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Prevalence of Rectal Chlamydial and Gonococcal Infections: A Systematic Review

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Abstract

We undertook a systematic review to examine rectal *Chlamydia trachomatis* (Ct) and *Neisseria gonorrhoeae* (Ng) infections in women and men who have sex with men (MSM). English-language publications measuring rectal Ct or Ng prevalence using nucleic acid amplification tests were eligible. Searching multiple electronic databases, we identified 115 eligible reports published between January 2000 and November 2016. Overall, the prevalence of rectal Ct (9%) was higher than that of rectal Ng (4.7%). Rectal Ct prevalence was similar in MSM (9%) and women (9.2%), whereas rectal Ng prevalence was higher in MSM (6.1%) than in women (1.7%). Generally, rectal Ct prevalence was similar in sexually transmitted disease clinics (9.1%) and nonsexual health clinics (8.6%), whereas rectal Ng prevalence was somewhat lower in sexually transmitted disease clinics (4.5%) than in nonsexual health clinics (6%). These infections seem to be relatively common across a range of populations and clinical settings, highlighting the need for additional research on these preventable, treatable conditions.

The sexually transmitted infections (STIs) chlamydia (caused by *Chlamydia trachomatis,* or Ct) and gonorrhea (caused by *Neisseria gonorrhoeae,* or Ng) are the 2 conditions most commonly reported to the Centers for Disease Control and Prevention (CDC), with more than 1.5 million and 468,000 annual cases in 2016, respectively.[1] Untreated urogenital Ct and Ng in women can lead to chronic pelvic pain, infertility, and other poor reproductive health outcomes, and to infertility and localized genital inflammation among men.[2] Although a large body of literature has described the epidemiology of urogenital Ct and Ng infections, relatively little is known about the epidemiology of rectal Ct and Ng.

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Most rectal STIs are acquired through receptive anal intercourse, with some data supporting possible transmission through oral-anal contact, through the gastrointestinal tract, and, in women, through autoinoculation from the vagina.[3–7] Men who have sex with men (MSM) account for most patients diagnosed with rectal Ct or Ng.[8] In the United States, MSM are also disproportionately affected by human immunodeficiency virus (HIV).[9,10] Several observational studies have identified an increased risk of HIV acquisition among MSM with a history of rectal Ct or Ng[11–14]: in both San Francisco and New York City, MSM diagnosed with a rectal Ct or Ng infection had significantly increased risk of subsequent HIV acquisition.[11,12] More recent studies among MSM in Atlanta and Washington State reported similar findings.[14,15]

Rectal STIs are also relatively common both among women who report anal sex[16] and women who deny anal sex.[7,17–20] In nationally representative data from 2010, 40% of women aged 20 to 49 years reported ever having anal sex, and more than 20% aged 20 to 39 years reported anal sex in the past year.[21] Although the long-term sequelae from untreated rectal Ct or Ng infections in women are unknown, untreated infections may be transmitted to susceptible male partners. Such onward transmission ultimately increases the risk of future urogenital infection in women and associated reproductive tract complications.

Screening programs have public health benefit when the prevalence of disease is relatively high, when the disease is serious (e.g., when untreated disease leads to substantial morbidity), when effective treatment is available, and when earlier identification and treatment leads to improved outcomes.[22–24] For STIs in particular, screening (with treatment) has the additional benefit of interrupting the chain of transmission of STIs from infected individuals to susceptible sex partners.

Published estimates of the prevalence of rectal Ct and Ng vary widely depending on the sex, age, location, and behavioral risk profile of the population examined. The lack of robust published data limits the development of evidence-based screening recommendations; currently, US Preventive Services Task Force has not put forth rectal STI screening recommendations for men or women. Sexually transmitted disease (STD) treatment guidelines from CDC recommend at least annual rectal STI screening for MSM who report receptive anal sex in the last 12 months, but make no rectal screening recommendation for women with behavioral exposure.[25,26] Clinical practice guidelines from CDC for HIV preexposure prophylaxis (PrEP) recommend screening patients for bacterial STIs every 6 months; for MSM only, the PrEP guidelines further state, “Do oral/rectal STI testing.”[26]

We undertook a systematic review of the published literature to document the prevalence of rectal Ct and Ng in MSM and women. Our goal was to describe the considerable burden of these 2 rectal STIs, to motivate future research to address current knowledge related to these infections. These gaps may include better understanding the consequences of untreated infections, the relationship between rectal infections and enhanced risk of HIV acquisition or HIV transmission, and the cost-effectiveness of screening and treating rectal STIs.

MATERIALS AND METHODS

Eligibility Criteria

Eligible studies were English-language publications that described data from MSM, cisgender, or transgender women aged 14 years and older, and that quantified the prevalence of rectal Ct or Ng using a nucleic acid amplification test (NAAT). We included cross-sectional studies and the baseline prevalence reported in prospective studies.

Excluded studies were those that assessed nonhuman subjects, focused exclusively on sexual assault survivors, used only culture diagnostic methods, reported results from tests of cure or previously positive patients, provided only combined prevalence of rectal Ct and Ng (i.e., not pathogen-specific prevalence estimates), computed incident infection, or were conducted strictly for the validation of new NAAT technology. Studies that reported testing for Ct or Ng at multiple anatomical sites for which the rectal-only prevalence could not be disaggregated were also excluded.

Search Strategy

We systematically searched electronic databases for relevant reports in MEDLINE through PubMed, Global Health through CAB Direct, Web of Science, Scopus, and Cochrane Library (January 1, 2000, through November 11, 2016). Studies before the year 2000 were not included because NAAT diagnostic techniques were rarely used before this time. The search strategy for MEDLINE is reported below (see Supplemental materials for additional search strategies).

All fields: ((chlamydia infections OR chlamydia trachomatis OR gonorrhea OR neisseria gonorrhoeae OR gonorrh* OR gonococcal OR chlamydia)) AND (rectal diseases OR rectum OR anal canal OR rectal OR anal OR rectum* OR anus OR anorectal).

Data Abstraction

One author (C.D.) screened titles and abstracts of all records identified through electronic searches and made initial judgements about eligibility. Two authors (A.N.T. and C.D.) then independently reviewed the full text of eligible articles.

One review author (C.D.) extracted relevant information from eligible articles using a standardized form. A second review author (A.N.T.) validated extracted data for 10% of studies. For each study, we recorded the following: (1) geographic location, (2) period of data collection, (3) population description and risk group (MSM, women, transgender women), (4) HIV status, (5) screening site (e.g., STD clinic), (6) NAAT type, (7) sample size, and (8) prevalence of rectal Ct and Ng.

Statistical Analysis

Prevalence estimates for rectal Ct and Ng were plotted separately by population (MSM vs. women) and screening site. To ease comparison across groups, we computed the weighted average prevalence for each subgroup. The weighted average prevalence is a sum of the weighted prevalence for each study, where the weight is the number of participants in a

given study divided by the total number of participants across all studies. Most studies presented unadjusted prevalence only, so no adjusted estimates are provided.

RESULTS

Results are presented according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines.[27]

Characteristics of Eligible Studies

Initial searches of MEDLINE, Global Health, Web of Science, Scopus, and Cochrane Library returned 3468 records (Fig. 1). We excluded 1151 duplicates and 1250 records published before January 1, 2000. We reviewed the title and abstract of the remaining 1067 records; after screening, 405 records advanced to full-text review. Of these, 290 (72%) were excluded for the following reasons: non-NAAT or diagnostic technique not reported (n = 82), results of rectal testing not reported (e.g., pharyngeal or urogenital results only; n = 47), no relevant data for inclusion in review (n = 34), NAAT validation study (n = 29), anatomical site of infection not distinguished (n = 23), population not defined as MSM or women (n = 17), no primary study data (e.g., editorials; n = 13), provided only combined rectal Ct/Ng prevalence estimate (n = 8), provided incidence estimates (n = 8), performed test of cure or repeated testing on previously positive patients (n = 5), analyzed data already included in review from another publication (n = 4), and included participants younger than 14 years (n = 2). In addition, 18 studies were excluded because of sampling designs that could critically bias prevalence estimates (e.g., assessed rectal infections only among patients with urogenital infections, or a sample size of <10). Ultimately, 115 publications are included in the review (Fig. 1).

Study Characteristics

Most included studies (82/115) focused only on MSM, 19 studies tested only women, and 14 studies tested both MSM and women. Geographic location varied considerably, but most studies were conducted in the United States (n = 36), Australia (n = 17), the United Kingdom (n = 13), and the Netherlands (n = 12). A variety of settings were represented, including STD/genitourinary medicine clinics (n = 63), HIV clinics (n = 12), and community-based organizations (n = 10). More than two thirds of included studies (n = 79; 68.7%) tested for both rectal Ct and rectal Ng; 36 (31.3%) tested for rectal Ct only. Included studies ranged in size from n = 12 to n = 55,444 records (Table 1).

Rectal Ct Prevalence

Prevalence of rectal Ct ranged from 0% to 30.5% across all studies and populations (median, 7.9%; weighted average, 9%). The prevalence of rectal Ct was similar among individuals in STD clinics (median, 8.2%; weighted average, 9.1%) and in non-sexual health clinics (median, 6.8%; weighted average, 8.6%; Fig. 2).[12,16–19,28–30,31–137] Prevalence was similar among MSM and cisgender women, with a median of 7.9% and a weighted average of 9% among MSM compared with a median of 7.1 % and a weighted average of 8.7% among cisgender women (Figs. 3A, B). Transgender women had a higher prevalence of rectal Ct compared with MSM and cisgender women, although only 3 publications presented data

separately for transwomen (median, 20.7%; weighted average, 26.5%; Fig. 3B). For studies that presented STI prevalence stratified by HIV status, prevalence of rectal Ct was higher among HIV-positive persons (median, 7.8%; weighted average, 8.8%) than among HIV-negative persons (median, 4.8%; weighted average, 5.7%; Supplemental Figure 1, http://links.lww.com/OLQ/A216).

Rectal Ng Prevalence

Across all studies and populations, the prevalence of rectal Ng ranged from 0% to 29% (median, 3.6%; weighted average,4.7%). The prevalence of rectal Ng was slightly lower among STD clinic attendees (median, 4%; weighted average, 4.5%) compared with nonsexual health clinics (median, 3.2%; weighted average, 6%; Fig. 4). Rectal Ng prevalence was considerably higher among MSM (median, 4.2%; weighted average, 6.1%) than among cisgender women (median, 1.1%; weighted average, 1.3%; Figs. 5A, B). Transgender women had a higher prevalence of rectal Ng than did both MSM and cisgender women (median, 20.8%; weighted average, 25.4%; Fig. 5B). By HIV status, the prevalence of rectal Ng was higher among HIV-positive persons (median, 4%; weighted average, 4.8%) than among HIV-negative persons (median, 1.4%; weighted average, 2.8%; Supplemental Fig. 2, http://links.lww.com/OLQ/A217).

DISCUSSION

In this systematic review of rectal Ct and Ng prevalence among MSM and women in a range of geographical and clinical settings, we observed a high burden of rectal STIs. Among MSM, the weighted average prevalences of rectal Ct and Ng were 9% and 6.1%, respectively. Fewer studies have explored the prevalence of rectal infections among women, and in our review, the weighted average prevalences for this population were 9.2% for rectal Ct and 1.7% for rectal Ng. Given the expected heterogeneity across studies and populations, we decided a priori not to produce pooled prevalence estimates for each infection, yet some patterns did emerge. Rectal Ct prevalence was higher than rectal Ng prevalence. Prevalence was similar between men and women for rectal Ct, but was higher in MSM than in women for rectal Ng. Although most studies were conducted in STD clinics, the burden of disease in other settings was also high.

What are the impacts of untreated rectal STIs? A small number of studies examining the longitudinal effect of rectal STIs in MSM have consistently reported elevated risk of HIV acquisition among MSM with recent rectal STI compared with MSM without a rectal STI.[11–14] This increased HIV risk may be a direct result of prevalent rectal infection (e.g., increased inflammation in the rectum leading to increased risk of HIV acquisition[138]), or rectal STI may be a marker of sexual risk that identifies those MSM more likely to encounter an HIV-infected sex partner (and who may benefit from HIV prevention interventions such as PrEP or risk reduction counseling). For example, a recent prospective cohort study found that, among a sample of initially HIV-negative MSM, the population-attributable fraction for rectal STIs was approximately 15%, after adjusting for the potential confounding effects of behavioral risk factors.[139] Although disentangling the direct and indirect effects of rectal STIs on HIV risk is challenging—given that critical confounders

such as condom use, partners' HIV status, and time-varying rectal inflammation are difficult to measure—methodologically rigorous analyses have concluded that rectal STIs are independently and likely causally associated with HIV acquisition.[15,140] Apart from any direct connection to HIV, curbing ongoing transmission of rectal Ng is also essential given the emerging threat of pathogen resistance to currently recommended Ng treatment.[141]

Our results are consistent with a recent review by Chan et al.[142s] Both that assessment and our review report a high burden of rectal infections among MSM and prevalences among screened women in excess of 1 %. Although the review by Chan et al. examined rectal and pharyngeal positivity, the current review is focused on rectal infections only. Our review also calculated weighted prevalence estimates, which we believe are a more robust summary measure of prevalence across the publications examined. In addition, our review included data from both cisgender and transgender women; transwomen in particular have a high prevalence of rectal infections and are often excluded from analyses or combined with MSM populations.

Although MSM experience the highest number of rectal STIs annually, the prevalence of rectal infections among women who undergo testing is notable. The proportion of US women reporting receptive anal sex seems to be increasing, and younger women—who have the highest prevalence of urogenital STIs—are also more likely to report recent anal sex.[1,21] Thus, we may expect the need for rectal STI testing in women to increase. Importantly, many women diagnosed with rectal Ct or Ng denied anal sex.[7,17,18] It is not clear if these findings represent an underreporting of anal sex among screened women, or if urogenital infections can migrate to the rectum through autoinoculation. More research on the prevalence and predictors of anal sex among women and on the sequelae of rectal infections is warranted.

The CDC's 2014 recommendation for PrEP for HIV prevention occurred at a time when STDs, including rectal Ct and Ng, were increasing among MSM populations.[26] Not all high-risk MSM use PrEP or use PrEP effectively, and awareness and uptake of PrEP among women is far lower than among MSM.[143] As PrEP becomes more accessible, data on the relationships between rectal STIs, PrEP use, and HIV incidence will be critical for isolating the contribution of rectal STIs to HIV transmission dynamics.

Nationally representative samples of MSM, as well as cisgender and transgender women, are the gold standard for estimating the population prevalence of rectal Ct and Ng. However, such studies would require enormous resources to be powered sufficiently to generate reliable prevalence estimates. In the absence of these studies, we are left with prevalence studies conducted among subsets of the target populations, including many of the publications included in this review. Most studies were conducted at STD or genitourinary medicine clinics; these patients are probably more likely to have more partners or engage in higher-risk behaviors. Consequently, prevalence of rectal STIs among participants recruited from these sites is likely to be higher than the prevalence in the general population. Because most rectal infections are asymptomatic,[74] screening coverage is also a critical factor in interpretation of these findings. In many settings, the more persons screened (especially those at higher risk), the more infections will be identified. Unfortunately, screening

coverage data were lacking for nearly all articles included in this review, and our prevalence estimates should therefore be considered in light of this limitation. Future assessments of the prevalence of rectal Ct and Ng should make an effort to quantify the proportion of the "at-risk" population included.

Our findings have important limitations. Patient factors and screening setting may impact screening coverage and limit the generalizability of results. We did not include unpublished results, and estimates may be affected by publication bias. When publication bias is present, studies reporting lower estimates are more likely to be missing; thus, estimates presented here may be inflated.[144] We also included only articles published in English, although we note that a past evaluation of possible bias concluded that restricting to English did not lead to bias in a systematic review.[144] We examined only studies of individuals aged 14 years and older, because the studies we identified that included younger children were generally focused on sexual abuse and thus not appropriate to combine with the bulk of the reviewed studies. Estimates presented are drawn from studies using highly sensitive NAAT; however, any misclassification of rectal infection status in the reviewed studies will also be present here. We were unable to estimate the proportion of rectal infections across studies which would be missed when only urogenital STI screening is performed, in other words, the proportion of rectal infections that occur in the absence of a concurrent urogenital infection. This is an essential consideration for control of rectal STIs, but it was not possible to calculate from the data provided in many studies. Finally, we did not exclude estimates based on study quality. Nearly all studies presented only unadjusted prevalence, and we do not know the impact of confounding on the estimates.

Considerable gaps exist in knowledge about the clinical, behavioral, and immunological factors associated with acquisition of rectal STIs, and the long-term sequelae for both MSM and women. We believe that better understanding of the correlates and consequences of rectal infections will lead to stronger evidence about the harms and benefits of screening for rectal infections and the development of evidence-based guidelines for screening and prevention. Although CDC's STD treatment guidelines recommend at least annual rectal STI screening for MSM reporting receptive anal intercourse in the last 12 months,[25] the uptake of these recommendations is poor: a 2010 medical record review of HIV-positive MSM seen in HIV clinics reported that only 2% to 9% of patients had been tested for rectal Ct and Ng in the last year.[66] The American Academy of Pediatrics recommends that all sexually experienced adolescent and young adult MSM be screened for rectal Ct/Ng every 3 to 6 months if they engage in receptive or insertive anal intercourse and have multiple or anonymous sex partners, have sex in conjunction with illicit drug use, or have sex with partners who participate in these activities.[145] Neither the STD treatment guidelines nor the American Academy of Pediatrics recommendations make specific screening recommendations for rectal STIs for adult or adolescent women. Given established associations with HIV the value of rectal STI screening likely goes beyond ameliorating the immediate morbidity (e.g., symptomatic disease) of a treatable STI. Furthermore, in the era of PrEP and HIV treatment as prevention, it is critical to better understand the potential role of untreated rectal STIs in increasing risk of HIV infection on a population level for both MSM and women. Understanding the non-HIV consequences of rectal STIs is also essential,

although designing longitudinal studies that are both ethical and permit capture of relevant behavioral, clinical, and immunologic data is an as-yet-unmet challenge.

In summary, this systematic review is one of the first comprehensive assessments of rectal STI prevalence across multiple populations and settings. Our review attempted to quantify prevalence in a robust way across a wide range of heterogeneous studies and evaluations of rectal STIs. Studies from a wide range of geographic areas suggest that rectal STIs are prevalent in both MSM and women. A more lucid understanding of the epidemiology and public health importance of rectal Ct and Ng will require further examination of associations between rectal STIs and HIV, especially in the context of PrEP; characterization of the clinical, behavioral, and immunologic correlates and consequences of rectal STIs; improved understanding of rectal immunology as it impacts STI and HIV susceptibility; assessment of anal sex practices and rectal STI prevalence in underrepresented populations including women and adolescents; and development of comprehensive screening guidelines with a goal of reducing morbidities associated with untreated rectal infections.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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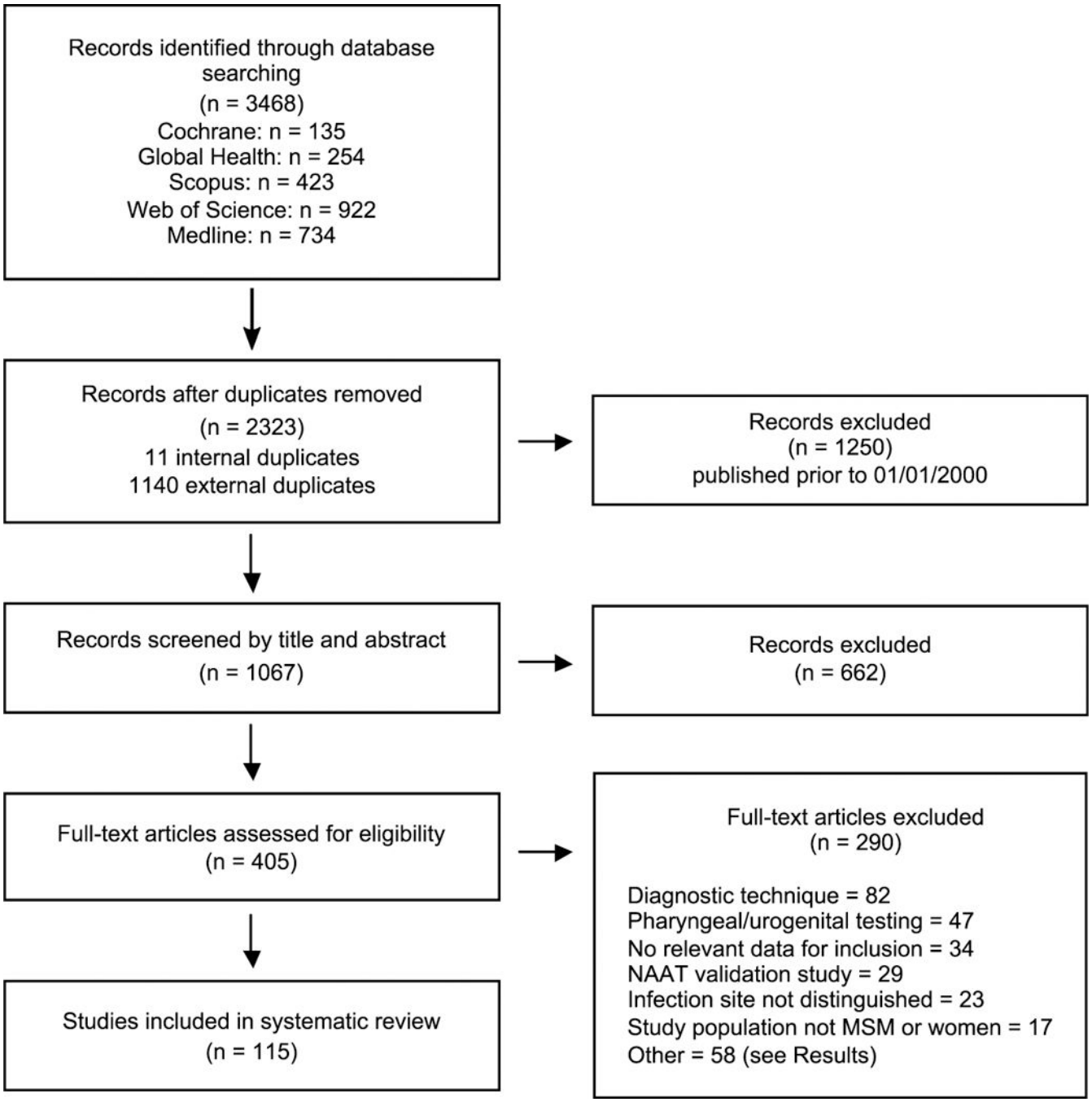

Figure 1.
Flow of information through the different phases of the systematic review.

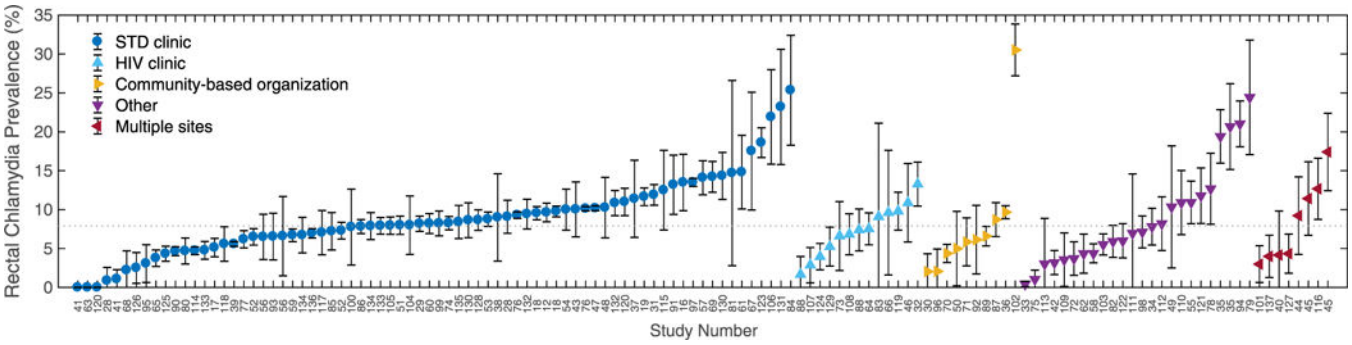

Figure 2.

Rectal chlamydia prevalence by study site; dashed line depicts unweighted median prevalence (7.9%).

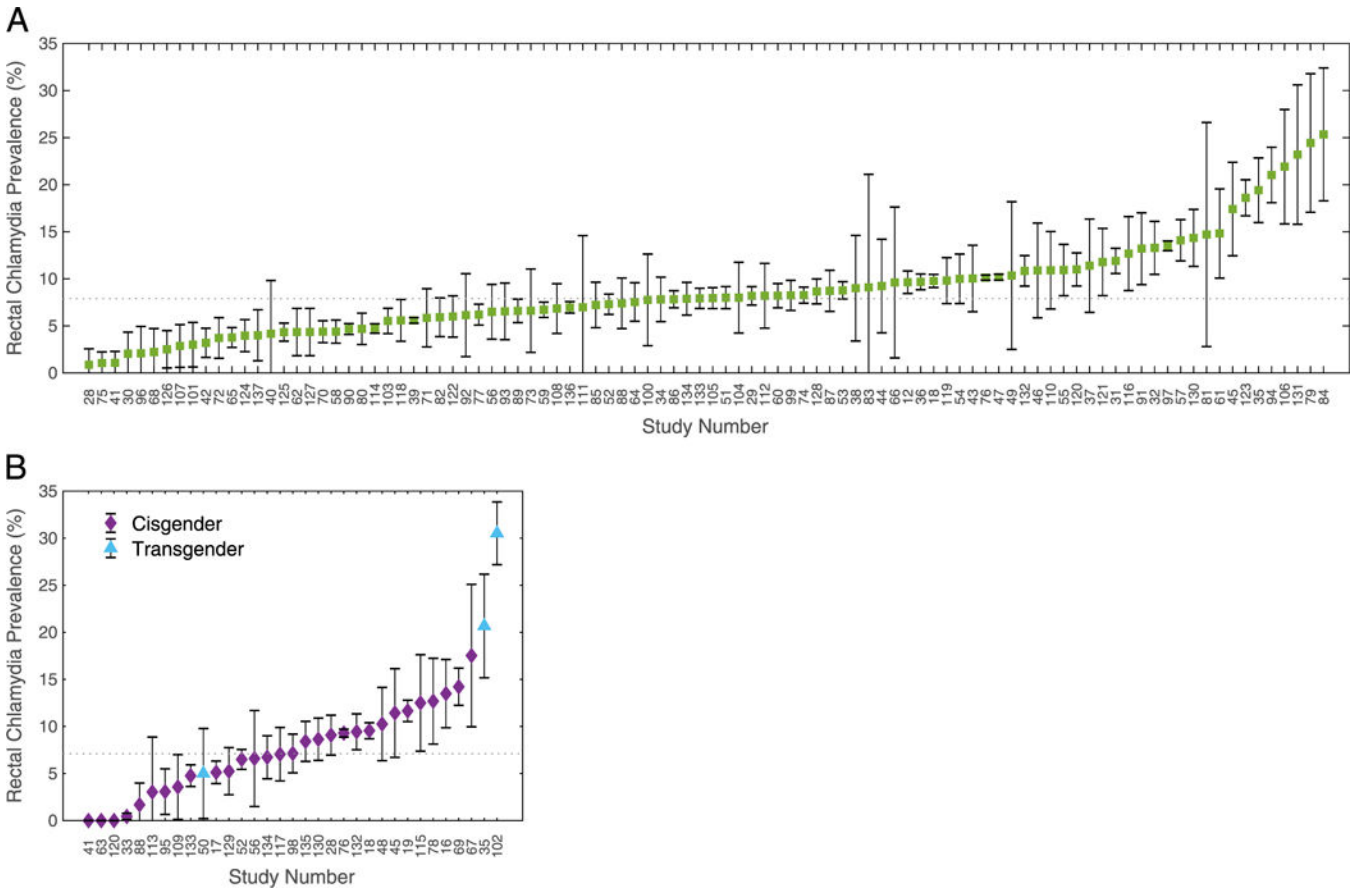

Figure 3.

Rectal chlamydia prevalence among MSM; dashed line depicts unweighted median prevalence (7.9%). B, Rectal chlamydia prevalence among women; dashed line depicts unweighted median prevalence (7.1%).

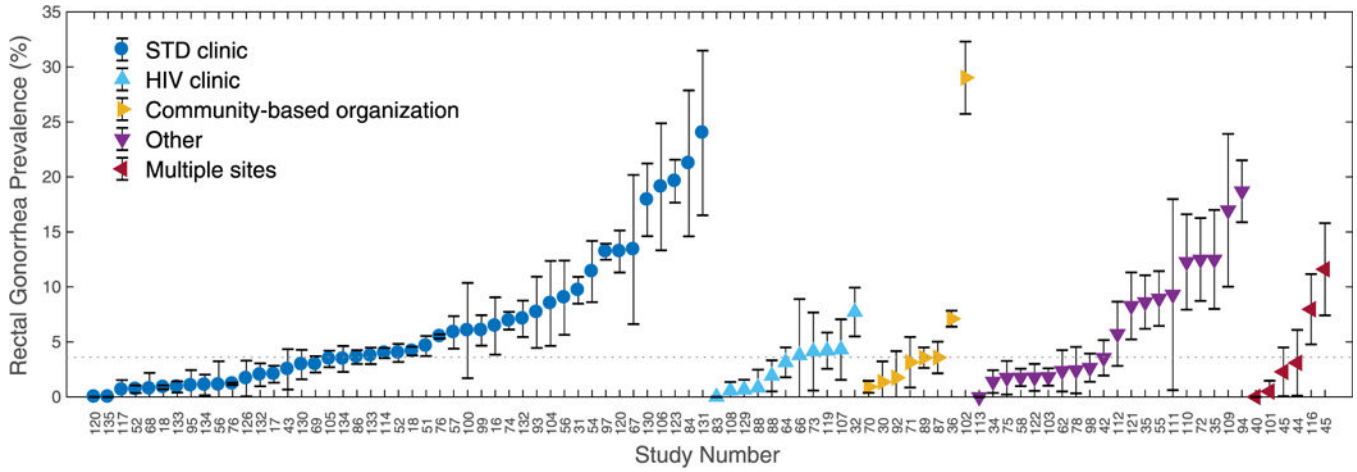

Figure 4.

Rectal gonorrhea prevalence by study site; dashed line depicts unweighted median prevalence (3.6%).

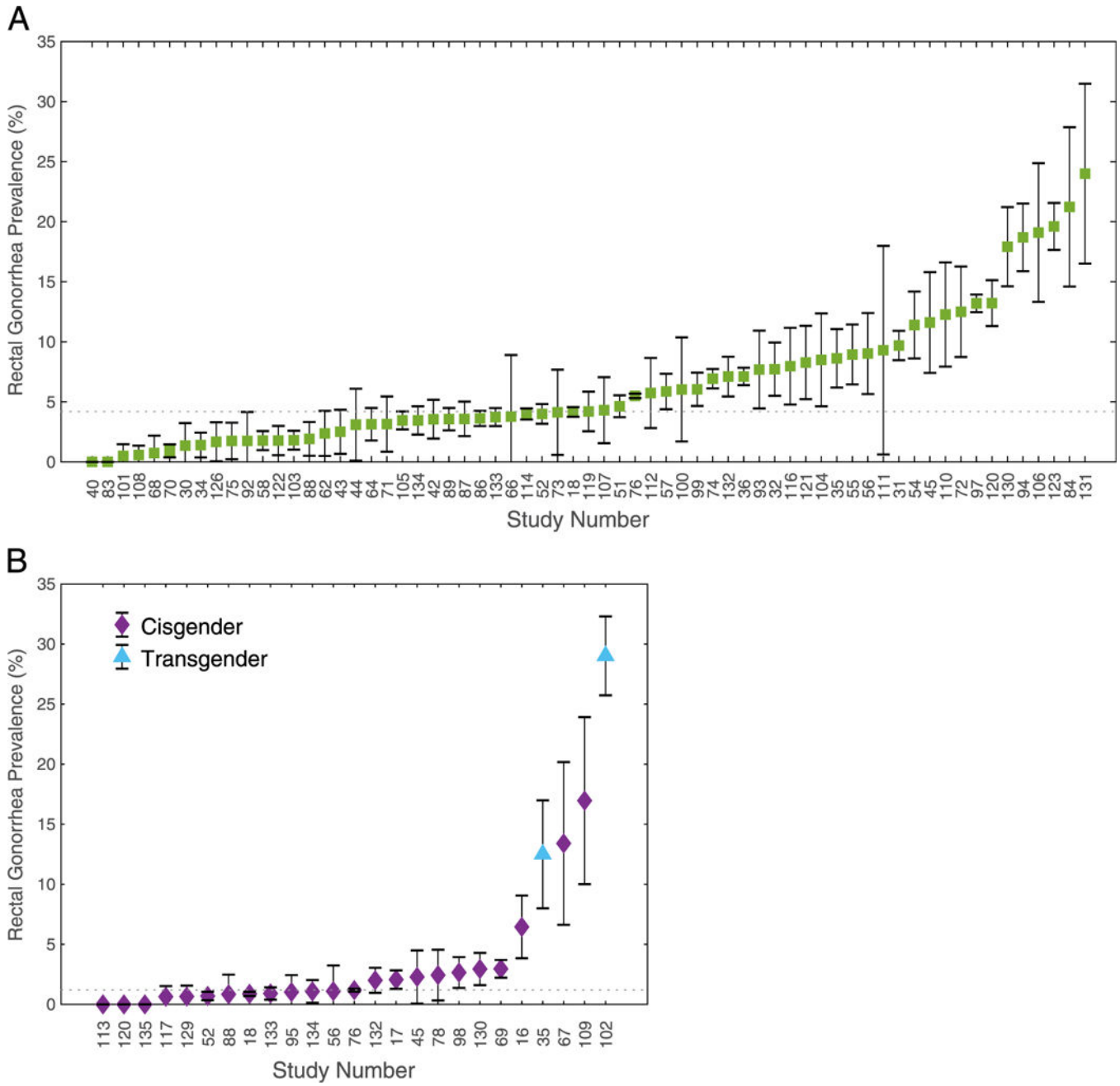

Figure 5.

Rectal gonorrhea prevalence among MSM; dashed line depicts unweighted median prevalence (4.2%). B, Rectal gonorrhea prevalence among women; dashed line depicts unweighted median prevalence (1.2%).

TABLE 1.

Characteristics of Eligible Studies in a Systematic Review of Prevalence of Rectal Chlamydial and Rectal Gonococcal Infections (n = 115)

Characteristics	n (%)
Rectal infection documented *	
Ct only	36 (31.3)
Ct and Ng	79 (68.7)
Population tested	
MSM only	82 (71.3)
Women only	19 (16.5)
MSM and women	14 (12.2)
Setting	
STD/genitourinary medicine clinic	63 (54.8)
HIV clinic	12 (10.4)
Community-based organization	10 (8.7)
Other	23 (20.0)
Multiple sites	7 (6.1)
Country	
United States	36 (31.3)
Australia	17 (14.8)
United Kingdom	13 (11.3)
The Netherlands	12 (10.4)
Germany	4 (3.5)
Canada	3 (2.6)
Indonesia	3 (2.6)
New Zealand	3 (2.6)
Argentina	2 (1.7)
Brazil	2 (1.7)
France	2 (1.7)
Kenya	2 (1.7)
Peru	2 (1.7)
South Africa	2 (1.7)
Botswana	1 (0.9)
China	1 (0.9)
El Salvador	1 (0.9)
Hong Kong	1 (0.9)
Ireland	1 (0.9)
Norway	1 (0.9)
Spain	1 (0.9)
Sweden	1 (0.9)
Switzerland	1 (0.9)
Tanzania	1 (0.9)

Characteristics	n (%)
Thailand	1 (0.9)
Uganda	1 (0.9)

* No study assessed rectal Ng only.