

1.3 Meningococcal disease

Summary

Number of cases, 2015: 75
 Number of cases, 2014: 82
 Number of cases, 2013: 81
 Crude incidence rate, 2015: 1.6/100,000

Between 1999 and 2012, a marked downward trend in invasive meningococcal disease (IMD) incidence was observed: in 1999 there were 536 cases (14.8/100,000) and in 2012 there were 66 cases (1.4/100,000), a decline of almost 88%. In 2015, however, 75 cases (1.6/100,000) of IMD were notified, seven fewer reported than in the previous year (n=82).

Typically, most cases in 2015 were diagnosed by blood/CSF culture testing, blood/CSF PCR testing or by detection of Gram negative diplococci in skin lesions/culture or in CSF specimens. Isolation of the organism from non-sterile sites (such as the eye, nose or throat) in clinically compatible cases is considered a possible case.

Of the 75 cases notified in 2015, 67 (89.3%) were case classified as confirmed and eight (10.7%) as possible. Confirmation of diagnosis by laboratory testing of cases has improved with time. In 2015, 89.3% (n=67/75) of cases were confirmed by laboratory testing in comparison to 83.0% (n=445/536) in 1999.

In 2015, 31 of the 67 confirmed cases (46.3%) were confirmed by PCR testing alone and another 12 confirmed cases (17.9%)

were diagnosed by culture of sterile specimens alone. Of the remaining 24 (35.8%) confirmed cases, all were diagnosed by both culture and PCR testing of sterile specimens. Additional laboratory testing was done on the 67 confirmed cases: four had positive CSF microscopy test results and one had a positive skin lesion culture.

Of the eight possible cases reported in 2015, one had a positive laboratory test result based on an eye culture in which serogroup 29E was identified.

In 2015, male cases (n=42) exceeded female cases (n=33), resulting in a male to female ratio of 1.3:1.0, following a consistent pattern observed since 2005. IMD cases in 2015 ranged in age from one month to 92 years (median age of 3 years).

Overall incidence in Ireland was 1.6/100,000 population in 2015. The incidence of IMD was highest in infants and young children. Age specific incidence rate (ASIR) was highest among infants <1 year of age (18.0/100,000; n=13), followed by children in the 1 to 4 years (5.3/100,000; n=15), and 15 to 19 year age groups (4.9/100,000; n=14) (Table 1, Figure 1). Figure 2 presents the number of IMD cases by gender and age group between 1999 and 2015 and shows the decline in numbers across all of the age groups, with the steepest declines observed in the <1, 5-9 and 10-24 year age groups following the introduction of the meningococcal C conjugate (MCC) vaccine in late 2000.

At regional level, incidence was highest in the HSE MW area

Table 1. Number of cases, deaths, age-group specific incidence rates per 100,000 population (calculated using Census 2011 denominator data) and case fatality ratios of IMD, Ireland, 2015

| Age Group | No. Cases | ASIR | No. Deaths | %CFR |
|-----------|-----------|------|------------|------|
| <1 | 13 | 18.0 | 0 | 0.0% |
| 1-4 | 15 | 5.3 | 1 | 6.7% |
| 5-9 | 8 | 2.5 | 0 | 0.0% |
| 10-14 | 4 | 1.3 | 0 | 0.0% |
| 15-19 | 14 | 4.9 | 1 | 7.1% |
| 20-24 | 2 | 0.7 | 0 | 0.0% |
| 25+ | 19 | 0.6 | 1 | 5.3% |
| All ages | 75 | 1.6 | 3 | 4.0% |

ASIR, age specific incidence rate per 100,000 population; %CFR, case fatality ratio

(2.4/100,000) and lowest in the HSE E area (1.1/100,000) (Table 2). No area had an incidence rate that was significantly different from the national rate (Figure 3). There were no imported cases identified in 2015.

Apart from the years 2003, 2013 and 2014, IMD cases have tended to occur most frequently in the first quarter of each calendar year (Figure 4).

Neisseria meningitidis serogroup B was the pathogen most

commonly associated with IMD in 2015 and accounted for 43 of the 75 (57.3%) notifications. However, this is a marked decline on what was previously reported between 2003 and 2014 when serogroup B accounted for more than 80% (n=1,703/2,031) of all IMD notifications (Figure 5).

In February 2015, a cluster of cases was reported in HSE S in Cork involving two siblings, aged 4 and 5 years with a serogroup B infection. Both cases recovered.

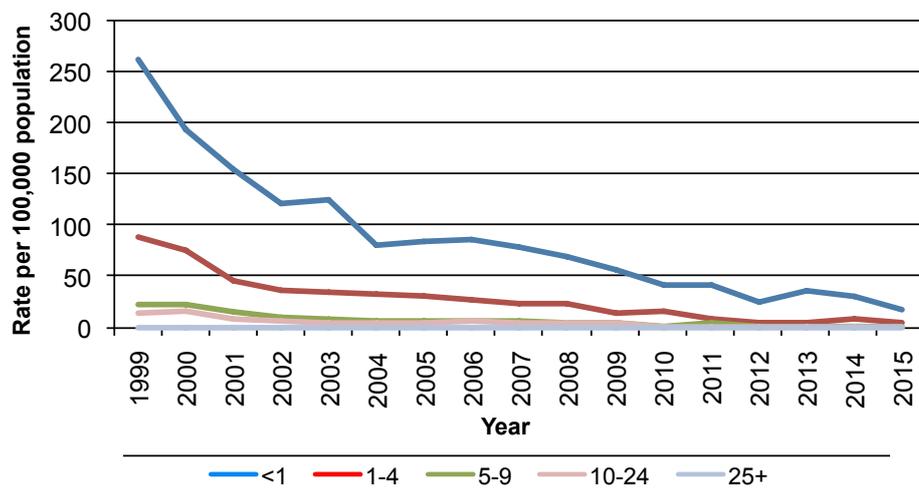


Figure 1. Age-specific rates per 100,000 population for invasive meningococcal disease (IMD), Ireland, 1999-2015

Table 2. Age specific incidence rates per 100,000 population (calculated using Census 2011 denominator data) of IMD by HSE area and age group, Ireland, 2015

| HSE Area | <1 | 1-4 | 5-9 | 10-14 | 15-19 | 20-24 | 25+ | Total |
|----------|------|------|------|-------|-------|-------|-----|-------|
| HSE E | 11.5 | 1.0 | 0.9 | 1.0 | 5.2 | 0.0 | 0.7 | 1.1 |
| HSE M | 20.7 | 5.2 | 0.0 | 4.9 | 11.3 | 0.0 | 0.6 | 2.1 |
| HSE MW | 17.5 | 17.5 | 11.4 | 0.0 | 0.0 | 4.1 | 0.0 | 2.4 |
| HSE NE | 39.0 | 3.2 | 0.0 | 0.0 | 14.7 | 0.0 | 0.0 | 1.8 |
| HSE NW | 0.0 | 6.3 | 5.3 | 0.0 | 18.0 | 0.0 | 0.6 | 2.3 |
| HSE SE | 26.2 | 6.5 | 2.8 | 5.7 | 0.0 | 0.0 | 0.6 | 1.8 |
| HSE S | 19.9 | 5.0 | 2.2 | 0.0 | 0.0 | 2.4 | 1.4 | 1.8 |
| HSE W | 15.1 | 11.5 | 3.2 | 0.0 | 0.0 | 0.0 | 0.7 | 1.6 |
| Ireland | 18.0 | 5.3 | 2.5 | 1.3 | 4.9 | 0.7 | 0.6 | 1.6 |

Table 3. Number of cases, deaths and case fatality ratios (%CFR) by year for meningococcal B and C disease, Ireland, 1999-2015

| Year | Meningococcal B | | | Meningococcal C | | |
|------|-----------------|------------|------|-----------------|------------|------|
| | No. Cases | No. Deaths | %CFR | No. Cases | No. Deaths | %CFR |
| 1999 | 292 | 12 | 4.1 | 135 | 5 | 3.7 |
| 2000 | 258 | 13 | 5.0 | 139 | 11 | 7.9 |
| 2001 | 245 | 8 | 3.3 | 35 | 3 | 8.6 |
| 2002 | 199 | 8 | 4.0 | 14 | 0 | 0.0 |
| 2003 | 206 | 11 | 5.3 | 5 | 1 | 20.0 |
| 2004 | 163 | 7 | 4.3 | 5 | 1 | 20.0 |
| 2005 | 169 | 5 | 3.0 | 5 | 0 | 0.0 |
| 2006 | 168 | 5 | 3.0 | 4 | 0 | 0.0 |
| 2007 | 158 | 6 | 3.8 | 2 | 0 | 0.0 |
| 2008 | 149 | 6 | 4.0 | 4 | 1 | 25.0 |
| 2009 | 119 | 6 | 5.0 | 5 | 0 | 0.0 |
| 2010 | 93 | 4 | 4.3 | 4 | 0 | 0.0 |
| 2011 | 84 | 2 | 2.4 | 2 | 0 | 0.0 |
| 2012 | 58 | 1 | 1.7 | 0 | 0 | 0.0 |
| 2013 | 68 | 4 | 5.9 | 1 | 0 | 0.0 |
| 2014 | 69 | 3 | 4.3 | 6 | 1 | 16.7 |
| 2015 | 43 | 2 | 4.7 | 11 | 0 | 0.0 |

%CFR, case fatality ratio

There were three IMD related notified deaths in 2015 (case fatality ratio of 4.0%) (age range 16 months to 92 years) (Table 1). The death in a 16 month old was reported to be due to a serogroup B infection, but the cause of death was not reported in the other two: one had a serogroup B infection and the other had a non-groupable infection. This compares to an annual average of 4.9 deaths between 2005 and 2014. In 2015, the %CFR was highest amongst cases 15-19 years of age (7.1%) as a result of one death among 14 cases. The next highest %CFR was 6.7% (n=1/15) among cases aged 1-4 years.

IMD due to serogroup C (MenC) has remained at relatively low levels between 2003 and 2014 with an average of 3.4 cases occurring annually. However, in 2015, the highest number of MenC cases (n=11) since 2002 was observed, aged between 4 months and 73 years (Table 3). Three of these six cases that were unvaccinated (aged between 4 months and 73 years) had no risk factors reported; there were four vaccine failures (aged 3 to 16 years) and the vaccination status of the remaining case was incomplete (aged 15-19 years).

Since 2003, 14 true vaccine failures have been recorded. Prior to the introduction of the MCC vaccine, serogroup C incidence rate in 1999 was 3.7/100,000 population; in 2015 it was 0.24/100,000.

The recent increase in MenC cases, which began in 2014, may be attributable to waning population herd immunity. Recent studies undertaken in the United Kingdom have reported waning immunity to serogroup C disease following infant vaccination in early childhood. Furthermore, protection given by vaccination at 12 months also wanes by the teenage years, but vaccination later in childhood provides higher levels of antibody that persist for longer.¹⁻⁴ Evidence shows that MCC vaccination significantly reduces nasopharyngeal carriage of the serogroup C meningococcus, providing indirect protection through herd immunity.⁵⁻⁶ The continuing increase in MenC cases in Ireland in 2015 may reflect a decline in this herd immunity.

The routine meningococcal C conjugate (MCC) vaccination programme in Ireland has recently changed in response

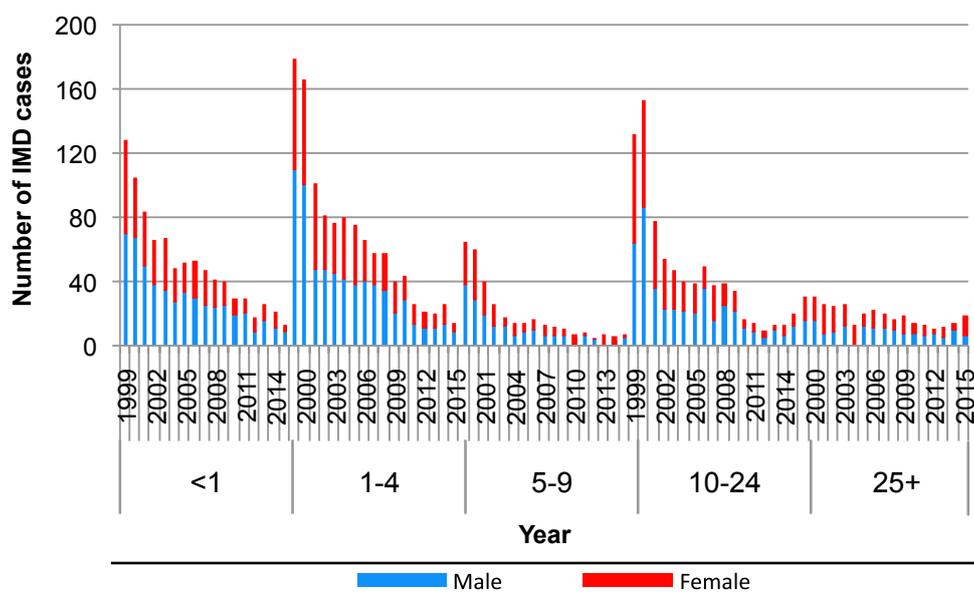


Figure 2. Number of IMD cases by gender and age group in Ireland, 1999-2015 (excludes one case with unknown gender details in 2009)

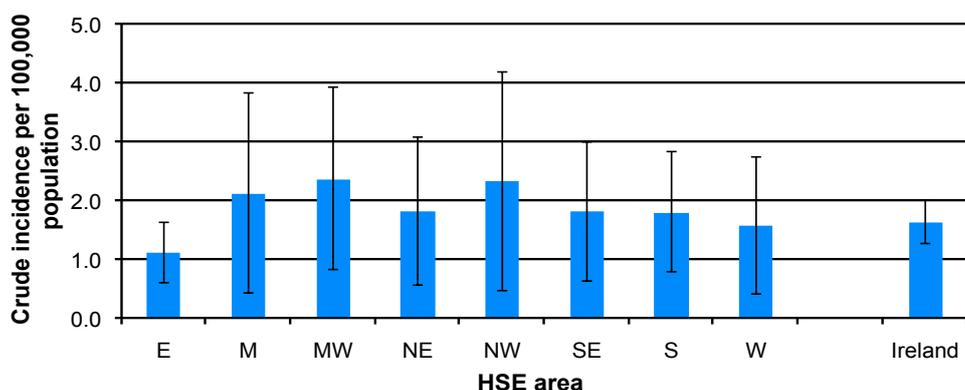


Figure 3. Crude incidence rates per 100,000 population with 95% confidence intervals for IMD notifications by HSE area, Ireland, 2015

to the recent increase in MenC cases and the emerging evidence of waning immunity. Instead of three doses of the MCC vaccine being administered to children at 4, 6 and 13 months of age, from July 2015 a single dose is given at 4 months, 13 months and at 12-13 years (if not previously vaccinated at >10 years of age) (<http://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/chapter13.pdf>).

The National Immunisation Advisory Committee (NIAC) also recommended a booster dose of the MCC vaccine for those considered at increased risk of MenC disease, and since 2011, the MCC vaccine booster has been recommended for close contacts of cases if their last dose was more than one year before. In August 2014, NIAC recommended an adolescent booster at 12-13 years to be offered in the first year of secondary level school. The adolescent booster MenC programme commenced in January 2015.

Despite the marked reduction in the overall incidence in the past decade, IMD is still an important public health concern due to its associated severity, high mortality rate and serious adverse sequelae. Complete IMD prevention

and control requires effective vaccination. Effective vaccines are now available against serogroups A, B, C, W135 and Y forms of the disease. In 2012, Bexsero®, a recombinant multicomponent vaccine (4CMenB) against serogroup B disease was approved by the European Medicines Agency. In March 2014, the United Kingdom's Joint Committee on Vaccination and Immunisation (JCVI) recommended the vaccination of infants against serogroup B.⁷ In Ireland, the primary childhood immunisation (PCI) schedule were updated in July 2016 so that all babies born on or after 1st October 2016 will be offered the MenB vaccine at 2, 4 and 12 months of age (<https://www.hse.ie/eng/health/immunisation/infomaterials/newsletter/newsletter23.pdf>). The MenB vaccine cannot be given at same time as MenC vaccine, which is given at 6 and 13 months of age.

The figures presented in this summary are based on data extracted from the Computerised Infectious Disease Reporting (CIDR) system on 26th August, 2016. These figures may differ from those published previously due to on-going updating of notification data on CIDR.

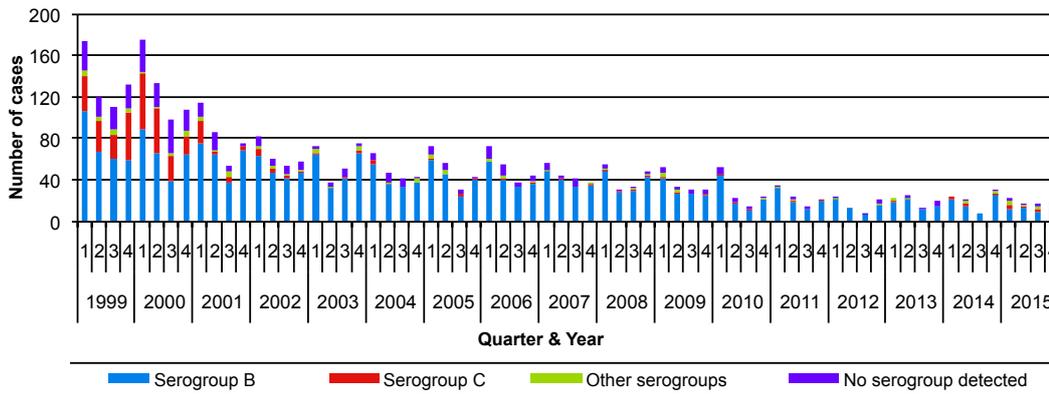


Figure 4. Number of IMD cases by quarter and serogroup, Ireland, 1999-2015

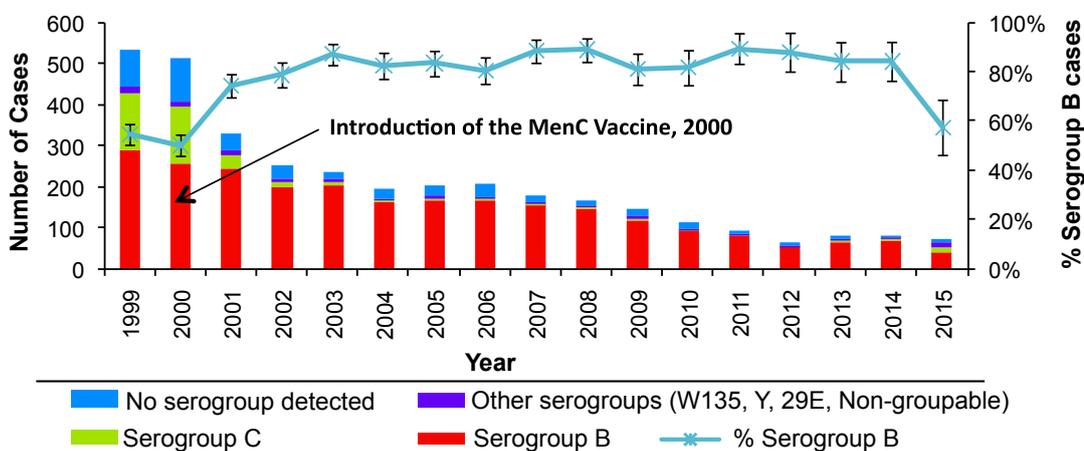


Figure 5. Number of IMD notifications in Ireland by serogroup and proportion of cases attributable to serogroup B with 95% confidence intervals, Ireland, 1999-2015

References

1. Borrow R, Andrews N, Findlow H, Waight P, Southern J, Crowley-Luke A, Stapley L, England A. Kinetics of antibody persistence following administration of a combination meningococcal serogroup C and haemophilus influenzae type b conjugate vaccine in healthy infants in the United Kingdom primed with a monovalent meningococcal serogroup C vaccine. *Clin Vaccine Immunol*. 2010 Jan;17(1):154-9.
2. Kitchin N, Southern J, Morris R, Borrow R, Fiquet A, Boissonard F, Thomas S, Miller E. Antibody persistence in UK pre-school children following primary series with an acellular pertussis-containing pentavalent vaccine given concomitantly with meningococcal group C conjugate vaccine, and response to a booster dose of an acellular pertussis-containing quadrivalent vaccine. *Vaccine*. 2009 Aug 13;27(37):5096-102.
3. Perrett KP, Winter AP, Kibwana E, Jin C, John TM, Yu LM, Borrow R, Curtis N, Pollard AJ. Antibody persistence after serogroup C meningococcal conjugate immunization of United Kingdom primary-school children in 1999-2000 and response to a booster: a phase 4 clinical trial. *Clin Infect Dis*. 2010 Jun 15;50(12):1601-10.
4. Snape MD, Kelly DF, Lewis S, Banner C, Kibwana L, Moore CE, Diggle L, John T, Yu LM, Borrow R, Borkowski A, Nau C, Pollard AJ. Seroprotection against serogroup C meningococcal disease in adolescents in the United Kingdom: observational study. *BMJ*. 2008 Jun 28;336(7659):1487-91.
5. Ramsay ME, Andrews NJ, Trotter CL, Kaczmarski EB, Miller E. Herd immunity from meningococcal serogroup C conjugate vaccination in England: database analysis. *BMJ*. 2003 Feb 15;326(7385):365-6.
6. Maiden MC, Ibarz-Pavón AB, Urwin R, Gray SJ, Andrews NJ, Clarke SC, Walker AM, Evans MR, Kroll JS, Neal KR, Ala'aldein DA, Crook DW, Cann K, Harrison S, Cunningham R, Baxter D, Kaczmarski E, Maclennan J, Cameron JC, Stuart JM. Impact of meningococcal serogroup C conjugate vaccines on carriage and herd immunity. *J Infect Dis*. 2008 Mar 1;197(5):737-43.
7. Public Health England. The Green Book. Immunisation against infectious disease, Children's health, Chapter 22, updated 28/ July/2015. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/448875/2904185_Green_Book_Chapter_22_v3_OW_July2015.PDF (accessed 21/08/2015)