

Review Article

# Meningococcal Disease Section 2: Epidemiology and Vaccination of Meningococcal Disease in Northern Ireland

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As a notifiable disease, the Public Health Agency Northern Ireland are responsible for collecting and collating data on the epidemiology of Invasive Meningococcal Disease (IMD). The epidemiology of IMD has varied considerably over the past two decades in Northern Ireland (Figure 1). The late 1990's saw cases more than double between 1996 and 2000.

Meningococcal Group C vaccine became available that overcame both these problems. This was introduced in late 1999 and had an immediate effect on Group C disease. Following widespread use of the vaccine in 2000, cases of Group C disease fell substantially, so that by 2004 onwards there were very few cases occurring (Figure 1).

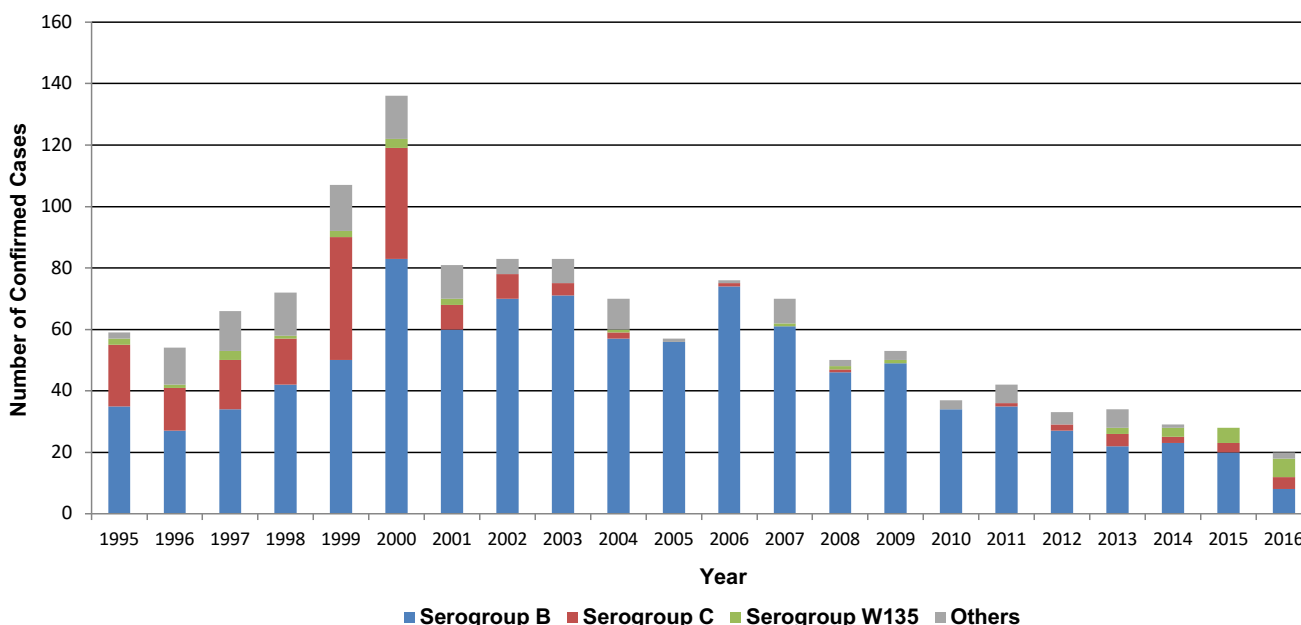


Fig 1. Number of confirmed cases in Northern Ireland of meningococcal disease by serogroup from 1995-2016.

(Source of data: Northern Ireland Public Health Agency; <http://www.publichealth.hscni.net/directorate-public-health/health-protection/meningococcal-disease>)

This was due to an increase in both Group B and Group C disease. Whilst in absolute numbers, Group B disease always remained the most common, Group C disease was increasing at a faster rate and there were serious concerns that it would overtake Group B, as the most common cause of disease.

At that time, there was no vaccine for Meningococcal Group B and although there was a polysaccharide vaccine for Meningococcal Group C, it had a number of significant drawbacks which made it unsuitable for a population-based campaign. It did not stimulate T cells, meaning there was no immunological memory, it produced only short-term protection and it did not work in infants under 18 months of age, who were at highest risk. However, in 1999, a conjugate

Meningococcal Group B disease continued to occur at relatively high levels until around 2007 when its incidence began to fall and for the last five years, the incidence of Meningococcal Group B disease has fallen to its lowest level since epidemiological monitoring began in the mid-1990s. A similar trend has been noted in the rest of the UK.

Figure 2 shows the age distribution of IMD in NI, which demonstrates that this is very much a disease of infants and

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TABLE 1:

A comparison of invasive meningococcal disease (IMD) incidence in 2016 between NI, ROI, England, Scotland and Wales.

	Northern Ireland <sup>a</sup>	Republic of Ireland <sup>b</sup> (2016)	England <sup>c</sup> (Epi Year 2015/16)	Scotland <sup>d</sup> (2016)	Wales <sup>e</sup> (2016)
Incidence (per 100,000 population)	1.1	1.8	1.5	2.0	1.4
No. of laboratory confirmed cases	20	87	805	106	44
Serogroup B (%)	8 (40.0%)	48 (55.2%)	444 (55.2%)	49 (46.2%)	33 (75.0%)
Serogroup C (%)	4 (20.0%)	22 (25.3%)	42 (5.2%)	13 (12.3%)	0 (0%)
Serogroup W (%)	6 (30.0%)	7 (8.0%)	210 (26.1%)	24 (22.6%)	4 (9.1%)
Serogroup Y (%)	Unknown	5 (5.75%)	101 (12.5%)	9 (8.5%)	6 (13.6%)
Others	2 (10.0%)	5 (5.75%)	8 (1.0%)	11 (10.4%)	1 (2.3%)

Sources of data: <sup>a</sup> Northern Ireland Public Health Agency; <sup>b</sup> Health Protection Surveillance Centre, Dublin; <sup>c</sup> Public Health England; <sup>d</sup> Health Protection Scotland; <sup>e</sup> Public Health Wales

young children, with a second but much smaller peak in late teenage years.

Table 1 details a comparison of IMD incidence in 2016 between NI, ROI, England, Scotland and Wales. The incidence of IMD is lowest in NI (1.1/100,000 population). Meningococcal Group B disease continues to constitute the most common group in NI (40%). An interesting and important phenomenon has developed over the past four years across the UK, which is an increasing number of Meningococcal Group W cases, due to a particular strain: MenW:cc11<sup>1</sup>. In 2016, NI had 30% of its confirmed cases of IMD attributed to Group W, which is the highest level in any of the neighbouring countries and the highest this has ever been in NI. It is particularly virulent and has caused outbreaks in other countries, notably in South America<sup>2</sup>. The situation has similarities to the increase in Men C in the late 1990s and action has therefore been taken (see Meningococcal ACWY vaccine) to tackle this rise in Group W cases<sup>3</sup>.

It is also worth mentioning the increase in Group C disease in NI, since 2011, to its current incidence of 20% (Table 1 & Figure 2). It remains unclear what has been the precipitating factor(s) leading to the re-emergence of this disease locally in Northern Ireland. Vaccine uptake rates for Group C have remained high in Northern Ireland since 2011, of greater than 94%<sup>4</sup>. Likewise, there has been a marked increase of Group C disease in the Republic of Ireland<sup>5</sup>. In England, the number of Group C cases reported in 2015/2016 was 45% (n=42) higher than the previous epidemiological year (n=29) and the highest in over a decade<sup>6</sup>.

## NI VACCINATION

### (i) Meningococcal Group C vaccines

Men A&C polysaccharide vaccines have been available since the 1970s, however as outlined above they had significant limitations. In 1999, a Men C conjugate vaccine became

available; this was introduced into the primary vaccine schedule, originally being given as a 3-dose schedule at 2, 3 and 4 months of age. During 2000, there was a catch-up programme for those aged up to 18 years and subsequently this was extended to everyone up to 25 years of age. This resulted in herd immunity as well as individual protection and led to the virtual elimination of the disease described above. There have been various changes to the schedule over the years resulting in the current schedule shown in Table 2.

TABLE 2:

Current meningococcal vaccines offered as part of the routine schedule in Northern Ireland as of September 2017.

Vaccine	Age
Meningococcal Group B	8 weeks
Meningococcal Group B	16 weeks
Meningococcal Group C (inc HiB)	1 year
Meningococcal Group B	1 year
Meningococcal ACWY	14 year olds
	First time university students (up to age of 25y)

PHL England 2015. The green book. Meningococcal, Chapter 22. 2015. [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/462629/2904512\\_Green\\_Book\\_Chapter\\_22\\_v6\\_0W.PDF](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/462629/2904512_Green_Book_Chapter_22_v6_0W.PDF)

### (ii) Meningococcal Group B vaccine

Meningococcal Group B vaccines were much more difficult to develop due to antigenic variation and commonality to human protein. However, the first vaccine has now been licensed in the UK and from September 2015, has been introduced into the primary immunisation programme. It is given as a three-dose schedule at 2, 4, and 12 months of age.

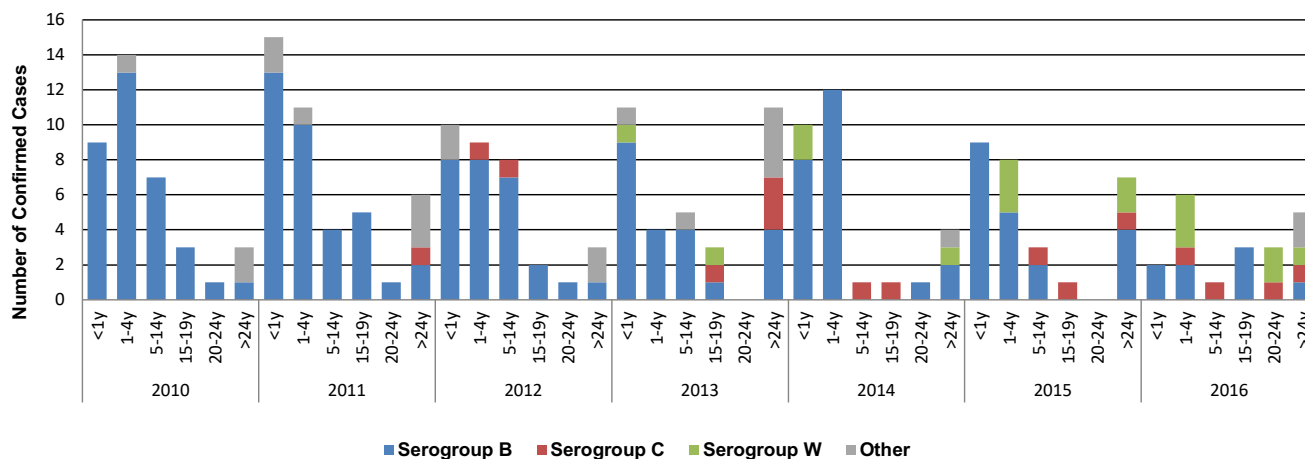


Fig 2. Distribution of confirmed cases of meningococcal disease in Northern Ireland by age and serogroup during the period 2010-2016. (Source of data: Northern Ireland Public Health Agency; <http://www.publichealth.hscni.net/directorate-public-health/health-protection/meningococcal-disease>)

Recently, a study was undertaken to estimate MenB vaccine coverage of invasive strains in England, Wales and NI, from 2007-8 compared to 2014-15, employing the Meningococcal Antigen Typing System (MATS)<sup>7</sup>. For NI, the MATS 2007-8, coverage was 77.8% (n=18 isolates) and for 2014-15, this was 62.5% (n=8 isolates), although this was not statistically different (p=0.418)<sup>7</sup>. During the same period, the combined England, Wales and NI data showed MATS coverage was 73.1% and 65.7%, respectively<sup>7</sup>. The significance of this data for Northern Ireland is that only 62.5% of culturable NI invasive serogroup B isolates would have been covered by the 4CMenB vaccine<sup>7</sup>. This is an important finding for NI healthcare professionals and parents alike, in that it emphasises the public health message that this new vaccine has not got total coverage for all serogroup B strains, hence prioritising the need for careful local monitoring of clonal types of serogroup B types circulating within NI at any given time. This will allow for the tracking of estimated 4CMenB vaccine efficacy locally.

Clinically, administration of the 4CMenB vaccine in infants has been associated with a high incidence of fever and parents are therefore advised to give three doses of paracetamol after their child has received the vaccine at two and four months of age.<sup>1</sup> Recently, an NI study of infants aged up to 180 days old, and presenting to the Paediatric A&E Department, The Royal Belfast Hospital for Sick Children, from 01 September 2015 through 31 January 2016, showed that 35 infants presented within four days after having received the 4CMenB vaccine<sup>8</sup>. This study estimated that this rate of presentation represented approximately 0.8% of the vaccinated population in the catchment area. Presenting symptoms varied amongst 13 signs, with fever (80%), irritability (71%), reduced feeding (63%) and fever & irritability (57%), being the most common presenting symptoms. All of these infants were given a final diagnosis of a vaccine-related reaction<sup>9</sup>.

### (iii) Meningococcal ACWY vaccines

Following an increase in cases of Meningococcal Group

W disease, the Joint Committee for Vaccination and Immunisation (JCVI) advised an urgent immunisation programme of Meningococcal ACWY vaccine to all teenagers aged 14-18 years old and those starting university for the first time. Initially in 2015, the vaccination implementation was phased, where all those in the age group (date of birth 2/7/96 to 1/7/97) were called by their GP for immunisation and various communication methods were implemented to raise awareness of those up to 25 years old going to university for the first time, to seek the immunisation from their GP<sup>10</sup>. Various data have since been published detailing the MenACWY vaccine uptake rates amongst NI teenagers and first-time university students.<sup>4,11</sup> A comprehensive survey was performed amongst first-time university students, who entered a NI University in September/October 2015 and who were eligible for MenACWY vaccination through the call and re-call GP programme<sup>11</sup>. The survey was completed by 1210 students, including 868 first-time freshers, from Healthcare related, Non-Healthcare related and Engineering/Computing faculties. Vaccine uptake amongst 18y old students was 90.7% and 87.3% in female and male cohorts, respectively, falling to 72.1% and 67.7% (19y cohort) and 32.7% and 39.6% (20-25y cohort), male and female, respectively<sup>11</sup>. The uptake rate of the MenACWY vaccine in this university cohort was markedly higher than the overall NI uptake rate within this age cohort (54%), with the lowest overall uptake being recorded in the Belfast area (45%)<sup>4</sup>.

Students reported that posters, clinics and talks were the preferred methods of communication and not social media<sup>11</sup>. Thirty percent of students falsely believed that administration of the MenACWY vaccine excluded the risk of contracting meningitis. This study concluded that for the successful introduction of any vaccination programme amongst university students, it is fundamental that a multidisciplinary team is established to inform and deliver such a programme in an efficient and timely manner<sup>11</sup>.

In 2016, there was a similar catch-up approach, where teenagers born between 2/7/97 and 1/7/99 were called by



their GP to be vaccinated. In addition, in 2016, Year 11 and Year 12 students were vaccinated at school by the NI School Health Service, where vaccine uptake was 79.4% and 78%, respectively<sup>4</sup>. Currently, as the “catch-up cohort” of 14-18-year olds have all been offered MenACWY vaccination, the vaccination of teenagers is now routinely offered by the NI School Health Service in year 11, with a catch-up opportunity in year 12.

Additionally, students aged up to 25 years and starting university for the first time and anyone in the previously eligible cohorts until they turn 25, who have not received the MenACWY vaccine should request this vaccine from their GP<sup>12,13</sup>. Meningococcal vaccines are also offered to patients in certain risk groups in line with recommendations from “Immunisations Against Infectious Disease”<sup>12</sup>.

**(iv) Changes in NI meningococcal epidemiology following recent modifications in the meningococcal vaccine schedule**

Recent changes in the NI meningococcal vaccination schedule, as detailed above, now require careful monitoring of the epidemiology of serogroup variations. It is important to monitor potential variations in serological epidemiology, whenever changes to the vaccination schedule are implemented.

There has been insufficient time to consider the potential effects in NI of the removal of the MenC vaccine at three months of age from July 2016. However, the JCVI has made this recommendation on account of:-

- (i) very few cases of invasive MenC disease in infants and young children in the UK, (ii) most cases of MenC disease is in the over 25 years age group, with a history of foreign

- travel or from persons coming to the UK from abroad, (iii) the MenB vaccine, Bexsero, “provides a degree of protection against invasive MenC disease, dependent on whether the vaccine provided protection against circulating strains”, (iv) that vaccination of teenagers should provide good herd immunity, (v) there is a very small risk that removal of the three month MenC vaccine now could increase the risk of exposure to MenC amongst infants in the short term and (vi) there is evidence from other European countries (The Netherlands and Switzerland) that good control of MenC in infancy is through herd protection and not through the employment of the MenC conjugate vaccination in infancy<sup>14</sup>.

This situation requires careful monitoring and analysis during the current and future epidemiological years.

To date, it is too premature to evaluate the effectiveness of the MenACWY vaccination in NI in teenagers/adolescents. In NI, cases of MenW since 2015 have been in the 1-4-year-old category (n=6; 54.5%) and in the >20 year old category (n=5; 45.5%) (Figure 2). Therefore, great reliance has been placed in effective herd immunity of our local teenage population and the MenACWY programme, as well as potential cross coverage of other non-Group B serogroups. In a recent study at the University of Nottingham, MenW carriage increased from 0.7% to 8%, from September 2015 through March 2016, in a population of University students, where the MenACWY vaccine uptake was 71%<sup>15</sup>. This study demonstrates that students may act as vehicles for the increased carriage and transmission of MenW even in the presence of the MenACWY vaccine<sup>15</sup>.

Other scenarios present in NI, which are unique to NI, namely the sharing of a land border with another EU member state,

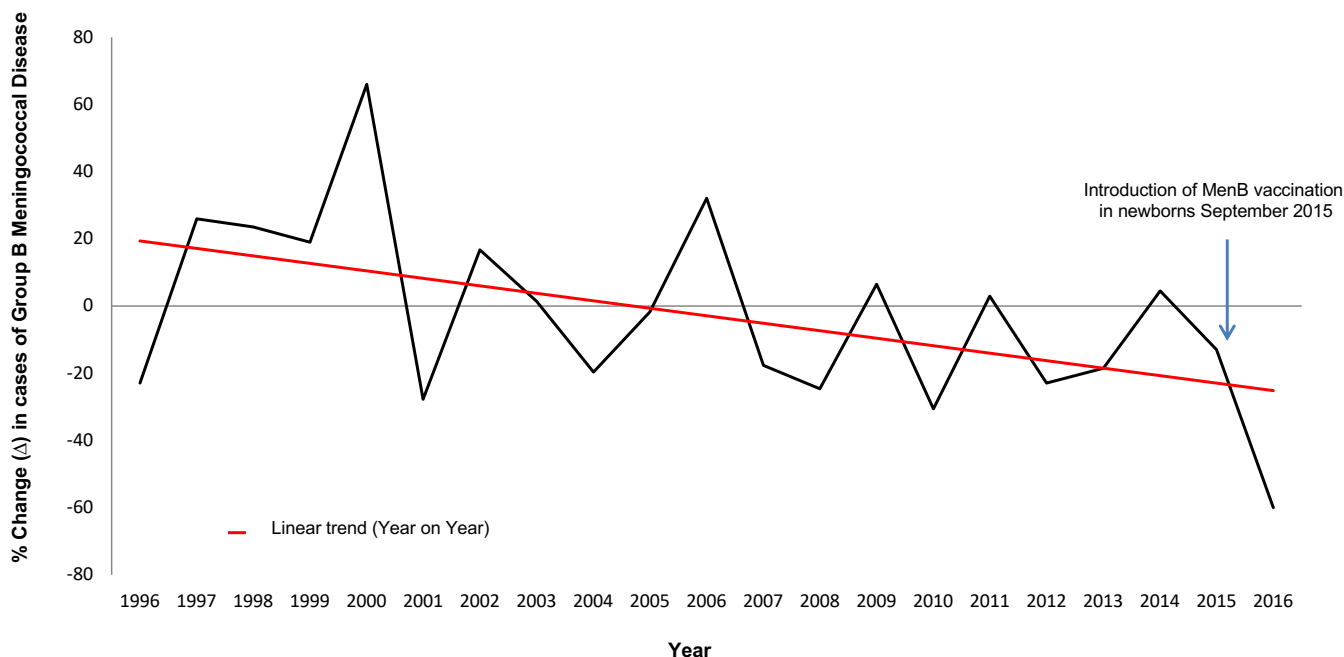


Fig 3. Year-on-year change on serogroup B meningococcal disease in Northern Ireland (1996-2016).

(Source of data: Northern Ireland Public Health Agency; <http://www.publichealth.hscni.net/directorate-public-health/health-protection/meningococcal-disease>)



with differences in their meningococcal vaccination schedule. The absence of the MenACWY vaccination programme in the Republic of Ireland has led to confusion amongst ROI university students and their parents, regarding access to the NI MenACWY vaccination programme. Operation of different meningococcal vaccination schedules in two jurisdictions on a single island presents a challenge to effective herd immunity and therefore requires careful monitoring.

In contrast to these scenarios, it is interesting to examine the changing epidemiology of MenB disease in NI, alongside the introduction of the MenB vaccine in newborns from September 2015. Figure 3 shows year-on-year changes in the incidence of MenB disease in NI from 1996 – 2016. Overall, there has been a marked reduction in MenB cases even in the absence of a MenB vaccine. However, there has been an unprecedented reduction of 77.8% of MenB cases in the <1 year olds, after the MenB vaccine was introduced in September 2015, which is higher than the 50% incidence rate ratio (IRR) reduction in MenB cases in England<sup>7</sup>.

#### (v) Travel Vaccines

A number of outbreaks of meningococcal disease have been linked to the Muslim Hajj pilgrimage to Mecca in Saudi Arabia, at first due to A strain in 1987<sup>16</sup> and then in 2000/2001 caused by the W135 strain<sup>17</sup>. Similar outbreaks occurred world-wide after pilgrims returned to their home countries. In response to these outbreaks, quadrivalent ACWY vaccination has been a compulsory entry requirement into Saudi Arabia for pilgrims, visitors and seasonal workers planning to travel to Saudi Arabia for Hajj and Umrah or during this period. The vaccine should be given to travellers over two years old, at least two to three weeks before travel, but not less than 10 days. In addition to these vaccine requirements, visitors entering Saudi Arabia from sub-Saharan countries (namely Benin, Burkina Faso, Cameroon, Chad, Central African Republic, Côte d'Ivoire, Eritrea, Ethiopia, Gambia, Guinea, Guinea-Bissau, Mali, Niger, Nigeria, Senegal, Sudan and South Sudan, also require antibiotic prophylaxis [ciprofloxacin; 1 x 500mg tablet] at port of entry to Saudi, to lower the rate of carriers among adults and children over 12 years<sup>18</sup>. The Saudi Arabian Embassy requires that visitors and workers submit a certificate of vaccination with the quadrivalent MenACYW135 vaccine against meningitis issued no more than three years and no less than 10 days before arrival in Saudi Arabia<sup>19</sup>.

The Muslim Council of Britain (MCB) has set up vaccination clinics in England, Wales and Scotland to facilitate administration of the vaccine at a subsidised cost of £35. This service does not include Northern Ireland. GP practices and Travel Clinics can be contacted for information on vaccination in Northern Ireland. The total population of the Muslim community in Northern Ireland (from the 2011 census) is around 4000 individuals, however, the Belfast Islamic Centre believe that this value is closer to 10,000 individuals drawn from 42 nationalities. It is not possible to give accurate estimation the number of people going to

Hajj or Umrah in Northern Ireland, as most travel for Hajj is organised by travel agencies in London and Dublin.

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