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HPV Infection and Diseases Among Men: Results from the HPV Infection in Men (HIM) Study

Infection with human papillomavirus (HPV) is the cause of several different diseases in men. Until recently, the natural history of HPV among males was relatively unknown. The *HPV infection in men (HIM)* Study was designed and implemented to fill this information gap.

The HIM Study: population and procedures

The *HIM Study* was a prospective study of the natural history of HPV infections in men in three countries. Participants were healthy men, aged 18-70 years, residents of southern Florida (USA), Sao Paulo (Brazil) or Cuernavaca (Mexico); and willing to comply with scheduled visits every 6 months for up to 7 years of follow-up. Study recruitment occurred between July 2005 and September 2009. A total of 4,299 men provided consent to participate.

At each study visit, questionnaire data and specimens from the genital area and anal canal, and oral rinse-and-gargle samples were obtained. Samples were analysed for the detection of individual HPV genotypes. Also, visually distinct external genital lesions such as genital warts (condyloma) and penile intraepithelial neoplasia (PeIN) were biopsied. Blood samples were also collected at each study visit to test for herpes simplex virus type 2 (HSV-2) serostatus and to measure serum antibodies against four HPV genotypes (HPV6, 11, 16, and 18). Finally, men provided a first-void urine specimen for Chlamydia trachomatis (CT) infection testing.

One of the most important findings to arise from the *HIM Study* was the observation that HPV natural history differs across anatomic sites. As shown in [Table 1](#), HPV prevalence is highest in the genitals, followed by the anal canal, and lowest in the oral cavity.

Genital HPV infection

At the external genitalia (coronal sulcus, glans penis, shaft and scrotum), HPV prevalence was high (50.4%) and did not vary with age ([Figure 1](#)). The incidence of a new genital HPV infection was correspondingly high (38.4 per 1,000 person-months) with a median duration of 7.5 months for any HPV ([Table 1](#)) (1).

Factors independently associated with genital HPV detection were race (lower risk among Asian men), condom use (lower risk among men who always use condoms), smoking (higher risk among current smokers), CT infection and HSV-2 serostatus (higher risk among antibody-positive men), and circumcision (lower risk for non-oncogenic HPV types only).

The rate of progression from infection to disease differed by HPV type. Whereas high rates of genital HPV infection progression to genital warts were observed (16-22% of men with a genital HPV6/11 infection developed an HPV6/11 condyloma), very low rates of disease progression to PeIN following genital HPV16 infection were noted (2).

Table 1

HPV natural history by anatomic site of infection in men. Ref. (1)

| ANY HPV TYPE | | | |
|--------------|------------|---|--------------------------------------|
| | Prevalence | Incidence rate per 1,000 person-months | Median time to clearance (months) |
| Genital HPV | 50.4% | 38.4 | 7.5 |
| Anal HPV* | 12.0% | 8.1 | -- |
| Oral HPV | 4.0% | 5.6 | 6.9 |

* Heterosexual men.

Anal HPV infection

Anal HPV prevalence differs by sexual behaviour. Anal canal HPV prevalence was 12.2% among men who have sex with women (MSW) and 47.2% among men who have sex with men (MSM) (Figure 2). Hence, although anal HPV infection is commonly acquired by both MSW and MSM, incident events and persistence occurred more often among MSM (3).

Oral HPV infection

Although genital and anal HPV prevalence was relatively common in the *HIM Study* cohort, oral HPV prevalence was rare (~4%). Oral HPV prevalence was lowest in the youngest age category (18-24 year old) and increased with increasing age, with men aged 55-74 years having the highest oral HPV prevalence (Figure 3). Newly acquired oral oncogenic HPV infections in healthy men were rare. However, once acquired, oral HPV16 had a high rate of persistence (4).

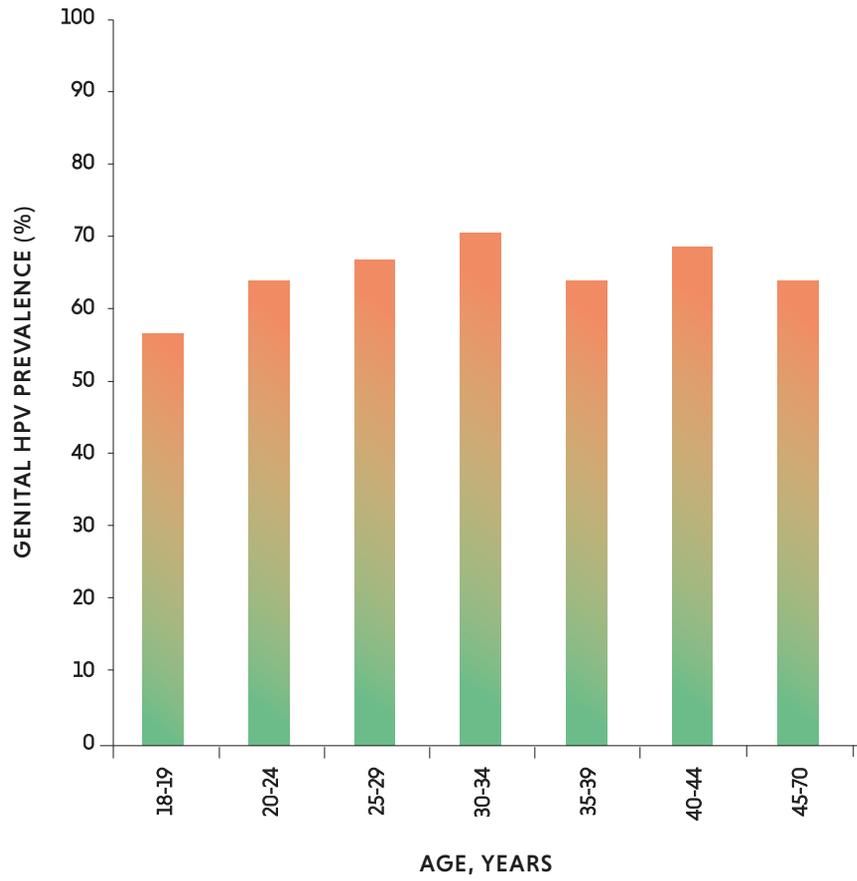
Anal canal HPV prevalence differs by sexual behavior, being higher in MSM (47,2%) than in MSW (12,2%)

HPV serology

While HPV is common among men, the antibody response to HPV appears to be much lower than observed among women. Indeed, HPV6, 11, 16, and 18 seroprevalence was relatively low at 8.1%, 13.9%, 12.7%, and 10.8%, respectively. Moreover, this response appears not to confer protection against subsequent infection. HPV seropositivity following natural infection with HPV6, 11, and 16 was not associated with protection against subsequent type specific genital infection, with only a possible protective effect against persistent HPV18 infection (5).

Figure 1

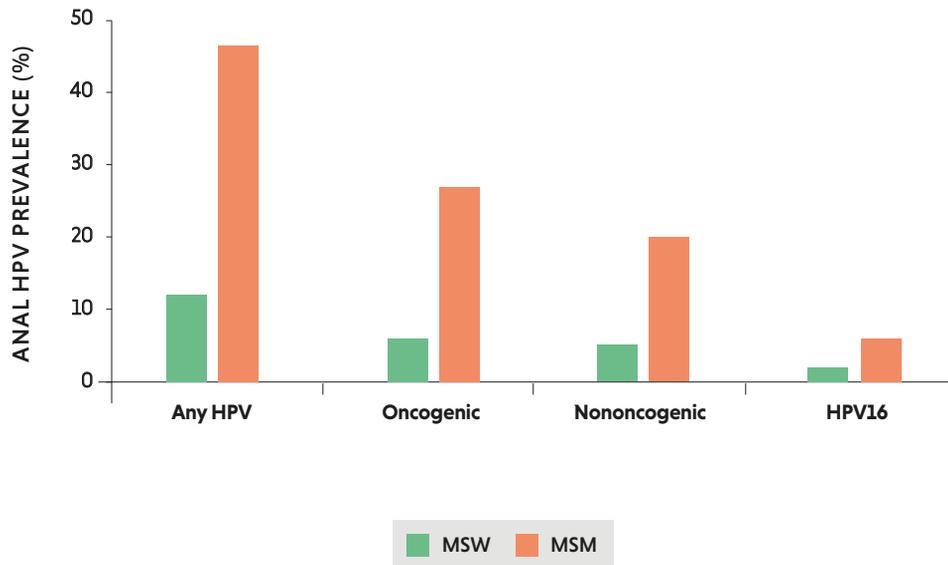
Age-specific prevalence of any genital HPV infection among men



Genital HPV prevalence remained high among all age groups. Ref. (1)

Figure 2

Anal canal HPV prevalence by sexual behavior



The HPV prevalence is higher in men who have sex with men (MSM) compared to men who have sex with women (MSW) for all HPV groups. Ref. (3)

Among men, the natural antibody response to HPV appears not to confer protection against subsequent infection

Heterosexual HPV transmission

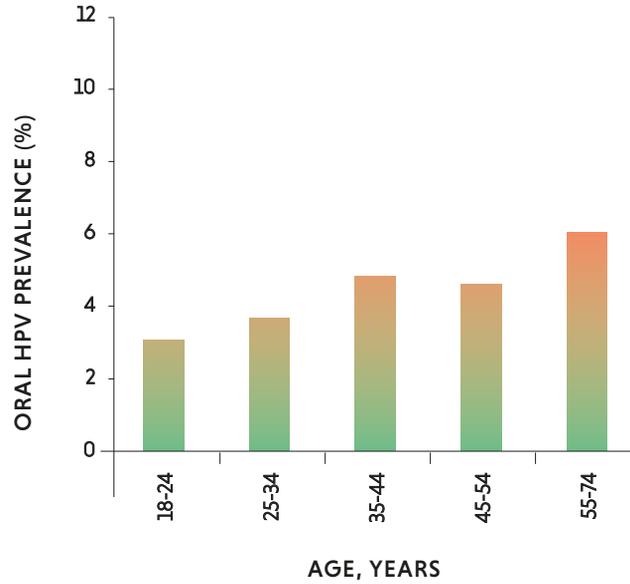
Among 65 discordant *HIM Study* heterosexual couples (the partners were discordant for ≥ 1 HPV type), HPV transmission was higher from females to males (12.3 per 1,000 person-months) than from males to females (7.3 per 1,000 person-months) (6).

Collectively, these findings demonstrate the susceptibility of men to HPV infection at multiple anatomic sites where HPV causes cancer and highlight the importance of HPV prevention programmes, such as gender-neutral HPV vaccination. ■



Figure 3

Age-specific prevalence of any oral HPV infection



Oral HPV prevalence was lowest in the youngest age category (18-24 year olds) and increased with increasing age, with men aged 55-74 years having the highest oral HPV prevalence. Ref. (4)

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