

Evidence based prevention of pneumococcal disease

**Assembling the evidence
and monitoring vaccine impact**

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Pneumococcus Surveillance



Why?

How?

Who?

Limitations

Outputs

Lessons

WHY?



In preparation for wider use of pneumococcal vaccines surveillance of invasive pneumococcal disease 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 (and other possible serotype) vaccines

- Use these data to inform policy and decision makers (JCVI)

- Monitor impact and effectiveness of vaccine programme

- Determine extent and scope of serotype replacement

How and Who? The Basics



Admitted with meningitis, pneumonia, etc

Microbiology
Labs in
England and
Wales



Blood/CSF
cultures



Hospitals
in England
and Wales

S pneumoniae Isolates sent for
serotyping to RSIL or Oxford

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



Electronic data captured/entered onto CFI Computer systems

Matching and deduplication

Final shared dataset containing
all information known to HPA

How and Who? Vaccine Effectiveness



Since launch of conjugate programme in September 2006 all IPD cases occurring in children eligible for immunisation actively followed up for vaccine history

Letters and questionnaires sent to general practitioners and clinicians requesting relevant information including vaccine history

Since Sept 2006 PCR diagnosis and serotype specific antigen test for culture negative CSF and empyema samples.

LIMITATIONS



Reporting of infections and submission of strains from laboratories and

of data from clinicians and GPs including immunisation record information, is

Entirely voluntary THANK YOU ALL VERY MUCH

Compliance with requests to submit strains and information is excellent overall

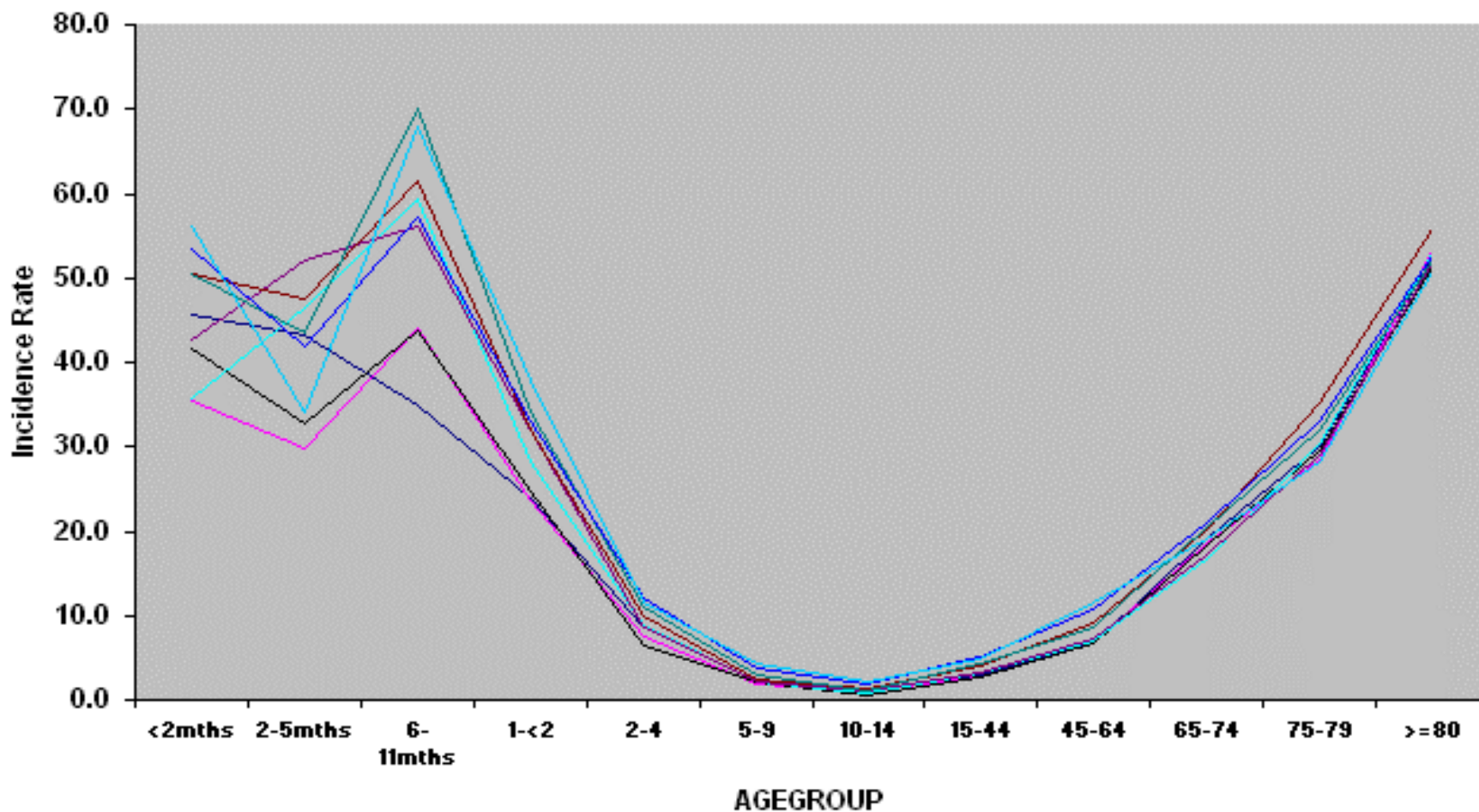
No major “holes” in the system but difficult to reliably determine absolute degree of under ascertainment

Efficiency and completeness of surveillance has increased each year thus complicating interpretation of trends

Incidence of Invasive Pneumococcal Disease per 100,000 population by age England & Wales 1998-2006

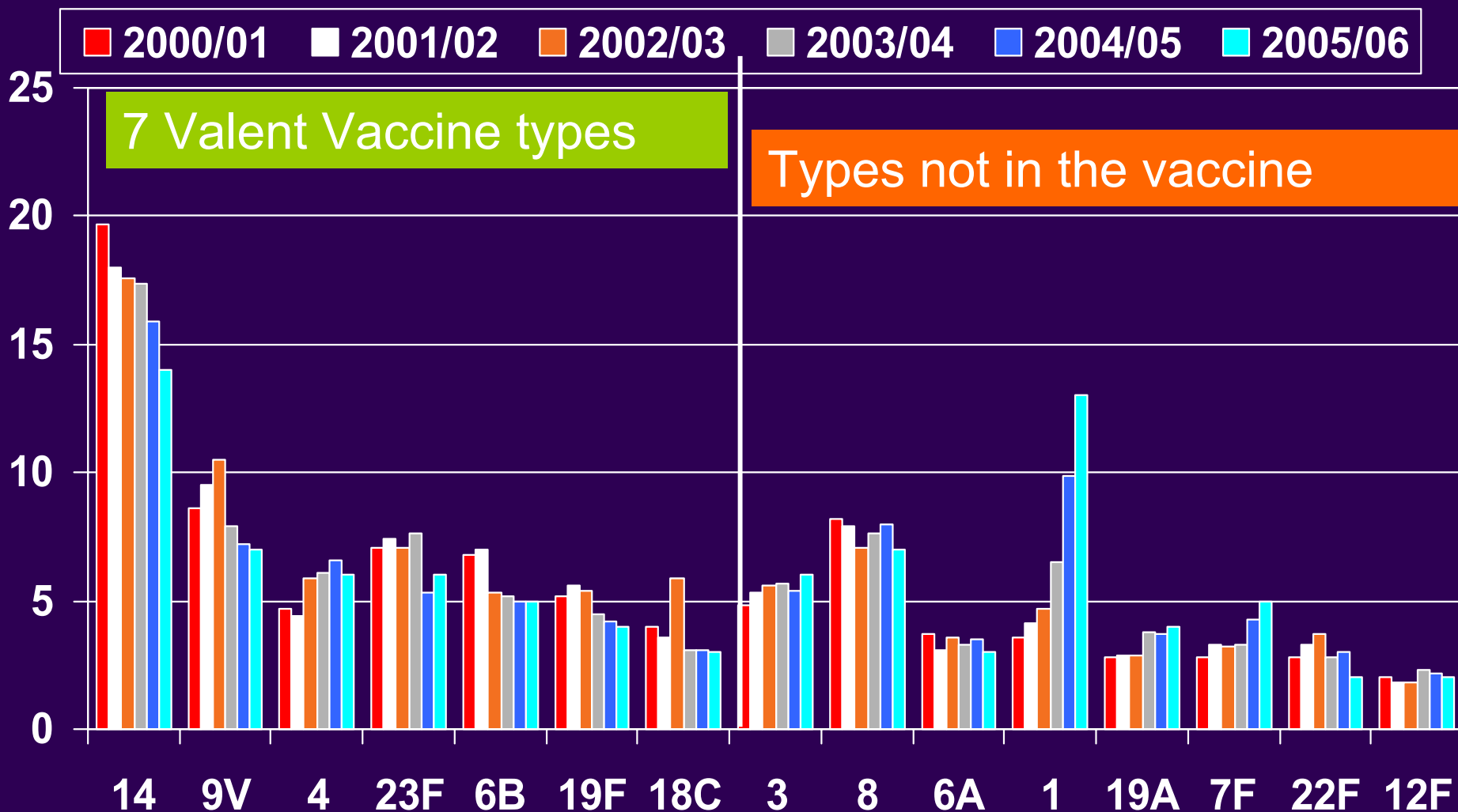


— 1998 — 1999 — 2000 — 2001 — 2002 — 2003 — 2004 — 2005 — 2006



Top 15 Serotypes (%) by epidemiological year

All ages combined



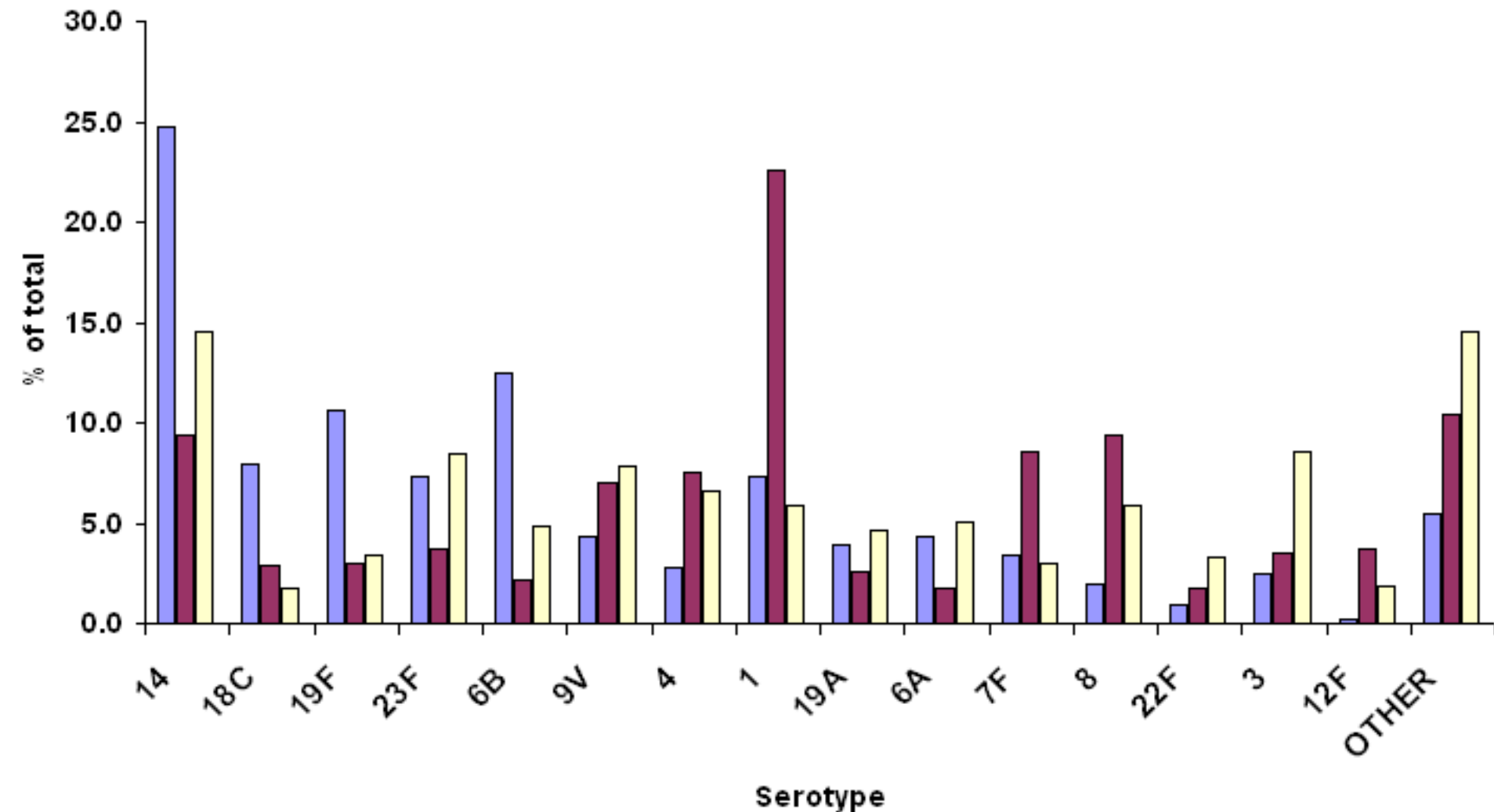
IPD Serotype Distribution 2005/2006

England and Wales

% of strains typed by age group



<5 years **5-64 years** **>=65 years**

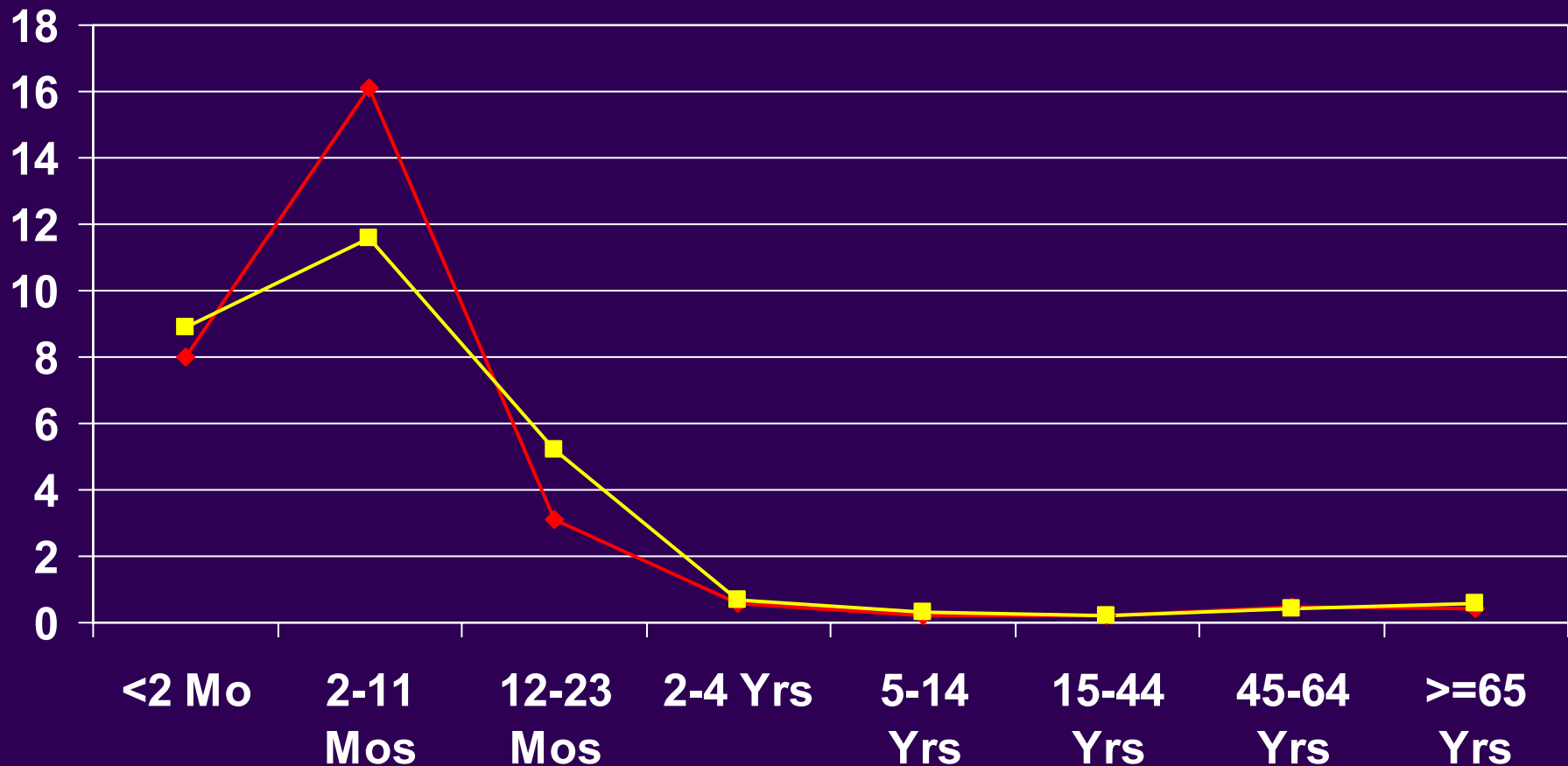


Pneumococcal Meningitis Incidence per 100,000 2004 & 2005

Johnson AP et al. J infect 2007;55:394-399



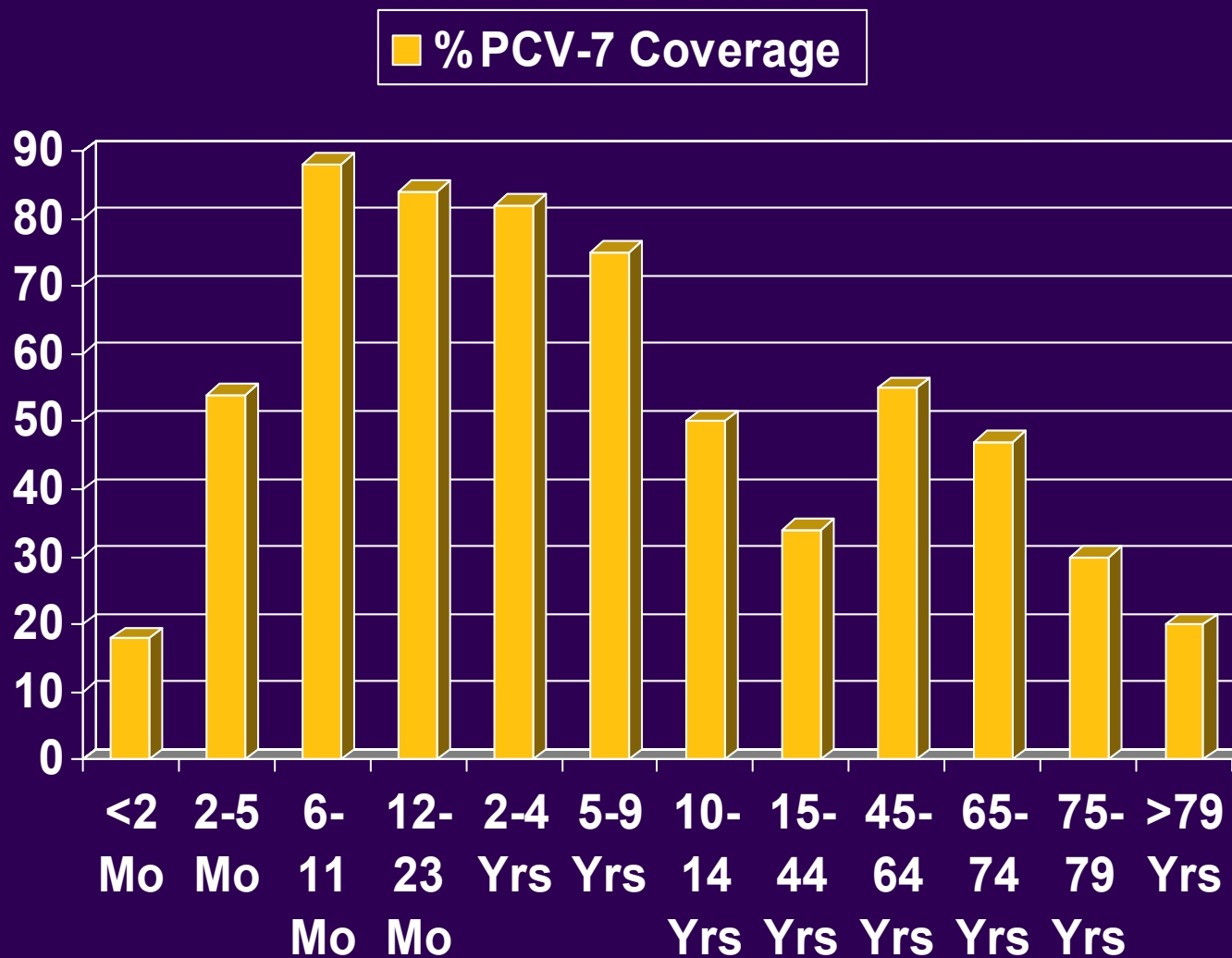
◆ Rate in 2004 ■ Rate in 2005



7-Valent Vaccine coverage of meningitis isolates 2005



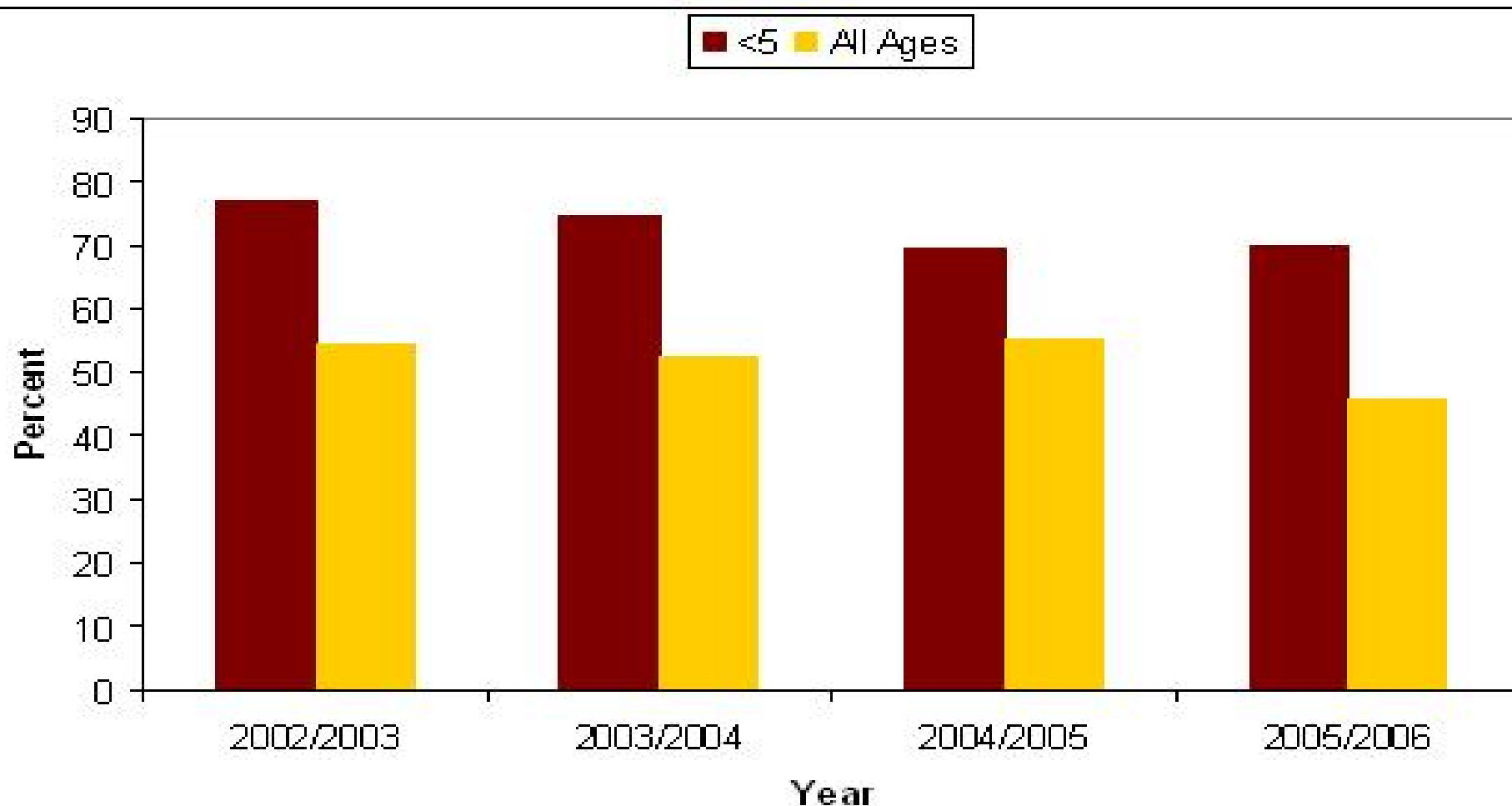
Johnson AP et al. J infect 2007;55:394-399



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



Surveillance Developments

Incorporation of non culture diagnosis and typing

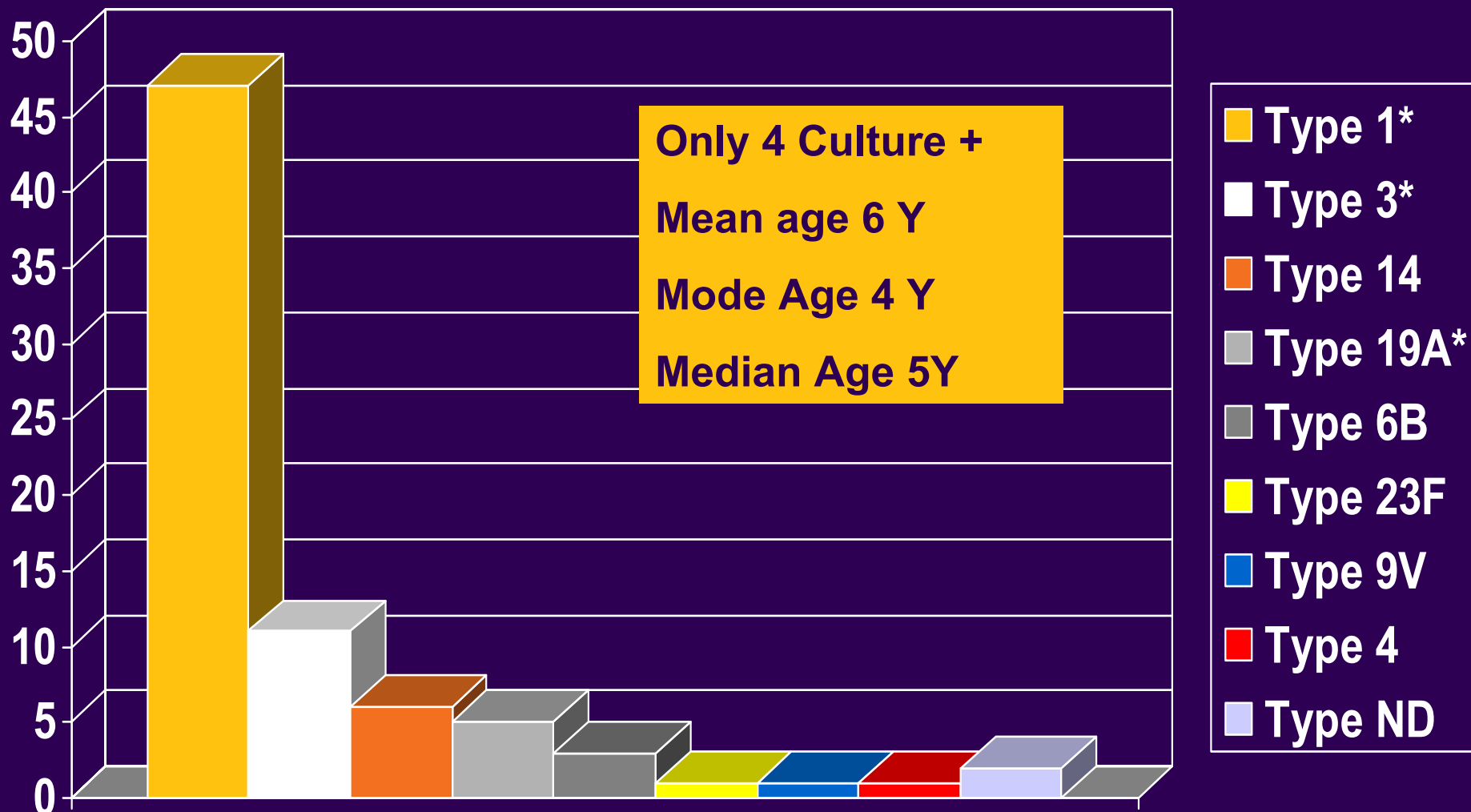


Sept 2006 contacted all microbiologists to alert them to provision of non culture diagnosis being launched in association with the implementation of PCV.

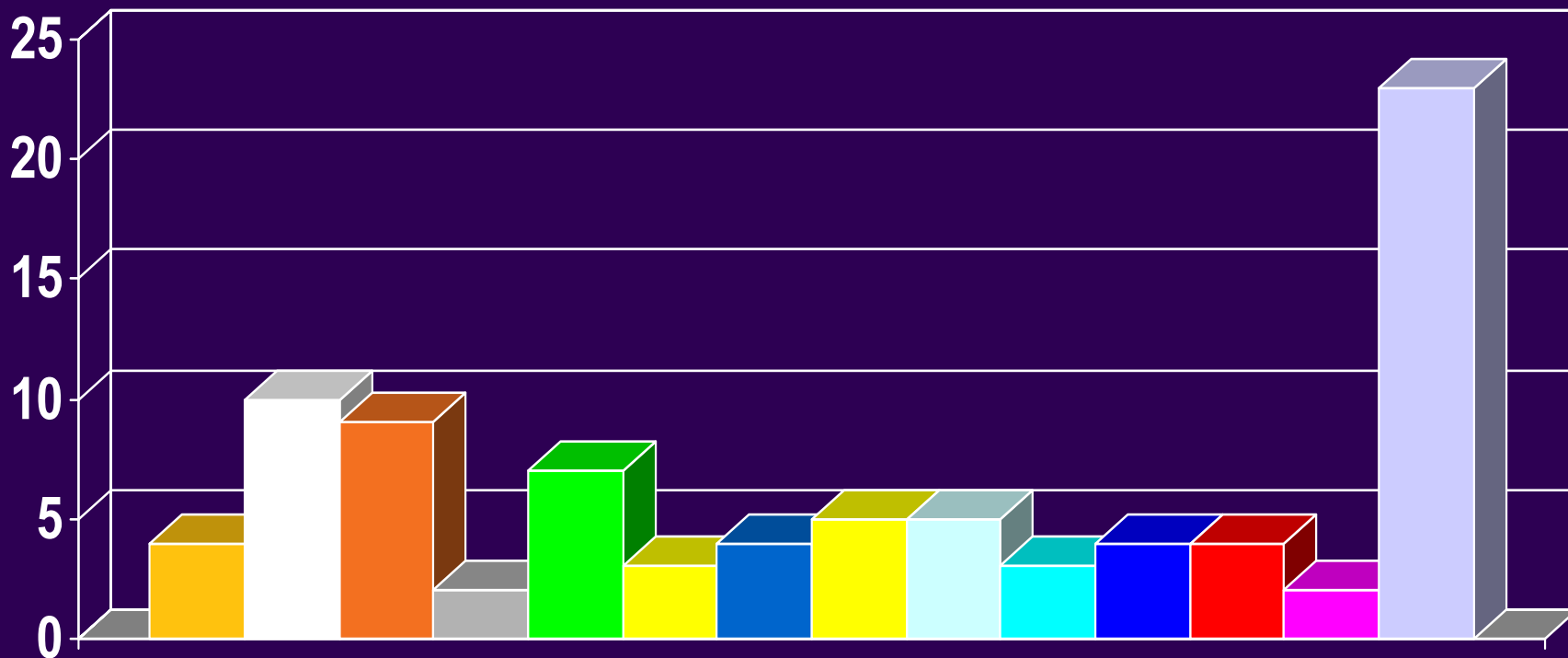
This entails sending CSF (all ages) or culture-negative empyema fluid from children aged 0-16 years with suspected pneumococcal infection to the HPA Meningococcal Reference Unit for testing using a multiplex PCR including the pneumolysin (ply) gene.

Pneumolysin PCR-positive CSFs and empyema fluid and DNA extracts from these samples are forwarded to RSIL at Cfl, Colindale, for serotype-specific antigen detection and reports issued to the originating laboratories, and incorporated within surveillance outputs.

Pleural/Empyema Fluids for type specific antigen detection Sept 2006 to Oct 2007: Age \leq 16 years, N = 77



CSFs for type specific antigen detection Sept 2006 to Oct 2007: All ages, N = 85



Type 1*

Type 3*

Type 14

Type 19A*

Type 6B

Type 23F

Type 9V

Type 18C

Type 7F*

Type 6A*

Type 8*

Type 4

Type 19F

Type ND

Assessment of Vaccine Impacts to date



Prof Goldblatt will be discussing overall effectiveness, vaccine schedules and vaccine failures later this morning.

Data on numbers of serotyped infections and serotype distribution calculated weekly and summary data presented on HPA website,

Also monitoring

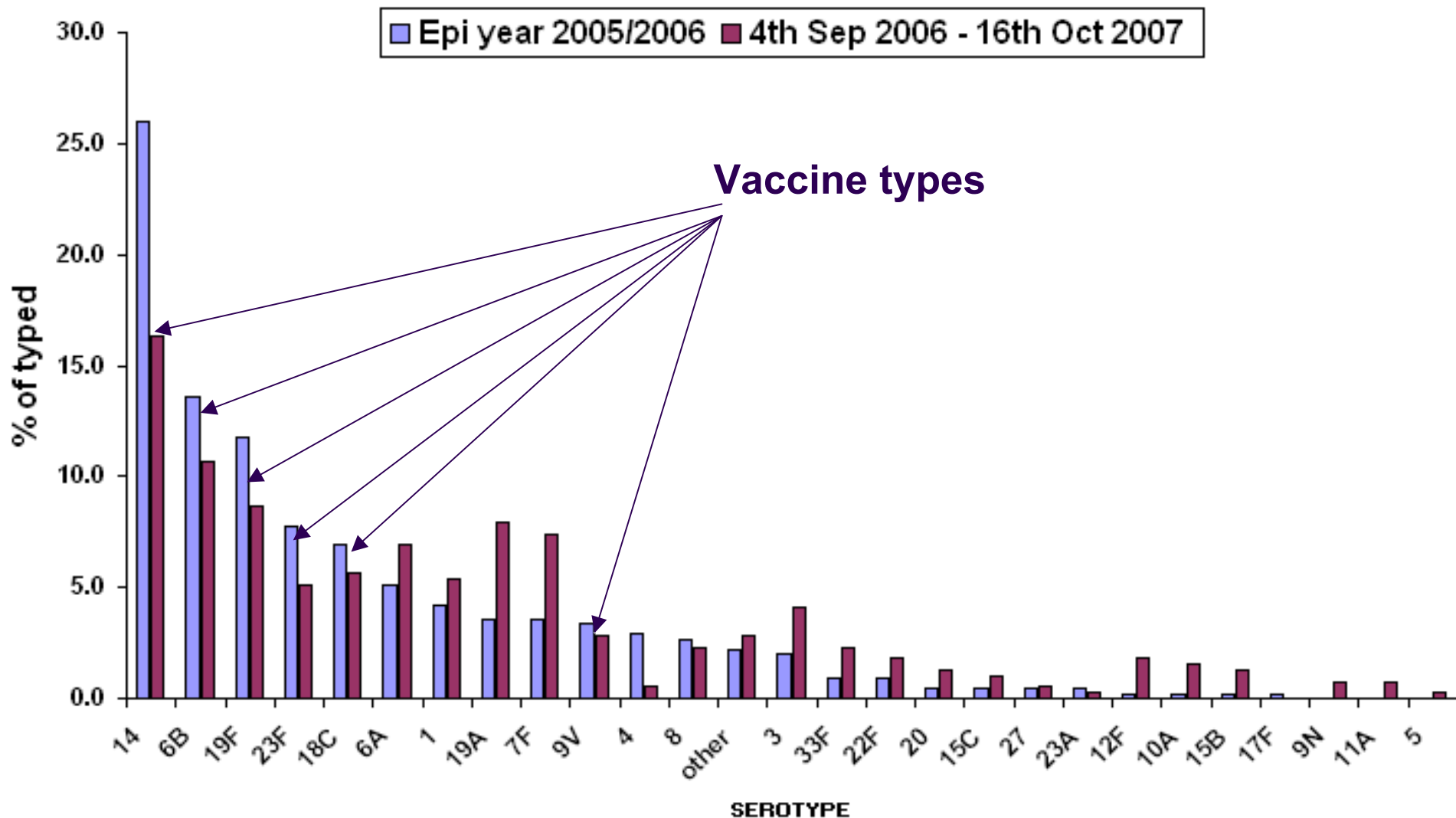
Potential replacement serotypes

Vaccine serotype disease in older non-vaccinated groups

Antimicrobial resistance

Impacts on genetic structure of pneumococcal population by MLST

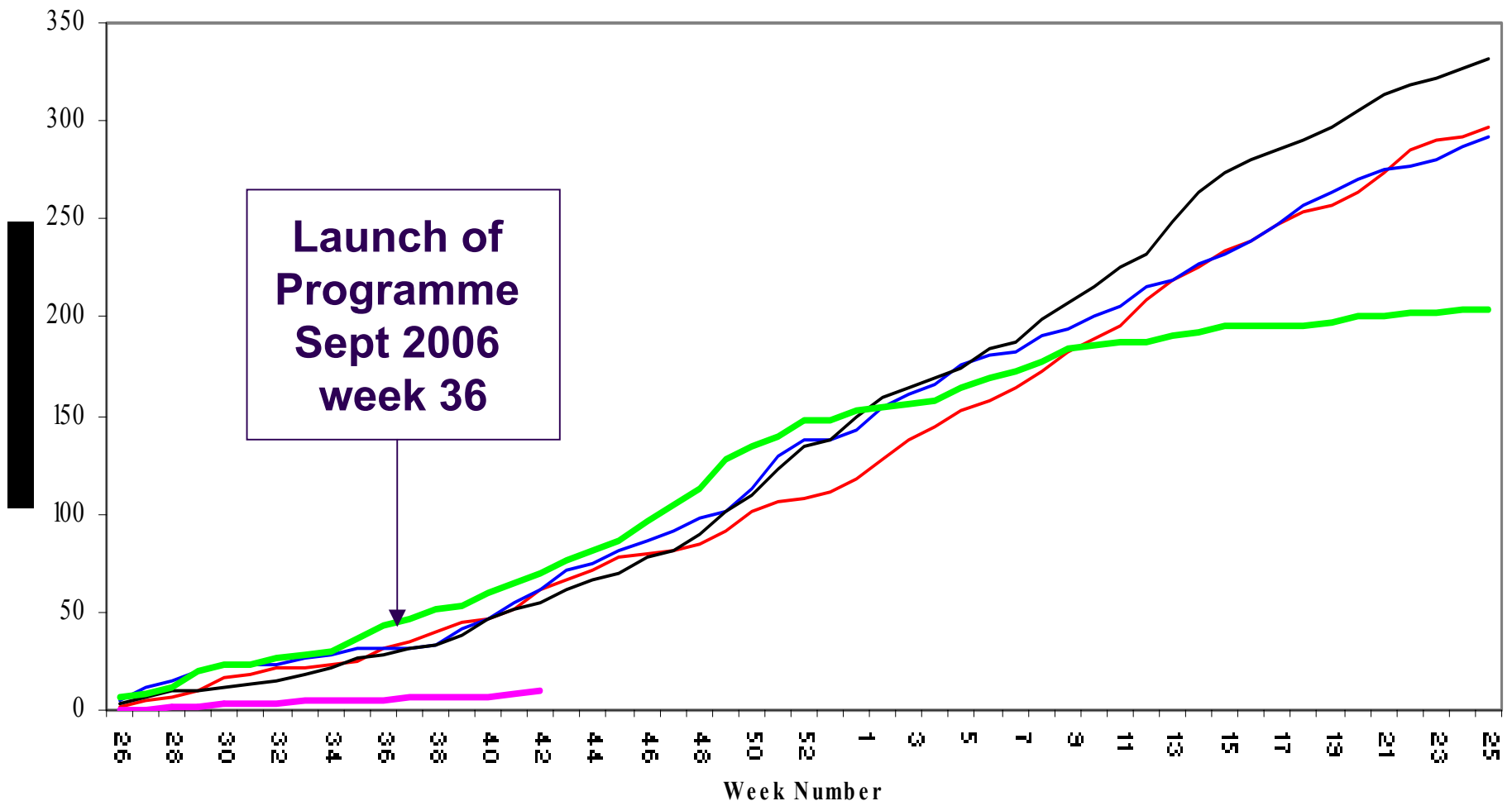
Serotype distribution for IPD cases in children < 2 years in 2005/6 vs surveillance cohort



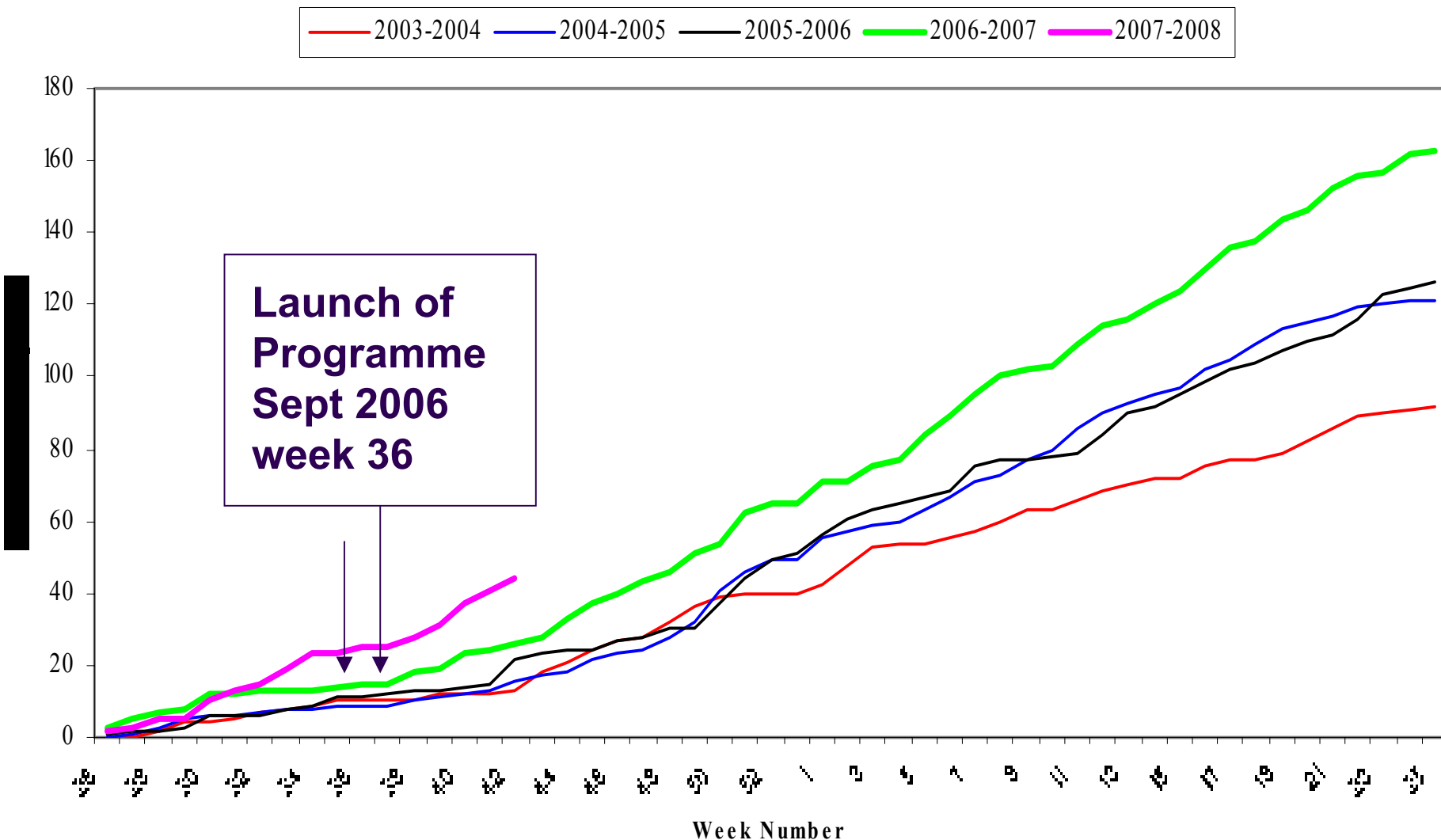
The impact on Invasive Pneumococcal Disease: Age 0-2 years serotypes in vaccine



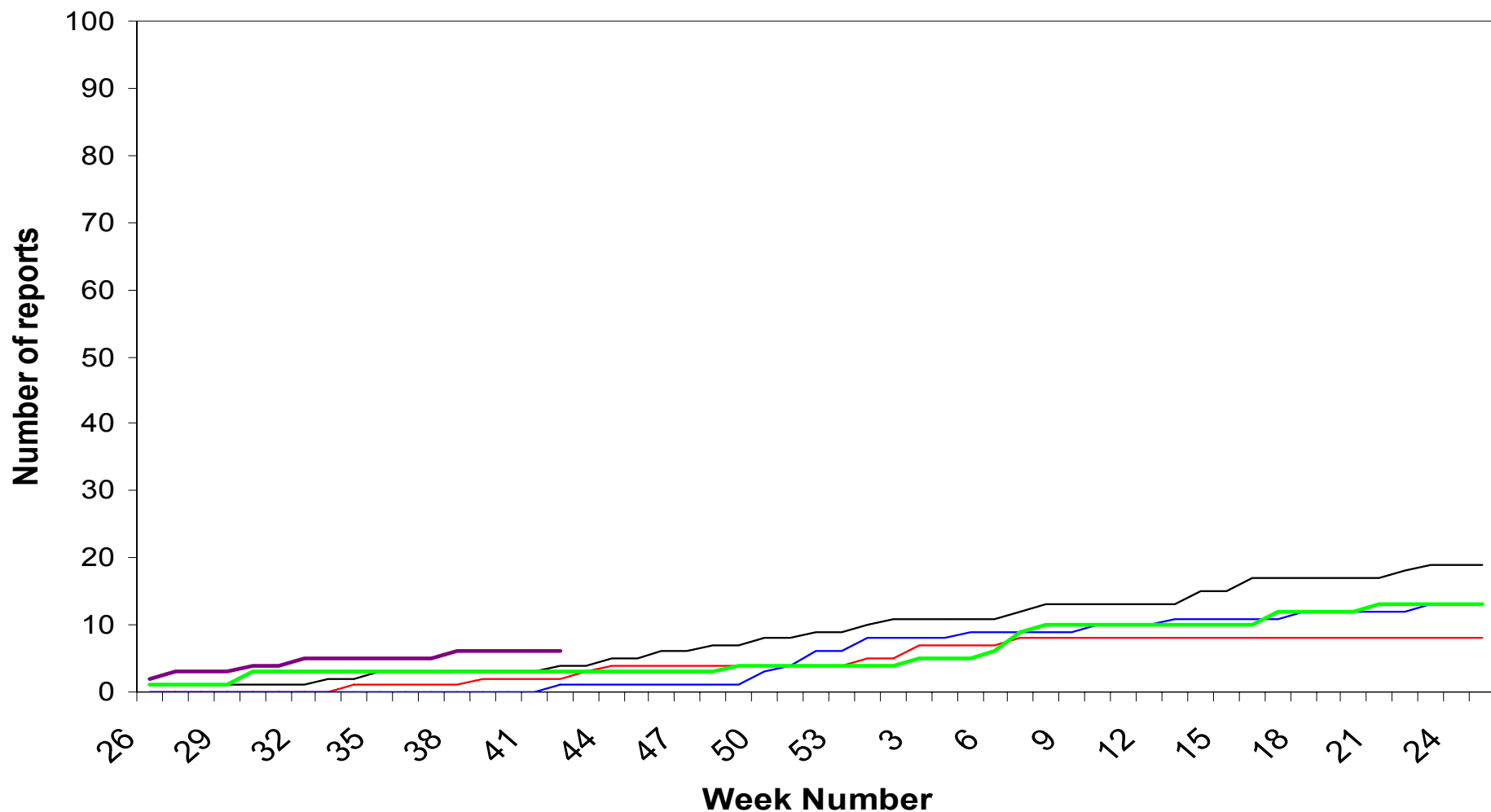
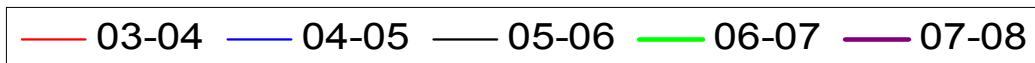
— 2003-2004 — 2004-2005 — 2005-2006 — 2006-2007 — 2007-2008



The impact on Invasive Pneumococcal Disease: Age 0-2 Years serotypes not in vaccine



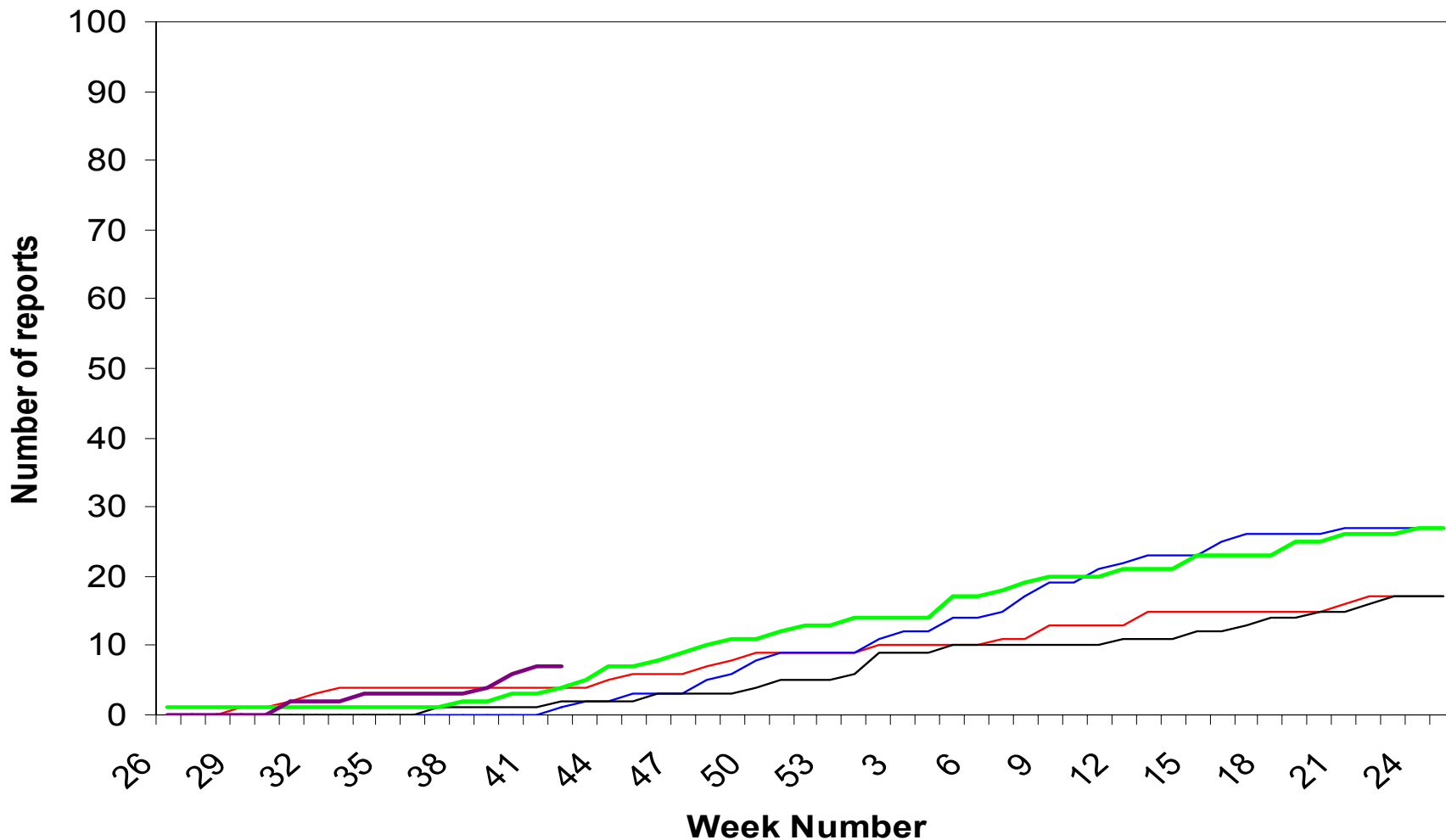
Serotype 1 IPD in vaccine eligible cohort



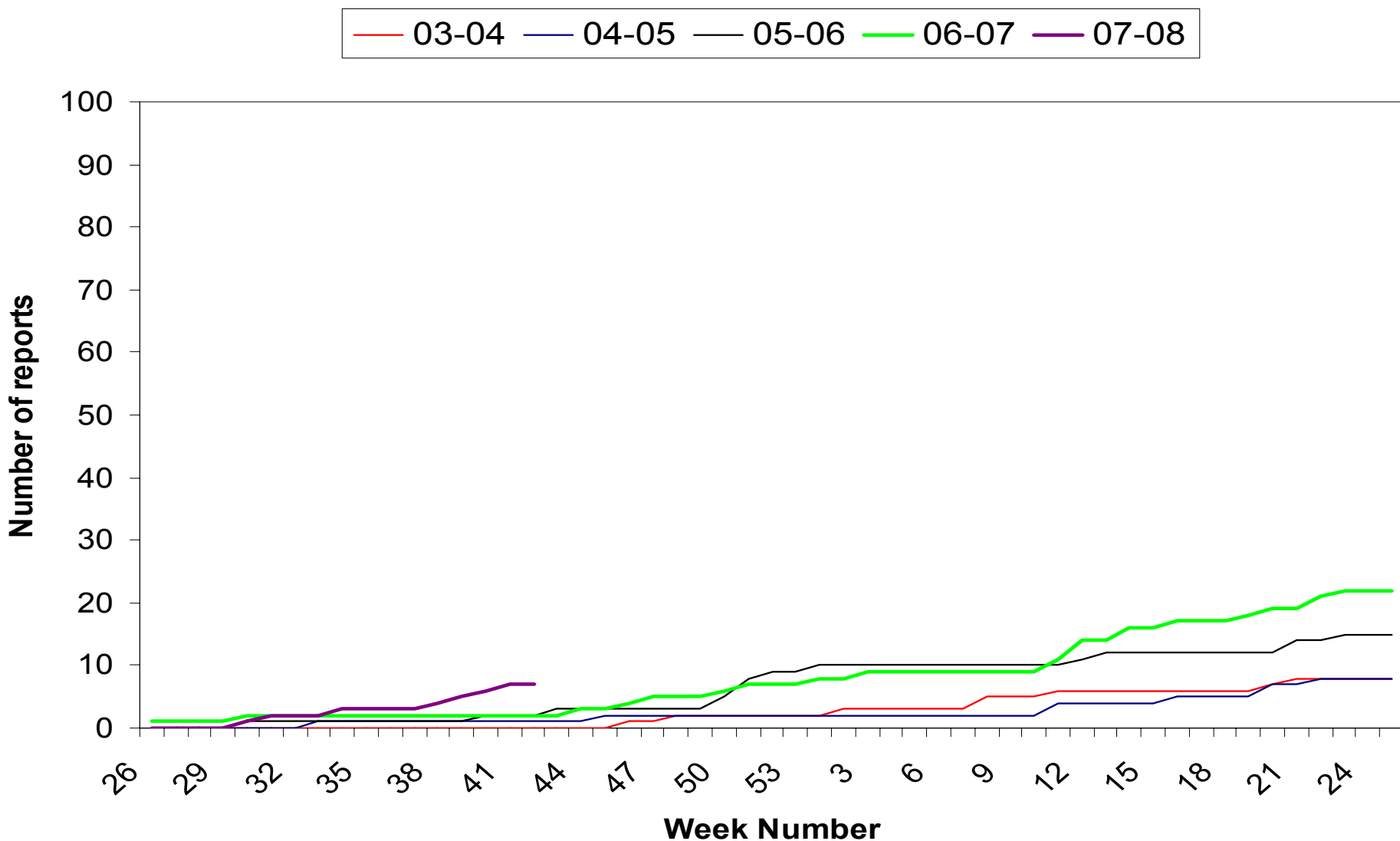
Serotype 19A IPD in vaccine eligible cohort



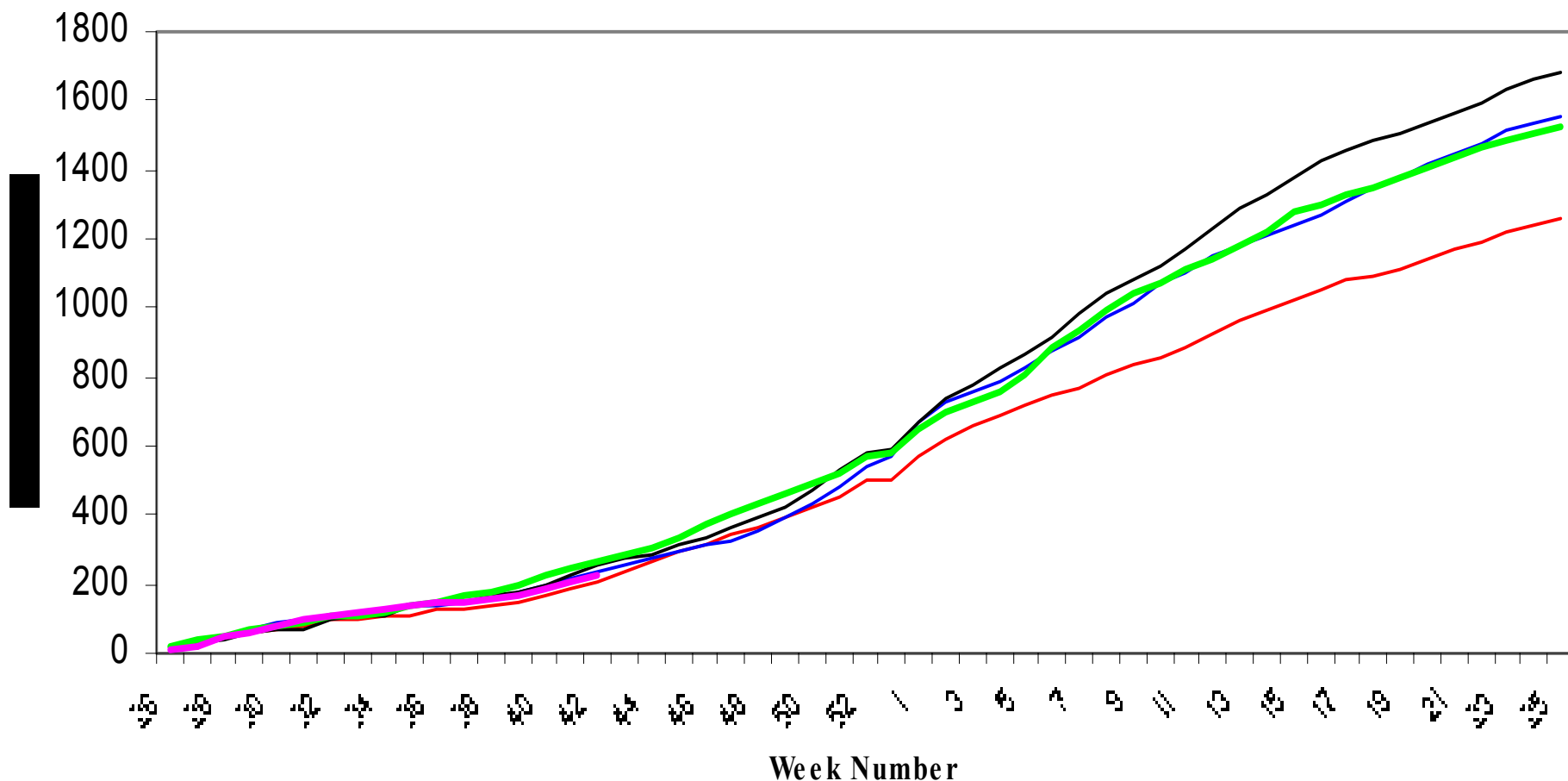
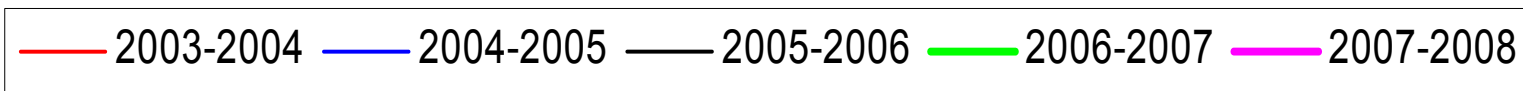
— 03-04 — 04-05 — 05-06 — 06-07 — 07-08



Serotype 7F IPD in vaccine eligible cohort



The impact on IPD: Age \geq 5 years Types IN Vaccine Herd Immunity? Not Yet



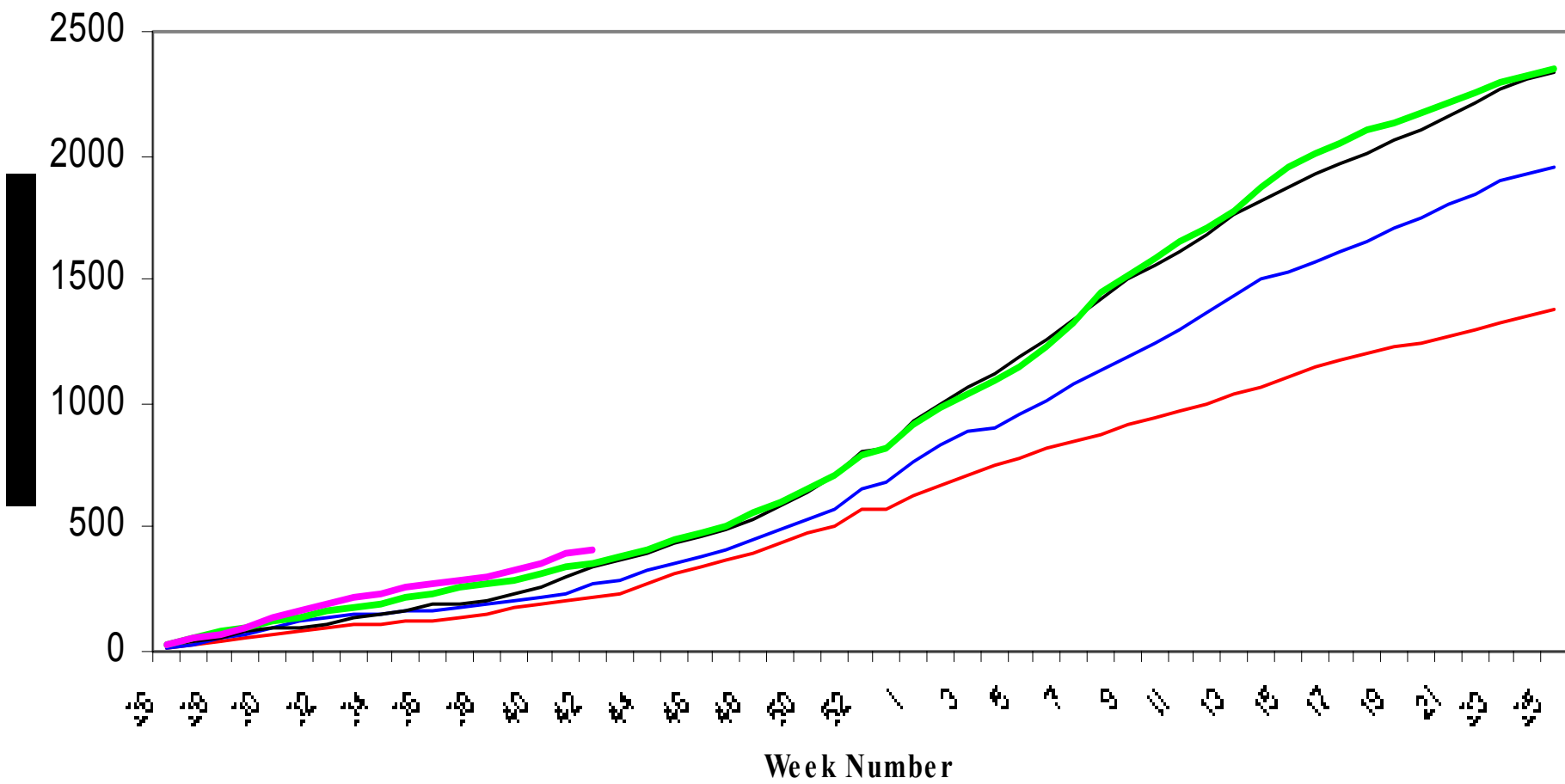
The impact on IPD: Age ≥ 5 years

NON vaccine types

Serotype Replacement ? Not Yet



— 2003-2004 — 2004-2005 — 2005-2006 — 2006-2007 — 2007-2008



Genetic characteristic of invasive pneumococci causing PCV failure in children between September 2006 and August 2007



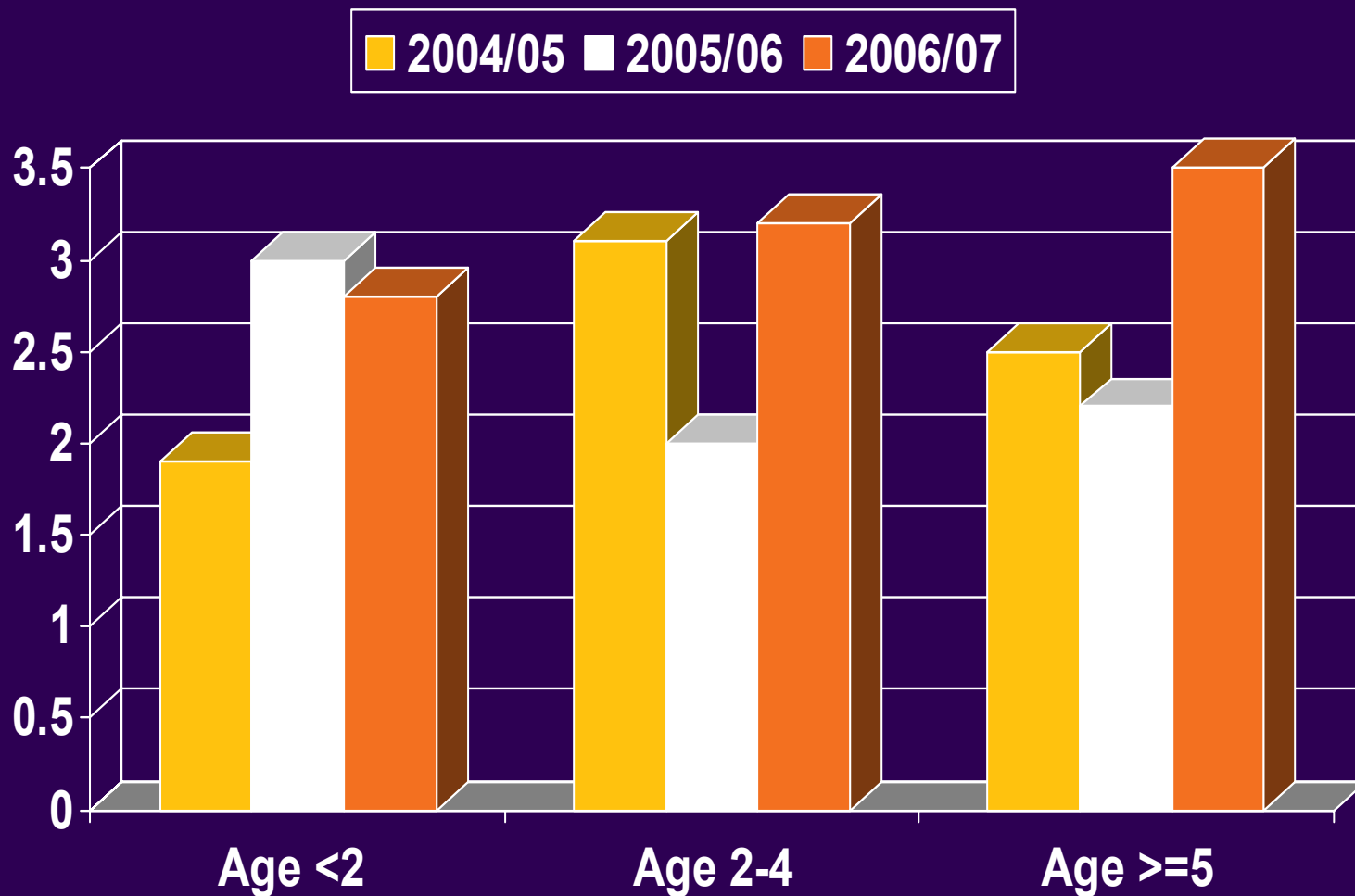
To date 13 of 18 strains associated with vaccine failure have been investigated by MLST (5 more in progress)

All show Sequence types typical for the serotypes involved

No evidence so far of vaccine failure being associated with particular Sequence types or capsule switching

Dr Bruno Pichon of Cfl has a poster at this meeting with much more information on this and genetic analysis of paediatric IPD isolates

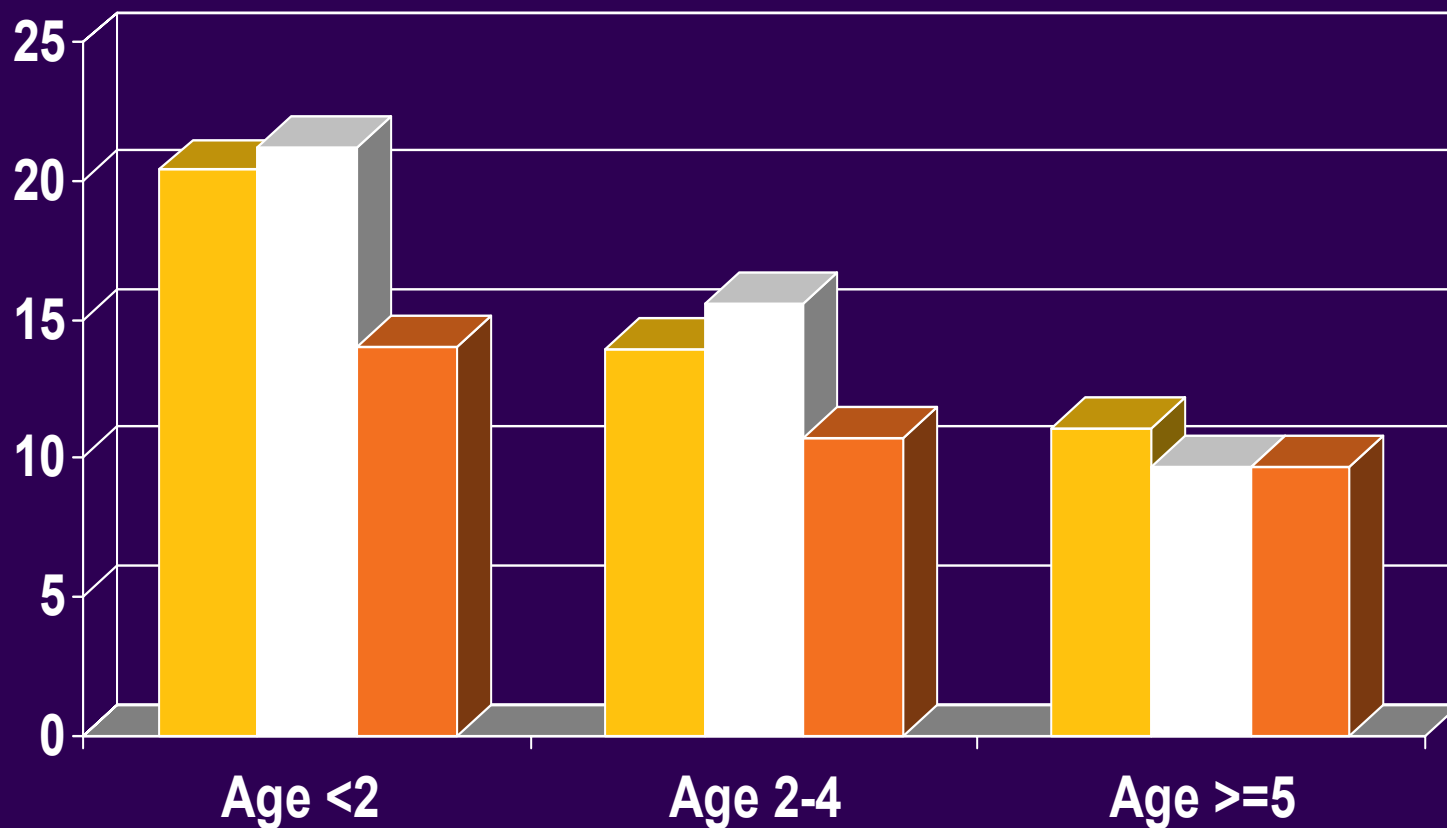
% Penicillin non-susceptible IPD Isolates Labbase Reports 1 Sept to 31st August each year



% Erythromycin resistance IPD Isolates Labbase Reports 1 Sept to 31 Aug each year N= 250 – 400 each year



■ 2004/05 ■ 2005/06 ■ 2006/07



CONCLUSIONS



- ❑ HPA Surveillance has provided evidence base for introduction of Prevenar™ to UK schedules
- ❑ Historical data on serotype distribution and IPD incidence in all age groups allows assessment of vaccine impact on both to be determined
- ❑ Ongoing surveillance will allow early detection of serotype shifts and thus identification of potential variations in effectiveness
- ❑ Ongoing molecular characterisation of IPD isolates will allow identification of capsule switching/genetic shifts
- ❑ There is no convincing evidence yet of either herd immunity or serotype replacement But.....↔ continuing surveillance
- ❑ Possible early decline in Erythromycin-resistant IPD in younger Children ↔ continuing surveillance

Acknowledgements



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