

1.3 Meningococcal Disease (*Neisseria meningitidis*) (invasive)

Summary

Number of cases, 2014: 82
 Number of cases, 2013: 81
 Number of cases, 2012: 66
 Crude incidence rate, 2014: 1.8/100,000

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 2014, however, 82 cases (1.8/100,000) of IMD were notified, similar to that reported in the previous year (n=81).

Typically, most cases in 2014 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 82 cases notified in 2014, 79 (96.3%) were case classified as confirmed and three (3.7%) as possible. Confirmation of diagnosis by laboratory testing of cases has improved with time. In 2014, 96.3% (n=79/82) of cases were confirmed by laboratory testing in comparison to 83.0% (n=445/536) in 1999.

In 2014, 49 of the 79 confirmed cases (62.0%) were confirmed by PCR testing alone and another eight confirmed cases (10.1%) were diagnosed by culture of

sterile specimens alone. Of the remaining 22 (27.9%) confirmed cases, all were diagnosed by both culture and PCR testing of sterile specimens. Additional laboratory testing was done on the 79 confirmed cases: one had a positive skin lesion culture and 11 had positive CSF microscopy test results.

Of the three possible cases reported in 2014, only one had a positive laboratory test result and it was based on an eye swab culture in which the peri-orbital cellulitis infection was attributable to a non-groupable strain.

In 2014, male cases (n=44) exceeded female cases (n=38), resulting in a male to female ratio of 1.2:1.0, following a consistent pattern observed since 2005. IMD cases in 2014 ranged in age from three weeks to 90 years (median age of 3 years).

Overall incidence in Ireland was 1.8/100,000 population in 2014. The incidence of IMD was highest in infants and young children. Age specific incidence rate (ASIR) was highest among infants <1 year of age (30.4/100,000; n=22), followed by children in the 1 to 4 year (9.2/100,000; n=26), and 15 to 19 year age groups (2.5/100,000; n=7) (table 1, figure 1).

Figure 2 presents the number of IMD cases by gender and age group between 1999 and 2014 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.

Table 1. Number of cases, deaths, age-group specific incidence rates per 1000,000 population (calculated using Census 2011 denominator data) and case fatality ratios of IMD, Ireland, 2014

Age Group	No. Cases	ASIR	No. Deaths	%CFR
<1	22	30.4	1	4.5%
1-4	26	9.2	1	0.0%
5-9	6	1.9	0	0.0%
10-14	3	1.0	0	7.1%
15-19	7	2.5	1	0.0%
20-24	3	1.0	0	0.0%
25+	15	0.5	1	0.0%
All ages	82	1.8	4	4.9%

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

At regional level incidence was highest in the HSE M area (3.5/100,000) and lowest in the HSE MW area (0.3/100,000) (table 2). Apart from HSE MW, no other area had an incidence rate that was significantly different from the national rate (figure 3). There were no imported cases identified in 2014.

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 2014 and accounted for 69 of the 82 (84.1%) notifications. Since 2002 serogroup B has consistently accounted for more than 80% of annual IMD notifications (figure 5).

One meningococcal outbreak was reported in 2014. The serogroup B outbreak occurred in a child care facility in the HSE NE in which two cases (age range one month to 20 years) were notified.

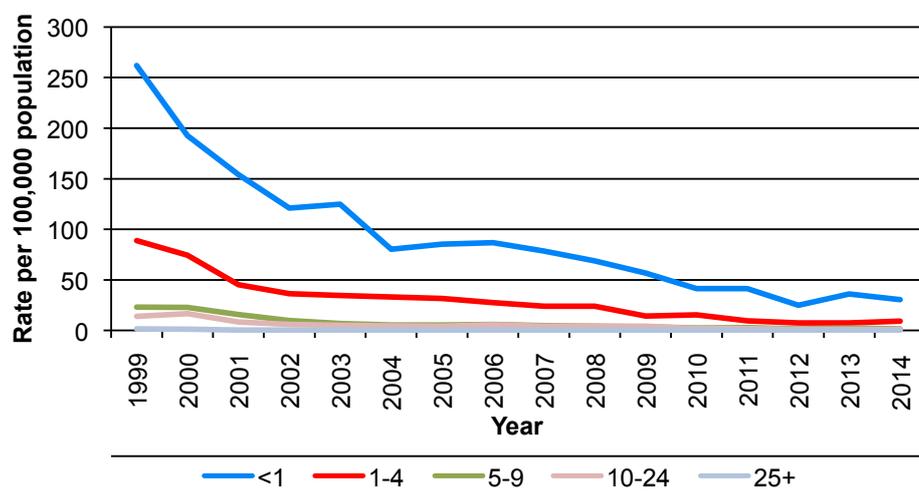


Figure 1. Age-specific rates per 100,000 population for invasive meningococcal disease (IMD), Ireland, 1999-2014

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, 2014

HSE Area	<1	1-4	5-9	10-14	15-19	20-24	25+	Total
HSE E	34.6	8.2	2.8	0.0	1.0	0.0	0.4	1.5
HSE M	62.2	26.2	4.5	0.0	0.0	0.0	0.6	3.5
HSE MW	0.0	4.4	0.0	0.0	0.0	0.0	0.0	0.3
HSE NE	78.0	16.0	0.0	3.1	0.0	0.0	0.7	3.2
HSE NW	25.7	6.3	0.0	0.0	6.0	6.7	0.0	1.5
HSE SE	39.2	9.7	0.0	0.0	0.0	0.0	0.6	1.6
HSE S	0.0	5.0	2.2	0.0	4.9	2.4	0.5	1.2
HSE W	0.0	3.8	3.2	6.8	10.8	3.6	1.3	2.7
Ireland	30.4	9.2	1.9	1.0	2.5	1.0	0.5	1.8

Table 3. Number of cases, deaths and case fatality ratios (%CFR) by year for meningococcal B and C disease, Ireland, 1999-2014

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	157	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%

%CFR, case fatality ratio

There were four IMD related notified deaths in 2014 (case fatality ratio of 4.9%) (age range 9 months to 90 years) (table 1). This compares to an annual average of five deaths between 2005 and 2013. In 2014, the %CFR was highest amongst cases 65+ years of age (20.0%) as a result of one death among five cases. The next highest %CFR was 14.3% (n=1/7) due to a MenC death in an adult aged 15-19 years.

All but one of the four IMD deaths in 2014 disease was due to serogroup B. This is in marked contrast to the 13 deaths due to serogroup B out of all 25 deaths reported in 2000. In the same year, 11 deaths were due to serogroup C disease.

IMD due to serogroup C (MenC) has remained at very low levels over the last decade with five cases or less occurring annually. However, in 2014, the highest number of MenC cases (n=6) since 2002 was observed, all aged between 18 and 72 years (table 3). Three of these six cases were unvaccinated and were aged

between 19 to 77 years with no risk factors reported; the vaccination status of the remaining three cases was unknown, they ranged in age between 18 and 53 years, two of whom were foreign born, including one who was a student who died.

Since 2003, 11 true vaccine failures have been recorded, the most recent of which occurred in 2013. Prior to the introduction of the MCC vaccine, serogroup C incidence rate in 1999 was 3.7/100,000 population; in 2014 it was 0.13/100,000.

The recent small increase in MenC cases may represent waning population herd immunity and would be consistent with recent studies undertaken in the United Kingdom which 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 There is

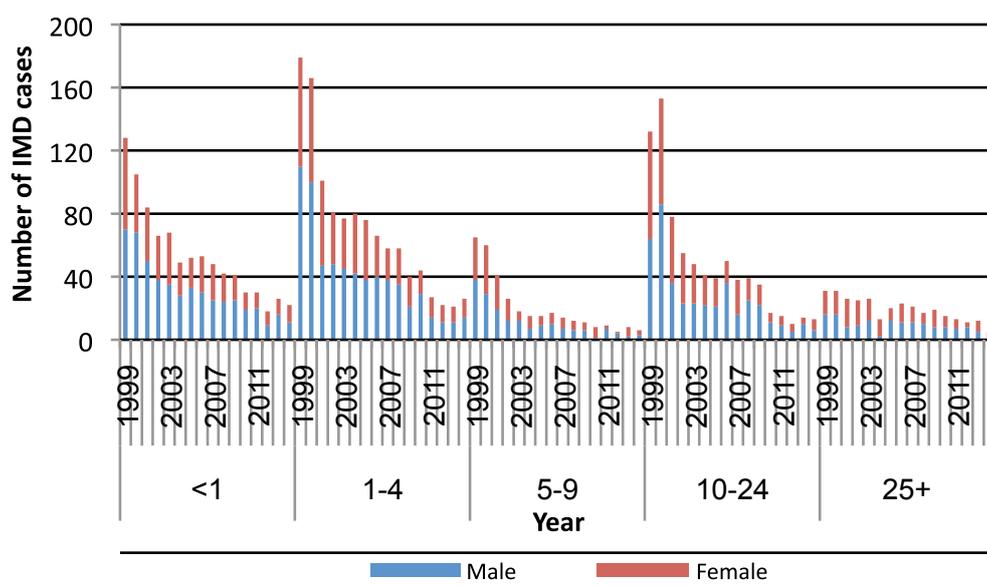


Figure 2. Number of IMD cases by gender and age group in Ireland, 1999-2014 (excludes one case with unknown gender details in 2009)

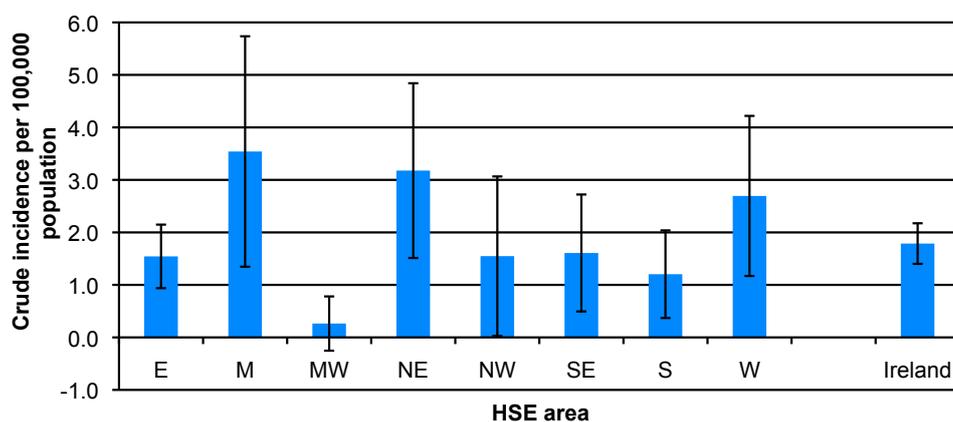


Figure 3. Crude incidence rates per 100,000 population with 95% confidence intervals for IMD notifications by HSE area, Ireland, 2014

evidence that shows that MCC vaccination significantly reduces nasopharyngeal carriage of the serogroup C meningococcus, providing indirect protection through herd immunity.⁵⁻⁶ The increase in MenC cases in Ireland in 2014 may reflect a decline in this herd immunity.

This emerging evidence of waning immunity and the recent increase in MenC cases has led to the routine MenC vaccination programme in Ireland being changed. Instead of three doses of meningococcal C conjugate (MCC) being administered to children at 4, 6 and 13 months of age, from July 2015 a single dose will be 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) has 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.

IMD is still an important public health concern due to its associated severity, high mortality rate and serious adverse sequelae, despite the marked reduction in the overall incidence in the past decade. Effective vaccination is necessary for complete IMD prevention and control. 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 August 2014, NIAC issued guidelines on how this vaccine should be administered in Ireland (<http://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/chapter13.pdf>). In September 2015, the National Immunisation

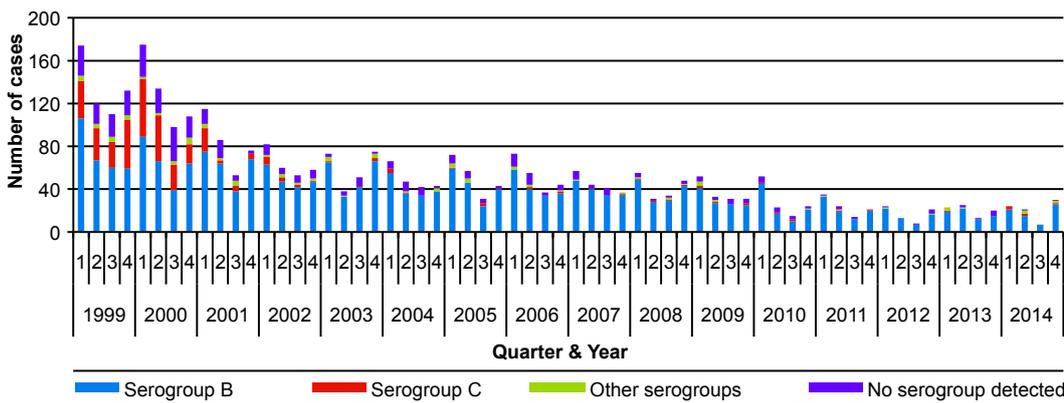


Figure 4. Number of IMD cases by quarter and serogroup, Ireland, 1999-2014

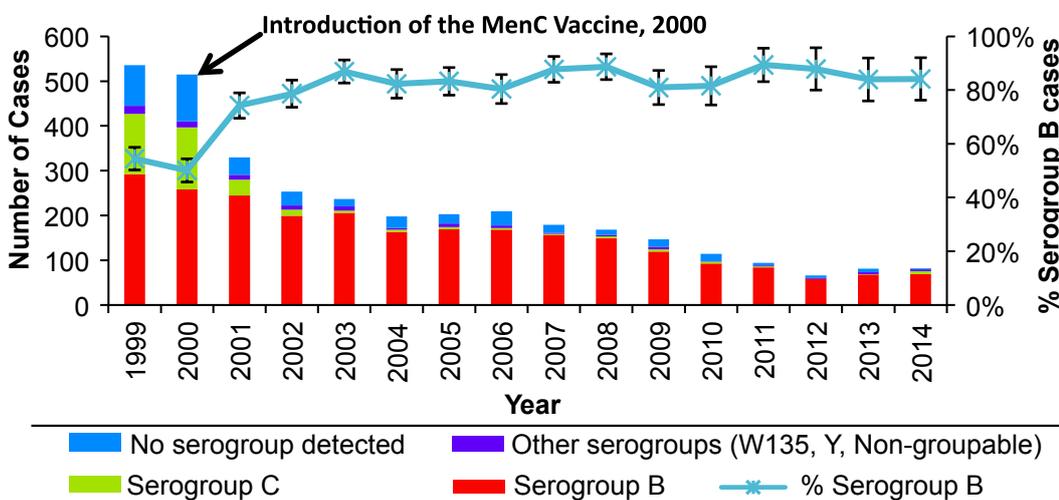


Figure 5. Number of IMD notifications in Ireland by serogroup and proportion of cases attributable to serogroup B with 95% confidence intervals, Ireland, 1999-2014

Office (NIO) included a universal MenB vaccination proposal in the HSE 2016 service plan. At the time of writing this report (September 2015), no decision has yet been made.

The figures presented in this summary are based on data extracted from the Computerised Infectious Disease Reporting (CIDR) system on 13th August, 2015. These figures may differ from those published previously due to on-going updating of notification data on CIDR.

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, Boisnard 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)