Journal of Infection 87 (2023) 385–391

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Epidemiological and strain characteristics of invasive meningococcal disease prior to, during and after COVID-19 pandemic restrictions in England

Stephen A. Clark [a,*], Helen Campbell [b], Sonia Ribeiro [b], Marta Bertran [b], Lloyd Walsh [a], Andrew Walker [a], Laura Willerton [a], Aiswarya Lekshmi [a], Xilian Bai [a], Jay Lucidarme [a], Shamez N. Ladhani [b,c], Ray Borrow [a]

[a] Meningococcal Reference Unit, UK Health Security Agency, Manchester Royal Infirmary, Manchester, UK
[b] Immunisation and Countermeasures Division, UK Health Security Agency, Colindale, London, UK
[c] Paediatric Infectious Diseases Research Group, St. George's University of London, Cranmer Terrace, London SW17 0RE, UK

ARTICLE INFO

Article history:
Accepted 5 September 2023
Available online 7 September 2023

Keywords:
Meningococcal
Neisseria meningitidis
COVID-19
Infectious disease
Epidemiology

SUMMARY

Objectives: In 2020, COVID-19 pandemic restrictions led to a major suppression of meningococcal disease in England. Here we describe the epidemiology of invasive meningococcal disease in the three years prior to the COVID-19 pandemic, and the three years immediately after the introduction of restrictions.
Methods: The UK Health Security Agency conducts national meningococcal disease surveillance in England consisting of laboratory-based case confirmation with strain characterisation by culture and/or molecular detection, as well as clinical follow-up of all cases.
Results: In the pre-pandemic period, 554–742 IMD cases were laboratory-confirmed per year. MenB caused 57.2% of cases, followed by MenW (22.7%), MenY (10.6%) and MenC (7.7%). The introduction of restrictions in late March 2020 led to a 73% reduction in IMD. After the removal of restrictions in 2021, a resurgence in MenB was observed, primarily in teenagers and young adults. During the following winter period (2022/23), MenB disease increased to the highest level since 2012 with cases rising across multiple age groups, however, cases in young children eligible for MenB vaccination remained lower than prior to the pandemic. MenACWY cases remained very low throughout the pandemic period.
Conclusions: Once pandemic restrictions in England were removed, MenB quickly rebounded- initially driven by a resurgence in teenagers/young adults, but later among other age groups. MenACWY cases remain very low due to the protection afforded by the adolescent MenACWY conjugate vaccine programme.

Introduction

Invasive meningococcal disease (IMD) is a bacterial illness characterised by rapid progression with non-specific symptoms often progressing to severe disease and/or death within 24 h, and, in many cases, survivors suffer long-term sequelae.[1] In England, serogroup C (MenC) IMD incidence fell rapidly after highly effective MenC conjugate vaccination programmes were introduced from 1999.[2] Additionally, serogroup B (MenB) IMD has also been declining over the same period, initially due to secular trends and, since 2015, because of a national infant MenB immunisation programme with 4CMenB.[3,4] A national increase in serogroup W (MenW) IMD caused by a highly virulent strain belonging to ST-11 clonal complex since 2009/10 led to emergency introduction of an adolescent MenACWY conjugate vaccine programme in 2015, which further contributed to a national decline in IMD cases.[5,6]

In late January 2020, the first cases of COVID-19 in England were confirmed. Incidence increased rapidly in subsequent weeks, prompting the UK government to implement the first national lockdown in late March 2020. From April 2020, the number of IMD cases in England reduced dramatically to a record low.[7] The transmission of other respiratory pathogens such as influenza, respiratory syncytial virus, *Streptococcus pneumoniae* and *Haemophilus influenzae* was also curbed leading to reductions in the corresponding diseases.[8] The suppression of IMD continued throughout 2020 and into 2021 due to multiple national and regional restrictions

* Correspondence to: Meningococcal Reference Unit, Manchester Royal Infirmary, 2nd Floor, Clinical Sciences Building 2, Oxford Rd, Manchester M13 9WL, UK.
E-mail address: stephen.clark@ukhsa.gov.uk (S.A. Clark).

https://doi.org/10.1016/j.jinf.2023.09.002

introduced to control the spread of SARS-CoV-2. December 2020 saw the approval and large-scale rollout of effective COVID-19 vaccines in the UK.

From March 2021, the national restrictions were gradually lifted, with the final measures removed in July 2021. In May 2023, the World Health Organization declared the COVID-19 Public Health Emergency over. Here we describe the epidemiological and strain characteristics of IMD in England in the three years prior to the COVID-19 pandemic, and during the first three pandemic years. We demonstrate the impact of COVID-19 restrictions on IMD and the re-emergence of the disease following their removal.

Methods

Case ascertainment

The UK Health Security Agency (UKHSA) Meningococcal Reference Unit (MRU) provides laboratory confirmation through characterisation of invasive meningococcal isolates submitted by National Health Service (NHS) laboratories across England, and provides free diagnostic meningococcal PCR testing for patients with suspected IMD. The Immunisation and vaccine preventable diseases division of UKHSA follows up all laboratory-confirmed cases for additional information under national IMD surveillance.

Strain characterisation

When a culture isolate was available, capsular group was determined serologically. Serogrouping and serotyping of cultured isolates were performed using monoclonal antibodies in a dot-blot ELISA assay.[9] Whole genome sequencing of all invasive meningococcal isolates was performed using Illumina sequencing technology as previously described.[10] Genomic data for isolates were uploaded to the publicly-accessible PubMLST Neisseria database on PubMLST.org.[11] Indexed multilocus sequence typing (MLST) data were downloaded from PubMLST. Genomic data were not available for 27/124 2022/23 isolates (23 MenB, two MenY and two MenW, 21.8% of total 2022/23 isolates) and so were omitted from the MLST analyses. A further seven MenB isolates and a non-groupable isolate (three from 2021/22 and five from 2022/23) had incomplete MLST allelic profiles and so sequence types (ST) could not be assigned. These were omitted from the ST analysis but clonal complex (CC) could be assigned from the partial profile for the CC analysis.

Detection and genogrouping of meningococcal DNA within clinical samples was achieved using Taqman real-time PCR screening assays.[12] A screening assay targeting the meningococcal *ctrA* and genogroup B-specific *csb* (*siaDb*) genes was initially used. Non-genogroup B meningococcal-positive samples were genogrouped using a secondary TaqMan assay targeting the genogroup W (*csw*), genogroup Y (*csy*) and genogroup C (*csc*) genes.

Statistical analysis

Whole population data are mainly descriptive. Annual incidence was calculated by age group using population estimates provided by the Office for National Statistics.[13] Annual data for pre-pandemic and pandemic years are presented from April to March because the first national lockdown was imposed in late March 2020 and the restrictions were eased from March 2021. The sample collection date was available for all submitted samples to the MRU and used as proxy for disease onset date. The significance of changes to ST distribution among MenB isolates was determined using Fisher's Exact Test (two-tailed) with a significance threshold of 0.05.

Results

Pre-pandemic IMD epidemiology (2017/18–2019/20)

In the three years leading up to the COVID-19 pandemic (2017/18, 2018/19 and 2019/20, April to March inclusive), 1864 IMD cases were confirmed in England. Annual IMD incidence declined from 1.33/100,000 in 2017/18 to 1.01/100,000 in 2018/19 and 0.98/100,000 in 2019/20 (mean annual incidence 1.11/100,000). In 2019/20, monthly IMD case numbers ranged from 23 (September) to 85 (December, Fig. 1).

MenB was the predominant capsular group prior to the introduction of COVID-19 restrictions, representing 57.2% (1066/1864) of IMD cases, followed by MenW (424/1864, 22.7%), MenY (197/1864, 10.6%) and MenC (143/1864, 7.7%) (Fig. 1).

There was a disproportionately high disease burden in younger age groups, with 35.5% (660/1860) of cases confirmed in 0–11 year-olds, and 18.4% (342/1860) among 12–24 year-olds. MenB was responsible for 76.5% (767/1002) of IMD cases in these younger age groups. Conversely, approximately two-thirds of IMD cases in adults aged ≥25 years were primarily caused by non-B groups, namely MenW (311/858, 36.2%), MenY (148/858, 17.2%), MenC (88/858, 10.3%) and other groups/non-groupable strains (14/858, 1.6%). The patient age was unknown for four cases which were excluded from this analysis.

During this pre-pandemic period, 9.0% (168/1864) of all IMD cases were fatal, comprising 5.8% (62/1066) of MenB cases, 14.0% (20/143) of MenC cases, 16.5% (70/424) of MenW cases and 7.6% (15/197) of MenY cases with a single fatal ungrouped case of 26 reported (3.8%). Overall mortality was 0.30 per 100,000 population per annum. Whilst the highest numbers of deaths occurred in those aged 65 years and older (19.1%, 78/408) then those aged 45–64 years (9.5%, 27/284), the highest mortality was seen among infants under 1 year of age at 1.73 deaths per 100,000 population, followed by those aged ≥65 years at 0.76 per 100,000 and 1–4-year-olds at 0.59 deaths per 100,000.

IMD in England following the introduction of COVID-19 restrictions

IMD during the first pandemic year (2020/21, April to March, inclusive)

In March 2020, the first national COVID-19 restrictions were introduced in England. During the following six months (April to September 2020), there was a 73% decline in the number of IMD cases in relation to the corresponding period of the previous year (Fig. 1). The low disease rates persisted into the winter months, with only 37 IMD cases confirmed between October 2020 and March 2021 (compared with 351 cases in the same period in 2019/20). Overall IMD incidence in England in 2020/21 was 0.16/100,000, with MenB representing 75.0% (69/92) of all IMD cases and very few MenW (n = 8), MenC (n = 7) or MenY (n = 4) cases.

During 2020/21, IMD reduced across all age groups with a 75.7% reduction in 0–11 years old, an 88.8% reduction in 12–24-year-olds and an 86.6% reduction among those aged ≥25 years (compared to 2019/20).

During this period, 12.0% (11/92) of all IMD cases were fatal comprising 11.6% (8/69) of MenB cases and 3 of 4 MenY cases with no fatalities in the remaining 19 cases of IMD. Overall mortality was low at 0.05 per 100,000 population per annum. There were five deaths in those aged 65 years and older (35.7%, 5/14), three deaths in infants under 1 year of age (14.3%, 3/21) and two further deaths in the remaining 57 cases.

IMD during the second pandemic year (2021/22, April to March, inclusive)

Between March and July 2021, the UK government gradually removed COVID-19 restrictions in England. During the first 5 months of 2021/22 (April to August 2021, inclusive), IMD figures remained

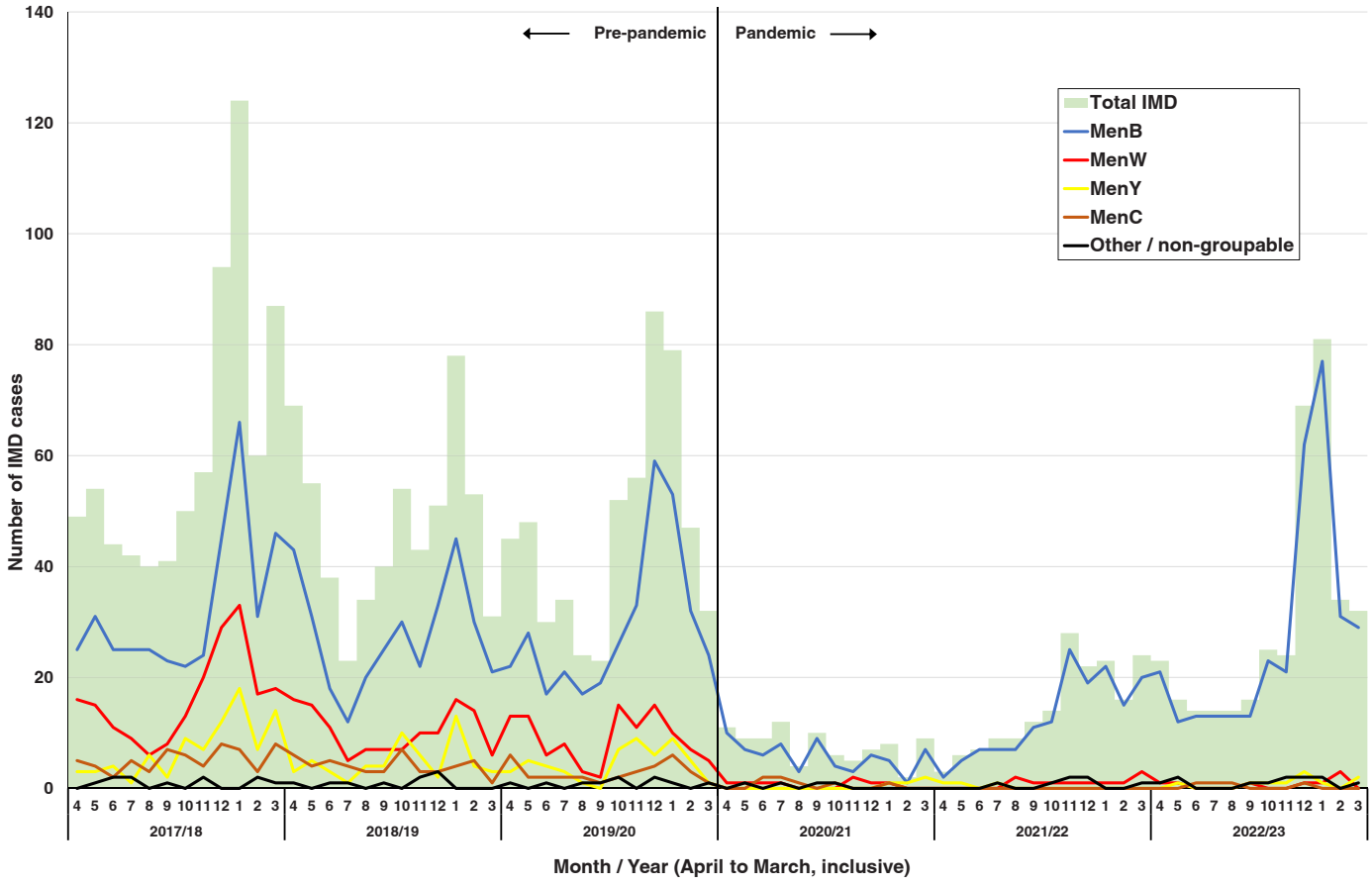

Fig. 1. Number of laboratory-confirmed English IMD cases per month: 2017/18–2022/23 (April to March, inclusive). Coloured lines represent the case numbers for each of the major capsular groups, and other/non-groupable cases are indicated in black. The green bars represent numbers of all IMD cases per month.

low with 34 cases, including 28 (82.4%) due to MenB strains (Fig. 1). MenB cases began to increase in September and October 2021, after removal of almost all social restrictions in July 2021, before a sharp rise in cases in November. The surge in IMD from September 2021 to March 2022 was primarily caused by MenB strains (124/139, 89.2%).

This re-emergence of IMD in 2021/22 was largely driven by cases in university age groups with 65 cases in those aged 18–24 years (37.6% of all IMD, 65/173). In comparison, the 18–24 age group saw only 9.8% (9/92) and 13.3% (248/1860) of all IMD cases in 2020/21 and the pre-pandemic period (2017/18–2019/20), respectively.

MenB disease among infants also increased with the number of cases almost doubling between 2020/21 and 2021/22 (18 cases vs. 33 cases, respectively). IMD in all other age groups remained similar to the preceding year (Fig. 2). Overall MenB IMD incidence increased from 0.12/100,000 to 0.27/100,000 between 2020/21 and 2021/22.

MenACWY IMD cases remained at a very low level across all ages in 2021/22 with only 12.1% of cases (n = 21/173) caused by non-B strains. Overall IMD incidence during 2021/22 was 0.31/100,000.

During the second pandemic year, 6.9% (12/173) of all IMD cases were fatal, comprising 6.6% (10/152) of MenB cases and single MenY and MenW fatalities in the remaining 19 cases of IMD. Overall mortality was low in 2020/21 at 0.02 per 100,000 population. There were four deaths in those aged 45–64 years (22.2%, 4/18), three deaths both in infants under 1 year of age (9.1%, 3/33) and those aged ≥65 years (18.8%, 3/16) with two further deaths in the remaining 106 cases.

IMD during the third pandemic year (2022/23, April to March, inclusive)

After the 2021/22 winter peak, IMD cases declined in line with expected seasonal changes and remained low during May-September 2022, with 14–16 monthly cases, almost all MenB (Fig. 1). From October 2022, a considerable increase in MenB disease was once again observed with monthly case numbers exceeding pre-pandemic levels in December 2022 (n = 62). January 2023 featured the highest number of monthly MenB IMD cases (n = 77) in England since 2012 (data not shown). Overall IMD incidence was 0.64/100,000 in 2022/23 and MenB incidence was 0.58/100,000.

MenACWY case numbers remained low and were responsible for only 5.8% (21/361) of all IMD cases, a reduction from 8.1% (14/172) in 2021/22. Most MenACWY cases occurred among ≥45-year-olds (n = 14/21, 66.7%), comprising five MenW, six MenY and three MenC cases. Conversely, only two MenW, four MenY and one MenC cases were confirmed in < 18-year-olds (Fig. 2). Twelve IMD cases in 2022/23 were caused by non-groupable/unencapsulated strains.

The patient age distribution among MenB cases changed in 2022/23 relative to the preceding year. Substantial increases in cases were observed in every age group except < 1 year-olds, where case numbers remained stable between 2021/22 and 2022/23 (33 and 32, respectively) (Fig. 2). In each of the adolescent and adult age groups (12 years or older), the number of MenB cases were higher in 2022/23 than at least one of the three pre-pandemic years (Fig. 2). MenB cases in those aged < 12 years remained lower in 2022/23 than all three pre-pandemic years (Fig. 2).

During the third pandemic year, 7.8% (28/361) of all IMD cases were fatal, comprising 6.7% (22/328) of MenB cases, 28.6% (2/7) of MenW cases and 20.0% (2/10) of MenY cases with two fatal ungrouped case of nine reported (22.2%). Overall mortality was 0.05 per 100,000 population per annum. There were 7 deaths in those aged ≥65 years (15.2%, 7/39) and in those aged 19–24 years (10.1%, 7/69) with the highest mortality again in infants under 1 year of age at

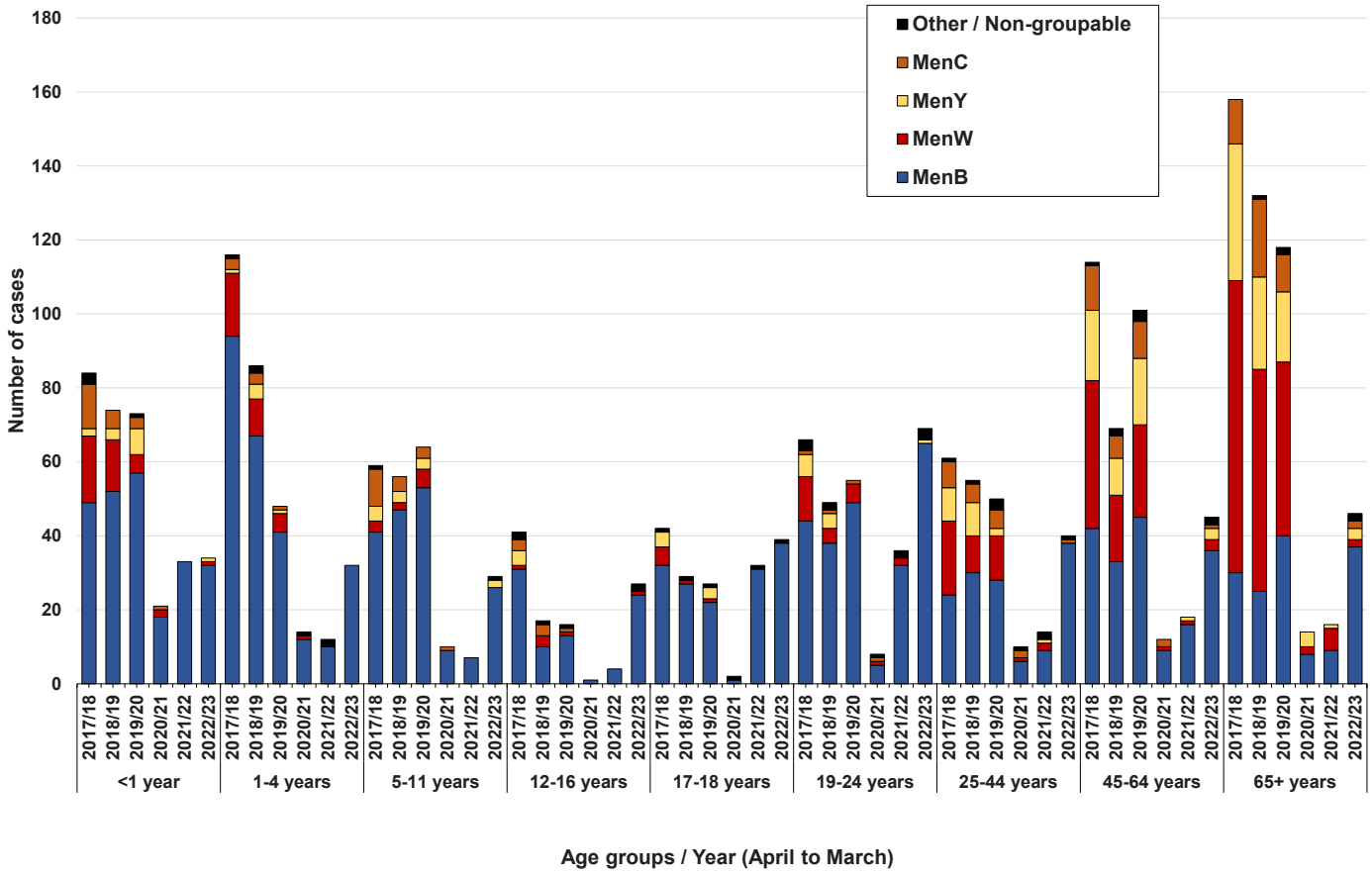

Fig. 2. English IMD cases by age group and year of confirmation (April to March, inclusive). Columns stratified by capsular group. Five cases (one from 2017/18, one from 2018/19, two from 2019/20 and one from 2021/22) were omitted due to lack of age data.

0.33 deaths per 100,000 population, followed by those aged 19–24 and 17–18 years at 0.17 and 0.16 per 100,000 respectively.

Strain characterisation

Between April 2017 and March 2023, 2490 English IMD cases were laboratory confirmed, including 1433 cases (57.6%) yielding a viable meningococcal isolate (751 MenB, 377 MenW, 173 MenY, 103 MenC and 29 other/non-groupable isolates). The remaining cases were confirmed by PCR only. The proportions of IMD cases confirmed by culture in the three pre-pandemic years ranged between 60.5% and 62.7%. During the pandemic years, the culture rate was comparatively lower with a range of 38.8% (2022/23) to 55.5% (2021/22).

Fig. 3 illustrates the CC distribution of MenB isolates received over the study period (23 isolates were omitted due to lack of genomic data, total n = 728). In almost all years, more than three quarters of the MenB isolates belonged to one of five major CC's, namely CC41/44, CC269, CC213, CC32 or CC461 (Fig. 3). The exception to this was the first pandemic year (2020/21) wherein a relatively high proportion of isolates (11/37, 29.7%) were singleton/unassigned or belonged to minor CCs (however the number of isolates for this year were low so this finding is unlikely to be significant). Other subtle variations were observed in the relative proportions of the major CCs, although no consistent changes were observed over the study period (Fig. 3).

To identify any strain changes beyond the CC level, the proportion of MenB isolates belonging to the most common STs (each represented by at least ten isolates) among the pre-pandemic (2017/18–2019/20) and pandemic (2020/21–2022/23) periods were calculated (Table 1). ST-485 (CC41/44) was the most common MenB ST overall and the proportion of isolates belonging to this ST doubled between the two periods (9.1–18.8%, p = 0.0004). The only other significant change occurred among ST-41 (CC41/44) strains, with the proportion of MenB isolates belonging to this sequence type reducing from 9.4% to 2.8% between the two periods (p = 0.0016).

Among non-MenB isolates, 93.6% (351/375) of MenW strains with available MLST data, including all 14 isolates since the beginning of the pandemic, belonged to CC11. Similarly, 86.4% (89/103) of MenC isolates belonged to CC11, while 90.1% (154/171) of MenY isolates belonged to CC23. No notable phylogenetic changes in these strains were observed over the study period, although isolate numbers in the pandemic years were low.

Discussion

COVID-19 mitigation measures, although variable in nature and timing across different countries, were associated with large and significant declines in the incidence of viral and bacterial respiratory diseases worldwide.[8] In England, a 73% reduction in IMD was observed in the months following the first national lockdown in March 2020, similar to reductions observed in other European countries.[14,15] Throughout 2020, national and local restrictions were implemented intermittently and guidance on precautionary behaviours (e.g. wearing of masks, social distancing etc.) was in place. The removal of the final restrictions occurred in July 2021 and, from November 2021, after students had returned to fulltime education, a substantial increase in MenB disease was observed, mainly in older teenagers and young adults. This age-specific pattern is most likely due to the traditionally higher rates of meningococcal carriage in

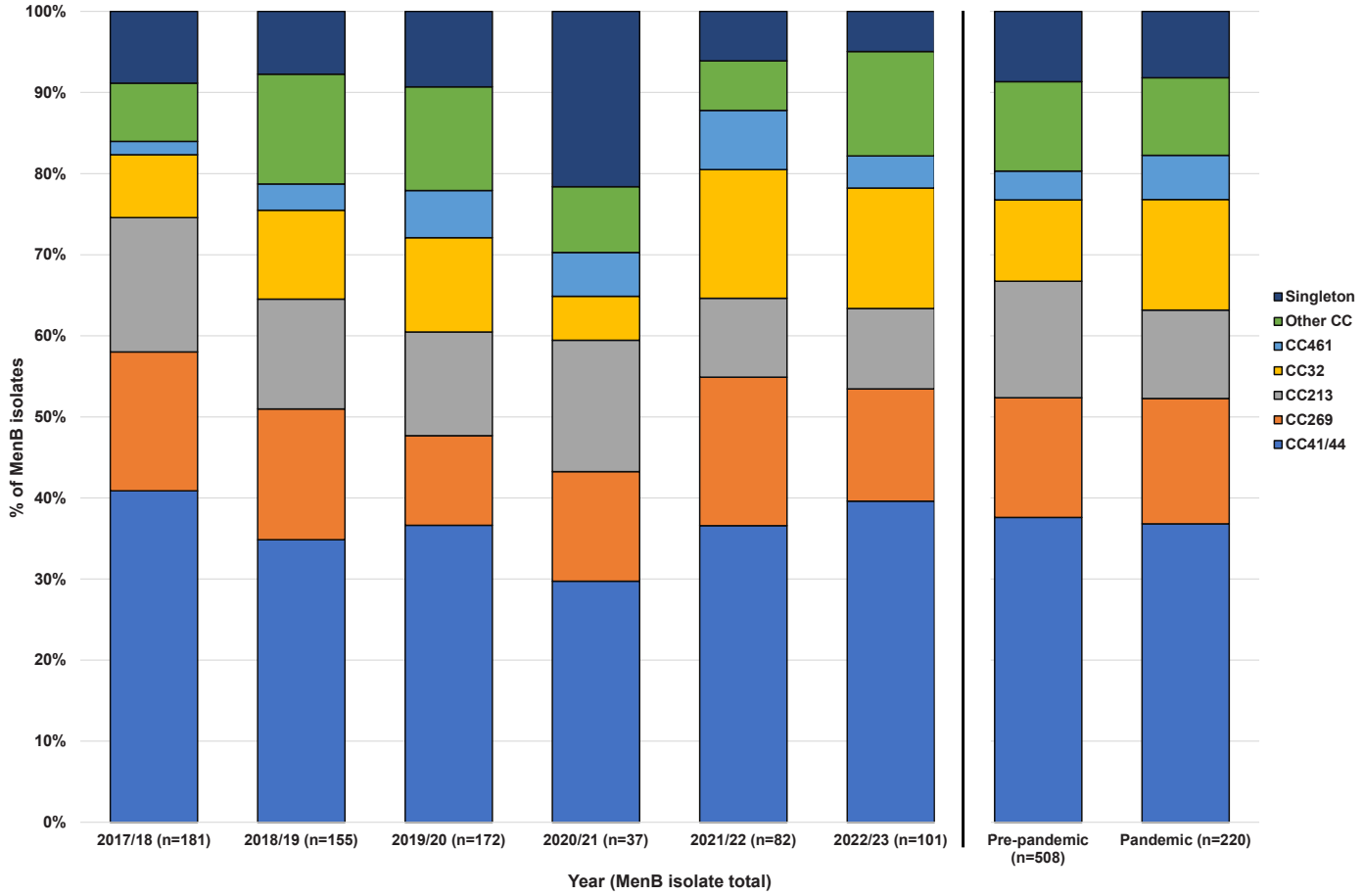

Fig. 3. Clonal complex distribution among English MenB isolates (n = 728): 2017/18–2022/23 (April and March, inclusive) and cumulative values for pre-pandemic (2017/18–2019/20) and pandemic (2021/22–2022/23) periods. Twenty-three MenB isolates from 2022/23 (18.5% of yearly total) were omitted due to lack of genomic data.

this population.[16] Specific behaviours commonly observed in this age group are associated with meningococcal transmission, and the sharing of university accommodation has been shown to increase IMD risk by more than 10-fold compared to age-matched non-students.[17,18] Consequently, in 2021/22, the commencement of higher education with little or no public health restrictions, involving the mixing of students from different parts of the country, will have contributed to the spike in MenB cases. Conversely, the low levels of IMD in older age groups in 2021/22 could reflect low levels of intergenerational mixing/transmission over this first year despite the removal of mandatory pandemic restrictions.

Interestingly, whilst the increase in MenB cases during 2021/22 occurred mainly in teenagers and young adults, the second winter period following easing of containment measures (2022/23) saw MenB cases increase across almost all age groups, except young children, most of whom had received 4CMenB as part of the national infant immunisation programme.[3] This pattern suggests a spread of invasive MenB strains from adolescents/young adults to other age groups over the preceding year. A similar pattern was observed with invasive pneumococcal disease where the first increase after easing of pandemic restrictions was observed in toddlers, who are the main nasopharyngeal carriers of pneumococci, followed by increases in older children and adults.[19] It is also important to note the possible influence of respiratory viral diseases which are known to be a preceding risk factor for IMD.[20] Indeed, a substantially higher level of influenza activity was reported in England in the final weeks of 2022 (relative to the preceding two years), which may have contributed to the corresponding sharp increase in IMD over this period, especially in older adults.[21]

An analysis of invasive MenB isolates obtained over the study period illustrates a reasonably stable picture with five major cc's continuing to predominate, however, significant shifts were observed in the proportion of cases caused by ST-485 and ST-41 (CC41/44) strains. The cause of these changes is unclear but the proportion of cases caused by ST-485 has been gradually increasing in England since 2010, and this strain has caused community-based outbreaks and clusters in England in recent years.[22]

Despite the increase in MenB disease, no corresponding increase in MenACWY disease was observed over the two years following the easing of restrictions. The most likely explanation is the ongoing protection afforded by the highly successful adolescent MenACWY conjugate vaccine programme. This vaccine was introduced into the UK national immunisation schedule in 2015 with high vaccine uptake of 71–86% obtained among 13–14 year-olds through the schools-based national immunisation programme.[23] Recent carriage surveys have demonstrated a reduction of MenACWY carriage in adolescent vaccinees following introduction of this vaccine.[24] The very low rates of MenACWY disease across all age groups clearly demonstrate the effectiveness of the vaccine at not only protecting adolescent vaccinees against the disease directly but also providing herd protection to other age groups by reducing carriage and onward transmission of MenACWY strains.

It is difficult to predict whether MenACWY disease rates will remain low in the future, especially after the disruption to school-based vaccine programmes observed during the pandemic when support for the national COVID-19 vaccination programme was prioritised. Recent mathematical modelling of the impact of MenACWY conjugate vaccination and the COVID-19 pandemic on

Table 1
Numbers of English MenB isolates belonging to the predominant STs (each represented by at least 10 isolates) in the pre-pandemic (2017/18–2019/20) and pandemic (2020/21–2022/23) periods. Seven isolates that were included in the CC analysis (two from 2021/22 and five from 2022/23) were omitted from the ST analysis due to incomplete MLST loci data.

Sequence type (clonal complex)	MenB isolates, n (% of period)		
	Pre-pandemic	Pandemic	Whole period
485 (CC41/44)	46 (9.1)	40 (18.8)	86 (11.9)
213 (CC213)	40 (7.9)	15 (7.0)	55 (7.6)
41 (CC41/44)	48 (9.4)	6 (2.8)	54 (7.5)
1161 (CC269)	21 (4.1)	16 (7.5)	37 (5.1)
1194 (CC41/44)	16 (3.1)	4 (1.9)	20 (2.8)
33 (CC32)	11 (2.2)	7 (3.3)	18 (2.5)
269 (CC269)	12 (2.4)	3 (1.4)	15 (2.1)
2314 (C41/44)	12 (2.4)	3 (1.4)	15 (2.1)
7460 (CC32)	6 (1.2)	8 (3.8)	14 (1.9)
275 (CC269)	10 (2.0)	1 (0.5)	11 (1.5)
1157 (CC1157)	8 (1.6)	3 (1.4)	11 (1.5)
1946 (CC461)	5 (1.0)	6 (2.8)	11 (1.5)
Other	273 (53.7)	101 (47.4)	374 (51.9)
Total	**508**	**213**	**721**

MenACWY strains in the UK has predicted that the suppressive impact on carriage would persist until at least 2025.[25] In the meantime, efforts are being made to catch up and improve adolescent immunisation uptake, especially in school-based programmes, but on-going surveillance will be important to monitor trends in serogroup-specific IMD in the coming years.

The key strength of this study was the use of data from comprehensive national surveillance linked to a national reference laboratory that provides free PCR confirmation and characterisation of invasive meningococcal isolates. Electronic linkage of national laboratory notifications with MRU data alongside the high rates of electronic surveillance questionnaire completion by UKHSA Health Protection Teams ensures high case ascertainment with detailed information for each individual case. Limitations include the limited strain characterisation in PCR-confirmed cases which constitute approximately one half of the confirmed IMD cases in England. Another limitation is the restricted scope of the surveillance questionnaire, although this was purposefully designed to be brief to ensure high completion rates and collect as much data as possible on underlying conditions, clinical presentation, disease severity and outcomes.

To conclude, MenB case numbers have recovered swiftly following the removal of COVID-19 containment measures in England, initially in adolescents and young adults, who are the main meningococcal carriers, and then across all age groups, reflecting the continuing transmission of MenB across the population. Reassuringly, there were fewer MenB cases in young children than prior to the pandemic due to the protection afforded by the national MenB infant immunisation programme, and cases caused by the other vaccine-preventable serogroups remain at a very low level because of the ongoing effectiveness of the adolescent MenACWY conjugate vaccine programme.

Funding source

This study was funded by the UK Health Security Agency as part of ongoing national surveillance.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: AL, AW, JL, LWa, LWi, RB, SAC and XB perform contract research on behalf of UK Health Security Agency for GlaxoSmithKline, Pfizer, and Sanofi Pasteur but receive no personal remuneration. SNL performs contract research on behalf of UK Health Security Agency and St. George's University of London for vaccine manufacturers but receives no personal remuneration.

Acknowledgements

The authors would like to thank all NHS and UKHSA staff who through their hard work contribute to national meningococcal surveillance.

References

1. Pace D, Pollard AJ. *Meningococcal disease: clinical presentation and sequelae. Vaccine* 2012;**30**(Suppl.2):B3–9. https://doi.org/10.1016/j.vaccine.2011.12.062
2. Borrow R, Abad R, Trotter C, van der Klis FRM, Vazquez JA. *Effectiveness of meningococcal serogroup C vaccine programmes. Vaccine* 2013;**31**:4477–86. https://doi.org/10.1016/j.vaccine.2013.07.083
3. Ladhani SN, Campbell H, Parikh SR, Saliba V, Borrow R, Ramsay M. *The introduction of the meningococcal B (MenB) vaccine (Bexsero®) into the national infant immunisation programme – new challenges for public health. J Infect* 2015;**71**:611–4. https://doi.org/10.1016/j.jinf.2015.09.035
4. Parikh SR, Campbell H, Bettinger JA, Harrison LH, Marshall HS, Martinon-Torres F, et al. *The everchanging epidemiology of meningococcal disease worldwide and the potential for prevention through vaccination. J Infect* 2020;**81**:483–98. https://doi.org/10.1016/j.jinf.2020.05.079
5. Lucidarme J, Hill DMC, Bratcher HB, Gray SJ, du Plessis M, Tsang RSW, et al. *Genomic resolution of an aggressive, widespread, diverse and expanding meningococcal serogroup B, C and W lineage. J Infect* 2015;**71**:544–52. https://doi.org/10.1016/j.jinf.2015.07.007
6. Campbell H, Andrews N, Parikh SR, White J, Edelstein M, Bai X, et al. *Impact of an adolescent meningococcal ACWY immunisation programme to control a national outbreak of group W meningococcal disease in England: a national surveillance and modelling study. Lancet Child Adolesc Health* 2022;**6**:96–105. https://doi.org/10.1016/S2352-4642(21)00335-7
7. Subbarao S, Campbell H, Ribeiro S, Clark SA, Lucidarme J, Ramsay M, et al. *Invasive meningococcal disease, 2011-2020, and Impact of the COVID-19 Pandemic, England. Emerg Infect Dis* 2021;**27**:2495–7. https://doi.org/10.3201/eid2709.204866
8. Brueggemann AB, Jansen van Rensburg MJ, Shaw D, McCarthy ND, Jolley KA, Maiden MCJ, et al. *Changes in the incidence of invasive disease due to Streptococcus pneumoniae, Haemophilus influenzae, and Neisseria meningitidis during the COVID-19 pandemic in 26 countries and territories in the Invasive Respiratory Infection Surveillance. Lancet Digit Heal* 2021;**3**:e360–70. https://doi.org/10.1016/S2589-7500(21)00077-7
9. Gray SJ, Trotter CL, Ramsay ME, Guiver M, Fox AJ, Borrow R, et al. *Epidemiology of meningococcal disease in England and Wales 1993/94 to 2003/04: contribution and experiences of the Meningococcal Reference Unit. J Med Microbiol* 2006;**55**:887–96. https://doi.org/10.1099/jmm.0.46288-0
10. Brehony C, Hill DM, Lucidarme J, Borrow R, Maiden MC. *Meningococcal vaccine antigen diversity in global databases. Eurosurveillance* 2015;**20**:1–9. https://doi.org/10.2807/1560-7917.ES.2015.20.49.30084
11. Jolley KA, Bray JE, Maiden MCJ. *Open-access bacterial population genomics: BIGSdb software, the PubMLST.org website and their applications. Wellcome Open Res* 2018;**3**:1–20. https://doi.org/10.12688/wellcomeopenres.14826.1
12. Corless CE, Guiver M, Borrow R, Edwards-Jones V, Fox AJ, Kaczmarski EB. *Simultaneous detection of Neisseria meningitidis, Haemophilus influenzae, and Streptococcus pneumoniae in suspected cases of meningitis and septicemia using real-time PCR. J Clin Microbiol* 2001;**39**:1553–8. https://doi.org/10.1128/JCM.39.4.1553
13. Office for National Statistics: estimates of the population for the UK, England, Wales, Scotland and Northern Ireland; 2022.
14. Steens A, Knol MJ, Freudenburg-De Graaf W, de Melker HE, van der Ende A, van Sorge NM. *Pathogen-and type-specific changes in invasive bacterial disease epidemiology during the first year of the COVID-19 pandemic in The Netherlands. Microorganisms* 2022;**10**(5):972. https://doi.org/10.3390/microorganisms10050972
15. Deghmane AE, Taha MK. *Changes in invasive Neisseria meningitidis and Haemophilus influenzae infections in France during the COVID-19 pandemic. Microorganisms* 2022;**10**(5):907. https://doi.org/10.3390/microorganisms10050907
16. Christensen H, May M, Bowen L, Hickman M, Trotter CL. *Meningococcal carriage by age: a systematic review and meta-analysis. Lancet Infect Dis* 2010;**10**:853–61. https://doi.org/10.1016/S1473-3099(10)70251-6
17. MacLennan J, Kafatos G, Neal K, Andrews N, Cameron JC, Roberts R, et al. *Social behavior and meningococcal carriage in British teenagers. Emerg Infect Dis* 2006;**12**:950–7.
18. Mandal S, Campbell H, Ribeiro S, Gray S, Carr T, White J, et al. *Risk of invasive meningococcal disease in university students in England and optimal strategies for protection using MenACWY vaccine. Vaccine* 2017;**35**:5814–8.
19. Bertran M, Amin-Chowdhury Z, Sheppard CL, Eletu S, Zamarreño DV, Ramsay ME, et al. *Increased incidence of invasive pneumococcal disease among children after COVID-19 pandemic, England. Emerg Infect Dis* 2022;**28**:1669–72. https://doi.org/10.3201/eid2808.220304

20. Jacobs JH, Viboud C, Tchetgen ET, Schwartz J, Steiner C, Simonsen L, et al. *The association of meningococcal disease with influenza in the united states, 1989-2009. PLoS One* 2014;**9**:1–8. https://doi.org/10.1371/journal.pone.0107486
21. UK Health Security Agency. Official Statistics Surveillance of influenza and other seasonal respiratory viruses in the UK, winter 2022 to 2023. UK Gov Off Stat; 2022. ⟨https://www.gov.uk/government/statistics/annual-flu-reports/surveillance-of-influenza-and-other-seasonal-respiratory-viruses-in-the-uk-winter-2022-to-2023⟩.
22. Clark SA, Lucidarme J, Lekshmi A, Walsh L, Willerton L, Walker A, et al. The expansion of a group B invasive meningococcal ST-485 (ST-41/44 clonal complex) strain in England: 2010–2022. 16th Congr. Eur. Meningococcal Haemophilus Dis. Soc., Dubrovnik, Croatia; 2023, p. 15–15.
23. Campbell H, Andrews N, Parikh SR, White J, Edelstein M, Bai X, et al. *Impact of an adolescent meningococcal ACWY immunisation programme to control a national outbreak of group W meningococcal disease in England: a national surveillance and modelling study. Lancet Child Adolesc Health* 2022;**6**:96–105.
24. Carr JP, MacLennan JM, Plested E, Bratcher HB, Harrison OB, Aley PK, et al. *Impact of meningococcal ACWY conjugate vaccines on pharyngeal carriage in adolescents: evidence for herd protection from the UK MenACWY programme. Clin Microbiol Infect* 2022;**28**(12):1649.e1–8. https://doi.org/10.1016/j.cmi.2022.07.004
25. Hadley L, Karachaliou Prasinou A, Christensen H, Ramsay ME, Trotter C. *Modelling the impact of COVID-19 on meningococcal carriage and disease in the UK. Epidemiol Infect* 2023;**151**:1–9. https://doi.org/10.2139/ssrn.3889421