

**Genomic surveillance and meningococcal group B vaccine coverage estimates after introduction of the vaccine into the national immunisation programme in the UK**

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**Background** In September, 2015, the meningococcal group B vaccine (Bexsero, GlaxoSmithKline) was introduced into the UK childhood immunisation schedule. Prelicensure coverage estimates used Meningococcal Antigen Typing System (MATS) to determine phenotype and function of circulating meningococci. Using whole-genome sequencing, we aimed to perform rapid, scalable, high-resolution analysis of peptide vaccine antigens in disease-causing meningococci before and after vaccine implementation.

**Methods** All culture-confirmed invasive meningococcal disease isolates from July 1, 2010, to June 30, 2016, from the UK underwent whole-genome sequencing (n=2994), representing 56·7% of cases reported to Public Health England. Genomes were hosted on the PubMLST database. The Bexsero Antigen Sequence Type (BAST) scheme was used to catalogue antigenic variants for comparison with the Bexsero type, BAST-1 (fHbp:1, NHBA:2, NadA:8, PorA VR1:7-2, PorA VR2:4). Statistical analysis was performed with R software (v3.2.4).

**Findings** Complete BASTs were obtained for 2915 isolates (97·4%). Within the fHbp family 1, variant 1 was only present in 105 (3·5%) of 2994 isolates. Variant 4 dominated since 2010–11 in BASTs 220, 226, and 229. From 2013–14 onwards, family 2 variants were more frequent than family 1 variants. NHBA variant 2 decreased from 373 (15·3%) of 2441 prevaccine isolates to 45 (9·4%) of 479 postvaccine (p=0·001). The most common variant was 29 (557/2994). NadA was absent in 2049 (70·1%) of 2921 isolates. PorA VR2 had 106 variants, most frequently variants 2 (n=542), 9 (350), and 4 (333). Genotypic matches to BAST-1 (≥1 antigen) decreased from 30·4% (167/550) to 15·5%

(83/536) over a 6 year period. Coverage including cross-reactive antigens was 60·2–69·0%. Genotype–phenotype modelling estimated coverage of 62·1% (95% CI 60·9–63·3), with no significant change before or after vaccine implementation.

**Interpretation** Recent clonal expansion of South American/UK serogroup W strain accounts for many antigenic changes, such as the increase in family 2 fHbp and NHBA variant 29. Cross-reactivity within the fHbp family 1 is a key determinant of vaccine immunogenicity. MATS coverage estimates of 73% (95% CI 57–87) were key to policy decisions for introduction of the vaccine in the UK. Analysis of recent disease isolates with genomic and genotype–phenotype correlations suggests that coverage estimates are lower but within the limits of previous MATS studies.

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### **Contributors**

MM and ERM were involved in conceptualisation and supervision of the study design. CR led this investigation and analysis and drafted the abstract. All authors reviewed the final abstract. CB originally set up the methodology and validation. Data were collected in laboratories in England, Wales, and Northern Ireland (RB); Scotland (AS); and Ireland (RC).

### **Declaration of interests**

MM has received grants and personal fees from Novartis outside the submitted work. ERM is a scientific adviser to GlaxoSmithKline and a member of the Scientific Advisory Board of LimmaTech Biologics AG, Zurich. All other authors declare no competing interests.