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Genomic surveillance of meningococcal capsular group B vaccine antigens in United Kingdom disease isolates, 2010 to 2016

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Background: The incidence of invasive meningococcal disease (IMD) is higher in the UK and Ireland compared to continental Europe or North America. In the UK, the epidemiology of endemic IMD is dynamic and due to multiple clonal complexes (cc), predominantly expressing capsular group B. In September 2015, 4CMenB vaccine, Bexsero®, was introduced into the UK immunisation schedule for infants at 2, 4, and 12 months of age. A novel nomenclature, Bexsero Antigen Sequence Type (BAST), was developed for describing Bexsero® vaccine antigens in meningococcal whole genome sequences (WGS). This study reports the prevalence of BASTs across six epidemiological years in the UK.

Material/methods: All culture-confirmed IMD cases from the UK between 2010/11 to 2015/16 (n=3010) underwent whole genome sequencing. The WGS were publicly-available on pubMLST.org/neisseria website. BASTs were analysed using the Bacterial Isolates Genome Database (BIGSdb) and embedded tools. Statistical analyses were performed using R v3.2.4. BAST describes genotypic variants and does not provide information on gene expression or cross-protection.

Results: Between 2010/11 and 2015/16, the studied IMD WGS included 31 cc (as described by multilocus sequence typing) and 800 BASTs, 21 BASTs accounted for 53.5% of isolates (1502/2808). When comparing 2010/11-2014/15 (pre-implementation) to 2015/16 (post-implementation of Bexsero), there were significant increases in BAST-2 ($p<0.00001$), BAST-221 ($p=0.02$), and BAST-8 ($p=0.002$) and decrease in BAST-220 ($p=0.02$). There were 0.27 BASTs/isolate across the whole study period, which fell from 0.42 in 2010/11 to 0.28 in 2015/16.

Conclusions: Despite the diversity represented by 800 BASTs, few occurred at high frequency. In common with previous studies, BASTs were strongly associated with cc. As such, secular changes in

cc led to increases in BAST-2 (W:cc11 South American/UK strain), BAST-221 (Y:cc23) and BAST-8 (C:cc11) and decrease in BAST-220 (B:cc41/44). The diversity represented by 0.27 BASTs/isolate was lower than other contemporaneous studies, however for these vaccines to be effective, either (i) one of the multiple antigens must be immunogenic or (ii) cross-reactivity must be a significant contributory factor in inducing host protection.