Circumcision to prevent HIV and other sexually transmitted infections in men who have sex with men: a systematic review and meta-analysis of global data

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Summary

Background Men who have sex with men (MSM) are disproportionately affected by HIV and other sexually transmitted infections (STIs) worldwide. Previous reviews investigating the role of circumcision in preventing HIV and other STIs among MSM were inconclusive. Many new studies have emerged in the past decade. To inform global prevention strategies for HIV and other STIs among MSM, we reviewed all available evidence on the associations between circumcision and HIV and other STIs among MSM.

Methods In this systematic review and meta-analysis, we searched PubMed, Web of Science, BioMed Central, Scopus, ResearchGate, Cochrane Library, Embase, PsycINFO, Google Scholar, and websites of international HIV and STI conferences for studies published before March 8, 2018. Interventional or observational studies containing original quantitative data describing associations between circumcision and incident or prevalent infection of HIV and other STIs among MSM were included. Studies were excluded if MSM could not be distinguished from men who have sex with women only. We calculated pooled odds ratios (ORs) and their 95% CIs using random-effect models. We assessed risk of bias using the Newcastle-Ottawa scale.

Findings We identified 62 observational studies including 119 248 MSM. Circumcision was associated with 23% reduced odds of HIV infection among MSM overall (OR 0·77, 95% CI 0·67–0·89; number of estimates [k]=45; heterogeneity I^2=77%). Circumcision was protective against HIV infection among MSM in countries of low and middle income (0·58, 0·41–0·83; k=23; I^2=77%) but not among MSM in high-income countries (0·99, 0·90–1·09; k=20; I^2=40%). Circumcision was associated with reduced odds of herpes simplex virus (HSV) infection among MSM overall (0·84, 0·75–0·95; k=5; I^2=0%) and penile human papillomavirus (HPV) infection among HIV-infected MSM (0·71, 0·51–0·99; k=3; I^2=0%).

Interpretation We found evidence that circumcision is likely to protect MSM from HIV infection, particularly in countries of low and middle income. Circumcision might also protect MSM from HSV and penile HPV infection. MSM should be included in campaigns promoting circumcision among men in countries of low and middle income. In view of the substantial proportion of MSM in countries of low and middle income who also have sex with women, well designed longitudinal studies differentiating MSM only and bisexual men are needed to clarify the effect of circumcision on male-to-male transmission of HIV and other STIs.

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Introduction

Men who have sex with men (MSM) are disproportionately affected by HIV worldwide.[1] Although pre-exposure prophylaxis (PrEP) for HIV, treatment of partners, and behavioural risk reduction are all effective in preventing HIV transmission among MSM, the HIV epidemic still contributes to substantial morbidity and mortality among this population.[2] MSM in countries of low and middle income are particularly affected.[2] Scant HIV prevention resources and entrenched stigma against MSM hamper access to HIV testing and treatment in countries of low and middle income.[2] Other sexually transmitted infections (STIs)—including syphilis, herpes simplex virus (HSV), gonorrhoea, chlamydia, and human papillomavirus (HPV)—also disproportionately affect MSM and could increase risk of HIV infection.[3] Evidence-based prevention approaches are urgently needed to optimise combination strategies to prevent HIV and other STIs among MSM.

The efficacy of male circumcision in preventing HIV among heterosexual men is well documented. In three randomised controlled trials undertaken in Africa, circumcision reduced the risk of female-to-male

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Research in context

Evidence before this study

Two previous systematic reviews and meta-analyses published in 2008 and 2011 found non-significant protective associations between circumcision and HIV infection and other sexually transmitted infections (STIs) among men who have sex with men (MSM). Since these reviews were published, a large amount of new evidence has emerged. A 2018 meta-analysis found circumcision was associated with a 20% reduced risk of HIV infection among MSM. However, this analysis included only 18 studies and did not include a substantial proportion of published data.

Added value of this study

We did a comprehensive updated review of associations between circumcision and HIV and other STIs among MSM. Our review included 62 observational studies and found that circumcision was associated with 23% reduced odds of HIV infection among MSM overall. This association was significantly stronger among MSM in countries of low and middle income compared with MSM in high-income countries. Circumcision was significantly associated with reduced odds of herpes simplex virus (HSV) infection among MSM overall and penile human papillomavirus (HPV) infection among MSM living with HIV.

Implications of all the available evidence

Our analysis suggests circumcision might protect MSM from HIV, HSV, and penile HPV infection. In view of the low quality of evidence and a substantial proportion of MSM in countries of low and middle income who also have sex with women, well designed longitudinal studies differentiating MSM from bisexual men are needed to clarify the effect of circumcision on male-to-male transmission of HIV and other STIs. MSM should be included in campaigns promoting circumcision among men in countries of low and middle income.

transmission of HIV by 50–60%.[4–6] The biological plausibility of circumcision to prevent HIV infection is also supported by immunohistological and histopathological studies that found a higher density of HIV target cells in the inner mucosa of the foreskin.[7,8]

It remains unclear whether MSM similarly benefit from circumcision.[9–11] Existing male circumcision programmes primarily target heterosexual men and have not actively promoted circumcision among MSM.[12] Two systematic reviews and meta-analyses from 2008[9] and 2011[10] have reported on associations between circumcision and HIV infection and other STIs among MSM. Analysing results from more than 20 observational studies, these meta-analyses found non-significant associations between circumcision and HIV infection and other STIs among MSM overall.[9,10] Significant protective associations between circumcision and HIV infection were identified in subanalyses of studies undertaken before the introduction of highly active antiretroviral therapy[9] and among MSM who primarily engage in insertive anal sex.[10] A meta-analysis from 2018[11] of 18 observational studies reported that circumcision was associated with 20% reduced odds of HIV infection among MSM overall (odds ratio [OR] 0·80, 95% CI 0·69–0·92), but not among MSM who primarily engage in insertive anal sex.

A large amount of new evidence has emerged in the past decade, particularly from countries of low and middle income.[13–50] To inform global prevention strategies for HIV and other STIs for MSM, we undertook an updated systematic review and meta-analysis of the association between circumcision and HIV and other STIs among MSM, stratifying important variables.

Methods

Search strategy and selection criteria

Our systematic review and meta-analysis was undertaken according to PRISMA[51] and MOOSE[52] guidelines. We searched PubMed, Web of Science, BioMed Central, Scopus, ResearchGate, Cochrane Library, Embase, PsycINFO, Google Scholar, and websites of five international HIV and STI conferences (World AIDS Conference, International AIDS Society Conference, Conference on Retroviruses and Opportunistic Infections, International Society for Sexually Transmitted Diseases Research Conference, and International Union against Sexually Transmitted Infections Conference) for studies published before March 8, 2018. We used the search terms ("circumcision", "circumcised", OR "uncircumcised") AND ("male sexual minorities", "male homosexuality", "men who have sex with men", "MSM", "homosexual", "gay", OR "bisexual"). References of retrieved full-text articles and other reviews were screened for additional eligible publications.

We included studies that recruited MSM, included circumcision status as a study variable, and reported estimates of associations between circumcision status and incident or prevalent HIV or other STIs among MSM. Interventional, cohort, case-control, and cross-sectional studies were all eligible for inclusion. Studies were excluded if MSM could not be distinguished from men who have sex with women only. We included multiple publications from one common study if each publication reported separate datasets.

Two of us (TY and HZ) independently did the literature search and assessed each study for inclusion. Disagreements were resolved through discussion with each other.

Data analysis

Two of us (TY and HZ) independently extracted the following study-level characteristics: first author, publication year, study country, years during which participants were recruited, study design, length of follow-up, recruitment setting, specific STIs and their infection sites, method of ascertaining HIV or STI status, method

of ascertaining circumcision status, sample size, mean or median age of participants, the proportion of circumcised MSM, the number of cases of HIV or other STIs among MSM by circumcision status, and association estimates of risk for HIV or other STIs comparing circumcised and uncircumcised MSM. Disagreements in extracted data were resolved through discussion with each other. Because other HIV prevention and treatment measures can mask the protective effect of circumcision, we also extracted the proportion of HIV-positive MSM receiving antiretroviral therapy (ART), the proportion of MSM self-reporting HIV testing history, and the proportion of MSM self-reporting consistent condom use, when available. To investigate effects of geographical, socioeconomic, and cultural factors, study countries were grouped by WHO region, income level,[53] and official position on lesbian, gay, bisexual, and transgender rights, as expressed in joint statements to the UN General Assembly or the UN Human Rights Council.[54]

The Newcastle-Ottawa scale was used to assess the methodological quality of included cohort and case-control studies.[55] An adapted version of the Newcastle-Ottawa scale developed by Herzog and colleagues[56] was used for cross-sectional studies. We planned to use a checklist developed by Downs and colleagues[57] to assess risk of bias of included interventional studies. Two of us (TY and HZ) independently assessed the risk of bias of included studies and quality of evidence. Any disagreement was resolved by discussion among all authors.

ORs were used to report associations between circumcision and HIV infection and other STIs among MSM, with an OR lower than 1·0 representing a protective effect of circumcision. ORs and their 95% CIs were extracted directly from reports when available, with adjusted ORs extracted preferentially over unadjusted ORs. If an included study did not report ORs, crude ORs were calculated from extracted data.

Because included studies differed in study design, we assumed a high potential for heterogeneity between included studies, and thus a random-effects model was used to calculate pooled effect sizes.[58] Our primary outcome was the pooled OR estimate of the association between circumcision and HIV infection in MSM. Our secondary outcomes were pooled OR estimates of the association between circumcision and STIs other than HIV infection in MSM. As in a previous meta-analysis,[9] we first calculated a pooled association estimate between circumcision and all STIs other than HIV as one composite outcome using the method developed by Borenstein and colleagues[59] to ensure the independence of individual effect sizes. We then calculated individual ORs for specific STIs when two or more studies reported outcomes for HPV, HSV, syphilis, chlamydia, gonorrhoea, or hepatitis B virus (HBV) infection. Additionally, we did random-effects cumulative meta-analyses to delineate temporal changes in the magnitude and direction of pooled association estimates as evidence accumulated over time.[60] Studies were sorted by year of publication and sequentially added to the analysis in chronological order, with pooled estimates recalculated with each added study.

The I^2 statistic was used to assess the level of heterogeneity across included studies, with values of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively.[61] If substantial heterogeneity was detected, we did univariate meta-regression analyses to investigate the proportion of between-study variance accounted for by study quality, participants' characteristics, and study characteristics. We were unable to do a multivariate meta-regression analysis because only a few included studies reported information for all study-level factors. We also did subgroup analyses by participant and study characteristics to compare pooled association estimates and heterogeneity. Publication bias was assessed using funnel plots and Egger's test.[62] Potential outliers were detected in a sensitivity analysis by removing each estimate one at a time and recalculating the pooled estimates. We also did sensitivity analyses by restricting ORs adjusted for potential confounders.

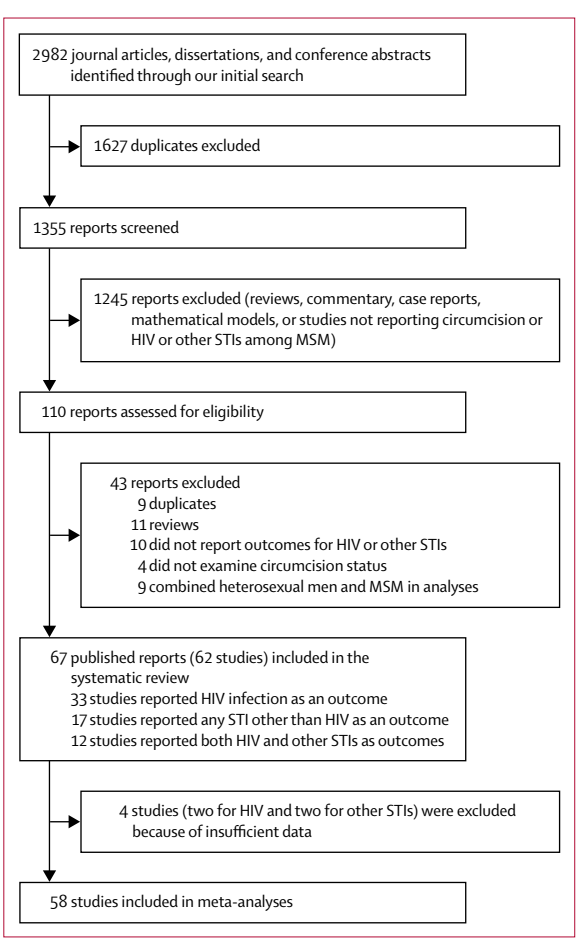

Figure 1: **Selection of reports for inclusion in meta-analyses**
STI=sexually transmitted infection. MSM=men who have sex with men.

	Studies (n)
Publication type	
Journal article	58
Conference abstract	7
Doctoral or Master's thesis	2
Study design	
Cohort*	15
Case-control†	2
Cross-sectional‡	45
WHO region§	
Americas	18
Western Pacific	19
Southeast Asia	9
Africa	6
Europe	5
Eastern Mediterranean	1
Income of country§	
High	26
Upper-middle	24
Lower-middle	7
Low	2
Official position on LGBT rights§	
Support	35
Oppose	4
Neither support nor oppose	21
Recruitment setting¶	
Non-clinic-based	40
Clinic-based	16

We identified 62 studies from 67 publications; one study split results into three parts and reported each part in different journals,[17,87,88] and another three studies[37,76,82] reported additional data in conference abstracts.[31,75,81] LGBT=lesbian, gay, bisexual, and transgender. *Four were retrospective cohort studies[15,49,69,85] and 11 were prospective cohort studies. †One study[84] was a nested case-control design. ‡Two studies[27,88] were cross-sectional analyses of a cohort study. §Studies were grouped according to country; three[15,69,85] were multinational cohort studies and one[67] did not report the country in which it was undertaken. ¶Six studies[20,49,68-70,85] did not provide information on recruitment setting.

Table: **Characteristics of included studies**

All data analyses were done using Stata version 14.1. Full details of the data extraction and analyses are provided in the appendix.

See Online for appendix

Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had access to all data in the study and had final responsibility for the decision to submit for publication.

Results

We identified 67 publications that were eligible for our analysis,[13–50,63–91] arising from 62 independent observational studies (119 248 participants). 33 studies only reported HIV infection as an outcome,[13–15,18,19,21,22,24,26,28–31,37,38,42,44,45,63,64,66,67,69,75–78,80–86,89,90] 17 reported STIs other than HIV as outcomes,[16,20,23,33,35,36,40,43,46–50,65,68,70,74] and 12 reported both HIV infection and other STIs as outcomes.[17,25,27,32,34,39,41,71–73,79,87,88,91] Four studies—two for HIV[15,29] and two for other STIs[65,70]—were excluded from the meta-analysis because they did not report data necessary to calculate ORs (figure 1).

The table summarises characteristics of included studies. Details of each study are presented in the appendix. Included studies were undertaken between 1989 and 2016 and published between 1993 and 2017. The number of MSM enrolled in each study ranged from 49 to 25 159. Mean or median age of MSM varied from 18 years to 46 years (median 29 years [IQR 26–34]; 58 studies). The proportion of circumcised men ranged from 4% to 96% (median 34% [IQR 17–66]; 56 studies). The proportion of HIV-infected MSM using ART at enrolment varied from 30% to 87% (median 66% [IQR 44–86]; five studies). The proportion of MSM self-reporting previous HIV testing ranged from 37% to 93% (median 53% [IQR 46–68]; 17 studies). Consistent condom use ranged from 12% to 83% (median 38% [IQR 27–54]; 20 studies).

Of 45 studies that examined the association between circumcision and HIV status among MSM, 29 reported non-significant associations. 11 studies found circumcision to have a significant protective association with HIV infection among all MSM.[18,41,42,63,64,67,73,76,83,86,90] Two studies found a significant protective association with circumcision only among MSM who primarily engage in insertive anal sex.[25,87] Two studies reported a significant protective association with circumcision only among bisexual men.[31,37,42] One of the included studies found circumcised MSM were at significantly increased odds of HIV infection.[45]

Of 29 studies that examined the association between circumcision and STIs other than HIV among MSM, 19 reported non-significant associations. One study reported that circumcision was associated with significantly less multiplicity of HPV genotypes and lower prevalence of high-risk HPV genotypes.[25] Another study reported a significant protective effect for penile HPV infection.[47] A further study found a significant protective association between circumcision and incident HPV infection among MSM who primarily engage in insertive anal intercourse.[17] Three studies reported a significant protective effect for syphilis infection.[32,73,88] A significant protective association between circumcision and HSV,[72] HBV,[49] and gonorrhoea infection[65] was reported by one study for each outcome. Circumcised MSM were at significantly increased odds of non-chlamydial non-gonococcal urethritis[74] and recurrent STI[70] in one study each.

43 studies (105 009 participants) were included in the meta-analysis of the association between circumcision and HIV infection in MSM. Circumcision was associated with 23% lower odds of HIV infection in MSM overall (OR 0·77, 95% CI 0·67–0·89; number of estimates [k]=45; I^2=77%). The cumulative meta-analysis suggested that this protective association became evident after 2011 (figure 2). In subgroup analyses (figure 3), this protective

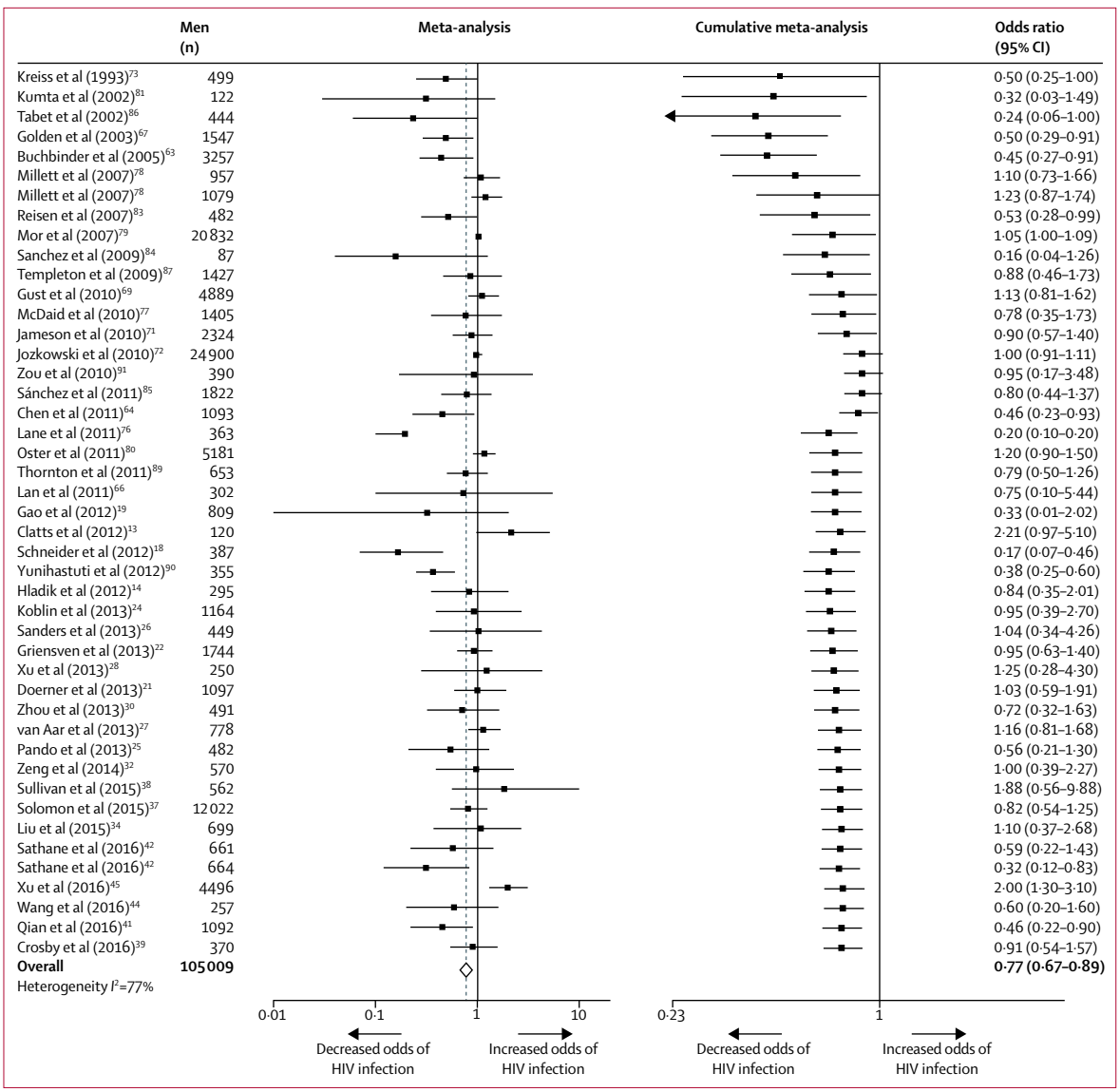

Figure 2: **Meta-analysis and cumulative meta-analysis of the association between circumcision and HIV infection among men who have sex with men**
In the cumulative meta-analysis, studies were sorted by year of publication and sequentially added to the analysis in chronological order, with pooled estimates recalculated with each added study. All estimates are independent. One study could contribute more than one estimate only when data from independent populations were analysed and reported separately. Blue vertical dotted line shows the overall odds ratio.

association was significantly stronger (95% CIs did not overlap) in countries of low and middle income (OR 0·58, 95% CI 0·41–0·83; k=23; I^2=77%) than in high-income countries (0·99, 0·90–1·09; k=20; I^2=40%). Compared with the overall pooled estimate, this protective association remained significant and was stronger among MSM from southeast Asia or Africa, those who primarily engage in insertive anal sex, younger MSM, non-clinic-based studies, and studies in which the proportion of MSM self-reporting consistent condom use was lower.

27 studies (61 411 participants) were included in the meta-analysis of associations between circumcision and STIs other than HIV. Circumcision was associated with reduced odds of any STI other than HIV (OR 0·91, 95% CI 0·83–1·00; k=29; I^2=8%), which became evident in available publications from 2013 (figure 4). In meta-analyses calculating associations between circumcision and specific STIs (figure 5), circumcision was associated with reduced odds of HSV infection among MSM overall (OR 0·84, 95% CI 0·75–0·95; k=5; I^2=0%). The significant protective association between circumcision and penile HPV infection was only observed among MSM living with HIV (0·71, 95% CI 0·51–0·99; k=3; I^2=0%). The odds of infection with anal HPV, syphilis, chlamydia, gonorrhoea, and HBV did not differ between circumcised and uncircumcised MSM.

Substantial heterogeneity (I^2=77%) was noted across studies that reported HIV infection as an outcome

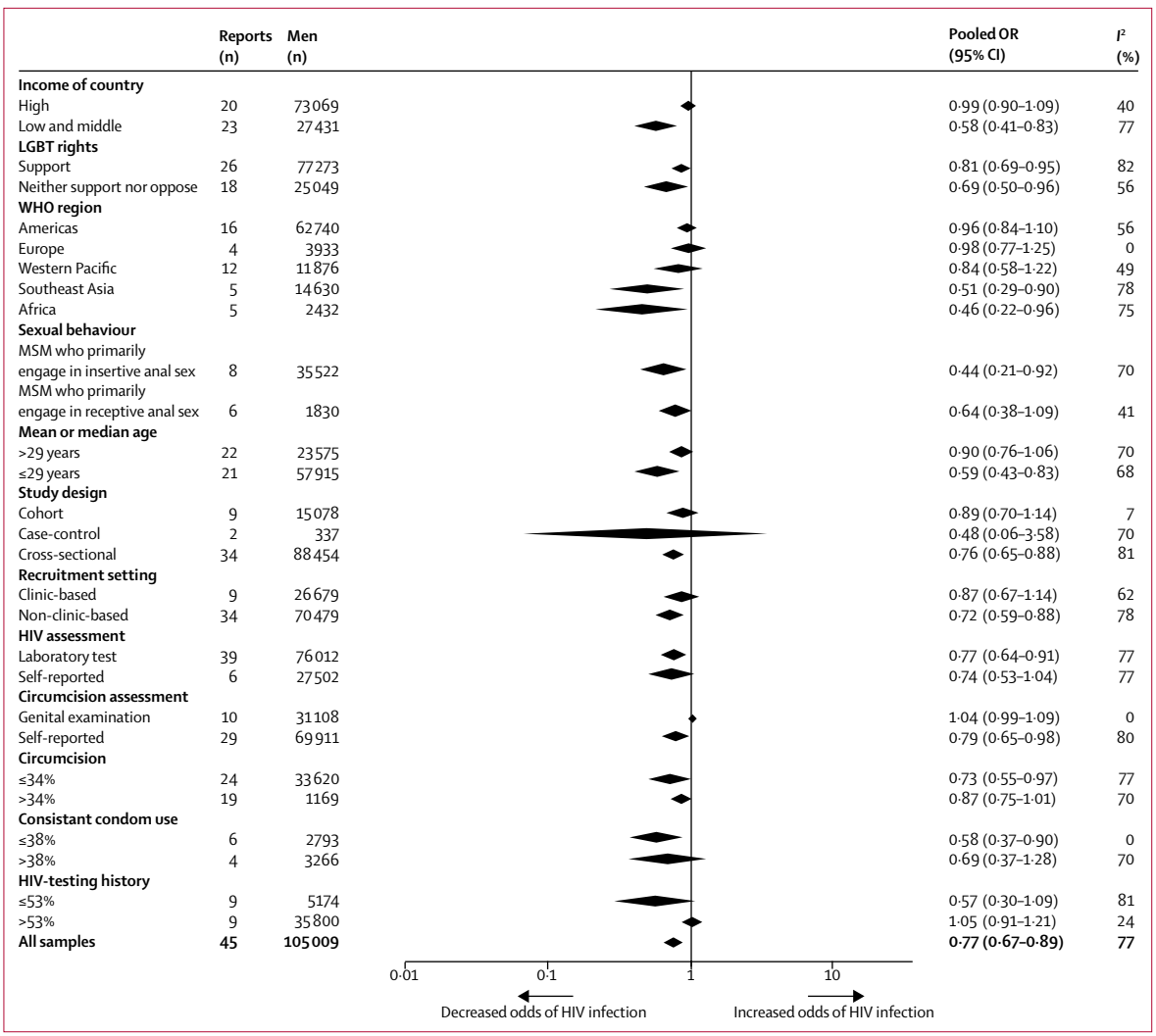

Figure 3: **Subgroup meta-analyses of the association between circumcision and HIV infection among men who have sex with men**
Cutoffs for continuous variables were median values. OR=odds ratio. MSM=men who have sex with men. LGBT=lesbian, gay, bisexual, and transgender.

(figure 2). In univariate meta-regression analyses, this high heterogeneity was accounted for by the income level of countries (R^2=19%; p=0·018), mean or median age of MSM (R^2=18%; p=0·018), and the proportion of MSM self-reporting HIV-testing history (R^2=34%; p=0·023; appendix). In subgroup analyses (figure 3), the high level of heterogeneity either disappeared or was substantially reduced in studies undertaken in Europe, in cohort studies, and in studies in which circumcision was ascertained by genital examination, the proportion of MSM self-reporting consistent condom use was lower, and the proportion of MSM with a history of HIV testing was higher (I^2 range 0–24%). Heterogeneity across studies that reported any STI other than HIV was low (I^2 range 0–28%), except for two studies that reported HBV infection, which had high heterogeneity (I^2=76%; figure 5).

Evidence of publication bias was found in studies reporting HIV infection (asymmetrical funnel plot and p=0·003 by Egger's test; appendix) and gonorrhoea infection (p=0·021 by Egger's test). Sensitivity analyses detected one study[76] as having some effect on the pooled association estimate between circumcision and HIV infection (appendix). Restricting the meta-analysis to 14 studies[18,30,42,45,63,64,71,73,76–78,80,83,89] that adjusted for potential confounders increased the magnitude of the protective association between circumcision and HIV infection (OR 0·64, 95% CI 0·45–0·93; k=16; I^2=87%). 32 (52%) of 62 studies were rated as low risk of bias with all remaining studies rated as high risk of bias (appendix).

Discussion

In this systematic review and meta-analysis of observational studies from countries of low and middle income and from high-income countries, we found that circumcision was associated with 23% reduced odds of HIV infection among MSM overall, with this protective

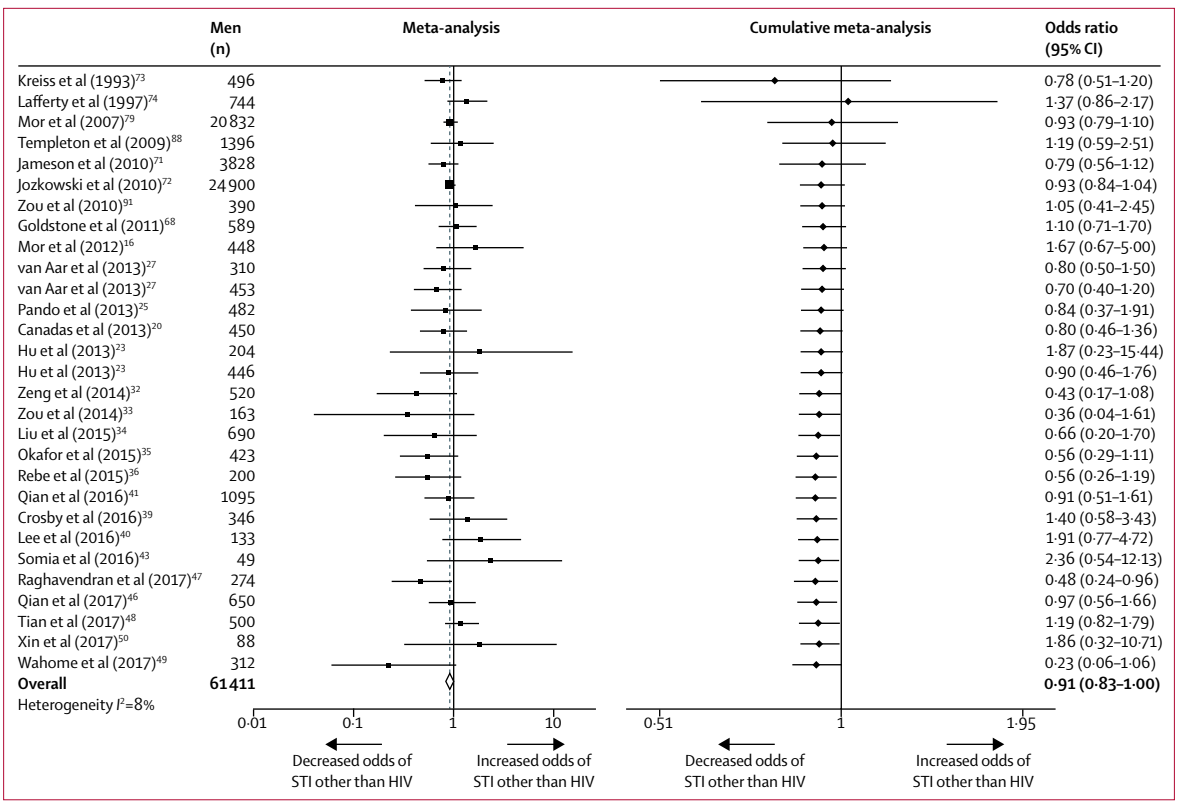

Figure 4: **Meta-analysis and cumulative meta-analysis of the association between circumcision and any sexually transmitted infection other than HIV among men who have sex with men**

In the cumulative meta-analysis, studies were sorted by year of publication and sequentially added to the analysis in chronological order, with pooled estimates recalculated with each added study. To ensure the independence of effects, each study contributed only one estimate unless data from independent populations were analysed and reported separately. If a study reported multiple individual association estimates between circumcision and different infection sites or STIs in the same population, a summary odds ratio of all STIs (excluding HIV) was calculated for that study population, using the formula developed by Borenstein and colleagues.[59] Blue vertical dotted line shows the overall odds ratio. STI=sexually transmitted infection.

association being stronger in countries of low and middle income. Circumcision was associated with significantly reduced odds of HSV infection among MSM overall and penile HPV infection among MSM living with HIV.

Our finding that circumcision is associated significantly with lower rates of HIV infection among MSM differs from those of two previous systematic reviews.[9,10] Compared with these reviews, we included 22 additional studies, of which 16 were from countries of low and middle income, a setting in which the association between circumcision and lower rates of HIV was especially pronounced. Additionally, in the cumulative meta-analysis, the significant protective effect of circumcision only became apparent in 2011, which is after the year of publication of the last comprehensive systematic review on this topic.[10] A systematic review published in 2018 included all men, and MSM was only a fraction of the analysis, and that review missed a substantial amount of existing evidence,[11] which could potentially lead to a biased conclusion with limited stratified findings.

The protective effect of circumcision against HIV infection was significantly stronger among MSM in countries of low and middle income compared with those in high-income countries. Several reasons could account for this difference. This enhanced protective effect could be attributable to the higher stability in anal sex role segregation, lower rates of circumcision, and higher HIV prevalence among MSM in countries of low and middle income.[92,93] Bisexual men represent a substantial proportion of MSM in countries of low and middle income, and could be another explanatory factor. Behavioural studies in China,[94] India,[37] Peru,[86] and sub-Saharan Africa[95] have found that 40–70% of MSM have also had sex with women, and nearly 30% are married to women.[37,95] Circumcision could be effective in reducing HIV acquisition among bisexual men by reducing female-to-male HIV transmission.[4–6] Rates of insertive anal intercourse are also higher among bisexual men,[94] the sex position for which circumcision offers direct benefit.[10] Additionally, fewer protective measures against HIV infection are available in countries of low and middle income compared with high-income countries.[2] Observational studies undertaken in these contexts might be affected less by other interventions that mask the effectiveness of circumcision to prevent infection. This interpretation is consistent with our

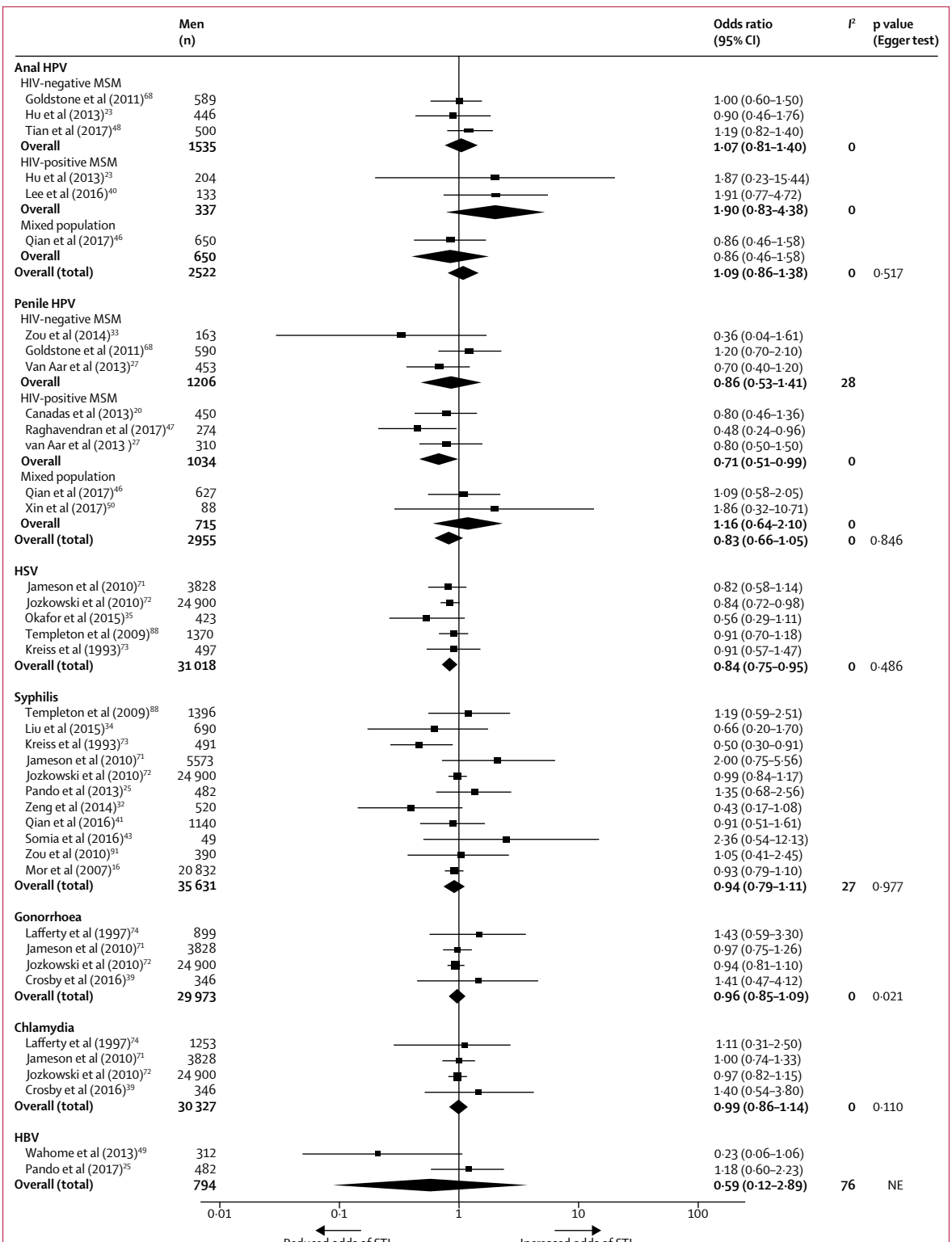

Figure 5: **Meta-analyses of the associations between circumcision and specific sexually transmitted infections among men who have sex with men**
Associations between circumcision and anal HPV infection and penile HPV infection were calculated separately and stratified by HIV status of participants. STI=sexually transmitted infection. MSM=men who have sex with men. HPV=human papillomavirus. HSV=herpes simplex virus, including both HSV-1 and HSV-2. HBV=hepatitis B virus. NE=not estimable.

subanalyses, which found the protective effect increased as the proportion of MSM receiving additional HIV protective measures (eg, condom use, HIV testing) decreased.

Circumcision was significantly associated with reduced odds of HSV infection among MSM overall. The protective association between circumcision and penile HPV infection was only significant among MSM living with HIV. This selective effect could be attributable to high HPV prevalence and increased susceptibility to HPV infection among people living with HIV.[96] Similar protective effects against HSV and HPV infection have also been described among heterosexual men.[97–99]

It is biologically plausible that circumcision could protect against HIV and other STIs. Circumcision decreases the number of target cells for pathogens to infect, eliminates a microenvironment favouring pathogen survival and replication, and reduces the potential for microabrasions during sexual intercourse that allow for the entry of pathogens into the body.[100] The protective association between circumcision and other STIs could be less apparent than the association with HIV infection because STIs other than HIV are transmitted more effectively through sexual behaviours besides anal intercourse (eg, syphilis transmission can occur via intimate skin-to-skin contact),[101] thereby reducing the protective effect of circumcision.

Our review has several limitations. First, our meta-analysis was based on observational data. More than half of included studies were cross-sectional and rated as having high risk of bias. However, the protective effect of circumcision was more apparent in non-clinic-based studies and studies that controlled for potential confounders, suggesting that the association between circumcision and lower rates of HIV infection might not be the result of confounding. Second, we found evidence of publication bias in our analysis. Disproportionate reporting of significant associations in published work can result in an overestimate of the protective effect of circumcision. Finally, only a few studies were included in several subgroup categories. Findings from these meta-analyses should be considered preliminary and warrant further investigation when more data become available.

Further research is needed to better characterise the effect of circumcision on HIV, HSV, and HPV transmission among MSM. Although randomised controlled trials of circumcision among MSM in countries of low and middle income could confirm this protective effect, evidence from this meta-analysis might not be strong enough to support development of a randomised trial. The protective effect of circumcision seen in countries of low and middle income could be accounted for by prevention of female-to-male HIV transmission among bisexual men rather than prevention of HIV transmission during anal sex. Because of the disparate anatomical and biological environments of the vagina and rectum, the effect of circumcision on transmission of HIV or other STIs during vaginal intercourse and anal intercourse might be different. Additionally, recruiting eligible participants for a randomised trial would be difficult because of widespread stigma against MSM in countries of low and middle income. Moreover, the willingness of MSM in countries of low and middle income to be circumcised is low: a study in China found that only 17% of MSM were willing to be circumcised;[102] and a study from Argentina found that 70% of uncircumcised MSM opted not to undergo circumcision even after being informed of the potential reduced risk of HIV infection.[25] In view of the paucity of high-quality cohort studies identified in this review, well-designed longitudinal studies are needed to further clarify the effect of circumcision on the transmission of HIV, HPV, and HSV during anal intercourse. Such longitudinal studies should differentiate MSM from bisexual men, to disentangle the effect of circumcision on male-to-male and female-to-male transmission of HIV and other STIs. It is essential to identify factors affecting the willingness to undergo circumcision among MSM in countries of low and middle income and design effective interventions to improve such willingness.

Our finding that circumcision is more likely to protect MSM in countries of low and middle income from HIV infection is promising in view of the high risk of HIV infection among MSM in these settings as a result of heavy stigma and restricted access to HIV prevention measures (eg, PrEP).[2] MSM in countries of low and middle income could benefit from advances in cheap, safe, and convenient circumcision surgical techniques (eg, Shang Ring).[103] Because circumcision as an HIV prevention measure targets all men regardless of sexual orientation, MSM in countries of low and middle income seeking circumcision would most likely experience less stigma when accessing this service. Although circumcision offers the most direct protection to MSM who primarily engage in insertive anal sex, high coverage of circumcision among MSM overall could reduce HIV prevalence at a population level and, therefore, indirectly protect MSM who engage in receptive anal sex. Our findings also suggest that interventions to increase circumcision among MSM could protect against other STIs, including HSV and HPV. Thus, MSM should not be excluded from campaigns promoting circumcision among men in countries of low and middle income, and mathematical modelling studies should be developed to assess the public health effect and cost-effectiveness of large-scale circumcision programmes for HIV prevention among MSM in individual countries of low and middle income.

Contributors

TY and HZ had the idea for the study, designed the protocol, and did the study selection and data extraction. TY, TF, N-YK, and HZ wrote the draft report. YCa, YCh, and JZ contributed to the statistical analysis. TF, LL, JX, JG, JL, CH, ZY, WC, C-YC, YH, ZL, KZ, GW, XM, and AEG critically revised the report.

Declaration of interests

We declare no competing interests.

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