Burden of HIV among female sex workers in low-income and middle-income countries: a systematic review and meta-analysis

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Summary

Background Female sex workers are a population who are at heightened risk of HIV infection secondary to biological, behavioural, and structural risk factors. However, three decades into the HIV pandemic, understanding of the burden of HIV among these women remains limited. We aimed to assess the burden of HIV in this population compared with that of other women of reproductive age.

Methods We searched PubMed, Embase, Global Health, SCOPUS, PsycINFO, Sociological Abstracts, CINAHL (Cumulative Index to Nursing and Allied Health Literature), Web of Science, and POPLine for studies of female sex workers in low-income and middle-income countries published between Jan 1, 2007, and June 25, 2011. Studies of any design that measured the prevalence or incidence of HIV among female sex workers, even if sex workers were not the main focus of the study, were included. Meta-analyses were done with the Mantel-Haenszel method with a random-effects model characterising an odds ratio for the prevalence of HIV among female sex workers compared with that for all women of reproductive age.

Findings Of 434 selected articles and surveillance reports, 102 were included in the analyses, representing 99 878 female sex workers in 50 countries. The overall HIV prevalence was 11·8% (95% CI 11·6–12·0) with a pooled odds ratio for HIV infection of 13·5 (95% CI 10·0–18·1) with wide intraregional ranges in the pooled HIV prevalence and odds ratios for HIV infection. In 26 countries with medium and high background HIV prevalence, 30·7% (95% CI 30·2–31·3; 8627 of 28 075) of sex workers were HIV-positive and the odds ratio for infection was 11·6 (95% CI 9·1–14·8).

Interpretation Although data characterising HIV risk among female sex workers is scarce, the burden of disease is disproportionately high. These data suggest an urgent need to scale up access to quality HIV prevention programmes. Considerations of the legal and policy environments in which sex workers operate and actions to address the important role of stigma, discrimination, and violence targeting female sex workers is needed.

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HIV infection in female sex workers varies by geographical epidemic typology, structure of sex work, and overlapping nature of HIV-risk behaviours such as injection drug use. Yet the heightened risk for HIV acquisition and transmission among sex workers operates through a similar variety of behavioural, biological or biomedical, and structural risks. Behavioural risk factors act at the level of the individual, with sex workers experiencing high-risk sexual exposures through high numbers of sexual partners and high concurrency of these partners. Biologically, the high prevalence of bacterial sexually transmitted infections (STIs) in sex workers and the synergistic relation between HIV and STIs compounds their risks and could lead to complications around reproductive health and childbearing. In some settings, protective sexual practices including consistent condom use and HIV testing are higher among sex workers than among women in the general population, although these rates remain low in many areas. HIV transmission among sex workers might also be driven, or exacerbated, by the intersection of injection drug use and sex work through increased parenteral exposures from shared injection equipment, sex with more HIV-positive partners, low condom use, and increased risk of other STIs such as syphilis and hepatitis C.

Structural risk factors indirectly heighten risk for HIV infection among sex workers by restricting access to preventive health and HIV and STI services and treatment. Structural factors also include the limiting influences of poverty, discrimination, and gender inequality as well as the damaging effects of physical and sexual violence, stigma, and social exclusion. Finally, structural factors such as the organisation and power dynamics of sex work and legal and regulatory policies regarding sex work have also been shown to contribute to sex workers’ increased risk of HIV infection by limiting their ability to negotiate safer sex. Health enabling environments, including safer work spaces, structural support for condom promotion and distribution, and community empowerment for sex workers have been shown to reduce structural risks for HIV infection.

Interventions targeting behavioural and structural-level risk factors for HIV among sex workers have proven successful for increasing protective behaviours and decreasing HIV and STI transmission. In fact, 44 of 87 countries with available data report that over 80% of sex workers used condoms with their last client. Despite these promising results and increasing number of initiatives, UNAIDS estimates that less than 50% of sex workers worldwide are covered by ongoing HIV prevention programmes. In view of this urgent need for HIV prevention and treatment among sex workers, there is still a lack of crucial information to guide global resource investment because most meta-analyses are limited to a single country or area. Systematic reviews and meta-analyses have been undertaken in other populations who are most at risk, including MSM and people who use drugs, to better characterise the relative burden of HIV to background rates. To date, however, such a review has not been completed for female sex workers, which is needed to better characterise the relative level of HIV risk among these women and to guide the allocation of resources and content of HIV prevention programmes and policies. The aim of this study is to characterise current burdens of HIV in female sex workers.

Methods

Search strategy and selection criteria

We searched PubMed, EMBASE, Global Health, SCOPUS, PsycINFO, Sociological Abstracts, CINAHL (Cumulative Index to Nursing and Allied Health Literature), Web of Science, and POPLine for studies published between Jan 1, 2007, and June 25, 2011. Articles and citations were downloaded, organised, and reviewed using the QUOSA information management software package (version 8.05) and EndNote (version X4). The search included MeSH terms for HIV or AIDS, and terms associated with sex work (prostitute [MeSH] or “sex work” or “female sex worker” or “commercial sex worker”). Other data sources included national surveillance system data reports, including AIDS indicator surveys, demographic health surveys, and integrated biobehavioral surveillance studies done by large international non-governmental organisations. Governmental surveillance reports were searched, including those from EuroHIV surveillance, US Centers for Disease Control and Prevention, Australian Surveillance Reports, Public Health Agency of Canada, Pan American Health Organization, and structured government-sponsored surveillance assessments from Asia. Expert researchers were contacted to identify unpublished or in-press data not identified through other search methods, although data were only included if the studies met all inclusion criteria.

Studies of any design were included that measured the prevalence or incidence of HIV among female sex workers, even if sex workers were not the main focus of the study. Studies were accepted if clear descriptions of HIV testing methods were included such as laboratory-derived HIV status with biological samples from blood, urine, or oral specimens. Only studies from countries defined as low income or middle income on the basis of The World Bank Atlas Method including all countries with a gross national income of US$12,275 per head or less were included. To be included, clear descriptions of the sampling, HIV testing, and analytical methods were required with sources including peer-reviewed journals and non-peer-reviewed publications meeting other criteria with online availability in the public domain. Studies published in English, French, Spanish, or Portuguese were included.
Studies were excluded if the sample size of female sex workers was less than 50 in a study including other populations or if the total sample size was less than 50 in studies that only included female sex workers. Additionally, studies that only included self-reported HIV status rather than biological testing were excluded from the analysis.

**Screening and data extraction**

All publications were originally screened by two independent reviewers (KM and TP) to include those that potentially included data about HIV prevalence, were not included in duplicate, and originated from low-income or middle-income countries. If either author classed a publication as relevant, the abstract was reviewed. Two independent reviewers (KM and TP) examined 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 author classed an article as relevant, a full-text copy was obtained. Review of these full-text articles was done by two independent reviewers (KM and TP). Subsequently, data were extracted by two trained coders with standardised data extraction forms that included details about study design, methods of recruitment, location, sample size, period of study, reported HIV prevalence, incidence, or both among female sex workers, HIV prevalence among comparison groups (if provided), and 95% CIs. Coders showed high agreement (90%), with discrepancies resolved through referral to a third senior study team member (SB).

**Methodological quality of each study was determined via assessment of sampling and recruitment methods, response rates, data reporting, and information about unmeasured biases and confounders.**

**Statistical analysis**

The prevalence for all reproductive age women in the general population was calculated using 2009 data from the UNAIDS report to assess the number of women, aged 15 years or older, living with HIV in each country as the numerator. The denominator used to measure HIV prevalence among women in the general population was assessed in two ways: data from the US Census Bureau International Division was used to assess the total number of women who were aged 15 years or older and also the total number of women of reproductive age, or those between the ages of 15 and 49 years. The meta-analysis represents the increased odds of being HIV seropositive for female sex workers compared with all women; it was completed with the Mantel-Haenszel method with a random-effects model with the assumption that the HIV prevalence in one country was independent of the HIV prevalence in other countries. A standard correction of 0·5 was added to all zero cells with STATA (version 11). Heterogeneity testing was done with the DerSimonian and Laird’s Q test. The data are presented in the form of forest plots including the odds ratio, its 95% CI, and the relative weight of any particular study in estimating the summary odds ratio for all countries.

Meta-analyses of subgroups of countries by prevalence level and region were also done. The following categorisation scheme classed the HIV prevalence among women of reproductive age or those aged 15–49 years as very low prevalence (<0·5% living with HIV), low prevalence (0·5–1·0%), medium prevalence (1·1–5·0%), and high prevalence (>5%).

A similar approach was used for systematic review of MSM in low-income and middle-income countries. As a sensitivity analysis, we used the two different aforementioned calculated background rates. No significant difference was detected between estimates calculated with these two methods. However, since women older than 49 years of age contribute relatively few infections in most low-income and middle-income countries, use of the background rate calculated with the numerator for women older than 15 years of age and the denominator for those aged between 15 and 49 years was deemed to be a more conservative approach. As of 2009, UNAIDS did not produce estimates of the number of people living with HIV in Afghanistan, Laos, and Albania and thus these countries were excluded from the meta-analysis.
To quantify the number of infections among women of reproductive age attributable to infections among female sex workers, estimates of HIV prevalence among female sex workers by country and region characterised primarily by Vandepitte and colleagues were used unless more recent data were available. When an estimate of the total number of female sex workers by country was available this estimate was used; otherwise a regional estimate was used. In each case, the lowest estimate in the range provided was used to be conservative. To complete the meta-analysis, we used estimates of the proportion of HIV cases among women attributable to female sex workers, by country.

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
Our search criteria identified 19 180 citations, of which

<table>
<thead>
<tr>
<th>Sample size</th>
<th>HIV prevalence among female sex workers (95% CI)</th>
<th>HIV prevalence among female population</th>
<th>Odds ratio (95% CI)</th>
<th>Prevalence level*</th>
<th>% HIV infections among female sex workers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Afghanistan</td>
<td>544</td>
<td>0.2% (0.0-0.5)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>9383</td>
<td>0.2% (0.1-0.3)</td>
<td>0.00%</td>
<td>47.8 (30.8-74.3)</td>
<td>Very low</td>
</tr>
<tr>
<td>Cambodia</td>
<td>160</td>
<td>0.2% (0.1-0.3)</td>
<td>0.06%</td>
<td>34.8 (24.1-50.3)</td>
<td>Low</td>
</tr>
<tr>
<td>China</td>
<td>18 177</td>
<td>0.2% (0.1-0.3)</td>
<td>0.06%</td>
<td>50.0 (46.0-54.4)</td>
<td>Very low</td>
</tr>
<tr>
<td>India</td>
<td>13 186</td>
<td>0.2% (0.1-0.3)</td>
<td>0.06%</td>
<td>54.3 (51.7-57.0)</td>
<td>Very low</td>
</tr>
<tr>
<td>Indonesia</td>
<td>7482</td>
<td>0.4% (0.4-0.5)</td>
<td>0.14%</td>
<td>38.0 (34.2-42.2)</td>
<td>Very low</td>
</tr>
<tr>
<td>Laos</td>
<td>1422</td>
<td>0.5% (0.1-0.9)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Malaysia</td>
<td>552</td>
<td>0.7% (0.8-1.3)</td>
<td>0.15%</td>
<td>81.2 (62.0-106.5)</td>
<td>Very low</td>
</tr>
<tr>
<td>Mongolia</td>
<td>931</td>
<td>0.00% (0.0-0.0)</td>
<td>0.02%</td>
<td>2.4 (0.2-39.3)</td>
<td>Very low</td>
</tr>
<tr>
<td>Nepal</td>
<td>1687</td>
<td>8.3% (7.0-9.6)</td>
<td>0.26%</td>
<td>35.0 (29.4-41.6)</td>
<td>Very low</td>
</tr>
<tr>
<td>Pakistan</td>
<td>5999</td>
<td>0.1% (0.0-0.1)</td>
<td>0.06%</td>
<td>0.8 (0.3-2.5)</td>
<td>Very low</td>
</tr>
<tr>
<td>Papua New Guinea</td>
<td>205</td>
<td>16.6% (11.5-21.7)</td>
<td>1.20%</td>
<td>16.1 (10.1-25.7)</td>
<td>Medium</td>
</tr>
<tr>
<td>Thailand</td>
<td>319</td>
<td>11.9% (8.4-15.5)</td>
<td>1.15%</td>
<td>11.6 (8.3-16.3)</td>
<td>Medium</td>
</tr>
<tr>
<td>Vietnam</td>
<td>3381</td>
<td>6.5% (5.7-7.3)</td>
<td>0.32%</td>
<td>22.0 (19.2-25.2)</td>
<td>Very low</td>
</tr>
<tr>
<td>Eastern Europe</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albania</td>
<td>92</td>
<td>1.1% (0.0-3.2)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Estonia</td>
<td>433</td>
<td>8.1% (5.5-10.7)</td>
<td>0.95%</td>
<td>9.1 (6.5-12.9)</td>
<td>Low</td>
</tr>
<tr>
<td>Georgia</td>
<td>234</td>
<td>0.4% (0.0-1.3)</td>
<td>0.13%</td>
<td>3.3 (0.5-23.8)</td>
<td>Very low</td>
</tr>
<tr>
<td>Ukraine</td>
<td>2278</td>
<td>12.9% (11.5-14.3)</td>
<td>1.46%</td>
<td>10.0 (8.9-11.3)</td>
<td>Medium</td>
</tr>
<tr>
<td>Latin America and the Caribbean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Argentina</td>
<td>625</td>
<td>3.2% (1.8-4.6)</td>
<td>0.34%</td>
<td>9.6 (6.1-15.0)</td>
<td>Very low</td>
</tr>
<tr>
<td>Brazil</td>
<td>90</td>
<td>6.7% (5.5-11.8)</td>
<td>0.47%</td>
<td>15.3 (6.7-34.9)</td>
<td>Very low</td>
</tr>
<tr>
<td>Chile</td>
<td>626</td>
<td>0.00% (0.0-0.0)</td>
<td>0.27%</td>
<td>0.3 (0.02-4.6)</td>
<td>Very low</td>
</tr>
<tr>
<td>Guatemala</td>
<td>1110</td>
<td>4.4% (3.2-5.6)</td>
<td>0.58%</td>
<td>7.9 (5.9-10.5)</td>
<td>Low</td>
</tr>
<tr>
<td>El Salvador</td>
<td>484</td>
<td>3.3% (1.7-4.9)</td>
<td>0.67%</td>
<td>5.1 (3.1-8.3)</td>
<td>Low</td>
</tr>
<tr>
<td>Guyana</td>
<td>450</td>
<td>27.6% (23.4-31.7)</td>
<td>1.48%</td>
<td>25.3 (20.5-31.2)</td>
<td>Medium</td>
</tr>
<tr>
<td>Honduras</td>
<td>493</td>
<td>9.7% (7.1-12.4)</td>
<td>0.59%</td>
<td>18.1 (13.5-24.5)</td>
<td>Low</td>
</tr>
<tr>
<td>Jamaica</td>
<td>433</td>
<td>8.8% (6.1-11.4)</td>
<td>1.31%</td>
<td>7.3 (5.2-10.1)</td>
<td>Medium</td>
</tr>
<tr>
<td>Mexico</td>
<td>4742</td>
<td>6.2% (5.6-6.9)</td>
<td>0.19%</td>
<td>35.0 (21.1-39.4)</td>
<td>Very low</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>460</td>
<td>2.2% (0.8-3.5)</td>
<td>0.13%</td>
<td>16.8 (8.9-31.4)</td>
<td>Very low</td>
</tr>
<tr>
<td>Paraguay</td>
<td>723</td>
<td>2.8% (1.6-4.0)</td>
<td>0.22%</td>
<td>12.8 (8.2-19.9)</td>
<td>Very low</td>
</tr>
<tr>
<td>Middle East and north Africa</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egypt</td>
<td>118</td>
<td>0.8% (0.0-2.5)</td>
<td>0.01%</td>
<td>73.2 (10.2-524.1)</td>
<td>Very low</td>
</tr>
<tr>
<td>Lebanon</td>
<td>96</td>
<td>0.00% (0.0-0.0)</td>
<td>0.10%</td>
<td>5.4 (0.34-87.5)</td>
<td>Very low</td>
</tr>
<tr>
<td>Somalia</td>
<td>237</td>
<td>5.5% (2.6-8.4)</td>
<td>0.67%</td>
<td>8.6 (4.9-15.0)</td>
<td>Low</td>
</tr>
<tr>
<td>Sudan</td>
<td>321</td>
<td>0.9% (0.0-2.0)</td>
<td>1.32%</td>
<td>0.7 (0.2-2.2)</td>
<td>Medium</td>
</tr>
<tr>
<td>Tunisia</td>
<td>188</td>
<td>0.00% (0.0-0.0)</td>
<td>0.03%</td>
<td>8.0 (0.5-128.7)</td>
<td>Very low</td>
</tr>
</tbody>
</table>

(Continues on next page)
2240 were unique records (figure 1). Of 434 selected articles and surveillance reports, data from 102 met inclusion criteria. These studies included 91 articles and 11 surveillance reports representing 99 878 female sex workers in 50 countries: 14 countries in Asia, four in the eastern Europe, 11 in Latin America and the Caribbean, five in the Middle East and north Africa, and 16 countries in sub-Saharan Africa (figure 1, table 1).

The overall HIV prevalence among female sex workers in all regions was 11.8% (95% CI 11.6–12.0; table 1) with notable variation by region, reflective of background rates of HIV. The highest prevalence of HIV was in sub-Saharan Africa, followed by eastern Europe, Latin America and the Caribbean, and Asia; the lowest rate was in the Middle East and north Africa (table 2).

The overall estimate for the odds ratio for a female sex worker to be living with HIV compared with all women of reproductive age in low-income and middle-income countries was 13.5 (95% CI 10.0–18.1; table 2).
countries was 13·5 (95% CI 10·0–18·1; table 2). The highest pooled odds ratio for HIV infection among sex workers was seen in Asia, followed by sub-Saharan Africa. The lowest odds ratio was seen in Latin America and the Caribbean (table 2). Sex workers from countries with very low or low HIV prevalence had higher odds of infection than did sex workers from countries with medium or high HIV prevalence among all women (figures 2, 3).

Sensitivity analyses compared whether there would be a difference in odds ratio when comparing the HIV prevalence rates among female sex workers with that of all women, including sex workers, or comparing them with women who do not sell sex. Globally, no substantially different magnitude in the ratio between these two scenarios was seen. However, in China, India, Malaysia, Egypt, and Rwanda a substantial increase was reported in the odds ratio of HIV infection among female sex workers when compared with women who do not sell sex rather than all women of reproductive age. In each of these countries, more than 20% of prevalent HIV infections among women were attributable to female sex workers (table 1). To be conservative, the odds ratios we report refer to the comparison of female sex workers with that of all women of reproductive age, including female sex workers.

**Discussion**

We identified consistent evidence of substantially higher levels of HIV among female sex workers compared with all women of reproductive age in low-income and middle-income countries in all regions with data. Although female sex workers have long been understood to be a key affected population, the scope and breadth of their disproportionate risk for HIV infection had to date not been systematically documented.

The largest sample size was available from Asia (table 1), where we reported the highest relative burden of disease (table 2). While some countries such as Thailand showed a trend towards higher prevalence in the 1990s, surveillance data have shown an increasingly concentrated HIV epidemic in populations who are most at risk. Responses such as the 100% condom campaign have been heralded as successes, though HIV prevalence has remained higher than 10% among female sex workers and the odds of infection remain ten-times higher than that of all Thai women, suggesting the need for complementary HIV prevention strategies including biomedical approaches, such as oral or topical chemoprophylaxis or treatment as prevention, and structural approaches. In India, the Avahan and Sonagachi combination HIV prevention programmes have had many targets such as addressing structural issues, including community empowerment, campaigns to address stigma, and structural policy support, as well as targeting high-risk sexual practices by increasing condom use during sex. Both programmes have been deemed to be successes and are being scaled up across the country. When reviewing the data from the past 5 years, female sex workers still carry more than a 50-times increased odds of HIV infection in India. Since HIV prevalence is a lagging indicator of substance use trends, time is needed to reveal the benefit of these programmes in terms of the absolute burden of HIV among female sex workers in India. Nonetheless, the disproportionate burden of HIV among these sex workers, even in settings where progressive

![Figure 2: Forest plot showing meta-analysis of risk of HIV infection among female sex workers compared with women aged 15-49 years in low-income and middle-income countries, 2007-11](image-url)
programmes exist, emphasises the need to increase coverage by increasing scale of prevention programmes and decreasing barriers to access.

HIV in Latin America and the Caribbean has remained a disease mostly concentrated among populations who are most at risk since the beginning of the epidemic.\textsuperscript{149} With low background prevalence and early recognition of the high risk among sex workers in Latin America and the Caribbean, HIV prevalence has a limited magnitude among sex workers in the region. Brazil famously declined USAID funding over the need to sign the “Prostitution Pledge”, which was mandated as part of the President’s Emergency Plan for AIDS Relief (PEPFAR) in 2003, and would have limited the ability to do comprehensive surveillance and service provision for sex workers.\textsuperscript{150,151} Consequently, Brazil has continued to invest in HIV prevention for sex workers throughout the country.\textsuperscript{152} In these analyses, Guyana was an anomaly in that female sex workers had more than 25-times increased odds of HIV infection. These analyses show that the HIV epidemic among female sex workers in Latin American and the Caribbean is not over, because these women have more than ten-times increased odds of having HIV than other women.

Sufficient data were not available to warrant meta-analyses of HIV prevalence among female sex workers in eastern Europe and the Middle East and north Africa. Most data in eastern Europe was derived from Ukraine, and in the Middle East and north Africa the combined data from the studies represented less than a thousand sex workers. The studies that have been done in these regions show that sex workers exist and that prevalence of HIV, although low in these settings, is concentrated among these women. In view of the importance of parenteral transmission of HIV through injection drug use in eastern Europe, characterisation of the synergies between epidemics of injection drug use and injection drug use among female sex workers in this region is important to guide prevention.

While wide variation in the prevalence of HIV exists across western, eastern, and southern Africa, the prevalence of HIV among female sex workers is high in each of these regions (table 1). Variation in the relative odds of infection among these women seems to be largely attributable to high background rates of HIV prevalence among all adults in hyperendemic zones, especially in southern regions of Africa. According to UNAIDS criteria, these countries have generalised epidemics because the HIV prevalence among women of reproductive age (as measured in antenatal clinics) is higher than 1%. Application of the system used by Stover and colleagues\textsuperscript{154} showed that these prevalence levels correspond to medium-prevalence and high-prevalence HIV epidemics. Overall, even in generalised epidemics in sub-Saharan Africa, female sex workers have more than 12-times increased odds of living with HIV as compared with all women. Similarly, in other medium and high HIV-prevalence settings, or generalised HIV epidemics, the odds ratio for HIV infection was high. These findings counter the notion that female sex workers play a less relevant part in the transmission of HIV in generalised epidemics.

The largest body of data about HIV prevalence among female sex workers in Africa was available from Kenya where in 2010, the Kenyan National AIDS and STI Control Program (NASCOP) developed a set of National Guidelines for HIV and STI Programmes for sex workers.\textsuperscript{155} These guidelines were developed in response to the Kenya National HIV Strategic Plan (KNASP III) 2009–13, which identified that female sex workers were a population who are most at risk and that barriers existed that limited their access to health and social services.

![Figure 3: Map of HIV prevalence among female sex workers in low-income and middle-income countries including data from 2007–11, categorised by HIV prevalence and pooled HIV prevalence estimates by region](image)
because some of their work is both criminalised and stigmatised by society. Encouragingly, incidence rates of HIV have been decreasing among some groups of female sex workers in Kenya, signalling decreasing HIV incidence in the general population.

In Pakistan, Chile, and Sudan the odds ratio for HIV associated with sex work suggested a trend towards this practice being protective, though this trend was not significant in any of these countries. Moreover, in Mongolia and Madagascar, the odds ratio for HIV among female sex workers was also not significantly increased. These results are likely to have some combination of truth and artefact. Non-probability samples of female sex workers could have underestimated the actual HIV prevalence in the population. However, in each of these countries except for Sudan, most prevalent HIV infections in 2009 were among men with risk factors including same-sex practices and injecting drug use. In Sudan, competing risk factors exist for HIV including migration and rape, which might, in part, account for these results.

Our study had several limitations. The focus on data from the past 5 years with an inclusion criterion of January, 2007, excluded data from many countries. While this exclusion represents a limitation, the aim of this study was to characterise current burdens of HIV in female sex workers. Any pooling of data comes at the risk of masking intra-country and inter-country variations in the risk status, including practices and HIV prevalence, and variations in the social contexts of female sex workers. Such masking in the variation of risk status is relevant in India and China, which have wide geographical variations in HIV prevalence and risk factors for HIV infection. Furthermore, these estimates are of limited generalisability since most studies were done in urban settings; female sex workers working in more rural settings, border areas, and truck stops were under-represented. The pooled estimates also mask differences between various contexts in which sex work is practised including establishment-based versus non-establishment-based sex work or additional risk factors among sex workers including injecting drug use and migration. There was significant heterogeneity of the HIV-prevalence results included in the meta-analysis, because these studies were from different populations of female sex workers in different countries. To account for this difference, a random-effects model was used for the meta-analysis.

The comparison of HIV prevalence rates among female sex workers and all women was conservative since HIV infections were included in the estimates provided by UNAIDS for all women of reproductive age. To address this issue, a sensitivity analysis was done to account for prevalent infections among women of reproductive age attributable to female sex workers, after which we undertook the meta-analysis. The size of the global pooled estimate did not change though it did change in certain countries where a high proportion of HIV in women is attributable to sex work. While the pooled analysis is limited in relation to the heterogeneity estimates by country, it does show the continued disease burden among female sex workers, and their continued need for services. A recent report on the investment framework for the global response to HIV/AIDS suggested that current allocation of resources for sex workers was adequate. This analysis, contextualised by evidence that female sex workers living with HIV have more sexual partners than other women of reproductive age living with HIV and have higher rates of STIs facilitating HIV transmission, suggests that more resources are needed to address these subepidemics.

This report shows that 50 of 145 low-income and middle-income countries have published data for the past 5 years that include biological assessments of HIV prevalence among female sex workers (figure 3). In other words, about two-thirds of low-income and middle-income countries do not have a current estimate of the burden of HIV in this population. Possible explanations for these gaps in the data include social stigma, criminalisation of sex work, and the “Prostitution Pledge”, which conflated the issue of sex work and human trafficking and substantially reduced research funding and investigator interest in this area.

These findings suggest an urgent need to scale up access to quality HIV-prevention programming and services among female sex workers because of their heightened burden of disease and likelihood of onward transmission through high numbers of sexual partners as clients. In view of the high burden of HIV among female sex workers and recent biomedical advances related to treatment as prevention, improvement of linkages to antiretroviral treatment, and retention in care, ongoing prevention for sex workers already living with HIV is crucial. The substantially increased odds of living with HIV among sex workers merits continued research regarding the role of not only behavioural but also structural factors associated with HIV in this population. Considerations of the legal and policy environments in which sex workers operate, and the important role of stigma, discrimination, and violence targeting female sex workers globally will be required to reduce the disproportionate disease burden among these women.

Contributors
SB, DK, and CB designed the study. SB and TP developed and implemented the search protocol. KM, AW, and TP abstracted data with SB acting as a tiebreaker at all stages. ALW developed the global prevalence map. MRD and SGS provided technical support at all stages. All authors wrote the report.

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

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References


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by the candidate vaccine protect against different HIV-1 clades (the RV1 44 trial was done in a clade E population, whereas most infections in sub-Saharan Africa are caused by clade C viruses)? What were the contributions of the RV 144 prime (ALVAC) and boost (AIDSVAX) to the reported protection? Can specific immune responses that correlate with protection be identified? Can the protective immune responses be enhanced to increase the strength and duration of vaccine-induced protection? Answers will come only from a rational and systematic research agenda that should include basic research, non-human-primate studies, phase 1 safety and immunogenicity trials of so-called improved vaccines, and carefully planned large-scale phase 2b efficacy trials.

Although the ALVAC-AIDSVAX prime-boost regimen resulted in slight protection in RV 144, two different versions of AIDSVAX alone did not protect against HIV infection when tested in injecting drug users in Bangkok,⁴ or in men who have sex with men in North America and Europe.⁵ Was the partial success of RV 144 because of the inclusion of the ALVAC prime (perhaps by induction of a different immune profile from that induced by immunisation with AIDSVAX alone), or was it because the study was done in a different population with low risk of HIV infection and reduced behavioural exposure to the virus?

Immune correlate studies such as that published by Haynes and colleagues⁴ could provide some answers. This case-control study generated the hypothesis that antibodies against the V1V2 region of glycoprotein 120 might have contributed to protection against HIV infection in RV 144, whereas high concentrations of IgA antibodies against glycoprotein 120 could have mitigated the effect of the protective antibodies. If these immune correlates are validated at least for this vaccine, they could guide the design of a new generation of vaccines with better efficacy and longevity. The short duration of protective immunity noted in RV 144—an issue also reported with non-HIV vaccines such as the cholera vaccine⁶—could be addressed with the use of adjuvants or boosters, or by basic research about the mechanisms of vaccine-induced immunological memory.⁷

Robb and colleagues’ work is important, not only because it strengthens the original findings from the RV 144 trial, but also because it identifies important variables to be considered when planning for and doing subsequent trials to confirm and explore the results of RV 144.

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# The politics and policies of HIV prevention in sex work

Decades into the HIV epidemic, we know surprisingly little about the relative burden of HIV among sex workers. UNAIDS estimates that less than 50% of sex workers have access to HIV prevention programmes worldwide.¹ HIV prevalence among sex workers is highly heterogeneous both across and within regions. In addition to individual and biological drivers (eg, the epidemic structure, co-infection with other sexually transmitted infections [STIs], and antiretroviral therapy [ART] coverage), structural features continue to play a crucial part in shaping risk of infection among sex workers and their clients, including work environment, violence, stigma, and the legal, cultural, and political contexts of sex work.²,³
In *The Lancet Infectious Diseases*, Stefan Baral and colleagues report a systematic review and meta-analysis of HIV burden among female sex workers in 50 low-income and middle-income countries. Female sex workers had an overall increased odds of HIV infection (odds ratio 13·5, 95% CI 10·0–18·1) relative to the general female population of reproductive age, with the highest odds in Asia (29·2, 95% CI 22·2–38·4) and lowest in Latin America and the Caribbean (12·0, 95% 7·3–19·7). Baral and colleagues show substantially high HIV prevalence levels across geographical regions and epidemic structures, including both concentrated epidemics and mature, generalised epidemics, as in sub-Saharan Africa where the pooled HIV prevalence was 36-9% (95% CI 36·2–37·5).

The heavy HIV burden points to the crucial need for urgent scale-up of comprehensive initiatives simultaneously targeting HIV prevention, ART access, and care among female sex workers, especially in view of the established role of treatment as prevention. Of concern, two-thirds of countries have no data on HIV burden in this group. As Baral and colleagues suggest, the dearth of data can be attributed in large part to the same structural barriers that increase risk of HIV and prevent engagement in interventions among female sex workers, including criminalised legal and policy environments, violence, stigma, and restrictive funding policies.

All too often moral debates dominate the public health response among sex workers, and science continues to take a backseat to punitive approaches and raid and rescue operations aimed at eliminating sex work. The US antiprostitution pledge enacted in 2003 continues to take a backseat to punitive approaches (eg, police crackdowns, raids), punitive sanctions, and the threat of violence can deter sex workers from accessing HIV prevention services, constrain their ability to negotiate condom use, and prevent the roll-out and rigorous assessment of HIV interventions.

Individual country and programme successes have made important progress regionally, but for the most part have not been met with global backing from international and governmental bodies, and face the same structural barriers to large-scale implementation and rigorous assessment. A systematic review of HIV and STI intervention studies among female sex workers in low-resource settings showed significant use of multicomponent and structural interventions (policy change and sex-work collectivisation), with only modest effects reported for behavioural interventions alone. Multipronged HIV-prevention strategies have been adopted in several countries (eg, safer sex-work environments), with the most well documented structural HIV interventions being those led by sex workers in India (Songachi and Avahan models).

The results stand as an important marker of the sheer scale of the HIV epidemic among female sex workers worldwide, and a call to action, both for investment in science and scale-up of evidence-based HIV-prevention interventions. With efforts to better characterise the epidemic in sex work and the response to it, research and interventions among the male client population and other subpopulations of sex workers (eg, male and transgender sex workers, migrant workers) are also crucial. As the epidemic matures in many settings, with some countries already reporting over 50% of sex workers living with HIV, comprehensive initiatives simultaneously targeting HIV prevention, ART access, and care are increasingly vital. As highlighted in a recent report by the UNAIDS advisory on sex work and HIV, removal of structural barriers (eg, criminalised laws and policies, violence) remains a necessary precondition to an effective HIV response in sex work worldwide.

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Linezolid for multidrug-resistant tuberculosis

Despite moderate early bactericidal activity and restricted activity in the murine model, linezolid has been used to treat fluoroquinolone-resistant multidrug-resistant (MDR) tuberculosis and extensively drug-resistant (XDR) tuberculosis with clinical improvement. Singla and colleagues reported unsupervised use of generic linezolid at 600 mg once or twice daily in 16 patients with XDR tuberculosis and 13 fluoroquinolone-resistant patients with MDR tuberculosis. With 90% of patients achieving sputum smear and culture conversion, and 72% attaining interim favourable outcome, the investigators concluded that linezolid was effective, cheap, and fairly safe for patients in India who had MDR-tuberculosis treatment failure. Although the reported rates of favourable outcome and major adverse events were comparable to those in two moderately large case series, the study should be interpreted with caution. The findings were uncontrolled, based on a small selected sample, interim with no definitive treatment outcomes, unsubstantiated by pharmacokinetic data, assessed without drug susceptibility testing of linezolid, and possibly confounded by linezolid of uncertain quality and unascertainable treatment adherence. Linezolid-resistant isolates of *Mycobacterium tuberculosis* have already emerged, and the optimum linezolid dosage to treat MDR tuberculosis is unknown. With no controlled trials, base therapy on anecdotal treatment successes with linezolid could be dangerous.

Since the advent of chemotherapy, the battle against tuberculosis has been haunted by the emergence of drug resistance. Use of streptomycin monotherapy to treat tuberculosis has shown that combination drug treatment is necessary to prevent the emergence of drug resistance and to ensure treatment success, irrespective of the antituberculosis activity of a drug. Linezolid-resistant tuberculosis, like other forms of drug-resistant tuberculosis, is a man-made problem that is associated with unreliable drug supply, erratic bioavailability, suboptimum prescription, and poor adherence to treatment. The activity of linezolid in the treatment of MDR tuberculosis will determine how quickly it can select out linezolid-resistant strains. Furthermore, because linezolid can have serious toxic effects after prolonged administration, treatment can easily be interrupted because of adverse reactions, thereby rendering the treatment regimen ineffective. Besides treatment failure, acquired drug resistance to both linezolid and remaining second-line drugs might develop and propagate within the community. In view of the unpredictable nature of treatment adherence, and the association between treatment-related side-effects and treatment default, programmatic management should use directly observed treatment plus reliable facilities for drug susceptibility testing to prevent the loss of linezolid and other drugs in our armamentarium, notably, newer-generation fluoroquinolones and second-line injectable drugs. Additionally, quality assurance is needed to ensure that patients receive drugs of internationally recognised standards. Political commitment to elimination of tuberculosis will help defray costs when potentially useful drugs are unaffordable.

Linezolid has been used at different dosing schedules to treat MDR tuberculosis, but the optimum dosage is unknown. Treatment with linezolid 600 mg twice daily for longer than 2–4 weeks is associated with reversible haemopoietic suppression and a high frequency of peripheral neuropathy. A small retrospective study suggested similar treatment effectiveness between linezolid 600 mg twice daily and once daily, but significantly fewer adverse events with the once-daily