Changes in invasive meningococcal disease in England before and after the first Covid-19 lockdown

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INTRODUCTION

- Rapid increase in the incidence of Covid-19 in February 2020 prompted the UK government to implement the first national lockdown in late March 2020 to reduce its transmission leading to a dramatic, almost immediate reduction in Invasive meningococcal disease (IMD) to a record low synonymous with other respiratory pathogens including *Streptococcus pneumoniae*.[1]
- We analysed the epidemiological and strain characteristics of cases in England in the three years prior to the COVID-19 pandemic, and during the first three pandemic years. During this period COVID control measures were implemented at differing levels from March 2020 before being finally withdrawn in July 2021.

METHODS

- IMD cases were confirmed by the UK Health Security Agency (UKHSA) Meningococcal Reference Unit (MRU) between April 2017 and March 2023, inclusive. Additional information was gathered as part of enhanced surveillance by the UKHSA Immunisation and Countermeasures Division. Annual data are presented from 1 April to 31 March..
- All isolates underwent phenotypic characterisation and whole genome sequence analysis using the Illumina platform. Draft genome sequences were deposited and interrogated on the PubMLST *Neisseria* database. PCR-only confirmed cases underwent genogrouping using Taqman real-time PCR assays .
- Indexed multilocus sequence typing (MLST) data were analysed. Isolates with incomplete/partial MLST allelic profiles were assigned clonal complex (CC) but omitted from Sequence Type (ST) analysis. Twenty-seven 2022/23 isolates were omitted from ST analyses as genomic data were unavailable.

RESULTS

- The number of IMD cases confirmed in England was 1864 from April 2017 to March 2020 and 626 from April 2020 to March 2023 with MenB remaining the predominant capsular group. Overall case fatality was 9.0% and 8.1% respectively. Highest mortality was observed among infants (<1 year of age).

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

- MenB was responsible for n=1066 (57.2%) cases (**Fig. 1**), with highest burden of disease in 0 to 11 year-olds (35.5%) followed by 18.4% among 12 to 24 year-olds **(Fig. 2).**
- Predominant capsular groups among the remaining 857 cases in adults aged ≥25 years were 36.2% MenW, 17.2% MenY, 10.3% MenC and 1.6% other groups/non-groupable strains (**Fig 2**).

IMD in England during national lockdown/COVID-19 restrictions

- An overall decline of 83.4% of IMD was observed across all age groups during 2020/21 compared to 2019/20 with 75.7% reduction in 0 to11 years old, 88.8% reduction in 12 to 24-year-olds and 86.6% reduction in ≥25 years olds. However, case fatality increased to 12% (11/92) with 75% (3/4) of MenY and 11.6% (8/69) of MenB cases being fatal.
- April to September 2020 saw 73% decline in IMD cases compared to preceding year with lower positivity rates in submitted samples[2]. There was 89.5% decline in cases confirmed between October 2020 and March 2021 compared to corresponding previous years (**Fig 1**).

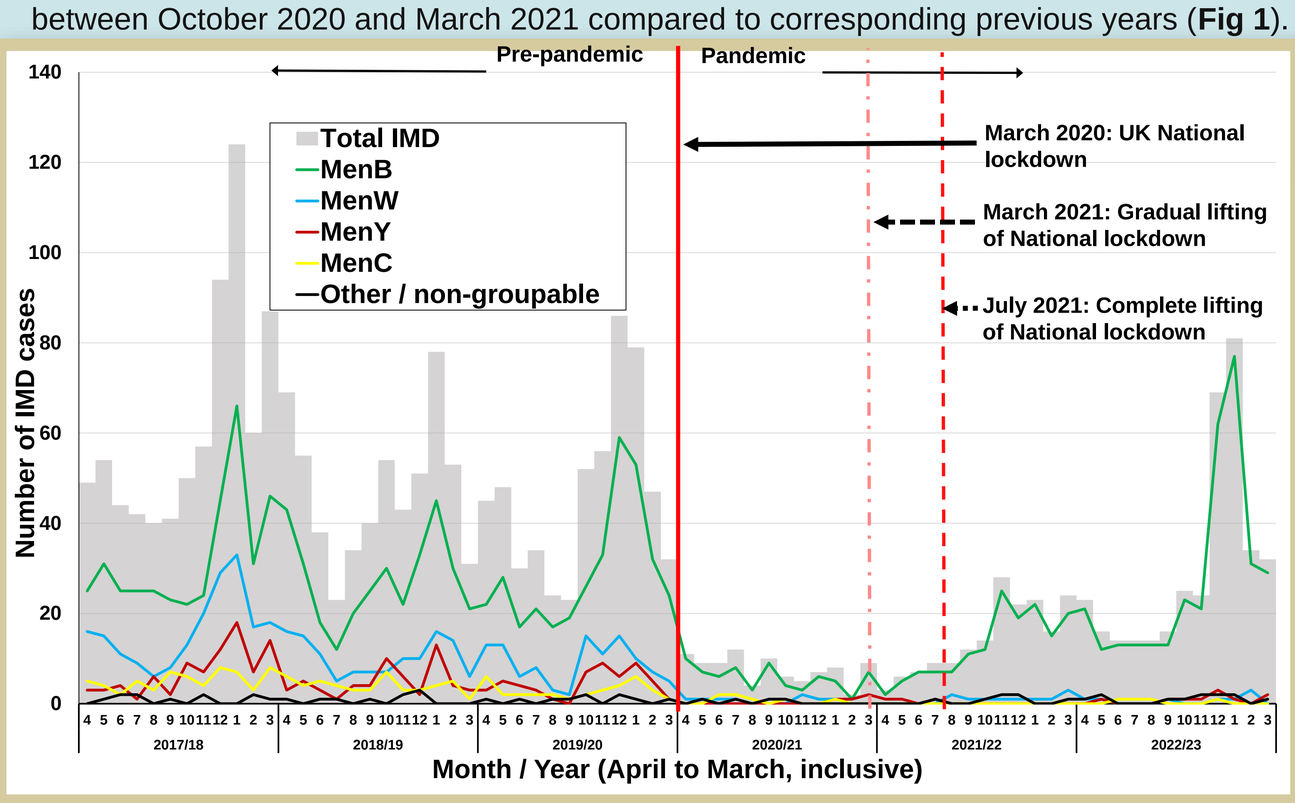

Figure 1. Number of laboratory-confirmed English IMD cases per month: 2017/18–2022/23. Coloured lines represent the case numbers for each of the major capsular groups, and black line shows other/non-groupable cases. Grey bars represent numbers of all IMD cases per month.

IMD in England during gradual to complete lifting of COVID-19 restrictions

- IMD cases remained low until August 2021 (**Fig. 2**). A sharp surge in IMD was recorded from September 2021 to March 2022, largely due to MenB strains. This was mostly driven by 37.6% of cases in university age groups (18 to 24 years). MenB disease among infants almost doubled between 2020/21 and 2021/22 (18 cases vs. 33 cases, respectively). ACYW cases remained very low accounting for 8.1% of all IMD.
- Total IMD cases rose to 361 in 2022/23 peaking October 2022. January 2023 had the highest number of monthly MenB IMD cases in England since 2012. The proportion of MenCWY cases was 5.8%.
- A substantial increase in cases was observed in all age groups except <1 year-olds among MenB cases in 2022/23 relative to the preceding year-**(Fig. 2**). Cases in those aged <12 years remained lower in 2022/23 than all three pre-pandemic years.

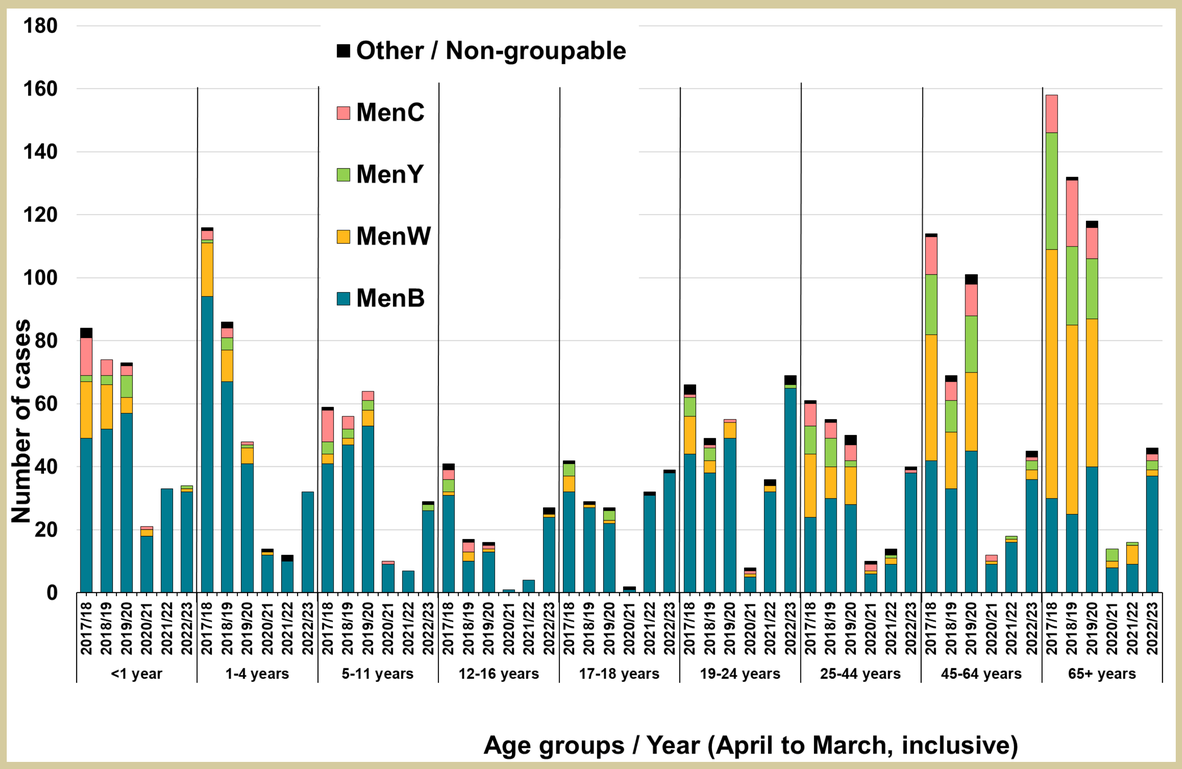

Figure 2. English IMD cases by age group and year of confirmation. Columns stratified by capsular group. Five cases (one from 2017/18, one from 2018/19, two from 2019/20 and one from 2021/22) were omitted due to lack of age data

MLST analysis

- Among all 2490 English IMD cases there was a culture rate of 57.6%. Relatively lower culture rates were observed during 2020/21 & 2021/22 (~55%) and 2022/23 (38.8%) versus >60% during the three pre-pandemic years.
- CC analysis: eight isolates; three from 2021/22 and five from 2022/23 had incomplete/partial MLST allelic profiles. >75% of the MenB isolates belonged to one of five major CC's, (CC41/44, CC269, CC213, CC32 or CC461). In all years except during 2020/21 29.7% isolates were singletons/ unassigned or belonged to minor CCs. (Fig. 3).
- ST analysis: Isolates belonging to ST-485 (CC41/44) doubled between the two periods (9.1–18.8%, p = 0.0004). MenB isolates belonging to ST-41 (CC41/44) reduced from 9.4% to 2.8% (p = 0.0016).

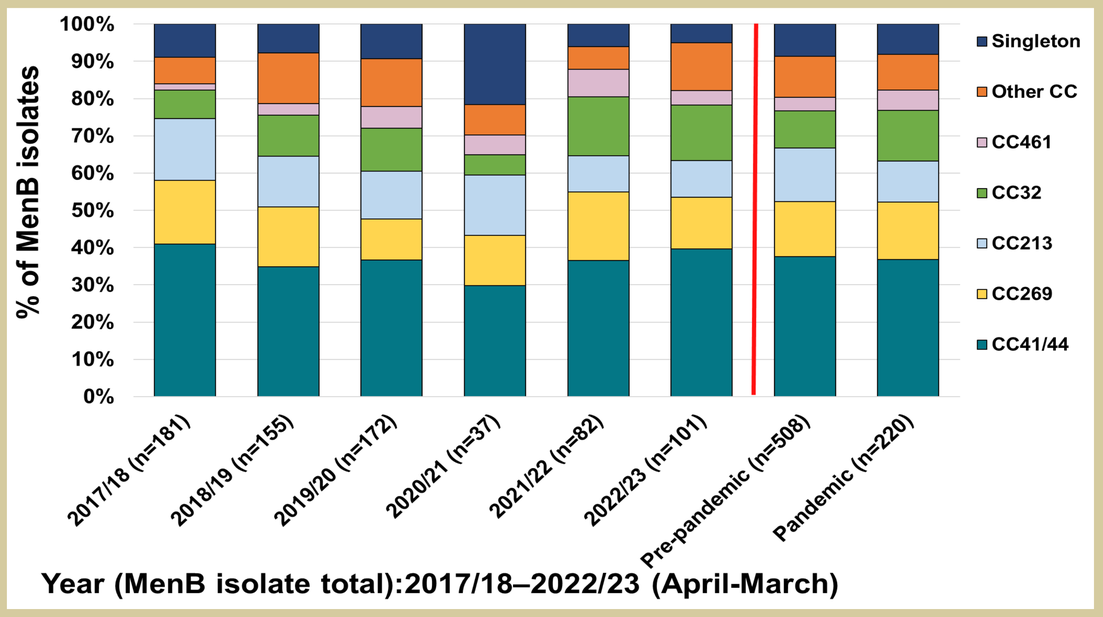

Figure 3. CC distribution among English MenB isolates (n = 728): cumulative values for pre-pandemic (2017/18–2019/20) and pandemic (2021/22–2022/23) periods. 23 MenB isolates from 2022/23 (18.5% of yearly total) were omitted due to lack of genomic data.

DISCUSSION & CONCLUSIONS

- **The initial increase in IMD post-restrictions was seen in university age groups (19-22 years) with the return of students to full time education. This may be expected with these being the peak ages for meningococcal carriage.**
- **IMD in older age groups in 2021/22 remained low which may reflect low levels of intergenerational mixing/transmission during that period.**
- **In 2022/23 MenB cases reached levels exceeding those pre-pandemic in all age groups other than those aged <12 years. Children up to 8 years would have been offered 4CMenB vaccine.**
- **Men ACWY cases remained low, likely due to the teenage MenACWY vaccination programme exerting good control.**
- **Close monitoring and catch-up programmes are required to minimise the effects of disruption of vaccination programmes observed during the pandemic**
- **Sub-strain fluctuations require continued surveillance as significant change in case numbers were observed in ST's associated with community-based outbreaks.**

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