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Social and behavioral predictors of two-doses 4CMenB vaccine series among adolescents enrolled in a cluster randomized controlled trial in Australia

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ABSTRACT

This study aimed to determine social and behavioral predictors of completing a course of 4CMenB vaccine in adolescents in a parallel cluster randomized controlled trial enrolling secondary school students (approximately 15–18 years of age) in South Australia. Participating schools were randomized to vaccination at baseline (intervention) or 12 months (control). Students assigned to the intervention group were excluded because they have received the first dose of 4CMenB vaccine at baseline. Logistic regression models examined factors associated with non-vaccination or incomplete 4CMenB doses. The study population comprised 11391 students. Overall, 8.3% (n = 946) received no doses and 91.7% (n = 10445) at least one dose. Of 10445 students who initiated their primary dose, 1334 (12.8%) did not complete the two-dose course. The final adjusted model indicated factors associated with non-vaccination in school students were older age (adjusted odds ratio; aOR 7.83, 95% CI: 4.13–14.82), smoking cigarettes (aOR 3.24, 95% CI: 1.93–5.44), exposure to passive smoke (aOR 2.64, 95% CI: 1.48–4.71), Aboriginal or Torres Strait Islander (aOR 1.77, 95% CI: 1.23–2.55), smoking water pipes (aOR 1.94, 95% CI:1.28–2.92), low socio-economic status (aOR 1.77, 95% CI:1.21–2.60), attending government schools (aOR 1.76, 95% CI: 1.28, 2.43) and participating in intimate kissing (aOR 1.40, 95% CI:1.10–1.79). Multivariable analysis for incomplete vaccination yielded similar findings. Social and behavioral predictors of non-vaccination or incomplete MenB doses were also known risk factors for carriage of *Neisseria meningitidis*. Immunization strategies to improve MenB vaccination completion need to be tailored to social behavior of adolescents.

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Introduction

Invasive meningococcal disease caused by *Neisseria meningitidis* infection is associated with high morbidity and mortality, responsible for 1.2 million cases of infection per year, as well as approximately 135,000 deaths worldwide.[1,2] The most important meningococcal disease-associated groups are A, B, C, W, X, and Y, serogroup B being one of the most predominant serogroups in Australia and other countries.[3,4] Exposure to *N. meningitidis* is common in the general population, leading to asymptomatic pharyngeal carriage, which may be transient or long term.[5]

Age influences carriage, with a rapid rise from 15 years of age to a peak at approximately 19 years in high-income countries, likely due to increases in the number and closeness of social contacts and exposure to risk factors in this age group.[6,7] Although invasive meningococcal disease incidence is highest in infants, a second peak occurs in adolescents/young adults.[4] Several countries, including Australia, recommend the licensed 4CMenB vaccine to provide protection against meningococcal B (MenB) disease in adolescents aged 15–19 years due to their higher risk of group B meningococcal disease.[3]

Despite the recommendation of MenB vaccination for adolescents, uptake of the vaccine in this age group has been suboptimal ranging between 17% to 22% for at least one dose of MenB in the USA.[8,9] One reason for low MenB vaccine uptake among adolescents is lack of routine and publicly funded MenB vaccination programs.[10,11] In the USA, MenB vaccine is recommended for adolescents or young adults aged 16–23 years (preferred age 16–18 years) on the basis of shared clinical decision-making.[12] In Australia, the MenB vaccine (4CMenB) is not funded in the National Immunization Program (NIP) for this age group, however South Australia has a state-funded MenB vaccine program for adolescents with 74% uptake for one dose and 66% for two doses in 15-year-olds in the first year of the program.[13] MenB vaccines are recently funded under the NIP in 2020 for people of all ages including adolescents with specified medical risk conditions, including defects in, or deficiency of, complement components, current or future treatment with eculizumab, or functional or anatomical asplenia. It is also funded for Aboriginal and Torres Strait Islander children ages less than 2 years of age.[14] While the recommendation for specific meningococcal vaccine use in each country depends on the predominant disease-causing serogroups,[15] low completion of multidose schedules is common among adolescents and young adults.[16] Although barriers and facilitators to vaccine uptake among adolescents have been extensively reviewed,[10,17–20] there is no comprehensive assessment of social and behavioral factors influencing non-vaccination or incompletion of MenB vaccine dose series in this group. This study aimed to determine demographic, social

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and behavioral predictors of non-vaccination or non-completion of the recommended two-dose of MenB vaccine series among adolescents aged 15–19 years.

Materials and methods

Study design and participants

This nested cohort study draws on data collected as part of a parallel cluster randomized controlled trial (RCT) enrolling secondary school students (approximately 15–18 years of age) throughout South Australia, in metropolitan and rural/remote areas from 2017 to 2018 to examine the impact of a two-dose 4CMenB vaccine series administered at least one month apart on the carriage of disease-associated meningococci in adolescent school students (ClinicalTrials.gov number, NCT03089086).[21] Students in the three final years of school were enrolled in the study. The trial's exclusion criteria were known pregnancy, previous anaphylactic reaction to 4CMenB, and receipt of a previous dose of 4CMenB. Over 90% (n = 237) of secondary schools in South Australia were randomized to intervention (4CMenB vaccination at baseline in 2017) or control (4CMenB vaccination at study 12 months in 2018) with randomization stratified by school size and socioeconomic status as measured by the Index of Community Socio-Educational Advantage (ICSEA). Approximately 62% of year 10 and 11 students in South Australia enrolled in the trial. Study details are described elsewhere.[21,22] In this analysis, only students from schools randomized to the control group were included as these students had not received the vaccine at baseline and therefore this allowed a comparison between students who declined offer/accepted offer at study completion. We cannot use baseline data as predictors to determine receipt of first dose for students assigned to the intervention group, since vaccination and baseline questionnaire were administered at the same visit for this group. Whereas, students assigned to the control group received their first dose at 12 months follow-up and second dose approximately 2-month after the first dose. Sociodemographic characteristics, health behaviors and social factors reported by students (control group) from their baseline questionnaire were assessed to examine factors associated with completing a two-dose course of 4CMenB vaccine in 2018. Students assigned to the control group that left school prior (mostly year 12 students in 2017) to either the first or second vaccination visit, were able to obtain their two-dose course of 4CMenB vaccine from their local immunization provider/council. Enough vaccine was provided through the study for all enrolled participants to receive 4CMenB vaccine free either at study enrollment or at study completion. Therefore, all control participants had access to free vaccine. Additionally, the State Government funded adolescent Meningococcal B (MenB) Immunization Program commenced on 1st of October 2018.[14] However, most school students from the control group who participated in the RCT received their second dose prior to commencement of the state funded program. Year 10 and 11 students were followed up in schools at 12 months, whereas the year 12 students only provided baseline data for the trial and were not in school at the end of the follow up period. To minimize the bias that might occur due to the difference in access to vaccination in this school year group, only students who were in years 10 and 11 at the first study visit in 2017 were included in this study.

Outcomes

The primary outcome was the proportion of adolescents in year 10 and 11 who did not receive two doses of the 4CMenB vaccine series. The secondary outcome was the proportion of adolescents in year 10 and 11 who received one vaccine dose but did not complete the two-dose course of 4CMenB vaccine series. Vaccination status was considered 'non-vaccination' if the adolescent did not receive any doses (zero doses) and "incomplete" if they did not receive the second dose of MenB vaccine with an interval of approximately 2 months (range 1–3 months).

Explanatory variables

Explanatory variables were selected based on the published literature, prior knowledge and variables included in the "B Part of It" study dataset. The students completed the baseline questionnaires on a separate form that only contained their study ID. No names were included on the forms to promote honest answers. Nurses provided hard copies of the questionnaires to students who were asked to complete it by themselves and advised that privacy would be maintained as the form only included a linking number. The questionnaire was later re-identified by subject number to link questionnaire data with carriage and demographic data. Internal quality checks, such as automatic range checks, were performed to identify data that appeared to be inconsistent, incomplete, or inaccurate. Factors measured at baseline that can potentially predict vaccination receipt at the study follow-up period were included. Baseline information on participants, age, gender, ethnicity, school characteristics, current smoking habit, number of people currently residing in their household, number of people in their house who smoke, recent partner, recent kissing and attendance at a party, pub, hotel were selected as exploratory variables predicting non-completion of MenB vaccine series among adolescents.

Statistical analysis

As this analysis involves the secondary use of data already collected in the high school RCT, no prespecified sample size calculation was undertaken. We first examined if demographic, school characteristics, behavioral variables measured at baseline were associated with receipt of two doses of 4CMenB vaccine at the 15-month follow-up. Logistic regression models with generalized estimating equations (GEEs) were used to estimate both the crude and adjusted odds ratios (aOR) and their corresponding 95% confidence intervals to determine factors associated with non-vaccination or incomplete two-dose course of 4CMenB vaccine among adolescents. To accommodate the potential correlations in vaccine receipt among students from the same school, the GEEs were used to account for clustering at the school level. In the mutually adjusted models, we included all covariates (i.e. age, gender, ethnicity/race, smoking status, relationship status, socioeconomic status (SES)) that were known

potential confounders associated with vaccination uptake among adolescents based on the published literature.[10,19,20,23] Given the relatively high follow-up rate and high adherence to the trial protocol in year 10 and 11 students, the overall missing information in either outcomes (vaccination status) or baseline (predictors) was minimal ranging between 0.1% to 6.9%. Therefore, all available data were used in the analyses. For all analyses, p values < .05 were considered statistically significant. All statistical analyses were performed using Stata version 15 (Stata Corp, College Station, Texas, USA). The protocol was approved by the Women's and Children's Health Network Human Research Ethics Committee.[21,22]

Results

A total of 34489 students were enrolled between April 1 and June 30, 2017. Overall, 11391 students in years 10 (n = 6117) and 11 (n = 5274) were included in our analysis, after excluding 18632 students assigned to receive 4CMenB vaccination at baseline, 4604 students in year 12 and 132 participants who withdrew from the study at any stage (Figure 1). The analysis included 5664 (49.72%) male students and 5727 (50.28%) female students from 112 participating secondary high schools in South Australia. Almost half of the participants (49.56%, n = 5649) at the baseline visit were 15 years old or younger (mean age, 15.61 ± 1.21 years). Students were predominantly Caucasian (69.15%, n = 7877) and from a low household overcrowding index (80.97%, n = 9223). Most (70.74%, n = 8058) of the students attended schools in metropolitan locations and just under half were from high Index of Relative Socioeconomic Disadvantage (IRSD) quintile (ICSEA) schools (47.23%, n = 5380). Baseline characteristics of the students are described in Table 1.

The overall percentage of students who received the first dose of 4CMenB at the 12 months follow up was 91.62% (n = 10,436) and 80.06% (n = 9,120) received 4CMenB vaccine at the second vaccination visit approximately spaced 2 months apart. The median time from first-dose vaccination to second-dose vaccination was 64 days (Interquartile range [IQR], 57–77 days). Of the 955 students who did not receive the vaccine at the first vaccination visit, only nine received the 4CMenB vaccine at a subsequent vaccination visit. Of the final 11391 students, 8.30% (n = 946) received no doses and 91.69% (n = 10445) at least one dose with an overall two-dose completion rate of 79.98% (n = 9111). Of the 10445 students who initiated their primary dose at the first or second vaccination visits, 1334 (12.77%) did not complete the two-dose course of 4CMenB vaccine series. The prevalence of disease-associated (A, B, C, W, X, Y) *N. meningitidis* carriage detected at baseline among adolescents who did not receive any doses 4CMenB vaccine (25/946, 2.64%) was significantly higher compared to those who received at least one dose of 4CMenB vaccine during the study period (135/10445, 1.29%; $p < .001$).

Univariate and multivariate associations among demographic, behavioral, and social predictors of non-vaccination (compared to receiving at least one 4CMenB vaccine dose) are shown in Table 2. In the multivariable logistic regression analyses, factors that increased the likelihood of non-vaccination included, being an older adolescent or young adult (age ≥18) (aOR 7.83, 95% CI: 4.13–14.83), smoking cigarettes (aOR 3.24, 95% CI: 1.93–5.44), exposure to passive smoke at home and outside the house (aOR 2.64, 95% CI: 1.48–

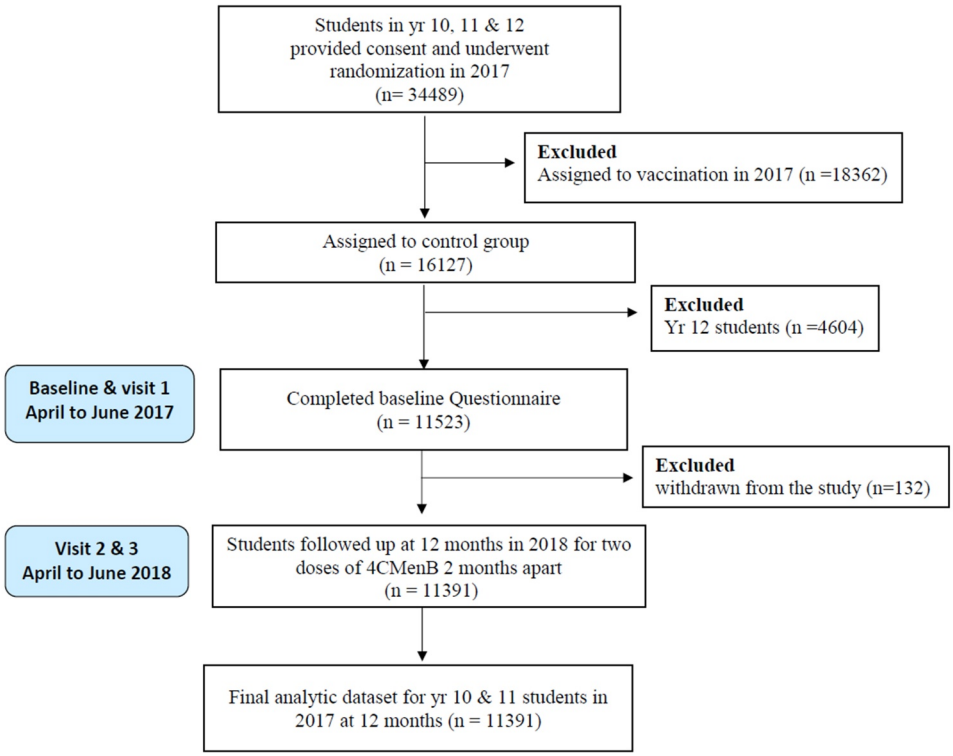

Figure 1. Participants' flow diagram.

Table 1. Baseline characteristics of year 10 and 11 students participating in school RCT, 2017–2018, South Australia.

Characteristic	Participants (N = 11391) n (%)
Gender	
Male	5664 (49.72)
Female	5727 (50.28)
Age (years)	
≤15	5649 (49.59)
16	4935 (43.32)
17	668 (5.86)
≥18	139 (1.22)
Age, mean (SD)	15.61 ± 1.21
Ethnicity	
Caucasian	7877 (69.15)
Aboriginal or Torres Strait Islander	305 (2.68)
Asian	1166 (10.24)
Others	1838 (16.14)
Missing	205 (1.80)
School ICSEA category	
<970 (low)	2443 (21.45)
970 to 1020 (medium)	3568 (31.32)
>1020 (high)	5380 (47.23)
School size	
< 60 students/year level	1496 (13.13)
60 to 119 students/year level	3855 (33.84)
>119 students/year level	6040 (53.02)
School location	
Metropolitan	8058 (70.74)
Provincial	2966 (26.04)
Remote	355 (3.12)
Very remote	12 (0.11)
School type	
Public	6392 (56.11)
Private	4999 (43.89)
Year of schooling	
10	6117 (53.70)
11	5274 (46.30)
Boarding student[a]	
Yes	186 (1.63)
No	11151 (97.89)
Missing	54 (0.47)
Smoked cigarettes in the last week	
Yes	179 (1.57)
No	11143 (97.90)
Missing	69 (0.61)
Smoked electronic cigarette in the last week	
Yes	126 (1.11)
No	11150 (97.88)
Missing	115 (1.01)
Smoked water-pipe in the last week	
Yes	277 (2.43)
No	10997 (96.54)
Missing	117 (1.03)
Nights out in a pub/club in last week	
0 times out in last week	9450 (82.96)
1 or more times out in last week	1883 (16.53)
Missing	58 (0.51)
People kissed in last week	
0 kissed in last week	9013 (79.12)
1 or more kissed in last week	2065 (18.13)
Missing	313 (2.75)
Current relationship status	
Not in relationship	9227 (81.00)
Relationship	2094 (18.38)
Missing	70 (0.61)
Number of persons per room (Household Crowding index)	
≤ 1.5	9223 (80.97)
>1.5 to ≤ 2	1009 (8.86)
>2	182 (1.60)
N/A boarding student	186 (1.63)
Missing	791 (6.94)
Resident smoking status	
Nonsmoking	7731 (67.87)
Smoking, outside the house	2455 (21.55)
Smoking, inside the house	318 (2.79)
Smoking, both inside and outside the house	90 (0.79)
N/A boarding student	186 (1.63)
Missing	611 (5.36)
Missing (including boarding students)	

SD, standard deviations; ICSEA, Index of Community Socio-Educational Advantage
Data are n (%) or mean (SD)
a: Students attending a residential secondary school where they live and study during the school year

4.71), smoking water pipes (aOR 1.94, 95% CI: 1.28–2.92), identifying as Aboriginal or Torres Strait Islander (aOR 1.77, 95% CI: 1.23–2.55), low ICSEA quintile (aOR 1.77, 95% CI: 1.21–2.60), attending Government schools (aOR 1.76, 95% CI: 1.28–2.43), participating in intimate kissing (aOR 1.40, 95% CI: 1.10–1.79), attending schools in metropolitan locations (aOR 1.31, 95% CI: 1.00–1.71) and having a partner (aOR 1.26, 95% CI: 1.02–1.57) (Table 2).

In the univariate analysis, smoking cigarettes, having a partner, participating in intimate kissing and attending government schools were associated with an increased likelihood of non-completion of the 4CMenB vaccine series, but these associations were not significant in the final adjusted model (Table 3). In the final adjusted model examining factors contributing to incomplete 4CMenB vaccination (compared to receiving two doses) similar associations of sociodemographic, social, and behavioral predictors of non-completion of the 4CMenB vaccine series were identified (Table 3). Additional significant predictors of incomplete 4CMenB vaccination status that were not associated with non-vaccination included living in overcrowded house (aOR 1.72, 95% CI: 1.06–2.78) and attendance at pubs or clubs (aOR 1.19, 95% CI: 1.00–1.42) (Table 3).

Discussion

This is the first study to evaluate social and behavioral factors associated with 4CMenB vaccine series completion among adolescents. Our analysis is based on a state-wide sample derived from the largest RCT cohort of adolescents vaccinated with 4CMenB to date as part of the school immunization program in South Australia.[21] Among approximately 11,000 adolescents included in our study, we observed 80% completion rate of the two-dose regimen within three months of the first dose. This suggests that a significant proportion of adolescents have missed opportunities for vaccination or initiate the series but do not complete the recommended two-dose of 4CMenB vaccine series. However, completion of the 4CMenB vaccine series in our study is impressively higher than a previous study in USA, with a completion rate of 58%.[23] A similar trend has been reported in 2017 for MenACWY vaccine uptake among adolescents in the USA where a coverage of at least one dose of MenACWY among

Table 2. Factors associated with non-vaccination (zero doses) of the two-dose schedule of 4CMenB vaccine among adolescents in year 10 and 11.

Variable	No doses n/N (%) 946/11391 (8.30)	Odds Ratio (OR) (95% CI)	P- value	Adjusted aOR [a] (95% CI)	P-value
Gender					
Female	452/5727 (7.89)	Reference		Reference	
Male	494/5664 (8.72)	1.11 (0.96, 1.29)	0.146	1.20 (1.03, 1.40)	0.013
Age					
≤15	362/5649 (6.41)	Reference	<0.001#	Reference	<0.001#
16	447/4935 (9.06)	1.45 (1.21, 1.73)	<0.001	1.46 (1.21, 1.76)	<0.001
17	87/668 (13.02)	2.18 (1.63, 2.91)	<0.001	1.89 (1.42, 2.52)	<0.001
≥18	50/139 (35.97)	8.20 (4.37, 15.40)	<0.001	7.83 (4.13, 14.83)	<0.001
Ethnicity					
Caucasian	597/7877 (7.58)	Reference	<0.001#	Reference	<0.001#
Aboriginal or Torres Strait Islander	56/305 (18.36)	2.74 (1.97, 3.80)	< 0.001	1.77 (1.23, 2.55)	0.003
Asian	73/1166 (6.26)	0.81 (0.52, 1.26)	0.363	0.64 (0.48, 0.87)	0.004
Others	200/1838 (10.88)	1.48 (1.18, 1.87)	0.001	1.20 (0.97, 1.50)	0.088
School socioeconomic status, ICSEA					
>1020 (high)	282/5380 (5.24)	Reference	<0.001#	Reference	0.011#
970 to 1020 (medium)	334/3568 (9.36)	1.86 (1.24, 2.80)	0.003	1.43 (1.03, 1.99)	0.029
<970 (low)	330/2443 (13.51)	2.82 (2.02, 3.93)	<0.001	1.77 (1.21, 2.60)	0.003
School location					
Rural	282/3333 (8.46)	Reference		Reference	
Metropolitan	664/8058 (8.24)	0.97 (0.70, 1.33)	0.860	1.31 (1.00, 1.71)	0.045
School size					
< 60 students/year level	102/1496 (6.82)	Reference	0.278#	Reference	0.724#
60 to 119 students/year level	299/3855 (7.76)	1.14 (0.76, 1.73)	0.508	0.99 (0.71, 1.38)	0.966
>119 students/year level	545/6040 (9.02)	1.35 (0.93, 1.96)	0.111	0.90 (0.65, 1.24)	0.532
School type					
Private	237/4999 (4.74)	Reference		Reference	
Public	709/6392 (11.09)	2.50 (1.88, 3.32)	<0.001	1.76 (1.28, 2.43)	<0.001
Boarding student [b]					
Yes	10/186 (5.38)	Reference		Reference	
No	931/11151 (8.35)	1.60 (0.96, 2.66)	0.068	1.15 (0.67, 1.99)	0.592
Smoked cigarettes in the last week					
No	872/11143 (7.83)	Reference		Reference	
Yes	68/179 (37.99)	7.21 (5.12, 10.15)	< 0.001	3.24 (1.93, 5.44)	<0.001
Smoked electronic cigarette in the last week					
No	903/11150 (8.10)	Reference		Reference	
Yes	23/126 (18.25)	2.53 (1.61, 3.96)	<0.001	0.74 (0.35, 1.56)	0.442
Smoked water-pipe in the last week					
No	855/10997 (7.77)	Reference		Reference	
Yes	72/277 (25.99)	4.16 (3.04, 5.70)	<0.001	1.94 (1.28, 2.92)	0.001
Residents smoking status [c]					
Nonsmoking	497/7731 (6.43)	Reference	<0.001#	Reference	<0.001#
Smoking, outside the house	311/2455 (12.67)	2.11 (1.74, 2.56)	<0.001	1.65 (1.34, 2.03)	<0.001
Smoking, inside the house	52/318 (16.35)	2.84 (2.01, 4.02)	<0.001	1.83 (1.27, 2.63)	0.001
Smoking, both inside and outside the house	19/90 (21.11)	3.89 (2.21, 6.84)	<0.001	2.64 (1.48, 4.71)	0.001
Nights out in a pub/club in last week					
0 times out in last week	739/9450 (7.82)	Reference		Reference	
1 or more times out in last week	201/1883 (10.67)	1.40 (1.20, 1.65)	<0.001	1.17 (0.97, 1.40)	0.115
People kissed in last week					
0 kissed in last week	629/9013 (6.98)	Reference		Reference	
1 or more kissed in last week	283/2065 (13.70)	2.11 (1.81, 2.47)	<0.001	1.40 (1.10, 1.79)	0.005
Current relationship status					
Not in relationship	661/9227 (7.16)	Reference		Reference	
In relationship	277/2094 (13.23)	1.97 (1.67, 2.32)	<0.001	1.26 (1.01, 1.57)	0.033
Number of persons per room (Household Crowding index) [c]					
≤ 1.5 persons per room	728/9223 (7.89)	Reference	0.020#	Reference	0.642#
>1.5 to ≤ 2 persons per room	96/1009 (9.51)	1.22 (0.89, 1.67)	0.201	0.91 (0.72, 1.13)	0.430
>2 persons per room	25/182 (13.74)	1.85 (1.22, 2.82)	0.004	1.22 (0.64, 2.31)	0.532

CI, confidence interval; SD, standard deviations; ICSEA, Index of Community Socio-Educational Advantage
A "Reference" is a group that we choose to be the reference so that all odds ratios will be a comparison to the reference group.
a: Mutually adjusted
b: Students attending a residential secondary school where they live and study during the school year
c: Boarding students (n = 186) have been omitted from the variable
Global *p*-value

adolescents age 13–17 years was estimated to be 85%, yet uptake of a booster dose at 16 years of age remains suboptimal at 44%.[24] On the basis of immunogenicity responses, completion of the two-dose 4CMenB vaccine course in adolescents is necessary for maximal protection against meningococcal B infection.[25] Focused efforts are required to overcome the drop off between the first and subsequent doses in school delivered immunization programs or in community or health facilities.

Table 3. Factors associated with receiving only one dose of 4CMenB vaccine among Adolescents in year 10 and 11.

Variable	Incomplete vaccine series n/N (%) 1334/10445 (12.77)	Odds ratio (OR) (95% CI)	P- value	Adjusted aOR [a] (95% CI)	P-value
Gender					
Female	617/5275 (11.70)	Reference		Reference	
Male	717/5170 (13.87)	1.21 (1.06,1.38)	0.003	1.25 (1.09, 1.44)	.002
Age					
≤15	656/5287 (12.41)	Reference	<0.001#	Reference	.001#
16	555/4888 (12.37)	0.99 (0.85, 1.16)	0.961	0.99 (0.83, 1.17)	.929
17	99/581 (17.04)	1.44 (1.12, 1.86)	0.004	1.40 (1.07, 1.84)	.014
≥18	24/89 (26.97)	2.60 (1.59, 4.24)	<0.001	2.42 (1.40, 4.18)	.001
Ethnicity					
Caucasian	876/7280 (12.03)	Reference	0.0002#	Reference	.004#
Aboriginal or Torres Strait Islander	60/249 (24.10)	2.32 (1.55, 3.46)	<0.001	2.02 (1.37, 2.96)	<.001
Asian	141/1093 (12.90)	1.08 (0.85, 1.37)	0.518	0.88 (0.69, 1.14)	.354
Others	223/1638 (13.61)	1.15 (0.98, 1.35)	0.081	0.97 (0.83, 1.14)	.780
School socioeconomic status, ICSEA					
>1020 (high)	531/5098 (10.42)	Reference	0.0002#	Reference	.002#
970 to 1020 (medium)	430/3234 (13.30)	1.31 (1.98, 1.76)	0.061	1.64 (1.23, 2.18)	.001
<970 (low)	373/2113 (17.65)	1.84 (1.37, 2.47)	<0.001	1.40 (1.04, 1.87)	.025
School location					
Rural	304/3051 (9.96)	Reference		Reference	
Metropolitan	1030/7394 (13.93)	1.46 (1.14, 1.86)	0.002	1.90 (1.49, 2.42)	<.001
School size					
< 60 students/year level	164/1394 (11.76) 428/3556	Reference	0.546#	Reference	.911#
60 to 119 students/year level	(12.04)	1.02 (0.71, 1.47)	0.890	0.93 (0.66, 1.32)	.716
>119 students/year level	742/5495 (13.50)	1.17 (0.84, 1.62)	0.348	0.92 (0.62, 1.34)	.676
School type					
Private	514/4762 (10.79)	Reference		Reference	
Public	820/5683 (14.43)	1.39 (1.07, 1.80)	0.013	1.07 (0.77, 1.47)	.661
Boarding student [b]					
Yes	16/176 (9.09)	Reference		Reference	
No	1307/10220 (12.79)	1.46 (0.78, 2.73)	0.229	0.71 (0.32, 1.58)	.412
Smoked cigarettes in the last week					
No	1285/10271 (12.51)	Reference		Reference	
Yes	35/111 (31.53)	3.22 (2.18, 4.75)	<0.001	1.51 (0.90, 2.51)	.112
Smoked electronic cigarette in the last week					
No	1280/10247 (12.49)	Reference		Reference	
Yes	31/103 (30.10)	3.01 (2.15, 4.21)	<0.001	1.60 (0.99, 2.58)	.053
Smoked water-pipe in the last week					
No	1255/10142 (12.37)	Reference		Reference	
Yes	58/205 (28.29)	2.79 (1.96, 3.96)	<0.001	1.83 (1.20, 2.77)	.004
Residents smoking status [c]					
Nonsmoking	798/7234 (11.03)	Reference	<0.001#	Reference	<.001#
Smoking, outside the house	362/2144 (16.88)	1.63 (1.41, 1.89)	<0.001	1.44 (1.24, 1.66)	<.001
Smoking, inside the house	66/266 (24.81)	2.66 (1.86, 3.78)	<0.001	2.03 (1.36, 3.02)	<.001
Smoking, both inside and outside the house	15/71 (21.13)	2.16 (1.24, 3.73)	0.006	1.90 (1.16, 3.13)	.011
Nights out in a pub/club in last week					
0 times out in last week	1078/8711 (12.38)	Reference		Reference	
1 or more times out in last week	244/1682 (14.51)	1.20 (1.03, 1.40)	0.019	1.19 (1.00, 1.42)	.039
People kissed in last week					
0 kissed in last week	992/8384 (11.83)	Reference		Reference	
1 or more kissed in last week	295/1782 (16.55)	1.47 (1.28, 1.69)	<0.001	1.22 (0.99, 1.50)	.051
Missing					
Current relationship status					
Not in relationship	1043/8566 (12.18)	Reference		Reference	.164
In relationship	281/1817 (15.47)	1.31 (1.14, 1.52)	<0.001	1.17 (0.93, 1.46)	
Number of persons per room (Household Crowding index) [c]	1040/8495 (12.24)	Reference	0.004#	Reference	.037#
≤ 1.5 persons per room	142/913 (15.55)	1.32 (1.05, 1.65)	0.016	1.18 (0.94, 1.48)	.146
>1.5 to ≤ 2 persons per room	34/157 (21.66)	1.98 (1.17, 3.34)	0.010	1.72 (1.06, 2.78)	.026
>2 persons per room					

CI, confidence interval; SD, standard deviations; ICSEA, Index of Community Socio-Educational Advantage
A "Reference" is a group that we choose to be the reference so that all odds ratios will be a comparison to the reference group.
a: Mutually adjusted
b: Students attending a residential secondary school where they live and study during the school year
c: Boarding students (n = 186) have been omitted from the variable
Global *p*-value

Although recent studies have demonstrated no discernible effect of recombinant MenB vaccines on disease-associated carriage,[21,26] there is still a need for direct protection of adolescents and young adults at an age of greater risk of invasive meningococcal disease.[7] Interestingly, it was found that groups of adolescents with the highest risk of carriage in the original

RCT[21] were least likely to be vaccinated or complete a two-dose series of 4CMenB in this study. The present study suggests that older adolescents, who are an important risk age-group for serogroup B meningococcal disease were more likely to be unvaccinated or have an incomplete course of the recommended two doses 4CMenB, consistent with previous studies of other meningococcal vaccines.[23,27] Although all students in our study were offered 4CMenB vaccine, school absenteeism in older adolescents is common which may contribute to non-vaccination or under vaccination in this age group. Additionally, parents are likely to be the primary decision-makers for early adolescent's vaccination compared to older adolescents who may be more participatory in vaccination decisions.[28] Interventions aimed at improving completion of 4CMenB series among older adolescents are needed and catch-up immunization campaigns should include sufficient information about and better access to the vaccine to help older adolescents make informed decisions about vaccination.[18] Furthermore, it is important to maintain high MenB vaccine series completion rates in younger adolescents before they enter the highest age-based risk period. This may maximize the likelihood of protection prior to entering the age group at highest risk of invasive meningococcal disease.[29]

Other sociodemographic factors associated with low completion of 4CMenB vaccine were male gender, although findings from a systematic review of studies of multi-dose vaccination in adolescents reported inconsistent results in relation to gender.[20] The RCT in South Australia demonstrated that students who identify as Aboriginal or Torres Strait Islander had almost double the carriage prevalence compared to students that identified as Caucasian[21] and they were twice more likely not to complete the 4CMenB vaccine series in this study. It is widely recognized that Aboriginal peoples in Australia have higher invasive meningococcal disease notification rates than non-Aboriginal peoples[30] with disease due to serogroup B being four times higher for Aboriginal people in 2017 (2.0/100 000) compared to non-Aboriginal people (0.5/100 000).[25] This suggests the need to improve strategies that are culturally appropriate, including active communication and better access in targeted campaigns for Aboriginal adolescents. For adolescents who missed the MenB vaccine doses delivered in school-based programs, catch up vaccine programs could incorporate Aboriginal Community Controlled Health Organization services to deliver culturally appropriate immunization resources and interventions for Aboriginal adolescents.

Social and behavioral factors, rather than age or gender, can explain the higher prevalence of meningococcal carriage among adolescents and young adults.[6] Importantly, our study demonstrates that social and behavioral factors such as active and passive cigarette smoking, waterpipe tobacco smoking, being in a relationship, intimate kissing, attending pubs and clubs, and household crowding were all strongly and independently associated with either non-vaccination or non-completion of the recommended two doses of MenB vaccine series, which are known predisposing risk factors for meningococcal carriage in adolescents and young adults.[21,31] Cigarette smoking,[32] passive smoking,[32] intimate kissing,[33] low socio-economic status,[34] overcrowded living,[34–36] identifying as Aboriginal or Torres Strait Islander,[37] attending nightclubs,[33,36] and have also inconsistently been found to be associated with developing invasive meningococcal disease. This highlights that targeted interventions to improve Men B vaccine coverage gap in adolescents with risk factors may also provide protection for those at highest risk of developing invasive meningococcal disease.[33] Administering meningococcal vaccine programs through schools provides an opportunity for parental participation in vaccination decisions and normalization of the process for adolescents. The school program also improves equitable access for adolescents from all socio-economic groups, particularly lower socio-economic groups where risk factors for carriage including smoking and household crowding are likely to be more prevalent.

The major strength of this study is the large sample size, representative of the adolescent population in South Australia. Another strength of the present study is the inclusion of extensive data on known risk factors for meningococcal carriage and disease. This enabled us to explore if predisposing factors for meningococcal carriage are also associated with vaccination behavior among adolescents. To improve retention rates, 20 USD iTunes cards were provided at the first study visit and 12-month follow up visit and text message reminders were sent prior to the school visits to notify parent/participants of when their first and second dose of vaccination will occur. There is evidence that financial incentives improve uptake of vaccines compared to standard practice.[18] There is also a risk the financial incentives may introduce bias, by being more appealing to adolescents with lower SES to complete the two-dose regimen. However, this is unlikely as students from low SES areas were less likely to have complete course of two-doses 4CMenB vaccine series. Another potential limitation is students that left school could not be identified. Furthermore, the fact that adolescents were all part of a study means that their social behavior might be different to adolescents partaking in the state government funded MenB immunization program,[14] although uptake in the study was almost as high as the state funded program.[13] Therefore, the estimated vaccine uptake and social and behavioral factors may differ for students receiving the vaccine via the standard school immunization program and the year 12 students that were excluded from our study.

Studies are needed to determine how to improve completion of vaccine doses in adolescents with consideration of co-designing strategies with young people. As behavioral risk factors were strongly associated with under-vaccination, strategies should focus on behavioral interventions or "nudges" to improve completion of two dose schedules, not only for meningococcal vaccines but also for human papillomavirus vaccine and COVID −19 vaccines when they become approved for young people.

Conclusions

The present study offers a robust evaluation of social and behavioral factors in predicting non-vaccination and completion of the two-dose 4CMenB vaccine series among adolescents. Many of the social and behavioral predictors of low 4CMenB vaccine uptake among adolescents identified in the current study were also known risk factors for carriage of *N. meningitidis* reflecting a higher risk population remaining unprotected. The study

findings can be used to co-design with adolescents, targeted interventions to improve coverage alongside the highly effective school-based immunization programs to maximize the uptake of vaccines recommended for adolescents.

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Disclosure of potential conflicts of interest

HSM is an investigator on vaccine trials sponsored by Industry (the GSK group of companies, Novavax, Pfizer). HSM's, MMc's and HM's institution receives funding for investigator-led studies from Industry (Pfizer, Sanofi-Pasteur and the GSK group of companies). HSM, HM and MM receive no personal payments from Industry.

Contribution to authorship

HM, MM and HSM have all contributed to the planning and design of the study, and to the interpretations of the data. HM performed data analyses and prepared the first draft of the manuscript. All named authors were involved in critically reviewing the content, and have approved the final version for publication.

Data availability statement

The datasets generated and/or analysed during the current study are available upon reasonable request to Prof. Helen Marshall (helen.marshall@adelaide.edu.au) and subject to regulatory approvals.

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