In silico prediction of 4CMenB coverage against invasive serogroup B Neisseria meningitidis isolates collected between 2010 and 2019.

Robert M. Mulhall[1], Holly Bratcher[2], Keith A Jolley[2], James Bray[2], Martin C. J. Maiden[2], Desiree Bennett[1], Robert Cunney[1,3].
[1] Irish Meningitidis and Sepsis Reference Laboratory, Children's Health Ireland at Temple Street , Dublin, Ireland.
[2] Department of Zoology, University of Oxford, Oxford, England.
[3] Department of Clinical Microbiology, RCSI Education and Research Centre, Beaumont Hospital, Dublin, Ireland.

INTRODUCTION

- *Neisseria meningitidis* (N.men) is an important cause of sepsis affecting primarily those under 5 years. Disease onset is rapid, and vaccination remains the most effective control strategy.
- Highly effective conjugate vaccines can control disease incidence due to MenC, MenW, MenY, but not MenB (as the B capsular polysaccharide is not immunogenic). Sub-capsular targets must be used instead.
- 4CMenB (Bexsero, GSK) is a "MenB substitute" vaccine which targets 4 individual surface proteins present on many meningococcal strains including MenB strains (1).
- Assessing strain coverage for sub capsular protein vaccines is complicated by high levels of diversity and differential levels of expression across the many different MenB strain types (**Fig 1**.)
- The Meningococcal antigen typing system (MATS) is an ELISA assay developed to capture the ability of vaccine elicited antibodies to recognise and bind to specific MenB strains, and correlate this with protective human serum bactericidal antibody (hSBA) titres.
- MATS was developed to estimate coverage against panels of meningococcal strains (1). The method is labour intensive, and time consuming and is not a available as a service by request.
- Genetic MATS (gMATS) is an *in silico* method developed in collaboration with Glaxo Smith Kline (GSK) and 18 different reference laboratories which can be used as a surrogate for MATS assay testing (2).

AIMS

1. To compare gMATS to previous MATS results for invasive MenB isolates collected between 2010 and 2013 in Ireland (3).
2. To estimate coverage for invasive MenB isolates collected between 2014 and 2019 using gMATS.

METHODS

- gMATS was developed by studying a large collection of invasive MenB isolates (n=3,912) to which MATS data and sequence data were available for the vaccine antigens. The study identified examples of 4CMenB peptide variants repeatedly predicted as positive by MATS (2).
- Invasive MenB isolates received to the IMSRL between 2010 and 2019 were whole genome sequenced and were available to study (n=215). Using the pubMLST platform we identified peptides reported in the gMATS study to estimate MATS positive phenotype among invasive MenB isolates, and therefore indirectly, estimated 4CMenB coverage (4).

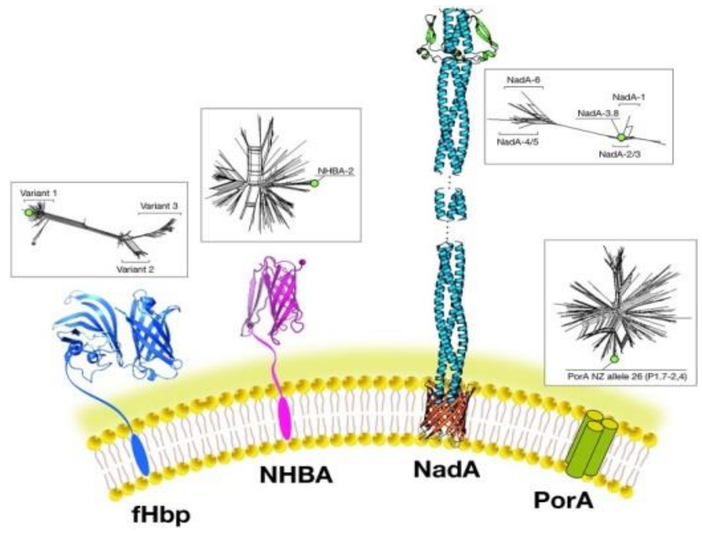

Fig 1. Shows the four sub-capsular targets of the 4CMenB vaccine.
Compared to the capsule polysaccharide, sub-capsular components are scarcely expressed (or may even be absent).
Across the various MenB strains the amount of these targets expressed will vary. Peptide composition also varies, which affects how well vaccine elicited antibodies recognise their respective targets on MenB strains.

RESULTS

- MATS data for Ireland generated prior to the 4CMenB vaccine introduction into the routine infant schedule allowed a direct comparison between MATS and gMATS (**Fig 2**).
- Over this period gMATS point estimates were consistently higher than MATS estimates, especially in 2010 and 2011.
- When the probability ranges of the estimates are compared there were no significant differences between the methods(as evidenced by overlapping confidence intervals of the two methods).
- Between 2014 and 2019 coverage remained within the range established between 2010 and 2013 until 2019, and was lowest in 2019 (65.8% [CI_{95}%], 73.7% to 57.9%).

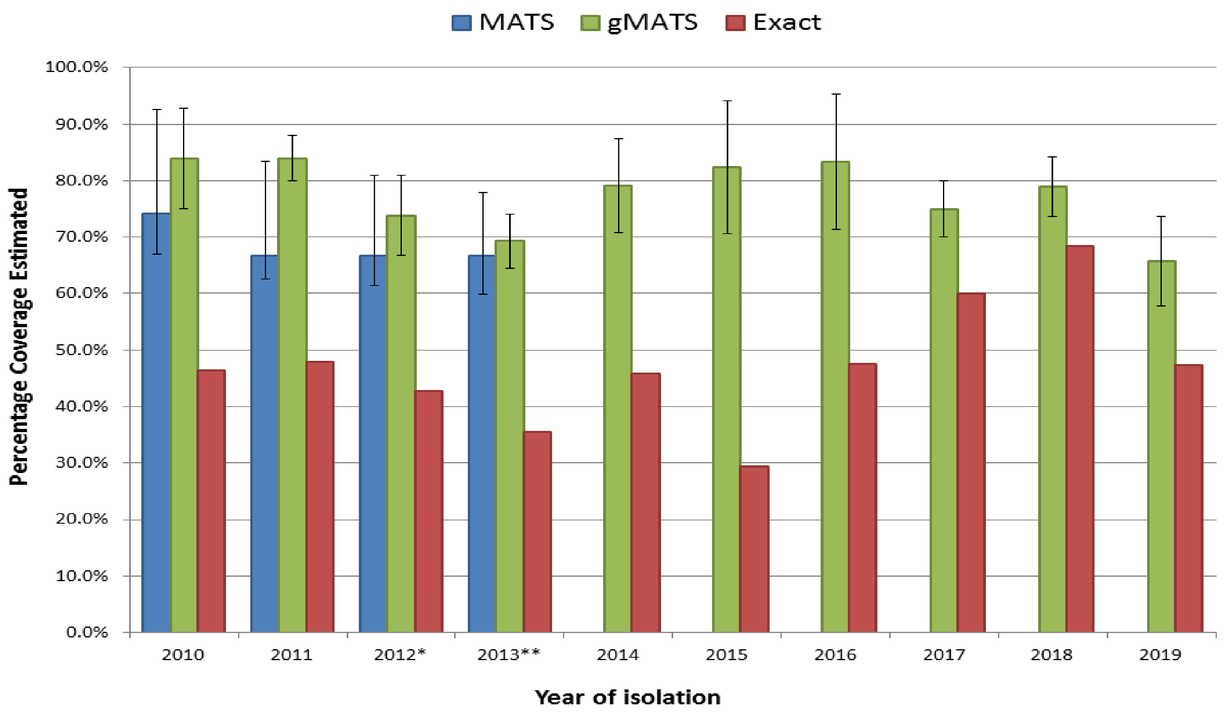

Fig 2. Shows estimated coverage against invasive MenB strains isolated in Ireland between 2010 and 2019 using MATS, gMATS and using the exact peptide components in the 4CMenB vaccine.

CONCLUSIONS

- gMATS estimations were largely consistent with MATS estimates where the methods could be directly compared.
- As part of post licensure surveillance of the 4CMenB in Ireland , MATS analysis of invasive MenB isolates collected between 2014 and 2019 will become available later this year which, together with the above data, will provide a better evaluation of the predictive capacity of the rapid *in silico* method gMATS.

ACKNOWLEDGMENTS

This work was funded by the National Immunisation Advisory Committee (NIAC). The study used the Neisseria MLST website (pubmlst.org/neisseria) developed by Keith Jolley, and supported by the European Union and the Wellcome Trust. We wish to thank Dr Angela Lee, the Oxford Genomics Centre, Wellcome Centre for Human Genetics, Roosevelt Drive, Oxford, OX3 7BN, who conducted the whole genome sequencing of the study isolates. We also thank all the students who participated in the study, and all those who welcomed us to the various institutes during isolate collection.

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