Worldwide burden of HIV in transgender women: a systematic review and meta-analysis

Stefan D Baral, Tonia Poteat, Susanne Strömdahl, Andrea L Wirtz, Thomas E Guadamuz, Chris Beyrer

Summary

Background Previous systematic reviews have identified a high prevalence of HIV infection in transgender women in the USA and in those who sell sex (compared with both female and male sex workers). However, little is known about the burden of HIV infection in transgender women worldwide. We aimed to better assess the relative HIV burden in all transgender women worldwide.

Methods We did a systematic review and meta-analysis of studies that assessed HIV infection burdens in transgender women that were published between Jan 1, 2000, and Nov 30, 2011. Meta-analysis was completed with the Mantel-Haenszel method, and random-effects modelling was used to compare HIV burdens in transgender women with that in adults in the countries for which data were available.

Findings Data were only available for countries with male-predominant HIV epidemics, which included the USA, six Asia-Pacific countries, five in Latin America, and three in Europe. The pooled HIV prevalence was 19·1% (95% CI 17·4–20·7) in 11 066 transgender women worldwide. In 7197 transgender women sampled in ten low-income and middle-income countries, HIV prevalence was 17·7% (95% CI 15·6–19·8). In 3869 transgender women sampled in five high-income countries, HIV prevalence was 21·6% (95% CI 18·8–24·3). The odds ratio for being infected with HIV in transgender women compared with all adults of reproductive age across the 15 countries was 48·8 (95% CI 21·2–76·3) and did not differ for those in low-income and middle-income countries compared with those in high-income countries.

Interpretation Our findings suggest that transgender women are a very high burden population for HIV and are in urgent need of prevention, treatment, and care services. The meta-analysis showed remarkable consistency and severity of the HIV disease burden among transgender women.

Introduction

The term transgender is used most often to refer to people whose gender identity or expression differs from their birth sex.1 Gender presentations and social categories vary greatly across cultures, and many different terms are used to describe individuals who live between or outside a male-female binary.2–4 For the purposes of this report, the terms male and female will be used to refer to biological sex, and the term man and woman will be used to refer to gender identity or expression. Transgender women, defined here as people who were assigned male at birth but who identify as women, have long been known to be at high risk for HIV acquisition and transmission. As of 2012, there remains a poor understanding of the burden of HIV among transgender women because of the limited inclusion of these populations in national HIV surveillance systems. In the few countries where epidemiological data for transgender women have been obtained, results have shown a disproportionate risk for HIV infection.

A 2008 meta-analysis by Herbst and colleagues’ at the US Centers for Disease Control and Prevention (CDC) identified 22 studies that reported HIV infection rates for transgender women. The average prevalence was 27·7% (range 16–68%) from the four studies that reported laboratory-confirmed HIV infections. African American transgender women had twice the prevalence of HIV infection (56·3%) than did those who were white (16·7%) or Hispanic (16·1%). When the results were averaged across the 18 studies where respondents self-reported their HIV serostatus, the average dropped to 11·8% (range 3–60%). Although selection bias might account for the difference in HIV prevalence between studies with self-reported HIV status and those with biologically confirmed HIV, CDC has reported that as many as 73% of the transgender women who tested HIV-positive were unaware of their status. Therefore, the difference in HIV prevalence between studies that used laboratory markers and those with only self-report provide support for the hypothesis that many transgender women might not be aware of their HIV status.5

One international systematic review and meta-analysis of HIV risk in a subset of transgender women was done by Operario and colleagues in 2008.6 This study compared HIV prevalence in transgender women sex workers versus transgender women who do not engage in sex work, male sex workers, and female sex workers. The investigators identified 25 studies including 6405 participants...
(3159 transgender women—2139 categorised as sex workers and 1020 categorised as non-sex workers—1633 male sex workers, and 1613 female sex workers) recruited from 14 countries on five continents. Although most studies were done in the USA, study populations also included transgender women in Spain, Singapore, Israel, Netherlands, Brazil, Belgium, Indonesia, Australia, Thailand, Uruguay, India, and Italy. Most sites were large metropolitan cities and all used convenience samples. Participants were recruited at venues that included HIV testing clinics, medical and community-based organisations serving transgender populations, street locations, and social and workplace venues. Six of the 25 studies established HIV status on the basis of self-report.

Overall crude HIV prevalence was 27.3% in transgender women engaging in sex work, 14.7% in those not engaging in sex work, 15.1% in male sex workers, and 4.5% in female sex workers. There was a significant difference in HIV prevalence in transgender women sex workers compared with all other pooled groups (odds ratio [OR] 1.46, 95% CI 1.02–2.09) and a significant difference between transgender sex workers and female sex workers (4.02, 1.60–10.11). Transgender sex workers were therefore more than four times more likely to be living with HIV than were female sex workers. Studies done outside of the USA showed higher HIV prevalence in transgender sex workers than in all other groups (OR 1.90, 95% CI 1.52–2.37), although studies within the USA did not show this difference (OR 1.24, 95% CI 0.72–2.12). These data highlight the disproportionate burden of HIV infections in transgender women sex workers compared with female sex workers.

We did a global systematic review to better assess the relative HIV burden among all transgender women worldwide. We then completed a meta-analysis comparing the burdens of HIV infection in these populations to those of adults of reproductive age in their countries to characterise the size of the burden of HIV borne by these women.

**Methods**

**Search strategy and selection criteria**

We searched PubMed, Embase, Global Health, Scopus, PsycINFO, Sociological Abstracts, Cumulative Index to Nursing and Allied Health Literature, Web of Science, POPLine, and LexisNexis. The WHO publications database was searched, as well as the National Library of Medicine’s Meeting Abstracts database. Searches were done in February, 2011, and repeated in November, 2011. Conference abstracts were searched from the online archives of the International AIDS Conference, the Conference on HIV Pathogenesis, Treatment, and Prevention, and the Conference on Retroviruses and Opportunistic Infections. Other data sources searched included national surveillance system data reports, including AIDS indicator surveys, demographic health surveys, and integrated biobehavioural surveillance studies done by large international non-governmental organisations. However, non-peer reviewed literature were not used on their own as sources of data. Rather, these documents guided secondary searches for further literature to ensure sensitive searches. Articles and citations were downloaded, organised, and reviewed with the QUOSA information management software package (version 8.05) and EndNote (version X4).

The search included medical subject headings (MeSH) terms for HIV or AIDS, and terms associated with transgender (transgender* OR “travesty” OR “koti” OR “hijra” OR “MTF” or “male to female transgender” OR transsexual* OR transvest* OR “mahuvahine” OR “mahu” OR “warai” OR katoey OR “cross dresser” OR “bantut” OR “nadleehi” OR “berdache” OR “xanith”). Gender identities are complex and fluid; a full explication of gender identities is beyond the scope of this text. Many terms have been used in the scientific literature to refer to transgender women. The aforementioned search terms represent those used in the international biomedical literature and are not inclusive of all local terms describing transgender women worldwide.

Studies of any design were included that measured the prevalence or incidence of HIV in transgender women. Studies were accepted if descriptions of HIV testing methods were included such as laboratory derived HIV status using biological samples from blood, urine, or oral specimens. To be included, detailed descriptions of the sampling, HIV testing, and analytical methods were needed, with sources including peer-reviewed journals and non-peer reviewed publications meeting other criteria and available online in the public domain. Studies published in English, French, and Spanish were included. Studies were excluded if the sample size of transgender women was less than 50. Studies were excluded if self-reported HIV status rather than biological testing was used to assess the burden of HIV. Finally, studies were excluded if the prevalence of HIV was presented in another study already included in the analysis.

This analysis focuses on people who were born male but identify as a different gender, in view of the evidence for a disproportionate burden of HIV in this population, irrespective of whether they had sexual reassignment surgery or altered their bodies with hormones, silicone injections, or surgical procedures. Most studies meeting the inclusion criteria did not describe the surgical status of the transgender women participants.

**Screening and data extraction**

The search described above was completed on Feb 22, 2011. After the removal of duplicates, titles were screened by two independent reviewers to exclude those that clearly did not include HIV prevalence data. If either reviewer thought a title relevant, the abstract was reviewed. Two independent reviewers (TP and MS) assessed the abstracts of the remaining articles and retained those that either clearly met the inclusion...
criteria or for whom the full text of the article had to be reviewed before a final decision about inclusion could be made. If either reviewer thought an article relevant, a full-text copy was obtained. A second search with the same search terms was done for the period Feb 22–Nov 30, 2011. Additional citations were identified and the titles were reviewed by two independent reviewers (TP and MS). The resulting abstracts were reviewed and articles were pulled for full text review. Full text review was completed by two independent reviewers (TP, MS, or SS). Data were extracted by two trained coders with standardised data extraction forms that included details about study design, methods of recruitment, location, sample size, reported HIV prevalence or incidence in transgender women, HIV prevalence in comparison groups (if provided), and CIs. Coders (TP, MS) showed high (90%) agreement, with discrepancies resolved through referral to a third senior study team member (SDB). Methodological quality of each study was assessed via evaluation of sampling and recruitment methods, response rates, data reporting, and information on unmeasured biases and confounders.

Meta-analysis
These methods have been described previously.7 Briefly, HIV prevalence data from different studies in transgender women were pooled and weighted by sample size for each country. The prevalence for the general population was calculated with the most recent UNAIDS estimates to assess the number of people living with HIV, aged 15 years or older, in each country as the numerator. US Census Bureau International Division was used to separately assess the total number of men and women who are aged 15 years or older and also the total number of men and women of reproductive age, or those between the ages of 15 and 49 years.7 The primary meta-analysis represents the increased odds of being HIV seropositive for transgender women compared with other people of reproductive age. However, separate analyses were also completed that compared HIV rates in transgender women with that of only men and with that of only women of reproductive age. Most infections are in people aged 15–49 years; thus, we decided to make the comparisons against people in this age range.

The meta-analysis was completed with the Mantel-Haenszel method with a random-effects model with the assumption that the HIV prevalence in one population or country was independent of the HIV prevalence in other countries. A standard correction of 0.5 is added to all zero cells by the statistical package used (STATA, version 11). Heterogeneity testing was completed with the DerSimonian and Laird Q test.7 Data are presented in forest plots including the OR, its 95% CI, and the relative weight of any particular study in estimating the summary OR for all countries.

Sensitivity analyses
Prevalent infections in transgender women comprise a portion of the prevalent infections in men and women used to characterise the denominator. Midpoint estimates of the prevalence of men who have sex with men (MSM) in the population and the prevalence of transgender women who were included in MSM estimates were obtained from Caceres and colleagues.9,10 Census data were then used to scale up these estimates to calculate the approximate number of MSM and transgender women by country.4 This estimate was then multiplied by the prevalence of HIV in transgender women in each country to approximate the number of HIV infections in each country. The Caceres method was focused on estimating the number of MSM and potentially underestimated the number of transgender women by excluding those who are not part of the MSM community (passing or post-transition transgender women who have sex with heterosexual male partners). However, these methods provided a range for the numbers of infections potentially attributable to transgender women in each of the countries studied. Meta-analyses were completed with and without these infections included as part of the background estimates.
and there was no statistical difference in view of the small proportion of males who are transgender women (data not shown).

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

Results
Figure 1 shows our study design. Across 15 countries with data that were included in this review, the pooled HIV prevalence was 19.1% (95% CI 17.4–20.7) for transgender women (table 1).11–48 In transgender women sampled in low-income and middle-income countries, HIV prevalence was 17.7% (95% CI 15.6–19.8); in high-income countries, HIV prevalence was 21.6% (18.8–24.3; table 2). The OR for infection with HIV as compared with all adults of reproductive age across all 15 countries was 48.8 (95% CI 21.2–76.3); the OR in low-income and middle-income countries was 50.0 (95% CI 26.5–94.3) and 46.3 (95% CI 30.3–70.7) in high-income countries (table 2) and was not statistically different across these strata.

All countries with studies meeting inclusion and exclusion criteria have male-predominant infections, defined as at least 50% of prevalent infections in 2009 being in men. Male predominance of HIV ranged from 59% in Brazil and Thailand to 75% in Peru. Concurrently, the HIV prevalence was higher in men of reproductive age in each of these countries than in women of reproductive age. Meta-analyses were completed to assess the measure of association between HIV in transgender women and that compared with men of reproductive age and also to women of reproductive age. Across all 15 countries, the relative odds for transgender women to have HIV compared with males was 35.5 (95% CI 23.0–54.6), whereas the odds compared with females was 78.0 (95% CI 48.7–124.8). In the five high-income countries included, the odds of transgender

<table>
<thead>
<tr>
<th>n</th>
<th>HIV prevalence in transgender women (95% CI)</th>
<th>Odds ratio (95% CI)</th>
<th>HIV prevalence in reproductive-age adults</th>
<th>HIV prevalence in reproductive-age males</th>
<th>Proportion of total HIV infections in men</th>
<th>Income level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina11–14</td>
<td>931</td>
<td>33.5% (28.3–38.8)</td>
<td>92.4 (80.6–105.8)</td>
<td>0.54%</td>
<td>0.73%</td>
<td>67.3%</td>
</tr>
<tr>
<td>Brazil15–17</td>
<td>638</td>
<td>33.1% (26.7–39.4)</td>
<td>85.3 (72.3–100.6)</td>
<td>0.58%</td>
<td>0.68%</td>
<td>59.2%</td>
</tr>
<tr>
<td>El Salvador18</td>
<td>67</td>
<td>19.4% (0.0–40.9)</td>
<td>23.2 (12.7–42.5)</td>
<td>1.03%</td>
<td>1.42%</td>
<td>65.6%</td>
</tr>
<tr>
<td>Peru19</td>
<td>450</td>
<td>28.9% (21.1–36.7)</td>
<td>84.7 (69.1–103.9)</td>
<td>0.48%</td>
<td>0.73%</td>
<td>75.3%</td>
</tr>
<tr>
<td>Uruguay20–22</td>
<td>260</td>
<td>18.8% (7.9–29.8)</td>
<td>38.3 (28.1–52.3)</td>
<td>0.60%</td>
<td>0.82%</td>
<td>67.7%</td>
</tr>
<tr>
<td>Australia23</td>
<td>133</td>
<td>4.5% (0.0–21.1)</td>
<td>24.9 (11.0–56.5)</td>
<td>0.19%</td>
<td>0.26%</td>
<td>69.0%</td>
</tr>
<tr>
<td>India24–26</td>
<td>135</td>
<td>43.7% (31.0–56.4)</td>
<td>208.0 (148.0–292.3)</td>
<td>0.37%</td>
<td>0.44%</td>
<td>61.7%</td>
</tr>
<tr>
<td>Indonesia27–29</td>
<td>1384</td>
<td>26.1% (21.6–30.6)</td>
<td>180.3 (159.9–203.3)</td>
<td>0.20%</td>
<td>0.32%</td>
<td>70.7%</td>
</tr>
<tr>
<td>Pakistan30–32</td>
<td>2643</td>
<td>2.2% (0.0–6.0)</td>
<td>21.9 (16.9–28.4)</td>
<td>0.10%</td>
<td>0.14%</td>
<td>70.5%</td>
</tr>
<tr>
<td>Thailand33–35</td>
<td>614</td>
<td>12.5% (5.1–19.9)</td>
<td>9.9 (7.8–12.6)</td>
<td>1.41%</td>
<td>1.71%</td>
<td>59.6%</td>
</tr>
<tr>
<td>Vietnam36</td>
<td>75</td>
<td>6.7% (0.0–28.5)</td>
<td>15.6 (6.3–38.8)</td>
<td>0.45%</td>
<td>0.73%</td>
<td>70.0%</td>
</tr>
<tr>
<td>Italy37–39</td>
<td>826</td>
<td>24.5% (18.5–30.4)</td>
<td>65.8 (56.1–77.1)</td>
<td>0.40%</td>
<td>0.65%</td>
<td>65.7%</td>
</tr>
<tr>
<td>Netherlands40–42</td>
<td>69</td>
<td>18.8% (0.0–40.1)</td>
<td>81.8 (44.1–149.5)</td>
<td>0.28%</td>
<td>0.39%</td>
<td>68.6%</td>
</tr>
<tr>
<td>Spain43–46</td>
<td>136</td>
<td>18.4% (3.2–33.6)</td>
<td>40.9 (26.5–63.1)</td>
<td>0.55%</td>
<td>0.81%</td>
<td>75.4%</td>
</tr>
<tr>
<td>USA47–49</td>
<td>2705</td>
<td>24.5% (18.5–30.4)</td>
<td>65.8 (56.1–77.1)</td>
<td>0.40%</td>
<td>0.65%</td>
<td>65.7%</td>
</tr>
<tr>
<td>Pooled estimate*</td>
<td>11 066</td>
<td>19.1% (17.4–20.7)</td>
<td>48.8 (31.2–76.3)</td>
<td>0.44%</td>
<td>0.58%</td>
<td>–</td>
</tr>
</tbody>
</table>

*Degrees of freedom=14, heterogeneity $I^2=98.5\%$, test of odds ratio=1, $z=16.21$, $p=0.0001$. Income level: M=middle-income; H=high-income.

Table 1: Meta-analyses of aggregate country data for HIV prevalence in transgender women versus all reproductive age adults, 2000–11

<table>
<thead>
<tr>
<th>Number of countries</th>
<th>Sample size of transgender women</th>
<th>Pooled transgender HIV prevalence (95% CI)</th>
<th>Background HIV prevalence</th>
<th>Background male HIV prevalence</th>
<th>Background female HIV prevalence</th>
<th>Pooled ORs (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low and middle income</td>
<td>10</td>
<td>7197</td>
<td>17.7% (15.6–19.8)</td>
<td>0.39%</td>
<td>0.49%</td>
<td>0.29%</td>
</tr>
<tr>
<td>High income</td>
<td>5</td>
<td>3869</td>
<td>21.6% (18.8–24.3)</td>
<td>0.69%</td>
<td>1.00%</td>
<td>0.37%</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>11 066</td>
<td>19.1% (17.4–20.7)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Table 2: Subgroup meta-analysis of pooled OR for HIV infection among transgender women by region and prevalence level
women having HIV compared with other males was 33·0 (95% CI 20·4–53·3) and with females was 79·7 (95% CI 60·0–106·0). In the ten low-income and middle-income countries included, the odds of transgender women having HIV compared with other males was 37·0 (95% CI 20·4–53·3) and compared with females was 79·7 (95% CI 60·0–106·0). In the ten low-income and middle-income countries included, the odds of transgender women having HIV compared with other males was 37·0 (95% CI 20·4–53·3) and compared with females was 79·7 (95% CI 60·0–106·0).

Discussion
Our findings suggest that transgender women are a very high burden population for HIV and are in urgent need of prevention, treatment, and care services. The findings of the meta-analysis of HIV infection rates are remarkable for the severity and consistency of disease burdens across these populations. This was true in all regions including Europe, Central and South America, Asia-Pacific, and the USA, and when stratified by income level of the country. Pooled ORs for HIV ranged from a low of 9·9 in Thailand to a high of 208·0 in India, but were consistently in the 20–90-times elevated range in most of the world (figure 2). This consistency is particularly notable in view of the wide cultural and social variability of transgender identities and communities, and of the political and legal contexts in which these communities live. How can this consistency be explained and what might these findings mean for transgender women, providers, and HIV programmes?

A primary driver of HIV infection in transgender women, similar to MSM, is the very high transmission probability of unprotected receptive anal intercourse. Since transgender women have been consistently identified as engaging in receptive anal sex with men, this biological vulnerability to HIV acquisition is undoubtedly an important factor in the high acquisition risk identified. Yet individual-level risks and sexual practices have been shown to be insufficient to explain disease burdens in other populations at high risk for HIV infection, most notably black MSM in the USA. Network level risks, particularly the HIV prevalence in subgroups, have emerged as crucial drivers of sustained HIV incidence in these populations.

This article identified data for HIV in transgender women in just 15 countries (figure 3). All these countries have predominant HIV epidemics in men, and all (except Pakistan, Vietnam, and Indonesia, which have high rates of injecting drug use, although again almost all users are men) have their highest rates of HIV infection in gay, bisexual, and other MSM. This finding too is probably important in understanding the very high rates of HIV infection in transgender women. Epidemics in transgender women happen in the wider context of high burden epidemics in men who have sex with males (irrespective of their sexual identity or partnerships with females), some of whom might also partner with transgender women. Additionally, transgender women are often included as a subgroup of MSM in epidemiological studies because many share risk behaviours with MSM, such as receptive anal intercourse, which is a much more efficient mode of HIV transmission than penile-vaginal intercourse. However, there remains a dearth of research on HIV acquisition risks from neovaginal intercourse after vaginoplasty, as well as from sex between transgender women and female partners. Transgender women in low-income countries have limited access to any types of sex-reassignment surgery. For example, even in Thailand where sex-reassignment is more accessible, only 11% of transgender women from three cities sampled had undergone surgery. Moreover, recruitment criteria for studies focused on MSM could inadvertently or inadvertently exclude transgender women because of gender identity or sexual practices. Together, these issues have complicated our understanding of epidemic transmission dynamics and prevalence estimates in these groups. A growing body of research seeks to address this by recruiting specifically transgender women.

Our analysis focused on transgender women, but there is also limited data for HIV risks in female-to-male transgender men, some of whom identify as gay and have exclusively or predominantly receptive anal sex with other men. Although transgender men have not traditionally been considered at risk for HIV, recent studies challenge this assumption. Between the years 2006 and 2010 in New York City, 11 (6%) of the 183 newly diagnosed HIV cases among transgender people were in transgender men. In a retrospective analysis of HIV status in attendees of sexually transmitted disease clinics from 2006 to 2009 in San Francisco, HIV infection rates were similar for transgender men (10%) and transgender women (11%).

The systematic review by Herbst and colleagues showed that high-risk sexual practices for HIV are common, and included unprotected receptive anal

<table>
<thead>
<tr>
<th>Weight</th>
<th>OR (95% CI)</th>
<th>Weight</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina29–34</td>
<td>93·3 (80·60–105·84)</td>
<td>Brazil26–27</td>
<td>85·29 (72·32–100·58)</td>
</tr>
<tr>
<td>El Salvador28</td>
<td>23·19 (12·65–42·49)</td>
<td>Peru20–30</td>
<td>84·73 (69·10–103·91)</td>
</tr>
<tr>
<td>Uruguay21,22</td>
<td>38·31 (28·06–52·21)</td>
<td>Vietnam24</td>
<td>34·21 (31·22–37·48)</td>
</tr>
<tr>
<td>Australia22</td>
<td>85·80 (69·10–103·91)</td>
<td>Indonesia27</td>
<td>7·02 (5·72–0·0001)</td>
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<tr>
<td>France</td>
<td>7·84 (5·72–0·0001)</td>
<td>Pakistan25–27</td>
<td>208·02 (148·06–292·27)</td>
</tr>
<tr>
<td>Thailand28</td>
<td>21·91 (16·89–28·42)</td>
<td>Russia</td>
<td>100·00 (100·00–0·0001)</td>
</tr>
<tr>
<td>USA</td>
<td>38·31 (28·06–52·21)</td>
<td>Vietnam24</td>
<td>48·78 (31·19–76·28)</td>
</tr>
</tbody>
</table>

Figure 2: Meta-analysis of risk of HIV infection in transgender women versus all adults 15–49 by country, 2000–11
intercourse and multiple sexual partners. Other individual-level risks for HIV include high rates of depression as well as risk of parenteral acquisition through illicit hormone and silicone injections. In addition to biological and network-level factors, the structural risks for HIV infection, such as social exclusion, economic marginalisation, and unmet healthcare needs, transcend the level of the individual and might also help explain why HIV rates are so high in transgender women compared with other adults. In many of the countries for which data were available, transgender women face stigma, social discrimination, and discrimination in health-care settings, which can lead to exclusion from HIV prevention and treatment services. Few health-care workers, from HIV counsellors to nurses and physicians, have received any training on addressing the specific health needs of transgender women. Consequently, consistent access to competent clinical prevention, treatment, or care services is rare, even in many high-income settings and even more so in low-income and middle-income settings. Physical and social violence targeted towards transgender women is commonly reported and might be an intermediate variable in the causal pathway towards HIV infection. Many transgender women engage in sex work and transactional sex because of employment discrimination and lack of other income opportunities. Sex work has been consistently associated with high HIV acquisition risks. And finally, transgender women have been noted to have high rates of substance use in some of the countries where data was available, including Thailand, USA, Brazil, Argentina, and Italy.

There are several limitations with the approach used for this meta-analysis. There is probably limited generalisability of pooled estimates to represent the rates of all transgender women in a country, especially in the countries where only small studies have been done. Traditional sampling methods such as time-location sampling, a method through which the study population is sampled randomly from within a sampling frame of times and venues such as brothels or clinics for sexually transmitted infections, might result in oversampling of transgender women who are sex workers or report any transactional sex or transgender women who are seeking medical care related to a sexually transmitted infection or HIV. Sampling biases could result in overestimation of the actual HIV prevalence in all transgender women in a country. To address this improved sampling frames are needed, such as is being done with the 2011 census in Nepal that allowed formal registration of third gender people. Studies have previously analysed HIV prevalence between transgender women who are sex workers and those who were not. For this article, we noted that unless the studies exclusively targeted transgender sex workers, the proportion of transgender participants with a history of sex work was often not described, rendering subgroup analysis by sex work impossible. Transgender women who have undergone medical and social transition might assimilate into the general population and not identify themselves as transgender. These women could be less...
likely to be accrued into epidemiological or prevention studies on transgender populations. Inclusion criteria requiring biological testing for HIV excluded a substantial number of studies where self-reported HIV prevalence was provided. However, in view of the low coverage of HIV testing and potential social desirability bias, objective evidence of HIV infection was deemed necessary. Thus, only data from publications and reports where methods of sampling and testing were described in detail were included in the analysis. Moreover, pooling hides the substantial intracountry spatial variation of the burden of HIV in large countries such as Brazil. Random-effects models were used to partly address the substantial heterogeneity of the HIV prevalence results included in the meta-analysis since these are studies from different populations of transgender women completed across different settings and contexts. Although a random-effects model for meta-analysis was deemed more appropriate, this approach does tend to equalise the weight of studies of different size and precision to the pooled estimate.56

In view of the limited worldwide data for transgender women and extraordinary disease burdens we have identified, the present HIV surveillance and prevention interventions for transgender women are clearly inadequate. Studies were available only in countries with male predominant epidemics probably attributable to same-sex practices among men, with no data available in generalised epidemics, including an absence of any quantitative data at all from Africa and the Pacific islands. The high burden of HIV is probably a function of both low coverage rates for effective interventions, and an insufficient range of interventions to reduce HIV infection risks for this population. Transgender-specific interventions are scarce, and no randomised trials of prevention technologies have included sufficient transgender participants to assess efficacy for these people. Consistent condom use with appropriate lubricants is an essential prevention method for anyone engaging in anal sex.57,9

Coverage of this basic intervention can be low in the lowest income settings. Acceptance and use of condoms remain challenging even where cost and access might not be barriers. The female condom could be an important alternative for transgender women, and this is an important area for acceptability research. Oral pre-exposure prophylaxis has shown efficacy in MSM for HIV prevention, and the iPrEx (Preexposure Prophylaxis Initiative) trial did include some transgender participants (in Thailand, Peru, and Brazil); therefore, this intervention could be promising.33 New interventions, most crucially a rectal microbicide that could reduce acquisition risk in anal sex, might be essential for transgender women. Inclusion of transgender women in rectal microbicide trials is arguably a research imperative for this population. Further, social and behavioural research that clarifies HIV risk contexts in this population will probably provide the link between efficacy in biomedical studies and real-world effectiveness of prevention, treatment, and care strategies. Structural change will also be essential. Transgender women and communities are emerging and advocating for their rights as citizens, and their full inclusion in the HIV response. The sexual orientation and gender identity strategy of the Global Fund is a welcome example of expanding efforts at such inclusion.80 Removing gender dysphoria/gender identity disorder from chapter 5 (mental and behavioural disorders) of the 11th International Classification of Diseases (ICD-11) could provide support for increased visibility of transgender people with less fear of being automatically labelled mentally ill. Greater visibility should be coupled with transgender people and communities having a stronger voice and be counted in national surveillance programmes and in HIV-focused research studies by disaggregating them from MSM. The findings of this meta-analysis make clear that urgency is needed to address this severe and widespread component of worldwide HIV.

Contributors
SDB, TEG, and CB devised the study design and wrote sections of the manuscript. SDB and TP developed the search protocol, which was implemented by TP, SS, and ALW. All authors contributed to the writing of the manuscript. TP, SS, and ALW abstracted data with SB acting as a tiebreaker at all stages. ALW also developed the global prevalence map.

Conflicts of interest
We declare that we have no conflicts of interest.

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References


40 Stephens SC, Bernstein KT, Philip SS. Male to female and female to transgender persons have different sexual risk behaviors yet similar rates of STDs and HIV. *AIDS Behav* 2011; 15: 683–86.


