

Meningococcal Antigen Typing System (MATS) conservatively estimated killing in the serum bactericidal assay using human complement (hSBA)

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BACKGROUND

- MATS can predict the strain coverage of multicomponent meningococcal serogroup B vaccine, 4CMenB, based on the quantity and cross reactivity of immune responses against factor H binding protein (fHbp), Neisseria Heparin Binding Antigen (NHBA), Neisserial Adhesin A (NadA), and PorA P1.4
- A comprehensive collection of 528 *Neisseria meningitidis* type B clinical isolates from England and Wales (98.7% of all 2007-08 cases) collected by the Health Protection Agency was **the reference epidemiological panel**. MATS relative potencies¹ were measured in ELISA to characterize fHbp, NadA and NHBA expression and the positive bactericidal threshold (PBT¹) classifier was used to calculate point predictions of 4CMenB coverage for all strains

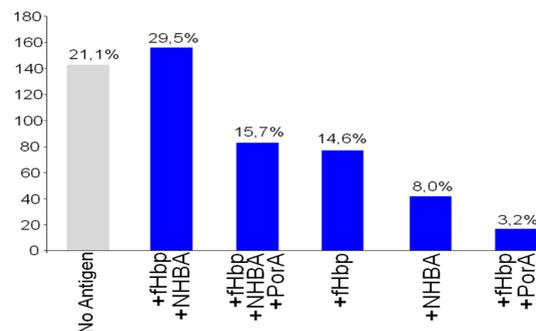
METHODS

Experimental validation of MATS coverage predictions was undertaken via **serum bactericidal antibody assay (SBA²)** for a representative sample of 40 strains

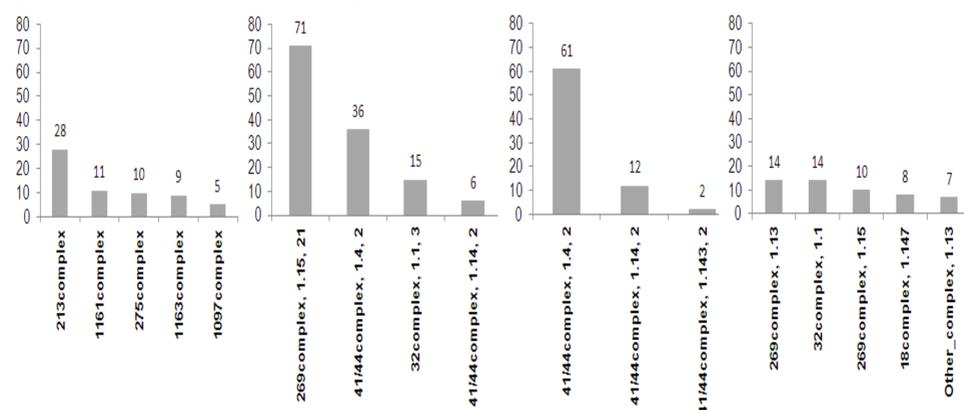
Stratified proportional sampling³ based on **MATS** and **genetic profile (MLST + antigen genotype)** was used to balance population characteristics in the sample

Two-level sample stratification:

MATS stratification: control for **coverage distribution** sampling bias using *empirical frequencies* of different coverage classes in the population

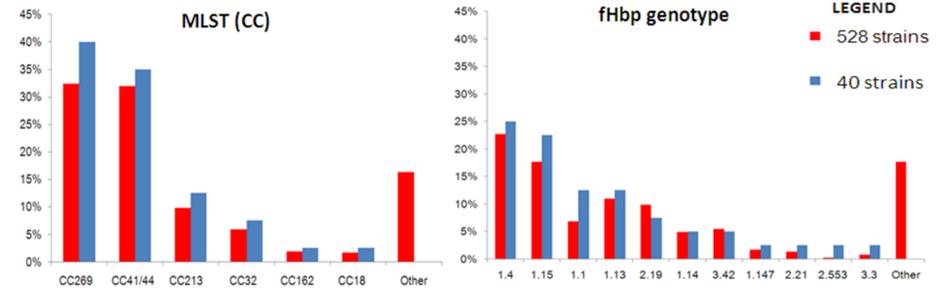
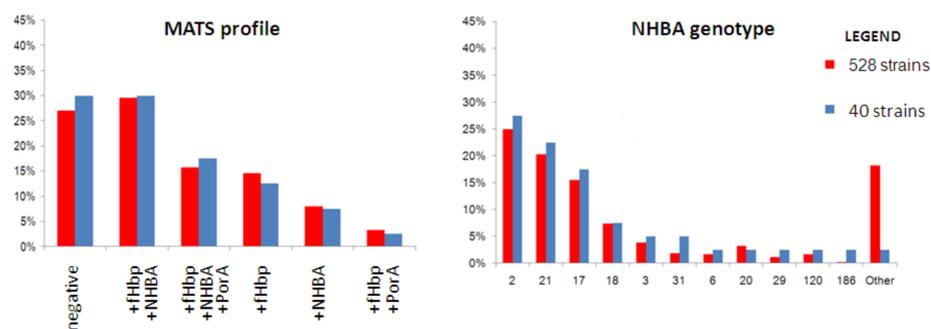


Genetic stratification within each MATS stratum: control for **genetic profile** sampling bias using multi-locus sequence type (MLST) and the genotype of relevant antigens



RESULTS

The random sample of 40 strains was proportionally representative of 98% of MATS phenotypes and >80% of MLST and vaccine antigen genotypes



- hSBA ON SELECTED STRAINS

SBA on selected strains was performed using pooled postimmune and control sera from participants in 2 clinical studies:

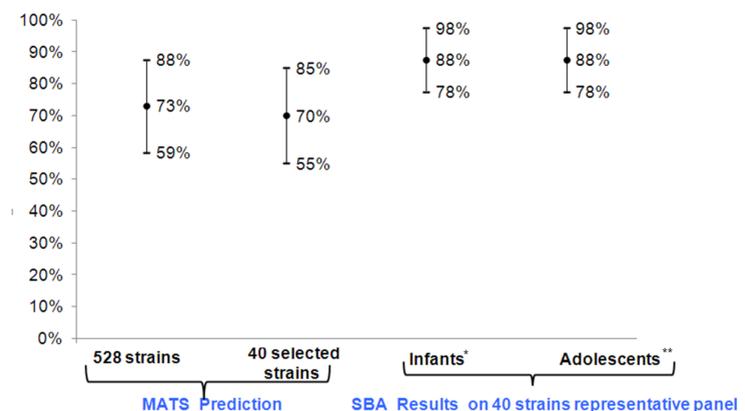
- Study 1:** pooled sera were derived from **13 subjects** before (control) and after 2 doses of 4CMenB (postimmune).
- Study 2:** pooled sera were derived from **109 infants** who received the primary series of 3 doses of routine vaccine starting at 2 months of age (control) and from **69 infants** who received a primary series of 3 4CMenB doses plus a booster in the 2nd year of life (postimmune).

- Coverage Comparisons

MATS coverage: intervals were estimated according to PBT definitions on the basis of MATS precision (reproducibility) determined during inter-laboratory standardization (Plikaytis, B. *et al*, in preparation): 19.78% (fHbp), 28.81% (NHBA) and 38.25% (NadA)

hSBA coverage: strains with a postimmune hSBA titer ≥ 8 and ≥ 4 -fold increase over control, with confidence intervals constructed on the basis of the binomial approximation

- Percentage of covered strains: MATS vs SBA results



* For infants, SBA results at post dose 4th are considered
 ** For adolescents, SBA results at dose 3rd are considered

CONCLUSION AND OUTLOOK

- The 40-strain panel selected for hSBA testing provided an unbiased sample that was proportionally representative of 98% of MATS phenotypes and >80% of MLST and vaccine antigen genotypes
- Based on MATS data, 73% (95%CI: 59-88%) of 528 strains of UK panel were predicted to be killed in the hSBA, while 70% (95%CI: 55-85%) of 40 selected strains were predicted to be killed in the hSBA.
- Experimental validation revealed that 88% (95%CI: 78-98%) and 88% (95%CI: 78-98%) of the selected strains were killed by pooled infant and adolescent sera respectively.
- These results confirm that MATS is a conservative measure of killing in the hSBA.

References

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