Title

Sustained Reduction in Sexual Behavior that May Pose a Risk of HIV Transmission Following Diagnosis During Early HIV Infection Among Gay Men in Vancouver, British Columbia

Journal

AIDS and Behavior, 22(7)

ISSN

1090-7165

Authors

Gilbert, Mark

Taylor, Darlene

Michelow, Warren

et al.

Publication Date

2018-07-01

DOI

10.1007/s10461-017-1702-0

Peer reviewed

HHS Public Access

Author manuscript

AIDS Behav. Author manuscript; available in PMC 2022 June 28.

Published in final edited form as:

AIDS Behav. 2021 June ; 25(6): 1839–1855. doi:10.1007/s10461-020-03113-8.

Change in Condom Use in Populations Newly Aware of HIV Diagnosis in the United States and Canada: A Systematic Review and Meta-Analysis

Mohsen Malekinejad[1,2,3],

Janet Blodgett[1,3],

Hacsi Horvath[1,2,3],

Andrea Parriott[1,3],

Angela B. Hutchinson[4],

Ram K. Shrestha[4],

Devon McCabe[1,3],

Paul Volberding[1,2,5],

James G. Kahn[1,2,3]

[1]Philip R. Lee Institute for Health Policy Studies, University of California, San Francisco, 3333 California Street, Suite 285, San Francisco, CA 94118, USA

[2]Global Health Sciences, University of California, San Francisco, San Francisco, CA, USA

[3]Consortium To Assess Prevention Economics, University of California, San Francisco, San Francisco, CA, USA

[4]Centers for Disease Control and Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Division of HIV/AIDS Prevention, Atlanta, GA, USA

[5]AIDS Research Institute, University of California, San Francisco, San Francisco, CA, USA

Abstract

HIV-infected individuals “aware” of their infection are more likely to use condoms, compared to HIV-infected “unaware” persons. To quantify this likelihood, we undertook a systematic review and meta-analysis of U.S. and Canadian studies. Twenty-one eligible studies included men who have sex with men (MSM; k = 15), persons who inject drugs (PWID; k = 2), and mixed populations of high-risk heterosexuals (HRH; k = 4). Risk ratios (RR) of “not always using condoms” with partners of any serostatus were lower among aware MSM (RR 0.44 [not significant]), PWID (RR 0.70) and HRH (RR 0.27); and, in aware MSM, with partners of

Mohsen Malekinejad, mmalekinejad@ucsf.edu.

Conflict of interest The authors declare that they have no conflicts of interest.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10461-020-03113-8) contains supplementary material, which is available to authorized users.

Research Involving Human Participants and/or Animals This review is a secondary analysis of published data and as such, did not involve human participants or animals.

Informed Consent This review is a secondary analysis of published data and as such, did not require informed consent.

HIV-uninfected or unknown status (RR 0.46). Aware individuals had lower “condomless sex likelihood” with HIV-uninfected or unknown status partners (MSM: RR 0.58; male PWID: RR 0.44; female PWID: RR 0.65; HRH: RR 0.35) and with partners of any serostatus (MSM only, RR 0.72). The association diminished over time. High risk of bias compromised evidence quality.

Keywords

HIV; Diagnosis; Risk behaviors; United states; Systematic review

Introduction

In both the United States (U.S.) and Canada, more than 14% of people living with HIV do not know they have the virus [1, 2]. Undiagnosed HIV infection is an important driver of the HIV epidemic in the U.S., Canada, and other countries [3]. Although annual incident cases of HIV infection in the U.S. have declined significantly in recent years—by 7% in the U.S. between 2014 (40,187 cases) and 2018 (37,515 cases)—new infections in Canada are estimated to have increased slightly, from 1,960 in 2014 to 2,160 in 2016 [2]. Nearly all people in the U.S. and Canada who become infected with HIV acquire it through having sex without correctly and consistently using condoms or through sharing drug injection equipment [2, 3].

In the U.S., Canada, and many other countries, a major strategy for reducing HIV transmission at the population level is to use HIV testing and counseling to identify previously undiagnosed HIV-infected people earlier, link or re-engage them to HIV care and treatment, initiate antiretroviral therapy (ART) as soon as possible, and retain them on ART [4]. Patients who are adherent to ART and whose HIV viral load is suppressed have improved health outcomes and pose effectively no risk of HIV transmission to HIV-uninfected partners [4-6]. Another important benefit of early HIV diagnosis is that persons who become aware of their HIV status may adopt less risky sexual and drug use behavior and thus break the chain of transmission.

Despite ART’s significant impact on HIV transmission risk, reduction in risky behaviors still plays a very important role for HIV-infected individuals. First, even if all HIV-infected people in the U.S. were linked to care and started on ART, achieving viral suppression takes several weeks to months [7], and during this period they are still infectious. Secondly, of all patients diagnosed with HIV in the U.S., nearly half do not have sustained viral suppression [8], with even higher proportions in certain transmission groups [9]. This is mainly due to obstacles in maintaining the high level of ART adherence necessary to maintain viral load suppression [10].

Rationale for Systematic Review

We conducted this review to generate updated quantitative effect estimates of knowledge of HIV status on condom use behavior among various populations at high risk of HIV in the U.S. and Canada. Health researchers and policy makers often rely on mathematical models to estimate the potential population health impact of public health interventions. In

this context, with the goal of informing HIV prevention efforts, serostatus awareness and its effects on condom use may be considered an important variable in such models, along with starting ART and achieving viral suppression. Thus, it is crucial to quantify in a nuanced way this risk behavior change in populations testing positive for HIV infection.

Although previous systematic reviews have quantified this behavior change [11, 12], there is a need to update these data using rigorous methodologies, as well as to assess effect sizes in different transmission groups, such as men who have sex with men (MSM), persons who inject drugs (PWID),and others. It is also necessary to assess the durability of the effect.

Methods

We followed Cochrane methods in our review process [13]. We developed our a priori review protocol and followed this protocol after its approval by our funder, the U.S. Centers for Disease Control and Prevention (CDC) (Online Appendix A). We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [14] guidelines for reporting our review. We used Grading of Recommendations Assessment, Development and Evaluation Guideline (GRADE) methods to assess evidence quality by outcome across the literature [15].

Study Eligibility

We included studies conducted in the U.S. or Canada (two adjacent North American countries with similar HIV epidemic patterns) that compared condom use behaviors of adults and adolescents who were aware of their HIV infection, with similar populations who were unaware of their HIV infection. Eligible studies could address general populations (i.e., participants who were not identified as members of sub-populations) and/or specific sub-populations at high risk of HIV transmission, such as MSM, men who have sex with men and women (MSMW), PWID, and heterosexuals deemed to be at elevated risk (details in Online Appendix A).

We included any study design with internal comparators. In other words, eligible studies had between-group behavioral comparisons (i.e., HIV-infected and aware of infection versus HIV-infected and unaware of infection [cross-sectional]) or within-group behavioral comparisons (i.e., behavior in a period before receiving an HIV diagnosis versus after receiving an HIV diagnosis [pre-post]).

We excluded studies with data collection completed before 1996 (the year in which triple-ART regimens became widely available in the U.S.). We had no restriction by publication or peer-review status (e.g., conference abstracts and other unpublished data were eligible) as long as sufficient quantitative data were provided to assess condom use behavior after HIV diagnosis. For non-peer-reviewed sources, we sought supplementary information from authors as deemed necessary. We excluded studies that examined the effects of multifaceted behavioral interventions unless it was possible to isolate the effect of knowing one’s HIV status.

We included studies that contained data on any condom use behaviors. As we anticipated, studies measured and reported condom use behavior outcomes in several ways. We created and used two standardized outcomes: (a)“condomless sex likelihood,” and (b) “not always using condoms” (Table 1).

Searches and Screening

We developed a comprehensive search strategy with relevant keywords and indexing terms (Online Appendix B) and searched PubMed, Scopus, PsycINFO, and the Cochrane Central Register of Controlled Trials. The search period was from January 1, 1996 to the search date (October 20, 2015; and updated through May 2018). We also searched available abstracts within the search period from the National HIV Prevention Conference, the International AIDS Society Conference on HIV Pathogenesis, Treatment & Prevention, and the International AIDS Conference. We examined the bibliographies of our included studies, the previous systematic reviews and other highly relevant articles. We later also examined studies that cited any of these papers. We included peer-reviewed papers, CDC Morbidity and Mortality Weekly Reports, and conference abstracts that were incidentally identified by co-authors.

We used EndNote software version X7 [16] to remove duplicate records. One reviewer excluded clearly irrelevant records, reviewing only titles. Two reviewers then independently examined the titles, abstracts and keywords of all records, excluding those not meeting eligibility criteria (< 5% disagreement). The remaining records were either eligible, or their eligibility could not be determined without full-text review. Two reviewers then independently applied our eligibility criteria to determine which studies were eligible for inclusion, and a third reviewer stood ready to serve as a neutral arbiter in case of disagreement that could not be resolved through discussion.

Data Extraction and Standardization

We developed and used a data collection sheet which captured the following data: complete citation; geographical setting; details of interventions and comparators; age, sex and other participant data; outcome definitions and descriptions; details of outcome assessment methods; study inclusion and exclusion criteria; length of follow-up for study outcomes; data necessary for assessing risk of bias. Two reviewers working independently extracted data and entered them into the data sheet. Reviewers cross-checked each other’s extracted data, corrected errors, and reconciled any disagreements as they arose. They also contacted study authors to obtain key data missing from reports.

Risk of Bias Assessment

We used the Cochrane instrument for assessing the risk of bias [13] in each study. Using this tool, we determined whether a study was at high, low, or unclear risk of bias in regard to randomization, allocation concealment, blinding of participants and study personnel, blinding of outcome assessors, missing data, selective outcome reporting, and other types of bias. For non-randomized studies, we additionally applied four criteria recommended by the GRADE Working Group [15]: failure of study investigators to develop and apply appropriate eligibility criteria; flawed measurement of exposure and outcome; failure to adequately

control confounding; and incomplete or inadequately short follow-up time. We used these assessments in our GRADE judgments about the quality of evidence for each outcome.

Data Analysis and Synthesis

For all included outcomes, we calculated risk ratios (RR) and their associated 95% confidence intervals (CI). We used the Zhang and Yu [17] method to calculate RR when studies reported odds ratios (OR) for non-rare outcomes. When studies did not report 95% CIs, we calculated 95% CIs from P-values or from the number engaging in and not engaging in the outcome behavior in each group. We excluded outcomes when there were insufficient data to estimate CIs and assumptions could not be made about sample sizes.

In preparation for conducting meta-analyses, we grouped effect size estimates (i.e., RR) according to the characteristics of three domains: (1) risk subgroup, (2) outcome, and (3) type of partner (see Table 1 for details).

We performed meta-analysis when we identified two or more conceptually combinable effect-size estimates. We used a random-effects meta-analytic model to calculate pooled RR and 95% CI, weighting by inverse of variance. We used a fixed-effect model to calculate an overall estimate within a study based on sub-group data [18]. For these analyses, we used Cochrane's Review Manager 5 software [19]. We assessed statistical heterogeneity using the I^2 statistic, which is reported as a percentage and reflects observed variation among pooled data that is due to heterogeneity rather than chance [13]. When more than two effect-size estimates were included in given pooled data, we conducted sensitivity analyses to assess the effect of each effect-size estimate on the overall estimate, by removing studies one at a time and recalculating the pooled estimate using the remaining effect-size estimates. We considered the new pooled estimate (after removing a study) to be "substantially" different from the overall estimate if the new pooled point estimate changed > 0.05 in either direction. We also explored funnel plot asymmetry by plotting the effect size (RR) of studies (x-axis) against log of the standard error of RR (y-axis) for meta-analyzed pooled estimates with ≥ 10 effect-size estimates.

Quality of Evidence

We used the GRADE approach to assess the quality of evidence for each outcome across studies [15]. In brief, the GRADE methodology defines "quality of evidence" as "the extent of our confidence that the estimate of effect is correct" [13]. The quality of evidence is rated in four levels: high, moderate, low or very low. Randomized controlled trials (RCTs) initially are considered to provide high-quality evidence, which can be downgraded in the event of the following: high risk of bias, indirectness of evidence, unexplained heterogeneity or inconsistency of results, imprecision of results, and high probability of publication bias. In contrast, non-RCTs initially provide low-quality evidence that, in the absence of other downgrading, can be graded up if there is a large magnitude of effect, confidence in an estimated effect despite plausible confounding, or a dose–response gradient. They can also be graded down for the same reasons as for RCTs, thus providing very low-quality evidence.

Results and Discussion

Study Screening Results

Two reviewers working independently screened a total of 6882 unique articles and excluded 6746 based on the titles and abstracts (Fig. 1). They assessed the full texts of the remaining 136 articles and excluded 115 because they did not meet our inclusion criteria (citations in Online Appendix C, with reasons for exclusion). We included 21 studies in the review [20-40]. Two conference abstracts [33, 38] were among the eligible records. We obtained additional data from the authors of one abstract [38]. For five studies [20, 22, 27, 34, 35], our team extracted data directly from a previously published systematic review [12], because we were unable to obtain the published papers for these studies and received no response when contacting study investigators.

Characteristics of Included Studies

Tables 2, 3 and 4 present a summary of key information about the included studies, such as setting, design, eligibility, sample size, and outcome assessed by risk group. Nine-teen studies were conducted in the U.S. and two in Canada. Although MSM studies comprised the majority (k = 15) of studies, we also found two studies of PWID and four of high-risk heterosexuals or mixed high-risk males and females. We did not identify studies for the general (non-high risk) population. Study designs included cross-sectional (k = 11) and pre-post (k = 10), including one pre-post study nested in a cross-sectional study [21]. Except for five studies that started data collection before 1996 and continued after 1996 [27, 34, 35, 37, 38], others collected data exclusively after 1996, with the most recent data collection being completed in 2014.

Only four studies reported the proportion of participants on ART and only two of these stratified results by ART status. Only one study reported the proportion of participants who were virally suppressed (i.e., reduced viral load to an undetectable level). For all cross-sectional studies and the one pre-post study, we were unable to ascertain the specific length of time between HIV diagnosis and follow-up when condom use behavior was assessed. In those that reported, it ranged from a median of one month to a median of 65.8 months.

Risk of Bias in Included Studies

Four study designs with various types of bias risk are graphically illustrated in Fig. 2. These study designs include: pre-post (within-group comparison) with participants recruited for HIV testing (k = 5) [27, 32, 34, 35, 38]; pre-post (within-group comparison) with participants self-selected for HIV testing (k = 4) [29, 33, 36, 40]; pre-post nested in a cross-sectional study (within-group comparison), with participants self-selected for HIV testing (k = 1) [21]; and cross-sectional double-arm, with participants self-selected for HIV testing (k = 11) [20, 22-24, 26, 28, 30, 31, 37, 39]. While data from all included studies were at high risk of bias due to the inherent limitations of observational studies, studies that recruited participants and were able to assess condom use behaviors before HIV testing avoided additional sources of biases (e.g., selection bias, recall bias) that were present in other study designs.

Change in "Not Always Using Condoms"

Most studies (k = 17) reported one or more condom use behavior outcomes (e.g., never used condoms, having unprotected vaginal or anal sex) that, together, could be transformed to "not always using condoms" (Table 5). In MSM, compared to HIV-infected unaware persons or before their own diagnoses, HIV-infected aware persons were marginally less likely to report "not always using condoms" with partners of any serostatus (k = 7, RR 0.59, 95% CI 0.34–1.04) and partners of HIV-uninfected or unknown serostatus (k = 6, RR 0.46, 95% CI 0.30–0.70). The effect of awareness on "not always using condoms" was also statistically significant in the overall analysis of this outcome that combined data across all studies, prioritizing partners of HIV-uninfected or unknown serostatus if data for both partner types was reported within the same study (k = 11, RR 0.44, 95% CI 0.33–0.59).

In male and female PWID, there was reduction in the risk of "not always using condoms" with partners of any serostatus (k = 1, RR 0.70, 95% CI 0.59–0.83 and k = 2, RR 0.52, 95% CI 0.38–0.70, respectively).

Reduction in this risk behavior with partners of any serostatus was relatively large in high-risk heterosexual men who have sex with women (MSW) (k = 1, RR 0.27, 95% CI 0.10–0.73), high-risk heterosexual women who have sex with men (WSM) (k = 2, RR 0.27, 95% CI 0.12–0.61), and populations comprising mixed high-risk males (k = 1, RR 0.37, 95% CI 0.33–0.41) and females (k = 1, RR 0.41, 95% CI 0.36–0.47).

"Not Always Using Condoms": Effect Size Change Over Time

Six of 17 MSM studies that reported the "not always using condoms" outcome after HIV diagnosis also measured the durability of the effect. Although this risk was significantly reduced (k = 3, RR 0.18, 95% CI 0.10–0.33) during the first six months (pooled shortest follow-up time), the risk reduction was attenuated and was also no longer statistically significant after 12 months (pooled longest follow-up time) after HIV diagnosis (k = 6, RR 0.75, 95% CI 0.54–1.03). We could not assess length of follow-up for any other group or outcome due to lack of data.

Change in "Condomless Sex Likelihood"

Only five studies reported on "condomless sex likelihood," defined as self-report of unprotected sex at last episode (k = 4) or based on the proportion of a set of episodes that were unprotected (k = 1) (Table 6). Compared to HIV-infected unaware MSM, HIV-infected aware MSM were less likely to have "condomless sex likelihood" with partners of any serostatus (k = 2 studies, RR 0.72, 95% CI 0.57–0.92) and with partners of HIV-uninfected or unknown status (k = 3, RR 0.54, 95% CI 0.46–0.65). A single study reporting on PWID reported that, compared to HIV-infected unaware persons, HIV-infected aware persons were less likely to have "condomless sex likelihood" with partners of HIV-uninfected or unknown HIV serostatus: male PWID (RR 0.44, 95% CI 0.33–0.58) and female PWID (RR 0.65, 95% CI 0.47–0.90). Similarly, a single study reporting on participants from mixed HIV risk profiles showed that compared to HIV-infected unaware persons, HIV-infected aware persons were less likely to have "condomless sex likelihood" with partners of HIV-uninfected or unknown serostatus: male participants (RR 0.41, 95% CI 0.35–0.48) and

female participants (RR 0.44, 95% CI 0.37–0.52). Finally, a single study that combined data for high-risk heterosexual male and female participants also reported lower risk of this outcome (k = 1, RR 0.35, 95% CI 0.24–0.51) [25].

Both Condom Use Outcomes Across Different Transmission Groups by Partner Type

Overall, across both condom use outcomes, all transmission groups, and all partner types, risky behaviors were lower among those aware of their HIV infection, although for certain subgroups there was a wide range of uncertainty around the point estimates (difference between lower and upper limits of CI ≥ 0.40), e.g. for not always using condom with any serostatus partner (WSM, MSW, MSM) and "condomless sex likelihood" with HIV-uninfected partner or partner of unknown serostatus (female PWID). Figure 3 illustrates the distribution of effect sizes for "not always using condoms" with partners of any serostatus (Fig. 3a) and "condomless sex likelihood" with HIV-uninfected partners or those of unknown serostatus (Fig. 3b), by risk-groups.

Quality of Evidence

The overall quality of evidence was low or very low for all included outcomes. This suggests that for each outcome, the true effect might be markedly different from the estimated effect. The GRADE summary tables are provided as supplementary material (Online Appendix D).

Sensitivity Analysis

Our sensitivity analysis on study inclusion (Online Appendix E), applicable only to MSM data analyses, found that pooled estimates were stable for some pooled data, but not for all. In "not always using condoms" outcome analyses, exclusion of certain studies substantially (> 0.05) changed pooled point estimates of the RRs. For partners of any serostatus, removing data from the CDC 2000 study [21] increased the estimate by 0.14, i.e., from RR 0.59 to RR 0.73. Also, the point estimate increased by 0.09 after removing Gilbert et al. 2018 [40] and decreased by 0.1 and 0.09 after removing Darrow et al. 1998 [28] and McFarland et al. 2011 [31], respectively. In studies that provided data for the longest follow-up time after 12 months, point estimates increased by 0.08 after removing Moskowitz 2008 [33] and 0.07 after removing Colfax et al. 2002; [27] and decreased by 0.09 after removing Khosropour et al. 2016 [29] and 0.05 after removing Darrow et al. 1998 [28].

Assessment of Publication Bias

We assessed funnel plot asymmetry for the overall "not always using condoms" outcome for MSM since it was the only meta-analyzed pooled estimate with ≥ 10 risk ratios in our model (Online Appendix F). The funnel plot shows an asymmetrical distribution of RR by the log of the standard error of RR, with most effect sizes clustered around the top of the pooled RR line and with only one small study at the bottom right of the plot. This suggests that our search strategies identified fewer studies with small sample sizes that reported unfavorable effect (i.e., increased risk of not always using condoms) than such studies with favorable effects.

Interpretation of Findings

Our systematic review identified 21 relevant studies of various study designs. We summarized the current evidence in respect to the effect of HIV diagnosis knowledge on condom use, among multiple groups at high risk of HIV transmission. Our review suggests that awareness of one's HIV diagnosis can in fact increase condom use. Although evidence quality for all outcomes was low or very low, the strength of the effect sizes and the consistency of results across transmission groups suggests that there likely is a strong effect. Compared to HIV-infected unaware people, HIV-infected aware people's risk of "not always using condoms" with partners of any serostatus, and their risk of "condomless sex likelihood" with HIV-uninfected or unknown status partners, were lower. For the outcome of "not always using condoms," RRs ranged by population from 0.27 to 0.70 and were not statistically significant in MSM. For the outcome of "condomless sex likelihood," RRs ranged by populations from 0.35 to 0.65.

Within MSM populations, the RR point estimates were smaller for partners of HIV-uninfected or of unknown serostatus than partner of any serostatus, for both outcome types. However, this observation does not take into account the overlapping CIs around the RR point estimates, which means these estimates may or may not be statistically significantly different. Further, with the exception of MSM, for all transmission groups the observed pattern is merely based on data from one or two studies. We also found that duration of follow-up mitigates the effect size with non-significant results with 12 months or greater follow-up, though this finding is limited, as we discuss below.

Overall, while evidence suggests knowledge of HIV diagnosis may help to substantially increase condom use, the magnitude of effect is uncertain. This is because evidence quality for all outcomes was low or very low. Due to the inherent limitations of observational studies, all studies were at high risk of bias. In most cases, outcomes were graded further down to very low-quality due to a high degree of statistical heterogeneity, as well as serious inconsistency (i.e., conflicting study results) in a few cases. This uncertainty in particular is prominent in regard to the effect size over time after the diagnosis. Only two of six studies that reported follow-up time of 12 months or longer for the outcome of not always using condoms [27, 33] showed statistically significant reduction in risk of this outcome at 12 months. While it is difficult to translate the increased condom use into changes in HIV incidence, it is encouraging that some of the strongest effects (in MSM, where we could assess timing) were observed soon after participants learned their HIV status, before initiating ART, thus suppressing viral load and reducing transmission risk.

This Review Versus Marks 2005 (A Similar Review with Pooled Data)

Our findings generally support the results of 11 studies in the review by Marks et al. [12], which reported a pooled estimate of 68% (95% CI 59–76%) reduction in prevalence of unprotected anal and vaginal sex in HIV-infected aware persons relative to HIV-infected unaware persons. As in the review by Marks et al. [12] we also found improved condom use behavior after HIV diagnosis. However, methodological and other differences limit parallel comparisons of our findings with those of Marks et al. [12].

In addition to capturing new studies published since Marks 2005 [12], our review offers more detailed analyses and incorporates several advances in systematic review/meta-analysis methodology and quality assessment, as follows. First, we identified and analyzed data by HIV transmission categories (e.g., MSM, PWID). Due to a high degree of heterogeneity; Marks 2005 had combined data across those categories. Second, we stratified data by sexual partner type instead of adjusting them based on the proportion of persons who might be at risk of HIV, as Marks 2005 had done. Third, we distinguished between two types of condom use outcomes that Marks 2005 did not do: "not always using condoms" and our defined "condomless sex likelihood." While the "not always using condoms" outcome is more frequently reported by studies and is a crude assessment of condom use behavior, our defined "condomless sex likelihood" outcome usually reflected specific episodes of sex, almost always the last episode. Fourth, our analysis also provided an assessment of length of time post-HIV diagnosis on condom use behaviors that was not reported by Marks 2005. Fifth, we thoroughly assessed and reported the risk of bias of primary studies as well as quality of evidence for each outcome using the GRADE system [15], thus providing a more standard description of the uncertainties around reported effect sizes.

Limitations and Cautionary Considerations

Since it is not ethical to randomize people to receive HIV test results versus not receiving them, studies that measure the effect of HIV infection knowledge are necessarily non-RCTs and are thus subject to inherently high risk of bias. Several studies also relied on historical data or memories of patients about their risk behavior before they were diagnosed with HIV infection. Thus, even if in our view this review provides the best available evidence, with low- and very low-quality evidence, the true effects of HIV diagnosis knowledge may be different from those we have calculated.

There was also substantial statistical heterogeneity ($I^2 > 60\%$) in several of the pooled analyses due to variations in study designs, settings, timing of outcomes measured since diagnosis, being on ART, and other unmeasured factors. We used random-effects models to account for these sources of heterogeneity, yielding wider 95% CIs. To optimally inform mathematical modeling and policy decisions, the uncertainty around point estimates should be given careful consideration. By combining across transmission groups, we would assume that study context (e.g., ongoing background activities such as HIV prevention and linkage to care interventions) is similar across these transmission groups. Further, by pooling across transmission groups, we would have artificially increased our sample size and increased the risk of type II error (i.e., detecting an effect when in fact there is no effect).

We observed funnel plot asymmetry for the one meta-analyzed pooled risk ratio ("not always using condoms" among MSM) that included more than 10 effect-size estimates. Although this asymmetry could be due to publication bias, it could also be due to significant heterogeneity of studies, or due to chance. In our efforts to minimize the risk of publication bias, we conducted a comprehensive search for scientific evidence including the grey literature pertaining to the U.S. and Canada on the effect of HIV diagnosis knowledge on condom use behavior. Further, we extracted data from all study designs in which the effect of HIV knowledge on condom use could be calculated.

Given the studies that we identified, our findings are mainly applicable to certain transmission groups in the U.S. Given the paucity of data, we were unable to assess the effect of being aware of one's HIV diagnosis in the presence and absence of receiving ART. Those who are diagnosed with HIV and receive treatment may differentially respond to HIV diagnosis knowledge compared to those without treatment. Further, it is also plausible that transmission groups with partners who have access to pre-exposure prophylaxis (PrEP) may respond differently to knowledge of HIV diagnosis. Nearly all studies, however, were conducted before PrEP became widely available.

Finally, men and women who are aware of their HIV status may adopt safer sexual practices other than condom use, such as serosorting, reduced number of partners, encouraging PrEP use in partners, and/or differential sexual positioning. We intend to assess the effect of HIV knowledge on a wider range of outcomes in future work.

Conclusion

Knowledge of HIV diagnosis substantially improves condom use risk behaviors among MSM, PWID, and high-risk heterosexual men and women, although this effect likely diminishes over time. While findings are generally consistent across populations and with partners of different serostatus, there are uncertainties around the magnitude of this effect due to statistical uncertainty as well as the generally very low-quality of evidence. Rigorous studies assessing HIV knowledge in the presence versus absence of ART, as well as the duration of effect, would be very useful to inform future policy and practice.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We would like to extend our special gratitude to Dr. Stephanie Sansom and Dr. Gary Marks at the Division of HIV/AIDS Prevention, CDC. We also would like to thank Amanda Viitanen for her assistance with data collection for a few studies, Erin Barker for providing support with updating citations, and authors of included studies who provided additional data not reported in their manuscripts.

Funding

Funding was provided by National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (Grant no. 5U38PS004649).

References

1. Centers for Disease Control and Prevention (CDC). Estimated HIV incidence and prevalence in the United States, 2010–2016. Atlanta, GA; 2019.
2. Challacombe L. The epidemiology of HIV in Canada. Canadian AIDS treatment information exchange (CATIE); 2018. https://www.catie.ca/fact-sheets/epidemiology/epidemiology-hiv-canada. Accessed 11 Nov 2020.
3. Centers for Disease Control and Prevention (CDC). HIV in the United States: at a glance. https://www.cdc.gov/hiv/statistics/overview/ataglance.html. Accessed 29 Jan 2018.
4. Centers for Disease Control and Prevention (CDC). Evidence of HIV treatment and viral suppression in preventing the sexual transmission of

HIV. August 2018. https://npin.cdc.gov/publication/evidence-hiv-treatment-and-viral-suppression-preventing-sexual-transmission-hiv. Accessed 11 Nov 2020

5. Anglemyer A, Rutherford GW, Horvath T, Baggaley RC, Egger M, Siegfried N. Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples. Cochrane Database Syst Rev. 2013. 10.1002/14651858.CD009153.
6. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Antiretroviral therapy for the prevention of HIV-1 transmission. N Engl J Med. 2016;375(9):830–9. [PubMed: 27424812]
7. Hall HI, Tang T, Westfall AO, Mugavero MJ. HIV care visits and time to viral suppression, 19 U.S. jurisdictions, and implications for treatment, prevention and the national HIV/AIDS strategy. PLoS ONE. 2013;8(12):e84318. [PubMed: 24391937]
8. Centers for Disease Control and Prevention (CDC). Understanding the HIV Care continuum. https://www.cdc.gov/hiv/pdf/library/factsheets/cdc-hiv-care-continuum.pdf. Accessed 4 Dec 2017.
9. Yehia BR, Fleishman JA, Metlay JP, Moore RD, Gebo KA. Sustained viral suppression in HIV-infected patients receiving antiretroviral therapy. JAMA. 2012;308(4):339–42. [PubMed: 22820781]
10. Benator DA, Elmi A, Rodriguez MD, Gale HB, Kan VL, Hoffman HJ, et al. True durability: HIV virologic suppression in an urban clinic and implications for timing of intensive adherence efforts and viral load monitoring. AIDS Behav. 2015;19(4):594–600. [PubMed: 25369887]
11. Crepaz N, Hart TA, Marks G. Highly active antiretroviral therapy and sexual risk behavior: a meta-analytic review. JAMA. 2004;292(2):224–36. [PubMed: 15249572]
12. Marks G, Crepaz N, Senterfitt JW, Janssen RS. Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: implications for HIV prevention programs. J Acquir Immune Defic Syndr. 2005;39(4):446–53. [PubMed: 16010168]
13. Higgins J, Green S, editors. Cochrane handbook for systematic reviews of interventions, Version 5.1.0. Available from: Handbook.cochrane.org. Accessed 11 Nov 2020: The Cochrane Collaboration; 2011.
14. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009;339:b2535. [PubMed: 19622551]
15. Schünemann H, BJ, Guyatt G, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. http://www.guidelinedevelopment.org/handbook/. Accessed 21 Jan 2018
16. EndNote version X7. Computer program Thomson; 2013.
17. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA. 1998;280(19):1690–1. [PubMed: 9832001]
18. Borenstein MHL, Higgins J, Rothstein H. Chapter 23: Independent subgroups within a study Introduction to Meta-Analysis. Chichester: Wiley; 2009. p. 217–23.
19. Review Manager (RevMan) version 5.3. Computer program. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration; 2014.
20. Buehler JW, Diaz T, Hersh BS, Chu SY. The supplement to HIV-AIDS Surveillance project: an approach for monitoring HIV risk behaviors. Public Health Rep. 1996;111(Suppl 1):133–7.
21. Centers for Disease Control and Prevention (CDC). Adoption of protective behaviors among persons with recent HIV infection and diagnosis—Alabama, New Jersey, and Tennessee, 1997–1998. MMWR Morb Mortal Wkly Rep. 2000;49(23):512–5. [PubMed: 10882290]
22. Centers for Disease Control and Prevention (CDC). Late versus early testing of HIV—16 Sites, United States, 2000–2003. MMWR Morb Mortal Wkly Rep. 2003;52(25):581–6. [PubMed: 12836626]
23. Centers for Disease Control and Prevention (CDC). HIV testing and risk behaviors among gay, bisexual, and other men who have sex with men—United States. MMWR Morb Mortal Wkly Rep. 2013;62(47):958–62. [PubMed: 24280915]
24. Centers for Disease Control and Prevention (CDC). HIV infection, risk, prevention, and testing behaviors among persons who inject drugs—National HIV behavioral surveillance: injection drug use, 20 U.S. cities, 2012. CDC; 2015.

25. Centers for Disease Control and Prevention (CDC). HIV infection, risk, prevention, and testing behaviors among heterosexuals at increased risk of HIV infection—National HIV behavioral surveillance, 20 U.S. cities, 2013. CDC; 2015.
26. Centers for Disease Control and Prevention (CDC). HIV infection risk, prevention, and testing behaviors among men who have sex with men—National HIV behavioral surveillance, 20 U.S. cities, 2014. CDC; 2016.
27. Colfax GN, Buchbinder SP, Cornelisse PG, Vittinghoff E, Mayer K, Celum C. Sexual risk behaviors and implications for secondary HIV transmission during and after HIV seroconversion. AIDS. 2002;16(11):1529–35. [PubMed: 12131191]
28. Darrow WW, Kurtz SP, Buckley AK, Patel KI, Stempel RR. Impact of HIV counseling and testing on HIV-infected men who have sex with men: the south beach health survey. AIDS Behav. 1998;2(2):115–26.
29. Khosropour CM, Dombrowski JC, Kerani RP, Katz DA, Barbee LA, Golden MR. Changes in condomless sex and serosorting among men who have sex with men after HIV diagnosis. J Acquir Immune Defic Syndr. 2016;73(4):475–81. [PubMed: 27792685]
30. Marks G, Millett GA, Bingham T, Bond L, Lauby J, Liau A, et al. Understanding differences in HIV sexual transmission among Latino and black men who have sex with men: the brothers y hermanos study. AIDS Behav. 2009;13(4):682–90. [PubMed: 18752064]
31. McFarland W, Chen YH, Raymond HF, Nguyen B, Colfax G, Mehrtens J, et al. HIV seroadaptation among individuals, within sexual dyads, and by sexual episodes, men who have sex with men, San Francisco, 2008. AIDS Care. 2011;23(3):261–8. [PubMed: 21347888]
32. Metsch LR, Feaster DJ, Gooden L, Schackman BR, Matheson T, Das M, et al. Effect of risk-reduction counseling with rapid HIV testing on risk of acquiring sexually transmitted infections: the AWARE randomized clinical trial. JAMA. 2013;310(16):1701–10. [PubMed: 24150466]
33. Moskowitz JM. Change in sexual risk behavior in people newly diagnosed with HIV [Poster]. Abstract #THPE0679. Mexico City, Mexico: International AIDS Conference; 2008.
34. Saah AJ, Hoover DR, Weng S, Carrington M, Mellors J, Rinaldo CR Jr, et al. Association of HLA profiles with early plasma viral load, CD4+ cell count and rate of progression to AIDS following acute HIV-1 infection. Multicenter AIDS cohort study. AIDS. 1998;12(16):2107–13. [PubMed: 9833851]
35. Smith DK, Warren DL, Vlahov D, Schuman P, Stein MD, Greenberg BL, et al. Design and baseline participant characteristics of the human immunodeficiency virus epidemiology research (HER) study: a prospective cohort study of human immunodeficiency virus infection in US women. Am J Epidemiol. 1997;146(6):459–69. [PubMed: 9290506]
36. Steward WT, Remien RH, Higgins JA, Dubrow R, Pinkerton SD, Sikkema KJ, et al. Behavior change following diagnosis with acute/early HIV infection-a move to serosorting with other HIV-infected individuals. The NIMH multisite acute HIV infection study: III. AIDS Behav. 2009;13(6):1054–60. [PubMed: 19504178]
37. Valleroy LA, MacKellar DA, Karon JM, Rosen DH, McFarland W, Shehan DA, et al. HIV prevalence and associated risks in young men who have sex with men young men's survey study group. JAMA. 2000;284(2):198–204. [PubMed: 10889593]
38. Vasarhelyi K MW, Anema A, Chan K, Hogg R, Montaner J. Changes in risk behaviour following HIV diagnosis and subsequent HAART initiation in men who have sex with men. Abstract #MOPE334. Rome, Italy: International AIDS Society Conference on HIV Pathogenesis; 2011.
39. Whitham HK, Sansom SL, Wejnert C, Finlayson T, Huang YA, An Q, et al. Sex practices by HIV awareness and engagement in the continuum of care among MSM: a National HIV behavioral surveillance analysis in 21 US cities. AIDS Behav. 2017;22:840–7.
40. Gilbert M, Taylor D, Michelow W, Grace D, Balshaw R, Kwag M, et al. Sustained reduction in sexual behavior that may pose a risk of HIV transmission following diagnosis during early HIV infection among gay men in Vancouver British Columbia. AIDS Behav. 2018;22(7):2068–78. [PubMed: 28168375]

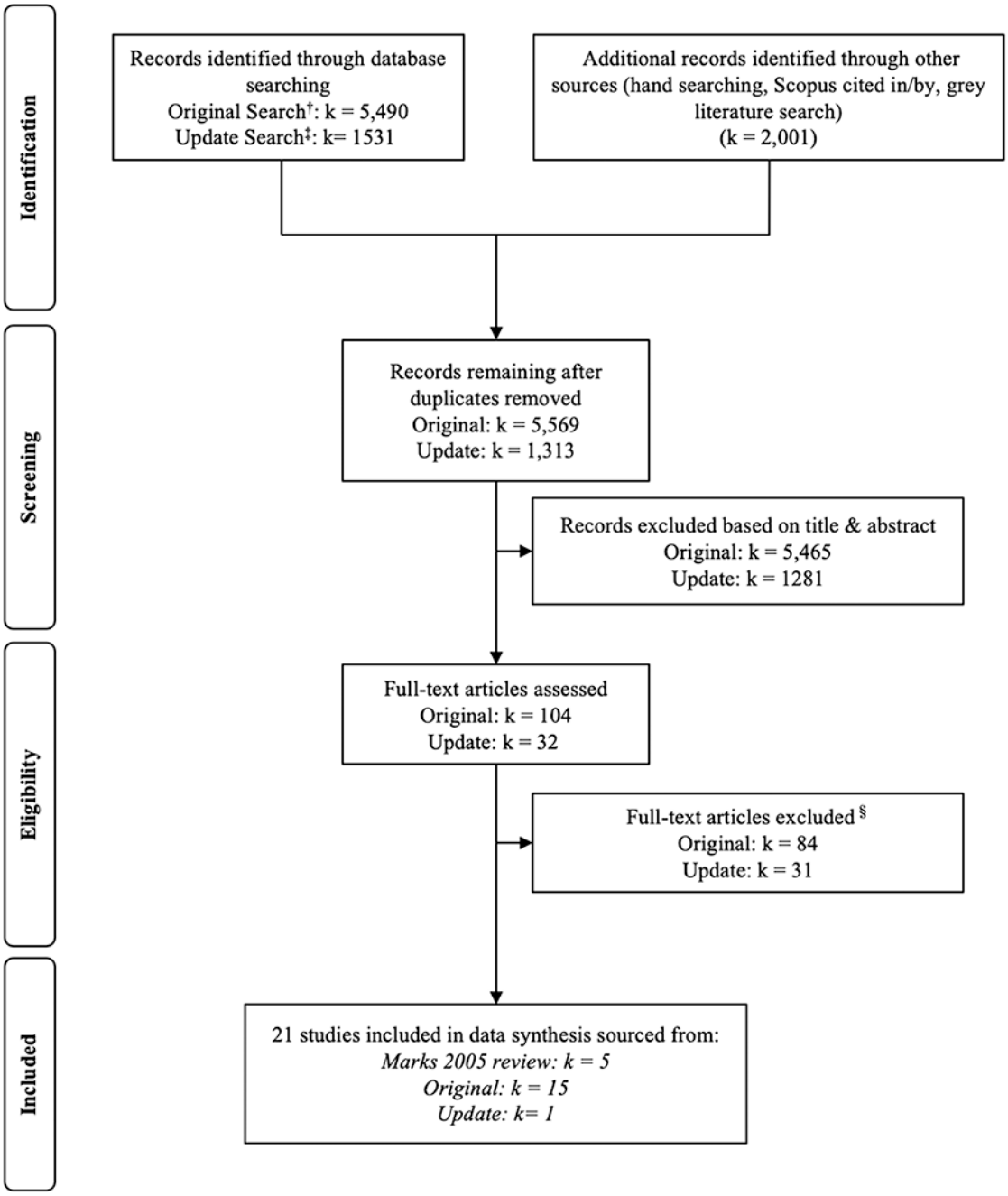

Fig. 1.

Identification and screening of citations: studies of the effect of knowledge of HIV infection on transmission risk behaviour. †Original database search (Jan 1, 1996–20 Oct 2015): SCOPUS, Web of Science, PubMed, PsycINFO, Cochrane Central Register of Controlled Trial. ‡Update database search (20 Oct 2015–8 May 2018): EMBASE, PubMed, PsycINFO, Cochrane Central Register of Controlled Trial. §Online Appendix C contains a list of records excluded at the full-text level with exclusion reasons

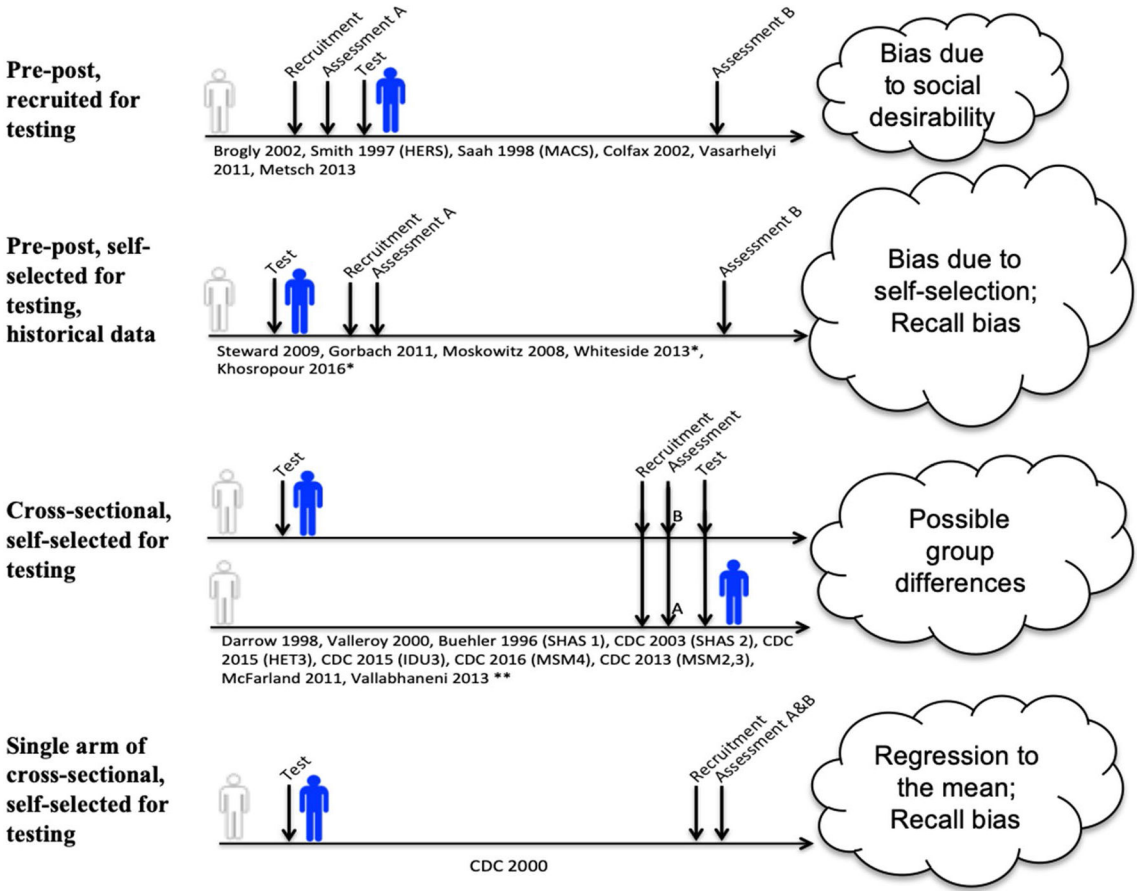

Fig. 2.

Study design and important risk of bias for included studies

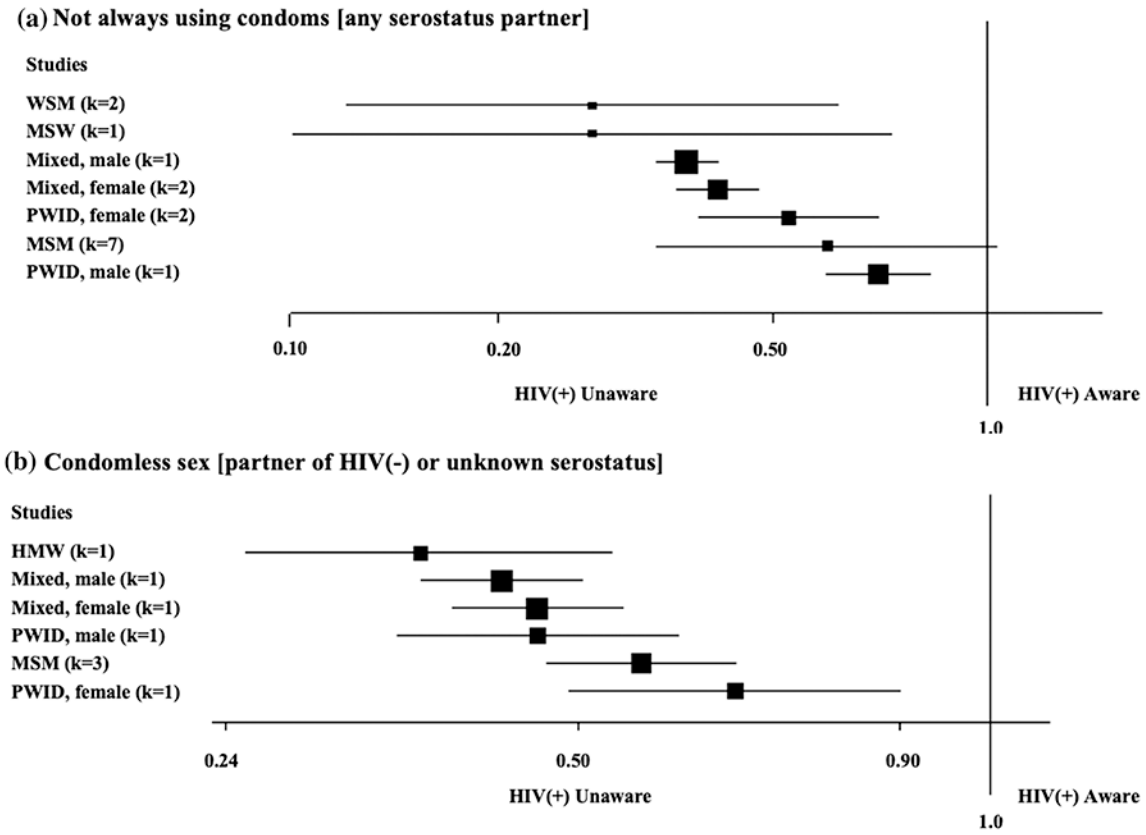

Fig. 3.

Forest plot of effect of HIV diagnosis by outcome type, population, and partner. †Risk ratios are sorted from smallest to largest from top to bottom. K: number of studies, HMW: Heterosexual men and women, Mixed: Mixed transmission groups, MSM: Men who have sex with men, MSW: Men who have sex with Women, POP: Population size, PWID: People who inject drugs, WSM: Women who have sex with men. †Results o separate meta-analytic data analysis and thus size of squares does not represent smaple sizes

Table 1

Outcome definitions and groupings for meta-analysis

Transmission group	Outcome	Type of partner
1 Men who have sex with men	**1** Not always using condoms: Self-report of having at least one episode of condomless sex in the recall period	Overall analysis: Combining across multiple partner types
2 Persons who inject drugs	Sub-analysis by duration:	Sub-analysis by:
3 Men who have sex with women	**a.** Shortest follow-up: shortest specified follow-up time at or after 12 months	**a.** Partner of any serostatus (unspecified)
4 Women who have sex with men	**b.** Longest follow-up: longest specified follow-up time at or after 12 months	**b.** Partner of HIV negative or unknown serostatus
5 Mixed risk: mix of multiple high-risk populations	**2.** Condomless sex likelihood: Self-report of having unprotected sex at last episode, or the proportion of a set of episodes that were unprotected	
Sub-analyses:		
a. Sex (male or female)		
b. Antiretroviral therapy status		

AIDS Behav. Author manuscript; available in PMC 2022 June 28.

Table 2

Characteristics of included studies: Men who have sex with men

Study	Setting/data collection year	Design	Eligibility	Sample	HIV+ diagnosis	Outcomes assessed[†]
CDC (2015) (MSM4)	20 US cities, 2014	Cross-sectional, participants self-selected for testing	Age ≥ 18 males, ever MSM history	N = 1888 Unaware: n = 468; White: 26% Age ≥ 30: 69%	Not interventional. Testing to validate participant self-report of HIV status, followed by survey	At baseline: • **Condomless sex last sex with HIV-discordant partners in past 12 months** • Condomless sex with any partners (male or female) in past 12 months
CDC [23] (MSM2, MSM3)	20 US cities, 2014	Cross-sectional, participants self-selected for testing	Age ≥ 18 males, MSM in past 12 months	**Cycle 2:** N = 1558 Unaware: n = 676; White: 17% Age ≥ 30: 82% **Cycle 3:** N = 1553 Unaware: n = 521; White: 30% Age ≥ 30: 69%	Not interventional. Testing to validate participant self-report of HIV status, followed by survey	At baseline: • **Unprotected sex at last sex with a partner of HIV-negative status or with unknown HIV status**
Colfax et al. [27][≠]	Seven US cities, 1995–1999	Single-arm pre-post, participants recruited for testing	Age ≥ 18 males, MSM in past 12 months	N = 66 White: 64% Age median: 31 (IQR 20–55) On ART: 70% (at 12 months)	Participants were in risk reduction program when diagnosed, and HIV+ participates offered enrolment in HIVNET observational cohort	At baseline and 12 months post diagnosis: • Insertive UAI with an at-risk partner in past 6 months
Darrow et al. [28]	Miami, Florida, 1996	Cross-sectional, participants self-selected for testing	Age ≥ 18 males, unmarried, ever MSM history	N = 51 Unaware: n = 14; 27.4% White: 53% Age mean (SD): 34 (6.4); range 23–9	All participants had received HTC over past median 65.8 months. Study baseline began with new HIV+ HTC	At baseline: • Insertive UAI with partner of HIV-negative status or with unknown HIV status in past 12 months
Gilbert et al. [40]	Vancouver, British Columbia 2009–2012	Single-arm pre-post, participants self-selected for testing	Age ≥ 19 males, ever MSM history, diagnosed with acute or recent HIV infection, English speaking	N = 25, including 241 dyads of sexual partners White: 72%, Age mean: 40,	Participants received HIV diagnosis in one of the six public health clinics and got routine counselling, support, and partner notification services, and referred to research coordinator for follow-up	At baseline, and 0–3 mon, 3–6.5 mon, 6.5–11 mon, and > 11 mon post diagnosis: • Condomless anal sex with serodiscordant or partner of unknown serostatus
Khosropour et al. [29]	Seattle, Washington, 2001–2013	Single-arm pre-post, participants self-selected for testing	Age ≥ 18 males, MSM in past 12 months	N = 186 White: 63% Age ≥ 25: 75%	HIV testing offered to MSM attending STI clinics not previously tested positive	At baseline and 1–2 years, 2–3 years and 3–4 years post diagnosis: • Condomless anal intercourse with HIV-uninfected partner

Study	Setting/data collection year	Design	Eligibility	Sample	HIV+ diagnosis	Outcomes assessed[†]
						• Condomless anal intercourse with partner of unknown HIV status
Metsch et al. [32][§]	Nine US cities, 2010–2011	Single-arm pre-post sub-group of randomized trial, participants recruited for testing	Age ≥ 18 males and female patients of STI clinics	N = 53 Males: n = 47 (89%) MSM: n = 38 (72%) White: 30% Age mean (SD): 35 (10)	Participants received HTC as a part of the study	At baseline and 6 months post diagnosis (all participants): • Unprotected proportion of all sex acts in past 6 months
Marks et al. [30]	Three US cities	Cross-sectional, participants self-selected for testing	Age ≥ 18 males, MSM in past 12 months, Black and Latio	N = 1007 Unaware = 142 White = 0% Median age: Black (43) and Latinos (32) 67% on ART past 3 mon	Not interventional. Testing to validate participant self-report of HIV status, followed by survey	At baseline: • UAI (insertive or receptive) in past 3 months
Moskowitz [33] ¶	San Francisco, California, 2003–2008	Single-arm pre-post, participants self-selected for testing	Age ≥ 18 males, most already tested HIV+	N = 59 No demographic data reported	Participants newly diagnosed with HIV+ prior to enrolment	At baseline and six additional times post diagnosis over the course of 18 months: • Insertive UAI with partner of HIV-negative status or with unknown HIV status
McFarland et al. [31]	San Francisco, California, 2007–2008	Cross-sectional, self-selected for testing	Age ≥ 18 males	N = 262 Unaware: n = 38; White: 50% Age ≥ 25: 86%	Participants tested as a part of the study	At baseline: • UAI past 6 months • 100% condom use past 6 months • UAI with partner of HIV-negative status or with unknown HIV status past 6 months
Saah et al. [34] (MACS)[‡]	Four US cities, 1987–2001	Single-arm pre-post, participants recruited for testing	Age ≥ 18 males, testing HIV+	N = 90 No demographic data reported	Participants tested as a part of the study	At baseline and every 6 months post diagnosis up to 18 months: • UAI with any partner in the past 12 months
Steward et al. [36]	Seven US cities	Single-arm pre-post, participants self-selected for testing	Age ≥ 18 males and females with documented early or acute HIV infection	N = 34 MSM: 93% White: 38% Age mean (SD): 33 (9.5)	Participants tested as a part of the study	At baseline and 3 months post diagnosis: • **Proportion of condom-protected sex acts**
Valleroy et al. [37]	Six US cities as well as the San Francisco Bay Area, 1994–1998	Cross-sectional, participants self-selected for testing	Age 15–22, males testing HIV+	N = 249 Unaware: n = 203; White: 16.5% Age ≥23: none	Participants tested as a part of the study	At baseline: • UAI (insertive or receptive) in past 6 months

Study	Setting/data collection year	Design	Eligibility	Sample	HIV+ diagnosis	Outcomes assessed†
Vasarhelyi et al. [38]¶	Vancouver, British Columbia, Canada, 1995–2004	Single-arm pre-post, participants recruited for testing	Age 15–30, males testing HIV+	N = 50 White: 64% Age median 25 (IQR 23–27)	Participants tested as a part of the study	At baseline and unspecified time post diagnosis (by being on ART or not only) • UAI with casual partner in past 12 months • UAI with regular partner in past 12 months
Whitham et al. [39]¶	21 US cities, three rounds of surveys 2008, 2011, 2014	Cross-sectional, participants self-selected for testing	Age ≥ 18 males, ever MSM history	N = 5935 Unaware = 1722 White = 40% Age: 18–24 (22.3%) 55 + (6.7%)	Not interventional. Testing to validate participant self-report of HIV status, followed by survey	At baseline: • Any condomless sex in past 12 months with any partner (on ART)

HIV + Positive HIV test result, *HTC* HIV testing & counseling, *IQR* Inter-quartile range, *MSM* Men who have sex with men, *SD* Standard deviation, *STI* Sexually-transmitted infection, *UAI* Unprotected anal intercourse

† Outcomes in bold are grouped as condomless sex likelihood

‡ Unpublished data reported in Marks 2005

§ Published and unpublished data

¶ Conference abstract

†† There is overlap with CDC 2014 and CDC 2016. There were three “aware” subgroups. For this analysis, we only included unaware and aware on ART—we excluded aware but out of care group and in care but not ART group, and only extracted data that are unique about being on ART

AIDS Behav. Author manuscript; available in PMC 2022 June 28.

Table 3

Characteristics of included studies: People who inject drugs

Study	Setting	Design	Eligibility	Sample	HIV+ diagnosis	Outcomes assessed[†]
CDC (IDU3) [24]	20 US cities	Cross-sectional, participants self-selected for testing	Males and females age ≥ 18 years, injection drug use in past 12 months	N = 903 Unaware: n = 326; Female: n = 271 (30%) White: 16.1% Age ≥ 30: 97% On ART: 62–70% of HIV+ aware	Testing to validate participant self-report of HIV status, followed by survey	At baseline: • **Condomless sex at last sex with HIV-discordant partners by gender** • Condomless sex with casual partners in past 12 months, by gender
Smith et al. [35] (HERS) ≠	Four cities in eastern US, 1993–2000	Single-arm pre-post, participants recruited for testing	Females age 16–55 reporting ≥ 1 HIV risk behaviours; 11/14 (79%) were PWID	N = 14 No demographic data reported	Participants tested as a part of the study	At baseline and 18 months post diagnosis: • Unprotected vaginal or anal sex with a casual partner (in past 6 months at baseline interview and past 12 month at follow-up)

HIV + Positive HIV test result, *PWID* People who inject drugs, *STI* Sexually-transmitted infection, *UAI* Unprotected anal intercourse

[†]Outcomes in bold are grouped as condomless sex likelihood

[≠]Unpublished data reported in Marks 2005

Table 4

Characteristics of included studies: Populations at mixed risk for HIV infection (including heterosexuals)

Study	Setting	Design	Eligibility	Sample	HIV+ diagnosis	Outcomes assessed[†]
Buehler et al. [20] (SHAS 1)[≠§]	Cities and regions in 12 US states, 1995–2000	Cross-sectional, participants self-selected for testing	Males and females at mixed risk of HIV infection	N = 9,419 Unaware: 236; White: 34%	HIV testing not part of the study	At baseline, participants within one month of HIV diagnosis ("unaware") compared to those at least 13 months after diagnosis ("aware"): • Unprotected anal or vaginal sex with any partner in the past 12 months
CDC 2015 (HET3) [25]	20 US cities, 2013	Cross-sectional, participants self-selected for testing	MSW and WSM, age 18–60, had sex with opposite sex partner in past 12 months; never MSM; never PWID	N = 171 Unaware: n = 76; 44% Female: 61% White: 1% Age ≥ 30: 90% On ART: 86–92% of HIV+ aware	Testing to validate participant self-report of HIV status, followed by survey	At baseline: • **Condomless sex last sex with HIV-discordant partners in past 12 months** • Condomless sex with casual partners in past 12 months
CDC [22] (SHAS 2)[≠§]	Cities and regions in 16 US states, 1995–2000[†]	Cross-sectional, participants self-selected for testing	Males and females at mixed risk of HIV infection	N = 3,658 Unaware: 3,218; Female: 27% Other demographic data not reported	HIV testing not part of the study	At baseline, "early testing" participants ("aware") were compared with those of "late testing": • **Condom use at last vaginal or anal sex with HIV-negative partner or partner with unknown HIV status**
CDC [21]	Alabama, New Jersey and Tennessee, 1997–1998	Single arm pre-post, nested in a cross-sectional study, participants self-selected for testing	MSW and WSM with documented recently-acquired HIV infection	N = 180 Female: 55% White: 27% Age ≥ 25: 47%	Participants reported dates of diagnosis	At baseline and median 6 months post diagnosis: • Any unprotected sex in past 6 months

HIV + Positive HIV test result, *MSM* Men who have sex with men, *PWID* People who inject drugs, *STI* Sexually-transmitted infection, *UAI* Unprotected anal intercourse, *WSM* Women who have sex with men

[†]Outcomes in bold are grouped as condomless sex likelihood

[≠]Unpublished data reported in Marks 2005

[†]Discrepancy: Marks 2005 reports "19 states." Only 16 states are named, and the title of the CDC study reporting these data includes "16 sites"

Table 5

Summary of evidence for the effect of knowledge of HIV infection on not always using condoms

Outcome	Number of data points	Risk ratio (95% CI) Pooled if ≥ 2 studies	I^2 (Q test p-value)	GRADE evidence quality	References (time since diagnosis)
Men who have sex with men					
Overall	11	**0.44 (0.33, 0.59)**	87% (0.00)	Very low	CDC [21] (6 mo); CDC 2016 (MSM4; NR); Colfax et al. [27] (12 mo); Darrow et al. [28] (65.8 mon); Gilbert et al. [40] (11 mon), Khosropour et al. [29] (1–2 yr); Marks et al. [30] (NR), McFarland et al. [31] (NR); Moskowitz [33] (12 mo); Saah et al. [34] (18 mo); Valleroy et al. [37] (NR)
With partner of any serostatus	7	0.59 (0.34, 1.04)	86% (0.00)	Very low	CDC [21] (6 mo); CDC 2016 (MSM4; NR); Darrow et al. [28] (65.8 mo); Gilbert et al. [40], McFarland et al. [31] (NR); Saah et al. [34] (18 mo); Valleroy et al. [37] (NR)
With partner of HIV (−) or unknown serostatus	6	**0.46 (0.30, 0.70)**	60% (0.03)	Very low	Colfax et al. [27] (12 mo); Darrow et al. [28] (65.8 mo); Khosropour et al. [29] (1–2 yr); Marks et al. [30] (NR), McFarland et al. [31] (NR); Moskowitz [33] (12 mo)
Overall, longest reported follow-up time and ≥ 12 months	6	0.75 (0.54, 1.03)	58% (0.05)	Very low	Colfax et al. [27] (12 mo); Darrow et al. [28] (65.8 mon); Gilbert et al. [40] (>11 mon); Khosropour et al. [29] (3–4 yr); Moskowitz [33] (12 mo); Saah et al. [34] (18 mo)
Overall, shortest reported follow-up time and ≤ 6 months	3	**0.18 (0.10, 0.33)**	0% (0.56)	Very low	CDC [21]; (6 mo); Gilbert et al. [40] (< 3 mon); Moskowitz [33] (3 mo)
With partner of HIV (−) or unknown status, HIV+ partner on ART	1	1.27 (0.69, 2.34)	–	Very low	Vasarhelyi et al. [38]
With partner of HIV (−) or unknown status, HIV+ partner not on ART	1	0.86 (0.54, 1.37)	–	Very low	Vasarhelyi et al. [38]
With partner of mixed serostatus, HIV+ partner on ART	1	1.2 (0.96, 1.09)	–	Very low	Whitham et al. [37]
People who inject drugs					
With partner of any serostatus, males	1	**0.70 (0.59, 0.83)**	**–**	Very low	CDC 2015 (IDU3) (NR)
With partner of any serostatus, females	2	**0.52 (0.38, 0.70)**	0% (0.89)	Very low	CDC 2015 (IDU3) (NR), Smith et al. [35] (18 mo)
Heterosexual: Men who have sex with Women					
With partner of any serostatus	1	**0.27 (0.10, 0.73)**	–	Very low	CDC 2015 (HET3) (NR)
Heterosexual: Women who have sex with men					
With partner of any serostatus	2	**0.27 (0.12, 0.61)**	83% (0.02)	Very low	CDC [21] (6 mo), CDC 2015 (HET3) (NR)
Mix of multiple transmission groups (including heterosexuals)					
With partner of any serostatus, males	1	**0.37 (0.33, 0.41)**	–	Very low	Beuhler 1996 (≥ 13 mo)
With partner of any serostatus, females	1	**0.41 (0.36, 0.47)**	–	Very low	Beuhler 1996 (≥ 13 mo)

mo = month, yr = year, NR = Not Reported

Bolding indicates statistical significance

Table 6

Summary of evidence for the effect of knowledge of HIV infection on condomless sex likelihood

Outcome	Number of data points	Risk Ratio (95% CI) Pooled if ≥ 2 studies	I^2 (Q test p-value)	GRADE evidence quality	References (time since diagnosis)
Men who have sex with men					
Overall	5	**0.58 (0.49, 0.69)**	57% (0.06)	Very low	CDC [26], CDC [23] (MSM2, NR)†; CDC [23] (MSM 3; NR)†; Metsch et al. [32] (6 mo); Steward et al. [36] (3 mo)
With partner of any serostatus	2	**0.72 (0.57, 0.92)**	0% (0.0)	Very low	Metsch et al. [32] (6mo); Steward et al. [36] (3 mo)
With partner of HIV (−) or unknown serostatus People who inject drugs	3	**0.54 (0.46, 0.65)**	57% (0.1)	Very low	CDC [26], CDC [23] (MSM2, NR)†; CDC [23] (MSM 3; NR)†
With partner of HIV (−) or unknown serostatus, male	1	**0.44 (0.33, 0.58)**	–	Very low	CDC 2015 (IDU3) (NR)
With partner of HIV (−) or unknown serostatus, female Heterosexual men and women	1	**0.65 (0.47, 0.90)**	–	Very low	CDC 2015 (IDU3) (NR)
With partner of HIV (−) or unknown serostatus Mix of multiple transmission groups	1	**0.35 (0.24, 0.51)**	–	Very low	CDC 2015 (HET) (NR)
With partner of HIV (−) or unknown status, males	1	**0.41 (0.35, 0.48)**	–	Very low	CDC [22] (NR)
With partner of HIV (−) or unknown status, females	1	**0.44 (0.37, 0.52)**	–	Very low	CDC [22] (NR)

Bold indicates statistical significance

mo = month, yr = year, NR = Not Reported

†Publication contributed two estimates, based on independent survey waves