A Cluster Randomised Controlled Trial in Senior School Students to Assess The Impact of 4CMENB on *N. meningitidis* Carriage and Determine Risk Factors for Carriage.

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Background

Understanding risk factors for carriage and determining whether protein-based MenB vaccines impact on carriage are important considerations for meningococcal immunisation programs. This study aimed to assess risk factors for carriage in baseline swabs obtained in the MenB vaccine herd immunity study, a cluster RCT to compare carriage prevalence of *Neisseria meningitidis* in vaccinated (4CMenB) and unvaccinated school students in South Australia.

Methods

All secondary schools were invited to participate and randomised to intervention (4CMenB at baseline) or control (4CMenB at 12 months) arms. Posterior pharyngeal swabs were obtained and risk factor questionnaires completed by all participating students at baseline and 12 months. Carriage was detected by *porA* real time PCR.

Risk factors for typeable and overall carriage at baseline in year 10, 11 and 12 students were identified using univariable and multivariable logistic regression models, with the clustering of students within schools accounted for using generalised estimating equations.

Results

Overall, 34,483 students attending 235 (>95%) secondary schools participated, including 17,925 (52%) females. The majority of students were from metropolitan (74%), followed by rural (23%) and remote (3%) schools. Only 1.8% of students reported they were smokers and 21.1% had a current upper respiratory tract infection (URTI).

Table 1: Risk factors for overall carriage

Characteristic	Level	Frequency (%)	Unadjusted OR		Adjusted OR	
			(95% CI)	P-value	(95% CI)	P-value
School ICSEA category (Index of Community Socio-Educational Advantage)	Low	229/6527 (3.51%)	1	0.53*	1	0.63*
	Medium	315/10369 (3.04%)	0.86 (0.66, 1.13)	0.28	1.01 (0.80, 1.26)	0.96
	High	539/17576 (3.07%)	0.87 (0.66, 1.15)	0.32	1.11 (0.84, 1.46)	0.46
School location	Metropolitan	765/25567 (2.99%)	1	0.02*	1	0.29*
	Provincial	256/7889 (3.25%)	1.09 (0.87, 1.36)	0.46	1.00 (0.77, 1.29)	0.97
	Remote/Very Remote	62/1016 (6.10%)	2.11 (1.24, 3.59)	0.006	1.53 (0.88, 2.65)	0.13
Age group**	<=15 years	209/11677 (1.79%)	1	<0.001*		
	16 years	341/11414 (2.99%)	1.69 (1.35, 2.11)	<0.001		
	17 years	445/9831 (4.53%)	2.60 (2.08, 3.25)	<0.001		
	>=18 years	88/1550 (5.68%)	3.30 (2.42, 4.52)	<0.001		
Sex	Male	524/16552 (3.17%)	1.02 (0.89, 1.16)	0.82	1.05 (0.91, 1.20)	0.50
Year of schooling	10	243/12756 (1.90%)	1	<0.001*	1	<0.001*
	11	340/11501 (2.96%)	1.57 (1.26, 1.95)	<0.001	1.42 (1.13, 1.78)	0.003
	12/13	500/10215 (4.89%)	2.65 (2.13, 3.30)	<0.001	2.16 (1.74, 2.69)	<0.001
Current cold or sore throat	Yes	287/7199 (3.99%)	1.38 (1.20, 1.59)	<0.001	1.28 (1.10, 1.49)	0.001
Antibiotics	Yes, currently taking	49/1651 (2.97%)	0.95 (0.69, 1.31)	0.75	0.84 (0.60, 1.17)	0.30
Smoked cigarette in last week	Yes	86/626 (13.74%)	5.26 (4.01, 6.90)	<0.001	2.31 (1.68, 3.18)	<0.001
Smoked e-cigarette in last week	Yes	36/369 (9.76%)	3.45 (2.34, 5.08)	<0.001	1.22 (0.75, 2.01)	0.42
Smoked water-pipe in last week	Yes	103/1042 (9.88%)	3.66 (2.89, 4.64)	<0.001	1.85 (1.40, 2.44)	<0.001
Pub/club visits in last week	>= 1 day	406/7053 (5.76%)	2.41 (2.05, 2.84)	<0.001	1.66 (1.41, 1.95)	<0.001
People kissed in last week	>= 1 person	449/7730 (5.81%)	2.56 (2.24, 2.94)	<0.001	1.67 (1.39, 2.01)	<0.001
In current relationship	Yes	364/7489 (4.86%)	1.87 (1.64, 2.13)	<0.001	1.10 (0.92, 1.32)	0.30
Boarding student	Yes	44/746 (5.90%)	1.98 (1.14, 3.44)	0.02	1.90 (0.98, 3.67)	0.06
Ethnicity	Caucasian	811/24696 (3.28%)	1	<0.001*	1	<0.001*
	Aboriginal/TSI	50/941 (5.31%)	1.65 (1.16, 2.36)	0.01	1.38 (1.00, 1.90)	0.05
	Asian	49/3383 (1.45%)	0.43 (0.31, 0.60)	<0.001	0.52 (0.37, 0.72)	<0.001
	Other	148/4853 (3.05%)	0.93 (0.77, 1.11)	0.41	1.02 (0.84, 1.24)	0.84

* Global p-value

** Excluded age from multivariable model due to correlation with school year

In multivariable analysis the odds of carriage was higher in year 11 compared to year 10 students (OR=1.42 [95% CI, 1.13, 1.78]), and higher again in year 12 students; (OR=2.16 [1.74, 2.69]). Asian ethnicity was the only characteristic that was associated with lower odds of carriage (OR=0.52 [0.37, 0.72]).

Modifiable risk factors including cigarette smoking (OR=2.31 [1.68, 3.18]) and water pipe use (OR=1.85 [1.40, 2.44]) were associated with increased carriage, but increased risk was not observed for e-cigarettes in the adjusted model.

Having a cold or sore throat was associated with carriage (OR=1.28 [1.10, 1.49]), whereas no reduction in carriage was found with current antibiotic use. Social factors such as attending a pub or club one or more days a week (OR=1.66 [1.41, 1.95]) and kissing one or more people in the past week were also independently associated with increased carriage (OR=1.67 [1.39, 2.01]), (Table 1).

Statistically significant predictors of typeable carriage (p < 0.05) in the multivariable model included school year, ethnicity, a current cold or sore throat, smoking (cigarette or water-pipe), days out and people kissed in the last week.

Conclusions

Immunisation programs should consider targeting risk groups for meningococcal carriage including senior students, smokers and waterpipe users.