

The impact of pneumococcal conjugate vaccine (PCV) in England and Wales- the first eighteen months



Dr Mary Slack

**Respiratory & Systemic Infection Laboratory
HPA Centre for Infections
Colindale, London, UK**

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Streptococcus pneumoniae- Host-pathogen interaction

- **Infects humans**
- **Colonisation of nasopharynx**
- **Outcome depends on:**
 - Intrinsic virulence of colonising serotype
 - Efficiency of host defence mechanisms
- **Transmission from asymptomatic infection is via droplets of respiratory secretions**

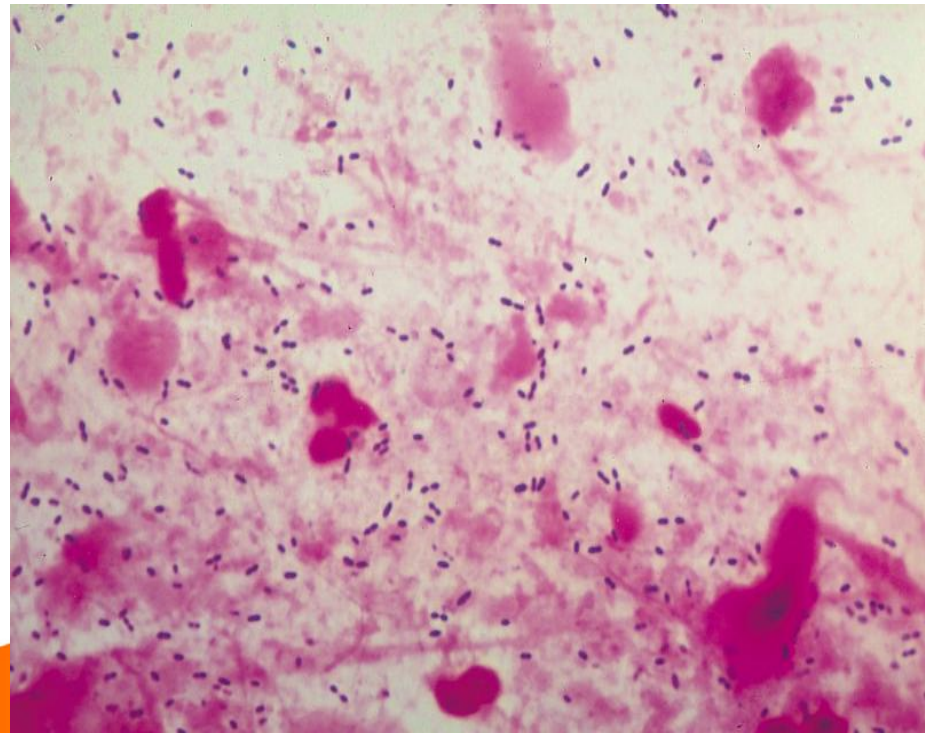
Pneumococcal Carriage

•Acquisition

- Pneumococci acquired very early in life
- Carriage rate:
 - 40-50% in children
 - 20-30% in adults
- Varies with serotype

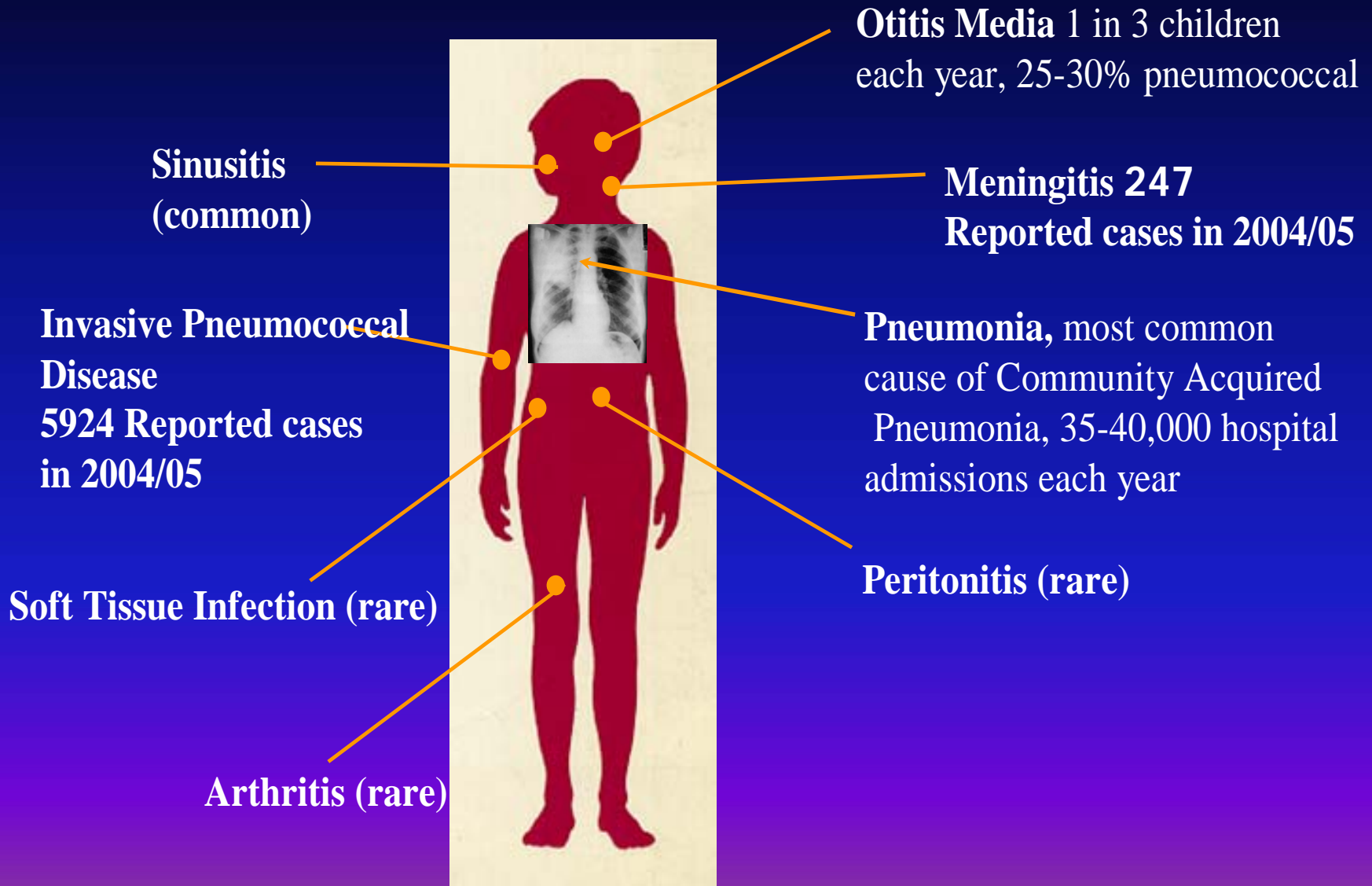
•Duration

- Longer in children than in adults
- Depends on serotype



The Clinical Spectrum of Pneumococcal Infection

Data relate to England and Wales in 2004/05





HPA Enhanced Surveillance of Pneumococcal disease

In preparation for wider use of pneumococcal vaccines surveillance of invasive pneumococcal disease was enhanced from 1996 onwards in order to:

- Determine disease burden**
- Determine age specific incidence**
- Determine serotype distribution**
- Estimate proportion of disease preventable by 23 and 7 valent vaccines**
- Use these data to inform policy and decision makers**

Methods

Capture basic data from routine reporting systems

- **age and sex, illness and outcome (where available)**

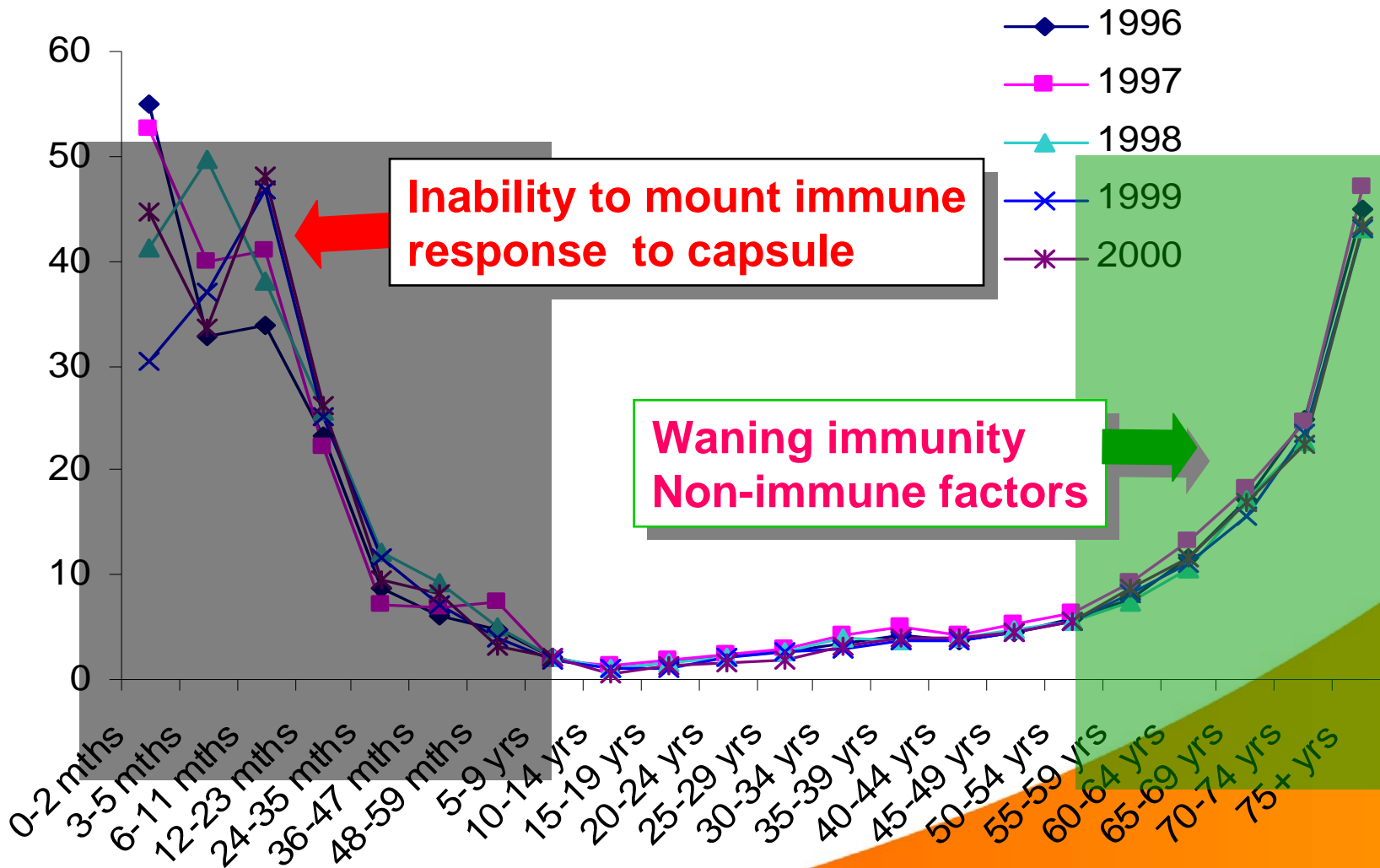
For all invasive pneumococcal infections reported by any route to the HPA each year and obtain bacterial isolates for serotyping wherever possible.

Linking laboratory reports of invasive disease (isolation from blood or CSF) to the Immunisation Dept of HPA Cfl, and,

Laboratory referrals of normally sterile site isolates to the HPA Streptococcus & Diphtheria Reference Unit of RSIL

To produce a single data set containing all information known to HPA regarding these infections.

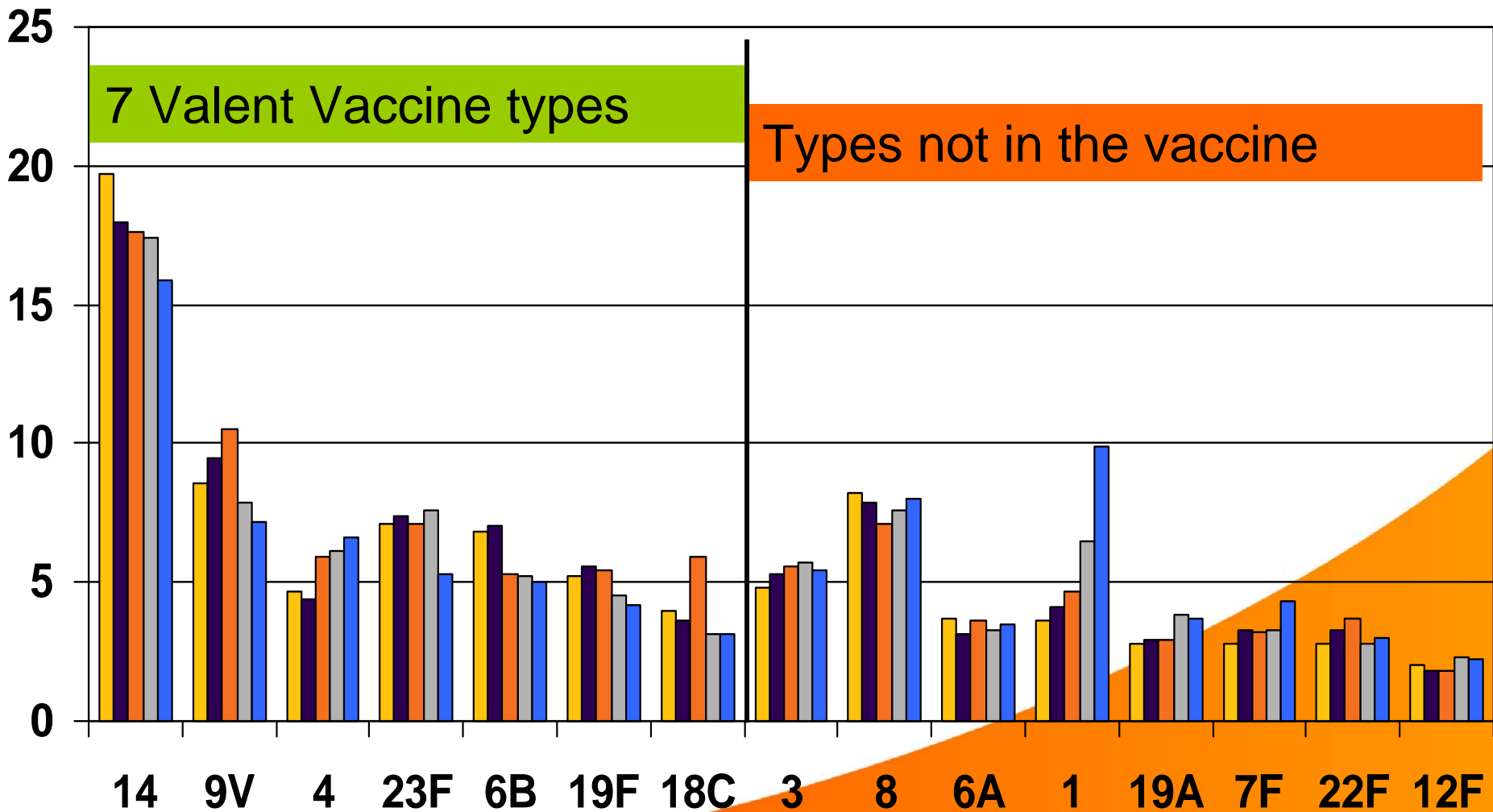
Annual incidence per 100,000 of invasive pneumococcal infection E&W, by age group and year, 1996-2000



Top 15 Serotypes (%) by epidemiological year



■ 2000/01
 ■ 2001/02
 ■ 2002/03
 ■ 2003/04
 ■ 2004/05

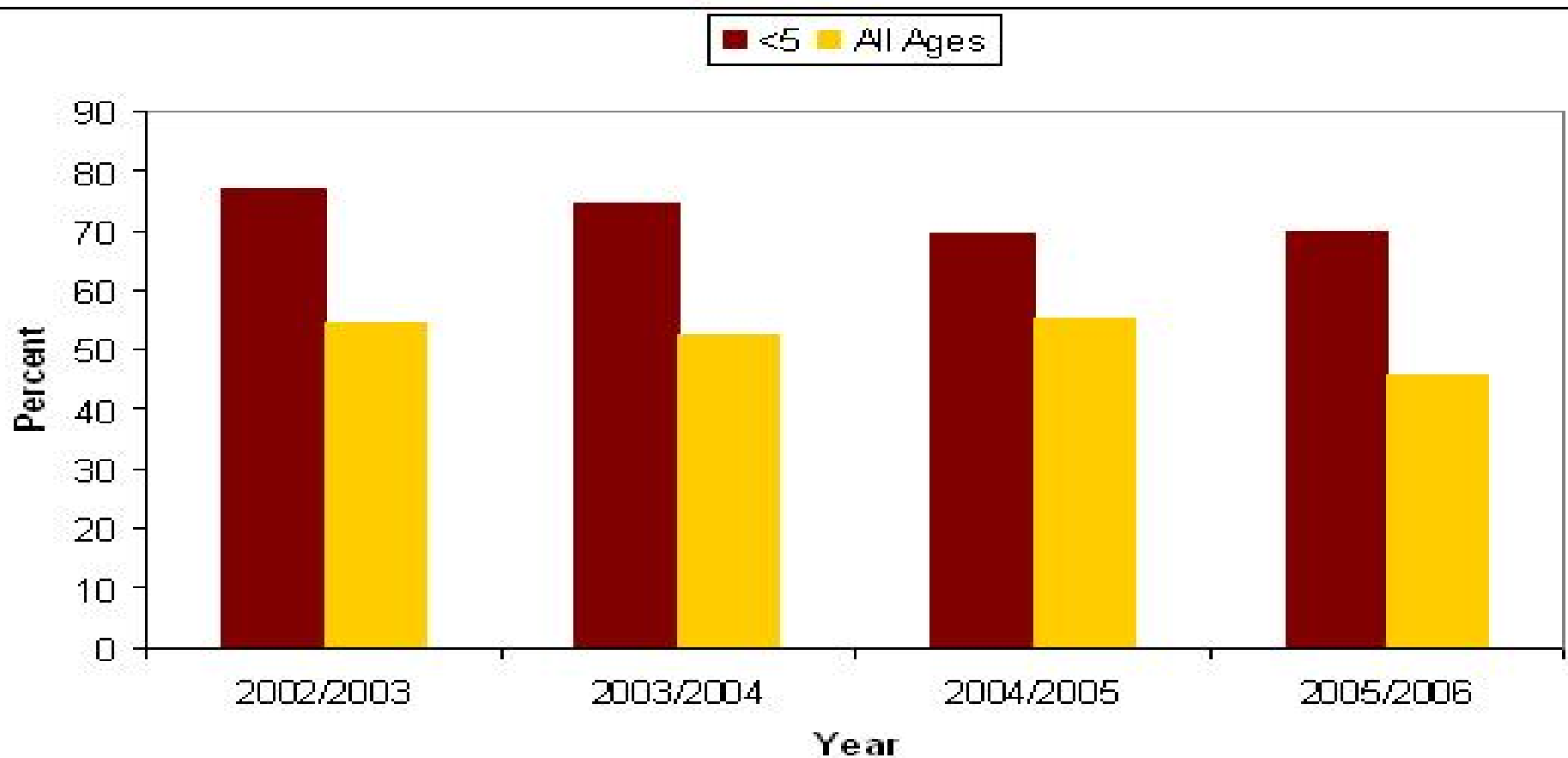


HPA Surveillance data



Percentage of the total cases of invasive pneumococcal disease (IPD) with a serotype contained in the 7-Valent Vaccine

Children - Under 5 yr vs all Ages – By epidemiological year



Pneumococcal polysaccharide vaccine



Produced from purified capsular polysaccharide;

Current vaccine contains 23 serotypes;

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;

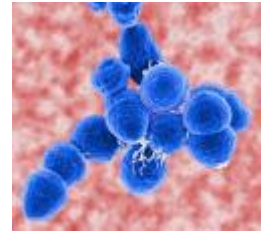
Seeks to prevent invasive and non-invasive (pneumonia and otitis media) disease.

- effective in young children;
- induces long-term memory;
- reduces Pneumococcal carriage and induces herd immunity.

The pneumococcal conjugate vaccine (PCV) Prevenar™



Over 90 serotypes of *Streptococcus pneumoniae* exist



The 7 valent conjugate vaccine (Prevenar™) contains 7 serotypes :

4 6B 9V 14 18C 19F 23F

New UK schedule from September 2006



2 months	DTaP₅/IPV/Hib + PCV
3 months	DTaP₅/IPV/Hib + MenC
4 months	DTaP₅/IPV/Hib + MenC + PCV (MenC can be given at 5 months)
12 months	Hib/Men C
13 months	MMR + PCV

Prevenar™ was introduced in England & Wales on September 4th 2006



CATCH – UP Campaign

- Children aged over 13 months and under 2 years,
born between 5/9/04 and 3/8/05

1 dose of PCV

- Children aged 8 months to 13 months, born
between 4/8/05 and 3/2/06

1 dose at routine 13 month visit

- Children aged over 2 months and under 8 months,
born between 4/2/06 and 3/7/06

**2 doses of PCV separated by 2 months,
with a further dose at routine 13 month
visit**

HPA Enhanced Pneumococcal Surveillance Activities



Following introduction PCV into routine infant immunisation schedule in UK on 04/09/06:

IPD surveillance by HPA was further enhanced to evaluate effects of PCV programme on:

- IPD rates in target age group and those not eligible for PCV
- Serotype distribution of IPD isolates
- Sequence type distribution of IPD isolates
- Antimicrobial susceptibility of IPD isolates

HPA Enhanced Surveillance of IPD



Microbiology
Labs in
England and
Wales



Hospitals
in England
and Wales

S. pneumoniae Isolates sent
for serotyping to RSIL

Reports of *S. pneumoniae*
isolates sent to CFI via CoSurv

Electronic data entered onto CFI Computer systems



Rapid telephone follow up to obtain
GP, Paediatrician and PCV
vaccination status

DATA transferred
electronically to ACCESS
study database



Clinical advice letters sent by
CFI to GP and paediatrician

ALL DATA
SHARED ON
JOINT
DATABASE
AT CFI



Antibody
results



HPA Manchester

May give a
dose of PCV
and send
blood to HPA
Manchester



Feed back results with further advice

Definition of Laboratory confirmed IPD and vaccine failures (VF)



Confirmed IPD

- Identification of *S. pneumoniae* in a normally sterile site by culture;
- Or, identification of *S. pneumoniae* DNA in CSF or pleural fluid by dual target PCR;
- Or, reference laboratory identification of *S. pneumoniae* capsular polysaccharide and serotype-specific antigen in CSF or pleural fluid.

Probable IPD

PCR positive in blood at low copy number, a clinical picture compatible with pneumococcal sepsis and no other pathogen identified

VF

- IPD within 14 days of a priming dose or 7 days of a booster dose

CASES OF IPD FOLLOWED UP to 13th March 2008



- **623 cases of IPD in children born since 04/09/2004**
- **555 (89%) serotyped – i.e. Isolate sent to RSIL**
 - Remaining 68 are from CoSurv reports to Centre For Infections but no isolate sent to RSIL for serotyping
- Immunisation status obtained for 617 (99%)
- 228 of total serotyped (41%) have a vaccine serotype
- **42 children have died**
 - 28 (66%) attributable to pneumococcal sepsis
- **143 children had pneumococcal meningitis**
 - Case fatality rate of meningitis was 13%
- 366 Bloods sent to HPA Manchester for serotype specific IgG responses and for total IgG

PCV vaccine failures



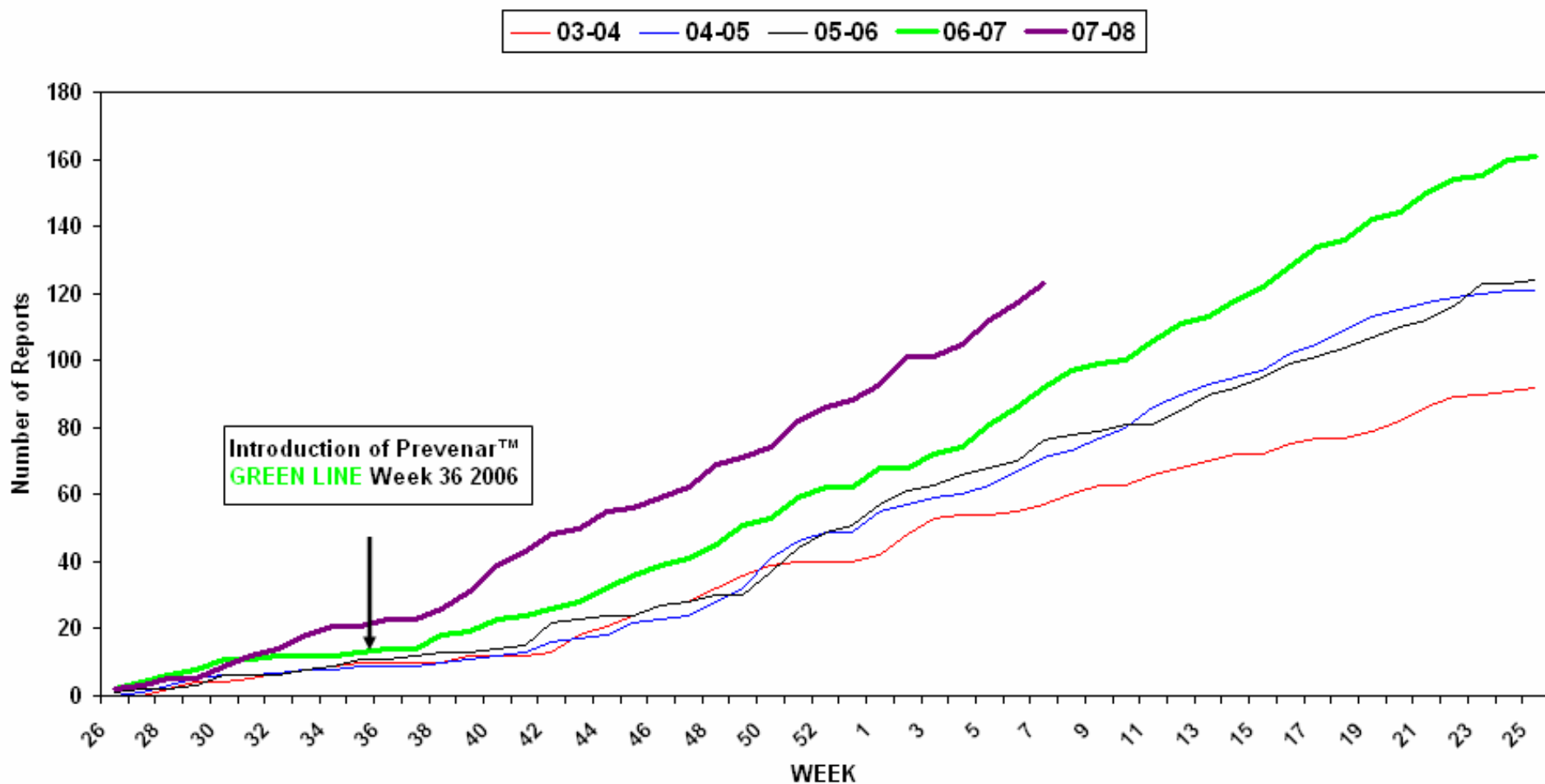
To date there have been 24 PCV failures:

COHORT	14	18C	19F	23F	6B	9V	TOTAL
Toddler Single Dose catch up			1	4	8	2	15
Two Dose Infant	1	1	2		5		9
TOTAL	1	1	3	4	13	2	24

The impact on Invasive Pneumococcal Disease (serotypes not in PCV) Children aged <2y



Cumulative weekly number of reports of Invasive Pneumococcal Disease due to any of the serotypes **NOT IN Prevenar™** : Children aged < 2 Years in England and Wales by Epidemiological Year: July-June (2003- To Date)

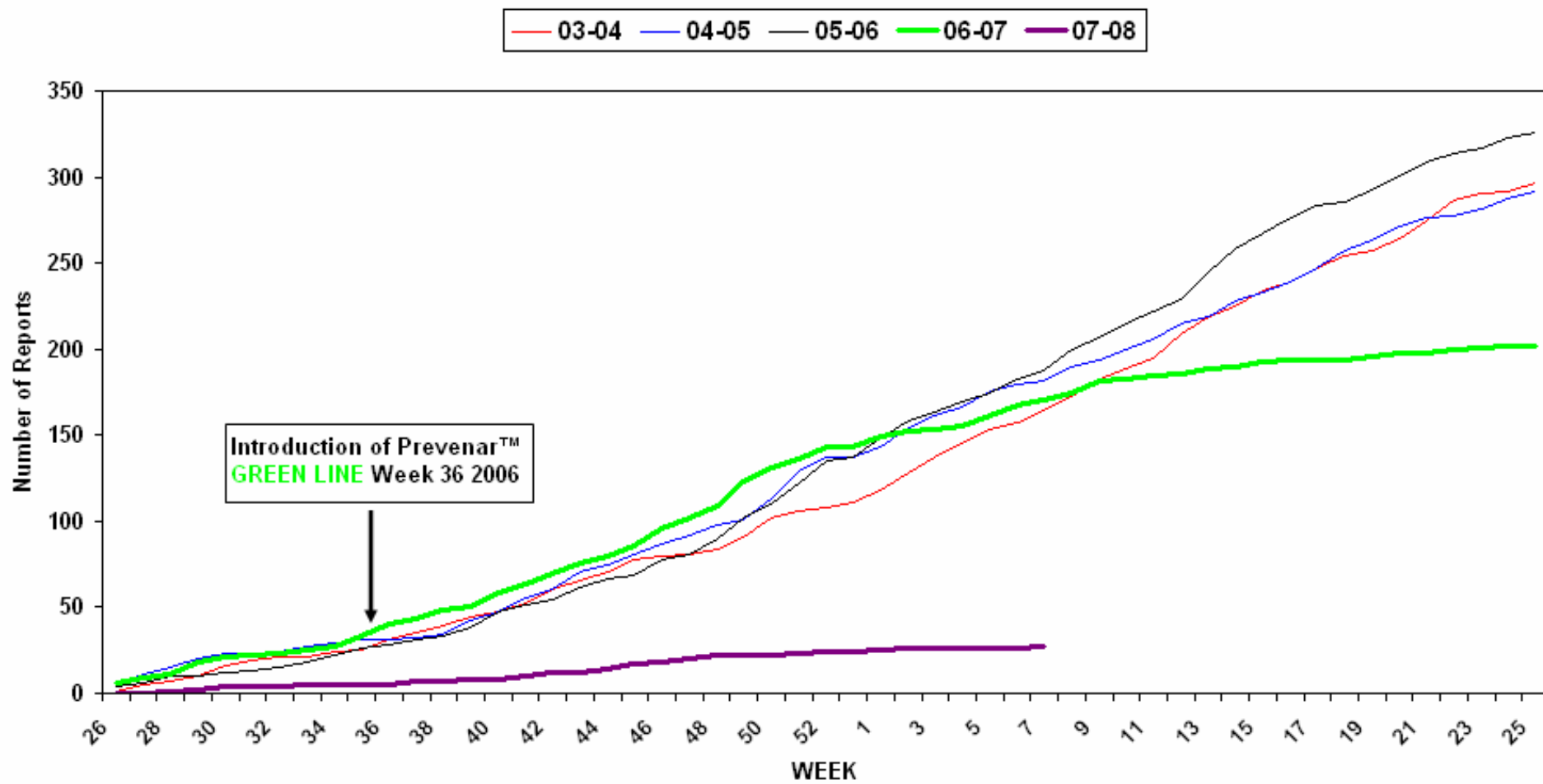


The impact on Invasive Pneumococcal Disease

(serotypes in PCV) Children aged <2y



Cumulative weekly number of reports of Invasive Pneumococcal Disease due to any of the seven serotypes in Prevenar™ : Children aged < 2 Years in England and Wales by Epidemiological Year: July-June (2003- To Date)

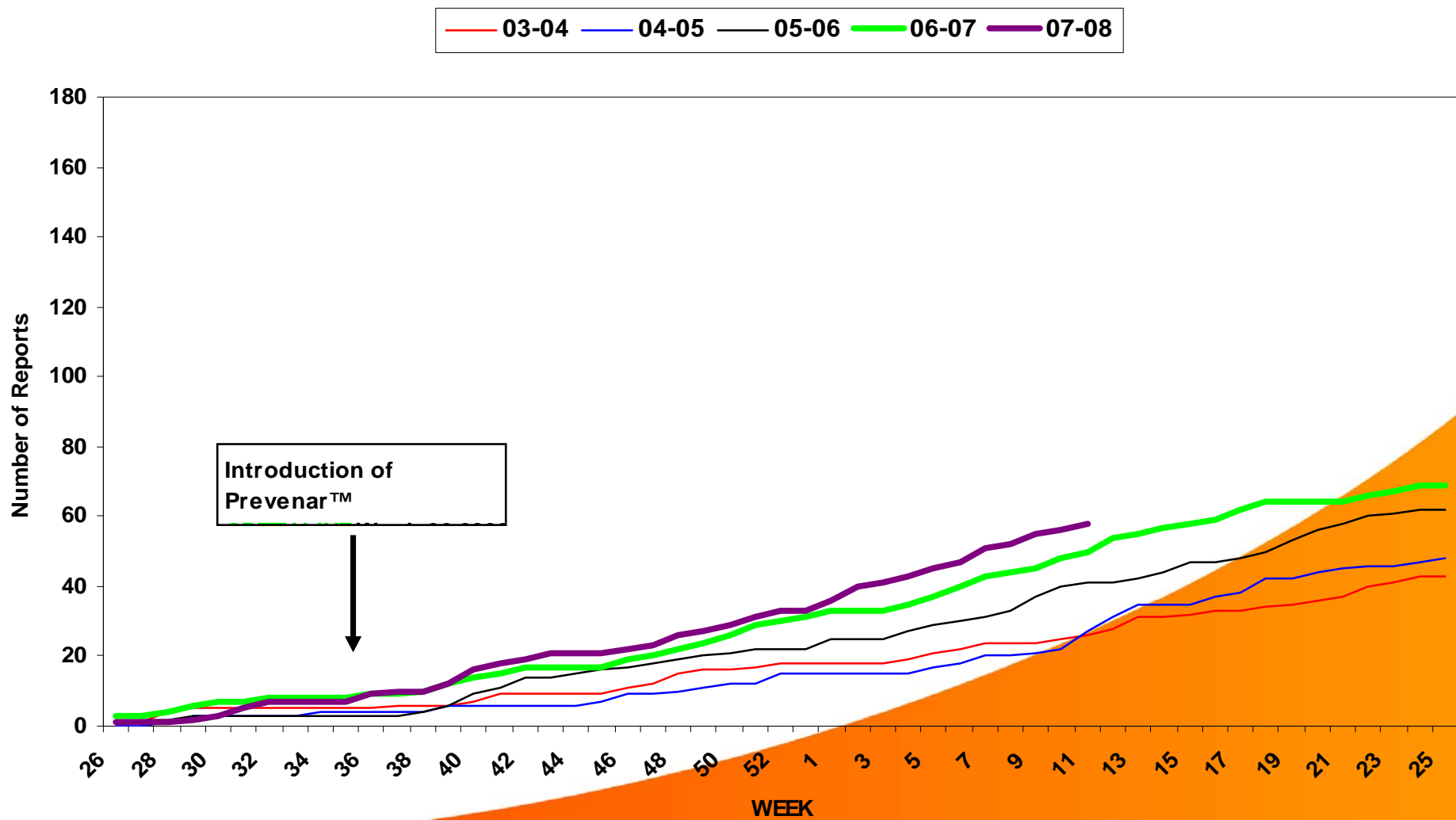


The impact on Invasive Pneumococcal Disease

(serotypes not in PCV) Children aged 2-4y



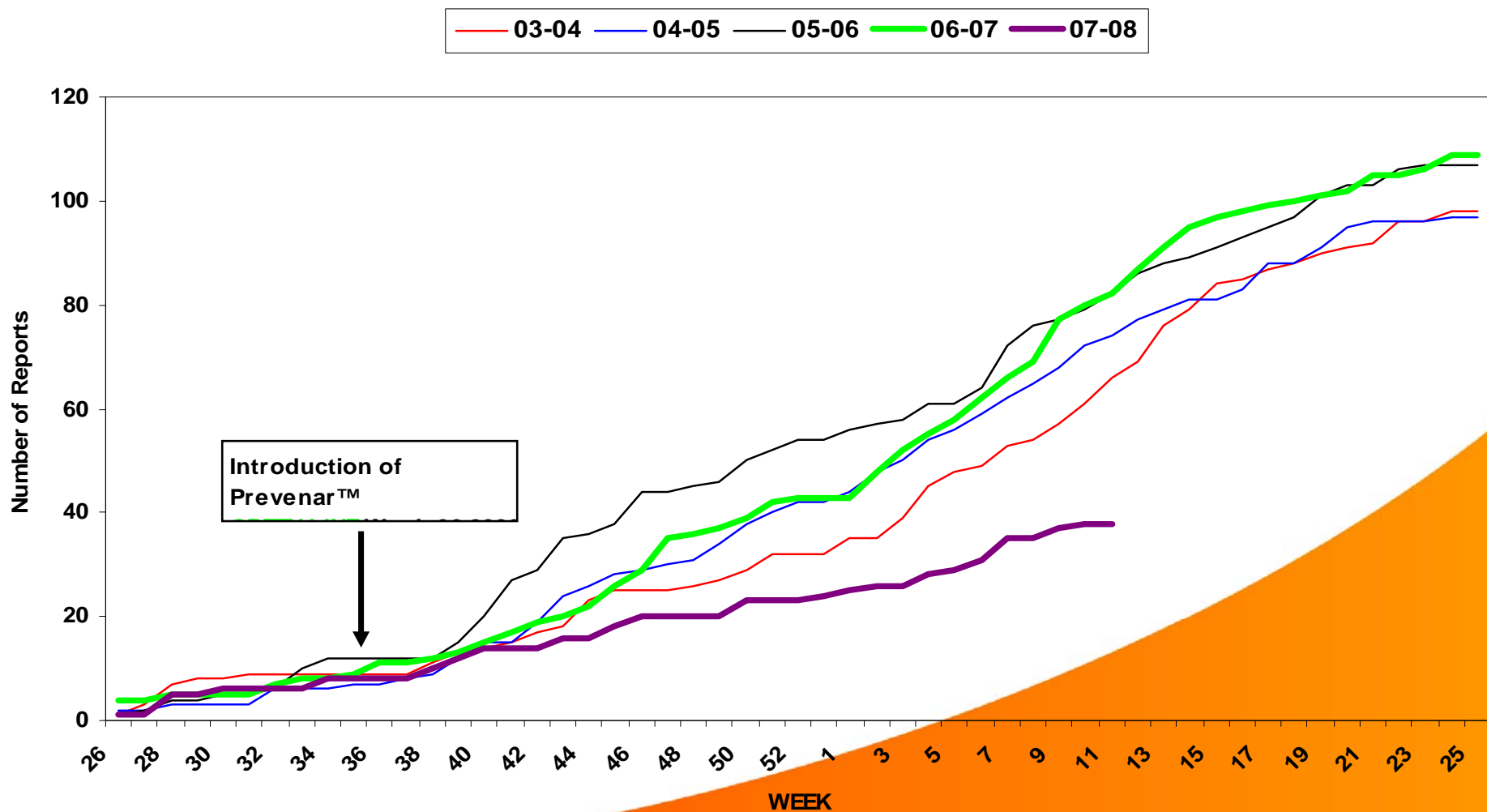
Cumulative weekly number of reports of Invasive Pneumococcal Disease due to any of the serotypes **NOT IN Prevenar™** : Children aged 2 to 4 years in England and Wales by Epidemiological Year: July-June (2003- To Date)



The impact on Invasive Pneumococcal Disease (serotypes in PCV) Children aged 2-4y



Cumulative weekly number of reports of Invasive Pneumococcal Disease due to any of the seven serotypes in Prevenar™ : Children aged 2 to 4 years in England and Wales by Epidemiological Year: July-June (2003- To Date)

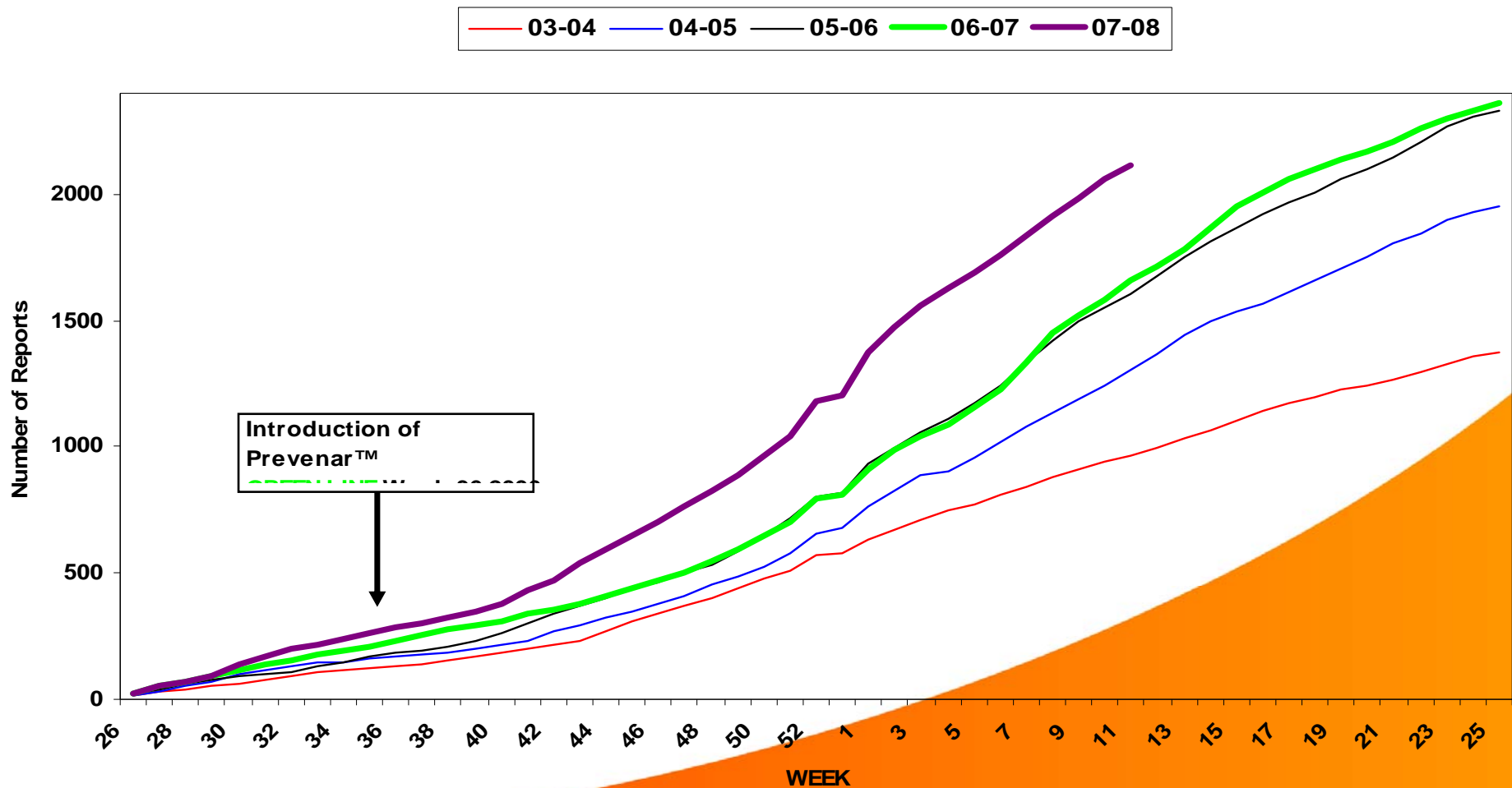


The impact on Invasive Pneumococcal Disease

(serotypes not in PCV) Aged >5y



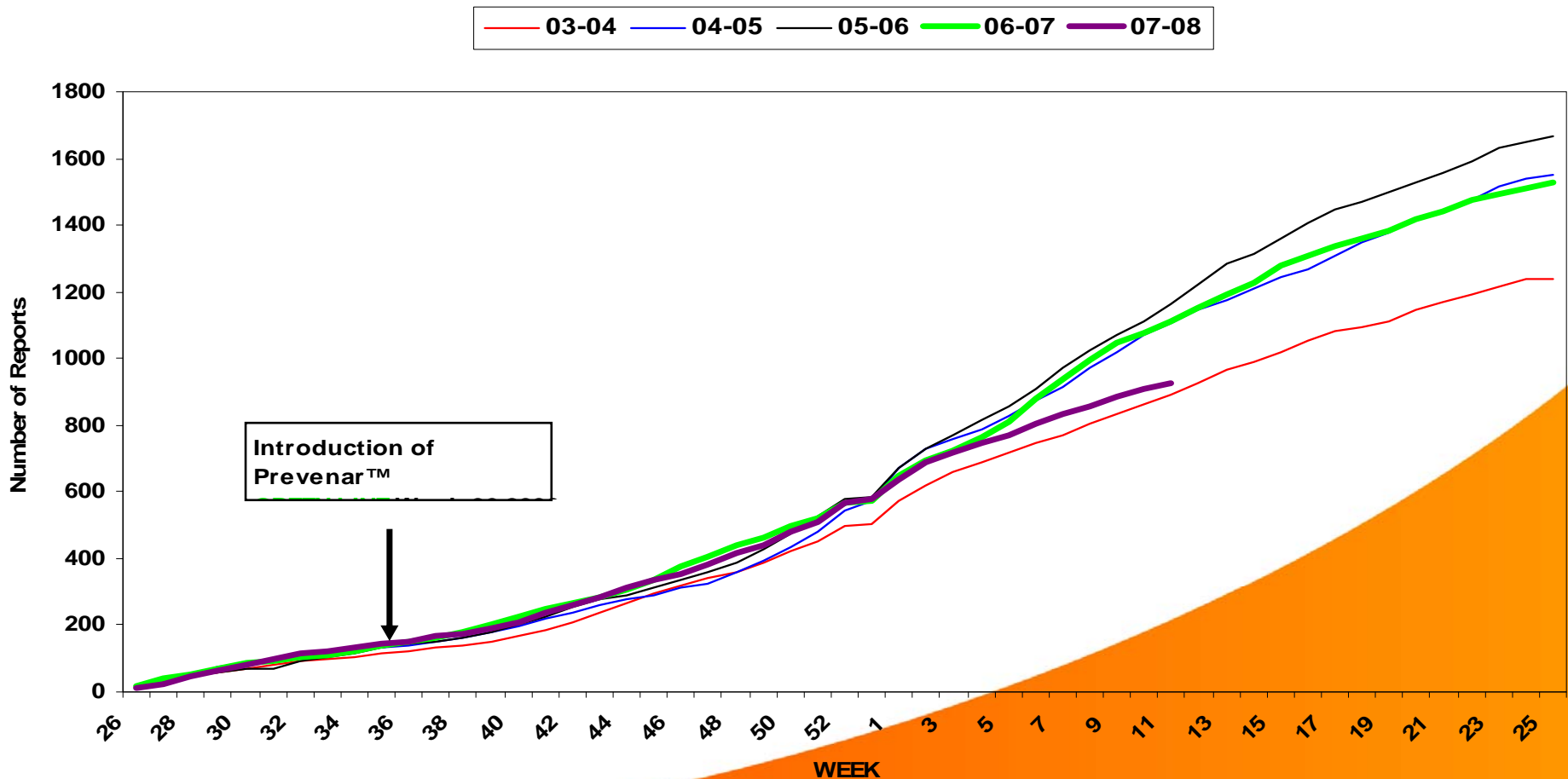
Cumulative weekly number of reports of Invasive Pneumococcal Disease due to any of the serotypes NOT IN Prevenar™ : Persons aged >5 Years in England and Wales by Epidemiological Year: July-June (2003- To Date)



The impact on Invasive Pneumococcal Disease (serotypes in PCV) Aged >5y



Cumulative weekly number of reports of Invasive Pneumococcal Disease due to any of the seven serotypes in Prevenar™ : Persons aged >5 Years in England and Wales by Epidemiological Year: July-June (2003- To Date)



Follow up of impact of PCV



MLST:

- All IPD isolates in children <5y
- Sample of IPD isolates from older groups

Antimicrobial Resistance:

- All IPD isolates screened for susceptibility to Penicillin, Erythromycin and Tetracycline by break-point method
- Any IPD isolate with reduced susceptibility will be further examined against an extended range of antimicrobials

MLST project funded by Meningitis Research Foundation

Updated data on HPA Website



- **Weekly updates on cumulative number of IPD cases by week of infection in <2y olds by:**

- Prevenar serotype

- Non-Prevenar serotype

- **5 weekly moving averages of IPD in all ages by :**

- Prevenar serotype

- Non-Prevenar serotype

- http://www.hpa.org.uk/infections/topics_az/pneumococcal/default.htm



Vaccine Efficacy

In First Year of Life

Early estimates ~ 90% for 2 doses

~ 65% for 1 dose

In Second Year of Life

~85% for 1 dose

CONCLUSIONS



- ❑ **There has been a marked reduction in the rate of cumulative increase of IPD cases caused by 7 serotypes in PCV since the introduction of Prevenar™**
- ❑ **Early estimates show good vaccine efficacy (90%) following a 2 dose primary schedule in infants and 85% after a single dose in one to two year olds**
- ❑ **Beginning to see evidence of herd immunity**
- ❑ **There is no convincing evidence yet of serotype replacement**

Acknowledgements



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PPV Immunisation of the elderly



Commenced August 2003 with those aged 80 or older

From April 2004 PPV offered to those aged 75+

From April 2005 PPV offered to those aged 65+

All serotyped IPD cases occurring in ages eligible for PPV followed up with GP to ascertain immunisation history, outcome of infection, underlying risk factors



Impact of 23 V programme in the elderly October 2003 to March 2007

5659 cases followed up

1319 cases had missing vaccination status

4340 cases of IPD for analysis

PPV Effectiveness in Elderly (Broome method)



TIME	CASE:CONTROL	VE (95% CI)
Unvaccinated	1787:208 (8.6 :1)	
<1y	306 : 66 (4.6 : 1)	47% (27% to 61%)
1-6 y	1043 : 175 (6.0 : 1)	23% (4% to 38%)
>6y	662 : 83 (8.0:1)	1% (-31% to 35%)