Male Circumcision and Human Papillomavirus Infection in Men: A Systematic Review and Meta-Analysis

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Background. We systematically reviewed the evidence for an association between male circumcision and Human Papillomavirus (HPV) infection and genital warts in men.

Methods. PubMed and Embase were searched to 15 September 2010. The measure of effect was the adjusted odds ratio (OR) or rate ratio (RR) when present and the crude estimate otherwise. Random effects meta-analyses were used to calculate summary measures of effect.

Results. We identified 23 papers about the association between circumcision and HPV DNA. Circumcised men were less likely to have prevalent genital HPV infection than uncircumcised men (summary OR, 0.57, 95% confidence interval [CI], 0.45–0.71) with between-study heterogeneity (P-heterogeneity = 0.006; I² = 50.5%; 19 studies). Similar summary associations were seen in clinical and methodological subgroups. The effect of circumcision was stronger at the glans/corona (OR, 0.47; 95% CI, 0.37–0.60) and urethra (OR, 0.35; 95% CI, 0.12–1.05) compared with sites more distal to the foreskin. There was weak evidence that circumcision was associated with decreased HPV incidence (summary RR, 0.75, 95% CI, 0.57–0.99; 3 studies) and increased HPV clearance (summary RR, 1.33; 95% CI, 0.89–1.98; 3 studies) but no evidence of an association with prevalent genital warts (OR, 0.93, 95% CI, 0.65–1.33; 15 studies).

Conclusions. Several countries are expanding access to voluntary medical male circumcision to reduce HIV prevalence. This could provide additional benefit in reducing HPV prevalence.

Three randomized controlled trials (RCTs) have shown that circumcision reduces the risk of HIV acquisition in heterosexual men by about 60%, and WHO/UNAIDS recommend that circumcision be added to current HIV prevention strategies [1]. Consequently, several countries with high prevalence of HIV are expanding access to safe male circumcision for HIV prevention.

Circumcision also reduces the risk of other sexually transmitted infections (STIs) including trichomonas vaginalis, herpes simplex virus type 2, and genital ulcer disease [2–5]. Proposed biological mechanisms include reduction of pathogen entry through abrasions in the thinly keratinized inner mucosal surface of the foreskin [6] and removal of the moist environment under the foreskin, which may favor pathogen survival and replication [7].

Human papillomavirus (HPV) infection is the major cause of genital warts and a necessary cause for cervical cancer. In men, HPV infection is strongly associated with anal cancer and some penile cancers [8]. There is inconclusive evidence to date that circumcision protects against genital HPV infection. A systematic review of studies published to March 2006 found no evidence of an association between circumcision and genital HPV (OR, 1.20; 95% CI, 0.80–1.79) [9]. However, this review was criticized methodologically, and a re-analysis of the same studies found a strongly protective effect (OR, 0.56; 95% CI, 0.39–0.82) [10]. An updated
meta-analysis using the same search strategy and including studies published to September 2007 found a similar effect (OR, 0.52; 95% CI, 0.33–0.82) [11].

The discrepancy between these findings is partly due to methodological challenges including the choice of anatomical sites for HPV sampling. For example, 1 study among HPV-infected men detected HPV more frequently at the penile shaft of circumcised than uncircumcised men [12]; it has been suggested that failure to sample the penile shaft results in underdetection of HPV in circumcised men compared with uncircumcised men [9]. However, other data suggest that observed differences in genital HPV prevalence between circumcised and uncircumcised men are not due to detection biases [10, 13]. Other methodological difficulties include the definition and methods used to ascertain the outcome.

Previous reviews included circumcision as a keyword in the search strategy. This may preferentially identify studies that found an association with circumcision status.

In this paper, we are reporting a systematic review and meta-analyses of the effect of circumcision on HPV and genital warts in men. This adds to previous reviews in several ways. We included several recent studies, including 3 RCTs; we also considered HPV incidence and clearance as outcomes; and we examined for the first time the association between circumcision and genital warts in detail. In addition, we used a comprehensive search strategy that did not include the keyword circumcision to avoid selection bias, and we undertook a priori defined subgroup analyses and meta-regression to allow in-depth analysis and to address methodological issues.

METHODS

Search Strategy
PubMed and Embase were searched up to 15 September 2010 (see Supplementary material for search terms). There were no language or publication date restrictions. All abstracts were reviewed independently by 2 authors (N. L. and H. W.), and papers likely to contain information on HPV risk factors were deemed potentially relevant. Full-text copies of these papers were obtained and reviewed. We also searched reference lists of relevant papers. We e-mailed authors when information was missing from published papers.

Inclusion Criteria
Studies of HPV infection were restricted to those detecting HPV DNA using Hybrid Capture 2 or PCR because of the low sensitivity and specificity of other DNA detection methods and the low sensitivity of serological HPV tests [14]. Eligible samples included HPV DNA sampled through exfoliated cytology of the male anogenital sites as well as semen, urine, and swabs of lesions or biopsy material. Studies of genital warts were eligible if they detected genital lesions through either self-report or clinical exam. Studies among men who had sex with men were excluded because circumcision is only likely to have a beneficial effect on those who practice insertive anal intercourse.

Data Extraction
A standardized prepiloted data extraction form in Microsoft ACCESS was used. Data were extracted independently by 2 authors (N. L. and H. W.), and any inconsistencies were discussed to reach consensus.

Study populations described in more than 1 paper were included only once; we used data from the paper with most detailed information. When more than 1 outcome (HPV prevalence, HPV incidence, HPV clearance, or genital warts) was evaluated in 1 study population, these were classified as separate studies.

Data Analysis
Meta-Analysis
The association between circumcision and genital HPV prevalence at any anatomical site was estimated using ORs. When ORs were not presented, crude ORs and 95% CI were calculated from the raw data. The effects of circumcision on HPV incidence and clearance were estimated using ORs or rate ratios (RR).

A best estimate of the effect for each study was selected to be the adjusted estimate when present and the crude estimate otherwise. Summary measures of effect were obtained from random effects meta-analysis. Meta-analyses of HPV incidence and clearance were limited to studies that presented the RR, because HPV infection was relatively common in all studies and the OR was likely to overestimate the RR (ie, lie further from unity). The effects of circumcision on prevalence of high- and low-risk HPV genotypes for cervical cancer were also evaluated separately.

The effect of circumcision on HPV included studies in which the majority of men were HIV-uninfected. The one study among HIV-positive men is presented separately, because the effect of circumcision on HPV may differ between HIV-positive and -negative men.

The effect of circumcision on HPV infection and genital warts may be biased if noncases are symptomatic for STIs because circumcision protects against some other STIs [2–5]. Therefore, study populations were categorized as high- or low-risk for other STIs (see Supplementary methods).

Publication bias was assessed via funnel plots and the Egger funnel plot asymmetry test [15]. Data were analyzed using Stata 11.1 (StataCorp, Texas).

Heterogeneity
Between-study heterogeneity was evaluated using $I^2$ and the $P$ value for heterogeneity (Cochrane’s Q statistic) [16]. To evaluate potential sources of heterogeneity, we compared $I^2$ values between clinical and methodological subgroups [16]. Summary estimates from subgroups were formally compared using meta-regression. We compared subgroups according to (1) adjustment for covariates, (2) ascertainment of circumcision status.
(clinical exam vs self-report), and (3) risk of STIs in the study population. For HPV studies, we also assessed (4) the range of HPV genotypes tested. For genital warts studies, we also assessed (5) current warts (vs history of warts) and (6) ascertainment of genital warts (clinical exam or cytology vs self-report).

**Anatomical Sampling of HPV**

Because anatomical distribution of HPV may vary by circumcision status [12, 17, 18], a sensitivity analysis was restricted to studies that measured HPV at a minimum at the following sites: glans/corona, penile shaft, and scrotum (sites with the highest prevalence). The effect of circumcision on HPV may also vary by anatomical site, representing a further potential source of heterogeneity. Therefore, we analyzed the effect of circumcision on prevalent HPV at different anatomical sites.

**Results**

**Results of Search Strategy**

We identified 3366 papers from the database searches and obtained the full text for 306 based on abstract reviews. Of the 306 papers, 269 were excluded based on the full text (Figure 1). An additional 6 papers were identified from references and review papers. Of the 43 papers for which data were extracted, 23 contained information on the association between circumcision and HPV DNA, and 16 contained information on genital warts. (One paper contained information on both outcomes.) A further 5 papers contained information only on penile cancer, the results of which are reported elsewhere.

**Description of Eligible HPV DNA Studies**

The 23 papers (30 studies) evaluating the effect of circumcision on HPV DNA prevalence, incidence, and/or clearance included subgroups from 3 RCTs and 4 cohort studies (Tables 1 and 2). Twenty-seven studies (22 papers) were among predominantly HIV-negative populations, and 3 studies (1 paper) were among exclusively HIV-positive men [33]. Twenty studies provided information on the association of circumcision and HPV prevalence [4, 12, 17–32] (Table 1), 5 studies on HPV incidence [25, 34, 36, 37] and 5 studies on HPV clearance [25, 34–36] (Table 2).

Study populations were from North America (10 studies), Central and South America (7 studies), Europe (5 studies), Africa (9 studies), and Asia (2 studies). Circumcision prevalence varied from 6% (the Netherlands) to more than 80% (the United States and South Korea). Circumcision status was

Figure 1. Flow chart of study selection for inclusion in the systematic review. Numbers in brackets represent number of studies. * Data extracted for a separate review (reported elsewhere). † Studies where majority of men are HIV negative.
<table>
<thead>
<tr>
<th>First author</th>
<th>Study design</th>
<th>Country and year of study</th>
<th>Study population (high/low risk&lt;sup&gt;a&lt;/sup&gt;)</th>
<th>Study size (% circumcised)</th>
<th>HPV prevalence</th>
<th>Sites sampled for HPV DNA&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Assessment of circumcision</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
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<td><strong>HIV-negative populations</strong>&lt;sup&gt;c&lt;/sup&gt;</td>
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<td><strong>Randomized controlled trials</strong></td>
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<td>Auvert [19] RCT&lt;sup&gt;d&lt;/sup&gt;</td>
<td>South Africa, 2002–2004</td>
<td>Men ages 18–24 y HIV negative at baseline, HIV prevalence at follow-up 7.3% (low risk)</td>
<td>1264 (51%)</td>
<td>19%&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Urethra</td>
<td>Clinical exam</td>
<td>0.54 (0.40–0.73)&lt;sup&gt;f&lt;/sup&gt;</td>
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<td>Tobian [4] RCT&lt;sup&gt;g&lt;/sup&gt;</td>
<td>Uganda, 2003–2006</td>
<td>Men ages 15–49 y HIV negative at baseline (low risk)</td>
<td>520 (45%)</td>
<td>44%&lt;sup&gt;h&lt;/sup&gt;</td>
<td>Glans/corona</td>
<td>Clinical exam</td>
<td>0.52 (0.36–0.76)&lt;sup&gt;f&lt;/sup&gt;</td>
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<td><strong>Observational studies</strong></td>
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<tr>
<td>Aynaud [20] Cross-sectional</td>
<td>France, published in 2002</td>
<td>Partners of women with HPV-associated genital lesions (low risk)</td>
<td>111 (20%)</td>
<td>23%&lt;sup&gt;i&lt;/sup&gt;</td>
<td>Semen</td>
<td>Clinical exam</td>
<td>0.95 (0.25–3.13)</td>
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<td>Baldwin [21] Cross-sectional</td>
<td>United States, 2000–2001</td>
<td>STI clinic attendees (high risk)</td>
<td>344 (67%)</td>
<td>27%&lt;sup&gt;i&lt;/sup&gt;</td>
<td>Glans/corona</td>
<td>Clinical exam</td>
<td>0.35 (0.21–0.57) 0.34 (0.20–0.57)&lt;sup&gt;h&lt;/sup&gt;</td>
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<td>Bleeker [22] Cross-sectional</td>
<td>Netherlands, 2002</td>
<td>Dermatology clinic attendees (low risk)</td>
<td>83 (16%)</td>
<td>25%&lt;sup&gt;i&lt;/sup&gt;</td>
<td>Foreskin and glans/corona</td>
<td>Clinical exam</td>
<td>0.87 (0.14–3.90)</td>
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<tr>
<td>Bleeker [22] Cross-sectional</td>
<td>Netherlands, 1995–2002</td>
<td>Partners of women with CIN (low risk)</td>
<td>170 (6%)</td>
<td>59%&lt;sup&gt;i&lt;/sup&gt;</td>
<td>Foreskin and glans/corona</td>
<td>Clinical exam</td>
<td>2.88 (0.55–28.5)</td>
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<tr>
<td>Castellsague [23] Cross-sectional</td>
<td>Spain, Colombia, Brazil, Thailand, and Philippines, 1985–1993</td>
<td>Husbands of women from case control study of cervical cancer (low risk)</td>
<td>1139 (26%)</td>
<td>16%&lt;sup&gt;i&lt;/sup&gt;</td>
<td>Urethra and glans/corona</td>
<td>Self-reported</td>
<td>0.24 (0.13–0.41) 0.37 (0.16–0.85)&lt;sup&gt;h&lt;/sup&gt;</td>
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<td>Giuliano [24] Cross-sectional</td>
<td>Brazil, Mexico, and US, 2005–2006</td>
<td>General, HIV negative (low risk)</td>
<td>988 (40%)</td>
<td>59%&lt;sup&gt;h&lt;/sup&gt;</td>
<td>Foreskin, glans/corona, shaft and scrotum</td>
<td>Clinical exam</td>
<td>1.03 (0.72–1.47) 0.70 (0.52–0.94)&lt;sup&gt;h&lt;/sup&gt;</td>
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<tr>
<td>Hernandez [17] Cross-sectional</td>
<td>US, 2004–2006</td>
<td>University population, HIV negative (low risk)</td>
<td>254 (77%)</td>
<td>83%&lt;sup&gt;h&lt;/sup&gt;</td>
<td>Glans/corona, shaft, scrotum, urethra, and semen&lt;sup&gt;g&lt;/sup&gt;</td>
<td>Clinical exam</td>
<td>0.74 (0.31–1.65) 0.49 (0.19–1.28)&lt;sup&gt;h&lt;/sup&gt;</td>
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<td>Lajous [25] Baseline data from cohort study</td>
<td>Mexico, 2000–2003</td>
<td>Military (high risk)</td>
<td>925 (10%)</td>
<td>42%&lt;sup&gt;i&lt;/sup&gt;</td>
<td>Urethra, glans/corona, shaft, and scrotum</td>
<td>Self-reported</td>
<td>0.47 (0.29–0.75)&lt;sup&gt;g&lt;/sup&gt; 0.48 (0.30–0.77)&lt;sup&gt;f&lt;/sup&gt;</td>
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<tr>
<td>Muller [26] Cross-sectional</td>
<td>South Africa, 2006–2008</td>
<td>Sexual health clinic attendees, HIV prevalence 49.5% (high risk)</td>
<td>208 (26%)</td>
<td>77%&lt;sup&gt;h&lt;/sup&gt;</td>
<td>Glans/corona, and shaft</td>
<td>Clinical exam</td>
<td>0.43 (0.21–0.85) 0.51 (0.21–1.25)&lt;sup&gt;h&lt;/sup&gt;</td>
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<td>Ng’ayo [27] Cross-sectional</td>
<td>Kenya, published 2008</td>
<td>Men working in the fishing industry, HIV prevalence 25.6% (high risk)</td>
<td>250 (7%)</td>
<td>58%&lt;sup&gt;h&lt;/sup&gt;</td>
<td>Glans/corona, shaft, scrotum, and perianal area</td>
<td>Probably clinician</td>
<td>0.56 (0.19–1.66)</td>
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<tr>
<td>First author</td>
<td>Study design</td>
<td>Country and year of study</td>
<td>Study population (high/low risk)</td>
<td>Study size (% circumcised)</td>
<td>HPV prevalence</td>
<td>Sites sampled for HPV DNA*</td>
<td>Assessment of circumcision</td>
<td>Crude OR (95% CI)</td>
<td>Adjusted OR (95% CI)</td>
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<tr>
<td>Nielson [18]</td>
<td>Cross-sectional</td>
<td>United States, 2002–2006</td>
<td>General, HIV negative (low risk)</td>
<td>463 (84%)</td>
<td>51%h</td>
<td>Foreskin, urethra, glans/corona, shaft, scrotum, perianal area, anus, and semen</td>
<td>Clinical exam</td>
<td>0.99 (.58–1.68)</td>
<td>0.53 (.28–.99)</td>
</tr>
<tr>
<td>Ogilvie [28]</td>
<td>Cross-sectional</td>
<td>Canada, published 2009</td>
<td>STI clinic attendees (high risk)</td>
<td>262 (50%)</td>
<td>70%h</td>
<td>Foreskin, glans/corona, shaft, and scrotum</td>
<td>Clinical exam</td>
<td>1.14 (.65–2.00)</td>
<td></td>
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<tr>
<td>Rombaldi [29]</td>
<td>Cross-sectional</td>
<td>Brazil, 2003–2004</td>
<td>Partners of women with CIN (low risk)</td>
<td>99 (10%)</td>
<td>55%m</td>
<td>Foreskin, urethra, glans/corona, and shaft</td>
<td>Not reported</td>
<td>2.09 (.44–13.20)</td>
<td></td>
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<tr>
<td>Shin [30]</td>
<td>Cross-sectional</td>
<td>South Korea, 2002</td>
<td>University and college students (low risk)</td>
<td>368 (88%)</td>
<td>9%v</td>
<td>Foreskin, urethra, glans/corona, shaft, and scrotum</td>
<td>Self-reported</td>
<td>1.31 (.38–7.00)</td>
<td>1.80 (.40–8.20)w</td>
</tr>
<tr>
<td>Svare [31]</td>
<td>Cross-sectional</td>
<td>Denmark, 1993</td>
<td>STI clinic attendees (high risk)</td>
<td>198 (12%)</td>
<td>45%x</td>
<td>Glans/corona, shaft, and scrotum</td>
<td>Not reported</td>
<td>0.21 (.05–.68)</td>
<td>0.20 (.06–.60)y</td>
</tr>
<tr>
<td>Vaccarella [32]</td>
<td>Cross-sectional</td>
<td>Mexico, 2003–2004</td>
<td>Vasectomy clinics (low risk)</td>
<td>779 (32%)</td>
<td>9%h</td>
<td>Glans/corona, shaft, and perianal area</td>
<td>Clinical exam</td>
<td>0.19 (.07–.44)</td>
<td>0.20 (.10–.40)y</td>
</tr>
<tr>
<td>Weaver [12]</td>
<td>Cross-sectional</td>
<td>United States, 2001–2002</td>
<td>University students (low risk)</td>
<td>317 (81%)</td>
<td>31%h*</td>
<td>Foreskin, glans/corona, shaft, scrotum, and urine</td>
<td>Clinical exam</td>
<td>1.05 (.53–2.15)</td>
<td></td>
</tr>
</tbody>
</table>

**HIV-positive populations**

<table>
<thead>
<tr>
<th>First author</th>
<th>Study design</th>
<th>Country and year of study</th>
<th>Study population</th>
<th>Study size (% circumcised)</th>
<th>HPV prevalence</th>
<th>Sites sampled for HPV DNA*</th>
<th>Assessment of circumcision</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Serwadda [33]</td>
<td>RCT</td>
<td>Uganda, 2003–2007</td>
<td>Men ages 15–49 y, HIV positive at baseline with CD4 cell counts 1350 cells/mL (low risk)</td>
<td>191 (45%)</td>
<td>64%†</td>
<td>Glans/corona</td>
<td>Clinical exam</td>
<td>0.49 (.26–.93)</td>
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</table>

Abbreviations: CD4 cells, T cells with CD4 receptor; CI, confidence interval; CIN, cervical intraepithelial neoplasia; OR, odds ratio; RCT, randomized controlled trial; STI, sexually transmitted infection.

* Study populations categorized as high or low risk for STIs (see Supplementary methods for details).

† Exfoliated cells collected by study clinician/nurse unless otherwise stated. It was assumed that HPV was sampled by clinician when the person sampling was not explicitly stated in the article but a clinical exam was undertaken. All semen samples were self collected.

‡ HIV negative populations = Populations in which the majority of participants are HIV negative; HIV positive populations = Populations that are all HIV positive.

* A subgroup (56%) of the randomized population was tested for HPV infection at 21-month visit.

† Thirteen HPV genotypes high-risk for cervical cancer were evaluated using reverse line blot (Roche Diagnostics) (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68).

‡ An adjusted prevalence risk ratio was presented in the paper; adjustment did not affect the magnitude or precision of the risk ratio compared to the crude estimate. In the South African trial, adjustment factors included ethnicity, age, education, lifetime number of sex partners, marital status, number of nonspousal partners in past 12 months, condom use in past 12 months, number of sex acts in past 12 months, HIV status, and in the Ugandan trial enrollment characteristics, rates of sex practices, and symptoms of STIs.

§ A subgroup (~80%) of the randomized population was tested for HPV infection at the 24-month visit.

‖ Thirty-seven HPV genotypes evaluated using reverse line blot (Roche Diagnostics).
evaluated by a clinician in 22 studies, self-reported in 5 studies, and not stated in 3 studies.

All studies measured HPV DNA using PCR, and 23 measured more than 24 high- and low-risk HPV genotypes for cervical cancer.

Anatomical Distribution of HPV

To assess whether failure to sample sufficient sites may underestimate HPV prevalence, we compared prevalence at specific anatomic sites by circumcision status among the 3 studies with this information [12, 17, 18]. The anatomical distribution of HPV was roughly similar between circumcised and uncircumcised men in 2 studies [17, 18] (Figure 2). The shaft was the most common site for infection in both circumcised (40% and 50%) and uncircumcised men (41% and 60%) followed by the glans/corona, scrotum, or foreskin (when sampled). In the third study [12], the shaft was the most common site among circumcised men (27%), followed by the scrotum and glans/corona. HPV prevalence was considerably higher at the foreskin (30%) than other sites in uncircumcised men.

Circumcision and HPV Prevalence

HPV prevalence was lower in circumcised than in uncircumcised men in 14 of the 19 studies among predominately HIV-negative men (Table 1). ORs ranged from 0.20 to 2.88. Meta-analysis indicated a strong protective effect overall (summary OR, 0.57; 95% CI, 0.45–0.71) but with substantial between-study heterogeneity ($P_{\text{heterogeneity}} = 0.006; I^2 = 50.5%$; Figure 3A). There was no evidence of publication bias from the funnel plot (available from the author on request) and Egger test ($P = 0.56$).

Estimates for high-risk HPV genotypes (summary OR, 0.59; 95% CI, 0.49–0.70) and low-risk (summary OR, 0.56; 95% CI, 0.45–0.70) were similar to those for any HPV genotype (see Supplementary material).

Heterogeneity

The strong protective effect of circumcision on HPV prevalence was seen consistently within the a priori defined subgroups (Figure 4). The adjusted estimates demonstrated a stronger effect (OR, 0.45; 95% CI, 0.33–0.61) compared with crude estimates (OR, 0.75; 95% CI, 0.55–1.02; $P$ value for meta-regression = 0.03), although heterogeneity remained among adjusted estimates ($P_{\text{heterogeneity}} = 0.02; I^2 = 54%$).

Similar summary estimates were observed among studies that ascertained circumcision status clinically and from self-report, and heterogeneity was observed within these 2 subgroups ($I^2 = 56\%$ and $39\%$, respectively) (Figure 4). There was no evidence that the effect of circumcision varied according to the risk of STIs in the population ($P = 0.49$) or the range of HPV genotypes examined ($P = 0.72$); considerable heterogeneity remained within these subgroups.
<table>
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<tr>
<th>First author</th>
<th>Study design, country, and year of study</th>
<th>Study population</th>
<th>Assessment of circumcision</th>
<th>Frequency of HPV sampling</th>
<th>Loss to follow-up (%)</th>
<th>Study size (circumcised)</th>
<th>Cumulative HPV incidence (12m)</th>
<th>Crude effect estimate (95% CI)</th>
<th>Adjusted effect estimate (95% CI)</th>
<th>Study size (circumcised)</th>
<th>Clearance of infections (95% CI)</th>
<th>Crude effect estimate</th>
<th>Adjusted effect estimate (95% CI)</th>
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<td>HIV-negative populationsa</td>
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<tr>
<td>Gray [34]</td>
<td>RCT, Uganda, 2003–2006</td>
<td>General, HIV-negative married men</td>
<td>Clinical exam</td>
<td>Baseline, 6 m, 12 m, and 24 m¹,c</td>
<td>n/a</td>
<td>840 (53%)</td>
<td>24%</td>
<td>RR, 0.67 (0.50–0.90)</td>
<td>RR, 0.67 (0.50–0.91)</td>
<td>645 (41%)</td>
<td>18.0 per 10 pyr (over 24 m)</td>
<td>RR, 1.36 (1.13–1.63)</td>
<td>RR, 1.39 (1.17–1.64)</td>
</tr>
<tr>
<td>Hernandez</td>
<td>Cohort, United States, 2004–2006</td>
<td>University students, HIV negative</td>
<td>Clinician</td>
<td>Every 2 m (mean follow-up 431d¹)</td>
<td>20%</td>
<td>Data not given¹</td>
<td></td>
<td></td>
<td></td>
<td>357 (81%)</td>
<td>64.8% (over 1y)</td>
<td>OR, 6.67 (0.1–∞)¹</td>
<td>OR, 8.33 (1.15–∞)¹</td>
</tr>
<tr>
<td>Lajous [25]</td>
<td>Cohort, Mexico, 2000–2003</td>
<td>Military, HIV negative</td>
<td>Self report</td>
<td>Baseline and 12 m follow-up²</td>
<td>67%¹</td>
<td>210 (17%)</td>
<td>21%</td>
<td>OR, 1.02 (0.42–2.50)</td>
<td>OR, 1.12 (0.45–2.80)</td>
<td>105 (11%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lu [36]</td>
<td>Cohort, United States, 2003–2005</td>
<td>General, HIV negative</td>
<td>Clinical exam</td>
<td>Every 6 m for 18 m²³</td>
<td>24%</td>
<td>285 (8%)</td>
<td>29%</td>
<td>RR, 1.10 (0.50–2.30)</td>
<td>RR, 0.80 (0.40–1.90)</td>
<td>285 (88%)</td>
<td>9.35 per 10 pyr cleared infections (median follow-up 15.5 m)</td>
<td>RR, 2.7 (1.3–5.7)</td>
<td>RR, 3.1 (1.2–8.2)³</td>
</tr>
<tr>
<td>Partridge [37]</td>
<td>Cohort, United States, 2003–2006</td>
<td>University students ages 18–20 y, HIV negative</td>
<td>Clinical exam</td>
<td>Every 4 m for 3 y period⁴</td>
<td>Not given⁴</td>
<td>240 (77%)</td>
<td>~35%</td>
<td>RR, 1.10 (0.60–2.00)</td>
<td>n/a</td>
<td>n/a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serwadda [33]</td>
<td>RCT, Uganda, 2003–2007</td>
<td>Men, ages 15–49 y, HIV positive at baseline</td>
<td>Clinical exam</td>
<td>Baseline and 24 m</td>
<td>n/a</td>
<td>174 (47%)</td>
<td>50%</td>
<td>RR, 0.74 (0.57–1.01)</td>
<td>RR, 0.68 (0.44–1.04)</td>
<td>174 (47%)</td>
<td>73.6% (over 24 m)</td>
<td>Not given</td>
<td>RR, 1.09 (0.94–1.27)</td>
</tr>
</tbody>
</table>

Abbreviations. CI, confidence interval; n/a, not applicable; OR, odds ratio; pyr = person years; RCT, randomized controlled trial; RR, rate ratio.

a HIV-negative populations = Populations where majority of participants are HIV negative; HIV-positive populations = populations that are all HIV positive.

b All participants were assayed at baseline and 24 months. 330/441 (75%) of participants randomly selected from the intervention arm were assayed at 6 and 12 months, and 321/399 (80%) and 314/399 (77%) of participants randomly selected from the control arm were assayed at 6 and 12 months respectively.

c HPV sampled from glans/corona.

d Men with both baseline and 24-month HPV samples were randomly selected: 441/835 (52.8%) of HIV-negative married men with samples at both time points in the intervention arm; 399/803 (49.7%) of HIV-positive married men with samples at both time points in the control arm.

e Fourteen high-risk HPV genotypes evaluated using reverse line blot (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) (Roche Diagnostics).

f Twelve-month cumulative incidence risk of high-risk HPV genotypes measured among 644 randomly selected samples.

g Results presented for high-risk HPV. Marginal evidence of an effect of circumcision on the incidence of low-risk HPV was also observed (crude RR, 0.84; 95% CI, 0.66–1.10).

h Adjusted for age, education, condom use, alcohol consumption with sex, and number of sex partners.

i Adjusted for age, education, number of sex partners, and condom use.

j HPV sampled from glans/coronal sulcus, shaft, and scrotum.

k Proportion of men who enrolled but did not complete more than 1 visit.

l Authors report no difference in HPV acquisition between circumcised and uncircumcised men, but data were not shown.

m Adjusted for age, ethnicity, birthplace, education, lifetime number of partners, history of sex with men, condom use, and history of genital warts.
Anatomical Site of HPV Sampling

To address possible underdetection of HPV, we first restricted analysis to the 10 studies that measured HPV at all of the glans/corona, penile shaft and scrotum. The effect was the same as for all studies (OR, 0.58; 95% CI, 0.40–0.82). However, there was still considerable between-study heterogeneity ($P = 0.003$; $I^2 = 63.8\%$).

The magnitude of the effect estimate varied by anatomical site of HPV sampling (Figure 4 and Supplementary material). There was some evidence of effect at the urethra (OR, 0.35; 95% CI, 0.12–1.05) and strong evidence of effect at the glans/corona (OR, 0.47; 95% CI, 0.37–0.60). There was less evidence of an association at sites more distal to the foreskin (shaft, scrotum, and anus) or in semen. Notably, there was very little heterogeneity between estimates from the glans/corona, shaft, and semen.

Circumcision and HPV Incidence

Four studies of predominately HIV-negative men evaluated the effect of circumcision on HPV incidence (Table 2), including 1 RCT from Uganda and cohort studies from Mexico and the United States [25, 34, 36, 37]. HPV incidence was relatively high in all 4 populations (21%–35% cumulative risk over 12 months).

Male circumcision was protective against incident infection in the RCT (adjusted RR, 0.67; 95% CI, 0.50–0.91) but not in the cohort studies [25, 36, 37]. The meta-analysis was restricted to the 3 studies, which reported a RR (1 study presented an OR) and showed some evidence of a protective effect of circumcision on HPV incidence (summary RR, 0.75; 95% CI, 0.57–0.99; $P_{-\text{heterogeneity}} = 0.35$; $I^2 = 5.8\%$).

Circumcision and HPV Clearance

Four studies looked at clearance of HPV infections where the majority of men were HIV negative [25, 34–36] (Table 2). Cleared infections were defined as follows: positive HPV status at baseline and negative HPV status for the same genotype 12 months later [25]; negative status following an initial positive status for the same HPV genotype over any 6-month period during 18 months of follow-up [36]; acquisition of an incident infection during follow-up followed by negative status for the same HPV genotype at ≥2 subsequent visits (every 2 months) [35]; and negative status following an initial positive status for the same HPV genotype between any 2 sequential visits (0, 6, 12, and 24 months) [34].

Three studies [25, 34, 36] showed strong evidence that circumcision was associated with increased clearance (Table 2). No effect of circumcision was observed (RR, 0.96; 95% CI, 0.71–1.32) in the remaining study [35]. The summary estimate for those studies that reported a RR (3 out of 4 studies) was 1.33 (95% CI, 0.89–1.98) with substantial between-study heterogeneity ($P_{-\text{heterogeneity}} = 0.03$; $I^2 = 73.0\%$).
One RCT of male circumcision was conducted among HIV-infected men [33] (Tables 1 and 2). This showed an effect of circumcision on prevalence of high-risk HPV genotypes 24 months after the procedure (OR, 0.49; 95% CI, 0.26–0.93). This study also showed a high incidence of HPV (50% over 24 months) and borderline evidence of a protective effect of circumcision on HPV incidence (RR, 0.68; 95% CI, 0.44–1.04) (Table 2). Cleared HPV infections were defined as participants who cleared an infection with the same HPV genotype between enrollment and 24-month follow-up. There was no evidence that circumcision was protective against clearance (RR, 1.09; 95% CI, 0.94–1.27) (Table 2).

Description of Genital Warts Studies
Sixteen studies from 15 papers (11 cross-sectional and 5 case control) evaluated the association of circumcision with prevalence of genital warts [22, 38–50] along with 1 cohort study on incidence [44] (Table 3). Circumcision prevalence varied from 21% (United Kingdom) to 87% (Kenya). Circumcision status was evaluated by a clinician in 11 studies, self-reported in 4, and the method not reported in 2. Warts were diagnosed clinically or cytologically in 14 studies and self-reported in 3 studies. Prevalence of warts ranged from 3.6%–62%. Only 2 studies adjusted for covariates, which included age and at least 1 measure of sexual behavior [40, 48]. One study presented insufficient information to calculate a 95% CI [51].

Association of Circumcision and Genital Warts
Overall, there was no evidence of an association of circumcision and prevalent genital warts, although there was marked between-study heterogeneity (summary OR, 0.93; 95% CI, 0.65–1.33; P-heterogeneity < .001; $I^2$ = 78.1%; Figure 3B). Similarly, no association was seen among the subgroups of studies evaluated (Figure 4). Considerable heterogeneity was observed between the estimates from many subgroups, although there was less heterogeneity among the studies that presented adjusted estimates ($I^2$ = 10.9%) and among populations at high risk for STIs ($I^2$ = 0%). There was no evidence of publication bias (Egger test P = 0.13).

DISCUSSION
Circumcised men are at substantially lower risk for prevalent genital HPV infection than non-circumcised men. Few studies assessed the effect of circumcision on HPV incidence or clearance, but data suggest strong evidence of an effect of...
Figure 3. Association between male circumcision and prevalence of any penile HPV genotypes (A) or genital warts (B) among predominantly HIV-negative populations. A subgroup of the randomized populations from the RCTs was tested for HPV infection (56% at 21-month visit in South Africa [19] and ~50% at 24-month visit in Uganda [4, 34]).
circumcision on reducing HPV incidence and weak evidence of an effect on increasing HPV clearance. There was no evidence of an association of circumcision with genital warts.

**Heterogeneity**
Most studies showed a protective effect of circumcision, but we observed considerable heterogeneity in the magnitude of the effect.

![Figure 4](image)

**Anatomical Site of HPV Sampling**
A key methodological issue for assessing the association of circumcision and genital HPV is the anatomical site of sampling [9, 10, 13]. A strong effect of circumcision amongst studies that measured HPV at all of the glans/corona, penile shaft and scrotum was observed (OR, 0.58; 95% CI, 0.40–0.82; n = 10), which indicated that there is still a strong overall effect even if there is a change in the distribution of HPV following circumcision.
<table>
<thead>
<tr>
<th>First Author</th>
<th>Study design</th>
<th>Country and year of study</th>
<th>Study population (high/low risk)</th>
<th>Study size</th>
<th>Genital warts</th>
<th>Current/past history of warts</th>
<th>Assessment of genital warts</th>
<th>Assessment of circumcision</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aynaud [39]</td>
<td>Cross-sectional</td>
<td>France, published 1999</td>
<td>Male partners of women with genital HPV infection (low risk)</td>
<td>210 (23%)</td>
<td>54%</td>
<td>Current warts</td>
<td>Clinical exam with acetic acid and penoscopy</td>
<td>Clinical exam</td>
<td>0.53 (0.28–1.02)</td>
<td></td>
</tr>
<tr>
<td>Aynaud [38]</td>
<td>Cross-sectional</td>
<td>France, 1991–1992</td>
<td>Male partners of women with genital condyloma or intraepithelial neoplasia (low risk)</td>
<td>1000 (26%)</td>
<td>50%</td>
<td>Current warts</td>
<td>Clinical exam with acetic acid and penoscopy</td>
<td>Clinical exam</td>
<td>0.76 (0.57–1.02)</td>
<td></td>
</tr>
<tr>
<td>Bleeker [22]</td>
<td>Cross-sectional</td>
<td>Netherlands, 2002</td>
<td>Dermatology clinic attendees (non-STI clinic) (low risk)</td>
<td>112 (17%)</td>
<td>14.2%</td>
<td>Current warts</td>
<td>Clinical exam with acetic acid and penoscopy</td>
<td>Clinical exam</td>
<td>0.00 (0.00–1.0)</td>
<td></td>
</tr>
<tr>
<td>Bleeker [22]</td>
<td>Cross-sectional</td>
<td>Netherlands, 1995–2002</td>
<td>Partners of women with CIN (low risk)</td>
<td>224 (4%)</td>
<td>62.0%</td>
<td>Current warts</td>
<td>Clinical exam with acetic acid and penoscopy</td>
<td>Clinical exam</td>
<td>1.20 (0.30–0.51)</td>
<td></td>
</tr>
<tr>
<td>Cook [40]</td>
<td>Cross-sectional</td>
<td>United States, 1990</td>
<td>STI clinic attendees (low risk)</td>
<td>1448 (83%)</td>
<td>16.7%</td>
<td>Current warts</td>
<td>Clinical exam</td>
<td>Clinical exam</td>
<td>2.03 (1.45–2.89)</td>
<td>1.43 (1.11–2.00)</td>
</tr>
<tr>
<td>Dave [41]</td>
<td>Cross-sectional</td>
<td>United Kingdom, 2000</td>
<td>General (low risk)</td>
<td>4777 (21%)</td>
<td>3.6%</td>
<td>History of warts</td>
<td>Self-reported</td>
<td>Self-reported</td>
<td>1.04 (0.67–1.63)</td>
<td></td>
</tr>
<tr>
<td>Dinh [42]</td>
<td>Cross-sectional</td>
<td>United States, 1999–2004</td>
<td>General (low risk)</td>
<td>4110 (72%)</td>
<td>3.9%</td>
<td>History of warts</td>
<td>Self-reported</td>
<td>Self-reported</td>
<td>1.94 (1.28–3.05)</td>
<td></td>
</tr>
<tr>
<td>Donovan [43]</td>
<td>Cross-sectional</td>
<td>Australia, 1990–1991</td>
<td>STI clinic attendees (high risk)</td>
<td>300 (62%)</td>
<td>16.7%</td>
<td>History of warts</td>
<td>Clinical exam</td>
<td>Clinical exam</td>
<td>0.92 (0.47–1.79)</td>
<td></td>
</tr>
<tr>
<td>Hart [51]</td>
<td>Cross-sectional</td>
<td>Australia, 1988–1991</td>
<td>STI clinic attendees (high risk)</td>
<td>12 170 (29%)</td>
<td>15%</td>
<td>Current warts</td>
<td>Clinical exam</td>
<td>Not stated</td>
<td>1.25 (P &lt; 0.001)</td>
<td></td>
</tr>
<tr>
<td>Lavreys [44]</td>
<td>Cohort</td>
<td>Kenya, 1993–1997</td>
<td>Trucking company employees (high risk)</td>
<td>746 (87%)</td>
<td>1.4 per 100 pyr</td>
<td>Current warts</td>
<td>Clinical exam</td>
<td>Clinical exam</td>
<td>RR, 0.77 (0.23–2.5)</td>
<td></td>
</tr>
<tr>
<td>Mallon [50]</td>
<td>Case control</td>
<td>United Kingdom, 1994–1997</td>
<td>Dermatology clinic attendees (low risk)</td>
<td>343 (48%)</td>
<td>Not available</td>
<td>History of warts</td>
<td>Clinical exam</td>
<td>Clinical exam</td>
<td>0.34 (0.14–0.77)</td>
<td></td>
</tr>
<tr>
<td>Mandal [45]</td>
<td>Cross-sectional</td>
<td>United Kingdom, published 1991</td>
<td>STI clinic attendees (high risk)</td>
<td>105 (16%)</td>
<td>27%</td>
<td>Current warts</td>
<td>Cytology of exfoliated cells</td>
<td>Not reported</td>
<td>1.60 (0.44–5.50)</td>
<td></td>
</tr>
<tr>
<td>First Author</td>
<td>Study design</td>
<td>Country and year of study</td>
<td>Study population (high/low risk*)</td>
<td>Study size</td>
<td>Genital warts</td>
<td>Current/past history of warts</td>
<td>Assessment of genital warts</td>
<td>Assessment of circumcision</td>
<td>Crude OR (95% CI)</td>
<td>Adjusted OR (95% CI)</td>
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<tr>
<td>Oriel [52]</td>
<td>Case control</td>
<td>United Kingdom, 1967–1970</td>
<td>STI Clinic attendees (high risk)</td>
<td>263 (28%)</td>
<td>Not available</td>
<td>Current warts</td>
<td>Clinical exam</td>
<td>Clinical exam</td>
<td>0.66 (0.36–1.22)</td>
<td></td>
</tr>
<tr>
<td>Parker [46]</td>
<td>Cross-sectional</td>
<td>Australia, 1981</td>
<td>STI clinic attendees (low risk)</td>
<td>568 (61%)</td>
<td>7.3%</td>
<td>Current warts</td>
<td>Clinical exam</td>
<td>Clinical exam</td>
<td>1.54 (0.98–2.42)</td>
<td></td>
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<tr>
<td>Tseng [47]</td>
<td>Case control</td>
<td>United States, 1975–1985</td>
<td>General (low risk)</td>
<td>100 (43%)</td>
<td>6.0%</td>
<td>History of warts</td>
<td>Self-reported</td>
<td>Self-reported</td>
<td>0.96 (0.12–7.53)</td>
<td></td>
</tr>
<tr>
<td>Van Den Eeden [48]</td>
<td>Case control</td>
<td>United States, 1987–1991</td>
<td>General (low risk)</td>
<td>237 (83%)</td>
<td>Not available</td>
<td>Current warts</td>
<td>Clinical exam</td>
<td>Self-reported</td>
<td>1.02 (0.47–2.27)</td>
<td>0.90 (0.40–2.00)</td>
</tr>
<tr>
<td>Wilson [49]</td>
<td>Case control</td>
<td>Canada, paper presented 1945</td>
<td>Military (low risk)</td>
<td>1018 (48%)</td>
<td>Not available</td>
<td>Current warts</td>
<td>Clinical exam</td>
<td>Clinical exam</td>
<td>0.00 (0.00–0.23)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; CIN, cervical intraepithelial neoplasia; OR, odds ratio; pyr, person years; RR, rate ratio; STI, sexually transmitted infection.
* Study populations categorized as high or low risk for STIs (see Supplementary methods for details).
* Proportion of entire study population circumcised for cross-section and cohort studies; proportion of controls circumcised for case-control studies.
** Warts were diagnosed by clinician, but the patients reported if this was the first time they sought medical attention for warts.
*** Both microscopic and macroscopic warts evaluated.
**** Penile flat lesions.
***** Controls were groups of patients without any STDs.
****** Participants with STIs other than genital warts were not included in the analysis.
******* Macroscopic warts evaluated.
******** Adjusted for age, ethnicity, number of sex partners in past month, place of residence, and other sexually transmitted infections.
********* Type of warts (micro- or macroscopic) not reported.
********** Patients reported that a doctor or healthcare professional had diagnosed them with warts.
*********** Proportion with history of genital warts.
************ 95% confidence interval not reported.
************* Incidence of genital warts (First appearance of warts during follow-up), where median follow-up was 21 and 20 months for uncircumcised and circumcised men, respectively.
************** Incidence rate ratio.
*************** Warts diagnosed clinically either on history or examination.
**************** All cases of warts were microscopic and had no macroscopic evidence of warts; exfoliated cells showed warty atypia with or without dyskaryosis through cytology.
***************** Comparison group comprised patients with gonorrhea but no genital warts.
****************** Age adjusted.
******************* Patients identified through cancer registry; neighborhood controls. Data presented from controls only.
******************** Warts that occurred more than 2 years before time of interview.
********************** Patients included men with incident genital warts; controls were age-matched men randomly selected from the same health cooperative.
*********************** Incident cases during 1987–1991, in which patients reported this as the first time medical attention was sought for warts.
************************ Adjusted for age, clinic, marital status, reference year, and number of sex partners.
Circumcised men were consistently less likely than uncircumcised men to have HPV infection at the glans/corona and the urethra. These site-specific effects possibly occur because the foreskin provides a suitable environment around the glans for HPV infection [13], and HPV type-specific concordance has been shown between the glans/corona and foreskin in uncircumcised men that possibly reflects simultaneous infection or autoinoculation [17]. The effect observed at the urethra is unlikely due to detection bias in uncircumcised men. In a nested substudy among men in the control group (who were offered circumcision at the end of the trial), Auvert et al (2009) showed that HPV prevalence did not differ in samples taken from the urethra before and after circumcision. There was less evidence of an effect at sites distal to the foreskin and semen. This may in part be due to lower statistical power because HPV prevalence is lower at the anus and in semen, or it may be a true site-specific differential effect of circumcision. Less heterogeneity was observed in some of the site-specific estimates compared with the estimates of HPV at any anatomical site. Assuming a true difference in the effect of circumcision by anatomical site, this would explain some of the heterogeneity in the effect estimates.

The residual heterogeneity seen in subgroup analyses is likely a reflection of the diversity in the methods used and sites sampled to assess HPV infection. The method used to sample HPV may be a source of heterogeneity. However, it would be difficult to interpret any observed variation between sampling method because this could be due to variation in (1) the person using the method, (2) the effectiveness of methods at different anatomical sites, or (3) the sampling method itself.

**Included Studies**

Our review included 14 additional papers not included in the most recent systematic review of circumcision and HPV infection [11], including 4 additional papers on incidence/clearance [33–36] and 1 among HIV-positive men [33]. We included 2 papers that were not identified by previous reviews because these papers did not include circumcision as a keyword [20, 29]. These 2 papers found no evidence of an effect on HPV prevalence, suggesting possible ascertainment bias when circumcision was used as a search term in a systematic search.

While the RCTs provided important additional information, the trials were designed to evaluate the association between circumcision and HIV incidence, not HPV. Only subgroups of men were tested for HPV infection (56% at a 21-month visit in South Africa [19], ~50% (HIV negative) and 22% (HIV positive) at a 24-month visit in Uganda [33, 34]). HPV was not measured at baseline in the South African trial, so the sequence of circumcision and outcome cannot be determined. In women, the median time to clearance of prevalent infections is 1 year [53], although 2 studies suggest it is <6 months in men [35, 54]. Nonetheless, the prevalence of HPV in the Ugandan trial declined considerably between baseline and follow up (62%–36%) among circumcised men but remained relatively high in uncircumcised men (63%–51%).

In addition to the published results from the Ugandan and South African RCTs, data from the Kenyan trial also showed a strong effect of male circumcision on HPV incidence (OR, 0.4; 95% CI, 0.3–0.5) and clearance (OR, 0.3; 95% CI; 0.3–0.5) [55].

**Genital Warts**

No effect of circumcision was observed on genital warts. The method for diagnosis of genital warts and histology of warts varied considerably between studies. However, we found a strong effect of circumcision on low-risk HPV genotypes, which included genotypes 6 and 11 that are commonly associated with warts, with little heterogeneity. There was insufficient information to look at individual HPV genotypes. The lack of effect on genital warts may in part be due to detection bias if genital warts are more commonly reported and/or detected in circumcised men.

**Implications for Women**

HPV prevalence is estimated to be between 15% and 71% among penile cancer cases [8], but it is not thought to be a necessary cause for penile cancer. However, HPV infection in men has consequences for female partners. The association between male circumcision and cervical cancer and HPV infection in female partners has been evaluated in a number of observational studies. Some studies showed a beneficial effect [23, 56], while others showed no evidence of any effect [57–60]. However, secondary analyses from a RCT of male circumcision on HIV infection among men and their female partners showed that female partners of circumcised HIV-negative men were at substantially reduced risk of becoming infected with high-risk HPV genotypes as compared with partners of uncircumcised men (incidence RR, 0.77; 95% CI, .63–.93) [61]. There was some evidence that circumcised men were at lower risk of incident infection with HPV genotypes 16 and 18, which are implicated in cervical neoplasia. Circumcised men were also more likely to clear these infections, although these results were not statistically significant [34]. Women would also benefit indirectly from a lower prevalence of HPV in their male partners.

**CONCLUSIONS**

Circumcision services are being expanded as an HIV prevention strategy, especially in countries in sub-Saharan Africa with high HIV prevalence. Sub-Saharan Africa has a high prevalence of HPV infection and a high incidence of invasive cervical cancer [62], but HPV vaccines are not yet available in many settings. Expansion of circumcision services in this region represents an opportunity to reduce HPV infection as well as HIV in men, with resulting benefit to women.
Supplementary Data

Supplementary data are available at http://www.jid.oxfordjournals.org/ online. Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyrighted.

The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

Acknowledgments. N. L., H. W., and S. T. designed the search strategy, N. L. and H. W. reviewed abstracts and papers and extracted the data. N. L. performed the meta-analysis and wrote the first draft of the paper. H. W., S. T., and I. S. commented in detail on the drafts and approved the final version.

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