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## Incidence, clearance and duration of cutaneous beta and gamma human papillomavirus anal infection

*To the Editor*

Mooij and colleagues have reported in this Journal that they found no evidence for a protective effect of naturally induced HPV antibodies on subsequent anogenital HPV infection in HIV-negative and HIV-infected men who have sex with men (MSM).[1] However, they only considered infections by mucosal HPV types, while in the anal canal it has been also shown the presence of cutaneous HPVs.[2–5] Recent studies have convincingly demonstrated that these HPVs are not confined to cutaneous epithelia but are in fact also detectable at mucosal sites, included the oral[2] and nasal mucosa.[6] We have previously reported the presence of HPVs of the β and γ genera in 27.2% and 27.7%, respectively, of anal samples collected from HIV-uninfected MSM.[4] However, it is currently unknown whether cutaneous HPVs may play a pathogenic role in the anal canal.

Due to the possible involvement of some β HPVs in the development of non melanoma skin cancer, interest in the natural history of the infection caused by cutaneous genotypes has been increasing. In fact, there has already been a study carried out on healthy men, which has evaluated the incidence and clearance of cutaneous HPV in normal skin and eyebrow hair.[7] However, to the best of our knowledge, the natural history of cutaneous HPV infection has yet to be investigated at anal level.

We estimated the incidence, clearance and duration of anal infection by β and γ HPVs in HIV-uninfected MSM, recruited among attendees of the STI/HIV Unit of the San Gallicano Dermatological Institute (Rome, Italy). The cohort included MSM who returned at least twice for anal sample collection and remained HIV-1 negative until the end of study. The other enrollment criteria and collection of anal swabs have been described elsewhere.[4] Type-specific multiplex genotyping PCR followed by hybridization with dyed bead-immobilized probes and detection by Luminex technology were used to reveal the presence of 43 β and 29 γ HPV genotypes.[4] Because of the interval censored nature of the data, a time homogenous two-state Markov model was used to estimate jointly the incidence and clearance rates for infection by: i) any β HPV; ii) any γ HPV; iii) any β and/or γ HPV (at least one HPV of either genus). The duration of infection was estimated as the median sojourn time in months. The study was approved by the local ethics committee (CE/564/11 and CE/436/14) and performed in accordance with the Declaration of Helsinki.

A total of 120 MSM, who were followed-up for a median of 12.0 months, were included, and 341 anal samples were collected (mean number per subject: 3; median interval between samplings: 6.4 months, IQR 5.9—7.3). Socio-demographic and sexual behavioral characteristics of the

**Table 1** Socio-demographic and behavioral characteristics of the study population.

| Variable | Median | IQR | |
|---|---|---|---|
| Age, years | 33.5 | 26.7 | 40.7 |
| Age at first intercourse, years | 20 | 17 | 24 |
| No. lifetime male partners | 60 | 23 | 200 |
| No. male partners in previous 6 months | 6 | 3 | 12 |
| | N | % | |
| Ethnicity | | | |
| Caucasian | 117 | 97.5 | |
| Other | 3 | 2.5 | |
| Educational level | | | |
| High school or less | 61 | 50.8 | |
| University | 57 | 47.5 | |
| Not specified | 2 | 1.7 | |
| Annual income | | | |
| <12,000 € | 54 | 45.0 | |
| 12,000–24,000 € | 52 | 43.4 | |
| >24,000 € | 13 | 10.8 | |
| Not specified | 1 | 0.8 | |
| No. lifetime male partners | | | |
| 1–8 | 6 | 5.0 | |
| 9–19 | 10 | 8.3 | |
| 20–49 | 28 | 23.3 | |
| ≥50 | 67 | 55.9 | |
| Not specified | 9 | 7.5 | |
| Receptive anal sex | | | |
| No | 27 | 22.5 | |
| Yes | 93 | 81.5 | |
| Condom use in receptive anal sex[a] | | | |
| No | 19 | 20.6 | |
| Yes | 74 | 79.4 | |
| Sex with occasional partner(s) | | | |
| No | 8 | 6.7 | |
| Yes | 111 | 92.5 | |
| Not specified | 1 | 0.8 | |
| History of STI | | | |
| No | 70 | 58.3 | |
| Ano-genital warts | 22 | 18.3 | |
| Other than ano-genital warts[b] | 26 | 21.7 | |
| Not specified | 2 | 1.7 | |

[a] For the 93 MSM who reported to practice receptive anal sex.
[b] Syphilis, gonorrhea (any site), genital herpes.

**Table 2** Incidence, clearance (and bootstrapped 95% CI), and median duration of anal infection by cutaneous HPVs in HIV-uninfected MSM.

| HPV infection | Incidence rate (95% CI) | Clearance rate (95% CI) | Median duration, months (IQR) |
|---|---|---|---|
| Any β | 70.7 (45.1–134.5) | 167.5 (102.2–350.6) | 5.9 (3.6–9.8) |
| Any γ | 65.7 (38.5–118.4) | 181.9 (123.0–307.8) | 5.5 (3.6–8.4) |
| Any β and/or γ | 108.6 (71.6–190.9) | 126.5 (83.5–222.8) | 7.9 (5.1–12.2) |