



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

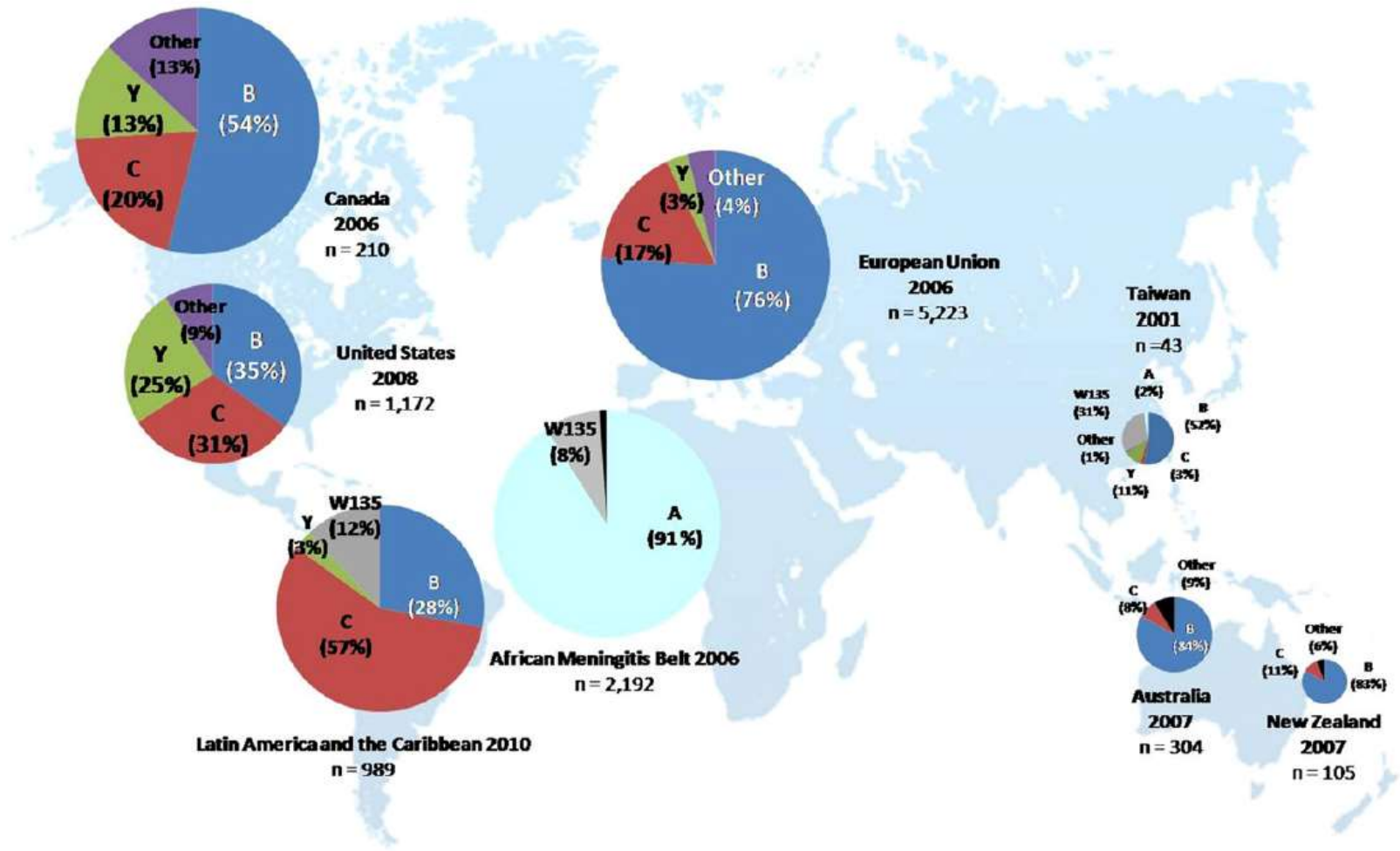
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Wellcome Trust Clinical Research Fellow, University of Oxford

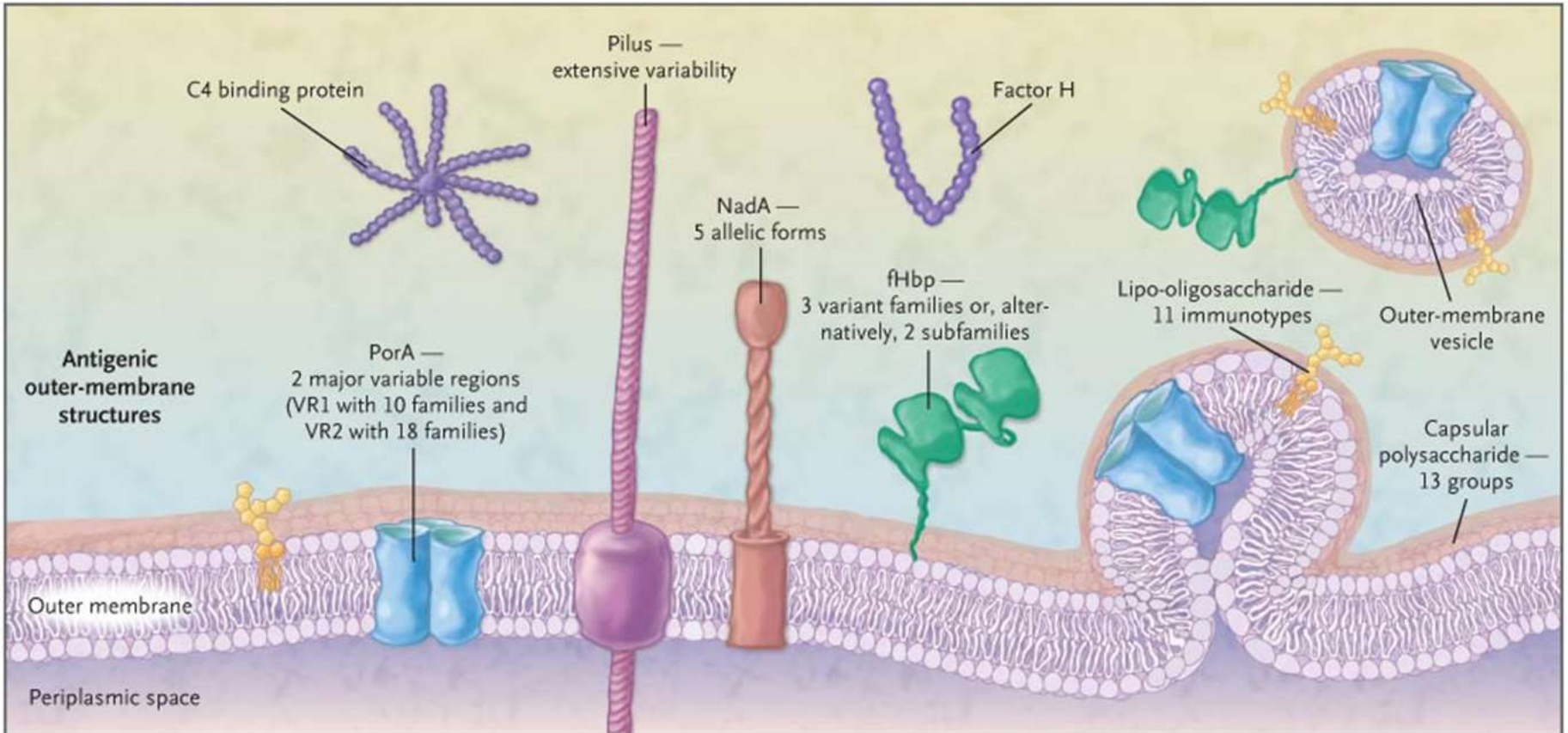
Paediatric Infectious Diseases, Immunology and Allergy Grid trainee, Great North Children's Hospital



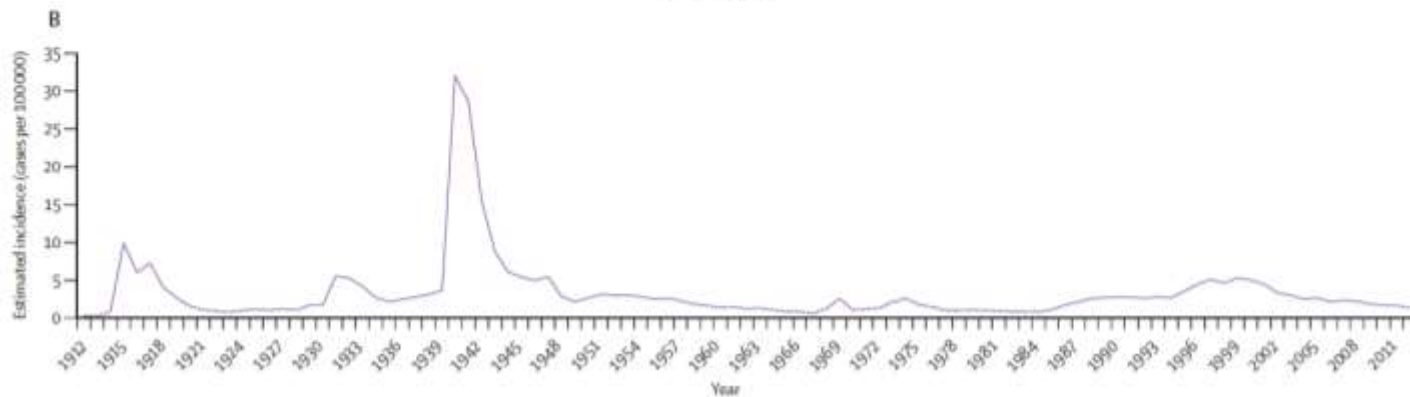
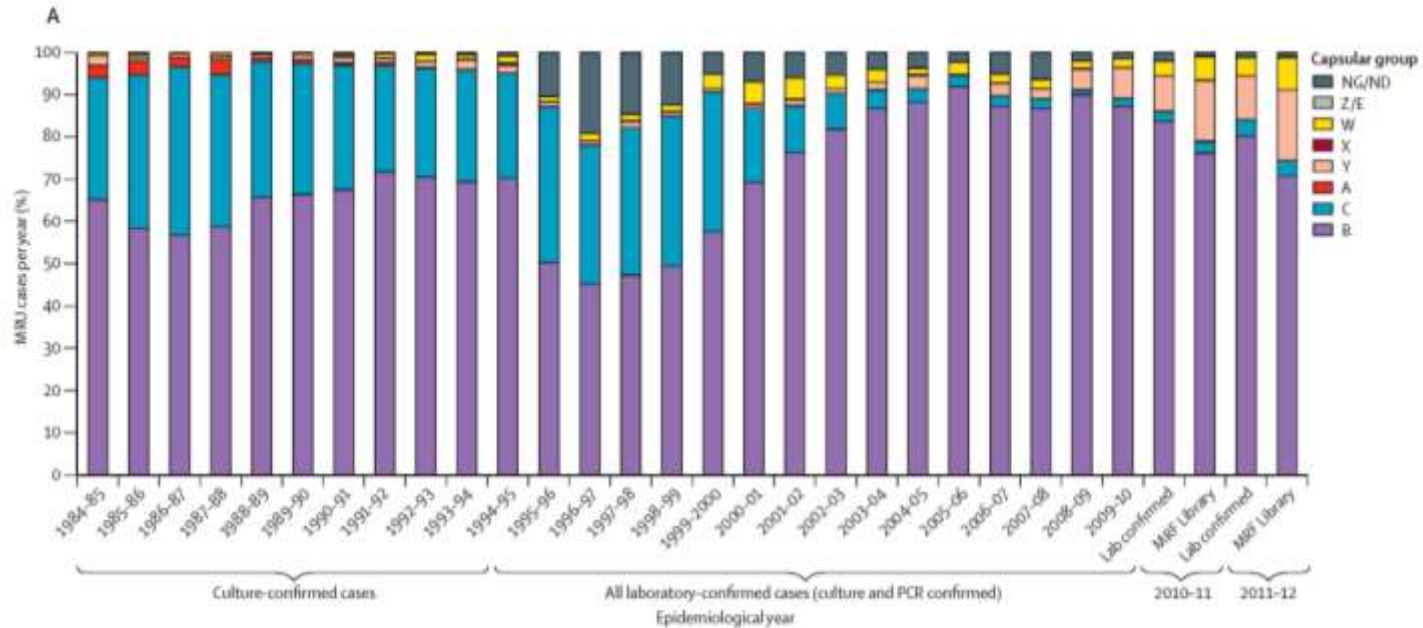
Global burden of disease



Capsular group B meningococcal protein vaccines



UK epidemiology



Hill **DMC** et al. Genomic epidemiology of age-associated meningococcal lineages in national surveillance: an observational cohort study. *Lancet Infectious Diseases* 2015;15:1420–8.

Broad aims

Using WGS of invasive meningococci to analyse the variation in Bexsero[®] vaccine antigens:

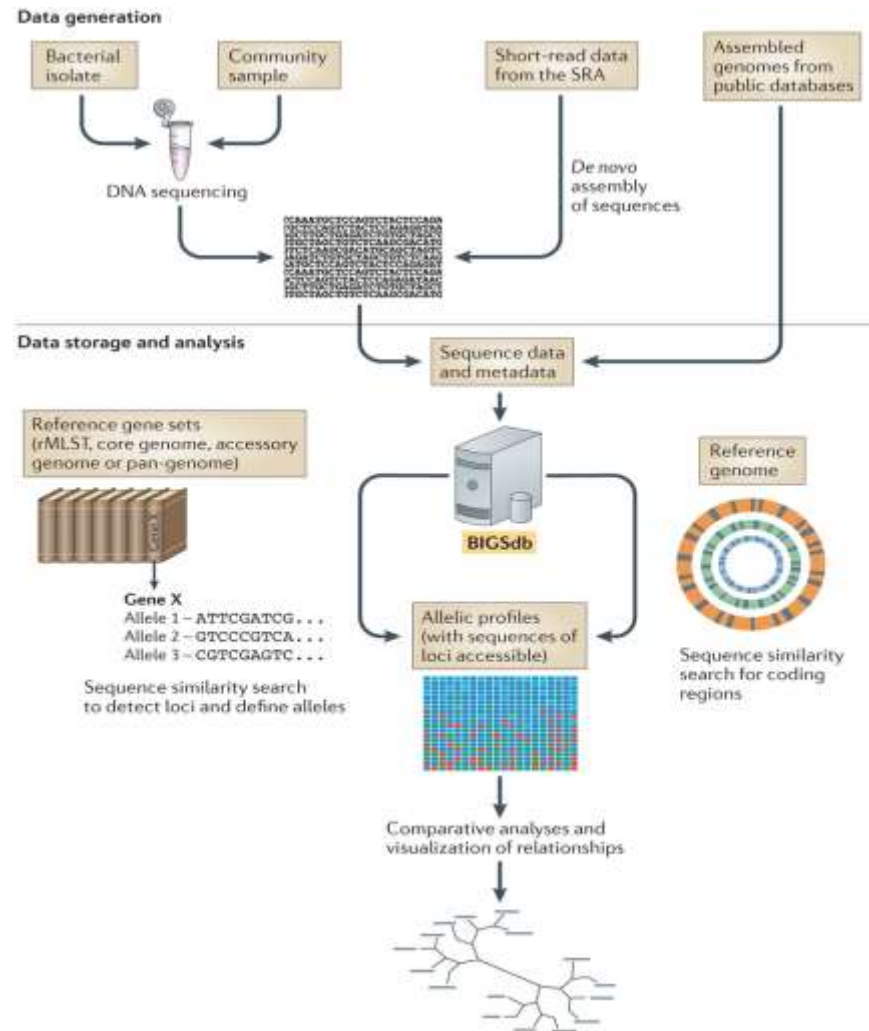
- Information about circulating strains in the UK causing disease
- Reference point prior to introducing Bexsero[®] as a potential selection pressure
- Inference about genomic coverage estimates (no prediction of protein expression or cross-reactivity)
- Information about vaccine reformulation

Objectives

Utilise rapid, scalable, and stable nomenclature Bexsero[®] Antigen Sequence Typing (BAST) to:

1. Determine the prevalence of Bexsero[®] Antigen Sequence Types (BASTs) in the UK disease isolates from 2010-16
2. Determine the incidence of fHbp, NHBA, NadA, PorA from 2010/11 to 2015/16
3. Estimate Bexsero[®] vaccine coverage for the UK in serogroup B and non-serogroup B disease isolates

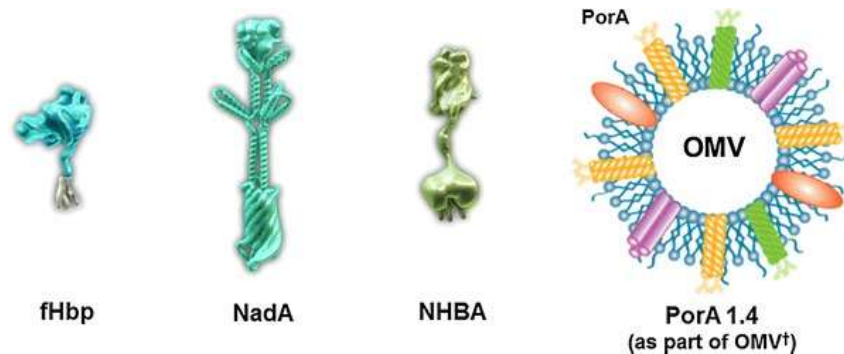
Methods



Bexsero[®] Antigen Sequence Type (BAST) design

Curated scheme for Bexsero[®] antigens was established within PubMLST.org/neisseria database

WGS allowed identification of deduced peptide sequences for each vaccine antigen

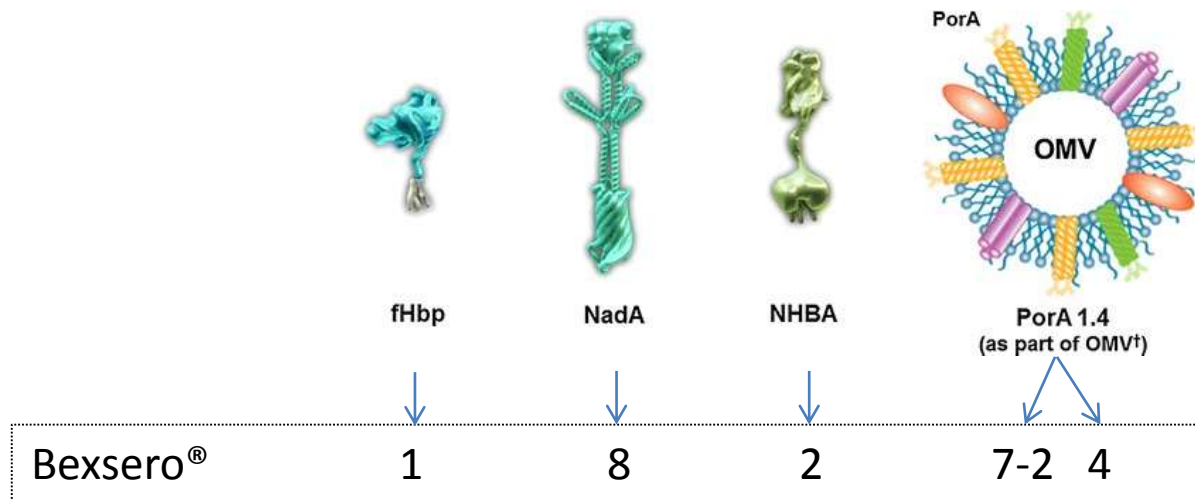


Brehony C et al. Distribution of Bexsero[®] Antigen Sequence Types (BASTs) in invasive meningococcal disease isolates: Implications for immunisation. *Vaccine*. 2016;34:4690-7 **O’Ryan et al.** A multi-component meningococcal serogroup B vaccine (4CMenB): the clinical development program. *Drugs*. 2014 74(1):15-30.

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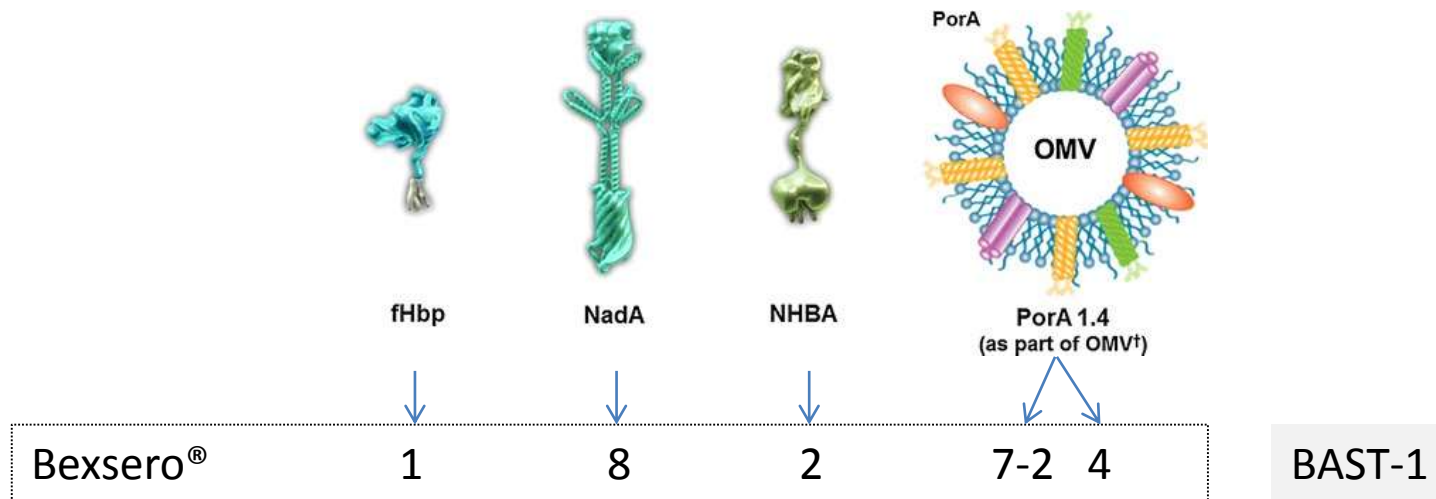


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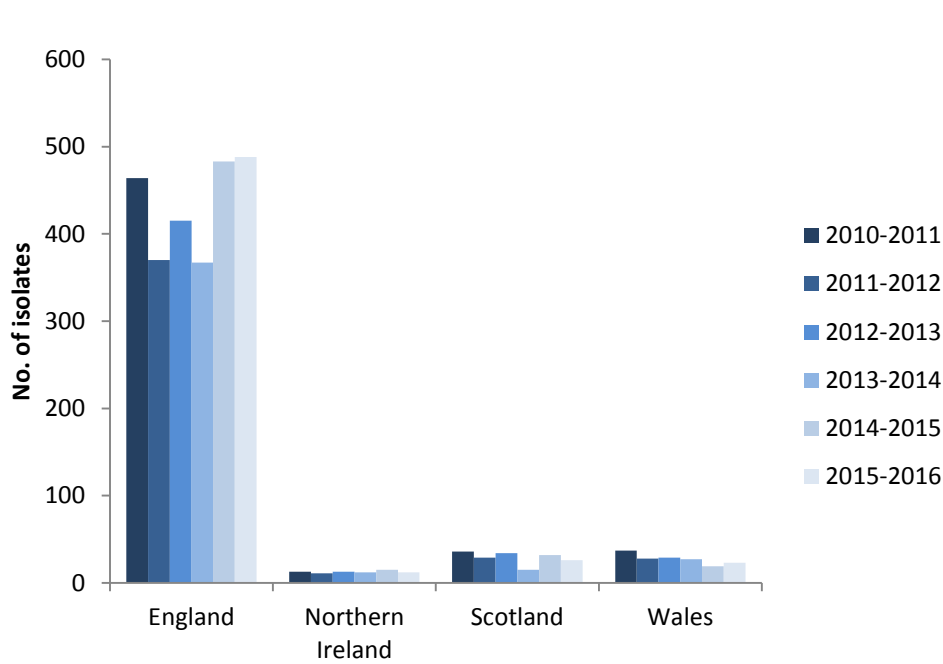
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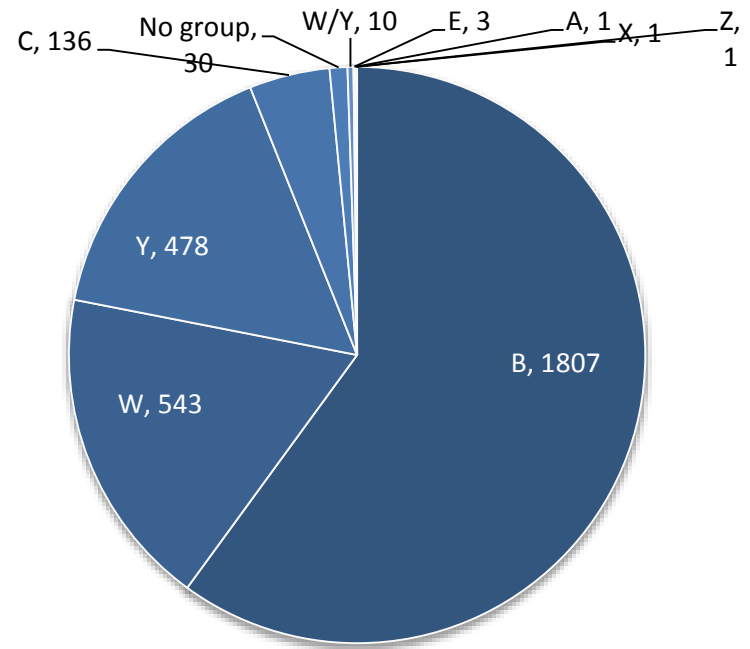
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Results

3010 genomes representing all culture-confirmed cases for epidemiological years **2010/11 to 2015/16** from **UK**

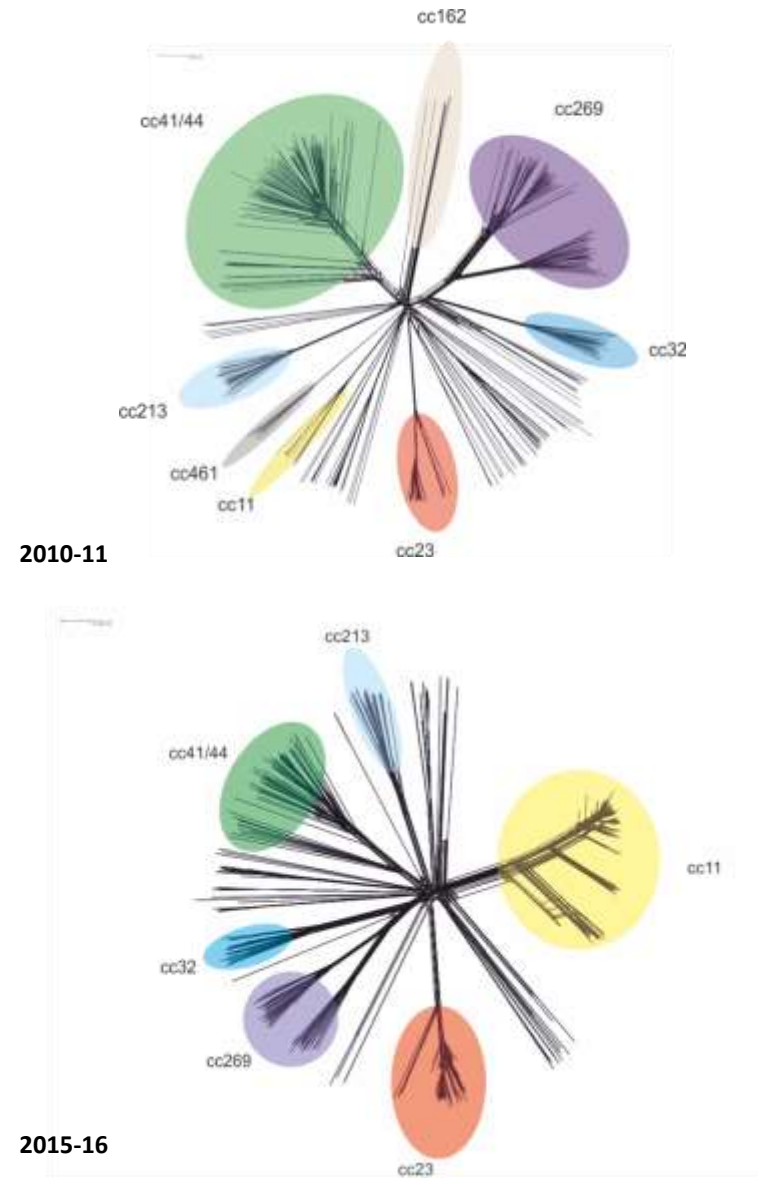
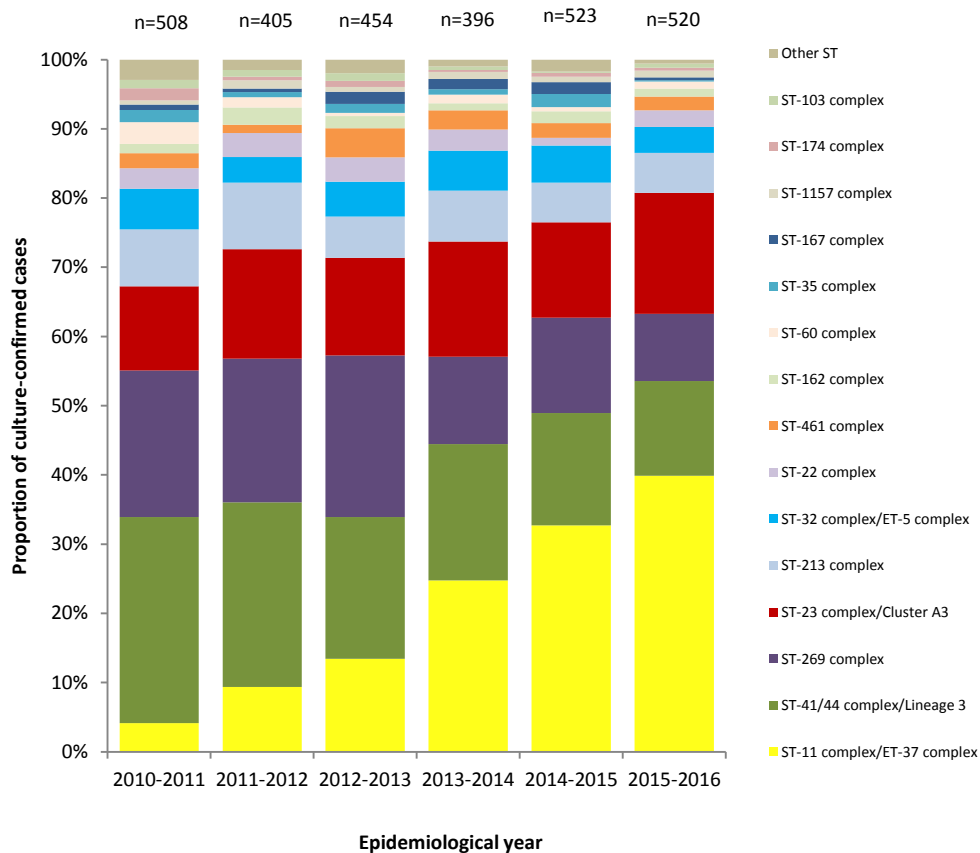


Geographic distribution

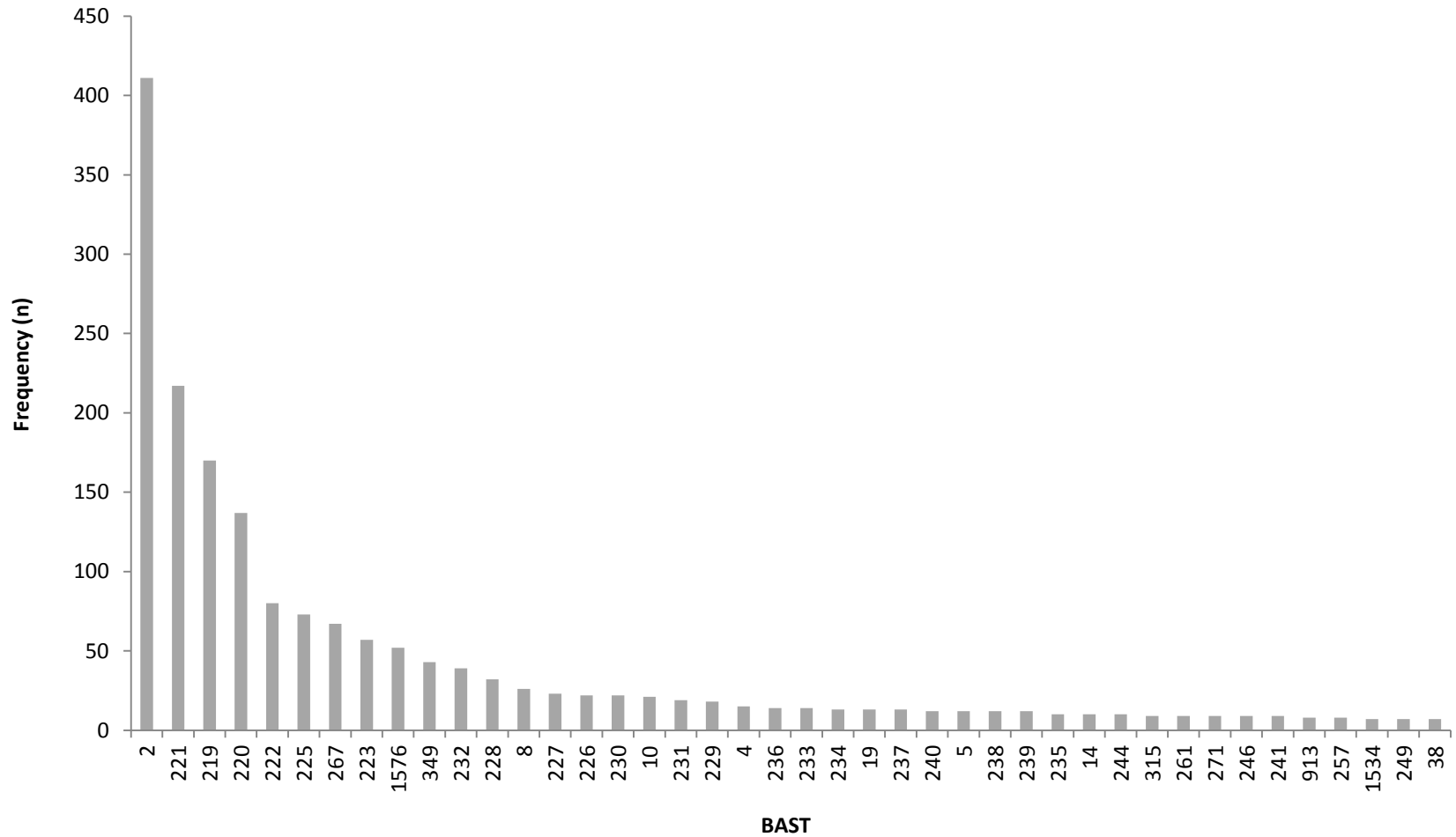


Serogroup distribution

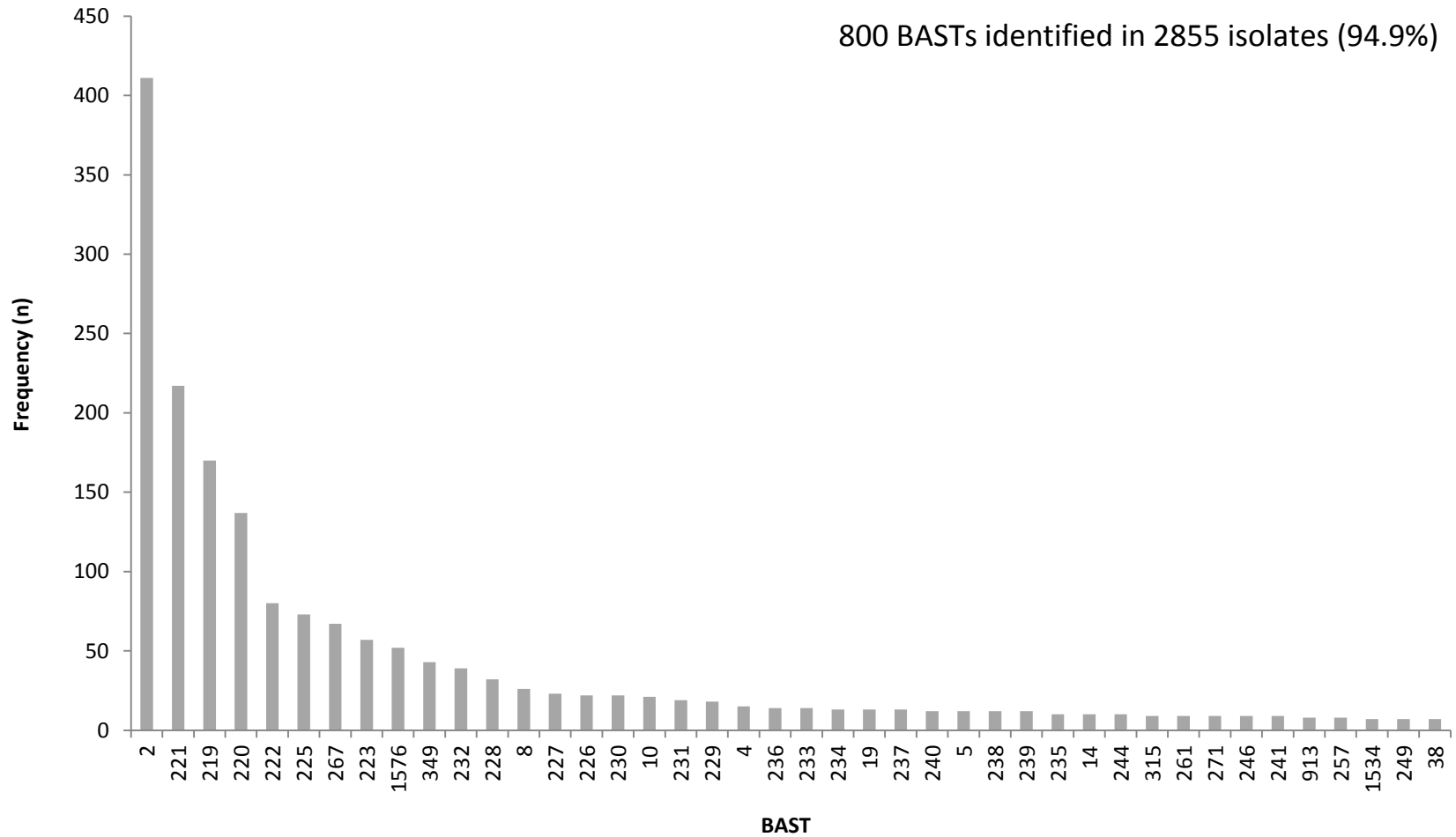
Endemic IMD clonal complexes



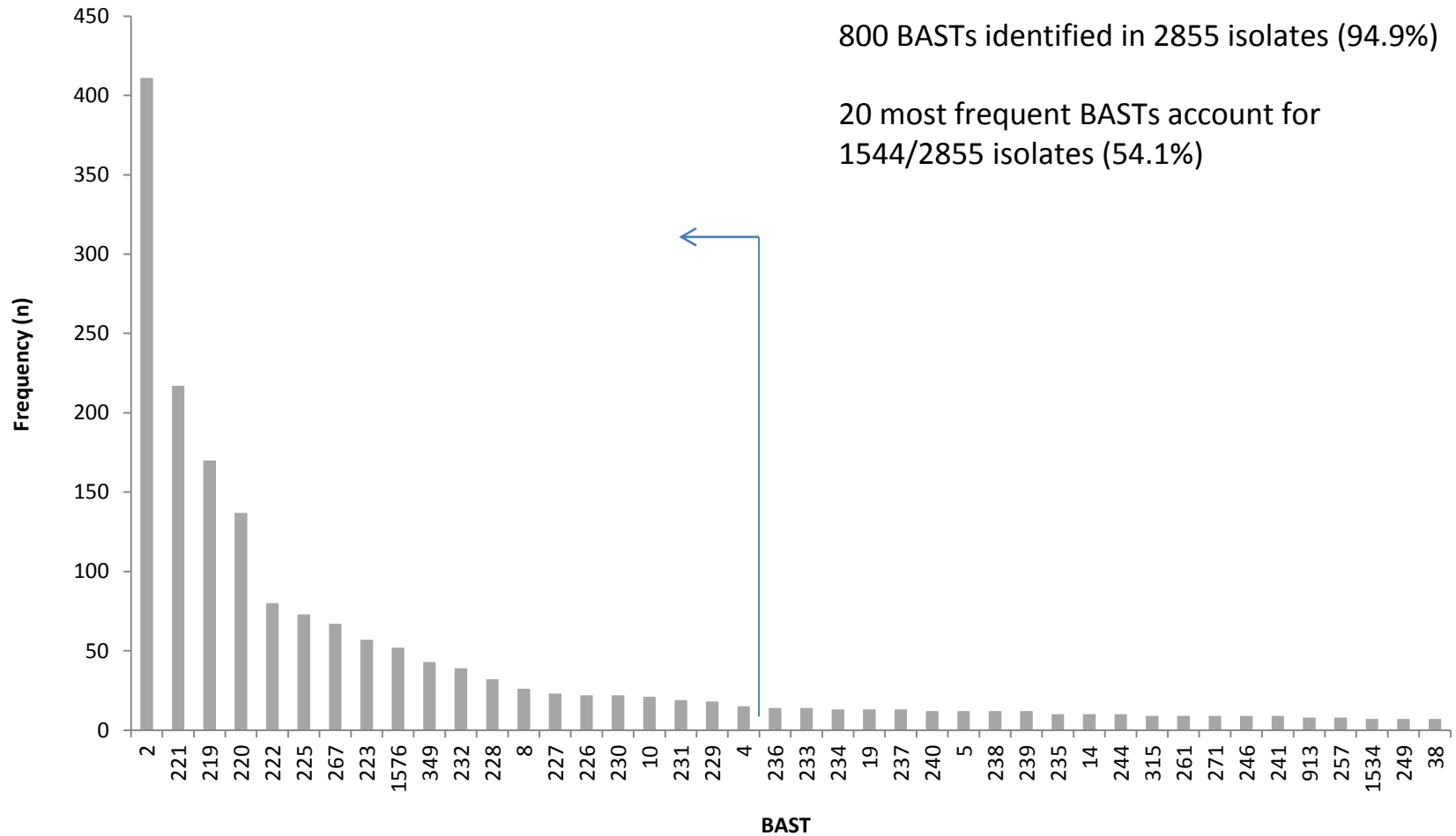
Frequency distribution of BASTs in the UK



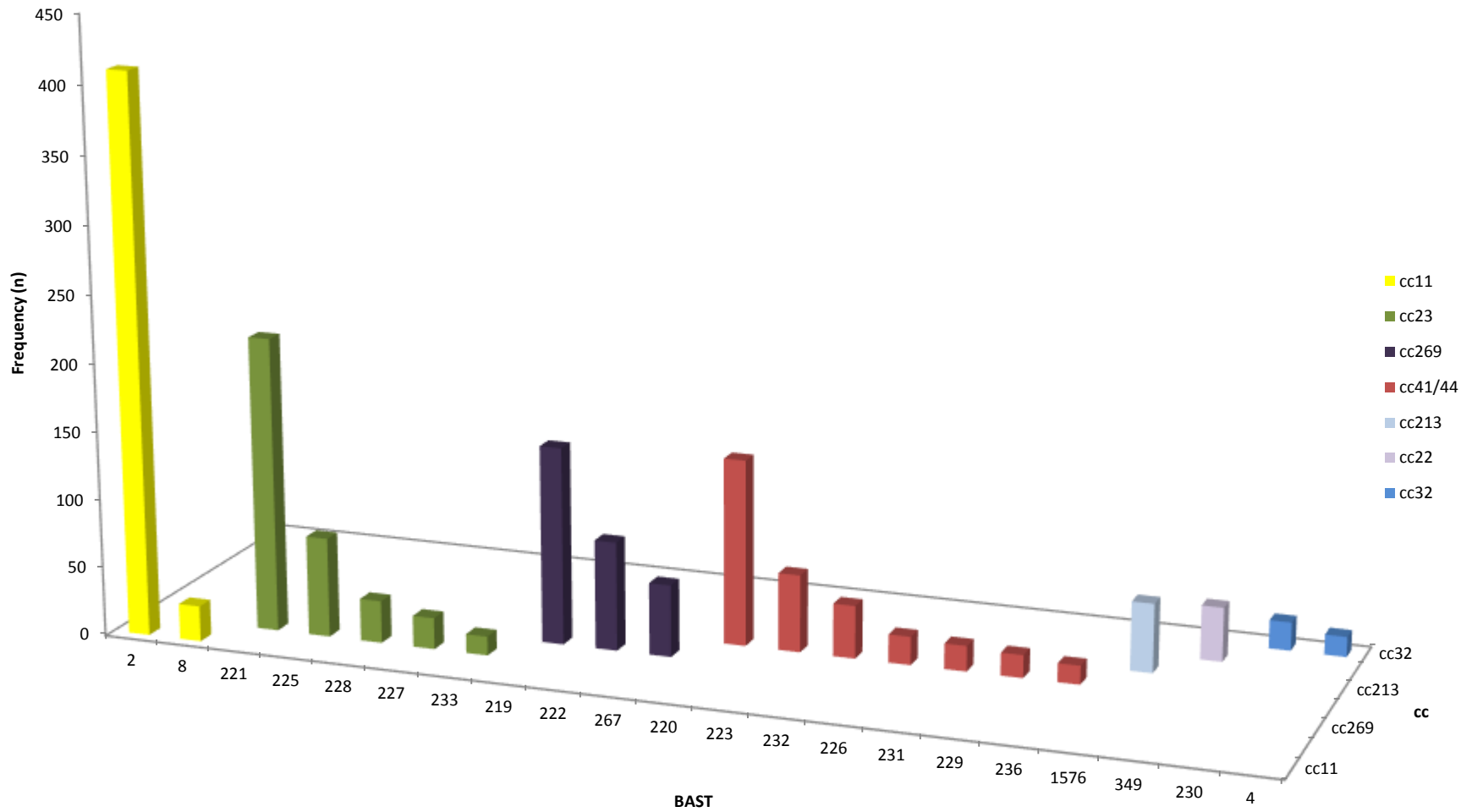
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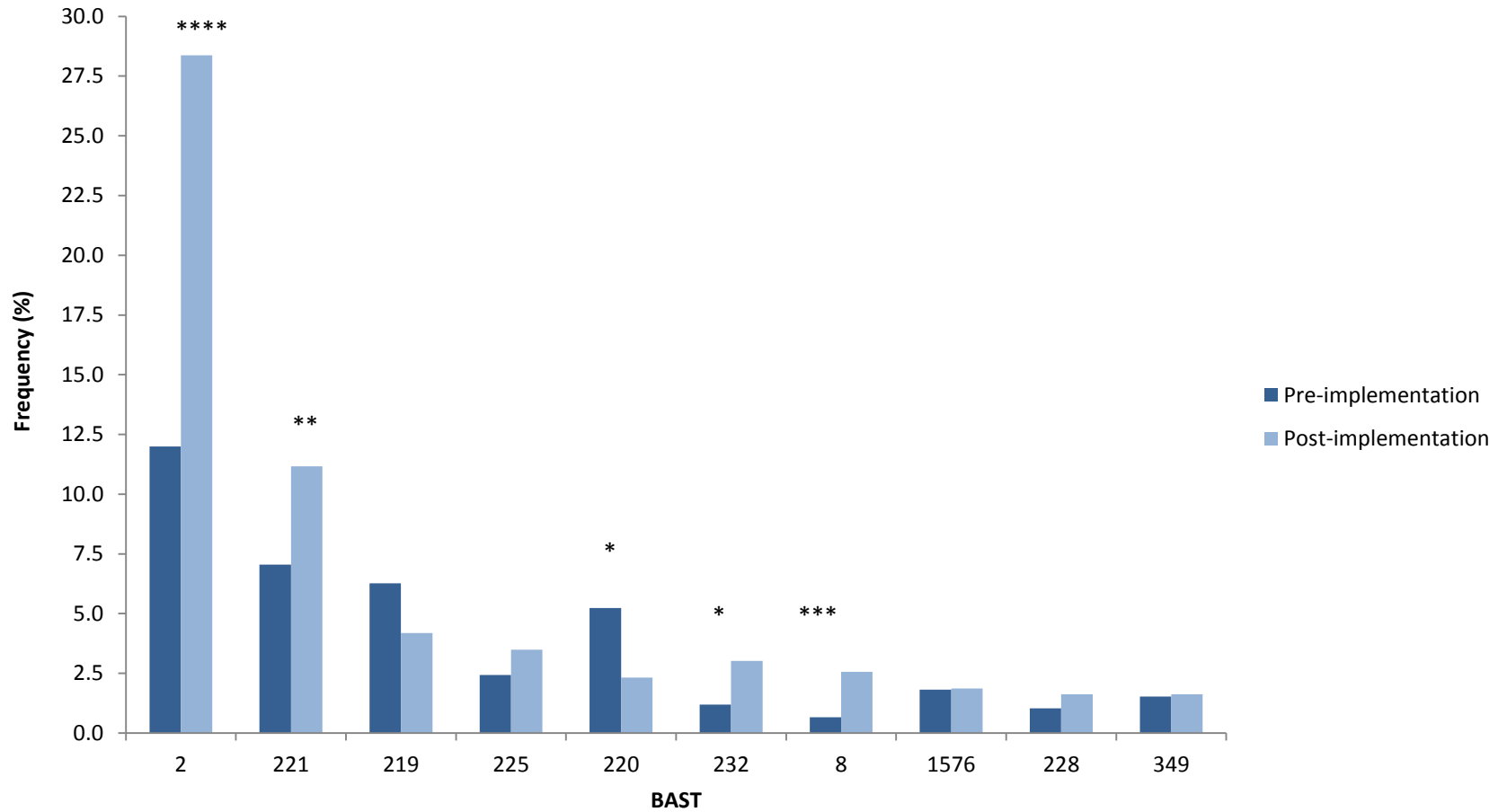
Frequency distribution of BASTs in the UK



Association of BAST with clonal complex



BAST prevalence



**** p<0.00001, *** p<0.0005, ** p<0.005, * p<0.05

Diversity of BASTs

Year	Unique BASTs (n)	Total isolates (n)	BASTs/isolate	Simpson's index of diversity (<i>D</i>)
2010/11	229	550	0.42	0.976
2011/12	187	438	0.43	0.977
2012/13	226	491	0.46	0.976
2013/14	176	421	0.42	0.960
2014/15	198	558	0.35	0.927
2015/16	153	552	0.28	0.908
Total	801	3010	0.27	0.964

Summary

Comprehensive evaluation of the population structure of Bexsero[®] antigenic variants.

A reference point prior to vaccine implementation.

BAST surveillance of meningococcal WGS can be done through publicly-available platforms i.e. pubMLST.org/neisseria

Rapid, scalable, and portable to other regions of the world.

Acknowledgments

Supervisors

Professor Martin Maiden, Professor Chris Tang
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The Maiden Lab

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Keith Jolley
James Bray
Jenny Maclennan

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Ray Borrow
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Scottish Haemophilus, Legionella, Meningococcus and Pneumococcus Reference Laboratory

Andrew Smith

