Impact of COVID-19 Containment Strategies and Meningococcal Conjugate ACWY Vaccination on Meningococcal Carriage in Adolescents

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Objectives: To examine if COVID-19 containment strategies were associated with reduced pharyngeal carriage of meningococci in adolescents. Also, to observe if carriage prevalence of meningococcal A, C, W and Y differed in meningococcal conjugate ACWY vaccinated and unvaccinated adolescents.

Design: Repeat cross-sectional study of pharyngeal carriage.

Setting: In 2020, recruitment commenced from February to March (pre-COVID-19) and recommenced from August to September (during COVID-19 measures) in South Australia.

Participants: Eligible participants were between 17 and 25 years of age and completed secondary school in South Australia in 2019.

Results: A total of 1338 school leavers were enrolled in 2020, with a mean age of 18.6 years (standard deviation 0.6). Pharyngeal carriage of disease-associated meningococci was higher during the COVID-19 period compared with the pre-COVID-19 period (41/600 [6.83%] vs. 27/738 [3.60%]; adjusted odds ratio [aOR], 2.03; 95% CI: 1.22–3.39; P = 0.01). Nongroupable carriage decreased during COVID period (1.67% vs. 3.79%; aOR, 0.45; 95% CI: 0.22–0.95). Pharyngeal carriage of groups A, C, W and Y was similar among school leavers vaccinated with meningococcal conjugate ACWY (7/257 [2.72%]) compared with those unvaccinated (29/1081 [2.68%]; aOR, 0.86; 95% CI: 0.37–2.02; P = 0.73). Clonal complex 41/44 predominated in both periods.

Conclusions: Meningococcal carriage prevalence was not impacted by public health strategies to reduce severe acute respiratory syndrome coronavirus 2 transmission and is unlikely to be the mechanism for lower meningococcal disease incidence. As international travel resumes and influenza recirculates, clinicians must remain vigilant for signs and symptoms of meningococcal disease. Vaccinating people at the highest risk of invasive meningococcal disease remains crucial despite containment strategies.

Keywords: meningococcal, carriage, COVID-19
function. Another potential factor could be reducing the transmission of meningococci through social distancing and quarantine.

This article examined differences in meningococcal carriage prevalence between adolescent school leavers in South Australia swabbed before and after introducing social distancing and lockdown measures in response to COVID-19, during a year of low influenza and IMD incidence. We also sought to detect differences in the prevalence of meningococcal A, C, W and Y carriage between MenACWY vaccinated and unvaccinated school leavers during the first year after the introduction of the MenACWY program in South Australia.

METHODS

Study Design

This analysis uses data from an investigator-led repeat cross-sectional “school leaver” study conducted in South Australia (2018–2020) that assessed meningococcal carriage in young adults the year after finishing school. This research is a secondary analysis of the final year of that study, in which oropharyngeal swabs were collected both before COVID containment strategies and after the easing of strategies in 2020. During 2017 and 2018, a cluster-randomized controlled trial conducted in South Australia provided 4CMenB vaccination at baseline (intervention) or after 12 months (control) to over 30,000 high school students (“B Part of it” study). After the randomized controlled trial, from 2019, both 4CMenB and MenACWY vaccines were made freely available for adolescents through the school immunization program in South Australia. In 2020, recruitment commenced on 24 February and continued until 4 March (hereafter “pre-COVID-19”). Recruitment was then paused because of COVID-19 restrictions and recommenced from 17 August until 11 September 2020 (hereafter “COVID-19-period”).

Figure 1. Timeline of COVID-19 restrictions in South Australia from January 25, to August 3, 2020.
Participants

Eligible adolescents must have completed secondary school in South Australia in 2019 and be between 17 and 25 years of age. Participants were recruited using mail-outs, text messages, education stalls during university orientation week, social media advertising and a Medicare mail-out to 18-year-olds in urban Adelaide and selected rural locations for generalizability in South Australia.

Study Process

Each participant provided written consent and had an oropharyngeal swab taken by trained nursing or medical staff. Questionnaires that identified potential risk factors for carriage were completed, and participants were reimbursed $40 for their time and travel costs. MenACWY and 4CMenB vaccination status was ascertained via the Australian Immunisation Register.

Swabs were placed in 2 mL skim milk-tryptone-glucose-glycerol medium and transported to the state-wide pathology service, SA Pathology. Direct screening for meningococcal DNA (\textit{porA} gene) was conducted using polymerase chain reaction (PCR), with further analysis conducted to determine the meningococcal genogroup (A, B, C, W, X or Y). Disease-associated carriage is defined as detection of the \textit{porA} gene and capsular genogroup for groups A, B, C, W, X or Y. Nongroupable carriage is defined as detection of the \textit{porA} gene and failure to detect any of the capsular genogroups listed above. As described previously, any samples yielding a \textit{porA} positive reverse transcription PCR were cultured for \textit{Neisseria} species on selective agar, and multilocus sequence typing and fine typing were defined using the PUBMLST database.

Statistical Analysis

As this is a secondary analysis/posthoc, sample size calculations for comparing specific time periods and comparisons based on MenACWY status were not conducted a priori. Logistic regression was used to examine the effects of COVID-19—a condition measure, MenACWY vaccination and 4CMenB vaccination on meningococcal carriage, with effects described as odds ratios (ORs) and 95% CIs. Participants who were vaccinated <28 days before their swab were considered unvaccinated for comparisons (ORs) and 95% CIs. Participants who were vaccinated <28 days before their swab were considered unvaccinated for comparisons between vaccinated and unvaccinated groups. Recruitment in 2020 was lower than anticipated owing to COVID-19 restrictions, resulting in low numbers of observed events. For this reason, variables used in the regression analysis were limited to the COVID-19 containment period, MenACWY vaccine and 4CMenB vaccine receipt. All analyses were performed using Stata v.15 (Statacorp, College Station, TX).

COVID-19 Restrictions in South Australia

After university orientation week in early March 2020, containment measures were progressively introduced by the state and federal government in response to the COVID-19 pandemic, with most nonessential gatherings and services effectively banned and shut down as of late March 2020. At the same time, foreign travelers were no longer able to come to Australia because of border measures introduced to curb the spread of the virus. Australian citizens could return but were required to undergo 14 days of quarantine. Study recruitment was paused until the easing of containment measures in August. During the heaviest restrictions, people were mandated to work or study from home, and environments conducive to the spread of respiratory droplets, such as pubs, clubs and entertainment venues, were shut. With the easing of restrictions, these venues were permitted to reopen with physical distancing and dramatically reduced capacity limits in place (Fig. 1).21,22

Ethics Approval

The study was approved by the Women’s and Children’s Health Network Human Research Ethics Committee and prospectively registered at ClinicalTrials.gov: NCT03419533.

RESULTS

A total of 1343 school leavers were enrolled in 2020. Five school leavers were excluded from all analyses of carriage prevalence because of missing swab data. Participants had a mean age of 18.6 years (standard deviation 0.6), and the majority were female (809 [60.9%]) (Table 1). Just over half of the participants were swabbed between February and March (738 [55.2%]), with the remainder swabbed between August and September (600 [44.8%]). Compared with the pre-COVID-19 period, the proportions of both 4CMenB-vaccinated and MenACWY-vaccinated participants were higher during the COVID-19-period (4CMenB: pre-COVID-19, 514/738 [69.6%], COVID-19-period 505/600 [84.2%], MenACWY: pre-COVID-19, 92/738 [12.5%], COVID-19-period, 165/600 [27.5%]). The proportion of school leavers spending 2 or more days out in the last week was dramatically reduced capacity limits in place (Fig. 1).21,22

TABLE 1. Participant Characteristics by COVID-19 Period

| Participant characteristics | Pre-COVID-19† | COVID-19† | Total‡ |
|----------------------------|---------------|-----------|--------|
| Age in years (N = 738) (N = 600) (N = 1338) | 18.33 (0.64) | 18.82 (0.41) | 18.55 (0.60) |
| IRSD quintile* | 1 (most disadvantaged) | 2 | 3 | 4 | 5 (least disadvantaged) |
| Mean (SD) | 118 (16.3) | 103 (14.2) | 137 (18.9) | 140 (19.3) | 228 (31.2) |
| 2 | 93 (15.7) | 85 (14.3) | 89 (15.0) | 144 (24.2) | 163 (30.8) |
| 3 | 211 (16.0) | 188 (14.3) | 226 (17.1) | 284 (21.5) | 409 (31.0) |
| 4 | 1 | 2 | 3 | 4 | 5 |
| 5 (least disadvantaged) | 32 (4.7) | 38 (5.6) | 46 (6.5) | 63 (9.1) | 70 (9.3) |
| Gender (female) | 210 (29.6) | 76 (12.8) | 286 (20.9) |
| Mean (SD) | 210 (21.9) | 430 (58.8) | 690 (60.9) |
| Meningococcal B vaccination (2 doses) | 514 (69.6) | 505 (84.2) | 1019 (76.2) |
| Mean (SD) | 92 (12.5) | 165 (27.5) | 257 (19.2) |
| Working status | 18 (2.4) | 11 (1.5) | 139 (18.9) | 557 (75.6) | 7 (0.9) |
| Full time work | 31 (5.2) | 76 (12.7) | 109 (18.2) | 274 (45.7) | 86 (14.3) |
| Part time work | 49 (3.7) | 87 (6.7) | 248 (18.5) | 831 (62.2) | 93 (7.0) |
| Part time work + study | 12 (2.0) | 32 (2.4) | 32 (2.4) | 62 (4.8) | 32 (2.4) |
| Smoking in the last week | 12 (2.0) | 32 (2.4) | 62 (4.8) | 32 (2.4) | 32 (2.4) |
| Smoking water pipe in last month | 9 (1.5) | 30 (2.2) | 30 (2.2) | 30 (2.2) | 30 (2.2) |
| Ethnicity | 13 (1.8) | 15 (2.5) | 28 (2.1) |
| Aboriginal Torres Strait Islander | 425 (59.9) | 464 (78.2) | 889 (68.2) |
| Caucasian | 425 (59.9) | 464 (78.2) | 889 (68.2) |
| Asian | 210 (29.6) | 76 (12.7) | 286 (21.9) |
| Middle Eastern | 11 (1.5) | 8 (1.3) | 19 (1.5) |
| African | 16 (2.3) | 3 (0.5) | 19 (1.5) |
| Other | 35 (4.9) | 27 (4.6) | 62 (4.8) |
| Days out in the last week | 368 (51.4) | 373 (62.5) | 741 (56.4) |
| None | 196 (27.4) | 162 (27.1) | 358 (27.3) |
| 1 | 152 (21.2) | 62 (10.4) | 214 (16.3) |
| 2 or more | 515 (71.7) | 420 (70.5) | 935 (71.2) |
| Drunk alcohol in last month | 446 (62.8) | 350 (59.6) | 796 (61.4) |
| None | 264 (37.2) | 237 (40.4) | 501 (38.6) |
| 1 or more | 213 (29.6) | 198 (33.2) | 411 (31.2) |

†Index of relative socio-economic disadvantage (IRSD).

‡n (%) presented unless otherwise indicated (excludes missing values).
days out in the last week halved in the COVID-19 period (62/597 [10.4%]) compared with pre-COVID-19 (152/716 [21.2%]). However, the proportion of people kissing 1 or more people in the last week was relatively consistent between the 2 periods. It was also similar between those kissing 2 or more people in the last week pre COVID-19 compared with during COVID-19 (3.8% vs. 3.6%). As well as those kissing 1 or more people while in a relationship (pre COVID-19 compared with during COVID-19 (3.8% vs. 3.6%). As

Pharyngeal carriage of disease-associated meningococci increased during the COVID-19 period compared with pre COVID-19 (41/600 [6.83%] vs. pre 27/738 [3.66%], adjusted OR [aOR], 2.03; 95% CI: 1.22–3.39; P=0.01). The increase was mostly because of changes in the carriage of groups B (aOR, 2.94; 95% CI: 1.50–5.79) and Y (aOR 2.76; 95% CI: 1.27–6.03), as per Tables 2 and 3. There was a decrease in nongroupable carriage in the COVID-19 period compared with the pre-COVID-19 period (10/600 [1.67%] vs. pre 28/738 [3.79%], aOR 0.45, 95% CI: 0.22–0.95; P=0.04).

Pharyngeal carriage of groups A, C, W and Y was similar among school leavers vaccinated with MenACYW (7/257 [2.72%]) compared with those unvaccinated (29/1081 [2.68%]; aOR, 0.86; 95% CI: 0.37–2.02; P = 0.73). No significant differences in carriage were detected between MenACYW vaccinated and unvaccinated

### TABLE 2. Carriage by COVID-19 Period and MenACWY Vaccination Status

| Genogroup‡ | Pre-COVID-19 | COVID-19 Period |
|------------|--------------|----------------|
|            | MenACWY | Unvaccinated (N = 646), n (%) | MenACWY | Vaccinated (N = 92), n (%) | Total Pre (N = 738), n (%) | MenACWY | Unvaccinated (N = 435), n (%) | MenACWY | Vaccinated (N = 165), n (%) | Total During (N = 600), n (%) |
| Disease-associated* | 26 (4.02) | 1 (0.99) | 27 (3.66) | 30 (6.90) | 11 (6.67) | 41 (6.83) |
| Groups A, C, W or Y | 13 (2.01) | 0 (0) | 13 (1.76) | 16 (3.68) | 7 (4.24) | 23 (3.83) |
| Any | 52 (8.05) | 3 (3.26) | 55 (7.45) | 39 (8.97) | 12 (7.27) | 51 (8.50) |
| Group A | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Group B | 12 (1.86) | 1 (1.09) | 13 (1.76) | 22 (5.06) | 8 (4.85) | 30 (5.00) |
| Group C | 1 (0.15) | 0 (0) | 1 (0.14) | 1 (0.23) | 1 (0.61) | 2 (0.33) |
| Group W | 3 (0.46) | 0 (0) | 3 (0.41) | 6 (1.35) | 2 (1.23) | 8 (1.33) |
| Group X | 1 (0.15) | 0 (0) | 1 (0.14) | 1 (0.23) | 1 (0.61) | 2 (0.33) |
| Group Y | 10 (1.55) | 0 (0) | 10 (1.36) | 15 (3.45) | 6 (3.64) | 21 (3.50) |
| Nongroupable† | 26 (4.02) | 2 (2.17) | 28 (3.79) | 9 (2.07) | 1 (0.61) | 10 (1.67) |

*“Disease-associated" and 'Groups A, C, W, Y' are less than the individual genogroup total because more than one isolate has been detected in some participants.

†“Nongroupable" carriage is defined as failure to detect genogroup A, B, C, W, X or Y, in those with porA detected.

‡Adjusted for all 3 exposures of interest. NOTE: All models are based on N = 1338 observations.

### TABLE 3. Unadjusted and Adjusted Analyses of Carriage Prevalence in School Leavers by COVID-19 Period, MenACWY, and MenB Vaccination Status in 2020

| Exposure by Genogroup | Unadjusted Effect | Adjusted Effect |
|------------------------|-------------------|-----------------|
|                        | Unadjusted OR (95% CI) | Unadjusted P | Adjusted OR (95% CI) | Adjusted P |
| Disease-associated* | 1.93 (1.17–3.18) | 0.01 | 2.03 (1.22–3.39) | 0.01 |
| COVID-19-period vs. pre-COVID-19 | 0.90 (0.47–1.70) | 0.74 | 0.77 (0.40–1.48) | 0.43 |
| MenACWY vaccinated vs. unvaccinated | 1.02 (0.57–1.81) | 0.95 | 0.91 (0.50–1.63) | 0.74 |
| Groups A, C, W or Y | 2.22 (1.12–4.43) | 0.02 | 2.35 (1.16–4.77) | 0.02 |
| COVID-19-period vs. pre-COVID-19 | 1.02 (0.44–2.35) | 0.97 | 0.86 (0.37–2.02) | 0.37 |
| MenACWY vaccinated vs. unvaccinated | 0.94 (0.44–2.01) | 0.87 | 0.80 (0.37–1.75) | 0.58 |
| Any | 1.15 (0.78–1.72) | 0.48 | 1.21 (0.81–1.82) | 0.36 |
| COVID-19-period vs. pre-COVID-19 | 0.67 (0.38–1.19) | 0.17 | 0.64 (0.36–1.13) | 0.13 |
| MenACWY vaccinated vs. unvaccinated | 1.08 (0.67–1.73) | 0.76 | 1.08 (0.67–1.75) | 0.75 |
| Group B | 2.94 (1.52–5.68) | 0.001 | 2.94 (1.50–5.79) | 0.002 |
| COVID-19-period vs. pre-COVID-19 | 1.12 (0.53–2.36) | 0.77 | 0.87 (0.41–1.87) | 0.72 |
| MenACWY vaccinated vs. unvaccinated | 1.38 (0.83–3.01) | 0.42 | 1.13 (0.51–2.50) | 0.76 |
| Group Y | 2.64 (1.23–5.65) | 0.01 | 2.76 (1.27–6.03) | 0.01 |
| COVID-19-period vs. pre-COVID-19 | 1.01 (0.41–2.49) | 0.98 | 0.82 (0.33–2.05) | 0.67 |
| MenACWY vaccinated vs. unvaccinated | 1.08 (0.46–2.52) | 0.87 | 0.89 (0.37–2.14) | 0.80 |
| Nongroupable† | 0.43 (0.21–0.89) | 0.02 | 0.45 (0.22–0.95) | 0.04 |
| COVID-19-period vs. pre-COVID-19 | 0.35 (0.11–1.16) | 0.09 | 0.41 (0.12–1.35) | 0.14 |
| MenACWY vaccinated vs. unvaccinated | 1.18 (0.54–2.60) | 0.68 | 1.44 (0.65–3.20) | 0.37 |

*“Disease-associated genogroups defined as genogroups A, B, C, W, X or Y.

†“Nongroupable" carriage is defined as failure to detect genogroup A, B, C, W, X or Y, in those with porA detected.

‡Adjusted for all 3 exposures of interest. NOTE: All models are based on N = 1338 observations.
school leavers for any individual genogroups or nongroupable carriage (Table 3).

Culturing of porA PCR-positive samples yielded 64 isolates (60% recovery: pre COVID-19, 29/55 [53%]; COVID-19 period 35/51 [69%]). The predominant clonal complexes (ccs) were as follows: cc41/44 (12/64 isolates, 19%); cc32 (10/64, 16%); and cc23 (7/64, 11%) (Table 4 and Fig. 2). The overall low number of individual ccs detected precluded regression analyses to compare changes in prevalence between periods.

**DISCUSSION**

Our findings indicate that COVID-19 restrictions did not result in a reduction in the carriage of meningococci. From late March 2020, South Australia was placed under “lockdown” restrictions to assist in limiting the spread of COVID-19 for approximately 2 months, and universities moved to online learning. Even as restrictions were gradually eased from June 2020, social distancing directives and the capping of numbers at pubs, clubs and private social gatherings were anticipated to have reduced meningococci transmission during this period. We found the opposite of the anticipated reduction, with significant increases in disease-associated meningococcal carriage. This increase was mainly driven by genogroups B and Y, among those swabbed during the COVID-19 period despite increased 4CMenB and MenACWY vaccine uptake. Of note, intimate kissing rates did not change during the period, which may explain no reduction in carriage. The circulation of some respiratory viruses such as rhinovirus also seemed unaffected by COVID-19 containment measures in Australia, contrary to the dramatic decrease in influenza notifications. 23 The difference is thought to be because of the closure of interjurisdictional and international borders, as influenza proliferation is usually aided by new seeding from the global influenza virus population. 23

Meningococcal carriage in university students typically increases as the year progresses. This increase is thought to be primarily because of increased uptake and participation in activities associated with carriage acquisition, such as smoking, intimate kissing and close contact in pubs, clubs and parties. 7 Although opportunities for large-group social interactions were limited in the COVID-19 period, any gatherings of smaller groups may have been sufficient in continuing to facilitate the spread of meningococci.

**TABLE 4. Clonal-Complexes of Recovered Isolates by COVID-19 Period**

| Clonal Complex | Pre-COVID | During COVID-19 | Total |
|----------------|-----------|-----------------|-------|
|                | n   | %   | n   | %   | n   | %   |
| 41/44*         | 4   | 13.8| 8   | 22.9| 12  | 18.8|
| 32             | 2   | 6.9 | 8   | 22.9| 10  | 15.6|
| 23             | 2   | 6.9 | 5   | 14.3| 7   | 10.9|
| 198            | 4   | 13.8| 2   | 5.7 | 6   | 9.4 |
| 35             | 3   | 10.3| 3   | 8.6 | 6   | 9.4 |
| 1157           | 3   | 10.3| 0   | 0.0 | 3   | 4.7 |
| 167            | 3   | 10.3| 2   | 5.7 | 5   | 7.9 |
| 22             | 3   | 10.3| 0   | 0.0 | 3   | 4.7 |
| 1136           | 1   | 3.4 | 1   | 2.9 | 2   | 3.1 |
| 162            | 0   | 0.0 | 1   | 2.9 | 1   | 1.6 |
| 269            | 1   | 3.4 | 0   | 0.0 | 1   | 1.6 |
| 4821           | 1   | 3.4 | 0   | 0.0 | 1   | 1.6 |
| 53             | 1   | 3.4 | 0   | 0.0 | 1   | 1.6 |
| 60             | 0   | 0.0 | 1   | 2.9 | 1   | 1.6 |
| No cc          | 3   | 10.3| 14.4| 1   | 10.9|
| Total          | 29  | 100 | 100 | 64  | 100 |

*Six were porA type P1.7-2,4.
Figure 2. GrapeTree analysis using cgMLST v1.0 on the PubMLST.org/neisseria website of 64 meningococci isolated from the 106 meningococcal positive participants by (A) genogroup; (B) cc. Open circles indicate isolates with no value (ie, unassigned to a cc).
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