









SHORT REPORT



## Human papillomavirus vaccine coverage in male-male partnerships attending a sexual health clinic in Melbourne, Australia

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### ABSTRACT

We aimed to investigate the sexual mixing by human papillomavirus (HPV) vaccination status in male-male partnerships and estimate the proportion of male-male partnerships protected against HPV. We analyzed male-male partnerships attending the Melbourne Sexual Health Center between 2018 and 2019. Data on self-reported HPV vaccination status were collected. Newman's assortativity coefficient was used to examine the sexual mixing by HPV vaccination status. Assortativity refers to the tendency of individuals to have partners with similar characteristics (i.e. same vaccination status). Of 321 male-male partnerships where both men reported their HPV vaccination status, 52.6% (95% CI: 47.0–58.2%) partnerships had both men vaccinated, 32.1% (95% CI: 27.0–37.5%) partnerships had only one man vaccinated, and 15.3% (95% CI: 11.5–19.7%) had both men unvaccinated. The assortativity on HPV vaccination status was moderate (assortativity coefficient = 0.265, 95% CI: 0.196–0.335). There were about 15% of male-male partnerships where both men were not protected against HPV. Interventions targeting vaccinated individuals to encourage their unvaccinated partners to be vaccinated might increase the HPV vaccine coverage.

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## Introduction


Australia has implemented school-based human papillomavirus (HPV) vaccination programs for girls and boys.<sup>1</sup> The Australian HPV vaccination program started in 2007 for schoolgirls aged 12–13 years, including a catch-up program for women aged up to 26 years until 2009. The program was extended to include schoolboys aged 12–13 years in 2013, with a catch-up program for boys aged up to 15 years until the end of 2014. In Australia, the HPV 3-dose vaccination coverage from the school-based program is relatively high for both girls (80%) and boys (76%) turning 15 years of age.<sup>2</sup> Numerous epidemiological studies have demonstrated a significant reduction in the prevalence of anogenital warts, vaccine-targeted HPV infections and precancerous cervical lesions in both women and men at a population level after implementing the HPV vaccination program.<sup>3–9</sup> Unvaccinated individuals may also receive herd protection from their vaccinated partners.<sup>10</sup> Past studies have estimated that about 47% of unvaccinated heterosexual men have a female partner vaccinated against HPV in Australia.<sup>11</sup> Although not all gay, bisexual, and other men who have sex with men (MSM) would have been eligible for the school-based HPV vaccination program, some men might have received the HPV vaccine from a time-limited HPV vaccination program that targeted MSM aged  $\leq 26$  years in 2017–2019 in Victoria, Australia.<sup>12,13</sup>

The proportion of unvaccinated individuals is critical to determining the critical vaccination threshold, or level of vaccination coverage that is necessary to bring the reproductive number ( $R_0$ )

down to less than one and achieve elimination.<sup>14–16</sup> The reduction in genital warts and HPV DNA in heterosexuals in Australia suggests that the levels of vaccination reached have been sufficient to achieve a reproductive number of less than one.<sup>4,8–10</sup> However, it is likely that HPV will be more difficult to control in MSM given their generally higher rate of partner change and indeed the high prevalence of HPV in MSM.<sup>16–19</sup> One of the key variables that will determine if the vaccination coverage in boys is sufficient is the sexual mixing among men in MSM population in relation to their HPV vaccination status. However, to date, there have been no studies examining whether an individual MSM's HPV vaccination status is associated with their partner's HPV vaccination status due to sexual mixing. If the HPV vaccination coverage for boys is about 70%, it is hypothesized that about 91% of random male-male partnerships are protected against HPV through the vaccination of one or both partners.<sup>16</sup> However, this proportion was estimated based on a hypothetical scenario and the vaccination coverage from the school-based HPV vaccination program. If there was assortative mixing by vaccination status, then up to 30% of partnerships could be unprotected; alternatively, if there was disassortative mixing by vaccination status, then almost all partnerships would be protected against HPV. The critical vaccination thresholds among boys that would be required for HPV control would therefore be quite different.

The HPV Infection and Transmission among Couples through Heterosexual Activity (HITCH) cohort study recruited 497 heterosexual couples and the findings showed

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that unvaccinated men receive some protection against HPV if their female partner is vaccinated against HPV.<sup>20</sup> Understanding the HPV vaccination status among couples can provide better estimates in modeling the HPV transmission between couples, particularly among male-male couples when there is a high burden of anal HPV infection and anal cancer in MSM and limited male HPV vaccination program globally. This study aimed to investigate the sexual mixing by HPV vaccination status in male-male partnerships (i.e. whether both individuals within a partnership were vaccinated or only one individual within a partnership was vaccinated) and estimate the proportion of male-male partnerships protected against HPV.

## Methods

### Study setting and design

This was a cross-sectional study using retrospective data collected at the Melbourne Sexual Health Center (MSHC) between 2018 and 2019. The MSHC is a public sexual health clinic in Victoria, Australia. New clients and returning clients who have not been seen for more than 3 months are invited to complete a questionnaire using computer-assisted self-interview (CASI) as part of the routine care and management. This questionnaire collects information on demographic characteristics, sexual practices, self-reported HPV vaccination and includes a question asking whether the client is attending the clinic with their partner. For clients attending the clinic with their partners, we also ask them to provide their partner's name. Additionally, if the clients reported their partner is also at the clinic, the clinician will record the partner's name and client ID on the medical file. Manual chart reviews were performed to verify the two individuals were partners and were seen at MSHC on the same day. This study was approved by the Alfred Hospital Ethics Committee, Melbourne, Australia (662/21). Informed consent was waived because of the retrospective nature of the study.

**Table 1.** Characteristics of 1030 men who have sex with men attending the Melbourne Sexual Health Centre with their male partner.

Characteristics	Median (IQR) or <i>n</i> (%)
Age (years), median (IQR)	29 (25–35)
Country of birth, <i>n</i> (%)	
Australia	478 (46.4%)
Outside Australia	520 (50.5%)
Unknown	32 (3.1%)
Number of male partners in the previous 12 months, median (IQR)	4 (2–9)
HIV status and PrEP use, <i>n</i> (%)	
HIV-positive	94 (9.1%)
HIV-negative taking PrEP	112 (10.9%)
HIV-negative not taking PrEP	824 (80.0%)
Self-reported HPV vaccination status, <i>n</i> (%)	
Vaccinated	558 (54.2%)
Unvaccinated	253 (24.6%)
Unsure/Unknown	219 (21.3%)

PrEP, pre-exposure prophylaxis; IQR, interquartile range.

### Inclusion and exclusion criteria

In this analysis, we only included male-male partnerships where both males aged 16 years or above, and both were seen on the same day (i.e. partners where one person was in attendance as a support person and not to be seen were not included). If the same male-male partnership attended MSHC more than once during the study period, only the first visit of the same male-male partnership was included and the subsequent visits were excluded. However, if one of the males attended MSHC more than once during the study period but with a different partner, they were considered as a new male-male partnership and were included in the analysis. Transgender individuals were not included because they were not asked to complete the questionnaire on CASI. The study period of 2018–2019 was selected so that men who received HPV vaccines from the Victorian time-limited HPV vaccination program in 2017 were included.<sup>12,13</sup> Men were asked whether they had received an HPV vaccine on CASI; men could choose 'yes', 'no' or 'unsure' for vaccination status.

### Statistical analyses

We calculated the proportion of male-male partnerships by HPV vaccination status. In the primary analysis, we excluded partnerships where at least one man was unsure about their HPV vaccination status.

The Victorian-based time-limited HPV vaccination program provided free HPV vaccine to MSM aged  $\leq 26$  years in 2017–2019. Hence, as of the end of 2019, MSM aged  $\leq 28$  years in Victoria would have been eligible to receive the HPV vaccine. We also performed a sensitivity analysis by restricting both men aged  $\leq 28$  years so that both men would have been eligible to receive the free HPV vaccine. Furthermore, individuals who were unsure about their HPV vaccination status might or might not have received the vaccine, and we included these individuals in the sensitivity analysis. In the first analysis, we classified these individuals into the 'unvaccinated' group; while in the second analysis, we classified these individuals into the 'vaccinated' group.

Assortativity, also known as homophily, refers to the tendency of individuals to have partners with similar characteristics (i.e. same vaccination status). We calculated Newman's assortativity coefficient to measure the assortative sexual mixing by HPV vaccination status in the male-male partnerships.<sup>21</sup> Newman's assortativity coefficient ranges between  $-1$  and  $+1$ . As per previous studies, we categorized the Newman's assortativity coefficient  $\geq 0.35$  as highly assortative,  $0.26$ – $0.34$  as moderately assortative,  $0.15$ – $0.25$  as minimally assortative, and  $< 0.15$  as disassortative.<sup>22–24</sup>

Logistic regression model, clustering on partnerships, was conducted to examine the association between individual's HPV vaccination status (i.e. dependent variable) and partner's HPV vaccination status (i.e. independent variable). Individuals who were unsure their HPV vaccination status were excluded from the logistic regression but partner's HPV vaccination status could be 'vaccinated', 'unvaccinated' or 'unsure'. Age, country of birth, HIV status, PrEP use and sex with women in the past 12 months were considered as

**Table 2.** Factors associated with HPV vaccination status among 811 men who have sex with men.

	n/N (%)	Odds ratios (95% CI)	P value	Adjusted odds ratios (95% CI)	P value
Partner's HPV vaccination status					
Vaccinated	338/441	3.12 (1.89–5.15)	<.001	2.95 (1.78–4.91)	<.001
Unvaccinated	103/201	1	Ref	1	Ref
Unsure	117/169	2.14 (1.34–3.43)	.002	2.11 (1.31–3.40)	.002
Age					
≤28	256/364	1.13 (0.82–1.58)	.438		
>28	302/447	1	Ref		
Country of birth					
Australia	293/390	1.69 (1.23–2.31)	.001	1.50 (1.10–2.04)	.009
Outside Australia	254/396	1	Ref	1	Ref
Unknown	11/25	0.44 (0.20–0.97)	.043	0.45 (0.21–0.98)	.045
HIV status and PrEP use					
HIV-positive	43/58	1.45 (0.75–2.81)	.267	1.36 (0.73–2.49)	.333
HIV-negative taking PrEP	87/108	2.10 (1.23–3.59)	.007	2.10 (1.24–3.54)	.006
HIV-negative not taking PrEP	428/645	1	Ref	1	Ref
Sex with women in the past 12 months					
No	541/790	1	Ref		
Yes	17/21	1.96 (0.65–5.93)	.235		

Note. There were 219 men who were unsure about their HPV vaccination status and were excluded from this analysis.

potential factors that might be associated with HPV vaccination and sexual mixing. Factors with  $p < .20$  in the univariable logistic regression analysis were included as a potential confounders in the multivariable logistic regression analysis. Crude and adjusted odds ratios (OR) and its 95% confidence intervals (CI) were reported.

All analyses were performed using Stata (version 17; Stata Corp., College Station, TX).

## Results

Between 2018 and 2019, 632 male-male partnerships attended the MSHC. We excluded 117 partnerships as they attended MSHC more than once during the study period, and only their first visits were included. Therefore, the remaining 515 partnerships (i.e. 1030 individuals) were included in the final analysis. Of the 1030 individuals, the median age was 29 (IQR 25–35) years (Table 1). Half (50%,  $n = 520$ ) were born outside Australia, and the top three countries were China (6%,  $n = 60$ ), Colombia (4%,  $n = 41$ ) and Malaysia (4%,  $n = 39$ ). There were 9% ( $n = 94$ ) of men living with HIV and 11% ( $n = 112$ ) of men taking HIV pre-exposure prophylaxis.

Of 1030 men, 54% ( $n = 558$ ) were vaccinated against HPV, 25% ( $n = 253$ ) were not vaccinated against HPV, and 21% ( $n = 219$ ) were unsure about their HPV vaccination status (Table 1). More Australian-born men were vaccinated compared to overseas-born men (61% [293/478] vs 49% [254/520];  $p < .001$ ). Of 515 partnerships, 38% ( $n = 194$ ) partnerships had at least one man who was unsure about their HPV vaccination status.

We excluded 194 partnerships where at least one man was unsure about their HPV vaccination status and included the remaining 321 partnerships (i.e. 642 men) in the primary analysis. Of 321 partnerships, 53% (95% CI: 47–58%; 169/321) partnerships had both men vaccinated, 32% (95% CI: 27–37%; 103/321) partnerships had only one man vaccinated, and 15% (95% CI: 12–20%; 49/321) had both men unvaccinated. The Newman's assortativity coefficient by HPV vaccination status was 0.265 (95% CI: 0.196–0.335), indicating moderate assortative mixing. After adjusting for HIV status, PrEP use and country of birth,

the odds of being vaccinated against HPV among men who had a vaccinated partner was 2.95 (95% CI: 1.78–4.91) times greater than those who had an unvaccinated partner (Table 2).

In the sensitivity analysis, there were 89 male-male partnerships where both men were aged ≤28 years old. Of 89 partnerships, 66% (95% CI: 55–76%; 59/89) partnerships had both men vaccinated, 21% (95% CI: 13–31%; 19/89) partnerships had only one man vaccinated, and 12% (95% CI: 6–21%; 11/89) had both men unvaccinated.

In the secondary analysis, men who were unsure about their HPV vaccination were reclassified as unvaccinated, the proportion of partnerships where both men were unvaccinated was 24% (95% CI: 21–28%; 126/515) (Table S1). The Newman's assortativity coefficient by HPV vaccination status was 0.169 (95% CI: 0.111–0.226), indicating minimal assortativity. However, if men who were unsure about their HPV vaccination were reclassified as vaccinated, the proportion of partnerships where both men were unvaccinated was 10% (95% CI: 7–12%; 49/515) (Table S2). The Newman's assortativity coefficient by HPV vaccination status was 0.192 (95% CI: 0.140–0.244), indicating minimal assortativity.

## Discussion

This cross-sectional study examined the mixing pattern between males according to their HPV vaccination status in 515 male-male partnerships attending an urban sexual health clinic in Melbourne, Victoria, Australia. Our findings suggest that male-male partnerships were minimally to moderately assortative on HPV vaccination status (i.e. minimal to moderate tendency of men to have partners with the same HPV vaccination status). About one in five MSM were unsure about their HPV vaccination status. It is also estimated that about 10% of male-male partnerships have both men unvaccinated (i.e. not protected against HPV).

For the first time, we estimated that 69% of men in regular relationships were vaccinated. If 31% of men were unvaccinated and they only had sex with unvaccinated men, 90% (i.e. 100% – (31%×31%)) of random male-male partnerships are protected against HPV or 10% (i.e. 100% – 90%) of random male-male

partnerships are not protected against HPV. This is similar to our estimates from empirical data that 7–28% of male-male partnerships are not protected against HPV. Furthermore, we also found that about one-third of the unvaccinated men would have received some protection from their vaccinated male partners. The high proportion of male-male partnerships that are protected against HPV is mainly due to the high HPV vaccination coverage for boys from the school-based program (i.e. 76% coverage for three doses)<sup>2</sup> as well as the implementation of the time-limited HPV vaccination catch-up program for young MSM aged up to 26 years.<sup>12,13</sup> Our estimate of only about 10% of partnerships being unprotected implies that with the current vaccination coverage in boys and MSM, it may be sufficient to reduce the burden of HPV among MSM in Australia.<sup>5</sup> Past studies have also demonstrated male-male partnerships are highly assortative on age,<sup>25</sup> which means men are more likely to mix with another man around the same age. Older men are not eligible for the school-based or time-limited catch-up program, and these men are more likely to be unvaccinated; thus, these men and their partners are less likely to be protected against HPV. This is also supported by our sensitivity analysis showing a higher proportion of partnerships had both men protected against HPV when they were both aged 28 years or under.

There is still 12% of partnerships aged  $\leq 28$  years had both men unvaccinated and 21% of partnerships had only man vaccinated despite the implementation implemented a free time-limited HPV vaccination program for MSM in Victoria.<sup>12,13</sup> High-risk HPV infection, particularly HPV16, in the anus is the primary cause of anal cancer. A meta-analysis published in 2019 has shown that MSM aged  $\geq 25$  years have a higher anal HPV16 prevalence compared to MSM aged  $< 25$  years (23% vs 15%),<sup>18</sup> this highlights the importance of receiving the HPV vaccine at an early age before they become sexually active or expose to HPV to maximize the degree of protection against HPV. Furthermore, partners may play an important role in influencing each other's health behaviors.<sup>26,27</sup> A US study of women aged 18–26 years reported that three quarters of vaccinated women would prefer their male partners are also vaccinated against HPV.<sup>28</sup> However, there have been no studies examining the preference of partner's HPV vaccination status in MSM. It will improve the population immunity and herd protection even if a small proportion of discordant partnerships became both vaccinated. Interventions such as recommending vaccinated individuals encouraging their partners to be vaccinated might increase the HPV vaccine coverage and HPV vaccine concordance rate in partnerships.

Innovative approaches targeting young MSM are required to increase the HPV vaccination uptake.<sup>29</sup> Smartphone dating apps have become the most common method in finding sexual partners among young MSM,<sup>30</sup> and the use of smartphone dating apps or mobile health (mHealth) can help to facilitate HPV vaccination.<sup>31</sup> Past studies have also shown the use of theory-based interventions with individually-tailored content about HPV and vaccination,<sup>32</sup> regular text messages,<sup>33–38</sup> and theoretically-informed mobile health (mHealth) tool with brief motivational interviewing,<sup>37</sup> can effectively increase HPV vaccination uptake. Furthermore, the use of clinical decision

support aids can provide reminders to clinicians to recommend appropriate vaccines based on the patient's profile.<sup>39–41</sup>

This study has several limitations. First, self-reporting bias might have occurred for HPV vaccination status. Past studies revealed that many MSM are unsure about their HPV vaccination status, with low sensitivity (48%) but reasonable specificity (86%) of self-reporting HPV vaccination status.<sup>42</sup> This suggests that only half of the vaccinated men correctly reported they were vaccinated and most unvaccinated men correctly reported they were not vaccinated; and therefore, we may have underestimated the HPV vaccination coverage in this study. However, we performed secondary analyses by reclassifying 'unsure' into either 'vaccinated' or 'unvaccinated' to provide lower and upper limits of the estimate. Second, this study was conducted at a single urban sexual health clinic, so our findings may not be generalizable to the whole MSM population and other settings, particularly settings with a low HPV vaccination coverage in men or settings without a male HPV vaccination program. Third, we might have overestimated the proportion of male-male partnerships not protected against HPV. We only estimated this proportion based on one partner, but men had a median of four partners in the past 12 months in our study, and these unvaccinated men might have received herd protection from vaccinated causal partners outside the partnerships.

To conclude, male-male partnerships have a minimal to moderate assortative mixing pattern on HPV vaccination status. Due to the assortative mixing, some unvaccinated men would have received herd protection from their vaccinated partner. There is about 7–28% of random male-male partnerships where both men may not be protected against HPV, but these men are likely to be sexually active and may have already been exposed to HPV and vaccinating these men may provide fewer benefits.

## Disclosure statement

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## Data availability

All data analyzed during this study are included in this article.

## Authors contribution

EPFC conceived the study and designed the study. TRP and HB were performed chart reviews to verify the partnerships. EPFC performed data analyses and wrote the first draft of the manuscript. EPFC, TRP, JJO, JT, ETA, MYC and CKF were involved in data interpretation, revising the manuscript for important intellectual content and approving the final version. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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