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## INTRODUCTION

*N. meningitidis* causes meningococcal disease mostly in young children, yet the bacterium is most commonly found in the oropharynx of adolescents and young adults. A recent study additionally confirms their presence in saliva samples from these age groups (1). If determinants of carriage and transmission of meningococci were better understood, approaches to disease control could be improved. The meningococcus GpC (MenC) conjugate vaccine catch up programme in 2000 reduced MenC carriage in adolescents and young adults and onward transmission through the UK population with consequent indirect ("herd") protection (2). We have described higher density carriage of upper respiratory tract bacteria, including pneumococcus, in pre-school children who have respiratory viral infections (3) and several studies have shown associations between influenza A and invasive meningococcal disease (IMD)(4,5), raising questions about the relationship between meningococcal carriage and respiratory viral infections.

We conducted the Bristol Meningococcus Natural History of Carriage (BrisMenNHC) longitudinal study between September 2014 and May 2015 to explore changes in the presence and carriage density of meningococcus over time. High density meningococcal carriage rates are low, as most carriage occurs at low density. We aimed to elucidate predictors of carriage and of high density carriage using this sample set. We investigated whether concurrent or antecedent respiratory viral infection is associated with the presence of meningococcal carriage and/or high density meningococcal carriage.

## STUDY DESIGN AND METHODS

- 5,456 pharyngeal swabs were collected from Bristol school students aged 15–19yrs, between September 2014 and May 2015, into 1.5mL skim milk-tryptone-glucose-glycerol (STGG) broth as part of a longitudinal study.
- 1,813 students were recruited for an initial swab, with 918 students taking part in a longitudinal part of the study in which pharyngeal swabs were collected from them monthly for 6 months.
- Bacterial and viral nucleic acids were extracted from the STGG broth using a QIA Symphony machine.
- Quantitative real-time polymerase chain reaction (qPCR) was used to identify the presence of *N. meningitidis* by identifying the *porA* gene (Ct≤35), as previously described (1).
- Respiratory viruses were detected using reverse transcriptase\* (rt)-PCR methods for the presence of a panel of 11 viruses: adenovirus (AdV), influenza A viruses (H1N1/09, seasonal H1N1 and H3N2) (FluA), influenza B (FluB), respiratory syncytial virus (RSV), human metapneumovirus (HMV), rhinovirus (RhV), parainfluenza virus types 1-3 (PF1-3) and enterovirus (EV). (\* for all viruses except ADV which is a DNA virus) as previously described (3).
- Data were analysed using logistic regression, including exact and mixed effects models as appropriate to take clustering and meningococcal carriage in a previous sample into account

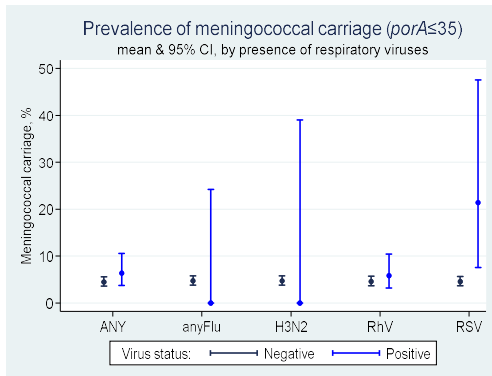
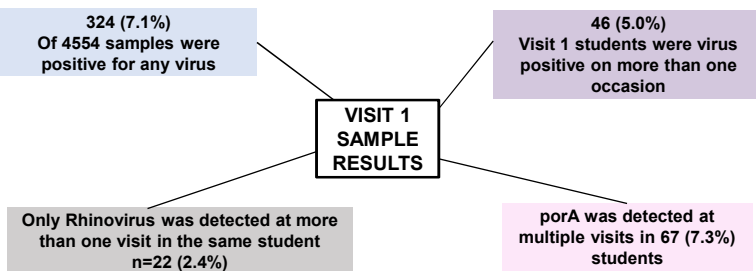
## RESULTS

### Results 1

Visit	Number (n)	Percentage(%)
All visits	255	4.7
1	85	4.7
2	42	5.0
3	32	4.4
4	35	5.1
5	24	3.4
6	37	5.4

### Results 1 – *N. meningitidis* *porA* detection rate per visit in pharyngeal swabs.

*N. meningitidis* *porA* overall and per visit detection rate (ct≤35) in pharyngeal swabs. Total n=5,456.



### Results 3 – Concurrent association of a respiratory virus and meningococcus at visit 1

There was weak evidence of an association between meningococcal carriage and RSV (OR 6.33, CI 1.10 to 25.3, P=0.02) but with very wide confidence interval. This association was not seen in later visits. No other associations between viral infection and detection of meningococcus were observed.

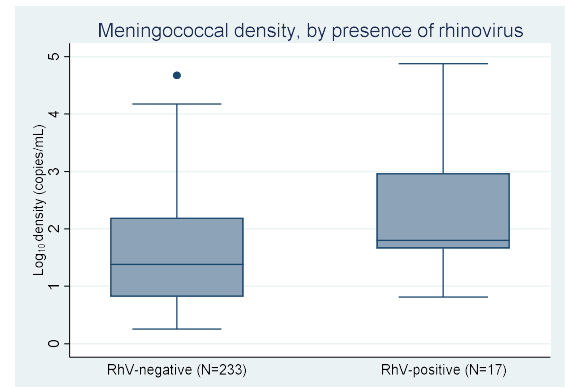
### Results 2

Virus	Number positive	Percentage positive(%)
Any virus	433	7.95
Rhinovirus	323	5.93
Any Flu virus	46	0.84
Respiratory syncytial virus	37	0.68
Any Parainfluenza virus	15	0.28
Adenovirus	11	0.20
Enterovirus	7	0.13
Human metapneumovirus	5	0.09

### Results 2 – Viral detection rate in pharyngeal swabs.

Number and percentage of respiratory viruses detected (ct≤35) in all study pharyngeal swabs, n=5,448. Any Flu virus includes any Flu A or Flu B virus detected; any parainfluenza virus incorporates parainfluenza viruses 1,2 & 3.

### Results 4



### Results 4 – Meningococcus density and association with viruses

- Only samples with any virus detected or RhV alone were detected in sufficient numbers to investigate a possible association with meningococcal density.
- The co-incident detection of RhV corresponded to an approximately 3 (95%CI 1.05–9.0) fold increase in density of meningococcus (p<0.043).
- There was no evidence that detection of any virus was associated with increased meningococcal density (p=0.70). The estimated increase in density was 1.2-fold (95% CI 0.50 to 2.8-fold).
- No association between the presence of RhV or any virus in the previous sample and meningococcal density in the following sample was found. Estimated effects of antecedent virus presence on mean log<sub>10</sub> density were +0.070 (CI -0.448 to 0.589, P=0.791) for RhV, and -0.045 log<sub>10</sub> units (CI -0.503 to 0.413, P=0.848) for any virus.

## CONCLUSIONS

- The overall viral detection rate was low in this sample set of healthy students, making it hard to investigate the relationship between viral infections and bacterial colonization.
- Rhinovirus was the most frequently detected respiratory virus with an overall detection rate of 5.93%.
- There was weak evidence in visit 1 samples of an association between the detection of respiratory syncytial virus and meningococcus.
- Intercurrent rhinovirus infection may be associated with an increase in meningococcal density, which potentially could increase the likelihood of onward transmission.
- No evidence was found in this analysis to suggest that viral infection may cause increased subsequent acquisition of meningococcus and higher carriage rates.
- Further analysis is planned including a second meningococcal gene target for PCR detection (*sodC*) which is expected to increase sensitivity of detection.

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