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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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Contributors

TY and HZ conceived the study, designed the protocol and conducted study selection and data extraction. TY, TF, NK, and HZ drafted the manuscript. Yong Cai, Yingqing Chen, JZ contributed to statistical analysis. TF, LL, JX, JG, JL, CH, ZY, WC, CC, YH, ZL, KZ, GW, XM, and AG critically revised the manuscript. TY, TF, and NK contributed equally to the manuscript.

Conflict of Interest Disclosures

We declare no competing interests.

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. A large number of new studies have emerged in the past decade. To inform global HIV/STI prevention strategies among MSM, we reviewed all available evidence on the associations between circumcision and HIV/STIs among MSM.

Methods—In this systematic review and meta-analysis, we searched PubMed, Web of Science, BioMed Central, Scopus, Research Gate, Cochrane Library, EMBASE, PsycINFO, Google Scholar, and websites of international HIV/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% confidence intervals (CIs) using random-effect models. We assessed risk of bias using the Newcastle-Ottawa scale.

Findings: We identified 62 observational studies involving a total of 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 LMICs (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 LMICs. Circumcision may also protect MSM from HSV and penile HPV infection. MSM should be included in campaigns promoting circumcision among men in LMICs. Given the substantial proportion of MSM in LMICs 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 HIV pre-exposure prophylaxis (PrEP), 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 MSM.[2] MSM in low- and middle-income countries (LMICs) are particularly impacted.[2] Limited HIV prevention resources and entrenched stigma against MSM hamper access to HIV testing and treatment in LMICs.[2] Other sexually transmitted infections (STIs), including syphilis, herpes simplex virus (HSV), gonorrhea, chlamydia, and human papillomavirus (HPV), also disproportionately affect MSM and may increase risk of HIV infection.[3] Evidence-based prevention approaches are urgently needed to optimize combination strategies to prevent HIV and other STIs among MSM.

The efficacy of male circumcision in preventing HIV among heterosexual men is well documented. Three randomized controlled trials (RCTs) conducted in Africa demonstrated that circumcision can reduce the risk of female-to-male transmission of HIV by 50% to 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 earlier systematic review and meta-analysis papers reported on the associations between circumcision and HIV infection and other STIs among MSM in 2008 and 2011.[9,10] Analyzing 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 sub-analyses of studies conducted before the introduction of highly active antiretroviral therapy[1] and among MSM who primarily engage in insertive anal sex.[10] A recent meta-analysis including 18 observational studies reported that circumcision was associated with 20% (95% confidence interval [CI] 0·69-0·92) reduced odds of HIV infection among MSM overall, however not among MSM who primarily engage in insertive anal sex.[11]

A large amount of new evidence has emerged, especially from LMICs, in the past decade.[13–50] To inform global HIV and STI prevention strategies for MSM, we conducted an updated systematic review and meta-analysis on the association between circumcision and HIV and other STIs among MSM, stratifying important parameters.

Methods

Search strategy and selection criteria

Our systematic review and meta-analysis was performed according to PRISMA and MOOSE guidelines.[51,52] We searched PubMed, Web of Science, BioMed Central, Scopus, Research Gate, Cochrane Library, EM BASE, PsycINFO, Google Scholar, and websites of five international HIV/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/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. We included multiple publications from one common study if each publication reported separate data sets.

Two authors (TY and HZ) independently performed the search and assessed each study for inclusion. Disagreements were resolved through discussion among the two authors.

Data analysis

Two authors (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/STI status, method of ascertaining circumcision status, sample size, mean or median age of participants, the proportion of circumcised MSM, the number of HIV/STI cases among MSM by circumcision status, and association estimates of HIV/STI risks comparing circumcised and uncircumcised MSM. Disagreements in extracted data were resolved through discussion among two authors (TY and HZ). Because other HIV prevention and treatment measures may mask the protective effect of circumcision, we also extracted the proportion of HIV-positive MSM receiving antiretroviral therapy (ART), proportion of MSM self-reporting HIV testing history, and proportion of MSM self-reporting consistent condom use, where available. To investigate effects of geographic, socioeconomic, and cultural factors, study countries were grouped by WHO region, income level,[53] and official position on lesbian, gay, bisexual, and transgender (LGBT) rights as expressed in joint statements to the United Nations General Assembly or the United Nations 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 *et al* was used for cross-sectional studies.[56] We planned to use a checklist developed by Downs *et al* to assess risk of bias of included interventional studies.[57] Two authors (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.

Odds ratios (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 articles where 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 a single composite outcome using the method developed by Borenstein *et al* to ensure the independence of individual effect sizes.[59] We then calculated individual ORs for specific STIs when two or more studies reported outcomes for HPV, HSV, syphilis, chlamydia, gonorrhea, or hepatitis B virus (HBV) infection. Additionally, we performed 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 performed univariate meta-regression analyses to explore the proportion of between-study variance explained by study quality, participant characteristics, and study characteristics. We were unable to perform a multivariate meta-regression analysis as only a small number of included studies reported information for all study-level factors. We also performed subgroup analyses by participant and study characteristics to compare pooled association estimates and heterogeneity. Publication bias was assessed using funnel plots and the Egger's test.[62] Potential outliners were detected in sensitivity analysis by removing each estimate one at a time and recalculating the pooled estimates. We also conducted sensitivity analyses by restricting ORs adjusted for potential confounders.

All data analyses were conducted using Stata version 14.1 (Stata Corp, College Station, TX, USA). Full details of the data extraction and analyses are provided in the appendix.

Role of the funding source

Study funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

We identified 67 eligible publications[12–49,63–91] arising from 62 independent observational studies (n=119248 participants). Thirty-three studies[12–14,17,18,20,21,23,25,27–30,36,37,41,43,44,46,63,64,66,67,69,75–78,80–86,89,90] only reported HIV infection as an outcome, 16 reported STIs other than HIV as outcomes,[19,22,32,34,35,42,45–49,65,68,70,74] and 13 reported both HIV infection and other STIs as outcomes.[15,16,24,26,31,33,38,40,71–73,79,86,88,91] Four studies (2 for HIV[15,29] and 2 for STIs[65,90]) were excluded from the meta-analysis because they failed to report data necessary to calculate ORs (figure1).

Table 1 summarizes characteristics of included studies. Details of each study are presented in the appendix. Included studies were conducted between 1989 and 2016 and published between 1993 and 2017. The number of MSM enrolled in each study ranged from 49 to 25159. Mean or median age of MSM varied from 18 to 46 years (median=29 years; 58

studies). The proportion of circumcised men ranged from 4% to 96% (median=34%; 56 studies). The proportion of HIV-infected MSM using ART at enrollment varied from 30% to 87% (median=66%; 5 studies). The proportion of MSM self-reporting previous HIV testing ranged from 37% to 93% (median= 53%; 17 studies), and consistent condom use ranged from 12% to 83% (median= 38%; 20 studies).

Of the 45 studies that examined the association between circumcision and HIV status among MSM, 29 reported non-significant associations. Eleven found circumcision to have a significant protective association with HIV infection among all MSM.[17,18,40,63,64,73,75,76,83,86,87,90] Two found a significant protective association with circumcision only among MSM who primarily engage in insertive anal sex.[24,86] Two reported a significant protective association with circumcision only among men who have sex with both men and women (MSMW).[30,36,41] One included studies that found circumcised MSM to be at significantly increased odds of HIV infection.[44]

Of the 29 studies that examined the association between circumcision and STIs other than HIV among MSM, 19 reported non-significant associations. One reported circumcision was associated with significantly less multiplicity of HPV genotypes and lower prevalence of high-risk HPV genotypes.[24] One reported a significant protective effect for penile HPV infection.[46] One found a significant protective association between circumcision and incident HPV infection among MSM who primarily engage in insertive anal intercourse.[16] Three reported a significant protective effect for syphilis infection.[31,73,88] A significant protective association between circumcision and HSV,[72] HBV,[48] and gonorrhea infection[65] was reported by one study, respectively. Circumcised MSM were at significantly increased odds of non-chlamydial non gonococcal urethritis[74] and recurrent STI[70] in one included study, respectively.

Forty-three studies (n=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 since 2011 (figure 2).

In subgroup analysis (figure 3), this protective association was significantly stronger (95% CIs did not overlap) in LMICs (0·58, 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 to the overall pooled estimate, this protective association remained significant and tended to be stronger among MSM from Southeast Asia or Africa, MSM 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. Details of all subgroup analyses are presented in Figure 3.

Twenty-seven studies (n=61411 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 from available publications in 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 (0·84, 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, gonorrhea, and HBV did not differ significantly between circumcised and uncircumcised MSM.

There was substantial heterogeneity (I^2=77%) across studies that reported HIV infection as an outcome. In univariate meta-regression analyses, this high heterogeneity was explained by the income level of countries (R^2=19%), mean or median age of MSM (R^2=18%) and the proportion of MSM self-reporting HIV-testing history (R^2=34%) (all p<0·05; appendix). In subgroup analyses (figure 3), the high level of heterogeneity disappeared, or was substantially reduced, in studies conducted in Europe, cohort studies, studies where circumcision was determined by genital examination, the proportion of MSM self-reporting consistent condom use was lower, and the proportion of MSM having HIV-testing history 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%).

There was evidence of publication bias in studies reporting HIV infection (asymmetrical funnel plot, and p=0·003 by Egger test; appendix) and gonorrhea infection (p=0·02 by Egger test). Sensitivity analyses detected one study[76] as having a large but statistically non-significant impact on the pooled association estimate between circumcision and HIV infection (appendix). Restricting the meta-analysis to the 13 studies[17,29,41,44,63,64,73,76,77,78,80,83,89] 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*=15; I^2=87%). Thirty-two (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 both LMICs and high-income countries, we found circumcision was associated with a 23% reduced odds of HIV infection among MSM overall, with this protective association being stronger in LMICs. 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 significantly associated with lower rates of HIV infection among MSM differs from two previous systematic reviews published in 2008 and 2011.[9,10] Compared to these reviews we included 22 additional studies,16 of which were from LMICs, a setting in which the association between circumcision and lower rates of HIV was particularly pronounced. Additionally, in cumulative meta-analysis the significant protective effect of circumcision only became apparent in 2011, after the publication of the last comprehensive systematic review on the subject.[10] The recent systematic review published in 2018 included all males and MSM was only a fraction of the analysis and that paper missed a significant amount of existing evidence,[11] which may potentially lead to a biased conclusion with limited stratified findings.

The protective effect of circumcision against HIV infection was significantly stronger among MSM in LMICs compared to MSM in high-income countries. Several reasons could explain this difference. Mathematical modelling studies suggest this enhanced protective effect may be due to the higher stability in anal sex role segregation, lower rates of circumcision, and higher HIV prevalence among MSM in LMICs.[92,93] MSMW represent a substantial proportion of MSM in LMICs and may be another explanatory factor. Behavioural studies in China, India, Peru, and sub-Saharan Africa have found that 40% to 70% of MSM have also had sex with women,[36,86,94,95] and nearly 30% are married to women.[36,95] Circumcision could be effective in reducing HIV acquisition among MSMW by reducing female-to-male HIV transmission.[4–6] Rates of insertive anal intercourse are also higher among MSMW,[94] the sex position for which circumcision offers direct benefit.[10] Additionally, fewer protective measures against HIV infection are available in LMICs compared to high-income countries.[2] Observational studies conducted in these contexts may be less impacted by other interventions that mask the effectiveness of circumcision to prevent infection. This interpretation is consistent with our sub-analyses which found the protective effect increased as the proportion of MSM receiving additional HIV protective measures (e.g. condom use, HIV testing) decreased.

Circumcision was found to be 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 may be due 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 may protect against HIV and other STIs. Circumcision decreases number of target cells for pathogens to infect, eliminates a microenvironment favoring pathogen survival and replication, and reduces the potential for micro-abrasions during sexual intercourse that allow for the entry of pathogens into the body.[100] The protective association between circumcision and other STIs may be less apparent than the association with HIV infection because other STIs are more effectively transmitted through sexual behaviors besides anal intercourse (e.g., syphilis transmission can occur via intimate skin to skin contact),[101] thereby reducing the protective effect of circumcision.

There are several limitations to this review. 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 may not be the result of confounding. Second, we found evidence of publication bias in our analysis. Disproportionate reporting of significant associations in the published literature may result in an overestimate of the protective effect of circumcision. Finally, only a small number of studies were included in several subgroup categories. Findings from these meta-analyses should be considered preliminary and warrant further investigation when more data becomes available.

Further research is needed to better characterize the effect of circumcision on HIV, HSV, and HPV transmission among MSM. Although RCTs of circumcision among MSM in LMICs could confirm this protective effect, evidence from this meta-analysis is not strong enough to support the development of an RCT. The protective effect of circumcision observed in LMICs may be explained by the prevention of female-to-male HIV transmission among MSMW rather than prevention of HIV transmission during anal sex. Because of the disparate anatomical and biological environment of vaginal and rectum, the effect of circumcision on HIV/STI transmission during vaginal intercourse and anal intercourse might be different. Additionally, recruiting eligible participants for an RCT would be difficult because of widespread stigma against MSM in LMICs. The willingness of being circumcised among MSM in LMICs is low. A study in 2009 in China found that only 17% of MSM were willing to be circumcised.[102] And a study conducted in Argentina found that 70% of uncircumcised MSM opted not to undergo circumcision after being informed of potential reduced risk of HIV infection.[24] Given 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 and MSMW so as 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 LMICs and design effective interventions to improve such willingness.

Our finding that circumcision is more likely to protect MSM in LMICs from HIV infection is promising given the high risk of HIV infection among MSM in these settings as a result of heavy stigma and restricted access to HIV prevention measures (e.g., PrEP).[2] MSM in LMICs could benefit from the advances in cheap, safe, and convenient circumcision surgical techniques (e.g., Shang Ring).[103] Because circumcision as an HIV prevention measure targets all men regardless of sexual orientation, MSM in LMICs seeking circumcision would 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 may 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 may protect against other STIs, including HSV and HPV. Consequently, MSM should not be excluded from campaigns promoting circumcision among men in LMICs, and mathematical modelling studies should be developed to evaluate the public health impact and cost-effectiveness of the large-scale circumcision programs for HIV prevention among MSM in individual LMICs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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Panel: Research in context

Evidence before this study

Two previous systematic reviews and meta-analyses published in 2008 and 2012 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. We conducted a comprehensive updated review of associations between circumcision and HIV and other STIs among MSM.

Added value of this study

Our review included 62 observational studies from both high-income countries and low- and middle-income countries (LMICs) and found that circumcision was associated with 23% reduced odds of HIV infection among MSM overall. This association was significantly stronger among MSM in LMICs compared to MSM in high-income countries. Circumcision was significantly associated with reduced odds of HSV infection among MSM overall and penile HPV infection among MSM living with HIV.

Implications of all the available evidence

Our analysis suggests circumcision may protect MSM from HIV, HSV, and penile HPV infection. Given the low quality of evidence and a substantial proportion of MSM in LMICs who also have sex with women, well-designed longitudinal studies differentiating MSM and men who have sex with men and women 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 LMICs.

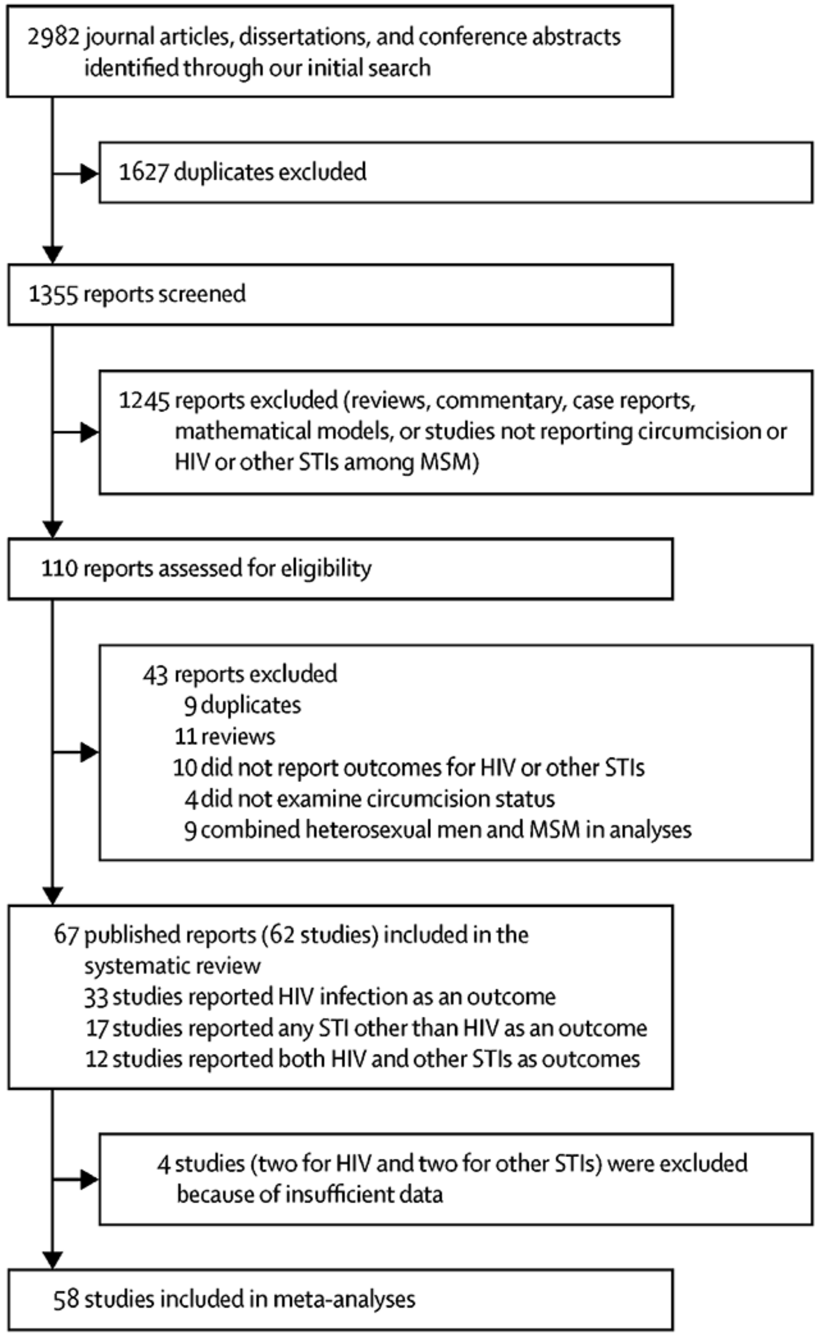

Figure 1.

Flow diagram of publication selection

Abbreviations: HIV, human immunodeficiency virus; STIs, sexually transmitted infections; MSM, men who have sex with men.

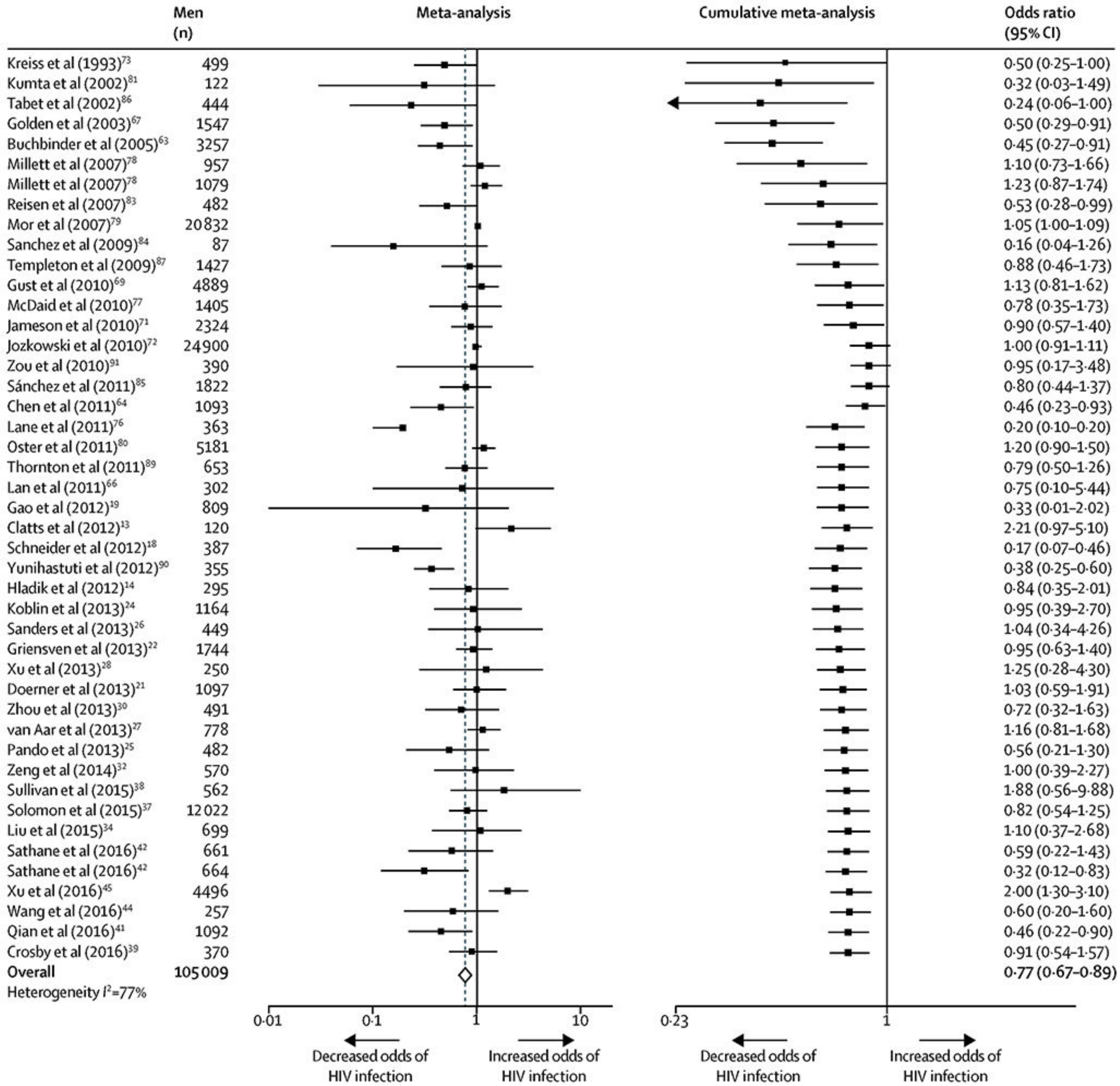

Figure 2.

Meta-analysis and cumulative meta-analysis of the association between circumcision and HIV infection among MSM

In 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 analyzed and reported separately.

Abbreviations: HIV, human immunodeficiency virus; MSM, men who have sex with men; CI, confidence interval.

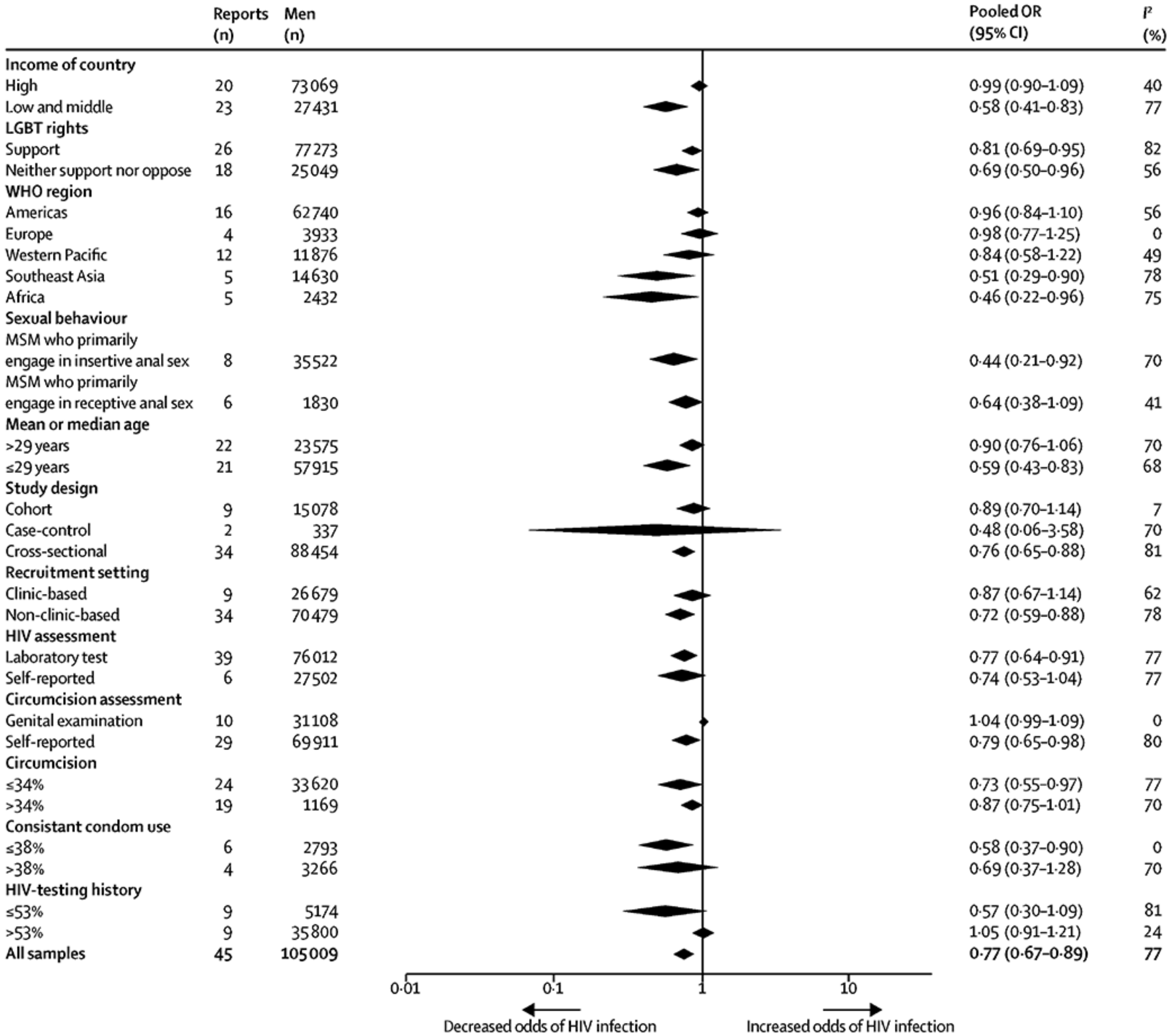

Figure 3.

Subgroup meta-analyses of the association between circumcision and HIV infection among MSM.

Cut-off points of continuous variables were medians.

Abbreviation: HIV, human immunodeficiency virus; CI, confidence interval; MSM; men who have sex with men; LGBT, lesbian, gay, bisexual, and transgender.

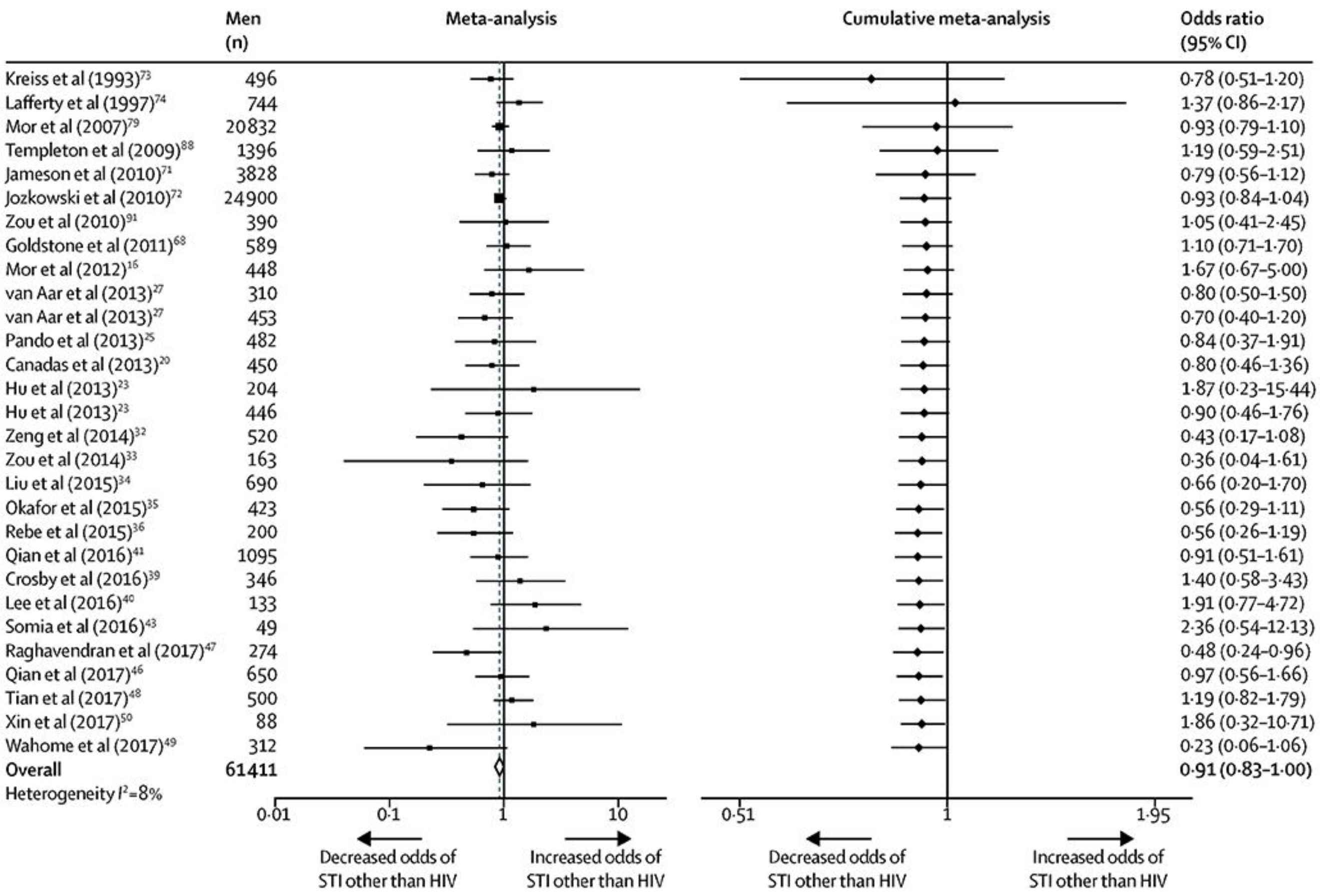

Figure 4.

Meta-analysis and cumulative meta-analysis of the association between circumcision and any STI other than HIV among MSM.

In 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 analyzed 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 OR of all STIs (excluding HIV) was calculated for that study population using the formula developed by Borenstein et al.[63]

Abbreviations: STI, sexually transmitted infection; HIV, human immunodeficiency virus; MSM, men who have sex with men; CI, confidence interval.

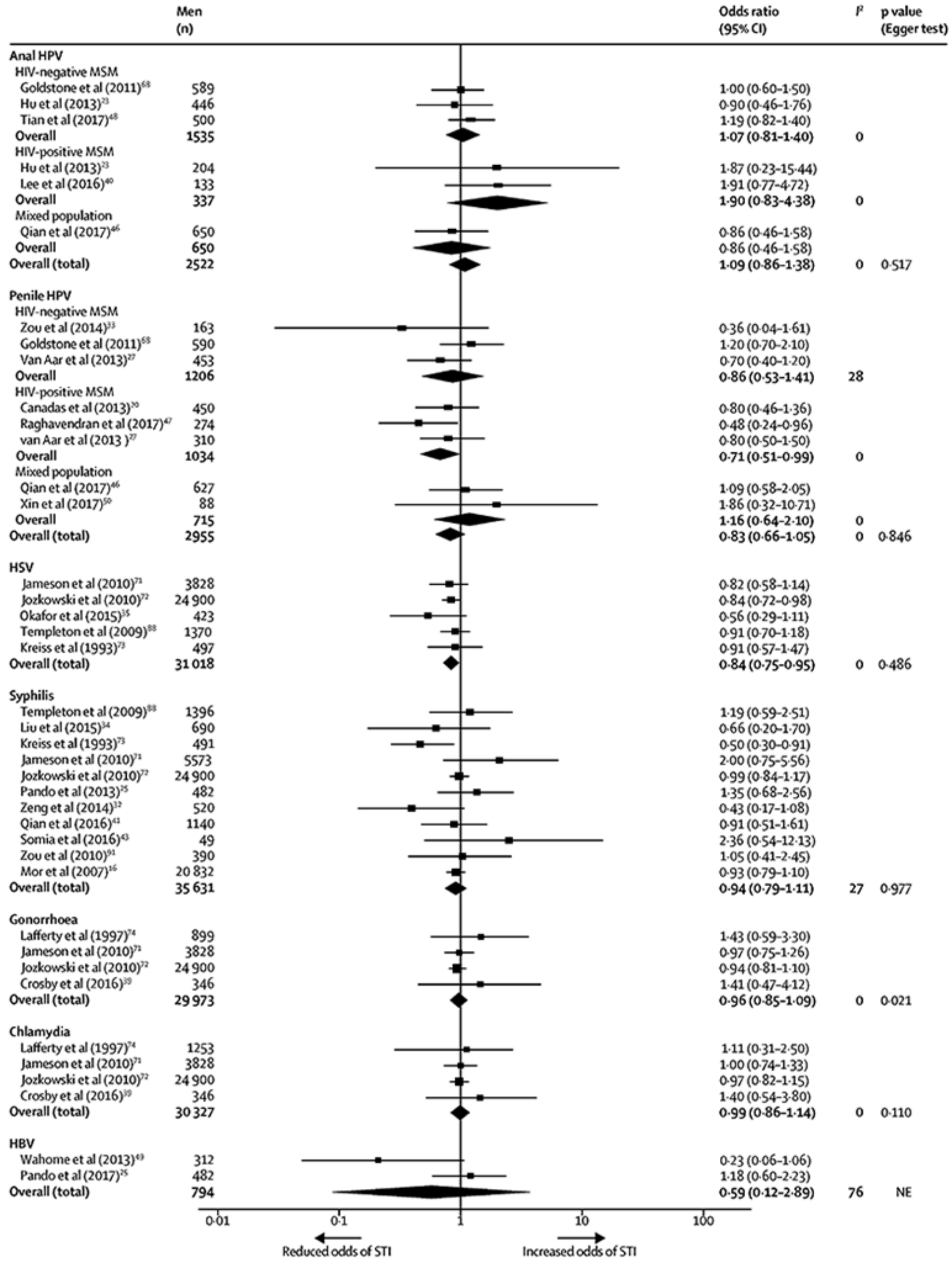

Figure 5.

Meta-analyses of the associations between circumcision and specific STIs among MSM. Associations between circumcision and anal HPV infection and penile HPV infection were calculated separately and stratified by HIV-status of participants.

Abbreviation: STI, sexually transmitted infection; MSM, men who have sex with men; CI, confidence interval; HIV, human immunodeficiency virus; HPV, human papillomavirus; HSV, herpes simplex virus, including both HSV-1 and HSV-2; HBV, hepatitis B virus.

Table 1.

Characteristics of included studies [*]

Characteristics	Number of studies
Publication type	
Journal article	58
Conference abstract	7
Doctoral/Master's thesis	2
Study design	
Cohort [†]	15
Case-control [‡]	2
Cross-sectional [§]	45
WHO region [¶]	
Americas	18
Western Pacific	19
South-East 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	21
Recruitment setting [//]	
Non-clinic-based	40
Clinic-based	16

WHO=world health organization. LGBT= lesbian, gay, bisexual, and transgender.

[*] We identified 62 studies from 67 publications; one study split results into three parts and reported each part in different journals,[16,87,88] and another three studies[36,76,82] reported additional data in conference abstracts.[30,75,81]

[†] Four retrospective cohort studies[14,48,69,85] and 11 prospective cohort study.

[‡] one study[84] was nest case-control in design.

[§] Two studies[26,88] were cross-sectional analyses of cohort study.

¶Studies were grouped according to study country. Numbers do not sum to a total of 62 because three studies[14,69,85] were multi-national cohort studies and one study[67] did not report the country in which it was conducted.

‖Numbers do not sum to a total of 62 because six studies[17,19,48,68–70] did not provide information on recruitment setting.