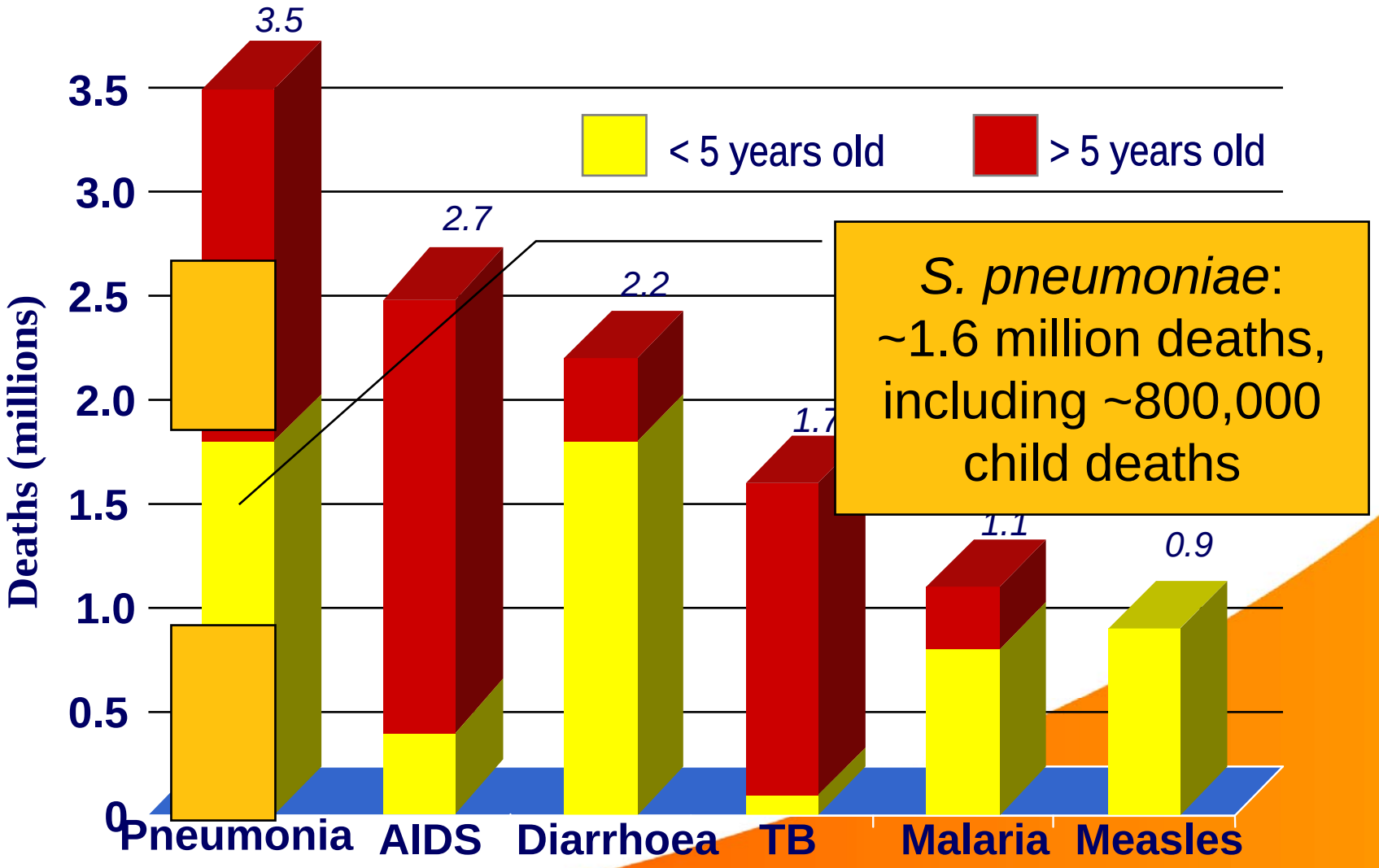
Pneumococcal vaccination in UK: an update

Dr Richard Pebody

Immunisation Department

Health Protection Agency Centre for Infections

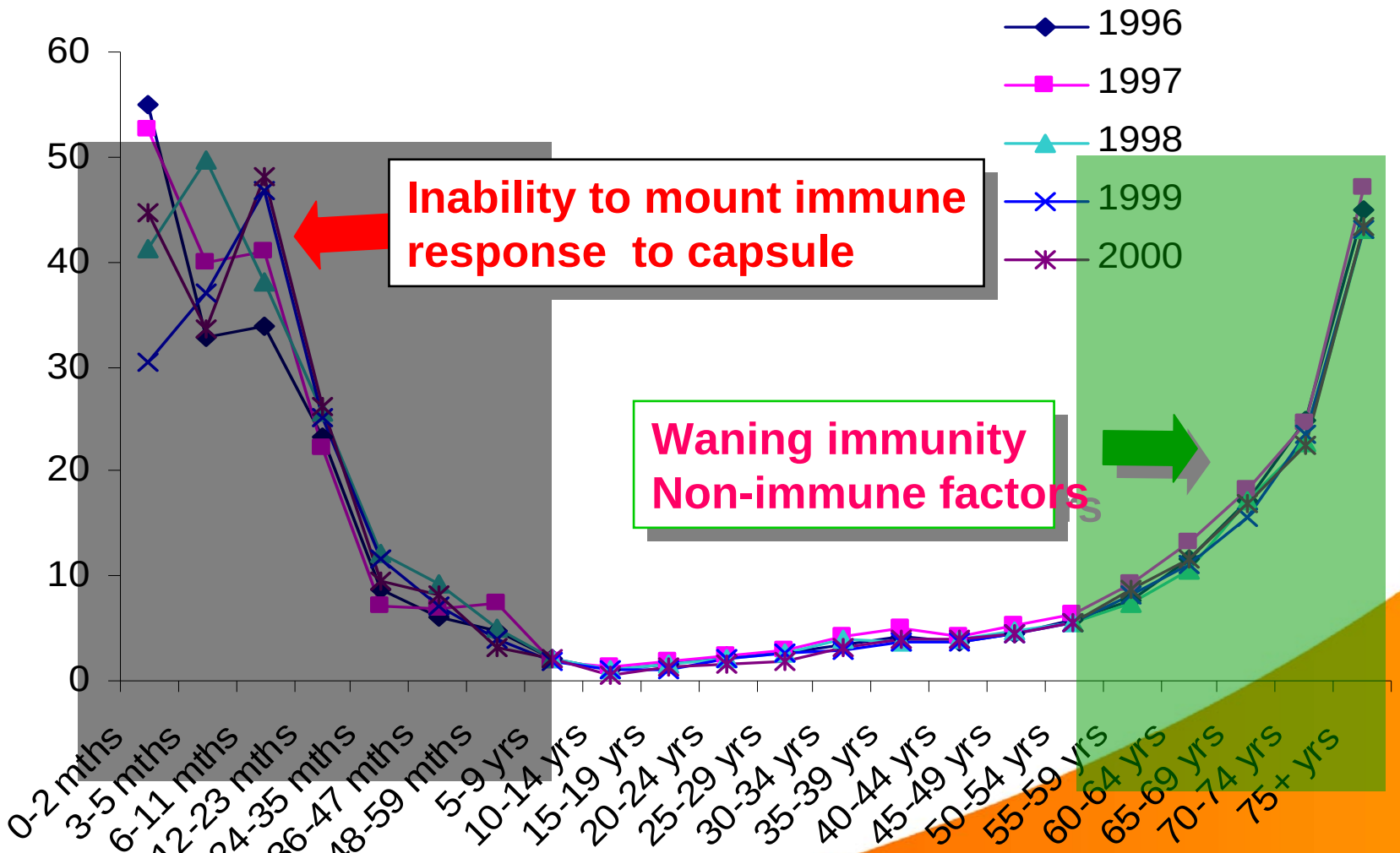
Leading infectious causes of mortality, 2000 WHO estimates



S. pneumoniae: ~1.6 million deaths, including ~800,000 child deaths

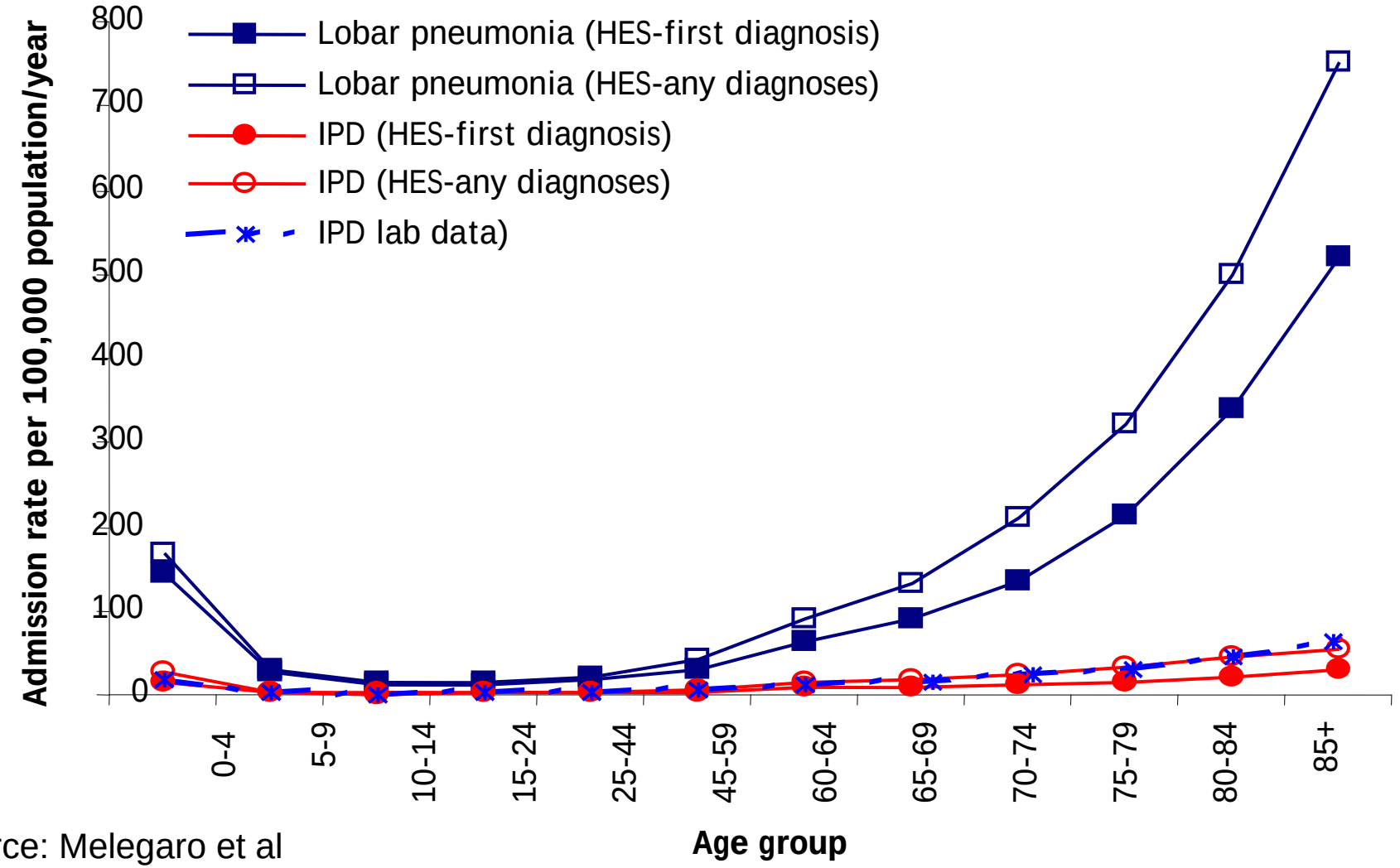
Source: WHO

Annual incidence per 100,000 of invasive pneumococcal infection E&W, by age group and year, 1996-2000



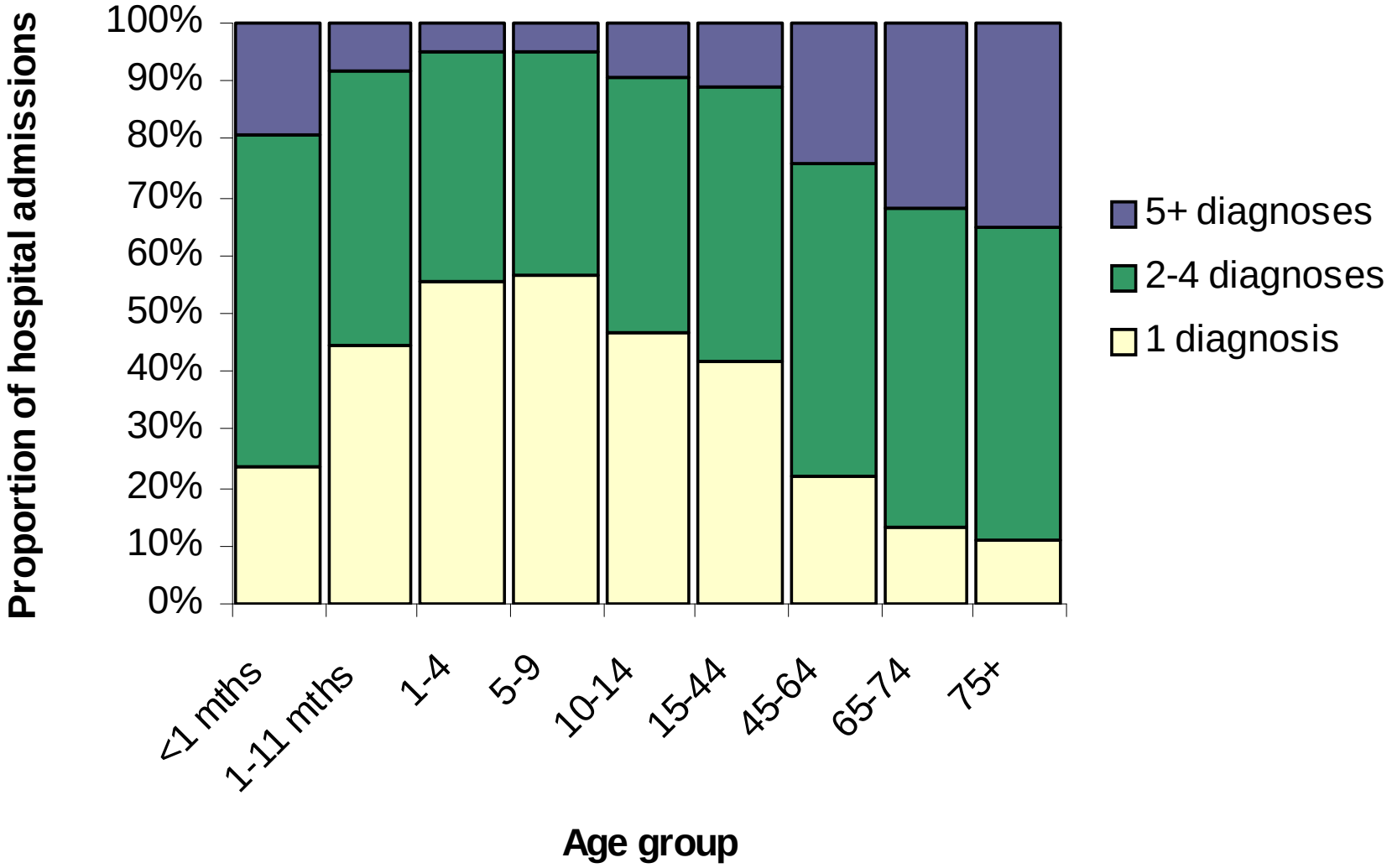
Burden of Pneumococcal disease

Hospital Episode Statistics (HES) England



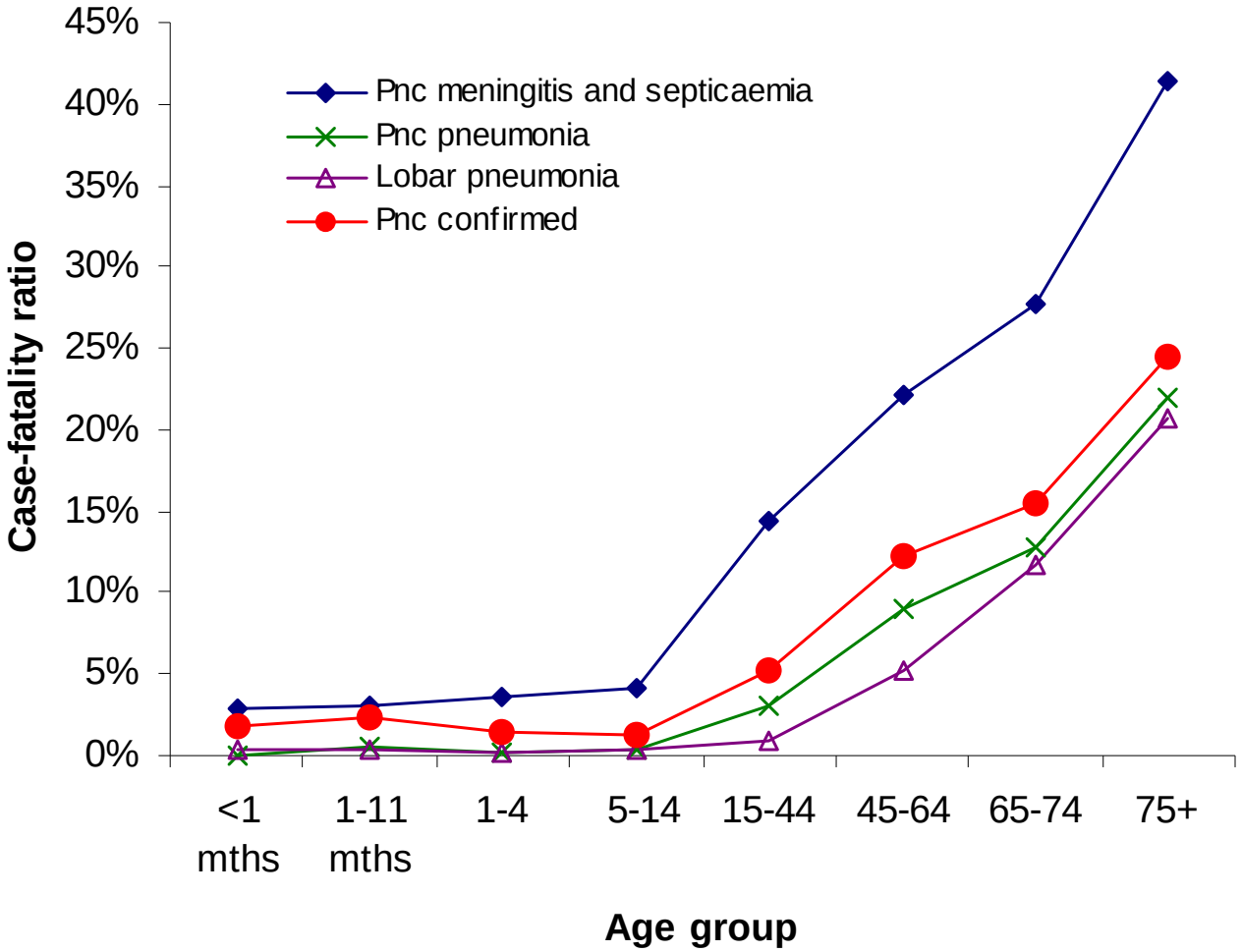
Source: Melegaro et al

Proportion of hospitalised pneumococcal cases reporting co-morbidity (1, 2-4 and 5+ diagnoses)



Source: Melegaro et al

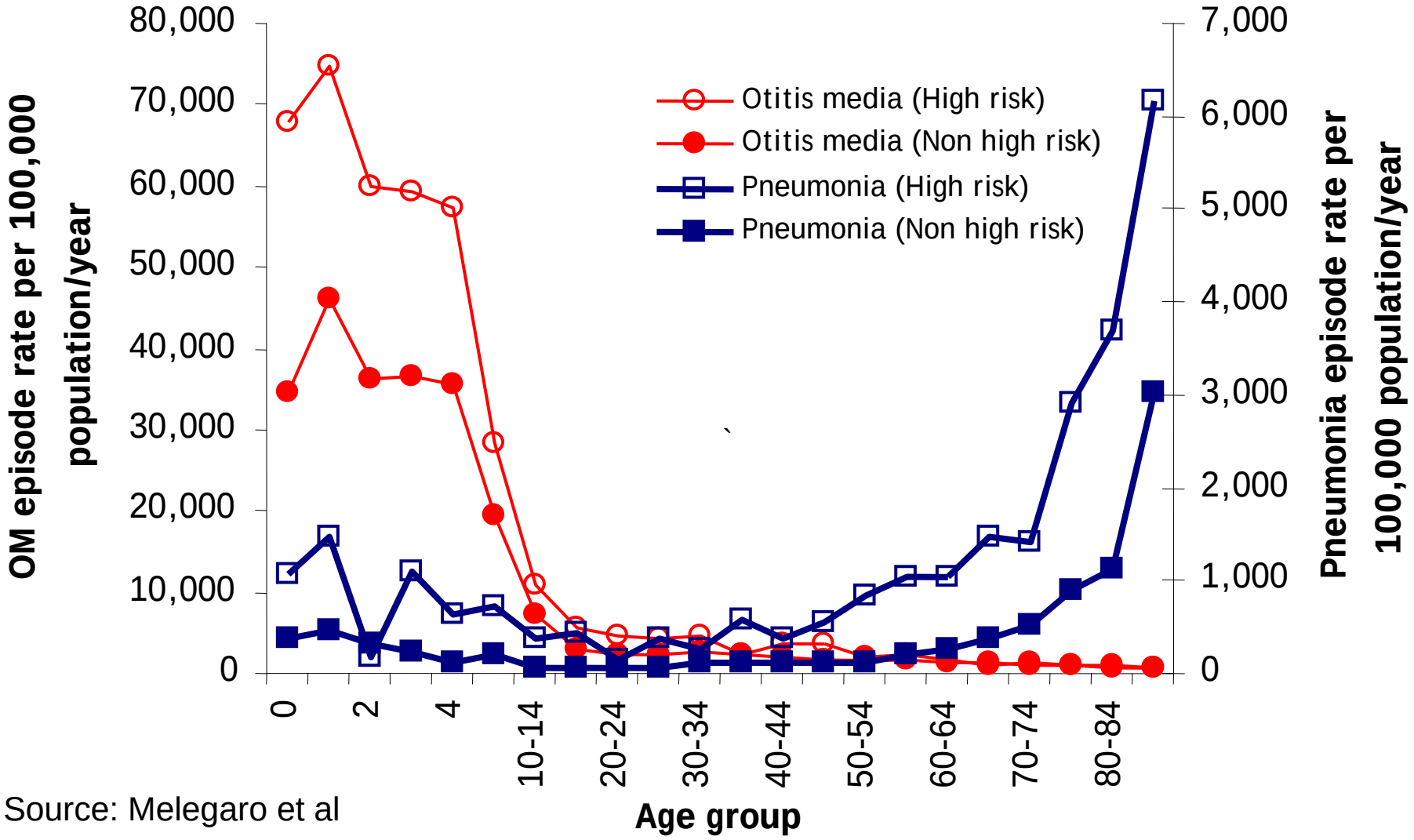
Case-fatality ratio by age of IPD, pneumococcal pneumonia and lobar pneumonia



Source: Melegaro et al

Burden of Pneumococcal disease

GP consultation rate for CAP and OM



Source: Melegaro et al

Pneumococcal polysaccharide vaccine

Produced from purified capsular polysaccharide;

Current vaccine contains 23 of the serotypes responsible for disease;

Protects against invasive disease:

–BUT

–poor antibody responses in young children;

–do not induce immunologic memory, short term protection;

–hyporesponsiveness on revaccination

–do not protect against non-invasive diseases e.g. otitis media;

–do not reduce nasopharyngeal carriage.

Pneumococcal conjugate vaccines

Pneumococcal conjugate vaccine contains 7 of the serotypes responsible for disease;

Seek to prevent invasive and non-invasive (pneumonia and otitis media) disease.

- effective in young children;
- induce long-term memory;
- reduce Pnc carriage and induce herd immunity.

Coverage of vaccine serotypes in England and Wales by age: 7-valent conjugate and 23-valent polysacc vaccine

Vaccine	<5yrs	5-64 yrs	64+ yrs
7-valent	**74.2** **(85.8)**	**42.3** **(51.2)**	**55.4** **(66.9)**
23-valent	**97.4**	**96.2**	**96.3**

Figures in ( ) based on assumption of full cross protection between serotypes within serogroups

Evolution of pneumococcal vaccination strategy in England and Wales

Polysaccharide vaccine (23-valent) licensed in 1989:

1992 until 2003	recommended for risk groups ≥2 year olds
post 2003	also recommended for elderly (>65 years)

Conjugate vaccine (7-valent) licensed in 2001:

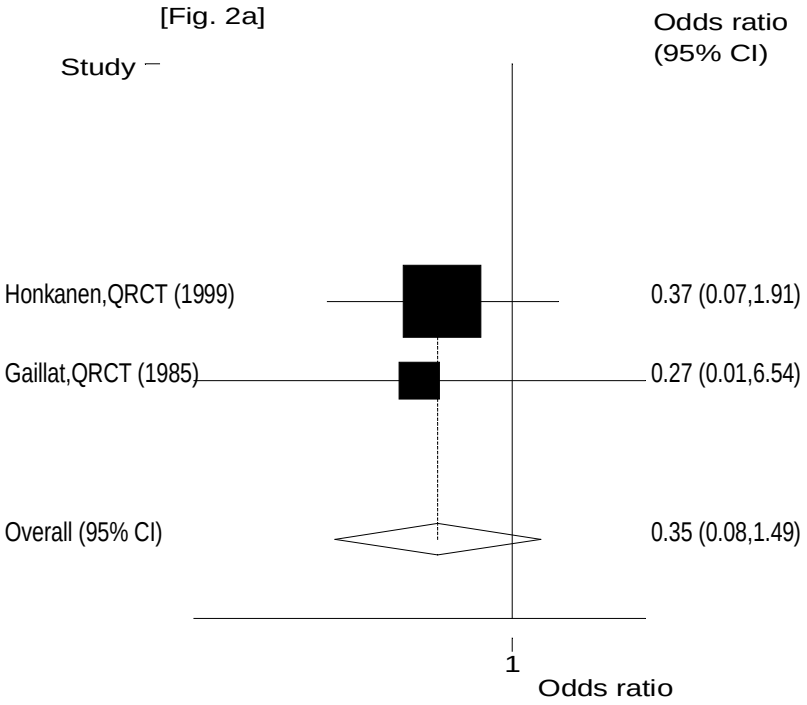
post 2002	recommended for risk groups <2 years old
post 2004	recommended for risk groups <5 years old
post 2006	recommended for all infants

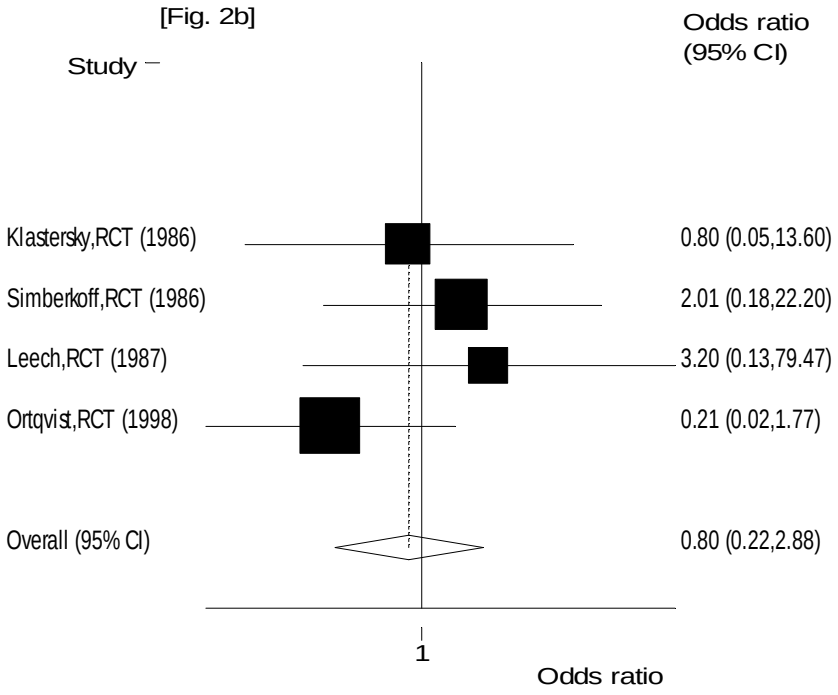
Health Protection Agency

Risk groups for whom vaccine indicated

- asplenics (including sickle cell & coeliac disease);
- chronic lung disease;
- chronic heart disease;
- chronic renal disease;
- chronic liver disease (including cirrhosis);
- diabetes mellitus;
- immunocompromised (disease or treatment);
- HIV infection (at any stage);
- persons with cochlear implants.

Meta-analysis of polysaccharide vaccine efficacy for IPD (Melegaro et al. 2004)



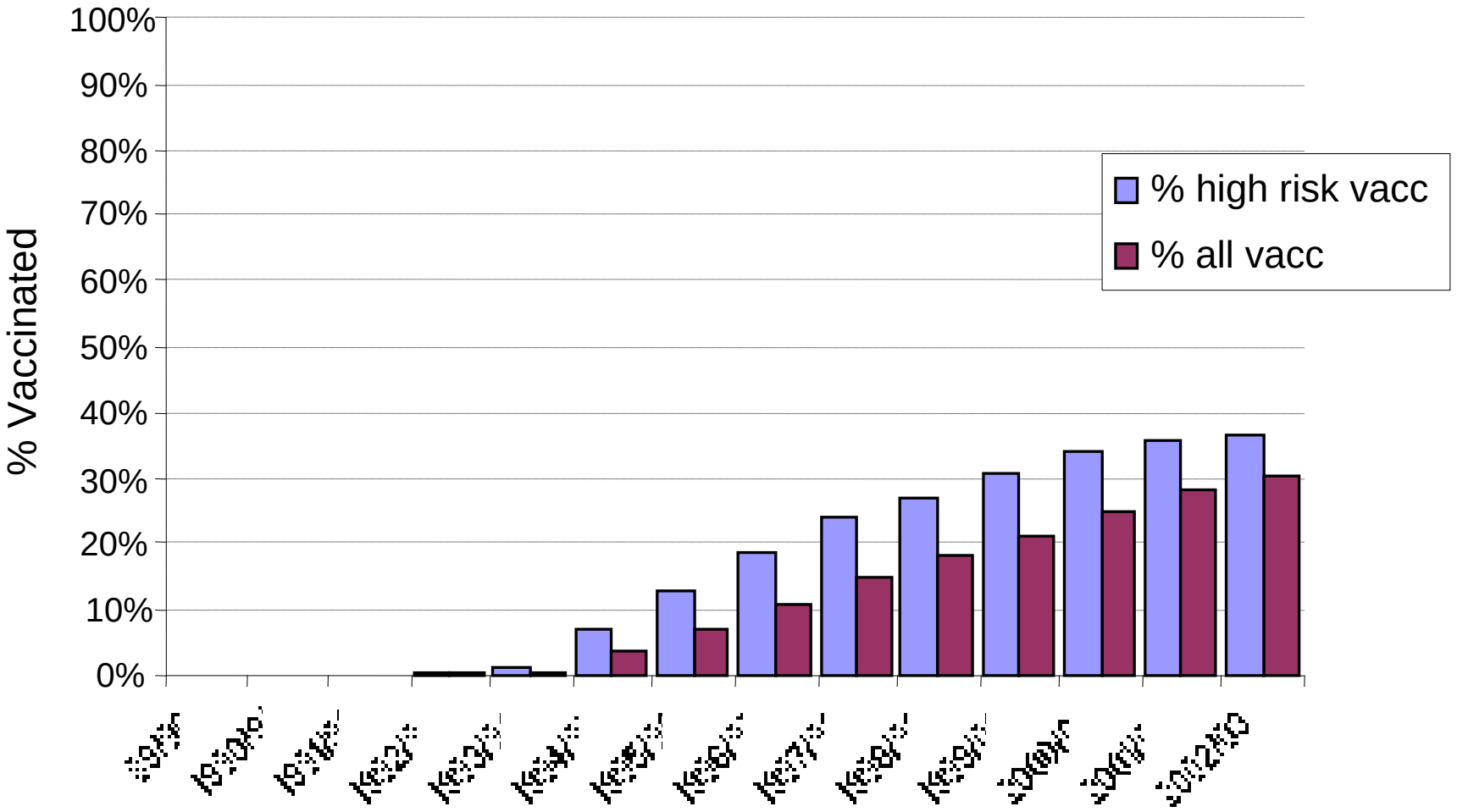


Little or no evidence of efficacy against pneumonia (not shown)

Limited evidence for efficacy against IPD in non-high risk individuals (left-hand panel & other studies)

Little or no evidence of efficacy against IPD in high risk population (right hand panel)

Polysaccharide vaccine coverage in high-risk population and all elderly >65 years, General Practice Research Database, 1989-2003



New polysaccharide programme for the elderly, England and Wales

from 20th August 2003:

all people ≥ aged 80 years

from 1st April 2004:

extended to all ≥ aged 75 years

from 1st April 2005:

extended to all ≥ aged 65 years

Enhanced pneumococcal surveillance

PPV coverage:

• 10 year historical coverage & previous 12 months uptake from GPs

– **From August 2004 for 80+**

– **From April 2005 for 75-79**

– **From April 2006 for 65-74**

Enhanced IPD surveillance:

- All serotyped IPD cases followed with GP to ascertain:
  - immunisation history;
  - outcome of infection;
  - underlying risk factors.

US pneumococcal conjugate vaccine efficacy trial: 2/4/6 months + 12 month booster

PCV efficacy against

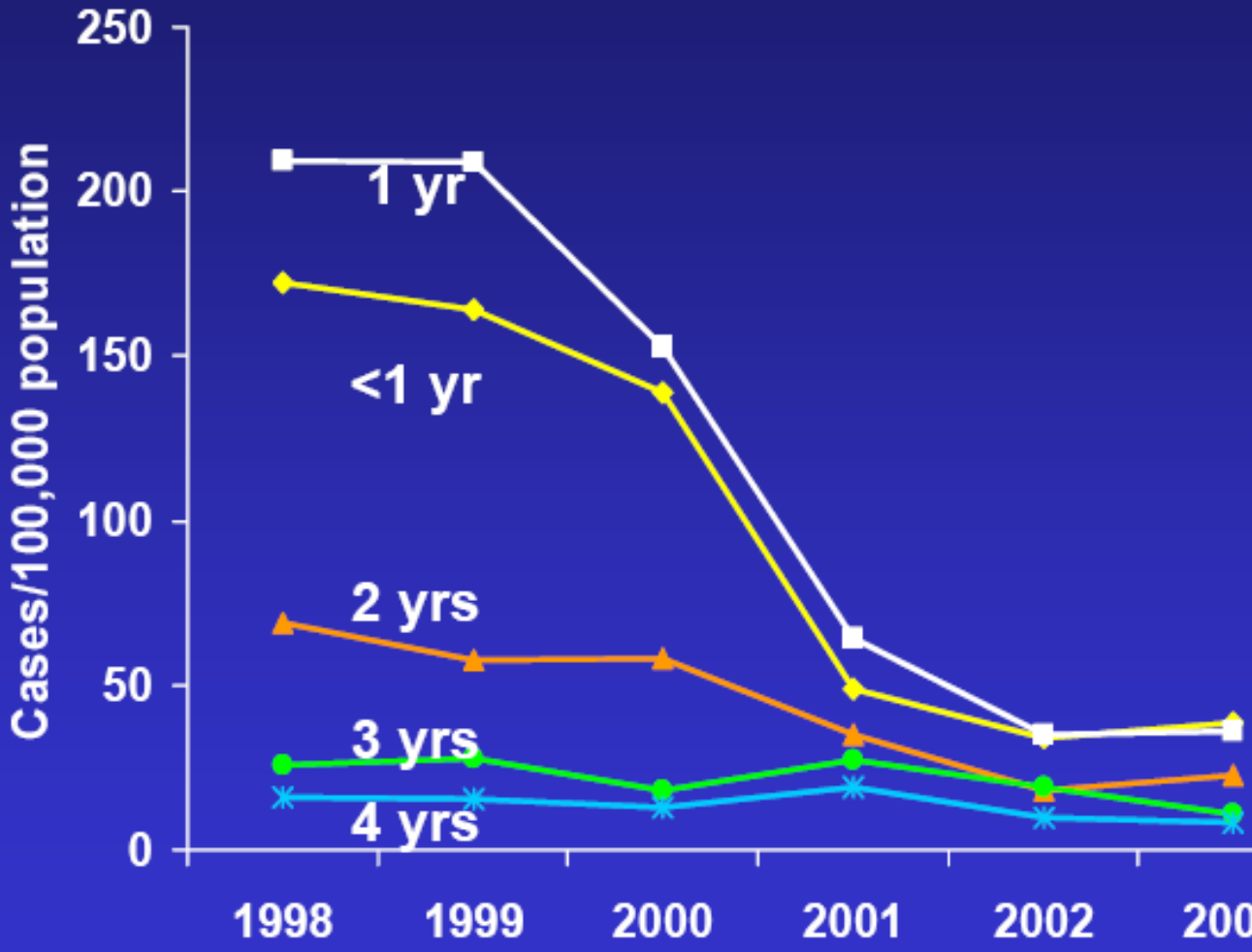
- Invasive disease vaccine serotypes (ST) **97.4%**
- Invasive disease vaccine ST 1+ dose **85.7%**
- Lobar pneumonia **73%**
- Any pneumonia with abnormal CXR **33%**
- Any otitis media episode **8.9%**
- Recurrent OM **11.9%**
- Ear tube placement **20.1%**

Finnish Prevenar Efficacy Trial against Serotype-specific Culture-confirmed Acute Pneumococcal Otitis Media (AOM) in Infants and Children

Episodes due to vaccine related serotypes	51% (27 to 97)
Any culture confirmed pneumococcal AOM	34% (21 to 45%)
AOM irrespective of aetiology	6% (-4 to 16%)
Episodes due to non-vaccine serotypes	- 33% (-80 to 1)

Eskola J, et al NEJM 2001

Invasive Pneumococcal Disease Rates by Age and Year Children <5 Years, ABCs, 1998-2003



2003 vs baseline

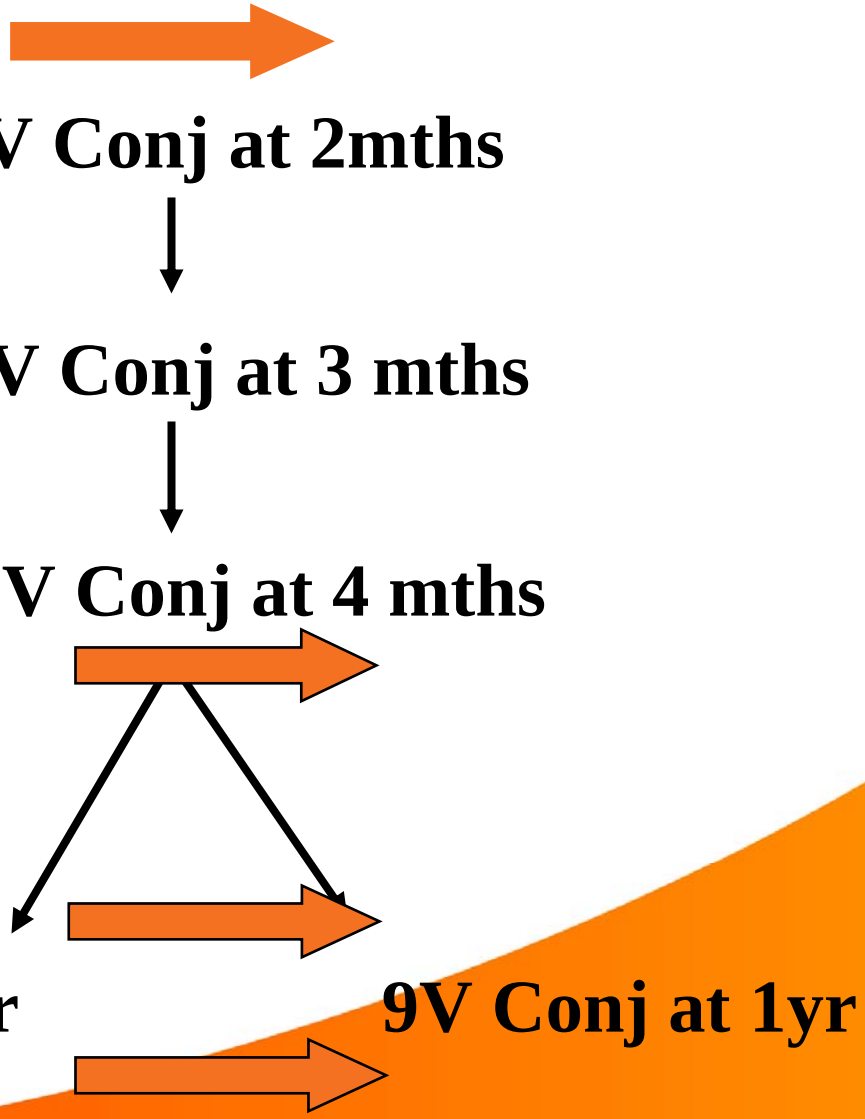
- 77% (<1 yr)
- 83% (1 yr)
- 64% (2 yr)
- 60% (3 yr)
- 48% (4 yr)

Source: ABCs (August 2003), Observed Rates
Sites: CA (SF co), CT, GA (20 co), MD (6 co), MN (7 co), NY (7 co), OR (3 co)

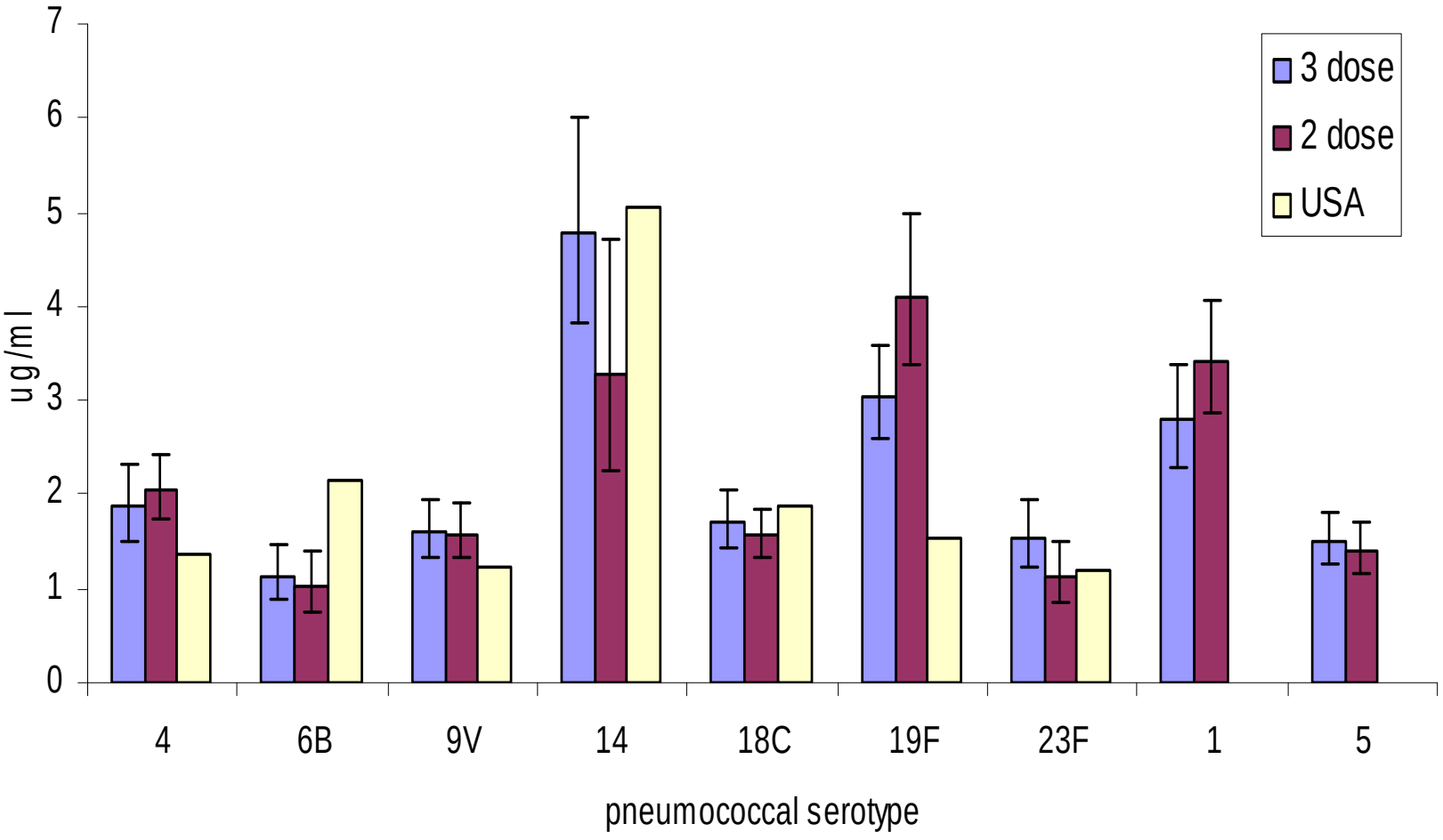
CDC

Design of infant trial, UK

PCV/PPV given concomitantly with $DTaP_3$/Hib-TT + MCC- CRM



Serotype-specific IgG GMCs after 3 doses (at 2/3/4 months) or 2 doses (at 2 and 4 months) of conjugate in UK infants compared with USA schedule*



*Data from Black et al PIDJ 2000

Source: Miller et al.

Vaccination schedule in the UK 2006

Primary immunisation

2 months

Diphtheria-tetanus-acellular pertussis, inactivated polio vaccine and *Haemophilus influenzae* type b	DTaP-Hib-IPV
Pneumococcal conjugate vaccine	PCV

3 months

Diphtheria-tetanus-acellular pertussis, inactivated polio vaccine and *Haemophilus influenzae* type b	DTaP-Hib-IPV
Meningococcal group C conjugate	MenC

4 months

Diphtheria-tetanus-acellular pertussis, inactivated polio vaccine and *Haemophilus influenzae* type b	DTaP-Hib-IPV
Meningococcal group C conjugate	MenC
Pneumococcal conjugate vaccine	PCV

13 months

Measles-mumps-rubella	MMR

Vaccination schedule in the UK 2006 (continued)

Booster immunisation

12 months

Haemophilus influenzae **type b – Meningococcal group C conjugate**	**Hib-MenC**

13 months

Pneumococcal conjugate vaccine	**PCV**

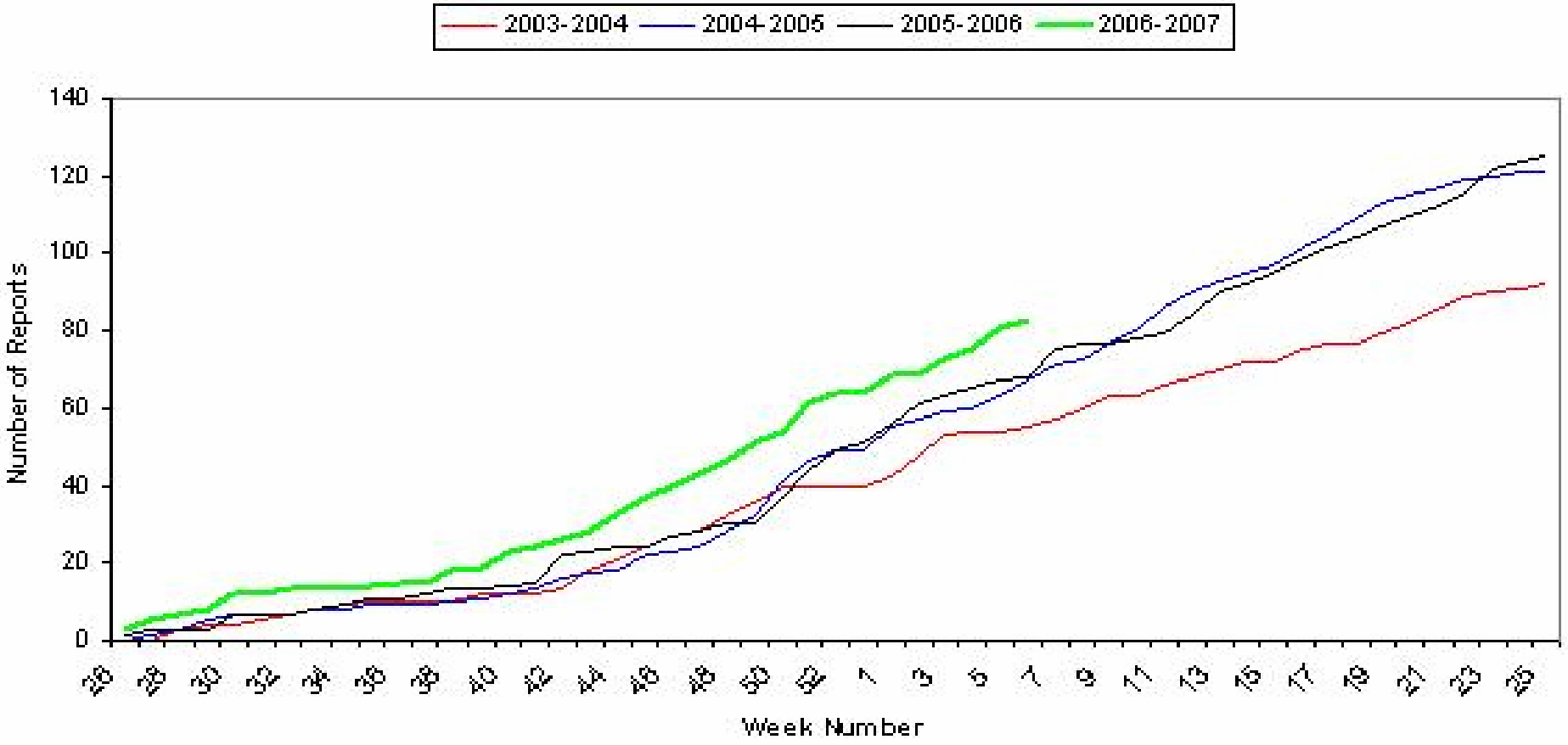
3½-5 years

Diphtheria-tetanus-acellular pertussis and inactivated polio vaccine	**DTaP-IPV or dTaP/IPV**
Measles-mumps-rubella	**MMR**

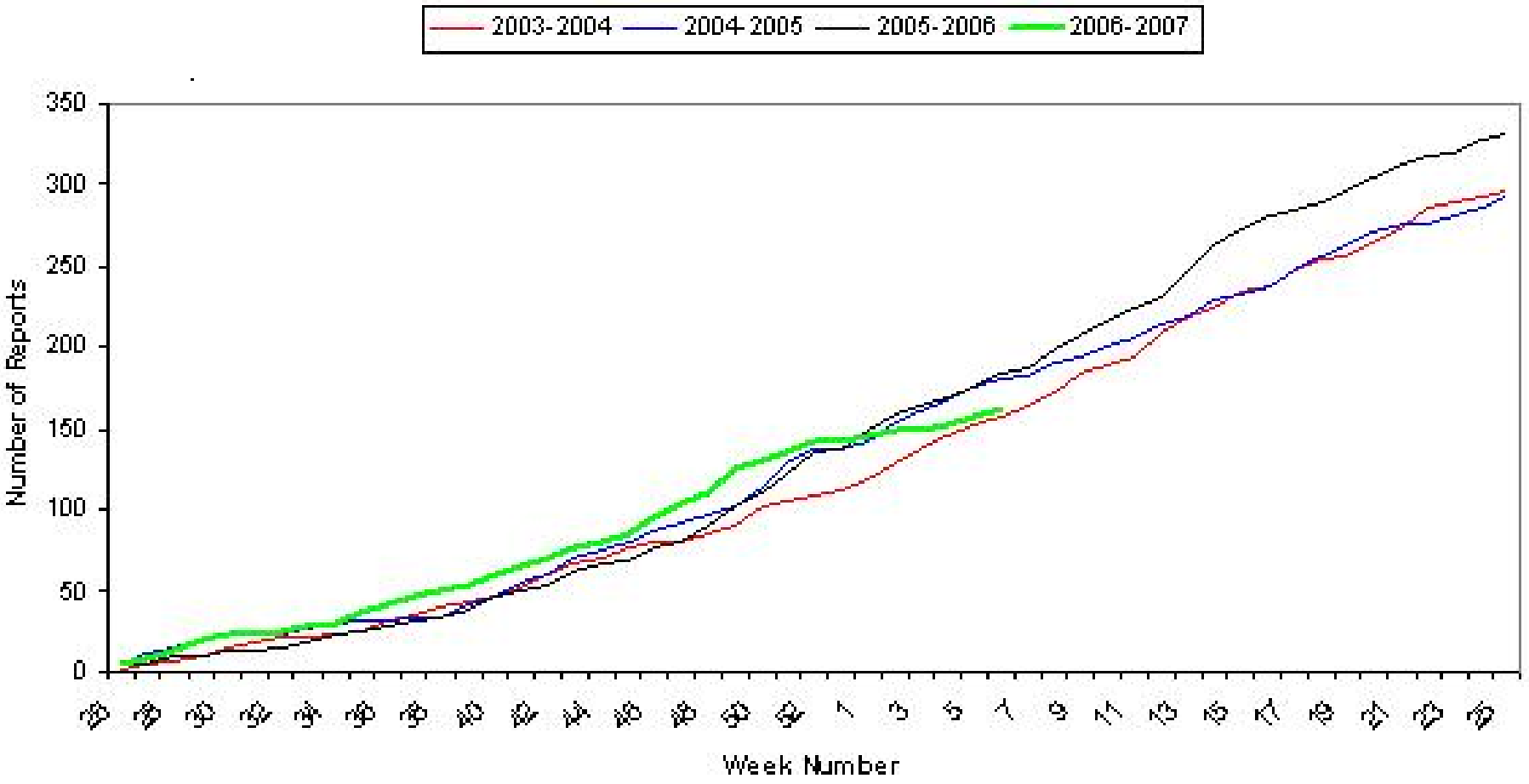
13-18 years

Tetanus-low dose diphtheria and inactivated polio vaccine	**Td-IPV**

Cumulative Weekly Number of Reports of Invasive Pneumococcal Disease Due To One of the Serotypes Not Present in Prevenar™ for Children Aged 0 - 2 Years in England and Wales by Epidemiological Year: July - June (2003 to Date)



Cumulative Weekly Number of Reports of Invasive Pneumococcal Disease Due To One of the Seven Serotypes Present in Prevenar™ for Children Aged 0-2 Years in England and Wales by Epidemiological Year: July-June (2003 to Date)



Current issues

Impact and effectiveness of current programme

Pneumococcal clusters

Emergence of non-7-valent PCV serotypes

Pneumococcal vaccine development:

10-valent and 13-valent vaccines in advanced stages of testing

At least one ‘common protein’ candidate approaching large-scale clinical evaluation

Acknowledgments

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Microbiologists, and General Practitioners across the country for referring IPD isolates, reporting infections and responding to all our (numerous) information requests.