Epidemiology and surveillance of meningococcal disease in England.

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Background

- The Public Health England (PHE) Meningococcal Reference Unit (MRU) has been providing data on invasive meningococcal disease for England since 1984.
- In November 1999 Meningococcal serogroup C conjugate (MCC) vaccine was introduced into the UK as part of the routine infant schedule and as a catch-up campaign for children under 18 years.
- From September 2013 MCC vaccine was offered to teenagers and university freshers. In August 2015 this was replaced by an ACWY conjugate vaccine programme with a catch-up component.
- From 1st September 2015, Bexsero® was introduced into the UK infant immunisation schedule primarily to prevent group B infection: for infants born after 1st May 2015. MCC infant vaccination stopped in July 2016 with a dose of MCC/Hib continuing to be offered at 12 months of age.

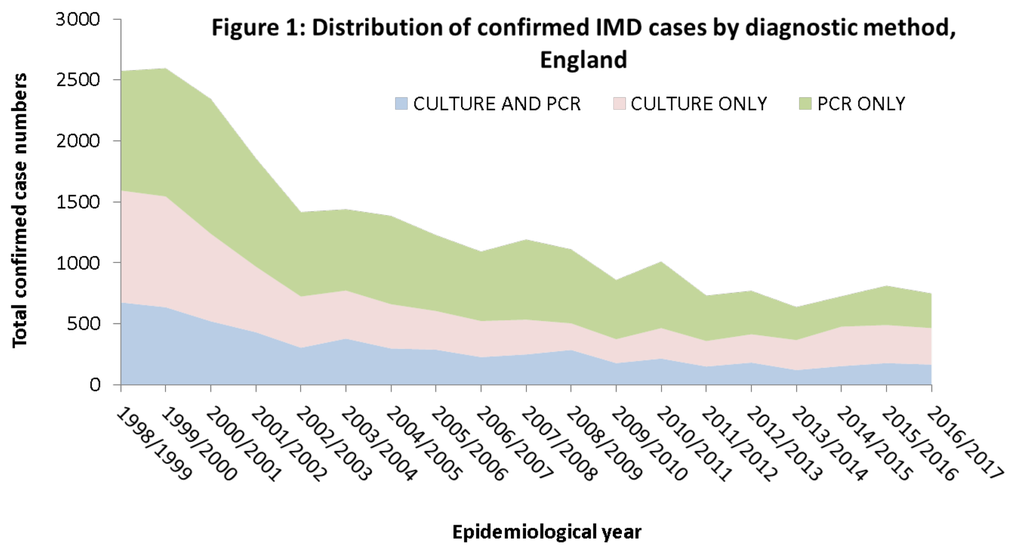
Methods

- Clinicians are required to notify all clinical cases of suspected invasive meningococcal disease via the local PHE Health Protection Teams to the PHE National Infection Service, Colindale, London.
- Since 1984, all microbiology laboratories in England have been encouraged to submit cultures of *Neisseria meningitidis* for characterisation to the MRU. Since October 1996, the MRU has provided a non-culture meningococcal PCR diagnostic service for England.
- Isolates are characterised by serogroup, serotype, and sero-subtype. MICs to 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 W characterisation and *mynB* for serogroup A. Routine characterisation of non-culture positives by *porA* and *fhbp* sequencing commenced in January 2012.
- Commencing epidemiological year 2010/11 all case isolates have been submitted for whole genome sequencing (WGS) as part of the Meningococcal Genome Library (MGL); 2010/11 to 2012/13 funded by The Meningitis Research Foundation (**http://www.meningitis.org/current-projects/genome**) in collaboration with PHE, University of Oxford and the Wellcome Trust Sanger Institute. From 2013/14 onwards WGS characterisation has been a collaboration between PHE and University of Oxford.

Results

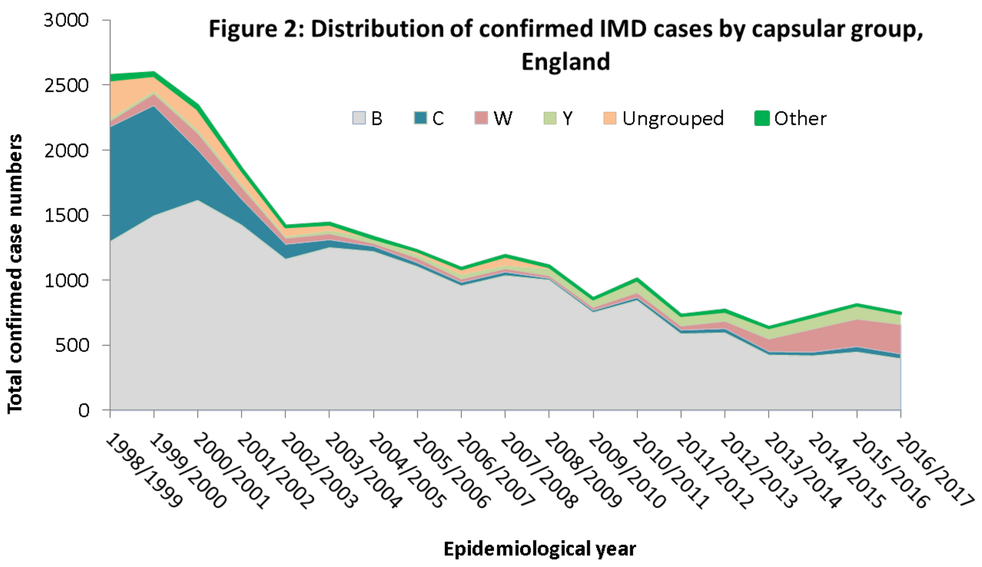
The incidence of laboratory-confirmed cases of all meningococcal disease peaked in 1999/00 and then decreased overall. Laboratory confirmed cases fell from 2,595 (in 1999/00) to a low of 636 in 2013/14; there were 747 cases in 2016/17 (Figure 1).

Figure 1: Distribution of confirmed IMD cases by diagnostic method, England



High levels of IMD in 1998/99 and 1999/00 were partly explained by better ascertainment resulting from the use of PCR (Figure 1). During 2016/17 38% (283) cases were confirmed by PCR only; this proportion has fallen in recent years from ~50% up to 2011/12. The decrease in total cases from 1999/00 has, in part, been due to the major reduction in Group C cases resulting from both direct and indirect (herd) protection from MCC vaccination (Figure 2). Since 2005/06, there have only been 13 - 33 serogroup C cases each epidemiological year in England. In 2015/16 however, this increased to the highest total in 12 years with 42 cases confirmed and there were 37 in 2016/17.

Figure 2: Distribution of confirmed IMD cases by capsular group, England



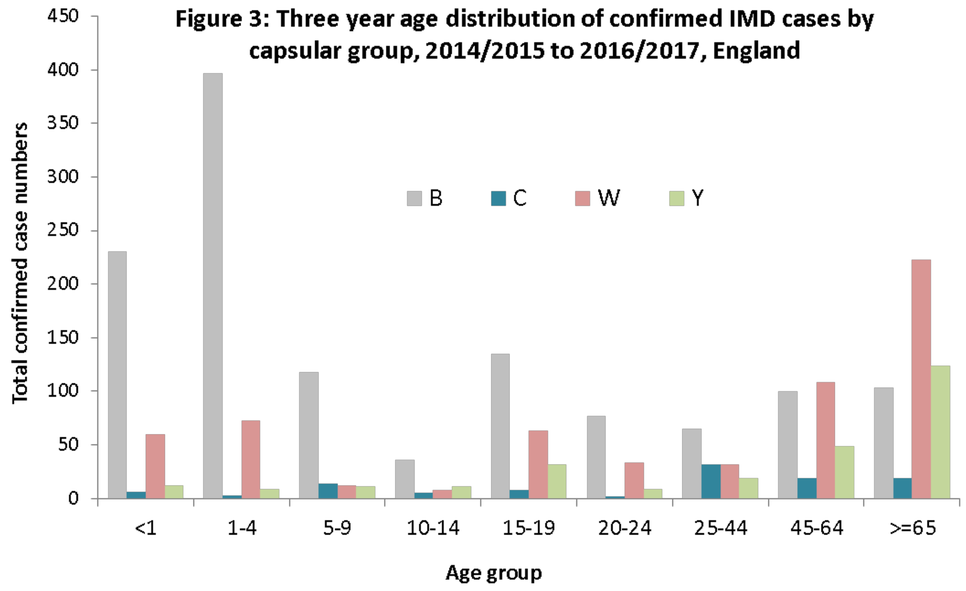
There has been an overall decrease in Group B cases in recent years from 1,614 (2000/01) to 447 (2015/16) and then to 396 cases in 2016/17 (Figure 2).

In 2016/17 Group B accounted for 53% of all confirmed cases with only 5% confirmed as Group C.

Group Y accounted for 11% (80 cases) in 2016/17: the proportion has remained similar in recent years even though the numbers of cases has varied slightly. The Group Y increase has been mainly due to a rise in cases confirmed in adults aged ≥45 (Figure 3).

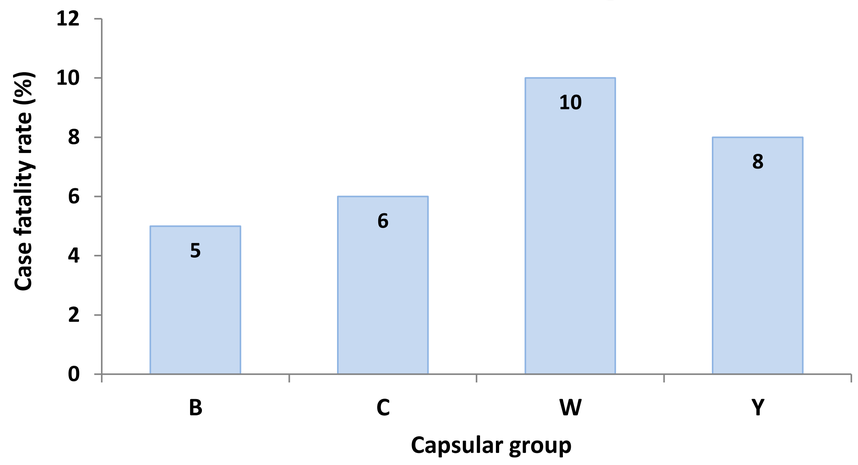
An increase was observed in Group W cases (often with severe disease and unusual presentation) from 95 cases in 2013/14, 176 cases in 2014/15 to 225 cases in 2016/17. In 2016/17 Group W represented 30% of all IMD, a substantial increase from 2% (19 cases) in 2008/09. The increase was almost entirely due to phenotype W:2a:P1.5,2 from 0 in 2008/09 to 133 case isolates in 2016/17; with W:2a accounting for 187 case isolates in 2016/17. WGS analysis implicated a single lineage[1]: 95% (190/200) of the UK group W case isolates in the MGL for 2015/16 were confirmed as cc11. Group W:cc11 cases were observed nationwide and across all ages (Figure 3), leading to the introduction of an ACWY conjugate vaccine programme for UK teenagers and university freshers commencing August 2015 as an emergency response measure.

Figure 3: Three year age distribution of confirmed IMD cases by capsular group, 2014/2015 to 2016/2017, England



A large proportion of the total IMD cases are observed in pre-school children aged under five years (Figure 3) accounting for 35% of all cases in 2014/15 to 2016/17, predominantly due to Group B. The proportion of cases in pre-school children has, however, steadily declined from 56% in 2006/07 to 29% in 2016/17 with a proportionate increase in the 45+ years age groups from 12% to 36% in the same period. These changes have been driven by continued decline in Group B disease with a concomitant increase in Groups Y and W. Distribution by capsular group is therefore also related to age, with non-group B infections forming a larger proportion of cases in older age groups. It is observed that fewer PCR investigations and therefore confirmations are made for elderly patients.

Figure 4: Case Fatality Rates (%) by capsular group based on confirmed cases of IMD and ONS certified deaths between 2014/2015 to 2016/2017, England



Group B cases continue to be associated with a relatively low case fatality rate (CFR) of 5%, based on the Office of National Statistics (ONS) recorded deaths and linked ONS/ MRU data over the last 3 years (Figure 4, *provisional data).* During this period group W accounted for 63 ONS deaths followed by Group B (59 deaths), group Y (23 deaths) and group C (7 deaths).

Discussion and Conclusions

- **Group B cases have fallen steadily since 2000/01 to a low of 396 (53%) of all cases in 2016/17; following the introduction of 4CMenB (Bexsero®) to UK infants post 1st September 2015 in addition to possible effects of the England public area indoor smoking ban introduced from 1st July 2007.**
- **The profile of IMD changed since MCC vaccine introduction. Group C disease has demonstrated historically low levels from 2008/09 with only 13 confirmed cases and with ~30 cases confirmed in each of the last 10 years but increased to 42 in 2015/16 and 37 in 2016/17.**
- **Given the waning effectiveness of MCC identified following a primary infant course and after a booster in the second year of life, a booster dose for teenagers was introduced in the academic year 2013/14 now superseded by the ACWY programme, to sustain the impact due to direct and indirect protection afforded by the MCC vaccine.**
- **In the light of the rapidly increasing Group W (cc11) disease from 2009/10 to 2014/15, ACWY conjugate vaccine was introduced from August 2015 (replacing the MCC booster) to protect teenagers and university freshers and is intended to induce herd protection.**
- **The age profile of cases of meningococcal disease has also altered, most recently with an increased proportion of cases in those aged 15 years and older. This is subsequent to increases observed in Group W and Y cases, together with the decrease in group B disease.**
- **Enhanced surveillance to carefully monitor any changes in IMD epidemiology (in vaccinated and unvaccinated age groups) following the introduction of Bexsero® and the MenACWY vaccine programme for teenagers in England is essential and ongoing.**

Reference

[1] Lucidarme *et al.*, 2015. J. Infect. 71 (5) Nov 2015; 544-552.