Epidemiology and surveillance of meningococcal disease in England.

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Public Health England

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Background

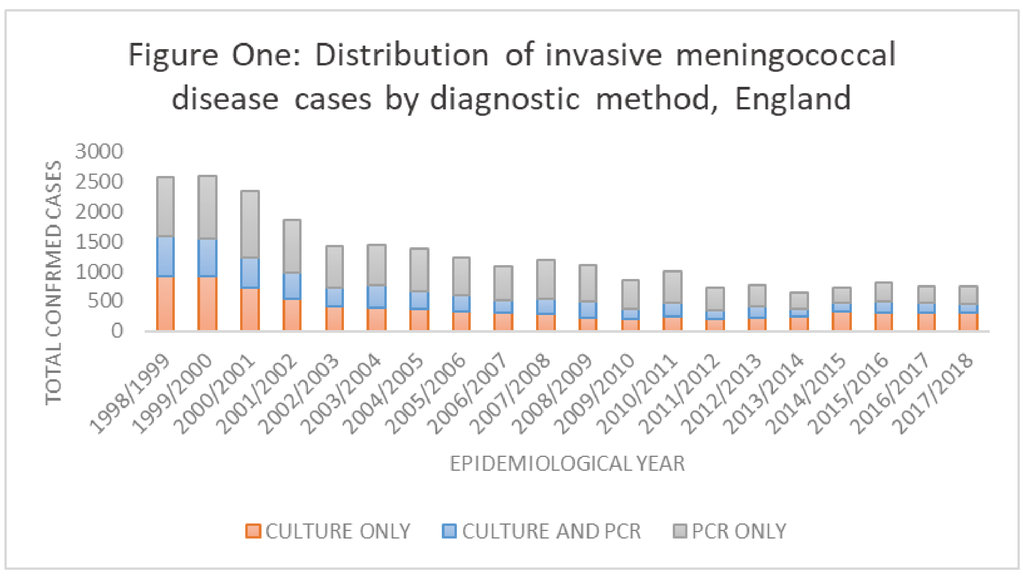
- The Public Health England (PHE) Meningococcal Reference Unit (MRU) has been providing data on invasive meningococcal disease for England since 1984.
- In November 1999 Meningococcal serogroup C conjugate (MCC) vaccine was introduced into the UK as part of the routine infant schedule and as a catch-up campaign for children under 18 years.
- England introduced a public area indoor smoking ban from 1st July 2007
- 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after a booster in the second year of life, a booster dose for teenagers was introduced in the academic year 2013/14 superseded by the ACWY programme, to sustain the impact of direct and indirect protection of the MCC vaccine.
- From 1st September 2015, 4CMenB (Bexsero®) was introduced into the UK immunisation schedule to prevent group B infection: for infants born after 1st May 2015[1]. MCC infant vaccination stopped in July 2016 with a dose of MCC/Hib continuing to be offered at 12 months.
- The age profile of cases of meningococcal disease also altered to the end of 2017/18, with an increased proportion of cases in those aged 45 years and older. This is subsequent to increases observed in Group W and Y cases, together with the decrease in group B disease.
- Commencing epidemiological year 2010/11 all case isolates have been submitted for whole genome sequencing (WGS) as part of the Meningitis Research Foundation (MRF) Meningococcus Genome Library (MGL); 2010/11 to 2012/13 funded by the MRF (**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.

Methods

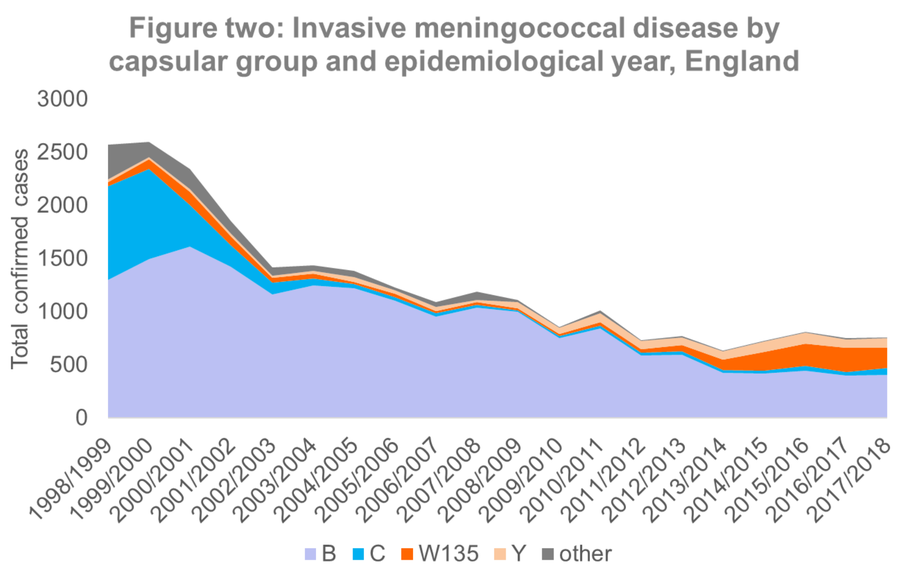
- Clinicians are required to notify all clinical cases of suspected invasive meningococcal disease via the local PHE Health Protection Teams to the PHE National Infection Service, Colindale, London.
- Since 1984, all microbiology laboratories in England have been encouraged to submit cultures of *Neisseria meningitidis* for characterisation to the MRU. Since October 1996, the MRU has provided a non-culture meningococcal PCR diagnostic service for England.
- 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.

Results

The incidence of laboratory-confirmed cases of all meningococcal disease peaked in1999/00 and then decreased overall. Laboratory confirmed cases fell from 2,595 (in 1999/00) to a low of 636 in 2013/14; there were 755 cases in 2017/18 (Figure one).



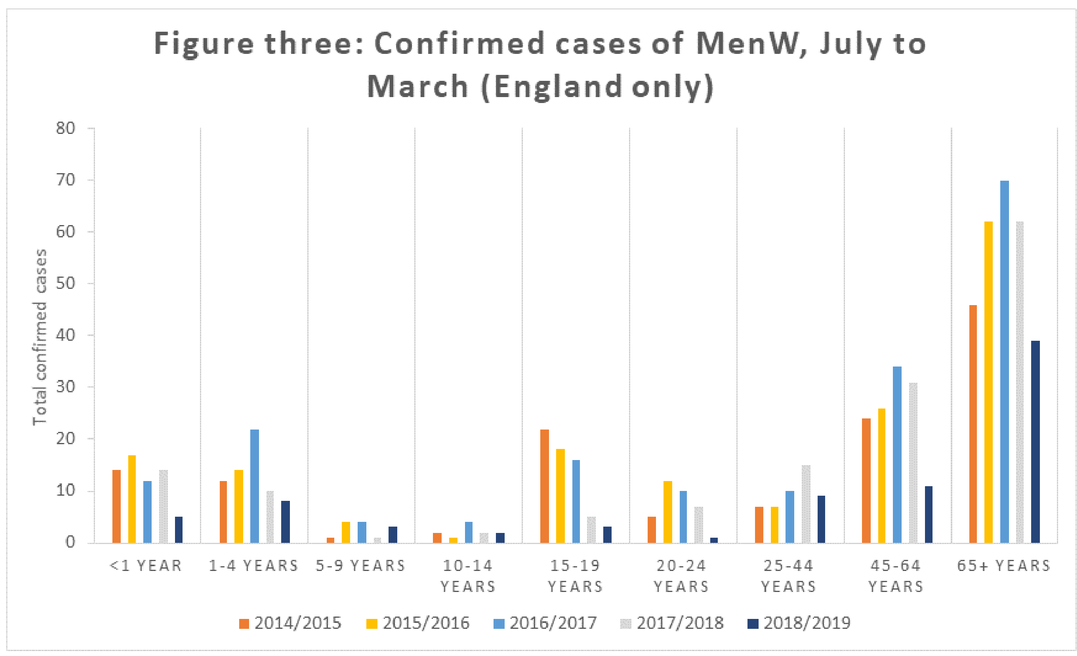
High levels of IMD in 1998/99 and 1999/00 were partly explained by better ascertainment resulting from the use of PCR (Figure 1). During 2017/18 39% (295) cases were confirmed by PCR only; this proportion has fallen in recent years from ~50% up to 2011/12. The decrease in total cases from 1999/00 has, in part, been due to the major reduction in Group C cases resulting from both direct and indirect (herd) protection from MCC vaccination (Figure two). Since 2005/06, there have only been 13 - 33 serogroup C cases each epidemiological year in England. This increased to 42 cases in 2015/16 and 64 cases in 2017/18, the highest total in 13 years and representing 8.5% of all IMD cases..



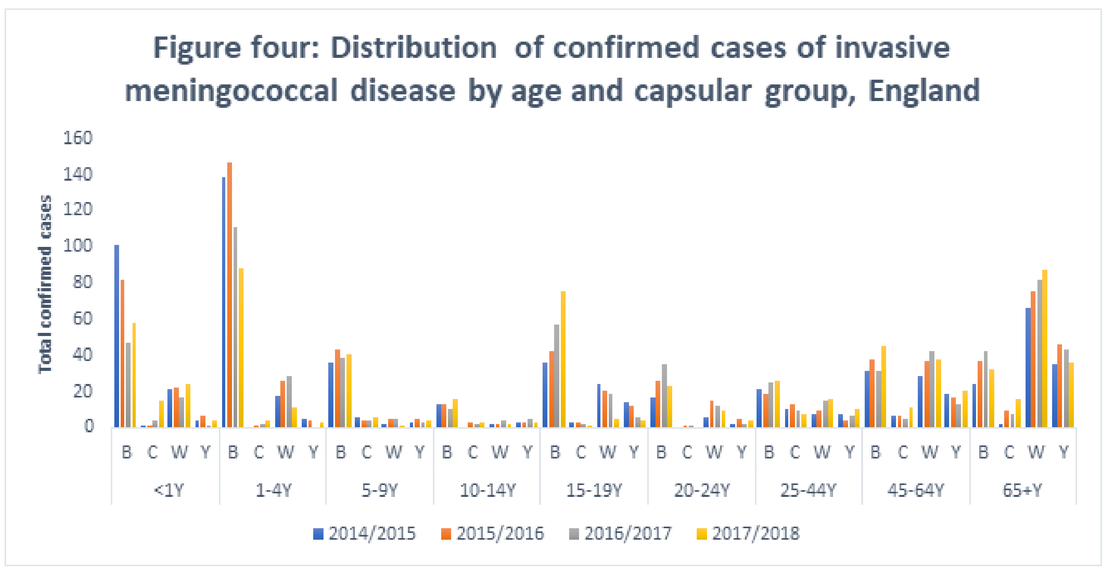
There has been an overall decrease in Group B cases in recent years from 1,424 (2001/02) to 397 (2016/17), (Figure two). In 2017/18 Group B accounted for 54% (404 cases) of all confirmed cases. With the UK national infant 4CmenB programme resulting in reduced disease in the targeted cohorts[1].

Group Y accounted for 12% (88 cases) in 2017/18: the proportion has remained similar in recent years (since peaking at 103 cases in 2015/16) with some small variation. The Group Y increase has been mainly due to a rise in cases confirmed in adults aged ≥45 (Figure two).

An increase was observed in Group W cases (often with severe disease and unusual presentation) from 19 cases (2% of all IMD cases) in 2008/09, 95 cases in 2013/14, 176 cases in 2014/15 peaking at 225 (30%) in 2016/17. In 2017/18 cases of Group W decreased to 193 representing 26% of all IMD. The cases were predominantly due to phenotype W:2a:P1.5,2 and confirmed as cc11 by WGS[2]. 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 three), leading to the introduction of an ACWY conjugate vaccine programme for UK teenagers and university freshers commencing August 2015 as an emergency response measure. Provisional data show a fall in MenW cases across all age groups in 2018/19 to date (Figure three).



A large proportion of the total IMD cases are observed in pre-school children aged under five years (Figure four) accounting for 40% of all cases in 2014/15 and 28% in 2017/18. Whilst cases in this age group have been predominantly due to Group B, this proportion has fallen from 83% of cases in 2014/15 to 70% in 2017/18. Cases in the 45+ years age groups accounted for 30% of all IMD increasing to 38% 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. MenACWY vaccination of young people may be having an impact on disease in older adults in 2018/19 (Figure four). It is observed that fewer PCR investigations and therefore confirmations are made for elderly patients.



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. 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), based on provisional data.
For 2017/18 CFR to date: is 4% for group B, 13% group C, 15% group W and 3% for group Y .

Discussion and Conclusions

- **Group B cases have fallen steadily since 2000/01 to a low of 396 (53%) in 2016/17 and maintained at 404 (54%) in 2017/18 of all IMD cases; where the introduction of 4CMenB (Bexsero®) to UK infants post 1st September 2015 has reduced B cases in the immunised population.**
- **The profile of IMD changed since MCC vaccine introduction; where Group C disease 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 has increased recently to 42 in 2015/16, 37 in 2016/17 and now 64 in 2017/18.**
- **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.**
- **Enhanced surveillance to carefully monitor any changes in IMD epidemiology (in vaccinated and unvaccinated age groups) following the introduction of infant Bexsero®, the MenACWY and MCC vaccine programmes in England is essential and ongoing.**

Reference: [1]Parikh R *et al*., (2016). Effectiveness and impact of a reduced infant schedule of 4CMenB vaccine against group B meningococcal disease in England: a national observational cohort study. The Lancet 388:31921-3.
[2]Lucidarme *et al*., 2015. J. Infect. 71 (5) Nov 2015; 544-552.