention:	CT-TAP
Comparison:	Chest x-ray, ultrasound, MRI, PET-CT
Outcome:	Sensitivity, specificity, diagnosis of hepatic & extrahepatic metastases
Clinical question 2.2.2 In patients diagnosed with rectal cancer with a potentially resectable liver lesion, is MRI of the liver superior to PET-CT in determining the presence of further liver lesions?	
Population:	Patients diagnosed with rectal cancer with a potentially resectable liver lesion
Intervention:	MRI
Comparison:	PET-CT
Outcome:	Sensitivity, specificity, diagnosis of additional lesions
Clinical question 2.2.3 In patients newly diagnosed with rectal cancer, is MRI superior to endorectal ultrasound in assessing the local extent of tumour?	
Population:	Patients newly diagnosed with rectal cancer
Intervention:	MRI
Comparison:	Endoanal ultrasound
Outcome:	Sensitivity, specificity, assessing local extent of tumour
Clinical question 2.2.4 In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed, is CT colonography necessary prior to surgery?	
Population:	Patients diagnosed with obstructing rectal cancer
Intervention:	No colonography (pre-operatively)
Comparison:	No CT colonography
Outcome:	Clinical effectiveness (diagnosis, treatment), sensitivity, specificity, safety and harms
Clinical question 2.2.5 In patients diagnosed with rectal cancer, is complete colonoscopy always necessary prior to surgery?	
Population:	Patients newly diagnosed with rectal cancer
Intervention:	Complete preoperative colonoscopy
Comparison:	Incomplete preoperative conventional colonoscopy
Outcome:	Clinical effectiveness (diagnosis, treatment), sensitivity, specificity, safety and harms

Clinical question 2.2.6 In patients diagnosed with rectal cancer, is there a minimum number of lymph nodes that need to be identified in a resection specimen and, if so, what is that number?	
Population:	Patients diagnosed with rectal cancer
Intervention:	Minimum threshold of lymph nodes sampled
Comparison:	Any number of lymph nodes sampled
Outcome:	Accuracy of staging, survival benefit
Clinical question 2.2.7 In patients diagnosed with rectal cancer, are the Haggitt and Kikuchi classification systems sufficiently applicable to recommend their use?	
Population:	Patients diagnosed with rectal cancer
Intervention:	Application of Haggitt (polypoid tumours) and Kikuchi (sessile tumours) classification systems
Comparison:	Non-application of Haggitt and Kikuchi classification systems
Outcome:	Accuracy of assessing local invasion
Clinical question 2.2.8 In patients diagnosed with rectal cancer receiving neoadjuvant chemoradiation: a) Should a tumour regression grading (TRG) system be employed b) If so, which one?	
Population:	Patients diagnosed with rectal cancer
Intervention:	3-point TRG system (Royal College of Path 2007 Dataset) 5-point TRG (Mandard 1994/Dworak 1997)
Comparison:	Non-application of a TRG system
Outcome:	Correlation with overall survival, reproducibility of TRG system, Prognosis

Restaging

Clinical question 2.3.1 In patients diagnosed with rectal cancer who have an apparent complete clinical response to chemoradiation, which radiological investigation best determines if the patient is a complete pathological responder**?**	
Population:	Patients diagnosed with rectal cancer with an apparently complete clinical response to chemoradiation
Intervention:	Digital rectal examination (DRE), endoscopy with biopsy, CT-TAP, PET-CT, carcinoembryogenic antigen (CEA) measurements, EMR, local resection, MRI, endorectal ultrasound, observation of lesion
Comparison:	Rectal resection with TME
Outcome:	ypT0N0M0, local recurrence, disease free survival, overall survival

Treatment: Emergency presentations

Clinical question 2.4.1 In patients diagnosed with obstructive rectal cancer, what is the role of stenting: (i) When intention of treatment is curative? (ii) When intention of treatment is palliative?	
Population:	Patients diagnosed with obstructive rectal cancer
Intervention:	Stenting
Comparison:	Immediate surgery
Outcome:	Bridge to surgery, tumour dissemination, palliation, safety, stoma rates, curative resection, mortality, perforation

Treatment: Patients with early rectal cancer

Clinical question 2.5.1 In predicted node negative patients diagnosed with T1 or T2 rectal cancer, what is the evidence for local resection without total mesorectal excision (TME)?	
Population:	Node negative patients diagnosed with T1 or T2 rectal cancer
Intervention:	Local resection without total mesorectal excision (TME)
Comparison:	Local resection with TME
Outcome:	Recurrence, overall survival
Clinical question 2.5.2 In patients with early-stage rectal cancer treated with local excision what pathological features indicate that radical surgery is required?	
Population:	Patients with early-stage rectal cancer who have had local excision
Intervention:	Pathological features on local excision specimen
Comparison:	-
Outcome:	Radical surgery required

Treatment: Patients receiving neoadjuvant therapy

Clinical question 2.6.1 In patients diagnosed with rectal cancer, what subgroups of patients would benefit from preoperative radiotherapy or chemoradiotherapy?	
Population:	Patients diagnosed with rectal cancer
Intervention:	Need for preoperative radiotherapy indicated by any of the following: MRI, endorectal ultrasound, endoscopy, surgical concern over ability to sphincter spare, tumour location, other patient specific factors
Comparison:	-
Outcome:	Recurrence, disease-free survival, overall survival, safety and harms
Clinical question 2.6.2 In patients diagnosed with rectal cancer who have an apparent complete clinical response to chemoradiotherapy, what is the evidence to support a watch and wait strategy?	
Population:	Patients diagnosed with rectal cancer with an apparent complete clinical response to chemoradiation being treated with curative intent

Intervention:	Local resection, abdomino-perineal excision of rectum, total mesorectal excision (TME)
Comparison:	Radical surgery, active surveillance
Outcome:	Recurrence, overall survival
Clinical question 2.6.3 In patients diagnosed with rectal cancer, how does short-course preoperative radiotherapy (SCPRT) compare with chemoradiotherapy for survival, toxicity, down-staging (or sphincter preservation), local recurrence rates, and postoperative complications?	
Population:	Patients diagnosed with rectal cancer undergoing SCPRT or LCPRT (+/- chemotherapy)
Intervention:	SCPRT or LCPRT (+/- chemo)
Comparison:	No SCPRT or LCPRT (+/- chemo)
Outcome:	Overall survival Toxicity, down-staging, pathological complete response rate, local recurrence, postoperative complications, sphincter preservation
Clinical question 2.6.4 In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiotherapy, is IMRT (intensity-modulated radiotherapy) superior to 3D-CRT (three-dimensional conformal radiotherapy) with regard to toxicity and outcomes?	
Population:	Patients diagnosed with rectal cancer undergoing neoadjuvant long-course chemoradiotherapy
Intervention:	IMRT
Comparison:	3D-CRT or 2D-CRT
Outcome:	Toxicity, pathological complete response rate, dosimetric parameters (example bowel and bladder dose & coverage), local recurrence, postoperative complications, overall survival
Clinical question 2.6.5 In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiotherapy, does addition of boost (e.g. EBRT, brachytherapy, simultaneous integrated boost, endocavitary contact x-ray) improve oncological outcomes?	
Population:	Patients diagnosed with rectal cancer being treated with adjuvant or neoadjuvant LCCRT
Intervention:	“Boost” following standard dose (45-50.4 Gy)
Comparison:	No “boost”
Outcome:	Toxicity, downstaging, pathological complete response rate, local recurrence, postoperative complications, overall survival

Treatment: Surgical techniques

Clinical question 2.7.1 In patients diagnosed with rectal cancer, what is the evidence for specific surgical techniques and the effectiveness of these techniques on patient outcomes?	
Population:	Patients diagnosed with rectal cancer
Intervention:	Laparoscopic surgery, abdomino-perineal excision of rectum (resection), total mesorectal excision (TME), robotic surgery
Comparison:	Radical surgery
Outcome:	Lymph node harvest, pathology scoring in macroscopic specimens, survival, recurrence – local and distant, morbidity, quality of life
Clinical question 2.7.2 In patients diagnosed with rectal cancer undergoing radical resection is minimally invasive or open total mesorectal excision (TME) more likely to preserve postoperative sexual and/or urinary function?	
Population:	Patients diagnosed with rectal cancer undergoing radical resection
Intervention:	Laparoscopic TME, robotic surgery
Comparison:	Open TME
Outcome:	Post-operative sexual/urinary function

Treatment: Patient receiving adjuvant therapy

Clinical question 2.8.1 In patients diagnosed with rectal cancer, does postoperative radiotherapy or chemoradiotherapy compensate for positive surgical margins?	
Population:	Patients diagnosed with rectal cancer with positive surgical margins
Intervention:	Postoperative radiotherapy/CRT
Comparison:	No postoperative radiotherapy/CRT
Outcome:	Local recurrence, overall survival

Treatment: Palliative care

Clinical question 2.9.1 When should palliative care be introduced for patients with cancer?	
Population:	Patients with cancer
Intervention:	Timing of palliative care
Comparison:	
Outcome:	Quality of life

Economics

Radiology What is the cost-effectiveness of various imaging modalities in staging patients with colorectal cancer?	
Population:	Patients diagnosed with colon or rectal cancer
Intervention:	Complete colonoscopy, CT colonography, CT-TAP (thorax, abdomen, pelvis), chest radiography, ultrasound, MRI, PET-CT
Comparison:	-
Outcome:	Cost-effectiveness analysis, cost-benefit analysis, cost-utility analysis, economic evaluation
Pathology What is the cost-effectiveness of processing lymph nodes or classifying pathological specimens in patients with colorectal cancer?	
Population:	Patients diagnosed with colon or rectal cancer
Intervention:	Processing lymph nodes (≤12 vs. 12) Classifying pathological specimens (Haggitt, Kikuchi, 3-point TRG system, 5-point TRG system)
Comparison:	-
Outcome:	Cost-effectiveness analysis, cost-benefit analysis, cost-utility analysis, economic evaluation
Gastroenterology What is the cost-effectiveness of gastroenterology services in patients with colorectal cancer?	
Population:	Patients diagnosed with colon or rectal cancer
Intervention:	Tattooing lesions during colonoscopy, preoperative colonoscopy, CT colonography, endoscopic mucosal resection, endoscopic submucosal dissection
Comparison:	-
Outcome:	Cost-effectiveness analysis, cost-benefit analysis, cost-utility analysis, economic evaluation
Surgery What is the cost-effectiveness of various surgical techniques in patients with colorectal cancer?	
Population:	Patients diagnosed with colon or rectal cancer
Intervention:	Laparoscopic surgery, colonic resection, mesocolon excision, complete mesocolic excision, stenting, abdomino-perineal excision, total mesorectal excision, robotic surgery, radical/open surgery, open low anterior surgery, endoscopic mucosal resection, endoscopic submucosal dissection, transanal excision, mesocolic section, curative resection, decompression, local resection
Comparison:	-
Outcome:	Cost-effectiveness analysis, cost-benefit analysis, cost-utility
Radiation Oncology What is the cost-effectiveness of radiotherapy in patients with colorectal cancer?	
Population:	Patients diagnosed with colon or rectal cancer
Intervention:	Short-course radiotherapy, Long-course radiotherapy, boost, intensity modulated radiotherapy (IMRT), 3D conformal radiotherapy (3DCRT), 2D conformal radiotherapy (2DCRT), postoperative radiotherapy (±chemotherapy)
Comparison:	-
Outcome:	Cost-effectiveness analysis, cost-benefit analysis, cost-utility analysis, economic evaluation

Appendix 3: Supporting tools

Downloading this guideline

This National Clinical Guideline will be available to download on the following websites:

- NCCP: https://www.hse.ie/eng/services/list/5/cancer/profinfo/guidelines/
- NCEC: https://health.gov.ie/national-patient-safety-office/ncec/national-clinical-guidelines/

Clinician information

- GP Electronic referral form - National Colorectal Cancer GP Referral for Symptomatic Patients https://www.hse.ie/eng/services/list/5/cancer/profinfo/resources/gpreferrals/gp-referral-pathway-for-suspected-colorectal-cancer.pdf
- NCCP Website: Information for Health Professionals https://www.hse.ie/eng/services/list/5/cancer/profinfo/
- Algorithms available in this guideline for clinicians:
  - **Figure 1** Staging algorithm recommended by the Guideline Development Group for patients with rectal cancer and suspected hepatic metastases

Patient information booklets/website

- Booklet - Sexual Wellbeing after breast or pelvic cancer treatments- a guide for women https://www.hse.ie/eng/services/list/5/cancer/patient/leaflets/sexual-wellbeing-after-breast-or-pelvic-cancer-treatment.pdf
- Booklet - Information for men on sexual wellbeing after pelvic cancer treatment- What you should know https://www.hse.ie/eng/services/list/5/cancer/profinfo/resources/booklets/pelvic%20cancer.pdf
- Booklet-Good bone health after cancer treatment- What you should know https://www.hse.ie/eng/services/list/5/cancer/patient/leaflets/good-bone-health-after-cancer-treatment.pdf
- Booklet - Irish Cancer Society. (2019) Understanding bowel (colorectal) and anal cancer booklet https://www.cancer.ie/cancer-information-and-support/cancer-types/bowel-cancer
- NCCP Colorectal cancer patient passport https://www.hse.ie/eng/services/list/5/cancer/profinfo/cancer-nursing-programme/patient%20passport.html
- NCCP Website: Patient Information https://www.hse.ie/eng/services/list/5/cancer/patient/

Service quality

- Department of Health (2017) National Cancer Strategy 2017-2026 https://health.gov.ie/blog/publications/national-cancer-strategy-2017-2026/
- Department of Health (2018) Framework for Public Involvement in Clinical Effectiveness Processes https://health.gov.ie/wp-content/uploads/2018/03/Final-WEB-COPY_PI-Framework-Feb-2018-1.pdf
- Department of Health (2018) NCEC Implementation Guide and Toolkit for National Clinical Guidelines https://www.gov.ie/en/collection/cd41ac-clinical-effectiveness-resources-and-learning/
- Health Information and Quality Authority (2012) National Standards for Safer Better Healthcare www.hiqa.ie/standards/health/safer-better-healthcare

Publications to assist with implementation of this guideline

- Department of Health (2017) Working Together for Health- A National Strategic Framework for Health and Social Care Workforce Planning https://health.gov.ie/blog/publications/working-together-for-health-a-national-strategic-framework-for-health-and-social-care-workforce-planning/
- Health Service Executive (2017) Palliative Care Services- Three Year Development Framework 2017-2019
- https://www.hse.ie/eng/services/publications/clinical-strategy-and-programmes/palliative-care-services-development-framework.pdf

- Department of Health (2017) Framework for Safe Nurse Staffing and Skill Mix in General and Specialist Medical and Surgical Care settings in Adult Hospitals in Ireland 2018
- https://health.gov.ie/blog/publications/framework-for-safe-nurse-staffing-and-skill-mix-in-general-and-specialist-medical-and-surgical-care-settings-in-ireland-2018/
- Department of Health (2014) Strategic Review of Medical Training and Career Structure
- https://health.gov.ie/blog/publications/strategic-review-of-medical-training-and-career-structure-final-report/
- Kumarasinghe et al., (2020) Pathological assessment of endoscopic resections of the gastrointestinal tract: a comprehensive clinicopathologic review. Mod Pathol ;33(6):986-1006. doi: 10.1038/s41379-019-0443-1.

Appendix 4: Systematic literature review protocol

National Cancer Control Programme

HSE Library Services
NCCP Guideline Development

SYSTEMATIC LITERATURE REVIEW PROTOCOL

Literature searches to answer clinical questions identified by the relevant tumour group will be conducted using the following procedure. Questions should only be submitted if they have not been adequately answered in the guidelines adopted by the tumour group, or where guidelines need to be updated. Guidelines should be identified in consultation with library services.

Tumour Group	1	PICO(T)		Analyse the clinical question using PICO(T) and complete a Clinical Query Request form. See below Annex 1: Clinical Query Request.
Tumour Group or Library Services	2	Question Category		Assign a question category, if appropriate: Therapy/Intervention □ Aetiology/Risk Factors □ Diagnosis □ Prognosis/Prediction □ Frequency/Rate □ Phenomena □ Other □
Library Services	3	Literature Search		Conduct searches of the following bibliographic databases in the order specified below using keywords implicit in the PICO(T) strategy and any identified subject headings:
		Cochrane	3.1	**Cochrane Library** Comprising: the Cochrane Database of Systematic Reviews; the Cochrane Central Register of Controlled Trials (Central); the Database of Abstracts of Reviews of Effects; the Health Technology Assessment Database; the NHS Economic Evaluation Database. Use MeSH and keyword searches to identify systematic reviews and other relevant studies.
		Point-of-Care	3.2	**Point-of-Care Reference Tools** One or more of the following point-of-care reference tools: BMJ Best Practice; DynaMed; UpToDate.
		Medline	3.3	**Medline** Use MeSH and keyword searches. Limit results using the 'Human' search filter. Unless otherwise specified by the tumour group or warranted by the specific clinical question, limit results to studies from the previous 5 years. Where appropriate, limit intervention questions according to the following priority: Medline clinical queries; Cochrane systematic reviews; other systematic reviews or meta-analyses; RCTs; systematic reviews of cohort or cross-sectional studies; cohort or cross-sectional studies; general Medline or other sources. Where appropriate, limit diagnosis, prognosis or aetiology questions according to the following priority: Medline clinical queries; systematic reviews of cohort or cross-sectional studies; cohort or cross-sectional studies; general Medline or other sources.
		Embase	3.4	**Embase** Repeat the Medline search strategy above using Embase, if available.
		Other Databases	3.5	**Other Bibliographic Databases** Repeat the Medline search strategy above using the Cumulative Index to Nursing and Allied Health Literature and/or PsycINFO, as appropriate.
		Other Sources	3.6	**Other Sources** Use any other sources for background or additional information, as appropriate. Other sources may include: PubMed, particularly for in-process or ahead-of-print citations; quality-assured, subject-specific Internet resources; clinical reference books; patient information materials; etc.
		Trial Registers	3.7	**Trial Registers** When a relevant trial is identified through searching the bibliographic databases, a search of trial registers should be carried out to identify any related trials which have been completed but whose findings have not been published or made available. The tumour group should be alerted to the presence of these unpublished trials. The following sources may be

			included:
		3.7.1	**ClinicalTrials.gov**: http://clinicaltrials.gov/
		3.7.2	**Cochrane Central Register of Controlled Trials (Central)**: http://www.thecochranelibrary.com/
		3.7.3	**EU Clinical Trials Register**: https://www.clinicaltrialsregister.eu/
		3.7.4	**International Prospective Register of Systematic Reviews (Prospero)**: http://www.crd.york.ac.uk/prospero/search.asp
		3.7.5	**WHO International Clinical Trials Registry**: http://apps.who.int/trialsearch/
		3.8	For questions relating to economic evaluations, use the SIGN economic studies filter for Medline as a basis for the search strategy: http://www.sign.ac.uk/methodology/filters.html#econ. The following source may also be consulted, if available: HEED: Health Economic Evaluations Database: http://onlinelibrary.wiley.com/book/10.1002/9780470510933.
Library Services	**4**	**Reference Management**	Retain an electronic record of the search strategy and all search results using the Zotero reference management utility.
Library Services	**5**	**Search Results**	Respond to the tumour group using the Clinical Query Response form to include: ▪ a copy of the search strategy ▪ bibliographic details of all search results identified ▪ optionally, a note of studies that seem to the librarian to be of particular relevance to the clinical question See below Annex 2: Clinical Question Response.
Library Services	**6**	**Retracted Publications**	**6.1** Set up an alert to review results lists returned to the tumour group to rapidly capture any articles that are subsequently retracted or withdrawn, and notify the tumour group accordingly.
Tumour Group or Library Services		**Retracted Publications**	**6.2** Review all articles included in recommendations of the completed guideline to confirm that they have not been subsequently retracted or withdrawn.
Library Services	**7**	**Summary of Search Strategy**	A summary of the search strategy is included as an addendum to the completed guideline. Complete the Clinical Question: Summary of Search Strategy form and return to the tumour group. See below Annex 3: Clinical Question: Summary of Search Strategy.
Library Services	**8**	**[Pre-External Review] Update of Literature Search**	Once internal review of the guideline has been completed, literature searches for all clinical questions should be updated to capture articles published in the interim between the original literature search and the final draft of the guideline. Updated literature searches should be conducted prior to submission of the guideline for external review. Respond to the tumour group as previous using the Clinical Query Response form to include: ▪ a copy of the search strategy ▪ bibliographic details of all search results identified ▪ optionally, a note of studies that seem to the librarian to be of particular relevance to the clinical question See below Annex 2: Clinical Question Response.

Annex 1-Clinical Question Request to Library

Your Contact Details	
Name	
Job Title	
Work Address	
Telephone	
Email	
Employee Number	
Please state your clinical question	
… and list any relevant keywords	
… or (optional) enter keywords under the following headings (PICO)	
PICO	
Population/Problem	
Intervention/Indicator	
Comparator/Control	
Outcome	

Is your question specific to any of the categories below?		
GENDER	AGE GROUP	DATE OF PUBLICATION
Male □ Female □	Infant (0 – 23 months) ❒ Child (2 – 12 years) ❒ Adolescent (13 – 18 years) ❒ Adult (19 – 65 years) ❒ Aged (> 65 years) □	Current year only □ 0 – 5 years ❒ > 5 years □

Question Type
Therapy/Intervention □
Aetiology/Risk Factors □
Diagnosis □
Prognosis/Prediction □
Frequency/Rate □
Phenomena □
Other □

Additional Information

Annex 2-Clinical Question Response from Library

Dear_____,

Thank you for your email. Please see attached in response to your clinical query and, below, details of the search strategy applied to your question. If you wish to source any of the references contained in these results, or to search further, please do not hesitate to contact us.

Best wishes,

_____.

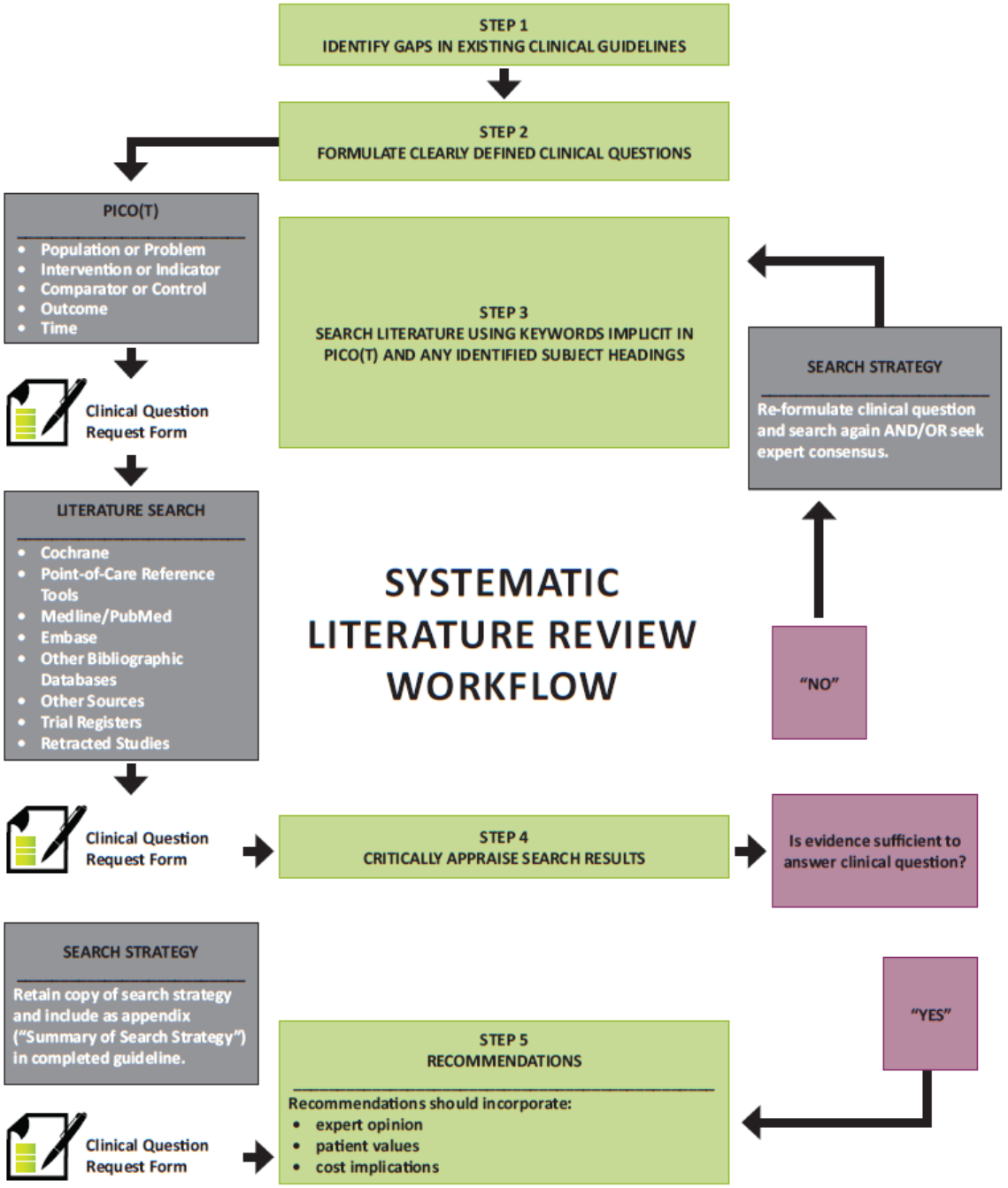
[ATTACH CLINICAL QUESTION REQUEST HERE]

Search Strategy		
Primary Database(s) Searched		
Search Strategy		
Other/Secondary Resources Searched		
Comments		
Contact		
Your Library Staff Contact		
Date		

Annex 3-Clinical Question: Summary of Search Strategy

Clinical Question		
PICO		
Population/Problem		
Intervention/Indicator		
Comparator/Control		
Outcome		
Is your question specific to any of the categories below?		
GENDER	AGE GROUP	DATE OF PUBLICATION
Male □ Female □	Infant (0 – 23 months) □ Child (2 – 12 years) □ Adolescent (13 – 18 years) □ Adult (19 – 65 years) □ Aged (> 65 years) □	Current year only □ 0 – 5 years □ > 5 years □
Question Type		
Therapy/Intervention □	Frequency/Rate □	
Aetiology/Risk Factors □	Phenomena □	
Diagnosis □	Other □	
Prognosis/Prediction □		
Search Strategy		
Primary Database(s) Searched		
Search Strategy	[Copy of base Medline and/or PubMed search strategy HERE. Include subject headings and search hits].	
Other/Secondary Resources Searched		
Search Strategy: Other Resources	[Copy of other search strategies HERE. Include subject headings and search hits].	
Comments	[Short paragraph describing search].	
Date		

*Annex 4-Systematic Literature Review Workflow**



* Based in part on "Figure 10: Systematic Literature Review" of SIGN 50: A Guideline Developer's Handbook. - Scottish Intercollegiate Guidelines Network (2011). SIGN 50: A Guideline Developer's Handbook. Revised ed. Edinburgh: Scottish Intercollegiate Guidelines Network.

Protocol designed by the HSE/hospital librarians in conjunction with the NCCP.

Appendix 5: Details of consultation process

As part of the consultation process, the draft guideline was circulated for review to this list of groups, committees and organisations. The guideline was also available on the NCCP website so it was accessible to all who wished to comment and feedback. All submissions and amendments from the national stakeholder and international expert review process are available on request from the Guideline Development Group. Further information regarding the consultation process can be found in section 3.10 External review.

Clinical leaders and healthcare managers	National Colorectal Clinical Leads group HSE Clinical Programme in Surgery HSE Clinical Programme in Radiology HSE Clinical Programme in Palliative Care HSE Clinical Programme in Medicines management & pharmacological interventions HSE Clinical Programmes in Renal Failure HSE Clinical Programme in Primary Care CEOs of the Hospital Groups CEOs of the designated cancer centres CEO/managers of the Cancer Network Hospitals
National groups, organisations, faculties & committees	Faculty of Surgery, RCSI Faculty of Radiology, RCSI Faculty of Pathology, RCSI Irish Society for Medical Oncologists (ISMO) Irish Association for Nurses in Oncology (IANO) Irish Stoma Care and Colorectal Nurses Association (ISCCNA) Irish College of General Practitioners (ICGP) Irish Association of Emergency Medicine Irish Association of Directors of Nursing and Midwifery Hospital Pharmacists Association of Ireland Oncology Pharmacists Special Interest Group Irish Association of Physicists in Medicine (IAMP)
Patient support and advocacy groups	HSE Patient Forum Irish Cancer Society Cancer Care West Marie Keating Foundation Gary Kelly Cancer Support Centre Purple House Support Group All Ireland Institute of Hospice and Palliative Care The Irish Hospice Foundation The Irish Association for Palliative Care ASH Ireland Stoma Support Groups nationwide
International Expert Review	Dr David Burling, Consultant Radiologist, St. Mark's Hospital, Harrow, UK Professor Brian Saunders, Professor of Endoscopy Practice, London North West Hospitals University Healthcare Trust, UK Professor Paul Horgan, Professor of Surgery, University of Glasgow, UK Mr Fergal Flemming, Assistant Professor of Surgery and Oncology, University of Rochester Medical Center, Rochester, New York, USA Dr Maria A. Hawkins, Professor of Radiation Oncology, University College London, UK Dr Amitabh Srivastava, Associate Professor of Pathology, Harvard Medical School, USA

Appendix 6: Economic Assessment

Key message

This budget impact assessment of the diagnosis, staging and treatment of rectal cancer is covered in two sections (Part A: Economic evidence summary and Part B: Budget Impact Analysis)

The report was compiled by:
Ms Rebecca Moore
Ms Keira Doherty-McCullough
Dr Helena Gibbons

The following people are thanked for the input they contributed:
Ms Michelle O'Neill, Senior Health Economist (HIQA)
Ms Margaret Morgan, Librarian (Midlands Regional Hospital)
Ms Nicola Fay, Regional Librarian (Midlands Regional Hospital)

Part A: Economic evidence summary

The Guideline Development Group undertook a literature search for evidence of clinical- and cost-effectiveness, cost and resource impact, including primary (research studies) and secondary (reviews) sources.

Methods

The literature sources searched are specified in the literature search strategy and include relevant resources, such as trial/guideline registries and relevant citation databases. The NCCP identified six economic questions pertaining to relevant areas within the guideline requiring cost-effectiveness analysis. Literature searches were carried out by HSE librarians and sifted by NCCP research staff. Selected literature was reviewed and quality appraised by the Guideline Development Group Health Economist to determine the cost of diagnosis, staging and treatment options. Using the SIGN economic literature checklist, a paper was determined to be too low quality to be used if the process of ensuring internal validity could not be established. A clearly focused question with an appropriate study design and measurable outcomes were important items considered in the overall assessment of study quality.

The estimated costs per quality adjusted life year (QALY) or life years gained (LYG) given in the following summaries are those reported within each study for the given year and national currency. These cost-effectiveness ratios have been complemented in brackets by euro estimates to correct for the purchasing power parity (PPP) between countries and health inflation to 2016-2017 costs as per the Health Information and Quality Authority's Economic Evaluation Guidelines (Health Information and Quality Authority (HIQA), 2014).

The following summaries report the conclusions regarding cost-effectiveness made by the authors of the reviewed literature. It is important to note that the thresholds of cost-effectiveness in other countries differ from that in Ireland and that statements of cost-effectiveness made in another context therefore may not be applicable to Ireland. While Ireland has no explicit cost-effectiveness threshold for non-drug interventions, cost-effectiveness ratios falling within the region of €45,000/QALY are conventionally considered cost-effective in Ireland.

Despite the conversion of the reported costs to PPP-adjusted 2016-2017 euro values it is also important to remember that there may still be a number of other factors which mean that cost-effectiveness ratios from other countries are not necessarily directly applicable to the Irish setting. For example, Ireland's discount rate is higher than that applied in the UK; so many interventions assessed in the UK would have less favourable ratios if the Irish discount rate was applied. Similarly, some analysis are conducted from the societal perspective and may account for more costs than are considered in Irish cost-effectiveness analyses (CEAs), which only account

for costs to the health sector. Accordingly, the euro-adjusted ratios reported here should only be considered broadly indicative of the level of cost-effectiveness rather than precisely adjusted estimates for the Irish health system.

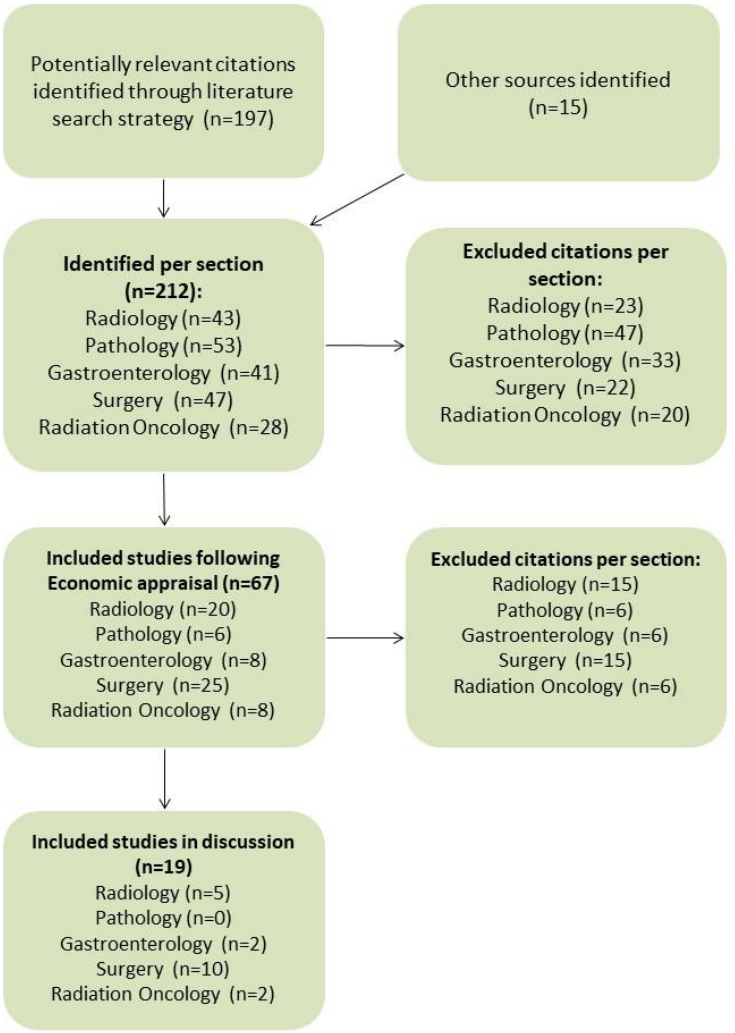


Figure 3 Economic literature review results breakdown

***Inclusion criteria**
Economic study
Applicable to the Irish healthcare system
Applicable to patient population/intervention/outcome
English Language
Relevant to guideline recommendations

***Exclusion criteria**
Not an economic study
Not in English language
Methodological or quality issues
Not applicable to Irish healthcare system
Not applicable to patient population/intervention/outcome
Not relevant to guideline recommendations

Table 15 Economic literature review protocol

ID	Search
1	Economics/
2	“costs and cost analysis”/
3	Cost allocation
4	Cost-benefit analysis/
5	Cost control/
6	Cost savings/
7	Cost of illness/
8	Cost sharing/
9	“deductibles and coinsurance”/
10	Medical savings accounts/
11	Health care costs/
12	Direct service costs/
13	Drug costs/
14	Employer health costs/
15	Hospital costs/
16	Health expenditures/
17	Capital expenditures/
18	Value of life/
19	Exp economics, hospital/
20	Exp economics, medical/
21	Economics, nursing/
22	Economics, pharmaceutical/
23	Exp “fees and changes”/
24	Exp budgets/
25	(low adj cost).mp.
26	(high adj cost).mp.
27	(health?care adj cost$).mp.
28	(fiscal or funding or financial or finance).tw.
29	(cost adj estimate$).mp.
30	(cost adj variable).mp.
31	(unit adj cost$).mp.
32	(economic$ or pharmacoeconomic$ or price$ or pricing).tw.
33	Or/1-32

Radiology

What is the cost-effectiveness of various imaging modalities in staging patients with colorectal cancer?

Of the 20 articles identified only five were relevant high quality economic studies assessing the cost-effectiveness of various imaging modalities in staging patients with colon or rectal cancer. The diagnostics included in the search were complete colonoscopy, CT colonography, CT-TAP, chest radiography, ultrasound, MRI, PET-CT.

The first study included was a very high quality health technology assessment from the UK under the NHS National Institute for Health Research Health Technology Assessment Programme. This study, "Brush et al. (2011) *The value of FDG positron emission tomography/computed tomography (PET/CT) in pre-operative staging of colorectal cancer: a systematic review and economic evaluation*" is a very comprehensive 192 page document. The research objectives were to "evaluate the diagnostic accuracy and therapeutic impact of PET-CT for the pre-operative staging of primary, recurrent and metastatic cancer using systematic review methods; undertake probabilistic decision-analytic modelling; and construct a value of information analysis". The systematic review did not find sufficient evidence for the use of PET-CT in primary colorectal cancer and only little supportive evidence in the use of PET-CT in pre-operative staging for recurrent and metastatic disease. The review judged the quality of the data identified to be generally of poor quality. The authors concluded that they could not support the use of PET-CT in staging primary colorectal cancer. The economic evaluations demonstrated a cost-effectiveness ratio of £21,409/QALY for recurrent rectal cancer, £6,189/QALY for recurrent colon cancer and £21,434 for metastatic disease.

Conclusions: PET-CT as an add-on imaging device is cost-effective in the preoperative staging of recurrent rectal and metastatic disease but not in primary colon or rectal cancer.

The second study by Halligan et al. (2015) "*Computed tomographic colonography compared with colonoscopy or barium enema for diagnosis of colorectal cancer in older symptomatic patients: two multicenter randomised trials with economic evaluation (the SIGGAR trials)"* is a 134 page long NHS National Institute for Health research health technology assessment. The cost-effectiveness is based on the SIGGAR trials and compares CT colonography with colonoscopy or barium enema in diagnosing symptomatic elderly patients. The objective was to examine the diagnostic efficacy, acceptability, safety and cost-effectiveness of CT colonography compared with BE or colonoscopy. The authors concluded that CT colonography detects more cancers and large polyps then barium enema and misses fewer cancers and improves patient experience but does increase follow-up investigations. The way in which results were delivered, quicker and face to face favoured colonoscopy however CT colonography improved patient experience in the short term. Compared to barium enema, CT colonography detected an extra serious colonic neoplasm for approximately £4,000. However detection rates were similar for CT colonography and colonoscopy and costs were also similar so there was not enough evidence for a solid recommendation.

Conclusions: No conclusions were possible.

In Huppertz et al. (2010) "*Whole-body MRI imaging versus sequential multimodal diagnostic algorithm for staging patients with rectal Cancer: Cost Analysis*", the direct and fixed costs of 33 patient were compared. Algorithm A included rectoscopy, endoscopic and abdominal ultrasound, chest x-ray, thoracic/abdominal CT in the case of positive findings in abdominal ultrasound or x-rays. The comparator was Algorithm B which consisted of rectoscopy followed by whole body MRI scanner. The study concluded that substantial savings are achievable with the use of whole-body MRI in pre-operative TNM staging of patients with rectal cancer compared to conventional work-up. The MRI option was deemed preferable to patients due to faster definitive diagnostic and to hospitals as the method involved less planning, personnel, steps and procedures and was thus easier to control. However, this study was a cost-minimisation study as the evidence for the superiority of the MRI scanner was not in the scope of the paper and was only based on one study Brown et al., (2003).

Conclusions: There is not enough evidence to conclude recommendations based on this study.

Yip et al. (2014) in "*Optimal imaging sequence for staging colorectal liver metastasis: Analysis of three hypothetical imaging strategies*" assessed inappropriate over investigations which can lead to delays in treatment and additional costs. Based on cost-analyses they concluded that a specialist multidisciplinary team should assess the initial CT of all patients with liver limited metastatic colorectal cancer, who are deemed fit for consideration for hepatectomy, prior to further radiological assessment by both PET-CT and MRI.

Conclusions: The most cost-effective option would be a specialist multidisciplinary team assessing the initial CT of all patients with liver limited metastatic colorectal cancer, who are deemed fit for consideration for hepatectomy, prior to further radiological assessment by both PET-CT and MRI.

In Zech et al. (2009)"*Health economic evaluation of three imaging strategies in patients with suspected colorectal liver metastasis: Gd-EOB-DTPA-enhanced MRI vs. extra cellular contrast-media enhanced MRI and 3-phase MDCT in Germany, Italy and Sweden*" the authors performed an economic evaluation of PV-MRI, ECCM-MRI and three-phase-MDCT as initial modalities in the work up of patients with metachronous colorectal liver metastasis. The authors concluded that PV-MRI with the lowest rate of further imaging needed can lead to cost-savings.

Conclusions: PV-MRI can lead to cost-savings.

Relevance to the guideline recommendation

The literature above discussed the cost-effectiveness of radiological modalities and techniques addressed within guidelines recommendations 2.2.1.3, 2.2.2.2, 2.2.4.1 and 2.2.5.2

Cost-effectiveness literature was available for recommendations 2.2.1.3 and 2.2.2.2. The recommendations discusses the use of PET-CT in patients with suspected liver metastases or used as a problem solving tool in patients with equivocal imaging results. This is supported by the cost-effectiveness literature which concluded that they could not support the use of PET-CT in staging primary colorectal cancer. The use of PET-CT in this cohort of patients should only be used after careful consideration of the patient at a multidisciplinary team meeting.

Cost-effectiveness literature was also available for CT colonography which is mentioned in recommendations 2.2.4.1, 2.2.5.1 and 2.2.5.2. Recommendation 2.2.4.1 advises that in patients with obstructing rectal cancer full colonic evaluation with CT colonography should be carried out to detect the presence of a synchronous tumour in patients where colonoscopy is not possible. Recommendation 2.2.5.1 advises that complete visualisation of the entire colon by colonoscopy is recommended prior to surgery. If colonoscopy is not possible CT colonography is the modality of choice.

A HTA addressed the use of CT colonography (compared with colonoscopy and barium enema) specifically in diagnosing colorectal cancer in older symptomatic patients (≥55 years) with symptoms suggestive of colorectal cancer. The cost-effectiveness analysis is not relevant to the recommendations made in this guideline, as the setting is different (i.e. diagnosing rectal cancer).

Cost-effectiveness literature was not available for recommendations 2.2.1.1, 2.2.1.2, 2.2.2.1, 2.2.3.1, 2.2.3.2. Recommendations 2.2.1.1 relates to the utility of CT-TAP as standard for initial staging of patients

Recommendations 2.2.1.2 and 2.2.2.1 relates to the utility of MRI and its role in the evaluation and resectability of liver metastases. Recommendation 2.2.3.1 relates to the use of MRI for locoregional staging. The cost-effectiveness literature detailed above is supportive of PV-MRI and Yip et al. states that patients who are deemed fit for consideration for hepatectomy; CT is more economically cost effective when assessed by a MDT prior to further radiological assessment by both PET-CT and MRI.

Recommendation 2.2.1.3 states that PET-CT is not a first line imaging tool and this is support by the cost-effectiveness data presented above.

Pathology

What is the cost-effectiveness of processing lymph nodes or classifying pathological specimens in patients with colorectal cancer?

We were unable to include any studies in this section. Of the six articles found in the literature that were included for full text extraction, there were no high quality cost-effectiveness studies relevant to the key question.

Relevance to the guideline recommendation
N/A

Gastroenterology

What is the cost-effectiveness of gastroenterology services for colorectal cancer?

Of the eight articles found in the literature search that were included for full text extraction only two were high quality. An additional study by Halligan et al. (2015) was found during the search for cost-effectiveness literature for the radiology economics question but is relevant to the gastroenterology recommendations made within this guideline.Law et al. (2016) compared the cost-effectiveness of endoscopic resection (ER) versus Laparoscopic resection (LR) in the management of complex colon polyps. The two strategies ER versus LR were compared in a hybrid markov model with a 10 year time horizon. In the first strategy the patient underwent ER followed by surveillance colonoscopy at three, six and 12 months any failed ER and residual adenoma at 12 months were referred for LR. Under strategy two, patients underwent LR as primary treatment. Performance was obtained for a systematic review of the literature. Medicare and Medicaid services were used to obtain costs and loss of utility. The results showed that LR was more costly and yielded fewer QALYs compared with ER. The cost of ER was $5,570 per patient with an average QALY of 9.64 while a LR was $1,8717 and yielded fewer QALYs (9.577). The authors concluded that ER is a cost-effective strategy for removal of complex colon polyps.

The second study to be included, Jayanna et al. (2016) undertook a cost-analysis of endoscopic mucosal resection versus surgery for large laterally spreading colorectal lesions. The authors concluded that EMR for large laterally spreading colorectal lesions is safer than surgery and savings of AU$8,839 and 2.81 inpatient nights can be achieved with a primary EMR strategy for large laterally spreading colorectal lesions in comparison with hypothetical ideal Survival outcome. Event specific costs were derived from Australian Refined Diagnostic Related Groups (AR-DRG).

The third study conducted by Haligan et al. (2015), "*Computed tomographic colonography compared with colonoscopy or barium enema for diagnosis of colorectal cancer in older symptomatic patients: two multicenter randomised trials with economic evaluation (the SIGGAR trials)"* is a 134 page long NHS National Institute for Health research health technology assessment. The cost-effectiveness is based on the SIGGAR trials and compares CT colonography with colonoscopy or barium enema in diagnosing symptomatic elderly patients. The objective was to examine the diagnostic efficacy, acceptability, safety and cost-effectiveness of CTC compared with BE or colonoscopy. The authors concluded that CTC detects more cancers and large polyps then BE and misses fewer cancers and improves patient experience but does increase follow-up investigations. They way in which results were delivered, quicker and face to face favoured colonoscopy however CTC improved patient experience in the short term. Compared to barium enema, CTC detected on extra serious colonic neoplasm for approximately £4,000. However detection rates were similar for CTC and colonoscopy and costs were also similar so there was not enough evidence for a solid recommendation.

Relevance to the guideline recommendation
The literature above discussed the cost-effectiveness of interventions in Section 2.2 Diagnosis and staging, Section 2.5 Treatment: Patients with early rectal cancer and Section 2.4 Treatment: Surgical techniques.

2.2.5.1 recommends that complete visualisation of the entire colon by colonoscopy should be performed prior to surgical intervention. 2.2.5.2 adds that in the event the patient is unsuitable for colonoscopy, CT colonography should be performed and these recommendations are supported by evidence from a meta-analysis, a number of randomised controlled trials, two population-based studies and an international guideline. The HTA conducted by Halligan et al. (2015) found that detection rates for cancer and large polyps were similar for CTC and colonoscopy, as were costs but added due to paucity of further evidence, a solid conclusion on cost-effectiveness could not be formed.

Surgery

What is the cost-effectiveness of various surgical techniques in patients with colorectal cancer?

Of the 25 articles identified, ten were relevant high quality economic studies assessing the cost-effectiveness of various surgical procedures in colon and rectal cancer. An additional economics analysis by NICE 2019 was sourced separately to the literature search carried out but was deemed relevant for this question.

The results of an economic analysis carried out by NICE 2019 which looks at the optimal surgical technique by comparing laparoscopic, open, TaTME and robotic approaches for rectal cancer. It has been suggested that the laparoscopic approach may be cost effective for rectal cancer surgery but there is uncertainty regarding the results largely driven by the uncertainty around some of the clinical effectiveness estimates especially around recurrence. A speculative analysis comparing the open, laparoscopic, robotic and TaTME approaches also suggests that the TaTME may be cost-effective.

Conclusion: The lack of clear data as well as the assumptions required to run this four-way comparison severely limit the conclusions that can be drawn from the analysis

The cost-effectiveness of laparoscopy in rectal cancer was assessed by authors Keller at al. (2014) in "*Cost-effectiveness of Laparoscopy in Rectal Cancer*". This was a case-matched study from the US conducted at a tertiary referral setting. 250 patients were included in the study through a review of a prospective database for elective laparoscopic rectal cancer resection which was matched to open cases. There was no significant difference in TNM stage, tumour distance from the anal verge or neoadjuvant therapy received between the two groups. The two groups were oncologically equivalent and there were no significant difference in postoperative complications, 30-day readmission, re-operation or mortality. However the laparoscopic group had significantly shorter stay and lower total hospital costs and more patients in the open resection group required intensive care. The average total cost for open surgery was USD $21,803 vs. USD $17,214 for laparoscopic surgery in this tertiary hospital setting.

Conclusion: Laparoscopy is cost-effective for rectal cancer surgery, improving patient outcomes and lowering costs in a US tertiary hospital setting.

Another study, "*Cost-savings for elective laparoscopic resection compared with open resection for colorectal cancer in a region of high uptak*e" by Thompson et al. (2014) also looked at the cost-effectiveness of laparoscopic surgery versus open resection. This study used hospital data from public hospitals in Queensland, Australia between 2009-2011. The results showed that the crude mean cost for laparoscopic resection was AUS $20,036 and for open resection was. AUS $22,780. The two procedures had the same length of surgery in this study but patients in the laparoscopic surgery group had shorter length of stay and fewer admissions to the ICU.

Conclusions: Laparoscopic resection for CRC was shown to be cost-saving when the technique is widely adopted and the surgeons are experienced in the technique.

Norwood et al. (2011) assessed the nursing and financial implications of laparoscopic colorectal-surgery in a paper titled "*The nursing and financial implications of laparoscopic colorectal surgery: data from a randomised controlled trial".* They looked at the cost of the nursing staff as according to the authors this topic was unaddressed. They included patients from the Australasian Laparoscopic Colon Cancer Study from one hospital in Australia. Of the 44 patients in the open surgery group an average of 80 hours nursing was needed and in the 53 patients in the laparoscopic arm 58.5 hours of nursing had been utilised. The cost of open surgery was AUS $9,698 and laparoscopic surgery AUS $10,951.

Conclusions: Laparoscopic surgery reduces nursing intensity versus open resection.

In a study from the US, "*Cost-effectiveness of Lparoscopic vs Open Resection for Colon and Rectal Cancer*", Jensen et al (2012) constructed a decision model with data from previously published studies. The results showed that Laparoscopic surgery yielded average savings of USD $4,283 per patient. There was no difference in QALYs (0.001 more QALY than open surgery). The only issue that would not make laparoscopic surgery more cost-effective was the postoperative hernia rates which needed to be equivalent or less than that of open surgery rates to ensure cost-effectiveness of Laparoscopic resection. The study from 2012 concluded that more surgeons, nurses and operating room staff needed to be trained in this procedure.

Conclusions: Laparoscopic resection is cost-effective versus open resection under almost all conditions.

Jordan et al (2014) assessed quality of life in the first six weeks after surgery to assess cost-effectiveness of Laparoscopic surgery versus open surgery in "*Laparoscopic versus Open colorectal resection for cancer polyps: a cost-effectiveness study*" as all other comparators of the two procedures according to the authors suggested the methods were equivalent. Using the EQ-5D quality of life measurement the laparoscopic group gained an average of 0.011207 QALYs. Incremental cost-effectiveness ratios showed the cost per QALY gained in the Laparoscopic surgery group was GBP £12,375 compared to the open surgery group.

Conclusion: Cost-Effective Acceptability Curves showed that at a willingness to pay threshold of GBP £30,000 there was a >65% chance that laparoscopic surgery would be cost-effective in the NHS.

In a study, "*Clinical effectiveness and cost-effectiveness of laparoscopic surgery for colorectal cancer: systematic reviews and economic evaluation*" Murray et al. (2006) pooled 20 different studies on laparoscopic surgery and pooled them into a Markov model. The results did not find Laparoscopic surgery to be more cost-effective as the outcomes were similar, except for a quicker recovery time with Laparoscopic surgery but the laparoscopic method was more costly and surgery times were also longer with laparoscopy. They concluded that Laparoscopy yielded an extra cost of GBP £250-300 per patient. The authors suggested that long-term follow-up of the RCT patients would make the results more robust.

Conclusions: Additional data on both costs and outcomes was deemed useful for further research, ideally from methodologically sound RCT's. However Laparoscopic surgery seemed more costly than open surgery this would vary depending on patient selection and surgery technique. This paper used data from 2000-2005.

Another study from the UK by Hernandez et al. (2008) "*Systematic review of economic evaluations of laparoscopic surgery for colorectal cancer*" undertook a systematic review of economic evaluations of laparoscopic surgery using published papers form 2000-2005. Five studies were included and the results were inconsistent. The authors concluded that laparoscopic surgery was generally more expensive but the effectiveness data was not consistent and unreliable.

Conclusions: Studies from 2000-2005 on the clinical and economic aspects of laparoscopic surgery were imprecise and unreliable.

Using the NHS perspective Roberts et al. (2015) paper "*Cost-Utility of operative versus non-operative treatment for colorectal liver metastasis*" wanted to find out if surgery was more cost-effective than non-surgical interventions (palliative care, including chemotherapy) for treating colorectal liver metastasis (CRLM) (Roberts et al., 2015). Results were conclusive and surgery had a mean survival of 41 months versus 21 months in the non surgical group. In addition, surgery was less costly €22,200 compared to €32,800 and yielded 4.017 QALYS versus 1.111 QALY.

Conclusion: Surgery to treat CRLM cost-effective as it is less costly and more effective than non-surgical intervention.

The cost-effectiveness of robotic surgery for rectal cancer focusing on short term outcomes was analysed by Kim et al. (2015). Two patient groups were retrospectively compared to ascertain the cost-effectiveness of robotic surgery versus laparoscopic surgery in patients with rectal cancer. Propensity matched scoring was used to reduce bias between the robotic surgery group and the laparoscopic surgery group. Costs and short term outcomes were compared. The short-term outcomes were similar between the groups, and 30-day post-surgery complications were not significantly different. In patients with robotic surgery with complications the postoperative course seemed to be milder. However the costs were $3,137 higher on average in the robotic surgery group.

Conclusions: Short term outcomes were similar in the two patient groups receiving either robotic surgery or laparoscopic surgery but costs were higher in the robotic surgery group, cost-effectiveness of robotic surgery was not demonstrated. It is not known how the South Korean costs would compare in the Irish healthcare setting.

Van den Broeck et al. (2009) in "*Transanal endoscopic microsurgery (TEM) versus endoscopic mucosal resection (EMR) for large rectal adenomas*" studied TEM versus EMR for large rectal adenomas the randomise controlled TREND trial. The costs and effects from a Dutch healthcare perspective were collected alongside the trial. The trial was not able to demonstrate statistical non-inferiority of EMR. There was no difference in quality of life. Nevertheless EMR could be considered a primary method because of a tendency of lower complication rates and a better cost-effectiveness ratio.

Conclusions: EMR saved approximately €3,000 per patient without any difference in QALYs and is thus the preferable treatment in terms of cost-effectiveness.

Relevance to the guideline recommendation

The literature above discussed the cost-effectiveness of surgical interventions and techniques which are addressed within this guideline for recommendations 2.7.1.1. and 2.7.2.1.

The cost-effectiveness literature suggests that TaTME may be cost effective but they cannot state this with absolute certainty due some of the estimates around disease recurrence. This is relevant to Recommendation 2.7.1.1 where high quality TME is recommended for patients with rectal cancer.

The cost-effectiveness literature detailed above concludes that laparoscopic approach is generally more cost effective than open procedures however the technique needs to be widely adopted with surgeons expertly trained. Recommendation 2.7.2.1 relates to post operative continence and sexual function but states there is no clear evidence in post operative genitourinary function between minimally invasive surgery and open TME. Evidence from a Cochrane review and a meta-analysis (Broholm et al., 2015) was used to support this recommendation regarding these important quality of life issues.

Radiation Oncology

What is the cost-effectiveness of radiotherapy in patients with colorectal cancer?

Of the eight articles found in the literature search that were included for full text extraction only two were high quality cost-effectiveness studies relevant to our interventions of interest: Short-course radiotherapy, long-course radiotherapy, boost, Intensity modulator radiotherapy, 3D conformal radiotherapy, 2D conformal radiotherapy, postoperative radiotherapy (+/- chemotherapy).

The first study of the two papers to be included, conducted by van der Brink et al. (2004) *Cost Utility Analysis of preoperative radiotherapy in patients with rectal cancer undergoing total mesorectal excision: A study of Dutch colorectal cancer group",* compared the societal costs and the quality adjusted life expectancy of patients undergoing mesorectal excision with or without short-term radiotherapy (5 x 5 Gy). A Markov model was constructed to predict the clinical and economical outcomes of preoperative radiotherapy with data from a randomised clinical trial. The results from the model estimated that the loss of quality of life was outweighed by the gain in life-expectancy, 0.39 years, and costs, $9,800. The cost-effectiveness ratio was $25,100/QALY.

Conclusions: Preoperative radiotherapy in patients with rectal cancer undergoing total mesorectal excision is cost effective. $25,000/QALY is below the Irish threshold of €40,000/QALY. The paper was of high quality and the Dutch healthcare setting is comparable to the Irish, however the paper is from 2003 and costs are presented in USD.

The second paper to be included was a study from Dahlberg et al. (2002),"*Cost-effectiveness of preoperative radiotherapy in rectal cancer: results from the Swedish rectal cancer trial*." In the study 98 randomised patients from the Swedish rectal cancer trial were followed for eight years and costs related to the treatment of rectal cancer and any associated complications were analysed. The irradiated group had 30% higher costs compared to the surgery alone group. However the higher recurrence rates for the surgery alone group contributed to an over-all increase in costs of 70 per cent. An average increase in costs of $5,000 per patient with an increase in mean survival generated a QALY of $3,650.

The paper's Swedish setting is comparable to an Irish setting. The study was of high quality based on a RCT that finished in 1997. Only caveat is that the paper is from 2003 and costs are presented in USD.
Conclusions: Preoperative radiotherapy in rectal cancer is cost effective as $3,650 per QALY is below the Irish threshold of €40,000/QALY.

Relevance to the guideline recommendation

The literature above discussed the cost-effectiveness of radiotherapy alone or with concurrent chemotherapy which is addressed within guidelines recommendation 2.8.1.1.

Recommendation 2.8.1.1 states that in patients with rectal cancer who have had a resection with a positive margin and have not received preoperative therapy than postoperative chemoradiotherapy is an acceptable salvage approach in. Neoadjuvant therapy is deemed cost effective by the literature presented above with Brink et al. (2004) estimating that the loss of quality of life was outweighed by the gain in life-expectancy.

Cost-effectiveness studies: Evidence tables

Radiology

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
Brush et al. (2011) *The value of FDG positron emission tomography/computed tomography (PET/CT) in pre-operative staging of colorectal cancer: a systematic review and economic evaluation* (United Kingdom)	FDG Positron emission tomography-computed tomography (FDG PET-CT).	HTA Systematic review of 5 studies. Unknown patient population.	**Model type:** Probabilistic decision-analytic model **Perspective:** UK NHS **Time horizon:** Not provided **Discount rate:** 3.5%	The economic evaluations demonstrated a cost-effectiveness ratio of £21,409/QALY for recurrent rectal cancer, £6,189/QALY for recurrent colon cancer and £21,434 for metastatic disease.	PET-CT as an add-on imaging device is cost-effective in the pre-operative staging of recurrent rectal and metastatic disease but not in primary colon or rectal cancer.	A lower confidence interval was used to calculate the standard error for use in the probabilistic analysis as it represented the widest range of uncertainty.	The recurrent models found FDG PET-CT as an add-on device to have an incremental cost-effectiveness ratio (ICER) of £21,409 per QALY in the rectal model and £6,189 per QALY in the colon model. The metastatic model produced an ICER of £21,434 per QALY. Considering the NICE monetary threshold of £20,000-£30,000 per QALY, these ICERs can be considered cost-effective.
Halligan et al. (2015) *Computed tomographic colonography compared with colonoscopy or*	CT colonography and colonoscopy vs. CT colonography and barium enema.	5,384 patients from 21 NHS hospitals	**Model type:** Markov model **Perspective:** NHS Secondary	CT colonography detected on extra serious	CT colonography detects more cancers and	Costs were analysed in relation to the benefits	Detection rates in BE trial were 7.3% for CTC compared to 5.6% for BE. CT

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barium enema for diagnosis of colorectal cancer in older symptomatic patients: two multicenter randomised trials with economic evaluation (The SIGGAR Trials) (United Kingdom)			care **Time horizon:** 5.2 years **Discount rate:** Not provided	colonic neoplasm for approximately £4,000.	large polyps then barium enema and misses fewer cancers and improves patient experience but does increase follow-up investigations.	of detecting extracolonic lesions separately from colonic lesions. Bootstrapping was used to estimate costs and cost differences. ICERS and their CI and a scatter plot were produced based on 1000 replicates.	colonography was better at detecting large polyps with no significant differences for cancer. CT colonography was associated with higher healthcare costs. The cost per large polyp or cancer detected as £4,235. ICERS amongst the studies varied from USD$2,144-USD$498,668 with a tendency for more recent studies to yield more favourable results.
Huppertz et al. (2010) *Whole-body MRI imaging versus sequential multimodal diagnostic algorithm for staging patients with rectal Cancer: Cost Analysis*	**Algorithm A:** included rectoscopy, endoscopic and abdominal ultrasound, chest x-ray, thoracic/abdominal CT in the case of	33 people with rectal cancer.	**Model type:** Cost minimisation **Perspective:** Not provided **Time horizon:** Not provided **Discount rate:**	This study was a cost-minimisation study as the evidence for the superiority of the MRI scanner was	The MRI option was deemed preferable to patients due to faster definitive diagnostic and to hospitals as	Activity based costing was used as the framework for cost analysis.	Costs could be substantially reduced by replacing the current sequential multimodal diagnostic algorithm with a

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
(Germany)	positive findings in abdominal ultrasound or x-rays. **Algorithm B:** which consisted of rectoscopy followed by whole body MRI scanner.		Not provided	not in the scope of the paper.	the method involved less planning, personnel, steps and procedures and was thus easier to control.		novel algorithm based on whole body MRI for the preoperative staging of rectal cancer.
Yip et al. (2014) *Optimal imaging sequence for staging colorectal liver metastasis: Analysis of three hypothetical imaging strategies* (United Kingdom)	CT, PET-CT and MRI and the use of appropriate imaging sequencing models.	644 patients with colorectal cancer	**Model type:** Not provided **Perspective:** Not provided **Time horizon:** Not provided **Discount rate:** Not provided	Upfront imaging pathway £2,700 compared to £2,440.73 for a sequential pathway and £2,381 for the hybrid pathway.	The most-cost effective option would be a specialist MDT assessing the initial CT of all patients with liver limited metastatic colorectal cancer, who are deemed fit for consideration for hepatectomy, prior to further radiological assessment by both PET-CT	Not provided	Based on cost analysis, assessment with initial CT followed by MDT with subsequent PET-CT and MRI imaging thereafter, was associated with shortest time to decision making and lowest cost.

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
					and MRI.		
Zech et al. (2009) *Health economic evaluation of three imaging strategies in patients with suspected colorectal liver metastasis: Gd-EOB-DTPA-enhanced MRI vs. extra cellular contrast-media enhanced MRI and 3-phase MDCT in Germany, Italy and Sweden* (Germany, Italy & Sweden)	PV-MRI, ECCM-MRI and three-phase-MDCT.	26 pairs of clinicians (One liver surgeon and one radiologist) from Germany, Italy and Sweden.	**Model type:** Decision tree model **Perspective:** Health care Payer **Time horizon:** Not provided **Discount rate:** Not provided	A strategy starting with PV-MRI was €959 and was cost-saving compared to ECCM-MRI (€1,123) and MDCT (€1,044) in Sweden. In Italy PV-MRI was cost-saving compared to ECCM-MRI and had total costs similar to MDCT.	According to the estimates, the proportion of high risk resectable, unresectable and non malignant categories were higher in the PV-MRI in comparison to ECCM-MRI and MDCT. In patients considered eligible for hepatic resections and scheduled for low risk resections, the proportion of "confirmed surgical plans" were estimated to be higher and	Results were presented to a third party where any areas in the uncertainty of the results were discussed and resolved.	PV-MRI with the lowest rate of further imaging needed can lead to cost-savings.

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
					the proportion of "modified surgical plans" lower following initial imaging with PV-MRI compared with ECCM-MRI and MDCT.		

Pathology

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
N/A							

Gastroenterology

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
Law et al. (2016) *Endoscopic resection is cost-effective compared with laparoscopic resection in the management of complex Colon polyps: an economic analysis* (United States)	Endoscopic resection (ER) vs laparoscopic resection (LR).	ER vs LR were evaluated in a hypothetical cohort of patients with complex colon polyps (CCPs). Reference case: a healthy 50-year-old patient who underwent an initial colonoscopy with identification of a complex, sessile colon polyp without features of deep submucosal invasion (>1000 mm).	**Model type:** Hybrid Markov model **Perspective:** Third-party payer **Time horizon:** 10 year **Discount rate:** None provided	The cost of ER of a CCP was $5,570. The cost of LR of a CCP was $18,717 per patient.	The probability of an adverse event with ER was 9.1%; however, the probability that an adverse event would require surgical intervention was 1.0%. After the index resection and routine surveillance colonoscopies at 3 to 6 months and 12 months, the probability of persistent adenomatous tissue was 7.2%.	Baseline estimates and costs were varied by using a sensitivity analysis through the ranges.	The cost of ER of a CCP was $5,570 per patient and yielded 9.640 QALYs. LR of a CCP cost $18,717 per patient and yielded fewer QALYs (9.577).
Jayanna et al. (2016) *Cost-analysis of endoscopic mucosal*	Endoscopic mucosal resection versus surgery for large laterally spreading	Endoscopic mucosal resection performed on 1489 colorectal	**Model type:** Surgical Management model **Perspective:**	EMR for large LSL is safer than surgery and savings of AU$8839 and 2.81 inpatient nights.	EMR performed at an appropriately experienced and resourced	Data was compared from patients who underwent EMR with those from	Endoscopic management produced a total cost-saving of US

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
resection vs surgery for large laterally spreading colorectal lesion (Australia)	colorectal lesions.	lesions in 1253 patients.	Not provided **Time horizon:** Not provided **Discount rate:** Not provided		tertiary centre should be first line treatment for patients with large laterally spreading colorectal lesion.	a model where all patients had surgery without complication. Event specific costs based on Australian refined diagnosis related group codes were used to estimate average costs per patient.	$10,284,909; the mean cost difference per patient was US $7602. In patient hospitalisation length of stay was reduced by 2.81 nights. This approach is likely to deliver substantial overall health expenditure savings.

Surgery

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
Roberts et al. (2015) *Cost-Utility of operative versus non-operative treatment for colorectal liver metastasis* (United Kingdom)	Resection for colorectal liver metastasis (CRLMs) compared with non-operative treatment (palliative care including chemotherapy).	Observational study of two patient cohorts. Operative cohort comprised consecutive patients undergoing CRLM resection between 1992 and 2001 (n=286). The non-operative cohort was identified from a review of patients who presented to a dedicated liver surgery multidisciplinary team between 2008 and 2010 (n=46).	**Model type:** Markov model **Perspective:** Healthcare provider perspective (UK NHS) **Time horizon:** Lifetime time horizon **Discount rate:** 3.5%	Non-operative treatment mean cost: €32,800 Operative strategy mean cost: €22,200	Median survival was 41 and 21 months in the operative and non-operative cohorts respectively (p< 0.001).	Probabilistic sensitivity analysis was carried out to examine the impact of uncertainties in the model parameters on the robustness of the model results. One-way sensitivity analysis was carried out to provide further insight into the impact of specific parameters on the model results.	The operative strategy dominated non-operative treatments, being less costly (€22,200 *vs.*€32,800) and more effective (4.017 *vs.* 1.111 QALYs gained). The results of extensive sensitivity analysis showed that the operative strategy dominated non-operative treatment in every scenario.
Kim et al. (2015) *Cost effectiveness of robotic surgery*	Robotic surgery (RS) compared with laparoscopic surgery (LS).	From January 2007- December 2011, 311 patients underwent	**Model type:** Cost-effectiveness analysis **Perspective:**	**RS:** Total hospital charges: $15,965.10 Operation: $1,0375.40	Most perioperative outcomes were similar between the groups	To reduce the selection bias, propensity score matching with a 1:1 ratio	Total hospital charges and patients' bill were higher in RS than in LS.

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
for rectal cancer focusing on short term outcomes (Korea)		totally RS and 560 patients conventional LS for rectal cancer in a single large-volume institution in Korea. As a result of the propensity score-matching, both groups included 251 patients.	Not provided **Time horizon:** 30 days **Discount rate:** Not provided	Anaesthesia: $1,028.50 Preoperative diagnosis: $1,175.70 Postoperative management: $3,317.00 Other: $56.40 **LS:** Total hospital charges:$11,933.00 Operation: $6,796.30 Anaesthesia: $875.30 Preoperative diagnosis: $1,184.80 Postoperative management: $3,010.20 Other: $66.50.	except for the OT. The OT was longer in RS than in LS, and the time to soft diet was earlier in RS than in LS. Complications and readmission rates within 30 days of surgery were not different between the 2 groups.	was performed according to a number of variables such as sex, age, year of operation, smoking status, BMI etc. Continuous variables were compared using Student t tests or Mann-Whitney U tests and categorical variables were compared using X2 or fisher exact tests.	The total hospital charges for patients who recovered with or without complications were higher in RS than in LS, although their short-term outcomes were similar. In patients with complications, the postoperative course after RS appeared to be milder than that of LS. Total hospital charges for patients who were readmitted due to complications were similar between the

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
							groups.
Keller at al (2014) *Cost-effectiveness of Laparoscopy in Rectal Cancer* (United States)	Elective laparoscopic rectal cancer resection versus open resection	Case matched study from the United States. n=254 patients undergoing elective rectal cancer resection (n=125 laparoscopic rectal cancer resections, n=129 open cases).	**Model type:** Cost-effectiveness analysis **Perspective:** Not provided **Time horizon:** Not provided **Discount rate:** Not provided	The average total cost for open surgery was USD $21,803 versus USD$17,214 for laparoscopic surgery in this tertiary hospital setting.	The two groups were oncologically equivalent and there were no significant difference in postoperative complications, 30-day readmission, re-operation or mortality. However the laparoscopic group had significantly shorter stay and lower total hospital costs and more patients in the open resection group required intensive care.	Data analysis was completed by using Student t test, the X2 test or fisher exact tests.	Laparoscopy is cost-effective for rectal cancer surgery improving patient outcomes and lowering costs. The average total cost for open surgery was USD $21,803 versus USD $17,214 for laparoscopic surgery.
Thompson et al (2014) *Cost-savings for elective*	Laparoscopic surgery versus open resection.	1,391 patients who received an elective resection for	**Model type:** Regression Model **Perspective:**	The results showed that the crude mean cost for laparoscopic resection was AUS	The two procedures had the same length of surgery in this		Laparoscopic surgery cost lower than open

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
laparoscopic resection compared with open resection for colorectal cancer in a region of high uptake (Australia)		colorectal cancer.	Not provided **Time horizon:** Not provided **Discount rate:** Not provided	$20,036 and for open resection was. AUS $22,780.	study but patients in the laparoscopic surgery group had shorter length of stay and fewer admissions to the ICU. Laparoscopic resection for CRC was shown to be cost-saving when the technique is widely adopted and the surgeons are experienced in the technique.		procedures but this could be due to a number of confounder factors
Norwood et al. (2011) *The nursing and financial implications of laparoscopic colorectal surgery: data from a randomised*	Laparoscopy versus open surgery.	Participants from the Australasian Laparoscopic Colon Cancer Study (ALCCaS) Data from 97 patients were analysed (laparoscopy, 53; open	**Model type:** Cost-effectiveness analysis **Perspective:** Healthcare **Time horizon:** Not provided **Discount rate:** Not provided	The total cost of the procedure from admission to discharge was AUS$ 9,916⁄£5,631 (AUS$ 4,694–90,397) in the open surgery group and AUS $10,951⁄£,6219 (AUS$ 6,505–66,236)	There was no statistical difference in the median LOS between the two groups. The median number of nursing hours per patient for	Subgroup analysis was performed according to anatomical resection which showed no significant differences in LOS, nursing	The median number of nursing hours required per patient was 80 in the open group and 58.5 in the laparoscopic group which

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
controlled trial (Australia)		surgery, 44).		in the laparoscopy group.	their total hospital stay was 80 (27.5–907) h in the open surgery group and 58.5 (15–684.5) h in the laparoscopy group (a saving of approximately 10 min per patient per hour).	time in minutes or cost.	represents a time saving of 10 minutes per patient. Nursing costs were less for laparoscopic procedures.
Jensen et al. (2012) *Cost-effectiveness of Laparoscopic vs Open Resection for Colon and Rectal Cancer* (United States)	Laparoscopy versus open surgery.	Data from previously published studies (randomised controlled trails where possible). Included sources of cost and QOL data related to laparoscopic and open resection of colon and rectal cancer.	**Model type:** Decision analysis model **Perspective:** Societal **Time horizon:** 5 years **Discount rate:** 3%	The results showed that laparoscopic surgery yielded average savings of USD $4,283 per patient. There was no difference in QALYs (0.001 more QALY than open surgery).	Laparoscopic resection is cost-effective versus open resection under almost all conditions. The only issue that would not make laparoscopic surgery more cost-effective was the post-operative hernia rates which needed to be	Sensitivity analyses were performed on all variables input into the model. A sensitivity model was also performed in which patients whose surgeries were converted from laparoscopic to open had higher costs	Laparoscopic resection resulted in a cost-savings of $4,238 and no difference in QALYS (0.001 more QALYS than open resection). Post-operative hernia rates needed to be equivalent or less than that of open

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
					equivalent or less than that of open surgery rates to ensure cost-effectiveness of laparoscopic resection.	related to the use of both laparoscopic and open equipment and additional operating room time.	surgery rates to ensure cost-effectiveness of laparoscopic resection.
Jordan et al. (2014) *Laparoscopic versus Open colorectal resection for cancer polyps: a cost-effectiveness study* (United Kingdom)	Laparoscopic versus open colorectal resection for cancer or polyps.	95 patients with either cancer or polyps requiring either laparoscopic (n=68) or open colorectal resection (n=27).	**Model type:** Multivariate regression model **Perspective:** National Health Service **Time horizon:** Not provided **Discount rate:** Not provided	Using the EQ-5D quality of life measurement the laparoscopic group gained an average of 0.011207 QALYs. Incremental cost-effectiveness ratios showed the cost per QALY gained in the laparoscopic surgery group was GBP £12,375 compared to the open surgery group. Cost-effective acceptability curves showed that at a willingness to pay threshold of GBP £30,000 there	The cost of the laparoscopic procedure was £1,037 higher than open due to cost of equipment. Staff cost were £190 lower due to shorter operative times. The open group had a longer mean length of stay which incurred a £897 higher bed day cost compared with a laparoscopic procedure. There was no	Uncertainty in the ICER point estimates are represented using confidence intervals, on the cost-effectiveness plan (CEP).	At 28 days the ICER calculated as the difference in adjusted means cost divided by the difference in adjusted mean QALYs, and showing the cost per QALY gained from laparoscopic compared to open surgery, was £12,375. Given the mean difference with QALYs (0.011207) and

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
				was a >65% chance that laparoscopic surgery would be cost-effective in the NHS.	significant difference in total cost between procedures because higher cost for laparoscopic surgery was offset by shorter length of stay.		costs (£139) observed, laparoscopic procedure times could be increased by 55 minutes (£197) and still achieve an ICER ≤ £30,000.
Murray et al. (2006) *Clinical effectiveness and cost-effectiveness of laparoscopic surgery for colorectal cancer: systematic reviews and economic evaluation* (United Kingdom)	Laparoscopically assisted and hand-assisted laparoscopic surgery (HALS) in comparison with open surgery for the treatment of colorectal cancer.	Systematic review involving 4,568 patients. (laparoscopic n=2,429 and open surgery n=2,139).	**Model type:** Markov model **Perspective:** Healthcare **Time horizon:** 25 years **Discount rate:** Not provided	Laparoscopy yielded an extra cost of GBP £250-300 per patient.	The results did not find laparoscopic surgery to be more cost-effective as the outcomes were similar, except for a quicker recovery time with laparoscopic surgery but the laparoscopic method was more costly and surgery times were also longer with	Beta distribution and triangular distribution was used to help evaluate uncertainty around the cost estimates. CECGs have also been used to illustrate uncertainty and these curves help show if a strategy or intervention is cost-effective.	Incremental cost per life-year, laparoscopic surgery appeared more costly and no more effective than open surgery. With respect to incremental cost per QALY, few data were available to differentiate between laparoscopic and open

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
					laparoscopy.		surgery. The results of the base-case analysis indicate that there is an approximately 40% chance that laparoscopic surgery is the more cost-effective intervention at a threshold willingness to pay for a QALY of £30,000.
Hernandez et al (2008) *Systematic review of economic evaluations of laparoscopic surgery for colorectal cancer* (United Kingdom)	Laparoscopic surgery versus open surgery for the treatment of colorectal cancer.	Systematic review (five studies were included and the results were inconsistent)with 1,421 participants in total.	**Model type:** Different models used per study **Perspective:** Societal and hospital **Time horizon:** Not provided **Discount rate:** Not provided	Most studies reported longer operational times and shorter length of stay with laparoscopic surgery but had similar long-term outcomes compared with open procedures.	Laparoscopic surgery was generally more expensive but the effectiveness data was inconsistent.	NHS-EED guidelines for reviewers were used to assess uncertainty across included studies. Data from all included studies were summarised and appraised	The evidence on cost-effectiveness was not consistent. Laparoscopic resection was generally more costly than open procedures. ICERs were

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
						in order to identify common results, variations and weaknesses. Where ICERs were not included but sufficient data was available, ICERS were estimated.	calculated for a number of outcomes
Van den Broek (2009) *Transanal endoscopic microsurgery versus endoscopic mucosal resection for large rectal adenomas (TREND-study)* (Netherlands)	Transanal endoscopic microsurgery versus endoscopic mucosal resection.	178 patients with large rectal adenomas	**Model type:** Randomised control trial protocol **Perspective:** Dutch healthcare **Time horizon:** 24 months **Discount rate:** Included in sensitivity analysis	Direct medical costs, out of-pocket expenses, and the indirect non-medical costs of production loss.	NA	Sensitivity analysis is planned – sampling variability, unit cost of surgery and endoscopic treatment, discount rates, rectal adenoma diameter and distances of the adenoma from the anal verge.	NA

Radiation Oncology

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
Van Der Brink et al. (2004) *Cost Utility Analysis of preoperative radiotherapy in patients with rectal cancer undergoing total mesorectal excision: A study of Dutch colorectal cancer group* (Netherlands)	Compared the societal costs and the quality adjusted life expectancy of patients undergoing mesorectal excision with or without short-term radiotherapy.	1,861 patients with rectal cancer undergoing total mesorectal excision.	**Model type:** A Markov model **Perspective:** Societal **Time horizon:** Not provided **Discount rate:** 3%	The results from the model estimated that the loss of quality of life was outweighed by the gain in life-expectancy, 0.39 years, and costs, $9,800. The cost-effectiveness ratio was $25,100/QALY	Preoperative radiotherapy in patients with rectal cancer undergoing total mesorectal excision is cost effective. $25,000/QALY is below the Irish threshold of €40,000/QALY.	Uncertainty was dealt with by performing subgroup analysis.	The results from the model estimated that the loss of quality of life was outweighed by the gain in life-expectancy, 0.39 years, and costs, $9,800. The cost-effectiveness ratio was $25,100/QALY
Dahlberg et al. (2002) *Cost-effectiveness of preoperative radiotherapy in rectal cancer: results from the Swedish rectal cancer trial*. (Sweden)	Radiotherapy versus surgery alone.	98 randomised patients from the Swedish rectal cancer trial.	**Model type:** A Markov model **Perspective:** Societal **Time horizon:** Not provided **Discount rate:** 3%	The irradiated group had 30% higher costs compared to the surgery alone group. However the higher recurrence rates for the surgery alone group contributed to an over-all increase in costs of 70 per cent. An average increase	There was an increased rate of recurrence in the surgery alone group and a survival benefit of 21 months with the addition of radiotherapy.	Sensitivity analysis were performed with variations of survival rates, local recurrence rates and different incidences for early and late adverse effects.	Preoperative radiotherapy in rectal cancer is cost effective as $3,650 per QALY is below the Irish threshold of €40,000/QALY.

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
				in costs of $5,000 per patient with an increase in mean survival generated a QALY of $3,650.			

Part B Budget Impact Analysis

For recommendations which affect resource requirements, the budget impact was calculated where data on cost was available. Additional resources where required will be sought through the HSE service planning process.

The burden of cancer is growing, and the disease is becoming a major economic expenditure for all developed countries. In 2008, the worldwide cost of cancer due to premature death and disability (not including direct medical costs) was estimated to be US$895 billion. This is not simply due to an increase in absolute numbers, but also the rate of increase of expenditure on cancer. Several drivers of cost, such as over-use, rapid expansion, and shortening life cycles of cancer technologies (such as medicines and imaging modalities), and the lack of suitable clinical research and integrated health economic studies, have converged with more defensive medical practice, a less informed regulatory system and a lack of evidence-based socio-political debate. (Sullivan et al., 2011)

"The cancer profession and industry should take responsibility and not accept a substandard evidence base and an ethos of very small benefit at whatever cost." (Sullivan et al., 2011)

Sullivan et al. (2011) believe that value and affordable cancer care can be introduced into the cancer policy lexicon without detracting from quality, and that the management tools, evidence, and methods are available to affect this transformation across all developed countries.

A population-based cost analysis illustrated the economic burden of cancer on the European Union (EU). In 2009, cancer was estimated to have cost the EU €126 billion, with healthcare costs accounting for €51 billion (40%) (Luengo-Fernandez et al., 2013). In Ireland, inpatient care costs were estimated to account for €417 million of cancer-related healthcare costs out of a total of €619 million. Drug expenditure accounted for a further €127 million, while primary, outpatient and emergency care were estimated at €32 million, €30 million and €13 million, respectively. Across the EU, lung cancer had the highest economic cost (€18.8 billion) when compared to breast (€15 billion), colorectal (€13.1 billion) and prostate (€8.43 billion) cancer.

A recent productivity loss analysis carried out in an Irish context (Pearce et al., 2016) projected that by 2030, premature death as a result of colorectal cancer will cause a value of €237,664 lost household per death and an overall productivity loss per population of €2.5 billion.

Information on the expected future trends of rectal cancer can be found in the epidemiology section of this guideline (Section 3.1 Epidemiology). Although some patients with rectal cancer may be treated in the private sector, all costing have been calculated on the assumption that all patients diagnosed annually with rectal cancer will attend publically and be treated within that system. This budget impact assessment focused on those recommendations considered to affect resource requirements, as determined by the Guideline Development Group at recommendation meetings held for each clinical question.

The National Cancer Strategy 2017-2026 (DOH, 2017) made a number of recommendations on how Irish cancer services should be organised, including hospital admissions policies, the organisation of hospital care including palliative care, infrastructure and staffing. The strategy encompasses a range of areas within cancer control, prevention, primary care from treatment to post treatment care and patient involvement, facilitating our healthcare system to operate to its full capacity. A number of recommendations (Table 19) made within the cancer strategy are relevant to the implementation of some of the guideline recommendations.

Measuring the performance and quality of cancer services is essential. The strategy also outlines a number of Key Performance Indicators (KPIs) (Table 20) that are relevant to how the NCCP proposes to evaluate the level of implementation of a number of recommendations made within the guideline.

All salaries used to calculate costs within this BIA, are based on the mid-point of the 2019 salary scale and are adjusted for pension (4%), pay related social insurance (10.95%) and overheads (25%). Salaries are rounded to the nearest thousand.

Salaries for consultant posts were calculated based on new entrants from 1st October 2012 and are based on the mid-point of contract type B on the 2019 salary scale for adjusted for pension (4%), pay related social insurance (10.95%) and overheads (25%). Salaries are rounded to the nearest thousand.

Budget impact analysis

The resource implications of implementing the recommendations were identified by the clinicians during meetings to discuss and develop the clinical recommendations. The Guideline Development Group complied with HIQA guidance on conducting this budget impact analysis.

The implementation plan (Appendix 7: Implementation plan) based on the NCEC Implementation Guide (Department of Health, 2018) details the guideline recommendation(s), the implementation barriers/enablers and gaps, the actions/tasks to implement the recommendation, which group/unit/organisation has lead responsibility for the task; an indicative timeframe for completion; some detail on expected outcomes and how they will be verified or measured. The implementation plan also details if there is an additional cost related to implementing the guideline in the context of a rectal cancer patient.

The capital costs of implementing the recommendations in the guideline are summarised in Table 16 and the revenue costs are summarised in Table 17. Each table details the additional resources required, the unit cost, unit of analysis, total cost per annum (2020-2021), and the total cost. In areas where additional resources are required these will be sought through the service planning process. Figures for funding approved by the National Service Plan may differ to those quoted below.

Table 16 Budget impact assessment of operational costs (excluding staff) in implementing recommendations

Operational costs (excluding staff)							
Recommendation	**Additional resource required**	**Unit cost**	**Number required**	**2020**	**2021**	**2022**	**Total cost**
Recommendation 2.2.1.1 **Initial staging** Contrast enhanced CT-TAP should be employed for the initial staging of patients diagnosed with rectal cancer.	CT-TAP (potential revenue costs for staffing included in Table 17)	€250 (SJH)	927[1]	€231,750	€231,750	€231,750	€695,250
Recommendation 2.2.1.2 **Hepatic metastases** Hepatocyte specific contrast enhanced MRI of the liver is the best modality for evaluation of liver metastases in patients with rectal cancer.	MRI (potential revenue costs for staffing included in Table 17)	€138 (SJH)	649[2]	€89,562	€89,562	€89,562	€268,686
Recommendation 2.2.1.3 **Extrahepatic metastases** Currently, PET-CT is not a first-line imaging modality for staging rectal cancer and can be used as a problem solving tool in patients with equivocal imaging findings following a discussion at a multidisciplinary team meeting.	PET-CT (potential revenue costs for staffing included in Table 17)	€1,199 (SJH)	Unknown[3]	TBD	TBD	TBD	TBD

[1] Estimated annual average incidence of rectum cancer (C20) and rectosigmoid junction cancer (C19) in Ireland, 2018–2020 (NCRI, 2020)

[2] Based on the estimated annual average incidence for rectum cancer (C20) and rectosigmoid junction cancer (C19) in Ireland, 2018–2020 (NCRI, 2020) and the percentage of rectal cancer patients treated with surgery within the first year (70%) (NCRI, 2018)

[3] The number of PET-CTs required is unknown. This is due to the nature of the recommendation with states that PET-CT is not a first line imaging modality but can be used for equivocal findings

Operational costs (excluding staff)							
Recommendation	**Additional resource required**	**Unit cost**	**Number required**	**2020**	**2021**	**2022**	**Total cost**
Recommendation 2.2.2.1 **Imaging for further liver lesions** Hepatocyte specific contrast enhanced MRI of the liver is the imaging modality of choice in patients with rectal cancer with a potentially resectable liver lesion to detect further liver lesions.	MRI (potential revenue costs for staffing included in Table 17)	€138 (SJH)	162[4]	€22,356	€22,356	€22,356	€67,067
Recommendation 2.2.2.2 **Imaging for further liver lesions** PET-CT can be considered in patients with potentially resectable liver lesion with equivocal imaging findings following discussion at a multidisciplinary team meeting.	PET- CT (potential revenue costs for staffing included in Table 17)	€1,199	Unknown[5]	TBD	TBD	TBD	TBD
Recommendation 2.2.3.1 Patients with rectal cancer should have an MRI for locoregional staging.	MRI (potential revenue costs for staffing included in Table 17)	€138 (SJH)	927[1]	€127,926	€127,926	€127,926	€383,778
Recommendation 2.2.3.2 When local expertise (surgical, radiology or gastroenterology) is available, preoperative endorectal ultrasound in low early rectal lesions may be considered to allow for surgical planning following discussion at a multidisciplinary team meeting.	TEUS (potential revenue costs for staffing included in Table 17)	€160 (HIQA CRC screening HTA)	N/A	N/A	N/A	N/A	N/A
Recommendation 2.2.4.1 In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available.	CT Colongraphy (potential revenue costs for staffing included in Table 17)	€550 (HIQA HTA)	23[6]	€40,150	€40,150	€40,150	€120,450

[4] Based on the estimated annual average incidence for rectum cancer (C20) and rectosigmoid junction cancer (C19) in Ireland, 2018 –2020 (NCRI, 2020), adjusted for the percentage of rectal cancer patients treated with surgery within the first year (70%) (NCRI, 2018), and of those number expected to have a metastases (25%) (NCRI, 2019a)

[5] The number of PET-CTs required is unknown due to the nature of the recommendation which states that PET-CT should be used in patients with equivocal findings

[6] Based on the estimated annual average incidence of rectum cancer (C20) and rectosigmoid junction cancer (C19) in Ireland, 2018–2020 (NCRI, 2020) and adjusted for the number of patients expected to undergo surgery (70%) (NCRI, 2018) and of those the number of patients expected to have a failed colonoscopy (11.3%) (Atkin et al., 2013).

Operational costs (excluding staff)							
Recommendation	**Additional resource required**	**Unit cost**	**Number required**	**2020**	**2021**	**2022**	**Total cost**
Recommendation 2.2.5.1 In patients with rectal cancer, complete visualisation of the entire colon by colonoscopy or CT colonography is recommended prior to surgery. CT colonography should only be performed in centres experienced in the technique	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.2.5.2 In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available.	CT Colonography (potential revenue costs for staffing included in Table 17)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.2.6.1 In patients undergoing surgery with rectal cancer, it is recommended to identify as many nodes as possible, all of which should be submitted for microscopic examination/evaluation. Overall, the median for the laboratory should be at least 12.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.2.7.1 In patients diagnosed with rectal cancer Haggitt and Kikuchi classification systems may be considered where deemed applicable but are not routinely recommended.	Nil (No additional resource required)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.2.8.1 In patients diagnosed with rectal cancer receiving neoadjuvant chemoradiation, it is recommended to employ the modified Ryan tumour regression grading system.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.3.1.1 In patients with primary rectal cancer, after chemoradiotherapy no radiological investigation to date reliably predicts a pathological complete response.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.3.1.2 In patients with primary rectal cancer following chemoradiotherapy where a non-operative strategy is planned frequent multimodal assessment and surveillance including DRE, endoscopy and imaging should be undertaken.	Nil (No additional resource required)	N/A	N/A	N/A	N/A	N/A	N/A

Operational costs (excluding staff)							
Recommendation	**Additional resource required**	**Unit cost**	**Number required**	**2020**	**2021**	**2022**	**Total cost**
Recommendation 2.4.1.1 **Curative intent** In select patients with obstructing upper rectal cancers stenting as a bridge to surgery may be considered.	Nil (potential revenue costs for staffing included in Table 17)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.4.1.2 **Palliative intent** Stenting can be considered for the palliation of patients with upper rectal cancer (i.e. in those who are not appropriate for immediate resection or in those with advanced disease)	Nil (potential revenue costs for staffing included in Table 17)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.5.1.1 For patients who present with predicted node negative T1 rectal cancer with favourable histopathological features, local excision may be considered.	Nil (potential revenue costs for staffing included in Table 17)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.5.1.2 For patients being treated with curative intent for T1 rectal cancer with unfavourable histopathological features or T2 cancers, TME is recommended.	Nil (potential revenue costs for staffing included in Table 17)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.5.2.1 In patients with rectal cancer who have undergone local excision radical surgery should be considered if adverse pathological features are present.	Nil (No additional resources as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.6.1.1 In patients with stage III rectal cancer preoperative short-course radiotherapy or chemoradiotherapy should be considered.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A

Operational costs (excluding staff)							
Recommendation	**Additional resource required**	**Unit cost**	**Number required**	**2020**	**2021**	**2022**	**Total cost**
Recommendation 2.6.2.1 In patients diagnosed with rectal cancer who have an apparent complete clinical response to chemoradiation radical surgery is the standard of care. However, a watch and wait approach should be discussed with the patient and may be considered following shared decision making.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.6.3.1 In patients diagnosed with rectal cancer where preoperative therapy has been recommended and the CRM is not threatened or involved short-course radiotherapy or chemoradiotherapy may be considered.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.6.3.2 In patients diagnosed with rectal cancer preoperative chemoradiotherapy is recommended for patients with a threatened or involved CRM.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.6.4.1 In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiotherapy IMRT and 3D-CRT techniques can both be considered.	Availability of RT across centres	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.6.5.1 In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiation the routine use of a boost is not recommended.	Nil (No additional resource required)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.6.5.2 In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiation boost can be considered in selected high risk patients.	Nil (No additional resource required)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.7.1.1 In patients with rectal cancer high quality total mesorectal excision (TME) surgery should be performed.	Nil (potential revenue costs for staffing included in Table 17)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.7.2.1 There is no clear evidence of difference in postoperative genitourinary function between minimally invasive and open total mesorectal excision (TME)	Nil (No additional resource required)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.8.1.1 In patients diagnosed with rectal cancer who have had a resection with a positive margin and have not received preoperative	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A

Operational costs (excluding staff)							
Recommendation	**Additional resource required**	**Unit cost**	**Number required**	**2020**	**2021**	**2022**	**Total cost**
radiotherapy then postoperative chemoradiotherapy is an acceptable salvage approach.							
Recommendation 2.9.1.1 For patients with cancer, early provision of palliative care can improve patient outcomes.	Nil (potential revenue costs for staffing included in Table 17)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.9.1.2 Assessment of palliative care needs should be an ongoing process throughout the course of a patient's cancer illness and services provided on the basis of identified need..	Nil (potential revenue costs for staffing included in Table 17)	N/A	N/A	N/A	N/A	N/A	N/A

Table 17 Budget impact assessment of staff costs of implementing recommendations

Profession	Relevant Recommendation(s)	Additional staff required	Unit cost	Number required	2020	FYC 2021	FYC 2022	Total cost
Radiology	2.2.1.1, 2.2.1.2, 2.2.1.3, 2.2.2.1, 2.2.2.2, 2.2.3.1, 2.2.4.1, 2.2.5.1, 2.2.5.2	Consultant radiologist	€204,944[7]	x WTE[8]				
Surgery	2.2.3.2, 2.5.1.1, 2.5.1.2, 2.7.1.1, 2.7.1.2	Consultant Colorectal surgeon	€204,944[7]	x WTE[8]				
Gastroenterology	2.4.1.1, 2.4.1.2	Consultant gastroenterologist	€204,944[7]	x WTE[8]				
Palliative	2.9.1.1, 2.9.2.1	Palliative Care Consultant	€204,944[7]	x WTE[8]				
Pathology	2.5.1.2	Consultant Histopathologist	€204,944[7]	x WTE[8]				
	2.5.1.2	Medical laboratory scientist	€61,953	x WTE[8]				
Nursing	2.9.1.1, 2.9.2.1	Palliative care CNS	€74,057	x WTE[8]				
Admin	All	Administrator (MDT, data management)	€64,453	x WTE[8]				
Total revenue costs of implementing the recommendations								TBD

Table 18 Total cost of implementing the guideline recommendations

Cost	2020	2021	2022	Total cost
Total operational costs for implementing recommendations	€511,744	€511,744	€511,744	€1,535,232
Total staff costs of implementing the recommendations				
Total cost of implementing the guideline				€1,535,232 + total revenue costs

[7] Salaries for consultant posts were calculated based on new entrants from 1st October 2012 and are based on the mid-point of contract type B on the 2019 salary scale for adjusted for pension (4%), pay related social insurance (10.95%) and overheads (25%). Salaries are rounded to the nearest thousand.

[8] Await outcome of surgical centralisation and workforce planning

Appendix 7: Implementation plan

Diagnosis and staging

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Rec. 2.2.1.1 **Initial staging** Contrast enhanced CT-TAP should be employed for the initial staging of patients diagnosed with rectal cancer. **Rec. 2.2.1.2** **Hepatic metastases** Hepatocyte specific contrast enhanced MRI of the liver is the best modality for evaluation of liver metastases in patients with rectal cancer. **Rec. 2.2.2.1** **Imaging for further liver lesions** Hepatocyte specific contrast enhanced MRI of the liver is the imaging modality of choice in patients with rectal cancer with a potentially resectable liver lesion to detect further liver lesions. **Rec. 2.2.3.1** Patients with rectal cancer should have an MRI for locoregional staging. **Rec. 2.2.1.3** **Extrahepatic metastases**	**Barrier:** Access to equipment **Enabler:** National Cancer Strategy recommendation no.14 (Capital investment plan).	Secure funding through the HSE service planning process for equipment. **National Cancer Strategy recommendation no.14.** The NCCP, working with the other Directorates in the HSE and with the Department of Health, will develop a rolling capital investment plan, to be reviewed annually, with the aim of ensuring that cancer facilities meet requirements	NCCP as per National Cancer Strategy recommendation no. 14.			X	**Outcome:** All patients with rectal cancer will have access to diagnostic equipment. **Verification:** Completed capital investment plan. Current programme of work by the NCCP based on cancer strategy recommendation 14.

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Currently, PET-CT is not a first-line imaging modality for staging rectal cancer and can be used as a problem solving tool in patients with equivocal imaging findings following a discussion at a multidisciplinary team meeting. **Rec. 2.2.2.2** **Imaging for further liver lesions** PET-CT can be considered in patients with potentially resectable liver lesion with equivocal imaging findings following discussion at a multidisciplinary team meeting. **Rec. 2.2.3.2** When local expertise (surgical, radiology or gastroenterology) is available, preoperative endorectal ultrasound in low early rectal lesions may be considered to allow for surgical planning following discussion at a multidisciplinary team meeting. **Rec. 2.2.4.1** In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be							

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available **Rec. 2.2.5.2** In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available.							
Rec. 2.2.1.1 **Initial staging** Contrast enhanced CT-TAP should be employed for the initial staging of patients diagnosed with rectal cancer. **Rec. 2.2.3.2** When local expertise (surgical, radiology or gastroenterology) is available, preoperative endorectal ultrasound in low early rectal lesions may be considered to allow for surgical planning following discussion at a multidisciplinary team	**Barrier:** Limited availability of appropriately trained radiology staff/personnel. **Enabler:** National Cancer Strategy recommendation 10, recommendation 16, recommendation 50 (Radiology training, consultant staffing, workforce planning)	**National Cancer Strategy recommendations no.10** The Department of Health will liaise with the Health and Education authorities with a view to increasing places in Third Level Institutions for the training of radiographers and sonographers.	DoH as per National Cancer Strategy recommendation No. 10.			X	**Verification:** Training provided/staff training records. Current programme of work by NCCP based on National Cancer Strategy recommendation no. 10.

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
meeting. **Rec. 2.2.4.1** In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available **Rec. 2.2.5.2** In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available.		**National Cancer Strategy recommendation no. 16.** The NCCP will ensure that consultant appointments for radiology, endoscopy and histopathology, where necessary, are made in conjunction with appointments in other disciplines such as surgery and medical oncology.	NCCP as per National Cancer Strategy recommendation No. 16.			X	**Verification:** Staff in place. No additional resources required. Current programme of work by NCCP based on National Cancer Strategy recommendation no. 16.
		National Cancer Strategy recommendation no. 50. The NCCP, aided by a crosssector group, will draw up a comprehensive workforce plan for cancer services. This will include an interim assessment of staffing needs at medical, nursing and health & social care professional levels by mid-2018[9].	NCCP as per National Cancer Strategy recommendation No. 50.			X	**Verification:** Completed workforce assessment. No additional resources required. Current programme of work by NCCP based on National Cancer Strategy recommendation no. 50.
Rec. 2.2.6.1 In patients undergoing surgery with rectal cancer, it is recommended to identify as	Current practice	Not applicable	Clinician				Not applicable

[9] Direct wording taken from the National Cancer Strategy (2017). Time frame for completion may differ.

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
many nodes as possible, all of which should be submitted for microscopic examination/evaluation. Overall, the median for the laboratory should be at least 12. **Rec. 2.2.7.1** In patients diagnosed with rectal cancer Haggitt and Kikuchi classification systems may be considered where deemed applicable but are not routinely recommended. **Rec. 2.2.8.1** In patients with primary rectal cancer, after chemoradiotherapy no radiological investigation to date reliably predicts a pathological complete response.							

Restaging

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Rec. 2.3.1.1 In patients with primary rectal cancer, after chemoradiotherapy no radiological investigation to date reliably predicts a pathological complete response. **Rec. 2.3.1.2** In patients with primary rectal cancer following chemoradiotherapy where a non-operative strategy is planned frequent multimodal assessment and surveillance including DRE, endoscopy and imaging should be undertaken.	Current practice	Not applicable	Clinician				Not applicable

Treatment: Emergency presentation

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Rec. 2.4.1.1 **Curative intent** In select patients with obstructing upper rectal cancers stenting as a bridge to surgery may be considered. **Rec. 2.4.1.2** **Palliative intent** Stenting can be considered for the palliation of patients with upper rectal cancer (i.e. in those who are not appropriate for immediate resection or in those with advanced disease)	**Barrier:** Limited availability of appropriately trained surgical staff. **Enabler:** National Cancer Strategy recommendation 14, recommendation 21 (Capital investment plan, centralisation).	**National Cancer Strategy Recommendations no.14.** The NCCP, working with the other Directorates in the HSE and with the Department of Health, will develop a rolling capital investment plan, to be reviewed annually, with the aim of ensuring that cancer facilities meet requirements.	NCCP as per National Cancer Strategy recommendation no. 14.			X	**Outcome:** All patients with rectal cancer will have access to surgical expertise. **Verification:** Completed capital investment plan. Current programme of work by the NCCP based on National Cancer Strategy recommendation no. 14 and no. 21.
		National Cancer Strategy Recommendations no.21. The NCCP will draw up a plan setting out the number/location of designated cancer centres in which surgery will take place for the various tumour types. Timescales for the implementation of the plan will be included for each tumour.	NCCP as per National National Cancer Strategy recommendation no. 21.				**Verification:** Designated cancer centres with surgical expertise in place for rectal cancer. **KPI 11** Complete centralisation of cancer surgical services

Treatment: Early rectal cancer

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Rec. 2.5.1.1 For patients who present with predicted node negative T1 rectal cancer with favourable histopathological features, local excision may be considered. **Rec. 2.5.1.2** For patients being treated with curative intent for T1 rectal cancer with unfavourable histopathological features or T2 cancers, TME is recommended. **Rec. 2.5.2.1** In patients with rectal cancer who have undergone local excision radical surgery should be considered if adverse pathological features are present.	**Barrier:** Limited availability of appropriately trained surgical staff. **Enabler:** National Cancer Strategy recommendation 14, recommendation 21 (Capital investment plan, centralisation).	**National Cancer Strategy recommendations no.14.** The NCCP, working with the other Directorates in the HSE and with the Department of Health, will develop a rolling capital investment plan, to be reviewed annually, with the aim of ensuring that cancer facilities meet requirements	NCCP as per National Cancer Strategy recommendation no. 14.			X	**Outcome:** All patients with rectal cancer will have access to surgical expertise. **Verification:** Completed capital investment plan. Current programme of work by the NCCP based on National cancer strategy recommendation no. 14 and no. 21.
		National Cancer Strategy recommendations no.21. The NCCP will draw up a plan setting out the number/location of designated cancer centres in which surgery will take place for the various tumour types. Timescales for the implementation of the plan will be included for each tumour.	NCCP as per National Cancer Strategy recommendation no. 21.			X	**Verification:** Designated cancer centres with surgical expertise in place for rectal cancer. **KPI 11** Complete centralisation of cancer surgical services

Treatment: Patients receiving neoadjuvant therapy

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Rec. 2.6.1.1. In patients with stage III rectal cancer preoperative short-course radiotherapy or chemoradiotherapy should be considered. **Rec. 2.6.1.2** In patients with rectal cancer, preoperative chemoradiotherapy is recommended for patients with a threatened or involved CRM. **Rec. 2.6.2.1** In patients diagnosed with rectal cancer who have an apparent complete clinical response to chemoradiation radical surgery is the standard of care. However, a watch and wait approach should be discussed with the patient and may be considered following shared decision making. **Rec. 2.6.3.1** In patients diagnosed with rectal cancer where preoperative therapy has been recommended and the CRM is not threatened or	Current practice	Not applicable	Clinician				Not applicable

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
involved short-course radiotherapy or chemoradiotherapy may be considered. **Rec. 2.6.3.2** In patients diagnosed with rectal cancer preoperative chemoradiotherapy is recommended for patients with a threatened or involved CRM. **Rec. 2.6.4.1** In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiotherapy IMRT and 3D-CRT techniques can both be considered. **Rec. 2.6.5.1** In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiation the routine use of a boost is not recommended. **Rec. 2.6.5.2** In patients diagnosed with rectal cancer undergoing neoadjuvant chemoradiation boost can be considered in selected high risk patients.							

Treatment: Surgical techniques

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Rec. 2.7.1.1 In patients with rectal cancer high quality total mesorectal excision (TME) surgery should be performed. **Rec. 2.7.2.1** There is no clear evidence of difference in postoperative genitourinary function between minimally invasive and open total mesorectal excision (TME)	**Barrier:** Limited availability of appropriately trained surgical staff. **Enabler:** National Cancer Strategy recommendation 14, recommendation 21 (Capital investment plan, centralisation).	**National Cancer Strategy recommendations no.14.** The NCCP, working with the other Directorates in the HSE and with the Department of Health, will develop a rolling capital investment plan, to be reviewed annually, with the aim of ensuring that cancer facilities meet requirements	NCCP as per National Cancer Strategy recommendation no. 14.			X	**Outcome:** All patients with rectal cancer will have access to surgical expertise. **Verification:** Completed capital investment plan. Current programme of work by the NCCP based on National Cancer Strategy recommendation no. 14 and no. 21.
		National Cancer Strategy recommendations no.21. The NCCP will draw up a plan setting out the number/location of designated cancer centres in which surgery will take place for the various tumour types. Timescales for the implementation of the plan will be included for each tumour.	NCCP as National Cancer Strategy recommendation no. 21.				**Verification:** Designated cancer centres with surgical expertise in place for rectal cancer. **KPI 11** Complete centralisation of cancer surgical services

Treatment: Patients receiving adjuvant therapy

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Rec. 2.8.1.1 In patients diagnosed with rectal cancer who have had a resection with a positive margin and have not received preoperative radiotherapy then postoperative chemoradiotherapy is an acceptable salvage approach.	Current practice	Not applicable	Clinician				Not applicable

Treatment: Palliative care

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Rec. 2.9.1.1 For patients with cancer, early provision of palliative care can improve patient outcomes. **Rec. 2.9.1.2** Assessment of palliative care needs should be an ongoing process throughout the course of a patient's cancer illness and services provided on the basis of identified need.	**Barrier:** Insufficient availability of specialist palliative care staff. **Enabler:** National Cancer Strategy recommendation 31, recommendation 32 (Specialist palliative care, identification of palliative care needs).	**National Cancer Strategy Recommendation no. 31.** Designated cancer centres will have a sufficient complement of specialist palliative care professionals, including psycho-oncologists, to meet the needs of patients and families (such services will be developed on a phased basis to be available over seven days a week.	HSE & designated cancer centres as per National Cancer Strategy recommendation no. 31.			X	**Outcome:** All patients with rectal cancer have access to palliative care. **Verification:** Staff in place. National Cancer Strategy KPI 19 - Increase the proportion of patients receiving specialist palliative care. Current programme of work based on National Cancer Strategy recommendation no. 31 (HSE and designated cancer centres) and 32 (HSE).
		National Cancer Strategy Recommendation no. 32. Oncology staff will have the training and education to ensure competence in the identification, assessment and management of patients with palliative care needs and all patients with cancer will have regular, standardised assessment of their needs.	HSE as per National Cancer Strategy recommendation no. 31.			X	**Verification:** Training and education provided. Staff training records.

A list of National Cancer Strategy (2017) recommendations, KPIs and NCCP KPIs that are mentioned in the implementation plan are detailed below:

Table 19 Cancer Strategy recommendations relevant to implementation (DOH, 2017)

No.	National Cancer Strategy recommendations relevant to implementation
Recommendation 10	The Department of Health will liaise with the Health and Educational authorities with a view to increasing places in third level institutions for the training of radiographers and sonographers.
Recommendation 13	Patients diagnosed with cancer will have their case formally discussed at a multi-disciplinary team meeting. The NCCP, working with the Hospital Groups, will oversee and support MDT composition, processes and reporting of outcomes.
Recommendation 14	The NCCP, working with the other directorates in the HSE and with the department of Health, will develop a rolling capital investment plan, to be reviewed annually, with the aim of ensuring that cancer facilities meet requirements
Recommendation 16	The NCCP will ensure that consultant appointments for radiology, endoscopy and histopathology where necessary, are made in conjunction with appointments in other disciplines such as surgery and medical oncology.
Recommendation 21	The NCCP will draw up a plan setting out the number/location of designated cancer centres in which surgery will take place for the various tumour types. Timescales for the implementation of the plan will be included for each type.
Recommendation 31	Designated cancer centres will have a sufficient complement of specialist palliative care professionals, including psycho-oncologists, to meet the needs of patients and families (such services will be developed on a phased basis to be available over seven days a week).
Recommendation 32	Oncology staff will have the training and education to ensure competence in the identification, assessment and management of patients with palliative care needs and all patients with cancer will have regular, standardised assessment of their needs.
Recommendation 50	The NCCP, aided by a cross- sector group, will draw up a comprehensive workforce plan for cancer services. This will include an interim assessment of staffing needs at medical, nursing and health & social care professional levels by mid-2018

Table 20 Key Performance Indicators relevant to implementation (DOH, 2017)

No.	National Cancer Strategy Key Performance Indicators relevant to implementation
Cancer strategy KPI 11	Complete centralisation of cancer surgical services
Cancer Strategy KPI 19	Increase proportion of patients receiving specialist palliative care

Table 21 Key Performance Indicators relevant to implementation (NCCP)

No.	NCCP Key Performance Indicators relevant to implementation
NCCP KPI No 3.	(i) For patients newly diagnosed with a primary rectal cancer, the interval between the discussion at the multidisciplinary meeting (MDM) and date of first surgical intervention where surgery is the first treatment shall be monitored. (ii) Systemic therapy shall be administered in a timely manner. (iii) Radiation therapy shall be carried out in a timely manner
NCCP KPI No 4.	All patients newly diagnosed with rectal cancer in the cancer centre shall be discussed at MDM.
NCCP KPI No 8.	Number of lymph nodes that are harvested from all newly diagnosed primary rectal cancer patients will be recorded
NCCP KPI No 10.	The proportion of newly diagnosed primary rectal cancer patients who receive radiotherapy pre or post operatively.

Appendix 8: Monitoring and audit

It is important that both the implementation of the guideline and patient outcomes are audited to ensure that this guideline positively impacts on patient care. A number of recommendations have been identified by the Guideline Development Group as areas suitable for audit, some specifically due to variation in practice Table 22.

There is a five stage approach to clinical audit which includes planning for audit, standard/criteria selection, measuring performance, making improvements and sustaining improvements. Each audit carried out will be expected to follow this process (HSE, 2019). Two Key Performance Indicators from the National Cancer Strategy 2016-2026 and 11 national KPIs for rectal cancer are outlined below which can be used to monitor the implementation of a number of guideline recommendations.

The audit criteria detailed in Table 23 will be monitored as KPIs from the National Cancer Strategy and the NCCP.

Table 22 Recommendations identified by the Guideline Development Group as areas suitable for audit

Diagnosis and staging
Recommendation 2.2.1.1 **Initial staging** Contrast enhanced CT-TAP should be employed for the initial staging of patients diagnosed with rectal cancer. **Recommendation 2.2.1.2** **Hepatic metastases** Hepatocyte specific contrast enhanced MRI of the liver is the best modality for evaluation of liver metastases in patients with rectal cancer. **Recommendation 2.2.1.3** **Extrahepatic metastases** Currently, PET-CT is not a first-line imaging modality for staging rectal cancer and can be used as a problem solving tool in patients with equivocal imaging findings following a discussion at a multidisciplinary team meeting. **Recommendation 2.2.2.1** **Imaging for further liver lesions** Hepatocyte specific contrast enhanced MRI of the liver is the imaging modality of choice in patients with rectal cancer with a potentially resectable liver lesion to detect further liver lesions. **Recommendation 2.2.2.2** **Imaging for further liver lesions** PET-CT can be considered in patients with potentially resectable liver lesion with equivocal imaging findings following discussion at a multidisciplinary team meeting. **Recommendation 2.2.3.1** Patients with rectal cancer should have an MRI for locoregional staging. **Recommendation 2.2.3.2** When local expertise (surgical, radiology or gastroenterology) is available, preoperative endorectal ultrasound in low early rectal lesions may be considered to allow for surgical planning following discussion at a multidisciplinary team meeting.

Recommendation 2.2.4.1
In patients diagnosed with rectal cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available

Recommendation 2.2.5.1
In patients with rectal cancer, complete visualisation of the entire colon by colonoscopy or CT colonography is recommended prior to surgery. CT colonography should only be performed in centres experienced in the technique

Recommendation 2.2.6.1
In patients undergoing surgery with rectal cancer, it is recommended to identify as many nodes as possible, all of which should be submitted for microscopic examination/evaluation. Overall, the median for the laboratory should be at least 12.

Palliative care

Recommendation 2.9.1.1
For patients with cancer, early provision of palliative care can improve patient outcomes.

Recommendation 2.9.1.2
Assessment of palliative care needs should be an ongoing process throughout the course of a patient's cancer illness and services provided on the basis of identified need.

Table 23 National Cancer Strategy and NCCP Key Performance Indicators relevant to implementation

No.	National Cancer Strategy Key Performance Indicators relevant to implementation
Cancer Strategy KPI 11	Complete centralisation of cancer surgical services
Cancer Strategy KPI 19	Increase proportion of patients receiving specialist palliative care
No.	**NCCP National Key Performance Indicators relevant to implementation**
NCCP No 1.	No. of newly diagnosed rectal cancer patients referred to the cancer centre
NCCP No 2.	Every patient newly diagnosed with rectal cancer should have a rigid sigmoidoscopy performed to determine the position of the tumour prior to any therapeutic intervention
NCCP No 3.	(i): For patients newly diagnosed with a primary rectal cancer, the interval between the discussion at the multidisciplinary meeting (MDM) and date of first surgical intervention where surgery is the first treatment shall be monitored (ii): Systemic therapy shall be administered in a timely manner (iii): Radiation therapy shall be carried out in a timely manner
NCCP No 4.	All patients newly diagnosed with rectal cancer in the cancer centre shall be discussed at MDM
NCCP No 5.	For patients with a primary rectal cancer, clinical TNM stage is recorded at prior to commencement of treatment
NCCP No 6.	The proportion of patients with a primary rectal cancer who undergo a radical surgical procedure that have an abdominoperineal resection (APR)
NCCP No 7.	(a) Distal margin status will be documented for all patients who have a radical surgical procedure for primary rectal cancer (b)Radial margin status will be documented for all patients who have a radical surgical procedure for primary rectal cancer (c) The percentage of patients whose marginal status is clear will be documented for all patients who have a radical surgical procedure for primary rectal cancer
NCCP No 8.	Number of lymph nodes that are harvested from all newly diagnosed primary rectal cancer patients will be recorded
NCCP No 9.	The number of newly diagnosed primary rectal cancer patients who have to return to theatre for any surgical procedure during their hospital stay

NCCP No 10.	The proportion of newly diagnosed primary rectal cancer patients who receive radiotherapy pre or post operatively
NCCP No 11.	Following surgery for primary rectal cancer, the percentage of patients with unscheduled re-admitted to hospital within 30 days of discharge following surgery

Appendix 9: Glossary of terms and abbreviations

Glossary

Definitions within the context of this document

Case Control Study	The observational epidemiologic study of persons with the disease (or other outcome variable) of interest and a suitable control (comparison, reference) group of persons without the disease. The relationship of an attribute to the disease is examined by comparing the diseased and non-diseased with regard to how frequently the attribute is present or, if quantitative, the levels of the attribute, in each of the groups. (CEBM website)
Case Series	A group or series of case reports involving patients who were given similar treatment. Reports of case series usually contain detailed information about the individual patients. This includes demographic information (for example, age, gender, ethnic origin) and information on diagnosis, treatment, response to treatment, and follow-up after treatment. (CEBM website)
Clinician	A healthcare professional such as a doctor involved in clinical practice.
Cohort study	The analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesised to influence the probability of occurrence of a given disease or other outcome. The main feature of cohort study is observation of large numbers over a long period (commonly years) with comparison of incidence rates in groups that differ in exposure levels. (CEBM website)
Validity	The extent to which a variable or intervention measures what it is supposed to measure or accomplishes what it is supposed to accomplish. The internal validity of a study refers to the integrity of the experimental design. The external validity of a study refers to the appropriateness by which its results can be applied to non-study patients or populations. (CEBM website)
Meta-analysis	A systematic review may or may not include a meta-analysis, which is a quantitative summary of the results. (CEBM website)
Randomised trial	An epidemiological experiment in which subjects in a population are randomly allocated into groups, usually called study and control groups, to receive or not receive an experimental preventive or therapeutic procedure, manoeuvre, or intervention. The results are assessed by rigorous comparison of rates of disease, death, recovery, or other appropriate outcome in the study and control groups. (CEBM website)
Systematic review	The application of strategies that limit bias in the assembly, critical appraisal, and synthesis of all relevant studies on a specific topic. Systematic reviews focus on peer-reviewed publications about a specific health problem and use rigorous, standardised methods for selecting and assessing articles. A systematic review differs from a meta-analysis in not including a quantitative summary of the results. (CEBM website)

Abbreviations

2D-CRT	Two-Dimensional Conformal Radiotherapy
3D-CRT	Three-Dimensional Conformal Radiotherapy
5FU	Fluorouracil
AGREE II	Appraisal of Guidelines for Research and Evaluation II
AJCC	American Joint Committee on Cancer
APR	Abdominoperineal Resection
ASCO	American Society of Clinical Oncology
BH	Beaumont Hospital
BIA	Budget Impact Analysis
CAP	College of American Pathologists
CCO	Chief Communications Officer
cCR	Complete Clinical Response
CDR	Clinical Decision Rule
CEA	Cost-Effectiveness Analysis
CEBM	Centre for Evidence-Based Medicine
CEO	Chief Executive Officer
CEP	Cost-Effectiveness Plan
CI	Confidence Interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CQ	Clinical Question
CRM	Circumferential Resection Margin
CRT	Chemoradiotherapy
CSO	Central Statistics Office
CRLM	Colorectal liver metastasis
CSO	Central Statistics Office
CT	Computed Tomography
CTC	Computed Tomographic Colonography
CT-TAP	Computed Tomography of Thorax, Abdomen and Pelvis
CTV	Clinical Target Volume
CUH	Cork University Hospital
DFS	Disease-Free Survival
DoH	Department of Health
DoHC	Department of Health and Children
EBP	Evidence-Based Practice
EBRT	External-Beam Radiotherapy
EMD	Extramural Depth
EMVI	Extramural Vascular Invasion
EU	European Union
EQ-5D	EuroQol-5D
EUS	Endoscopic Ultrasound
GDG	Guideline Development Group
GI	Gastrointestinal
GTV	Gross Target Volume
GUH	Galway University Hospital
HALS	Hand assisted laparoscopic surgery
HEED	Health Economics Evaluation Database
HIQA	Health Information and Quality Authority
HR	Hazard Ratio
HSE	Health Service Executive

IAMP	Irish Association of Physicists in Medicine
IANO	Irish Association for Nurses in Oncology
ICER	incremental cost-effectiveness ratio
ICU	Intensive Care Unit
ICD-O	International Classification of Diseases for Oncology
ICGP	Irish College of General Practitioners
IIEF	International Index of Erectile Function
IMRT	Intensity-Modulated Radiotherapy
IPSS	International Prostate Symptom Scores
ISCCNA	Irish Stoma Care and Colorectal Nurses Association
ISMO	Irish Society for Medical Oncologists
IV	Intravenous
KPI	Key Performance Indicators
LOS	Length of Stay
LAR	Low Anterior Resection
LCPRT	Long-Course Preoperative Radiotherapy
LSL	laterally spreading colonic lesions
LV5FU	Leucovorin/Fluorouracil
LV	Leucovorin
MDCT	Multidetector computed tomography
MDT	Multidisciplinary team meeting
MeSH	Medical Subject Headings
MMUH	Mater Misericordiae University Hospital
MUH	Mercy University Hospital
MRC	Medical Research Council
MRF	Mesorectal Fascia
MRI	Magnetic Resonance Imaging
MSK	Memorial Sloan Kettering
n/a	Not applicable
NALA	National Adult Literacy Agency
NCCN	National Comprehensive Cancer Network
NCCP	National Cancer Control Programme
NCEC	National Clinical Effectiveness Committee
NCRI	National Cancer Registry Ireland
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NMSC	Non-Melanoma Skin Cancer
NPSO	National Patient Safety Office
NSS	National Screening Service
OLOLH	Our Lady's of Lourdes Hospital
OR	Odds Ratio
OS	Overall Survival
OT	Operation time
PET-CT	Positron Emission Tomography-Computed Tomography
PFS	Progression-Free Survival
PH	Portunicula Hospital
PICO(T)	Population/Patient; Intervention; Comparison/Control; Outcome (Time)
PTV	Planning Target Volume
QALY	Quality-Adjusted Life Year
QOL	Quality Of Life
QUB	Queens University Belfast

RCPath	The Royal College of Pathologists
RCSI	Royal College of Surgeons in Ireland
RCT	Randomised Controlled Trial
RR	Risk Ratio
RT	Radiotherapy
SCPRT	Short-Course Preoperative Radiotherapy
SEMS	Self-Expanding Metal Stent
SFH	St. Francis' Hospice
SIGN	Scottish Intercollegiate Guideline Network
SJH	St. James' Hospital
SLRON	St. Luke's Radiation Oncology Network
SVUH	St. Vincent's University Hospital
TAE	Transanal Excision
TAMIS	Transanal Minimally Invasive Surgery
TCD	Trinity College Dublin
TEM	Transanal Endoscopic Microsurgery
TEUS	Transrectal Endoscopic Ultrasound
TME	Total Mesorectal Excision
TRG	Tumour Regression Grading
TNM	Tumour, Node, Metastasis
TUH	Tallaght University Hospital
USA	United States of America
USD	United States Dollar
US	United States
UK	United Kingdom
UCD	University College Dublin
UHW	University Hospital Waterford
UL	University Hospital Limerick
WHO	World Health Organization

Appendix 10: Levels of evidence & grading systems

Table 24 Levels of evidence for diagnostic studies (Oxford CEBM, 2009)

1a	Systematic review (with homogeneity*) of Level 1 diagnostic studies; clinical decision rule (CDR") with 1b studies from different clinical centres.
1b	Validating** cohort study with good reference standards" " "; or CDR tested within one clinical centre.
1c	Absolute SpPins (specificity) and SnNouts (sensitivity)" ".
2a	Systematic review (with homogeneity*) of Level >2 diagnostic studies.
2b	Exploratory** cohort study with good reference standards; CDR after deviation, or validated only on split-samples§§§ or databases.
3a	Systematic review (with homogeneity*) of 3b and better studies.
3b	Non-consecutive study; or without consistently applied reference standards.
4	Case-control study, poor or non-independent reference standard.
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or first principles.

* By homogeneity we mean a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a "-" at the end of their designated level.

" Clinical Decision Rule (these are algorithms or scoring systems that lead to a prognostic estimation or a diagnostic category).

** Validating studies test the quality of a specific diagnostic test, based on prior evidence. An exploratory study collects information and trawls the data (e.g. using a regression analysis) to find which factors are 'significant'.

" " " Good reference standards are independent of the test, and applied blindly or objectively to applied to all patients. Poor reference standards are haphazardly applied, but still independent of the test. Use of a non-independent reference standard (where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference') implies a level 4 study.

" " An "Absolute SpPin" is a diagnostic finding whose Specificity is so high that a positive result rules-in the diagnosis. An "Absolute SnNout" is a diagnostic finding whose Sensitivity is so high that a negative result rules-out the diagnosis.

§§§ Split-sample validation is achieved by collecting all the information in a single tranche, then artificially dividing this into "derivation" and "validation"samples.

Table 25 Grades of recommendations for diagnostic studies (Oxford CEBM, 2009)

A	Consistent level 1 studies.
B	Consistent level 2 or 3 studies; or Extrapolations from level 1 studies.
C	Level 4 studies; or Extrapolations from level 2 or 3 studies.
D	Level 5 evidence; or Troublingly inconsistent or inconclusive studies of any level.

Extrapolations are where data is used in a situation that has potentially clinically important differences than the original study situation.

Table 26 Levels of evidence for interventional studies (SIGN grading system 1999-2012)

1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias.
1+	Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias.
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias.
2++	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal.
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal.
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal.
3	Non-analytic studies (e.g. case reports, case series).
4	Expert opinion.

Table 27 Grades of recommendations for interventional studies (SIGN grading system 1999-2012)

A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results.
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+.
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++.
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+.

Note: the grade of recommendation does not necessarily reflect the clinical importance of the recommendation.

Good Practice Point
Recommended best practice based on the clinical experience of the Guideline Development Group.

Practical considerations around patient care
Are statements developed with patients on issues that were important to them with regards to their own experience of the diagnosis, staging and treatment of their cancer.

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