Contents lists available at ScienceDirect



International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Anal human papillomavirus prevalence and risk factors among men who have sex with men in Vietnam



Le Anh Tuan, MD, PhD, first author^{a,†}, Kiesha Prem, PhD, co-first author^{b,†}, Quang Duy Pham, MD, PhD, Co-author^c, Zheng Quan Toh, PhD, Co-author^{d,e}, Hau Phuc Tran, MD, PhD, Co-author^c, Phuc Duy Nguyen, MSc, Co-author^c, Chu Thi Ngoc Mai, BSc, Co-author^a, Le Thi Khanh Ly, BSc, Co-author^a, Van Cao, PhD, Co-author^c, Tam-Duong Le-Ha, PhD, Co-author^c, Nguyen Anh Tuan, PhD, Co-author^a, Mark Jit, PhD, Co-author^{b,f,g}, Kathryn Bright, BN, Co-author^d, Marc Brisson, PhD, co author^{h,i}, Thuong Vu Nguyen, MD, PhD, Co-author^c, Suzanne Garland, MD, PhD^{d,j}, Dang Duc Anh, PhD^a, Nguyen Van Trang, PhD, Corresponding author^{a,#,*}, Kim Mulholland, MD, PhD, Co-corresponding author^{b,d,e,#}

^a National Institute of Hygiene and Epidemiology, Hanoi, Vietnam

^b London School of Hygiene and Tropical Medicine, London, UK

^c Pasteur Institute in Ho Chi Minh City, Ho Chi Minh City, Vietnam

^d Infection and Immunity, Murdoch Children's Research Institute, VIC, Australia

^e Department of Paediatrics, The University of Melbourne, VIC, Australia

f School of Public Health, University of Hong Kong, Hong Kong, SAR, China

^g Public Health England, Modelling and Economics Unit, London, UK

^h Centre de recherche du CHU de Québec, Université Laval, Québec, QC, Canada

ⁱ Department of Social and Preventive Medicine, Université Laval, Québec, Canada

^j Centre for Women's Infectious Diseases, The Royal Women's Hospital, Melbourne, Department of Obstetrics and Gynaecology, University of Melbourne, Australia

ARTICLE INFO

Article history: Received 25 March 2021 Revised 24 August 2021 Accepted 7 September 2021

Keywords: Men who have sex with men MSM HPV Risk factors Vietnam

ABSTRACT

Objectives: Men who have sex with men (MSM) are at risk of human papillomavirus (HPV)-related cancers, while published data are scarce. This study determined HPV prevalence and risk factors in MSM in Vietnam to inform HPV prevention strategies in this key population.

Methods: A cross-sectional study of 799 MSM aged 16-50 years was conducted in Vietnam in 2017-2018. Information was collected on risk behaviours, and knowledge of HPV and anal cancer; rectal swabs were taken to detect anal HPV infection. An in-house polymerase chain reaction and Genoflow HPV array test kit were used for HPV detection and genotyping.

Results: The median age of the study participants was 25 years (range 18-52). Overall prevalence of any HPV and HPV16/18 infection was 32.3% and 11.0%, respectively. A higher prevalence of high-risk HPV infection to all 14 types tested was found in Ho Chi Minh City (30.9%) than in Hanoi (18.4%). High-risk HPV infection was associated with inconsistent condom use and history of engaging in sex under the influence of drugs (adjusted odds ratio (aOR), 2.27; 95% CI, 1.48-10.67), as well as having multiple sexual partners (aOR, 1.01; 95% CI, 1.00–1.02).

Conclusions: High-risk anal HPV infections in Vietnamese MSM were significantly associated with risky sexual behaviours. A targeted HPV vaccination strategy would have substantial benefit for MSM in Vietnam.

© 2021 The Author(s). Published by Elsevier Ltd on behalf of International Society for Infectious

Diseases. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

https://doi.org/10.1016/j.ijid.2021.09.016

Introduction

Human papillomavirus (HPV) infection is the most common sexually transmitted infection globally, affecting both men and women (Crosbie et al., 2013). Although the majority of HPV infections are asymptomatic and transient (Dunne et al., 2006), persistent HPV infections can lead to a range of diseases from benign anogenital warts (90% caused by HPV6/11) to life-threatening diseases such as anogenital and some oropharyngeal cancers (>70% caused by HPV16/18) (Daling et al., 2004; Frisch et al., 1999; Garland et al., 2009; Hoots et al., 2009; Parkin and Bray, 2006; Vaccarella et al., 2010).

As with cervical cancer, most anal cancers are squamous cell carcinomas, and 90% of them are caused by HPV infection, particularly with HPV16 (Daling et al., 2004; Frisch et al., 1999; Hillman et al., 2014; Parkin and Bray, 2006). Anal cancer incidence and mortality have risen sharply over the last decade (Deshmukh et al., 2020; Nelson et al., 2013). Most cases have been recorded in high-income countries, while data are scarce in low-income and middle-income countries (Islami et al., 2016). The age standardized rate of anal cancer in Vietnam is 0.3 per 100,000 males per year (http://hpvcentre.net/statistics/reports. VNM.pdf). Compared with heterosexual men and women, MSM are at increased risk of HPV infection and HPV-associated diseases, such as anogenital warts and anal cancer, due to risky sexual behaviours such as practicing anal intercourse and having multiple sexual partners (Daling et al., 2004; Daling et al., 1982; Grulich et al., 2012; Machalek et al., 2012; Nyitray et al., 2016; Palefsky et al., 2011). Furthermore, they are often not targeted by HPV vaccination and, unlike heterosexual men, MSM are unlikely to benefit from herd effects from girls-only HPV vaccination (Ali et al., 2013).

There are currently three licensed prophylactic HPV vaccines (Cervarix®, bivalent - 2vHPV; Gardasil®, quadrivalent -4vHPV; and Gardasil®9, nonavalent - 9vHPV) that protect against HPV16/18 infections. Both the 4vHPV and 9vHPV protect against 90% of anogenital warts cases. The 9vHPV protects against an additional five high-risk HPV types: HPV31/33/45/52 and 58. These three vaccines will likely protect against anal cancers caused by these HPV types, although only 4vHPV and 9vHPV are currently licensed for the prevention of anal cancer. The 4vHPV has demonstrated 50.3% and 77.5% efficacy against anal intraepithelial neoplasia, the precursor of anal cancer, in young men who were previously infected with HPV and those who were HPV-naïve, respectively (Palefsky et al., 2011).

In Vietnam, little is known about the epidemiology and prevalence of HPV among MSM. There are currently no HPV prevention programs for MSM and men who have sex with women because the HPV vaccine is yet to be recommended for males in Vietnam. Access to HPV screening and testing in the MSM population remains limited, unless they present with symptoms of sexually transmitted infections. This cross-sectional study was conducted to determine the demographic, behavioural patterns and HPV preva-

* Corresponding author.

lence among MSM in two of the largest cities in Vietnam – Hanoi and Ho Chi Minh City (HCMC) – to inform HPV prevention strategies for MSM in Vietnam.

Methods

Ethics approval

The study was reviewed and approved by the ethics review boards of the National Institute of Hygiene and Epidemiology (NIHE), Vietnam (IRB-VN01057-13/2017) and London School of Hygiene & Tropical Medicine, UK (reference number: 14207).

Study design and population

This community-based, cross-sectional study was conducted in Hanoi and HCMC between December 2017 and February 2018. Men aged 16-50 years who reported a history of having anal sex with men in the last month prior to their first study visit were recruited. The respondent-driven sampling (RDS) method was used to recruit this "hard-to-reach" study population of participants. The RDS sampling process began with the recruitment of "seed" members among the MSM population. First, seeds were selected through discussions with peer educators and staff of outreach programmes. Study-participated seeds were then asked to randomly recruit a maximum of three other members of their population from their network to the study by distributing invitation coupons to introduce subsequent participants. Thereafter, each MSM recruited and enrolled in the study received up to three recruitment coupons used to recruit their peers into the study. Each coupon was uniquely coded to link recruiters with those recruited. If the recruitment chains "dried up", new seeds were selected based on the inclusion criteria. In Hanoi, 399 MSM were recruited through three seeds and five waves of the RDS recruitment process, while in HCMC, 400 MSM were recruited through 15 seeds and six waves (Appendix 1). All participants provided written informed consent to answer the questionnaire and to have anal swabs taken. Individuals were allowed to participate in this study only once. No participants withdrew from the study after providing consent.

Data collection

Participants completed a face-to-face interview with study nurse/staff on questionnaires related to the demographics, sexual behaviour, knowledge of HPV and associated diseases, as well as their willingness to be vaccinated. An anal swab specimen was collected from each participant by a trained medical professional. The swab was placed in a tube containing 1 ml of specimen transport media (Qiagen, Germany). On the same day, the samples were sent for processing at the laboratories in the National Institute of Hygiene and Epidemiology (NIHE) in Hanoi or Pasteur Institute in HCMC. In the laboratory, the swabs were vortexed in the transport media, aliquoted and stored at -30 °C until further analysis.

HPV detection and genotyping test

HPV detection and genotyping were performed using a twostep method. First, nucleic acid extraction was performed using Cador pathogen 96 Qiacube HT kit (Qiagen, Hilden, Germany) on the automated platform, followed by amplification with PGMY9/11 by polymerase chain reaction (PCR) to detect HPV-DNA; HLA was used as the internal control (Human papillomavirus laboratory manual, 2010). HPV-DNA-positive samples by PCR were subjected to genotyping by Genoflow HPV array test kit (Diagcor, Hongkong), which detected 33 HPV types (14 high-risk types, 3 probable highrisk types and 16 low-risk types): (i) high-risk and probable highrisk types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68,

E-mail addresses: lat@nihe.org (L.A. Tuan), kiesha.prem@lshtm.ac.uk (K. Prem), duyquang.pham@gmail.com (Q.D. Pham), zheng.quantoh@mcri.edu.au (Z.Q. Toh), hautran68@gmail.com (H.P. Tran), phucnguyenduy@gmail.com (P.D. Nguyen), chumai93@gmail.com (C.T.N. Mai), lethikhanhlyb_t59@hus.edu.vn (L.T.K. Ly), vancao.pasteur@gmail.com (V. Cao), lehatamduong@gmail.com (T.-D. Le-Ha), nat@nihe.org.vn (N.A. Tuan), mark.jit@lshtm.ac.uk (M. Jit), kathrynbright59@gmail.com (K. Bright), marc.brisson@crchudequebec.ulaval.ca (M. Brisson), nguyenthuong@yahoo.com (T.V. Nguyen), suzanne.garland@thewomens.org.au (S. Garland), dda@nihe.org.vn (D.D. Anh), nvt@nihe.org.vn (N.V. Trang), Kim.Mulholland@lshtm.ac.uk (K. Mulholland).

[†] joint first authors

[#] joint corresponding authors

73, 82; and (ii) low-risk types: 6, 11, 40, 42, 43, 44, 54, 55, 57, 61, 70, 71, 72, 81, 26/84 (Clifford et al., 2005; Walboomers et al., 1999). The kit was authorised for in-vitro diagnostic usage and qualified by the World Health Organization (WHO) HPV LabNet for high-risk HPV detection and genotyping.

The human leukocyte antigen (HLA) and beta-globulin genes were used as internal controls for the PGMY9/11 PCR assay and Genoflow kit, respectively. Samples negative for HLA gene were considered invalid. For each laboratory, external quality assurance was performed on a panel of 40 previously tested samples prior to screening test by HPV LabNet at the Western Pacific WHO reference laboratory, Melbourne, Australia. There was ~90% agreement between labs for all samples, and some discordant/missed results were found for certain tested hrHPV genotypes: 4/20 for HPV16, 1/12 for HPV18, 1/4 for HPV31, 2/12 for HPV39, 2/7 for HPV45, 3/9 for HPV56, 2/17 for HPV58, and 3/16 for HPV 66.

Statistical analyses

The overall and type-specific prevalence of anal HPV infection from Hanoi and HCMC were calculated. In these analyses, HPV genotypes were classified based on IARCs classification. The RDSadjustment methods (Gile and Handcock, 2010) were used to estimate 95% confidence intervals (CI) of HPV infection (Clopper and Pearson, 1934). Between-city differences were evaluated using Chisquare test or Fisher's exact test for categorical variables and Student's *t*-test or Mann-Whitney U test for continuous variables, where appropriate. Logistic regression was performed to determine participants' sociodemographics and sexual behaviours that were associated with high-risk anal HPV infection at the time of screening. Variables with a significance level of p < 0.10 in the bivariate analyses were included in the multivariable model. Nested models were compared using the likelihood ratio test. Data analyses were performed in R version 3.6.3 (Team, 2018).

Results

Participant characteristics

From December 2017 to February 2018, a total of 799 MSM with the median age of 25 years (range: 18-52) from Hanoi and HCMC completed the questionnaires. Participants' sociodemographic, behavioural, and clinical characteristics are presented in Table 1. Overall, the age of sexual debut, duration of sexual activity, and number of sex partners in the last 12 months were similar for MSM between both cities (Table 1). Conversely, a higher proportion of MSM from Hanoi (58.9%) attained at least college education compared with MSM from HCMC (26.0%), while more risky behaviours such as drug use, sex under drug influence (chemsex), group sex, and inconsistent condom use were more generally observed for MSM from HCMC than from Hanoi. Generally, the proportions of MSM had good knowledge of HPV, preventative measures and anal cancer in Hanoi were higher than in HCMC (at 5.0%, 25.3% and 21.8% in Hanoi compared with 0%, 0.8% and 1.3% in HCMC, respectively). All MSM participating in this study did not get vaccinated for reasons such as: don't know HPV vaccine (86.98%), don't know where to get vaccine (14.5%) and other reasons (4.0%) (Table 1).

HPV prevalence

Of the 799 MSM who were screened, HPV DNA was detected in 238 (29.8%). The RDS-adjusted prevalence of any HPV, any highrisk HPV and HPV-16/18 infections among all subjects were 32.3% (95% CI: 28.4–36.1%), 24.5% (95% CI: 21.1–27.9%) and 11.0% (95% CI: 8.5–13.4%), respectively. Prevalence of high-risk HPV was almost two-fold higher in HCMC (RDS-adjusted prevalence, 30.9; 95% CI: 25.6–36.2%) than in Hanoi (RDS-adjusted prevalence, 18.4; 95% CI: 15.2–21.5%). The most common HPV types among MSM in HCMC and Hanoi were HPV52 and HPV39, respectively, followed by HPV66/68, HPV18 and HPV16 in both cities. Figure 1 depicts the prevalence of the individual high-risk and low-risk HPV genotypes in MSM in Hanoi and HCMC, as well as the prevalence of vaccine-preventable HPV types. Overall, the prevalence of vaccine-preventable HPV types. Overall, the prevalence of vaccine-preventable HPV infection was 10.5% (95% CI: 5.8–15.2%) for the 2vHPV genotypes, 17.0% (95% CI: 11.5–22.5%) for the 4vHPV and 20.9% (95% CI: 14.9–26.9%) for the 9vHPV. Almost a quarter (23.0%) of the MSM aged < 25 years were infected with a vaccine-preventable genotype (Figure 2).

Risk factors

The unadjusted and adjusted association between high-risk anal HPV infection and demographic and behavioural characteristics of the participants are summarised in Table 2. In Hanoi, MSM who reported inconsistent condom use with a regular partner and sex workers were associated with a two-fold (aOR, 2.03; 95% CI, 1.14-3.60) and four-fold (aOR, 4.22; 95% CI, 0.46-38.76) higher prevalence of high-risk HPV infection, respectively. In HCMC, higher prevalence's of high-risk HPV infection were found in MSM who, in the last year, had engaged in chemsex (aOR, 2.27; 95% CI, 1.48-10.67) or had multiple sex partners (aOR, 1.01; 95% CI, 1.00-1.02, for every additional partner). Interestingly, older MSM in Hanoi, but not HCMC, were associated with a lower prevalence of highrisk HPV infection (aOR, 0.88; 95% CI, 0.77-1.03). Prevalence and risk factors for high-risk anal HPV infection among MSM differed across the two cities (Figure 2). Unlike in HCMC, infection with a high-risk HPV genotype among MSM in Hanoi appeared to attenuate with the number of years of being sexually active (Figure 2).

Discussion

In this largest community-based HPV prevalence survey of MSM in both northern and southern Vietnam, it was found that one in three MSM had detectable anal HPV, and among them, one in four harboured at least one high-risk HPV genotype. In the current cohort, the high-risk HPV genotypes were significantly associated with risky sexual behaviours such as inconsistent condom use, having multiple sexual partners and chemsex.

The prevalence of high-risk anal HPV infection observed in this survey of MSM was comparable with the prevalence rates previously reported in Vietnam (Le et al., 2019; Vu et al., 2013), although it did find higher high-risk anal HPV infections in HCMC than in Hanoi. Higher HPV prevalence was also observed in a previous study of male sex workers where the prevalence was highest in Ho Chi Minh City (59%), followed by Hanoi (19%) and Nha Trang (6%) (Vu et al., 2013). Compared to the other countries in Asia, such as Thailand (30) and China (28), lower HPV prevalence was observed. This observation could be attributed to the study design and study population, as well as small sample sizes that may overestimate or underestimate the HPV prevalence in the community. In other studies, higher prevalence rates were often found in studies performed in sexual health clinics (Chow et al., 2019; Milošević et al., 2010; ; Supindham et al., 2015) since selection criteria in these clinic-based recruitments are usually biased toward higherrisk men.

Persistent infection with high-risk anal HPV genotypes is a real risk for anal cancer (Hoots et al., 2009; Lin et al., 2018; Machalek et al., 2012). Compared to heterosexual men and women, MSM are disproportionately more likely to have an anal HPV infection, which is related a precursors to anal cancer. Previous stud-

Table 1

Sociodemographic, behavioural characteristics, and HPV prevalence of participants (n = 799).

Characteristics	Hanoi (n = 399)	HCMC $(n = 400)$	Total $(n = 799)$
Demographics			
Age (years)			
mean (SD)	25.8 (5.6)	29.4 (9)	27.6 (7.7)
median (range)	24 (19-48)	26 (18-52)	25 (18-52)
Attained college education and above, n (%)	235 (58.9)	104 (26)	339 (42.4)
Marital status, n (%)			
never married	355 (89)	365 (91.2)	720 (90.1)
married	7 (1.8)	4 (1)	11 (1.4)
ever married (separated, divorced, widowed)	37 (9.2)	31 (7.8)	68 (8.5)
Living arrangements			
alone	133 (33.3)	108 (27)	241 (30.2)
with female partner	9 (2.3)	4 (1)	13 (1.6)
with male partner	20 (5.0)	50 (12.5)	70 (8.8)
with friends	168 (42.1)	37 (9.2)	205 (25.7)
others	69 (17.3)	201 (50.2)	270 (33.8)
Behaviours			
Ever smoked	96 (24.1)	150 (37.5)	246 (30.8)
Ever consumed alcohol	285 (71.5)	273 (68.2)	558 (69.8)
Ever consumed drugs	20 (5)	48 (12)	68 (8.5)
Ever engaged in chemsex [§]	7 (1.8)	16 (4)	23 (2.9)
Ever had in-group sex	29 (7.3)	55 (13.8)	84 (10.5)
Inconsistent condom use with regular sex partner	214 (53.6)	242 (60.5)	456 (57.1)
Inconsistent condom use with casual sex partner	2 (0.5)	77 (19.2)	79 (9.9)
Inconsistent condom use with sex worker	6 (1.5)	22 (5.5)	28 (3.5)
Ever had sex with both male and female partners	94 (23.6)	79 (19.8)	173 (21.7)
Age of sex debut, in years, median (range)	18 (12-34)	18 (11-47)	18 (11-47)
Duration of sexual activity, in years, median (range)	7 (2-28)	8.2 (2-35)	8 (2-35)
Number of sex partners in the last 12 months, median (range)	2 (1-12)	2 (1-240)	2 (1-240)
HPV prevalence			
Any HPV infection	106 (26.6)	132 (33)	238 (29.8)
Any high-risk HPV infection [†]	76 (19)	116 (29)	192 (24)
HPV 16/18 infection	36 (9)	49 (12.2)	85 (10.6)
HPV vaccine			
Got HPV vaccine	0(0)	0 (0)	0(0)
Reasons not to get vaccinated			
don't know	305 (76.44)	390 (97.50)	695 (86.98)
unnecessary	10 (2.51)	5 (1.25)	15 (1.88)
worry about side effects	3 (0.75)	0 (0)	3 (0.38)
expensive vaccine price	7 (1.75)	2 (0.50)	9 (1.13)
don't know where to get vaccine	115 (28.82)	1 (0.25)	116 (14.52)
inconvenient location	5 (1.25)	0 (0)	5 (0.63)
fear of being stigmatized	12 (3.01)	0 (0)	12 (1.50)
don't provide to male	6 (1.50)	3 (0.75)	9 (1.13)
others	4 (1.00)	2 (0.50)	6 (0.75)

HCMC, Ho Chi Minh City; SD, standard deviation

[†] High-risk HPV types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66/68

§ Chemsex: intentional sex under the influence of psychoactive drugs

ies have found that high-risk sexual behaviours such as engaging in sex work, receptive anal intercourse, inconsistent condom use, and high number of sexual partners are the strongest risk factors for anal HPV infection (Colon-Lopez et al., 2014; Dunne E. F. et al., 2006; Muller et al., 2016; Nyitray et al., 2011; Tian et al., 2017; Zou et al., 2014). Similarly, the current study found that inconsistent condom use, having multiple sexual partners and chemsex significantly increased the risk of high-risk HPV infections, although this differed between HCMC and Hanoi, which might explain the higher prevalence of any and high-risk HPV infections among MSM in HCMC than in Hanoi.

The two most prevalent high-risk HPV in each city were HPV52 or HPV39 for HCMC and Hanoi, respectively, and HPV66/68. These HPV types are not included in the 2vHPV or 4vHPV, and only HPV52 is in the 9vHPV. Despite these, the proportion of anal cancers attributed to these HPV types in Vietnam is unclear, and more studies are needed to address this research gap to inform HPV prevention strategies. An interesting observation observed in Hanoi but not HCMC is that the high-risk HPV genotype appears to attenuate with the number of years of being sexually active, suggesting the possibility of natural immunity or latent infection.

Based on studies conducted in 2015, there are more than 52,000 and 30,000 MSM in HCMC and in Hanoi, respectively (Safarnejad et al., 2017; Son et al., 2019). This large population of MSM in two of the largest cities in Vietnam are at risk of anal cancers as well as other HPV-associated diseases such as oropharyngeal cancers and anogenital warts. HPV vaccination is the best way to prevent HPV infections and HPV-associated diseases. The introduction of girls-only HPV vaccination would confer protection for heterosexual men only if the coverage were high. However. MSM are unlikely to benefit from herd effects of a girls-only vaccination programme. Evidence emerging from epidemiological and modelling studies has led to the introduction of targeted MSM HPV vaccination programmes in the United Kingdom and Australia (Datta et al., 2019; Zhang et al., 2017). Therefore, a targeted HPV vaccination strategy for MSM in Vietnam could have substantial benefits. Future work investigating the willingness to receive HPV vaccination is crucial to the feasibility of HPV vaccination strategies for MSM in Vietnam.

This study had some limitations, including that the participant identification was based on RDS recruitment and may not have represented individuals outside the participants' networks. The

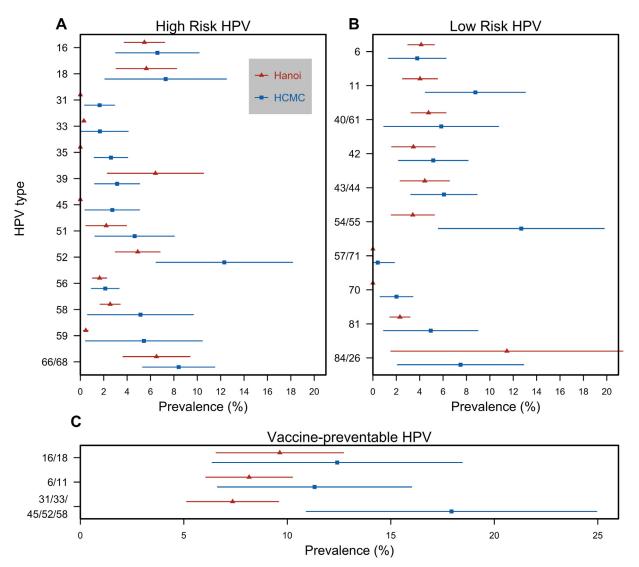


Figure 1. Prevalence of high-risk and low-risk HPV types among MSM in Hanoi and HCMC after adjusting for respondent-driven sampling, 2017–2018. Respondent-driven sampling method was used to estimate 95% CI of HPV infection for north Vietnam, Hanoi (in red) and south Vietnam, HCMC (in blue). The high-risk HPV types included 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66/68 and the low-risk HPV types included 6, 11, 34, 40, 42, 43, 44, 62, 84, 89, 61, 54, 83, 81, 55.

study focused on the age range 16-50 years, which is considered to be the sexually active period of MSM in Vietnam, thus might have affected the generalizability of the results for the MSM population. In addition, it was unable to capture information on persistent HPV infection, which is an appropriate surrogate for anogenital precancers or cancers (Daling et al., 2004; Frisch et al., 1999; Parkin and Bray, 2006). Other limitations included the study findings on sexual activity - in last sex act, the past month, the past 12 months - that were subject to recall bias. In addition, human immunodeficiency virus (HIV) infection status of the study participants, a major risk factor for HPV infection, was not collected, so there was no correlation with HPV prevalence (Clifford et al., 2006; Orlando et al., 2008; Palefsky and Holly, 2003). The national HIV surveillance, however, reported HIV prevalence of 10.9% among MSM in Hanoi (Hanoi Medical University-National HIV/AIDS conference, 2018) and 13.6% among MSM in HCMC (Nguyen et al., 2021). Nevertheless, this study did identify risk factors associated with anal HPV infection among MSM in Hanoi and HCMC.

In conclusion, this study identified several sociodemographic and behavioural factors associated with the prevalence of incident anal HPV infection, as well as the HPV genotypes circulating among MSM in the two largest cities of Vietnam. The findings have significant implications for the prevention of anal cancer among MSM in Vietnam and Asia in general. The study highlights the need for better education on safe sex practices and HPV disease awareness in men. The study also suggests that MSM should be considered for future HPV vaccination programs; it is already available for MSM in the UK, Canada and Australia.

Author contributions

KM and NVT conceptualised the study. KM, NVT, HPT, NAT and SG contributed to study design. LAT and QDP were involved in data collection. KP, MJ, MB, KB, PDN, TVN and NVT contributed to statistical analysis and made the figures. VC and TDLH performed laboratory testing. KP and LAT conducted the literature review. KP, ZQT, LAT wrote the initial draft. All authors contributed equally to data interpretation, critically reviewed the manuscript and approved the final version.

Ethics approval

The study was reviewed and approved by the ethics review boards of the National Institute of Hygiene and Epidemiology

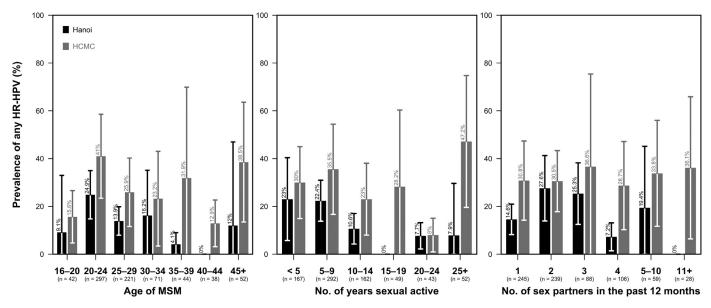


Figure 2. Correlates of high-risk anal HPV infection among MSM in Hanoi and HCMC, 2017–2018. Respondent-driven sampling method was used to estimate prevalence and their 95% CI of HPV infection for north Vietnam, Hanoi (in black) and south Vietnam, HCMC (in grey) and how it correlates to age, number of years since sexual debut, and number of sex partners in the past 12 months. The numbers of respondent in each bin are presented in parentheses. The high-risk HPV types included 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66/68.

Table 2

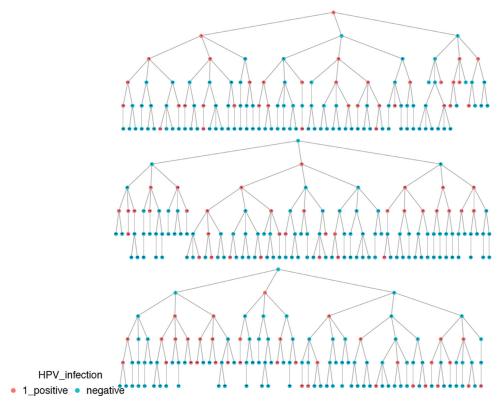
Correlations of factors associated with high-risk HPV infection.

	Hanoi (n = 399)						HCMC^{\S} (n = 400)					
Variables	Any I N	high- n	risk HP %	V [†] P	Bivariate analysis OR (95% CI)*	Multivariate analysis OR (95% CI)*	Any I N	high-ri n	sk HPV %	Р	Bivariate analysis OR (95% CI)*	Multivariate analysis OR (95% CI)*
Age, in years					0.91 (0.85-0.96)	0.88 (0.77-1.03)					0.97 (0.95-1.00)	0.94 (0.87-1.02)
Attained college education	235	44	18.7	1	0.95 (0.57-1.58)	0.90 (0.51-1.58)	104	40	38.5	0.02	1.81 (1.12-2.92)	1.87 (1.06-3.30)
and above												
Marital status												
never married	355	73	20.6	0.04	1		365	110	30.1	0.06	1	
married	7	1	14.3		0.64 (0.08-5.45)		4	2	50		2.32 (0.32-16.75)	
ever married (i.e.	37	2	5.4		0.22 (0.05-0.95)		31	4	12.9		0.34 (0.11-1.01)	
separated, divorced,												
widowed)												
Living arrangements												
alone	133	20	15	0.66	1		108	34	31.5	0.72	1	
with female partner	9	2	22.2		1.61 (0.31-8.40)		4	2	50		2.18 (0.28-16.34)	
with male partner	20	3	15		1 (0.27-3.73)		50	13	26		0.76 (0.36-1.62)	
with friends	168	36	21.4		1.54 (0.84-2.82)		37	12	32.4		1.04 (0.47-2.33)	
others (parents, siblings)	69	15	21.7		1.57 (0.74-3.31)		201	55	27.4		0.82 (0.49-1.37)	
Ever smoked	96	17	17.7	0.67	0.89 (0.49-1.62)	1.12 (0.54-2.32)	150	31	20.7	0.01	0.51 (0.31-0.82)	0.58 (0.31-1.08)
Ever consumed alcohol	285	59	20.7	0.21	1.49 (0.82-2.69)	1.72 (0.90-3.28)	273	73	26.7	0.18	0.71 (0.45-1.13)	0.72 (0.42-1.21)
Ever consumed drugs	20	1	5	0.14	0.21 (0.03-1.63)		48	16	33.3	0.59	1.26 (0.66-2.40)	
Ever engaged in chemsex	7	0	0	0.35			16	8	50	0.11	2.56 (0.93-7.02)	2.27 (1.48-10.67)
Ever had in-group sex	29	5	17.2	0.87	0.88 (0.32-2.38)		55	20	36.4	0.26	1.48 (0.81-2.70)	
Inconsistent condom use	214	50	23.4	0.02	1.86 (1.10-3.15)	2.03 (1.14-3.60)	242	66	27.3	0.41	0.81 (0.52-1.26)	0.85 (0.50-1.47)
with regular sex partner												
Inconsistent condom use	2	0	0	1			77	19	24.7	0.43	0.76 (0.43-1.35)	
with casual sex partner												
Inconsistent condom use	6	3	50	0.11	4.38 (0.85-22.37)	4.22 (0.46-38.76)	22	5	22.7	0.67	0.71 (0.25-1.97)	0.73 (0.15-3.61)
with sex worker												
Ever had sex with both	94	19	20.2	1	1.10 (0.62-1.97)		79	21	26.6	0.7	0.86 (0.49-1.50)	
male and female partners												
Duration of sexual activity,					0.90 (0.84-0.96)						0.98 (0.96-1.01)	
in years, median (range)												
Number of sex partners in					1.01 (0.85-1.21)	1.08 (0.88-1.32)					1.01 (1.00-1.02)	1.01 (1-1.02)
the last 12 months,												
median (range)												

OR, odds ratio, and its 95% confidence interval (CI) are presented in the brackets

[†] High-risk HPV types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66/68

§ HCMC: Ho Chi Minh City



The dot represents 1 person. Each dot can branched to up to 3 dots.

(NIHE), Vietnam (IRB-VN01057-13/2017) and London School of Hygiene & Tropical Medicine, UK (reference number: 14207).

Funding statement

This work was supported by the UK Medical Research Council (MRC), and Vietnamese Ministry of Science and Technology as part of the UK-Vietnam Research Collaboration (Newton Fund), project number HNQT/SPDP/03.16.

Declaration of Competing Interest

The authors have declared no competing interest.

Acknowledgements

The authors thank participants for their involvement in the study. The authors would also like to thank all staff from HIV/AIDS Centers of Hanoi and HCMC for their help in the field implementation and data collection.

Appendix 1. Recruitment chart for MSM.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2021.09.016.

References

- Ali H, Guy RJ, Wand H, Read TR, Regan DG, Grulich AE, et al. Decline in in-patient treatments of genital warts among young Australians following the national HPV vaccination program. BMC Infect Dis 2013;13:140. doi:10.1186/1471-2334-13-140.
- Chow EPF, Danielewski JA, Murray GL, Fehler G, Chen MY, Bradshaw CS, et al. Anal human papillomavirus infections in young unvaccinated men who have sex with men attending a sexual health clinic for HPV vaccination in Melbourne, Australia. Vaccine 2019;37(43):6271–5. doi:10.1016/j.vaccine.2019.08.066.

- Clifford GM, Gallus S, Herrero R, Muñoz N, Snijders PJF, Vaccarella S, et al. Worldwide distribution of human papillomavirus types in cytologically normal women in the International Agency for Research on Cancer HPV prevalence surveys: A pooled analysis. Lancet 2005;366(9490):991–8. doi:10.1016/S0140-6736(05)67069-9.
- Clifford GM, Gonçalves MAG, Franceschi S. Human papillomavirus types among women infected with HIV: A meta-analysis. AIDS 2006;20(18):2337–44. doi:10.1097/01.aids.0000253361.63578.14.
- Clopper CJ, Pearson ES. The Use of Confidence or Fiducial Limits Illustrated in the Case of the Binomial. Biometrika 1934;26(4):404–13. doi:10.2307/2331986.
- Colon-Lopez V, Ortiz AP, Del Toro-Mejias L, Clatts MC, Palefsky JM. Epidemiology of anal HPV infection in high-risk men attending a sexually transmitted infection clinic in Puerto Rico. PLoS One 2014;9(1):e83209. doi:10.1371/journal.pone.0083209.
- Crosbie EJ, Einstein MH, Franceschi S, Kitchener HC. Human papillomavirus and cervical cancer. Lancet 2013;382(9895):889–99. doi:10.1016/S0140-6736(13)60022-7.
- Daling JR, Madeleine MM, Johnson LG, Schwartz SM, Shera KA, Wurscher MA, et al. Human papillomavirus, smoking, and sexual practices in the etiology of anal cancer. Cancer 2004;101(2):270–80. doi:10.1002/cncr.20365.
- Daling JR, Weiss NS, Klopfenstein LL, Cochran LE, Chow W, Daifuku R. Correlates of Homosexual Behavior and the Incidence of Anal Cancer. JAMA: J American Med Association 1982;247(14):1988–90.
- Datta S, Pink J, Medley GF, Petrou S, Staniszewska S, Underwood M, et al. Assessing the cost-effectiveness of HPV vaccination strategies for adolescent girls and boys in the UK. BMC Infectious Diseases 2019;19(1):1–16. doi:10.1186/s12879-019-4108-y.
- Deshmukh AA, Suk R, Shiels MS, Sonawane K, Nyitray AG, Liu Y, et al. Recent trends in squamous cell carcinoma of the anus incidence and mortality in the united states, 2001-2015. J National Cancer Inst 2020;112(8):829–38. doi:10.1093/jinci/djz219.
- Dunne EF, Nielson CM, Stone KM, Markowitz LE, Giuliano AR. Prevalence of HPV Infection among Men: A Systematic Review of the Literature. J Infect Dis 2006;194(8):1044–57. doi:10.1086/507432.
- Frisch M, Fenger C, Van Den Brule AJC, Sørensen P, Meijer CJLM, Walboomers JMM, et al. Variants of squamous cell carcinoma of the anal canal and perianal skin and their relation to human papillomaviruses. Cancer Research 1999;59(3):753–7.
- Garland SM, Steben M, Sings HL, James M, Lu S, Railkar R, et al. Natural history of genital warts: analysis of the placebo arm of 2 randomized phase III trials of a quadrivalent human papillomavirus (types 6, 11, 16, and 18) vaccine. J Infect Dis 2009;199(6):805–14. doi:<u>10.1086/597071</u>.
- Gile KJ, Handcock MS. Respondent-Driven Sampling: An Assessment of Current Methodology. Sociol Methodol 2010;40(1):285–327. doi:10.1111/j.1467-9531.2010.01223.x.

Grulich AE, Poynten IM, MacHalek DA, Jin F, Templeton DJ, Hillman RJ. The epidemiology of anal cancer. Sex Health 2012;9(6):504–8. doi:10.1071/SH12070.

- Hillman RJ, Garland SM, Gunathilake MP, Stevens M, Kumaradevan N, Lemech C, et al. Human papillomavirus (HPV) genotypes in an Australian sample of anal cancers. Int J Cancer 2014;135(4):996–1001. doi:10.1002/ijc.28730.
- Hoots BE, Palefsky JM, Pimenta JM, Smith JS. Human papillomavirus type distribution in anal cancer and anal intraepithelial lesions. Int J Cancer 2009;124(10):2375–83. doi:10.1002/ijc.24215.
- Islami F, Ferlay J, Lortet-Tieulent J, Bray F, Jemal A. International trends in anal cancer incidence rates. Int J of Epidemiology 2016;46(3):924–38 dyw276-dyw. doi:10.1093/ije/dyw276.
- Le HHL, Bi X, Ishizaki A, Van Le H, Nguyen TV, Ichimura H. Low concordance of oral and genital HPV infection among male patients with sexually transmitted infections in Vietnam. BMC Infect Dis 2019;19(1):578–86. doi:10.1186/s12879-019-4175-0.
- Lin C, Franceschi S, Clifford GM. Human papillomavirus types from infection to cancer in the anus, according to sex and HIV status: a systematic review and meta-analysis. Lancet Infect Dis 2018;18(2):198–206. doi:10.1016/S1473-3099(17)30653-9.
- Machalek DA, Poynten M, Jin F, Fairley CK, Farnsworth A, Garland SM, et al. Anal human papillomavirus infection and associated neoplastic lesions in men who have sex with men: A systematic review and meta-analysis. Lancet Oncol 2012;13(5):487–500. doi:10.1016/S1470-2045(12)70080-3.
- Milošević M, Poljak M, Mlakar B. Anal HPV infection in Slovenian men who have sex with men. Central European J Med 2010;5(6):698–703. doi:10.2478/s11536-010-0019-4.
- Muller EE, Rebe K, Chirwa TF, Struthers H, McIntyre J, Lewis DA. The prevalence of human papillomavirus infections and associated risk factors in men-who-havesex-with-men in Cape Town, South Africa. BMC Infect Dis 2016;16(1):440–53. doi:10.1186/s12879-016-1706-9.
- Nelson RA, Levine AM, Bernstein L, Smith DD, Lai LL. Changing patterns of anal canal carcinoma in the United States. J Clin Oncol 2013;31(12):1569–75. doi:10.1200/JCO.2012.45.2524.
- Nguyen TV, Tran HP, Khuu NV, Nguyen PD, Le TN, Hoang CD, et al. Increases in both HIV and syphilis among men who have sex with men in Vietnam: Urgent need for comprehensive responses. Int J STD AIDS 2021 9564624211036421. doi:10.1177/09564624211036421.
- Nyitray AG, Carvalho da Silva RJ, Baggio ML, Lu B, Smith D, Abrahamsen M, et al. Age-specific prevalence of and risk factors for anal human papillomavirus (HPV) among men who have sex with women and men who have sex with men: the HPV in men (HIM) study. J Infect Dis 2011;203(1):49–57. doi:10.1093/infdis/jiq021.
- Nyitray AG, Carvalho Da Silva RJ, Chang M, Baggio ML, Ingles DJ, Abrahamsen M, et al. Incidence, duration, persistence, and factors associated with high-risk anal human papillomavirus persistence among HIV-negative men who have sex with men: A multinational study. Clin Infect Dis 2016;62(11):1367–74. doi:10.1093/cid/ciw140.
- Orlando G, Tanzi E, Beretta R, Amendola A, Fasolo MM, Bianchi S, et al. Human papillomavirus genotypes and anal-related lesions among HIV-1infected men in Milan. J Acuir Immune Defic Syndr 2008(1):129–31. doi:10.1097/qai.0b013e318156ec7b.

- Palefsky JM, Giuliano AR, Goldstone S, Moreira ED, Aranda C, Jessen H, et al. HPV vaccine against anal HPV infection and anal intraepithelial neoplasia. N Engl J Med 2011;365(17):1576–85. doi:10.1056/NEJMoa1010971.
- Palefsky JM, Holly EA. Chapter 6: Immunosuppression and Coinfection with HIV. JNCI Monographs 2003;2003(31):41–6. doi:10.1093/oxfordjournals.jncimonographs.a003481.
 Parkin DM, Bray F. Chapter 2: The burden of HPV-related cancers. Vaccine
- Parkin DM, Bray F. Chapter 2: The burden of HPV-related cancers. Vaccine 2006;24(SUPPL 3):11–25. doi:<u>10.1016/j.vaccine.2006.05.111</u>.
- Safarnejad A, Nga NT, Son VH. Population Size Estimation of Men Who Have Sex with Men in Ho Chi Minh City and Nghe An Using Social App Multiplier Method. J Urban Health 2017;94(3):339–49. doi:<u>10.1007/s11524-016-0123-0</u>.
- Son VH, Safarnejad A, Nga NT, Linh VM, Tu LTC, Manh PD, et al. Estimation of the Population Size of Men Who Have Sex With Men in Vietnam: Social App Multiplier Method. JMIR Public Health Surveill 2019;5(2) e12451-e. doi:10.2196/12451.
- Supindham T, Chariyalertsak S, Utaipat U, Miura T, Ruanpeng D, Chotirosniramit N, et al. High prevalence and genotype diversity of anal HPV infection among MSM in Northern Thailand. PLoS ONE 2015;10(5):e0124499. doi:10.1371/journal.pone.0124499.
- Team RC. R: A Language and Environment for Statistical Computing; 2018 Vienna, Austria.
- Tian T, Mijiti P, Bingxue H, Fadong Z, Ainiwaer A, Guoyao S, et al. Prevalence and risk factors of anal human papillomavirus infection among HIV-negative men who have sex with men in Urumqi city of Xinjiang Uyghur Autonomous Region, China. PLoS One 2017;12(11). doi:10.1371/journal.pone.0187928.
- Vaccarella S, Franceschi S, Snijders PJF, Herrero R, Meijer CJLM, Plummer M, et al. Concurrent Infection with Multiple Human Papillomavirus Types: Pooled Analysis of the IARC HPV Prevalence Surveys. Cancer Epidemiology Biomarkers & Prevention 2010;19(2):503–10. doi:10.1158/1055-9965.EPI-09-0983.
- Vu VD, Le GM, Nguyen SM, Clatts MC, Goldsamt LA. P3.112 High Prevalence of Gonorrhoea and HPV Among Male Sex Workers in Three Cities of Vietnam: Challenges in Addressing HIV Epidemic Among MSM Populations. Sex Transmit Infect 2013;89(Suppl 1) A182.2-A. doi:10.1136/sextrans-2013-051184.0571.
- Walboomers JMM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. J Pathol 1999;189(1):12–19. doi:10.1002/(SICI)1096-9896(199909)189:1<12::AID-PATH431>3.0.CO;2-F.
- Zhang L, Regan DG, Ong JJ, Gambhir M, Chow EPF, Zou H, et al. Targeted human papillomavirus vaccination for young men who have sex with men in Australia yields significant population benefits and is cost-effective. Vaccine 2017;35(37):4923–9. doi:10.1016/j.vaccine.2017.07.078.
- Zou H, Tabrizi SN, Grulich AE, Garland SM, Hocking JS, Bradshaw CS, et al. Early acquisition of anogenital human papillomavirus among teenage men who have sex with men. J Infect Dis 2014;209(5):642–51. doi:10.1093/infdis/jit626.
- World Health Organization. Human papillomavirus laboratory manual. 1st ed. World Health Organization; 2010 2009 1st ed, 2 edp WHO/IVB/102-WHO/IVB/2.