Human Immunodeficiency Virus Infection Is Associated With Increased Meningococcal Carriage Acquisition Among First-year Students in 2 South African Universities

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Background. Invasive meningococcal disease clusters occur among university students and may reflect higher carriage prevalence among this population. We aimed to measure meningococcal carriage prevalence, acquisition, and risk factors among first-year university students in South Africa.

Methods. In summer–autumn 2017, after consenting to participate, we collected oropharyngeal swabs and questionnaires on carriage risk factors and tested students for HIV at 2 universities, during registration week (survey 1) and 6–8 weeks later (survey 2). Meningococci were detected by culture and polymerase chain reaction.

Results. We enrolled 2120 students at registration. Mean age was 18.5 years, 59% (1252/2120) were female and 0.8% (16/1984) had HIV. Seventy-eight percent of students returned for survey 2 (1655/2120). Among the cohort, carriage prevalence was 4.7% (77/1655) at registration, increasing to 7.9% (130/1655) at survey 2: 5.0% (83) acquired new carriage, 2.8% (47) had persistent carriage, 1.8% (30) cleared the initial carriage, and 90.3% (1495) remained carriage free. At both surveys, nongenogroupable meningococci predominated, followed by genogroups Y, B, W, and C. On multinomial analysis, risk factors for carriage acquisition included attending nightclubs (adjusted relative risk ratio [aRRR], 2.1; 95% CI, 1.1–4.0), having intimate kissing partners (aRRR, 1.8; 95% CI, 1.1–2.9) and HIV (aRRR, 5.0; 95% CI, 1.1–24.4).

Conclusions. Meningococcal carriage among first-year university students increased after 2 months. Sociobehavioral risk factors were associated with increased carriage for all analyses. HIV was associated with carriage acquisition. Until vaccination programs become mandatory in South African universities, data suggest that students with HIV could benefit most from meningococcal vaccination.

Keywords. meningococcus; Neisseria meningitidis; carriage; Southern Africa; risk factors.

Neisseria meningitidis (meningococcus) is spread from human to human, the main ecological niche being the mucosa of the human oropharynx [1]. Neisseria meningitidis carriage is a prerequisite for ongoing transmission and invasion of the organism leading to meningococcal bacteremia or meningitis [2]. Understanding meningococcal carriage dynamics in a population is important for understanding disease epidemiology and transmission, and determining vaccination strategies for disease prevention.

The polysaccharide capsule surrounding the meningococcus is its most important virulence factor. Almost all isolates causing invasive meningococcal disease (IMD) are encapsulated, with serogroups A, B, C, W, and Y being the most frequent causes of IMD globally [3]. However, the majority of carriage isolates are nongroupable/unencapsulated and these isolates rarely cause disease, as either there is phase variation in the expression of the capsule, capsular synthesis genes have been inactivated, or there is an absence of genes required for capsule production (capsule null phenotype) [4, 5]. Carriage isolates that are sero-/genogroupable may be responsible for the spread of meningococcal disease in the community.

Invasive meningococcal disease is seasonal, peaking in May to October each year in South Africa, but it also fluctuates over periods of 10 to 15 years [2, 6]. Following the emergence of serogroup W in South Africa in 2005, IMD incidence has declined in recent years (0.2 cases per 100 000 population in 2016) [6, 7]. Human immunodeficiency virus (HIV) infection has been associated with increased risk of IMD, particularly serogroup W, which causes more severe disease and IMD in men who have
sex with men [8–10]. Thirty-seven percent of patients with IMD in South Africa are living with HIV (in a background population HIV prevalence of 13%) [6, 11]. Recommendations for meningococcal vaccination of high-risk groups (including persons with HIV and those entering universities) have been published; however, meningococcal vaccine uptake is minimal in South Africa [12, 13]. While data on IMD incidence and risk factors are available, there are currently no published data on meningococcal carriage prevalence in any population in southern Africa or by HIV status.

Meningococcal carriage prevalence increases with age, peaking at 23% in 19- to 24-year-olds in industrialized countries [14]. However, in the African meningitis belt, an area of 26 countries in sub-Saharan Africa extending from Senegal to Ethiopia, carriage peaks at a younger age (10–14 years) and occurs at a lower rate (5%) [15, 16]. Despite this low carriage rate and huge successes with MenAfriVac controlling serogroup A IMD, periodic large-scale meningococcal epidemics still occur in this region [17, 18].

Even though carriage peaks in adolescence, carriage prevalence is often higher in young adults living in semiconfined populations such as university campuses or in army barracks [19, 20]. This may be due to mixing of diverse meningococcal strains brought in by carriers from different areas, resulting in a rapid meningococcal carriage acquisition among new students or recruits, which usually plateaus after 1 month [21]. Globally, studies on university campuses have shown varied carriage rates among students, ranging from 46% in the United Kingdom and 15% in the United States to 9% in Australia [22–24]. Spreading of new meningococcal strains is enhanced by behavioral risk factors associated with meningococcal carriage, such as smoking (active and passive), attendance at pubs/nightclubs, and intimate kissing [14, 19]. Some studies have suggested carriage of Streptococcus pneumoniae to be higher in adults with HIV; however, it is not known whether HIV coinfection is also a risk factor for meningococcal carriage and/or acquisition [25–27].

We aimed to describe the meningococcal carriage prevalence and risk factors for carriage among first-year university students in South Africa at 2 time points and to determine whether HIV coinfection was associated with meningococcal carriage acquisition, persistence, and clearance among students 2 months after starting university.

METHODS

We performed a cross-sectional study to determine the prevalence of meningococcal carriage among university students at 2 time points (survey 1 and survey 2), with a nested cohort study to determine the acquisition, persistence, and clearance of meningococcal carriage. The study population included first-year university students registering at the start of the 2017 academic year at 2 large universities: University of the Witwatersrand (Wits) in Gauteng Province or University of Cape Town (UCT) in Western Cape Province. The student populations are diverse and draw from all 9 provinces of South Africa. Combined, approximately 14 000 first-year students register each year at the 2 universities. The cohort of students included those participating in both cross-sectional studies: at registration (survey 1) and 6–8 weeks later (survey 2). Sample size was calculated using OpenEpi (https://www.openepi.com/SampleSize/SSCC.htm), assuming differences in the acquisition of meningococcal carriage in a cohort of students with and without HIV coinfection. Calculations were for repeat measurements assuming an HIV prevalence of 7% and initial meningococcal carriage prevalence of 4%. Our target was to enroll 3000 students (see Supplementary Methods).

The South African university year begins in late summer. Survey 1 of the study occurred during registration week at Wits from 30 January until 3 February 2017, and at UCT from 27 February until 8 March 2017. Survey 2 occurred 6–8 weeks later for each site in the autumn: 14–17 March 2017 at Wits and 18–21 April 2017 at UCT.

Study recruitment and sample collection took place on campus at both sites. There was no random selection of the students. All students were informed of the study via e-mail and the study was introduced at student welcome lectures. Study teams were centrally situated on campus with signage inviting students to participate. Interested participants were requested to sign an informed-consent form prior to enrollment. Participants were allocated a unique study number to link the questionnaire, HIV test performed (UniGold Recombingen HIV-1/2; Trinity Biotech). Oropharyngeal swabs were taken using flocked swabs (Copan Diagnostics), ensuring the oropharynx, both tonsillar beds, and posterior pharyngeal wall were touched using a figure-of-8 motion and avoiding the tongue or teeth. Rapid HIV-antibody detection tests (Alere Determine HIV-1/2; Abbott) were used on finger-prick blood samples. Persons testing positive for HIV had a second confirmatory rapid HIV test performed (UniGold Recombingen HIV-1/2; Trinity Biotech). Oropharyngeal swabs were taken using flocked swabs (Copan Diagnostics), ensuring the oropharynx, both tonsillar beds, and posterior pharyngeal wall were touched using a figure-of-8 motion and avoiding the tongue or teeth. The oropharyngeal swabs were placed directly into Todd-Hewitt broth (Media Mage Products), a selective enrichment medium, and incubated within 6–8 hours at 37°C for 24 hours [28]. In the laboratory, a 500-µL aliquot of broth was stored at −70°C for polymerase chain reaction (PCR) later. After
overnight incubation, 100 µL of broth was plated onto Thayer-Martinson, New York City, and 5% blood agar (Diagnostic Media Products) and incubated for 48 hours in 5% CO₂. Matrix-assisted laser desorption/ionization–time-of-flight mass spectrometry was used to identify all isolates. Meningococcal isolates were serogrouped by slide agglutination using monovalent antibodies to capsular polysaccharide A, C, W, X, Y, and Z and monoclonal antibodies to polysaccharide B. All stored broths underwent real-time PCR to detect the sodC gene [29]. The ctrA and genogrouping real-time PCR (ABCEHWXYZ) was performed on all meningococcal isolates and sodC-positive swabs [30, 31]. ctrA-Negative and genogroup PCR-negative meningococci were considered nongenogroupable. Participants were classified as meningococcal carriers if _N. meningitidis_ was cultured or the sodC gene was detected on PCR. No interventions to eliminate carriage were given to meningococcal colonized subjects in this nonoutbreak setting.

Data from surveys 1 and 2 (questionnaire, oropharyngeal swab, and HIV test) were linked using the unique study number. All statistical analyses were done using Stata version 14.0 (StataCorp). _P_ values less than .05 were considered statistically significant. Variables with _P_ values less than .2 in univariate analysis were evaluated in the multivariable models using manual backward elimination.

Carriage prevalence and risk factors for carriage of meningococci were determined from the cross-sectional study of first-year university students from survey 1. Carriage prevalence was determined by day of study enrolment, and percentage changes ((rate ratio − 1) × 100) in carriage were calculated to demonstrate the increase in carriage during registration at the universities and over time from survey 1 to survey 2. Prevalence of carriage by genogroup distribution was reported.

Univariate and multivariable logistic regression models were used to determine significant risk factors associated with meningococcal carriage at each of the 2 time points. Acquisition, persistence, and clearance of meningococcal carriage 6–8 weeks following registration were determined from the cohort at the second survey (see Supplementary Methods for definitions). Multinomial regression was performed to compare those who never carried meningococci (baseline category) with the carrier acquisition and carrier persistence groups (see Supplementary Methods).

The study was approved by the Wits Health Research Ethics Committee (Medical) (M160672) as well as that of the UCT (Ref395_2016). All participants gave written consent to be enrolled in the study.

**RESULTS**

Survey 1

In the summer of 2017, we enrolled 2137 first-year students into a cross-sectional meningococcal carriage study (survey 1). Seventeen students were excluded from the study; 6 did not consent to an oropharyngeal swab and 11 did not complete the questionnaire (Figure 1). The mean age of the students was 18.5 years (SD, 1.5 years) and the majority were female (59.1%, 1252/2120). Most students were from Gauteng (43%, 914/2120).
and Western Cape Provinces (19%, 410/2120). Twenty-eight percent (600/2120) of students lived in a university residence, and 27% (581/2120) were current cigarette smokers. Of those tested for HIV at enrollment, 0.8% (16/1984) had HIV infection.

Overall meningococcal carriage was 4.6% (98/2120) and carriage prevalence increased significantly over the 5 days of enrolment (3.2-fold increase from day 1 [1.8%] to day 5 [5.9%]) (Figure 2). Meningococci were isolated from 65 of 2120 (3.1%) swabs, with the remaining meningococci (33/2120, 1.6%) identified by PCR only. No human DNA was detected on 0.6% (13/2120) of swabs. The overall meningococcal carriage prevalence by genogroup was 1.8% (38) nongroupable, 1.1% (24) MenY, 0.8% (16) MenB, 0.2% (4) MenW, and 0.1% (2) MenC of the 2120 swabs (Table 1).

On multivariable analysis, compared with Gauteng Province, students were twice as likely to carry meningococcus if their home province was KwaZulu-Natal (adjusted odds ratio [aOR], 2.1; 95% confidence interval [CI], 1.1–4.2) and 3 times as likely for the Western Cape (aOR, 2.7; 95% CI, 1.6–4.5). Carriage was more likely if they lived in a university residence (aOR, 2.0; 95% CI, 1.2–3.4) or an apartment with other students (aOR, 2.1; 95% CI, 1.2–3.9) compared with living with their family, or if they attended a nightclub (aOR, 1.8; 95% CI, 1.1–3.0) or had at least 1 intimate kissing partner (aOR, 2.8; 95% CI, 1.8–4.5) in the previous 2 weeks (Table 2).

Survey 2
In the autumn of 2017, 6–8 weeks following survey 1, we repeated the survey at the same 2 universities. Across the 2 sites, 1785 students were enrolled, but 10 were excluded due to not completing the questionnaire (n = 3) or missing the oropharyngeal swab (n = 7) (Figure 1). Overall meningococcal carriage at survey 2 was 7.5%, a 1.6-fold increase (95% CI, 1.3–2.1) from survey 1. Three percent of swabs were culture positive (3.4%, 60/1775) and an additional 4.2% (74/1775) were detected using PCR only. No human DNA was detected on 1.5% (28/1775) of swabs. The overall meningococcal carriage prevalence by genogroup was 3.5% (63) nongroupable, 1.5% (27) MenY, 0.9% (16) MenB, 0.1% (2) MenW, 0.1% (2) MenC, 0.1% (1) MenX, and 0.1% (1) MenZ of the 1775 swabs (Table 1).

Cohort Analysis
Of the 1775 students who participated in survey 2, 93% (1655/1775) had participated in survey 1. Carriage at survey 1 for this cohort was 4.7% (77/1655) and increased 1.7-fold (95% CI, 1.3–2.3) to 7.9% (130/1655) for survey 2. Factors associated with meningococcal carriage at surveys 1 and 2 were similar for the cohort and cross-sectional study (Table 2 and Supplementary Tables 1–4).

In the cohort, 90.3% (1495/1655) of students never carried meningococcus in their oropharynx, 5.0% (83) acquired meningococcus after 6–8 weeks of university life, 2.8% (47) had persistence of meningococcal carriage during the study period, and 1.8% (30) cleared their initial meningococcal carriage by the second survey. On further analysis, only 1 student in the persistent carrier group had different genogroups at the second survey (initially genogroup B then genogroup Y).

On multivariable analysis, among the 5% who acquired meningococcal carriage, risk factors for genogroupable meningococcal carriage included pub attendance (aOR, 7.9; 95% CI, 1.8–35.3), having intimate kissing partners (aOR, 15.4; 95%...
CI, 3.1–75.8), and having had a recent upper respiratory tract infection (aOR, 5.3; 95% CI, 1.4–19.6) (Table 3).

On multinomial analysis, compared with those who never carried meningococci, risk factors for acquiring meningococcal carriage included attending nightclubs (adjusted relative risk ratio [aRRR], 2.1; 95% CI, 1.1–4.0), having intimate kissing partners (aRRR, 1.8; 95% CI, 1.1–2.9), and having HIV (aRRR, 5.0; 95% CI, 1.1–24.4).

Persistence of meningococcal carriage across the study period associated with being male (aRRR, 2.5; 95% CI, 1.3–4.6), attending the UCT (aRRR, 2.1; 95% CI, 1.1–4.0), and attending pubs (aRRR, 3.0; 95% CI, 1.4–6.3) (Table 4).

**DISCUSSION**

Meningococcal carriage among first-year university students in South Africa was 5% upon registration, increasing by 63% to 8% after 2 months on campus. At both time points, nongroupable strains predominated, followed by Y and B genogroups. Human immunodeficiency virus infection was a risk factor for meningococcal carriage acquisition; it was not associated with baseline meningococcal carriage. Significant risk factors for meningococcal carriage included home province, male gender, intimate kissing, and nightclub attendance.

Although meningococcal carriage among South African university students was lower than in studies in the United Kingdom [24, 32], it is comparable to more recent carriage studies among adolescents in Australia (6%) and Italy (5%) [22, 33]. The warmer summers and milder winters in these countries and South Africa may affect meningococcal transmission, explaining the lower prevalence as, globally, behavioral risk factors remain fairly similar [14, 19].

In our study, the risk factors associated with meningococcal carriage included being male, attending nightclubs, and having at least 1 intimate kissing partner in the previous 2 weeks. Smoking was not an independent risk factor for carriage, although the prevalence of smoking (27%) and smoke exposure (65%) was high among the students, compared with a national prevalence of 18% and 47%, respectively, among South African adults in 2012 [34]. Smoking showed collinearity with nightclub and pub attendance, which were strongly associated with carriage.

Although HIV prevalence was lower than expected, underlying HIV infection was associated with meningococcal carriage acquisition. Human immunodeficiency virus has previously been associated with increased risk of meningococcal disease and more severe disease, and some countries have included

| Table 1. Carriage Prevalence by University Site, Day of Enrollment, Laboratory Testing, and Genogroup for Surveys 1 and 2: South Africa, 2017 |
|---|---|---|---|---|---|
| Day of study enrollment | Total Enrolled | NM Carriers, n (%) | Total Enrolled, n | NM Carriers, n (%) | Percentage Change From Day 1 % (95% CI) | Percentage Change From Survey 1 to 2% (95% CI) |
| Day 1 | 2120 | 217 | 4 (1.8) | ... | ... | ... |
| Day 2 | 677 | 32 (4.7) | ... | ... | 156 (~9.1 to 898) | ... |
| Day 3 | 341 | 10 (2.9) | ... | ... | 59 (~54 to 595) | ... |
| Day 4 | 477 | 27 (5.7) | ... | ... | 207 (7 to 1108) | ... |
| Day 5 | 408 | 24 (5.9) | ... | 219 (10 to 1165) | ... |
| Total participants | 2120 | 98 (4.6) | 1775 | 134 (7.5) | 63 (25 to 114) | ... |
| University of Witwatersrand | 1219 | 34 (2.8) | 993 | 67 (6.7) | 142 (~58 to 277) | ... |
| University of Cape Town | 901 | 64 (7.1) | 782 | 67 (8.6) | 21 (~16 to 73) | ... |
| Laboratory test results | 2120 | 65 (3.1) | 1775 | 60 (3.4) | 10 (~24 to 59) | ... |
| PCR positive only | 2120 | 33 (1.6) | 1775 | 34 (4.2) | 168 (75 to 317) | ... |
| Genogroup | 2120 | 0 (0) | 1775 | 0 (0) | ... | ... |
| A | 2120 | 16 (0.8) | 1775 | 16 (0.9) | 19 (~44 to 155) | ... |
| B | 2120 | 2 (0.1) | 1775 | 2 (0.11) | 19 (~91 to 1548) | ... |
| C | 2120 | 4 (0.2) | 1775 | 2 (0.11) | 40 (~95 to 317) | ... |
| W | 2120 | 1 (0.0) | 1775 | 1 (0.06) | 19 (~99 to 9276) | ... |
| X | 2120 | 24 (1.1) | 1775 | 27 (1.52) | 34 (~25 to 143) | ... |
| Y | 2120 | 0 (0) | 1775 | 1 (0.06) | ... | ... |
| Z | 2120 | 38 (1.8) | 1775 | 63 (3.5) | 98 (30 to 205) | ... |
| Nongroupable | 2120 | 3 (0.1) | 1775 | 2 (0.1) | ~20 (~93 to 595) | ... |
| Other | 2120 | 3 (0.1) | 1775 | 2 (0.1) | ... | ... |

Abbreviations: NM, Neisseria meningitidis; PCR, polymerase chain reaction.

aAll culture-positive swabs were also sodC PCR positive.
bIncludes 2 E and 1 non-ABCEHWXYZ from survey 1, and 1 E and 1 non-ABCEHWXYZ from survey 2. No genogroup A was detected at either time point. Ten meningococcal positive swabs in survey 1 and 20 from survey 2 were sodC positive yet had inconclusive genotyping.
Table 2. Multivariable Analysis of Risk Factors for Meningococcal Carriage Among First-year University Students at Registration (Survey 1): South Africa, 2017

| Characteristics                          | All, N | Meningococcal Carriers, n (%) | Univariate Analysis | Multivariable Analysis |
|------------------------------------------|--------|------------------------------|---------------------|------------------------|
| Number of students                      | 2120   | 98 (4.6)                     | OR (95% CI)         | P                      | OR (95% CI) | P |
| University                               |        |                              |                     |                        |            |   |
| Witwatersrand                            | 1219   | 34 (2.8)                     | Ref                 |                        |            |   |
| Cape Town                                | 901    | 64 (7.1)                     | 2.7 (1.7–4.1)       | .125                   | 1.9 (1.8–4.5) | .178 |
| Home province                            |        |                              |                     |                        |            |   |
| Eastern Cape                             | 117    | 7 (6.0)                      | 1.9 (1.8–4.5)       | .125                   | 1.9 (1.8–4.5) | .178 |
| Free State                               | 51     | 3 (5.9)                      | 1.9 (1.6–6.5)       | .301                   | 1.8 (1.5–6.5) | .344 |
| Gauteng                                  | 914    | 29 (3.2)                     | Ref                 |                        |            |   |
| KwaZulu-Natal                            | 179    | 15 (8.4)                     | 2.8 (1.5–5.3)       | .002                   | 2.1 (1.1–4.2) | .032 |
| Limpopo                                  | 183    | 1 (0.6)                      | 0.2 (1.1–1.2)       | .080                   | 0.2 (1.1–1.3) | .094 |
| Mpumalanga                               | 90     | 3 (3.3)                      | 1.1 (1.3–3.5)       | .934                   | 1.1 (1.3–3.6) | .951 |
| Northern Cape                            | 26     | 1 (3.9)                      | 1.2 (1.2–9.3)       | .848                   | 1.1 (1.7–17.8) | .991 |
| North West                               | 54     | 0 (0)                        |                     |                        |            |   |
| Western Cape                             | 410    | 37 (9.0)                     | 3.0 (1.8–5.0)       | <.001                  | 2.7 (1.6–4.5) | <.001 |
| Outside South Africa                     | 96     | 2 (2.1)                      | 0.7 (2.2–8.6)       | .559                   | 0.7 (2.2–3.0) | .606 |
| Median age, years                        | 18.5   | 18.53                        |                     | .451                   | ...         |   |
| Sex                                      |        |                              |                     |                        |            |   |
| Male                                     | 868    | 50 (5.8)                     | 1.5 (1.1–2.3)       | .039                   | 1.5 (0.9–2.3) | .067 |
| Female                                   | 1252   | 48 (3.8)                     | Ref                 |                        |            |   |
| Living arrangements                      |        |                              |                     |                        |            |   |
| House/apartment, with family             | 1116   | 40 (3.6)                     | Ref                 |                        |            |   |
| House/apartment, with other students     | 404    | 23 (5.7)                     | 1.6 (1.9–2.8)       | .071                   | 2.1 (1.2–3.9) | .012 |
| University residence/hostel/dormitory    | 600    | 35 (5.8)                     | 1.7 (1.1–2.7)       | .031                   | 2.0 (1.2–3.4) | .007 |
| Shares a room                            |        |                              |                     |                        |            |   |
| No                                       | 1268   | 65 (5.1)                     | Ref                 |                        |            |   |
| Yes                                      | 852    | 33 (3.9)                     | 0.8 (1.5–1.1)       | .179                   | ...         |   |
| Current cigarette smoker*                |        |                              |                     |                        |            |   |
| No                                       | 1539   | 52 (3.4)                     | Ref                 |                        |            |   |
| Yes                                      | 581    | 46 (7.9)                     | 2.5 (1.6–3.7)       | <.001                  | 1.2 (1.7–1.9) | .533 |
| Smoke exposure*                          |        |                              |                     |                        |            |   |
| No                                       | 741    | 20 (2.7)                     | Ref                 |                        |            |   |
| Yes                                      | 1379   | 78 (5.7)                     | 2.2 (1.3–3.6)       | .002                   | 1.3 (1.7–2.2) | .385 |
| Nightclub attendance*                    |        |                              |                     |                        |            |   |
| No                                       | 1714   | 56 (3.3)                     | Ref                 |                        |            |   |
| Yes                                      | 406    | 42 (10.3)                    | 3.4 (2.3–5.2)       | <.001                  | 1.8 (1.1–3.0) | .018 |
| Pub/bar attendance*                      |        |                              |                     |                        |            |   |
| No                                       | 1646   | 58 (3.5)                     | Ref                 |                        |            |   |
| Yes                                      | 474    | 40 (8.4)                     | 2.5 (1.7–3.8)       | <.001                  | ...         |   |
| Party attendance*                        |        |                              |                     |                        |            |   |
| No                                       | 1502   | 55 (3.7)                     | Ref                 |                        |            |   |
| Yes                                      | 618    | 43 (7.0)                     | 2.0 (1.3–3.0)       | .001                   | 0.8 (0.5–1.3) | .375 |
| Intimate kissing*                        |        |                              |                     |                        |            |   |
| No                                       | 1260   | 29 (2.3)                     | Ref                 |                        |            |   |
| Yes                                      | 860    | 69 (8.0)                     | 3.7 (2.4–5.8)       | <.001                  | 2.8 (1.8–4.5) | <.001 |
| Recent upper respiratory tract infection*|        |                              |                     |                        |            |   |
| No                                       | 1215   | 61 (5.0)                     | Ref                 |                        |            |   |
| Yes                                      | 779    | 32 (4.1)                     | 0.8 (1.5–1.3)       | .346                   | ...         |   |
| Antibiotic use*                          |        |                              |                     |                        |            |   |
| No                                       | 1651   | 86 (5.2)                     | Ref                 |                        |            |   |
| Yes                                      | 359    | 10 (2.8)                     | 0.5 (1.3–1.1)       | .055                   | ...         |   |
| HIV                                      |        |                              |                     |                        |            |   |
| Uninfected                               | 1968   | 90 (4.6)                     | ...                 | ...                    |            |   |
HIV in the criteria for meningococcal vaccination requirement [35, 36]. However, an association between HIV infection and increased risk of carriage acquisition has not been previously reported. This new finding, if validated in other studies and settings, may be important in emphasizing the need for IMD prevention through vaccination in population groups with a high HIV prevalence.

There were significant geographic differences in carriage prevalence among participants, especially in the initial survey. These differences reflect the higher incidence of meningococcal disease in the provinces with higher carriage. The provinces with higher disease are all coastal. Some provincial differences may be related to variations in lifestyle and living conditions. For example, residing in the Western Cape Province was associated with higher odds of carrying meningococcus. Other studies have shown this province to have the highest incidence of meningococcal disease, as well as the highest prevalence of smokers (37%) nationally [6, 34].

As with other carriage studies, nongroupable meningococci were the most prevalent among our participants [28, 37, 38]. Genogroup Y was the next most predominant. Serogroup Y is the fourth most predominant cause of invasive disease in South Africa and is associated with HIV coinfection, raising concern for those persons with HIV who are at higher risk of acquiring carriage [6]. Genogroup B was the third most predominant in causing carriage in this survey and the most predominant cause of invasive disease in 2016 [6]. Odds were higher for acquiring nongroupable meningococci if students attended pubs, had intimate kissing partners, or had a recent upper respiratory tract infection. Although no cases of meningococcal disease were reported among the study population during our surveys, acquisition of nongroupable meningococci is thought to drive risk of disease.

Currently, only quadrivalent conjugate meningococcal vaccines targeting serogroups A, C, W, and Y are available in South Africa. Knowing the circulating geno-/serogroups driving carriage and invasive disease in South Africa will assist policymakers to decide which meningococcal vaccine(s) to include in future vaccination campaigns should meningococcal B vaccines be registered for use in South Africa.

Limitations
Peak carriage prevalence among students in our study was 8%, much lower than university settings in the Western world [23, 24]. By only targeting first-year students, we have no reliable data for South Africa on how carriage rates change with age. Considering the lower age seen in the meningitis belt, it is possible that the observed relatively low carriage rate is a reflection of carriage peaking at a younger age in our setting [15]. Overall, 1% (41/3895) of swabs did not contain human DNA, an indicator of poor-quality specimens. These swabs may have missed meningococcus in those students. In light of previous HIV surveys at university campuses, we expected a higher HIV prevalence among our target population [39]. The prevalence of HIV in first-year students on admission to university may be lower than in the university population as a whole [39]. Even with this low HIV prevalence and not meeting our target sample size, we found a significant association between HIV and carriage acquisition.

Our study found less carriage acquisition than other university-based studies, especially among the students studying in the Western Cape Province. The delayed start of the academic year due to student protests disrupting examinations from the previous year meant that mixing of the students may have occurred prior to the official registration week—hence, the higher initial carriage rate at UCT [40]. However, we were able to show
### Table 3. Multivariable Analysis of Risk Factors for Carriage Acquisition of Nongenogroupable Versus Genogroupable Meningococci Among First-year University Students 2 Months After Registration (Survey 2 Cohort): South Africa, 2017

| Characteristics                          | Nongenogroupable Meningococci, n (%) | Genogroupable Meningococci, n (%) | Univariate Analysis | Multivariable Analysis |
|-----------------------------------------|--------------------------------------|-----------------------------------|---------------------|------------------------|
|                                         | OR (95% CI)                           | P                                  | OR (95% CI)         | P                      |
| Number of students                      | 57 (69)                              | 26 (31)                           | ...                 | ...                    |
| University                              |                                      |                                   |                     |                        |
| Witwatersrand                           | 42 (69)                              | 5 (11)                            | Reference           | ...                    |
| Cape Town                               | 15 (42)                              | 21 (58)                           | 11.8 (3.8–36.8)     | <.001                  |
| Sex                                     |                                      |                                   |                     |                        |
| Male                                    | 29 (81)                              | 7 (19)                            | 0.4 (1.1–1.0)       | .045                   |
| Female                                  | 28 (60)                              | 19 (40)                           | Reference           | ...                    |
| Living arrangements                     |                                      |                                   |                     |                        |
| House/apartment, with family            | 24 (75)                              | 8 (25)                            | Reference           | ...                    |
| House/apartment, with other students    | 15 (94)                              | 1 (6)                             | 0.2 (0.2–1.8)       | .147                   |
| University residence/ hostel/dormitory   | 18 (51)                              | 17 (49)                           | 2.8 (1.0–8.0)       | .049                   |
| Shares a room                           |                                      |                                   |                     |                        |
| No                                      | 35 (66)                              | 18 (34)                           | Reference           | ...                    |
| Yes                                     | 22 (73)                              | 8 (27)                            | 0.7 (0.3–1.9)       | .492                   |
| Current cigarette smoker*               |                                      |                                   |                     |                        |
| No                                      | 45 (80)                              | 11 (20)                           | Reference           | ...                    |
| Yes                                     | 12 (44)                              | 15 (56)                           | 5.1 (1.9–14.0)      | .001                   |
| Smoke exposure*                         |                                      |                                   |                     |                        |
| No                                      | 19 (76)                              | 6 (24)                            | Reference           | ...                    |
| Yes                                     | 38 (66)                              | 20 (34)                           | 1.7 (1.6–4.8)       | .347                   |
| Nightclub attendance*                   |                                      |                                   |                     |                        |
| No                                      | 45 (80)                              | 11 (20)                           | Reference           | ...                    |
| Yes                                     | 12 (44)                              | 15 (56)                           | 5.1 (1.9–14.0)      | .001                   |
| Pub/bar attendance*                     |                                      |                                   |                     |                        |
| No                                      | 51 (80)                              | 13 (20)                           | Reference           | Reference              |
| Yes                                     | 6 (32)                               | 13 (68)                           | 8.5 (2.7–26.7)      | <.001                  |
| Party attendance*                       |                                      |                                   |                     |                        |
| No                                      | 41 (80)                              | 10 (20)                           | Reference           | ...                    |
| Yes                                     | 16 (50)                              | 16 (50)                           | 4.1 (1.5–10.9)      | .005                   |
| Intimate kissing*                       |                                      |                                   |                     |                        |
| No                                      | 36 (92)                              | 3 (8)                             | Reference           | Reference              |
| Yes                                     | 21 (48)                              | 23 (52)                           | 13.1 (5.3–49.1)     | <.001                  |
| Recent upper respiratory tract infection*|                                      |                                   |                     |                        |
| No                                      | 37 (86)                              | 6 (14)                            | Reference           | Reference              |
| Yes                                     | 18 (49)                              | 19 (51)                           | 6.5 (2.2–19.1)      | .001                   |
| Antibiotic use*                         |                                      |                                   |                     |                        |
| No                                      | 42 (67)                              | 21 (33)                           | Reference           | ...                    |
| Yes                                     | 12 (75)                              | 4 (25)                            | 0.7 (0.2–2.3)       | .524                   |
| HIV                                     |                                      |                                   |                     |                        |
| Uninfected                              | 52 (68)                              | 25 (32)                           | ...                 | ...                    |
| Infected                                | 2 (100)                              | 0 (0)                             | ...                 | .330                   |
| Received a meningococcal vaccine        |                                      |                                   |                     |                        |
| No                                      | 38 (75)                              | 13 (25)                           | Reference           | ...                    |
| Yes                                     | 4 (67)                               | 2 (33)                            | 1.5 (1.2–8.9)       | .681                   |
| Chronic lung disease                    |                                      |                                   |                     |                        |
| No                                      | 53 (69)                              | 24 (31)                           | Reference           | ...                    |
| Yes                                     | 4 (67)                               | 2 (33)                            | 1.1 (1.2–6.4)       | .912                   |
| Diabetes                                |                                      |                                   |                     |                        |
| No                                      | 57 (69)                              | 26 (31)                           | ...                 | ...                    |
| Yes                                     | 0 (0)                                | 0 (0)                             | ...                 | ...                    |

N = 83. Genogroupable indicates any capsular genogroup. Nongenogroupable indicates cnl, NG on polymerase chain reaction, neg ACWZYXHE.

Abbreviations: CI, confidence interval; cnl, capsular null locus; HIV, human immunodeficiency virus; neg, negative; NG, nongenogroupable; OR, odds ratio.

*In the previous month.

*In the previous 2 weeks.
Table 4. Multinomial Analysis of Factors Associated With Meningococcal (*Neisseria meningitidis*) Carriage Status Among First-year University Students 2 Months After Registration: South Africa, 2017

| Characteristics                              | All Students, N | Never an NM Carrier, n or n/N (%) | Acquired NM Carriage, n or n/N (%) | RRR (95% CI) | aRRR (95% CI) | Retained NM Carriage, n or n/N (%) | RRR (95% CI) | aRRR (95% CI) |
|----------------------------------------------|----------------|-----------------------------------|------------------------------------|--------------|--------------|------------------------------------|--------------|--------------|
| Number of students                          | 1625           | 1495 (92.0)                       | 83 (5.1)                           | ...          | ...          | 47 (2.9)                           | ...          | ...          |
| University                                  |                |                                   |                                    |              |              |                                   |              |              |
| Witwatersrand                               | 881            | 818/881 (92.9)                    | 47/881 (5.3)                       | Ref          | 16/881 (1.8) | Ref                                | ...          | ...          |
| Cape Town                                   | 744            | 677/744 (90.8)                    | 36/744 (4.8)                       | 0.9 (0.6–1.4)| 0.8 (0.5–1.3)| 31/744 (4.2)                       | 2.3 (1.3–4.3)| 2.1 (1.1–4.0)|
| Sex                                         |                |                                   |                                    |              |              |                                   |              |              |
| Male                                        | 638            | 573/638 (89.9)                    | 36/638 (5.6)                       | 1.2 (0.8–1.9)| 1.3 (0.8–2.1)| 29/638 (4.6)                       | 2.6 (1.4–4.7)| 2.5 (1.3–4.6)|
| Female                                      | 987            | 922/987 (93.4)                    | 47/987 (4.8)                       | Ref          | 18/987 (1.8) | Ref                                | ...          | ...          |
| Living arrangements                         |                |                                   |                                    |              |              |                                   |              |              |
| House/apartment, with family                | 647            | 599/647 (92.6)                    | 32/647 (5.0)                       | Ref          | 16/647 (2.5) | Ref                                | ...          | ...          |
| House/apartment, with other students         | 413            | 382/413 (92.5)                    | 16/413 (3.9)                       | 0.8 (0.4–1.4)| ...          | 15/413 (3.6)                       | 1.5 (1.7–3.0)| ...          |
| University residence/hostel/dormitory        | 565            | 514/565 (91.0)                    | 35/565 (6.2)                       | 1.3 (0.8–2.1)| ...          | 16/565 (2.8)                       | 1.2 (0.6–2.4)| ...          |
| Shares a room                               |                |                                   |                                    |              |              |                                   |              |              |
| No                                          | 937            | 856/937 (91.4)                    | 53/937 (5.7)                       | Ref          | 28/937 (3.0) | Ref                                | ...          | ...          |
| Yes                                         | 688            | 639/688 (92.9)                    | 30/688 (4.4)                       | 0.8 (0.5–1.2)| ...          | 19/688 (2.8)                       | 0.9 (0.5–1.6)| ...          |
| Current cigarette smokera                   |                |                                   |                                    |              |              |                                   |              |              |
| No                                          | 1138           | 1056/1138 (92.8)                  | 56/1138 (4.9)                      | Ref          | 26/1138 (2.3)| Ref                                | ...          | ...          |
| Yes                                         | 487            | 439/487 (90.1)                    | 27/487 (5.5)                       | 1.2 (0.7–1.9)| ...          | 21/487 (4.3)                       | 1.9 (1.1–3.5)| ...          |
| Smoke exposurea                             |                |                                   |                                    |              |              |                                   | ...          | ...          |
| No                                          | 521            | 484/521 (92.9)                    | 25/521 (4.8)                       | Ref          | 12/521 (2.3) | Ref                                | ...          | ...          |
| Yes                                         | 1104           | 1011/1104 (91.6)                  | 58/1104 (5.3)                      | 1.1 (0.7–1.8)| ...          | 35/1104 (3.2)                      | 1.4 (0.7–2.7)| ...          |
| Nightclub attendanceb                       |                |                                   |                                    |              |              |                                   |              |              |
| No                                          | 1250           | 1165/1250 (93.2)                  | 56/1250 (4.5)                      | Ref          | 29/1250 (2.3)| Ref                                | ...          | ...          |
| Yes                                         | 375            | 330/375 (88.0)                    | 27/375 (7.2)                       | 1.7 (1.1–2.7)| 2.1 (1.1–4.0)| 18/375 (4.8)                       | 2.2 (1.2–4.0)| 0.7 (0.3–1.6)|
| Pub/bar attendanceb                         |                |                                   |                                    |              |              |                                   |              |              |
| No                                          | 1234           | 1148/1234 (93.0)                  | 64/1234 (5.2)                      | Ref          | 22/1234 (1.8)| Ref                                | ...          | ...          |
| Yes                                         | 391            | 347/391 (88.8)                    | 19/391 (4.9)                       | 0.9 (0.6–1.7)| 0.5 (0.3–1.0)| 25/391 (6.4)                       | 3.8 (2.1–6.8)| 3.0 (1.4–6.3)|
| Party attendanceb                           |                |                                   |                                    |              |              |                                   | ...          | ...          |
| No                                          | 1103           | 1026/1103 (93.0)                  | 51/1103 (4.6)                      | Ref          | 26/1103 (2.4)| Ref                                | ...          | ...          |
| Yes                                         | 522            | 469/522 (89.9)                    | 32/522 (6.1)                       | 1.4 (0.9–2.2)| ...          | 21/522 (4.0)                       | 1.8 (0.9–3.2)| ...          |
| Intimate kissingb                           |                |                                   |                                    |              |              |                                   |              |              |
| No                                          | 968            | 908/968 (93.6)                    | 39/968 (4.0)                       | Ref          | 21/968 (2.2) | Ref                                | ...          | ...          |
| Yes                                         | 657            | 587/657 (89.4)                    | 44/657 (6.7)                       | 1.7 (1.1–2.7)| 1.8 (1.1–2.9)| 26/657 (4.0)                       | 1.9 (1.1–3.4)| 1.4 (0.7–2.6)|
| Recent upper respiratory tract infectionm   |                |                                   |                                    |              |              |                                   | ...          | ...          |
| No                                          | 828            | 761/828 (91.9)                    | 43/828 (5.2)                       | Ref          | 24/828 (2.9) | Ref                                | ...          | ...          |
| Yes                                         | 720            | 662/720 (91.9)                    | 37/720 (5.1)                       | 0.9 (0.6–1.6)| ...          | 21/720 (2.9)                       | 1.1 (0.6–1.8)| ...          |
| Antibiotic usea                             |                |                                   |                                    |              |              |                                   | ...          | ...          |
| No                                          | 1302           | 1199/1302 (92.1)                  | 63/1302 (4.8)                      | Ref          | 40/1302 (3.1)| Ref                                | ...          | ...          |
| Yes                                         | 238            | 216/238 (90.8)                    | 16/238 (6.7)                       | 1.4 (0.8–2.5)| ...          | 62/238 (2.5)                       | 0.8 (0.3–2.0)| ...          |
A rapid increase in carriage during the first survey at both universities, as seen in other studies conducted at registration [21]. Our swabbing techniques and detection of meningococci were standard across the sites and surveys; therefore, these factors are unlikely to be the cause for the observed difference. Persistence of carriage was not confirmed by whole-genome sequencing of the isolates; therefore, estimates of meningococcal persistence could have overestimated the actual rates.

Conclusions
Neisseria meningitidis carriage among first-year university students in South Africa was low initially, with a moderate acquisition of carriage between the 2 surveys. Nongroupable strains predominated, followed by Y, B, C, and W genogroups. Significant risk factors for meningococcal carriage at both time points included male sex, intimate kissing, and nightclub attendance. Human immunodeficiency virus is known to be associated with increased risk of IMD and more severe IMD; however, this is the first study that has shown an association between HIV infection and meningococcal carriage acquisition. These data suggest that students with HIV could benefit most from receiving meningococcal vaccination.

Supplementary Data
Supplementary materials are available at Clinical Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes
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Potential conflicts of interest.
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Table 4. Continued

| Characteristics | All Students, N | Never an NM carrier, n or n/N (%) | Acquired NM Carriage, n or n/N (%) | Retained NM Carriage, n or n/N (%) | RRR (95% CI) | aRRR (95% CI) | RRR (95% CI) | aRRR (95% CI) |
|-----------------|----------------|-----------------------------------|-----------------------------------|-----------------------------------|-------------|--------------|-------------|--------------|
| HIV             |                |                                   |                                   |                                   |             |              |             |              |
| Uninfected      | 1552           | 1430/1552 (92.1)                  | 77/1552 (5.0)                     | Ref                               |             |              |             |              |
| Infected        | 10             | 8/10 (80.0)                       | 2/10 (20.0)                       | 4.6 (.9–22)                       | 5.0 (1.1–24.4) |             |             |              |
| Received a meningococcal vaccine | | | | | | | | |
| No              | 1060           | 986/1060 (93.0)                   | 51/1060 (4.8)                     | Ref                               |             |              |             |              |
| Yes             | 85             | 77/85 (90.6)                      | 6/85 (7.1)                        | 1.5 (1.6–3.6)                     | ...         | ...          | 2.85 (2.4) | 1.1 (1.3–4.8) |
| Chronic lung disease | | | | | | | | |
| No              | 1531           | 1410/1531 (92.1)                  | 77/1531 (5.0)                     | Ref                               |             |              |             |              |
| Yes             | 94             | 85/94 (90.4)                      | 6/94 (6.4)                        | 1.3 (1.5–3.1)                     | ...         | ...          | 3.9/3.4    | 1.1 (1.3–3.7) |
| Diabetes        |                |                                   |                                   |                                   |             |              |             |              |
| No              | 1616           | 1486/1616 (92.0)                  | 83/1616 (5.1)                     | Ref                               |             |              |             |              |
| Yes             | 9              | 9/9 (100)                         | 0/9 (0.0)                         | ...                               | ...         | ...          | 0/9 (0.0)  | ...          |

Abbreviations: aRRR, adjusted relative risk ratio; CI, confidence interval; HIV, human immunodeficiency virus; NM, Neisseria meningitidis; Ref, reference; RRR, relative risk ratio.

aIn the previous month.

bIn the previous 2 weeks.

Never an NM carrier
Acquired NM Carriage
Retained NM Carriage
