

Background

- The HPA Meningococcal Reference Unit (MRU) has been providing data on meningococcal disease for England and Wales since 1984
- The methods used to ascertain meningococcal disease, to characterise the organism, and to determine the incidence between 1995 – 2004 are described.
- Meningococcal serogroup C conjugate (MCC) vaccine was introduced into the UK population in November 1999

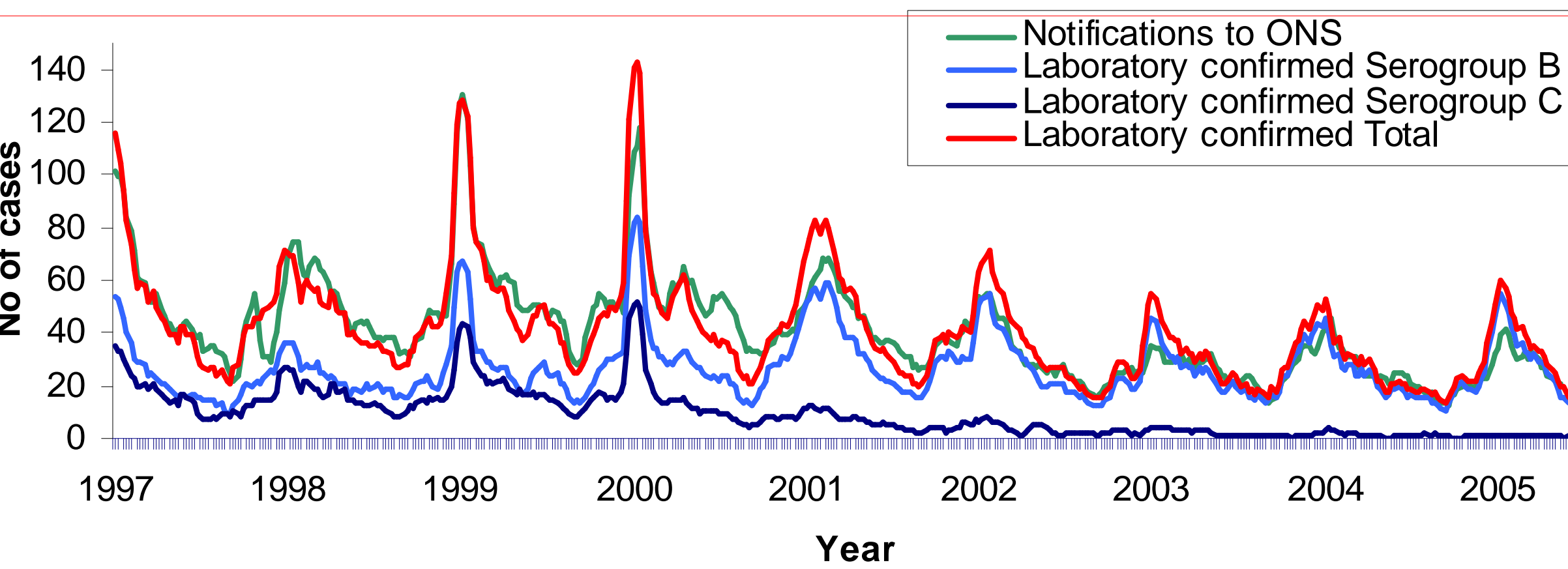
Methods

- Clinicians are required to notify all clinical cases of suspected meningococcal meningitis and septicaemia via the local Health Protection Units to the HPA Centre for Infections
- Since 1984, all microbiology laboratories have been encouraged to submit cultures of *N meningitidis* for characterisation to the MRU. Since October 1996, the MRU has provided a non-culture meningococcal PCR diagnostic service for England and Wales
- Isolates are characterised by serogroup, serotype and sero-subtype. MICs to therapeutic and prophylactic antibiotics (penicillin, cefotaxime, rifampicin and ciprofloxacin) are also determined.
- Non-culture confirmation is based on real-time Taqman® PCR assays; *ctrA* for detection, *siaD* for serogroup B, C, Y or W135 characterisation and *mynA* for serogroup A.
- Currently approximately 45% of cases are confirmed by PCR alone.

Results

Good case ascertainment of meningococcal disease is demonstrated in Figure 1 by the close correlation between the number of clinical notifications and of laboratory confirmed cases, particularly in more recent years.

Figure 1 - Laboratory Confirmed Cases of Meningococcal Disease in England & Wales Five Weekly Moving Averages: 1997 to 2005



The incidence and numbers of laboratory-confirmed cases increased between 1995 and 1999, followed by a decrease to 2004 (Figure 2). The increase was partly explained by better ascertainment resulting from the use of PCR. The decrease from 2000 is due to a major reduction in serogroup C cases resulting from MCC vaccination (Figure 3).

Figure 2 - Incidence and numbers of Laboratory confirmed cases of meningococcal disease in England and Wales 1995-2004

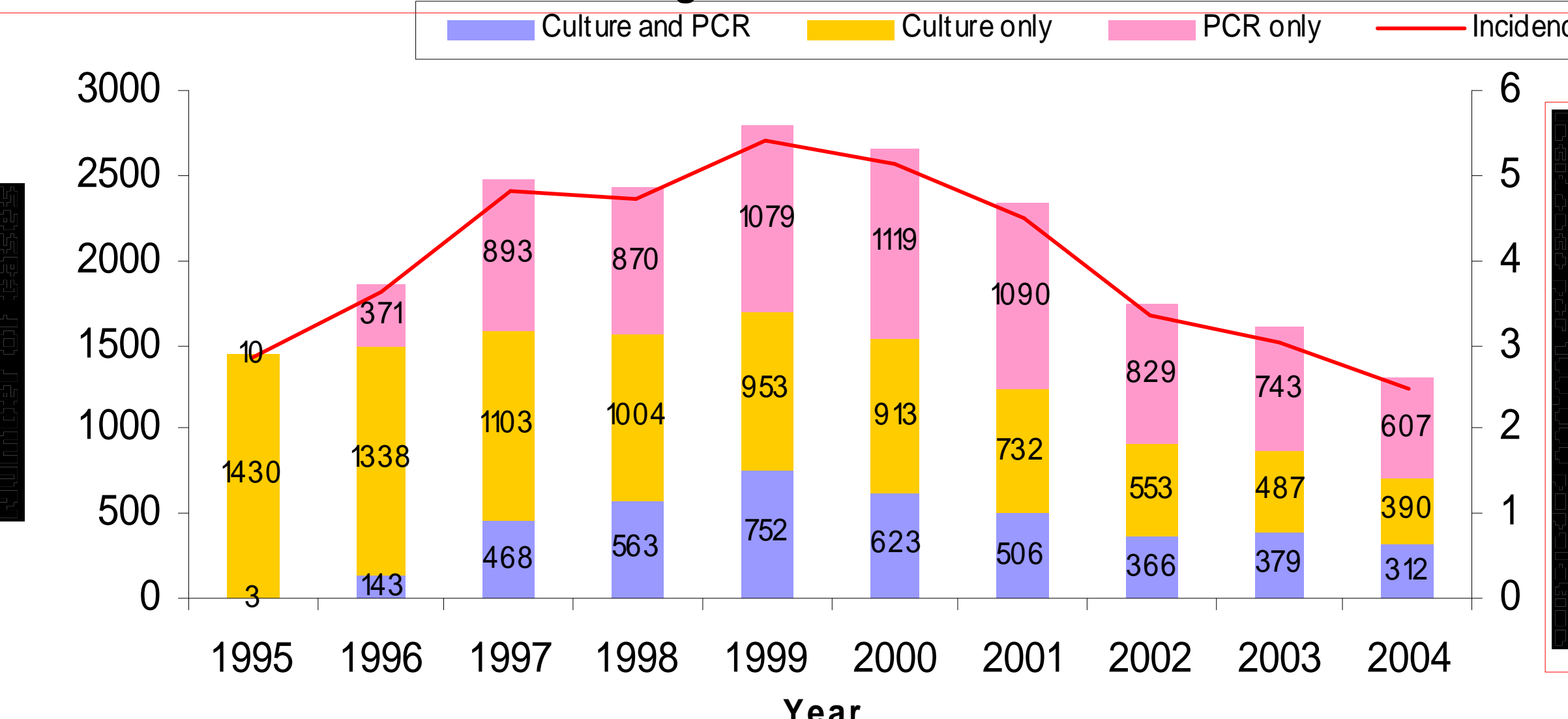
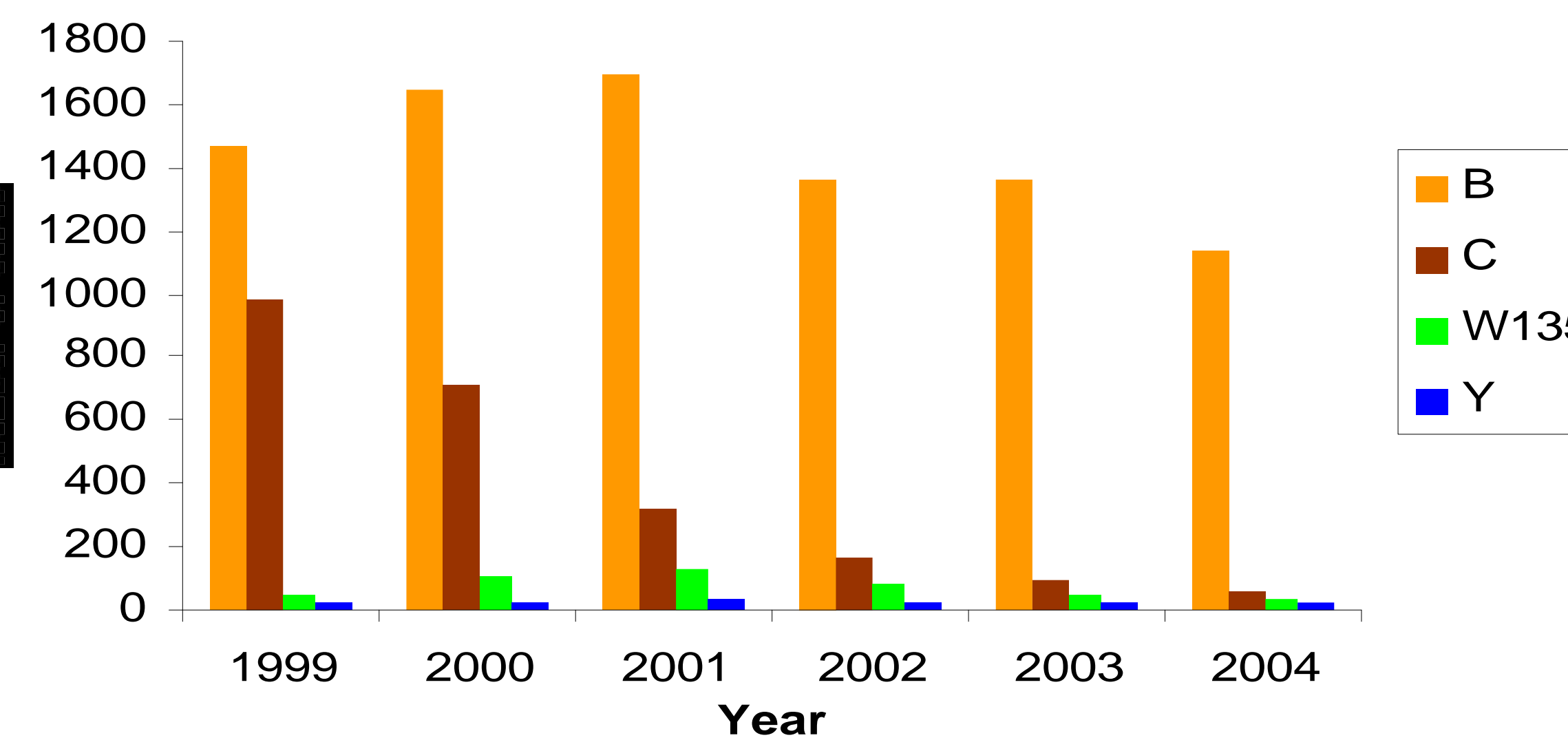
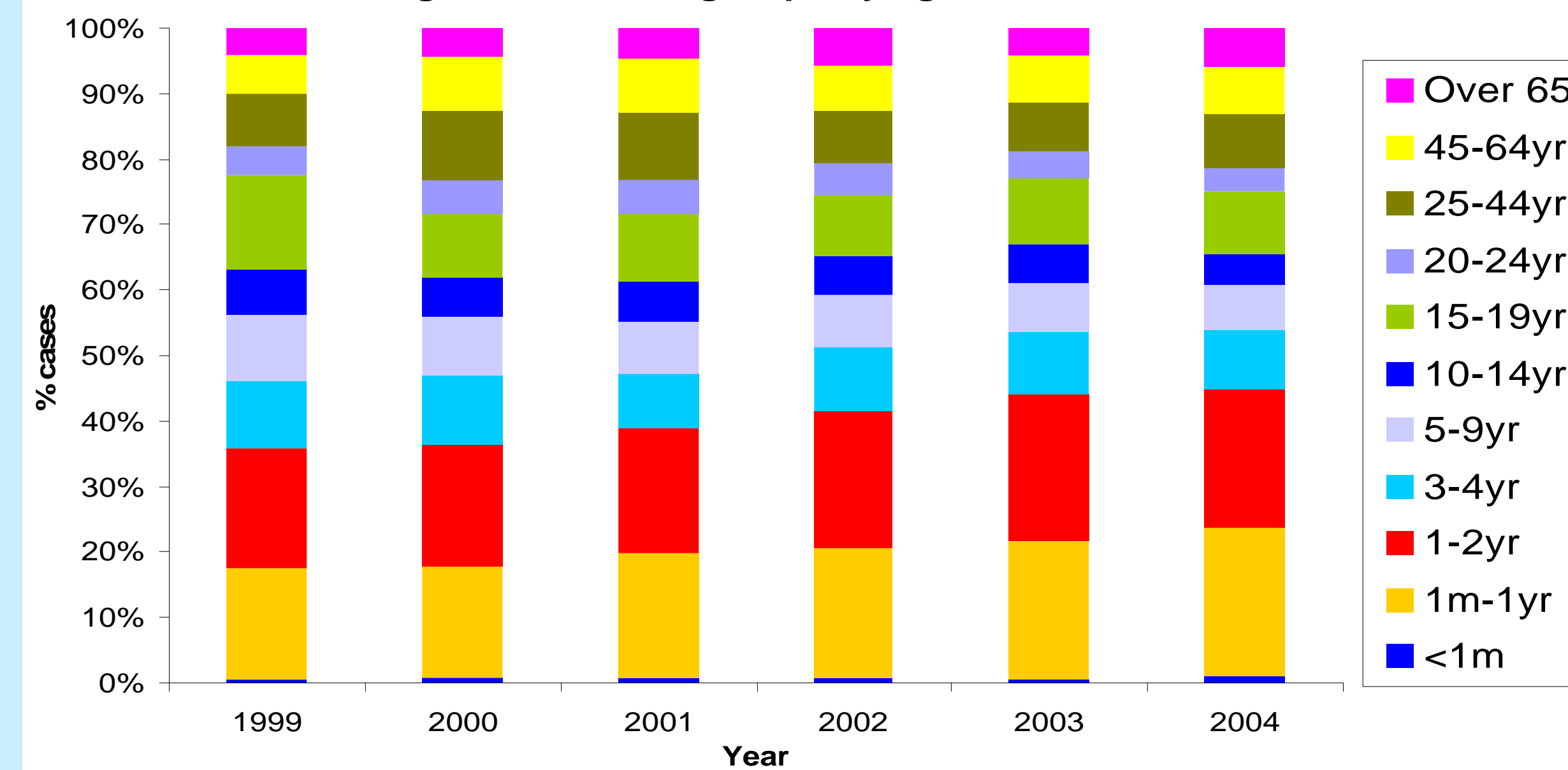


Figure 3 - Serogroups present in England and Wales 1995-2004



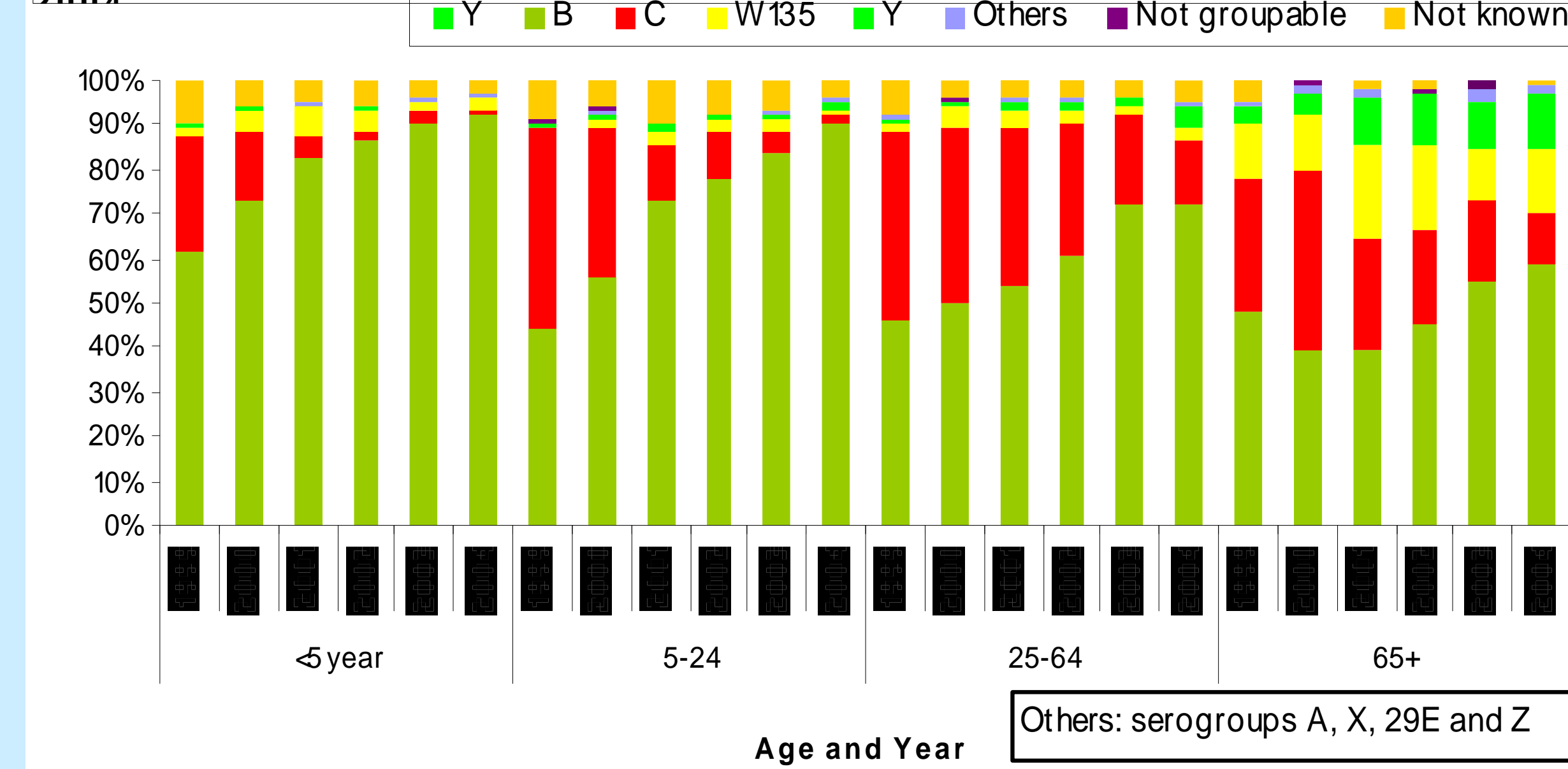
Overall, a large proportion of cases are observed in pre-school children aged under five years (Figure 4). Since 1999, this proportion has increased as the numbers of cases in older individuals has declined, mainly due to the decline in serogroup C disease (Figure 3).

Figure 4 - All serogroups by age band 1999-2004



Serogroup distribution is also related to age (Figure 5), with non-serogroup B infections forming a larger proportion of cases in older age groups. The major reduction in proportion of serogroup C cases after 1999 can be seen across all age groups, but particularly in those under 25.

Figure 5 - Proportion of serogroups for different ages in England and Wales 1999-2004

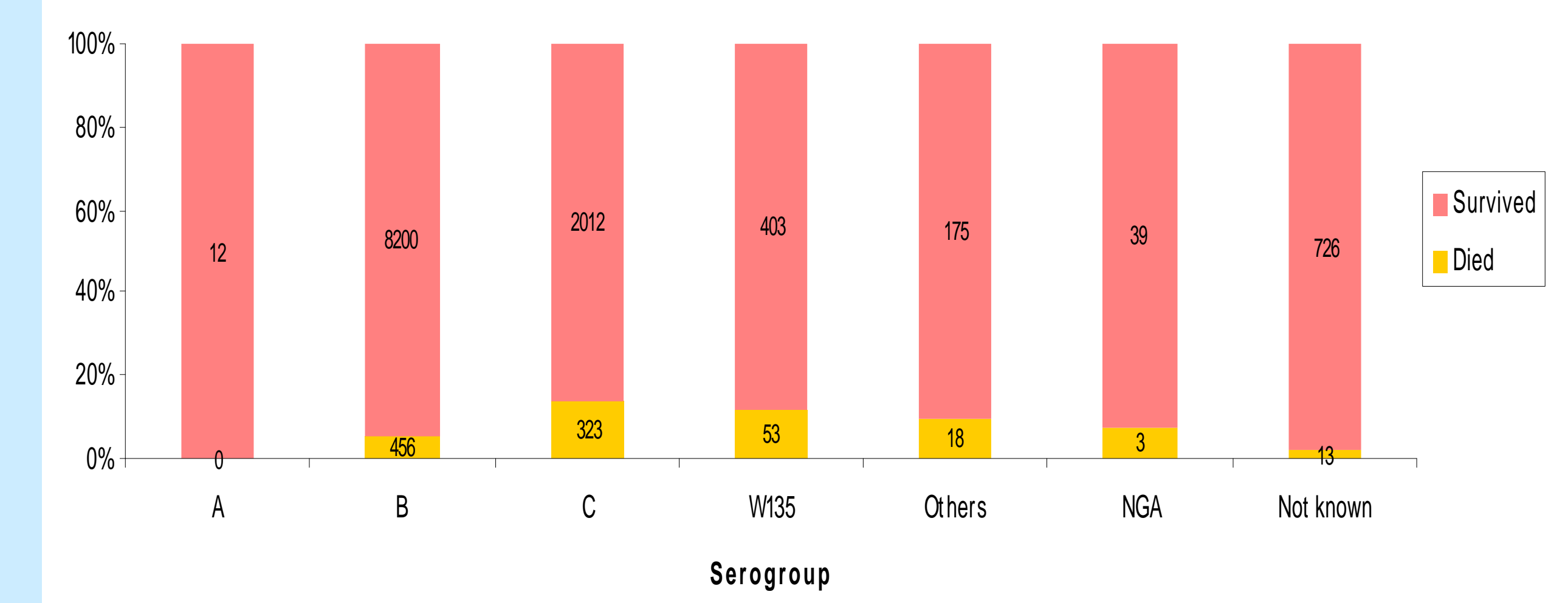


Figures 6a and 6b show the relationship between disease outcome and clonal complex (CC) and serogroup respectively.

Figure 6a - Association between disease outcome and clonal complex



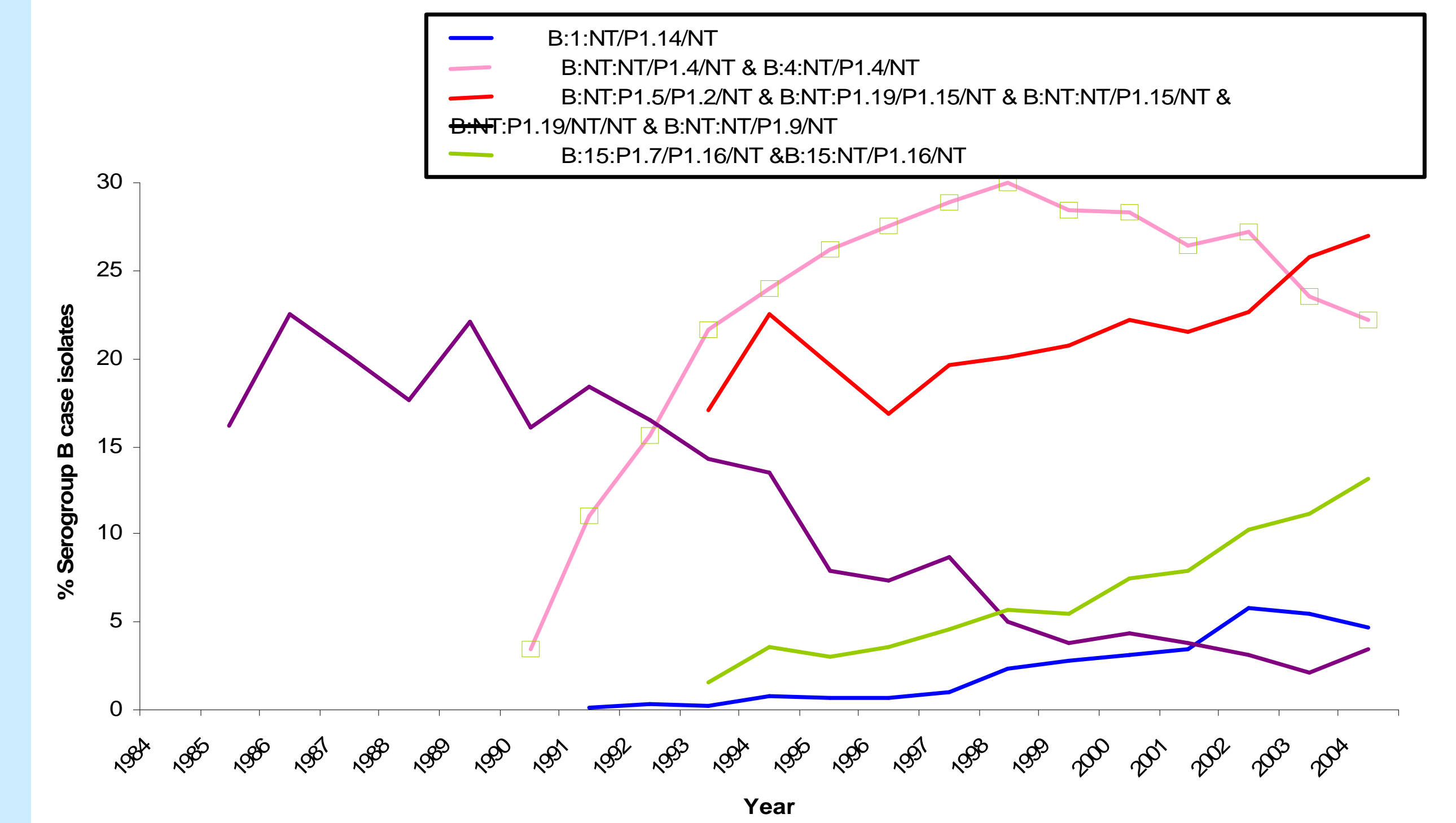
Figure 6b - Association between disease outcome and serogroup



Serogroups C and W135 are most likely to result in adverse outcome with case fatality rates of 13.8% and 11.7% respectively. This is probably due to the association of 'hypervirulent' CC ST-11 (ET37) with these serogroups in recent years.

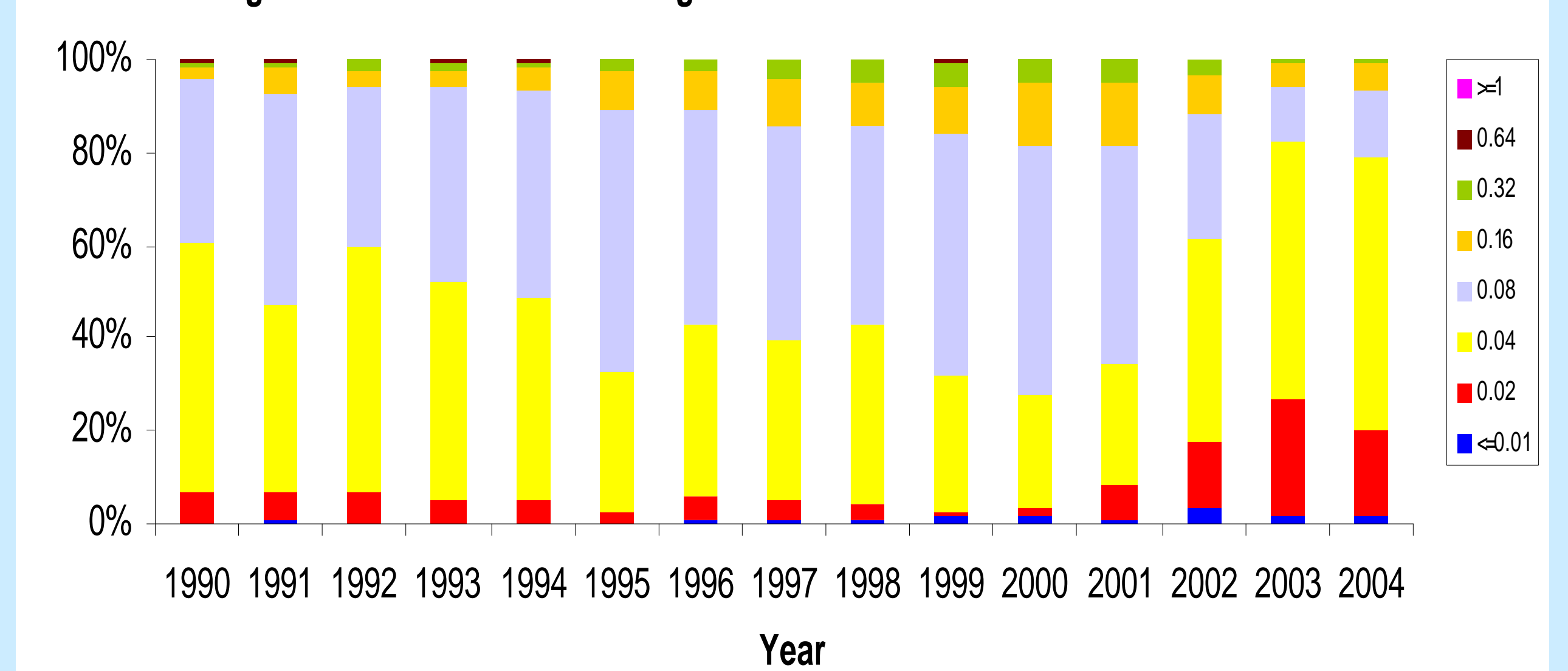
The predominant serogroup B phenotypes (Figure 7) varied over the years. Some strains such as B:15:P1.7 and B:15:P1.7,16 (representing CC ST-32), and B:4:P1.4 and B:4:NT, (representing CC ST-41/44) have declined naturally, while others such as B:NT:P1.9, B:NT:P1.19, B:NT:P1.15,19, B:NT:P1.15, B:NT:P1.5,2 (representing CC ST-269) have increased. Specifically, B:NT:P1.9 rose from 1.5% (1993) to 13.2% (2004). B:1:P1.14 isolates (representing CC ST-213) have also shown a steady increase from <0.5% (1992) to 5% (2004).

Figure 7 - Trends in predominant serogroup B case isolates 1985-2004



The proportion of isolates with a penicillin minimum inhibitory concentration (MIC) of or below 0.08µg/ml varied between 82% - 95% in the years 1990 and 2004.

Figure 8 - Penicillin MICs of England and Wales case isolates 1984-2004



Conclusions

- There has been major reduction of serogroup C disease following the introduction of MCC vaccine and there is evidence of herd immunity
- Serogroup B disease is now responsible for >85% of laboratory confirmed cases
- The increase in serogroup B observed up to 1999 has now reversed and cases fell by 35% between 2001 and 2004
- There is natural phenotypic and genotypic variation amongst all serogroups but particularly serogroup B