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Syphilis in Drug Users in Low and Middle Income Countries

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Abstract

Background—Genital ulcer disease (GUD), including syphilis, is an important cause of morbidity in low and middle income (LMI) countries and syphilis transmission is associated with HIV transmission.

Methods—We conducted a literature review to evaluate syphilis infection among drug users in LMI countries for the period 1995–2007. Countries were categorized using the World Bank Atlas method (The World Bank, 2007) according to 2006 gross national income per capita.

Results—Thirty-two studies were included (N=13,848 subjects), mostly from Southeast Asia with some from Latin America, Eastern Europe, Central and East Asia, North Africa and the Middle East but none from regions such as Sub-Saharan Africa. The median prevalence of overall lifetime syphilis (N=32 studies) was 11.1% (interquartile range: 6.3% to 15.3%) and of HIV (N=31 studies) was 1.1% (interquartile range: 0.22% to 5.50%). There was a modest relation (r=0.27) between HIV and syphilis prevalence. Median syphilis prevalence by gender was 4.0% (interquartile range: 3.4% to 6.6%) among males (N=11 studies) and 19.9% (interquartile range: 11.4% to 36.0%) among females (N=6 studies). There was a strong relation (r= 0.68) between syphilis prevalence and female gender that may be related to female sex work.

Conclusion—Drug users in LMI countries have a high prevalence of syphilis but data are limited and, in some regions, entirely lacking. Further data are needed, including studies targeting the risks of women. Interventions to promote safer sex, testing, counseling and education, as well as health care worker awareness, should be integrated in harm reduction programs and health care settings to prevent new syphilis infections and reduce HIV transmission among drug users and their partners in LMI countries.

Keywords

syphilis; genital ulcer disease; drug user; sexual risk behaviors; HIV; developing countries

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Introduction

There is a long-standing relationship between sexually transmitted infections (STIs) and illicit drug use. Up to 60% of injection drug users (IDUs) report histories of STIs (Nelson et al., 1991) and high rates are also seen among non-injection drug users (NIDUs), such as users of crack cocaine (Ross et al., 2002). STIs, including syphilis, have been shown to be independent risk factors for the sexual transmission of human immunodeficiency virus (HIV) (Lyles et al., 2007; Buchacz et al., 2005; Phipps et al., 2005; Browne et al., 2003; Harrell et al., 2003; Kalichman et al., 2000; Greenblatt et al., 1988). Additionally, untreated STIs can cause infertility, debilitating illness and death. Unlike HIV, many STIs can be easily treated and cured if diagnosed.

There are substantial gaps in our understanding of global syphilis epidemiology. Worldwide, there were 11.76 million reported new cases of syphilis in 1999 (World Health Organization, 2001) as shown in Table 1, the most recent year in which aggregate data are available. Drug users are an important target group for the prevention of both syphilis and HIV due primarily to frequent high-risk sexual behaviors, including commercial sex work to obtain money for drugs. In addition, drug users that have non-drug using sex partners often constitute a “bridge group”, through which they may facilitate the spread of STIs to non-drug using populations (Strathdee et al., 2008; Steinbrook et al., 2007; Liu et al., 2006; Ruan et al, 2006; Hahn et al., 1989). Despite having a high prevalence and incidence of STIs internationally, drug users can be a difficult-to-reach population who may be incompletely or inconsistently engaged in longitudinal or preventive health care, and for whom adherence to therapeutic interventions can be problematic.

We conducted a review of literature summarizing syphilis prevalence and associated factors among drug users in LMI countries to document syphilis prevalence and to explore related risk factors. Knowledge of these risk factors can be used to facilitate the development of targeted and effective interventions to reduce risky sexual and drug related behaviors and encourage early and effective treatment.

Methods

Searches of literature published from January 1995 to May 2007 were conducted via a PubMed portal on NCBI Entrez Databases. The following search terms were used: (Syphilis OR Treponema pallidum) AND (intravenous drug use OR intravenous drug abuse OR drug misuse OR drug addict OR injecting drug use OR drug abuse OR IDU). We supplemented the search with manual footnote chasing and review of relevant journals and supplements. The search revealed 448 papers. Figure 1 illustrates the process used to retrieve, screen and select studies for this review.

We included all primary research papers written in English or containing an English abstract. Only one paper was not published in English and the relevant data was extracted from the English abstract. All papers and abstracts that were included contained primary data on syphilis infection in people living in LMI countries who reported cocaine, crack, amphetamine, heroin, morphine, opiates, barbiturates, diazepam, sedatives and other illicit drug use via injecting, snorting, smoking or ingesting.

Countries were categorized by income groups according to 2006 gross national income (GNI) per capita. The World Bank Atlas method (The World Bank, 2007) groups countries as low income ($905 or less), lower-middle income ($906–3,595), upper-middle income ($3,596–11,115), and high income ($11,116 or more). Low, lower-middle, and upper-middle income countries (referred to as LMI) were included in this review.

To increase precision and reduce bias in estimating syphilis prevalence, we excluded papers in which selection of subjects was based on syphilis status, as this was our outcome of interest, and those that included non-drug users when this population could not be separated from the entire sample. Papers including alcohol or marijuana as participants' sole drug use were excluded. Finally, to be certain that the diagnosis of syphilis was accurate in the papers under review, we excluded those that based syphilis status on self-report, including only those that used serologic testing for syphilis.

Data were transcribed onto a coding form developed by reviewing those used in other reviews, such as the HCV Synthesis Project (Scheinmann et al., 2007). The coding form included type of study (cohort vs. cross sectional); diagnostic tests and prevalence; demographics and other characteristics of the subjects such as age, gender, type of drug used and route of administration; sexual history and current sexual practices including condom usage, if working as a sex worker and if had sex with a sex worker. The principal outcomes were cases of syphilis organized into three categories: active syphilis, unspecified syphilis, and the total lifetime prevalence of syphilis. Total lifetime syphilis is the sum of active and unspecified. Subjects were considered to have active syphilis if they had a positive RPR or VDRL with a titer $\geq$ 1:8 and a positive confirmatory TPHA, FTA-ABS test, or TPPA test or if the authors explicitly stated that they were reporting laboratory-confirmed active cases (Mandell et al., 2005). Patients were considered to have unspecified syphilis if they had positive treponemal tests and or RPR or VDRL tests with a titer < 1:8. The list of diagnostic tests used in each study is located in Table 2.

The *meta* package (Schwarzer, 2007) of the freely-available, open-source R program (R Development Core Team, 2008) was used to test prevalences for heterogeneity. Testing revealed significant heterogeneity among the identified studies precluding pooling of syphilis or HIV prevalence. Testing for heterogeneity revealed $\chi^2 = 1085.76$, degrees of freedom = 31, $p < 0.0001$ for overall syphilis data and $\chi^2 = 18573.1$, degrees of freedom = 30, $p < 0.0001$ for HIV data. We therefore report these data in terms of median and unweighted interquartile ranges.

Results

Twenty-nine published papers were included (Abdala et al., 2003; Altaf et al., 2007; Azim et al., 2000; Azim et al., 2001; Azim et al., 2004; Azim et al., 2006; Baqi et al., 1998; Beyrer et al., 2004; Carey et al., 2006; Chen et al., 2005; de Carvalho et al., 1996; Dowe et al., 2001; El Ghazzawi et al., 1995; Frost et al., 2007; Go et al., 2006; Karapetyan et al., 2002; Kurbanov et al., 2003; Liu et al., 2006; Ostrovskii et al., 1999; Panda et al., 2002; Panda et al., 2007; Panda et al., 1997; Panda et al., 1998; Peak et al., 1995; Rhodes et al., 2006; Platt et al., 2007; Ruan et al., 2004; Rumi et al., 2000; Wai et al., 1996). Two papers (Azim et al., 2004 and Peak et al., 1995) were serial cross-sectional studies involving data from multiple years; these papers were thus listed as two and four separate studies, respectively. Two papers by different authors clearly describe the same study and thus were considered one study (Rhodes et al., 2006 and Platt et al., 2007). Thus, our sample of 29 papers included 32 studies described in Table 2.

The total sample (13,848 subjects, 252 of whom were not tested for syphilis due to study methodology) ranged from a study of 18 HIV positive subjects presenting at an HIV clinic in Uzbekistan (Kurbanov et al., 2003) to a study of 1,865 subjects entering a heroin or methamphetamine drug treatment facility in Thailand (Beyrer et al., 2004), with a mean of 433 subjects and a median of 271 subjects per study.

Study methodology and available details varied. Investigators of 12 studies did at least part of their recruitment from drug treatment programs, while another 14 recruited in part from street outreach. Other recruitment sites included storefront (N=6), syringe exchange programs (N=5), community setting (N=4), medical setting (N=3) and jails (N=1). Some investigators recruited from more than one site, thus the sum of the locations exceeds the total number of studies. Most studies were cross-sectional (n=30); the remaining two were a retrospective case-control and baseline data from a cohort study.

We recorded all types of drugs used regardless of method of administration. Twenty two studies included only IDU: nine included subjects who injected heroin or buprenorphine only; eight reported injection of heroin, benzodiazepines and other pharmaceutical agents, in addition to the use of opium, buprenorphine, cocaine, methamphetamine, ephedrine, cannabis, crack, barbiturates and methadone. The remaining five IDU-only studies did not specify type of drugs injected. One study reported 100% NIDU using alcohol, cannabis, and cocaine. The remaining nine studies consisted of a mix of IDU and NIDU using amphetamines, opiates, cocaine, crack, pheniramine, meclizine/promethazine, diazepam/lorazepam, buprenorphine, cannabis, barbiturates, alcohol, nitrazepan, pentazocine, pethidine, chloropheniramine and other tranquilizer tablets.

Among the 29 studies reporting gender, 81.1% of subjects were men and 18.9% were women. Eight studies included only men and three included only women, while the remaining 18 studies were primarily men (range 56.8 – 99.6%). The three women-only studies (Azim et al., 2006; Chen et al., 2005; Wai et al., 1996) included a high proportion of sex workers (48%, 63% and 100%). Among the 21 studies reporting age, the mean age was 30.5 years.

The prevalence of total syphilis (active and unspecified) in all studies, ranged from 1.0% in a mostly male IDU study in Vietnam (Go et al., 2006) to 60.3% in an IDU study among female sex workers in Bangladesh (Azim et al., 2006), with a median of 11.1% (interquartile range: 6.3% to 15.3%). The prevalence of active syphilis, in the 11 studies reporting active cases, ranged from 0.0% in an IDU/NIDU study in India (Panda et al., 2002) to 15.3% in an IDU study in China (Ruan et al., 2004), with a median of 6.23% (interquartile range: 2.98% to 10.8%). Prevalence of unspecified syphilis, in the 27 studies that did not distinguish between active and lifetime syphilis, ranged from 1.0 % in an IDU study in Vietnam (Go et al., 2006) to 51.2% in a study of IDU sex workers from Bangladesh (Azim et al., 2006), with a median of 11.0% (interquartile range: 6.3% to 13.9%). There was no association between World Bank country income groups (low, lower-middle, and upper-middle) and observed syphilis rates. No studies distinguished among primary, secondary, and tertiary syphilis. Table 3 summarizes the overall, active and unspecified syphilis.

HIV prevalence, in the thirty-one studies that reported HIV prevalence, ranged from 0.0% to 100%, with a median of 1.1% (interquartile range: 0.2% to 5.5%; see Table 3). Kurbanov et al. included only HIV-positive subjects (Kurbanov et al., 2003). There was a modest correlation (r=0.27) between HIV and overall syphilis prevalence. Eight studies reported rates of syphilis/HIV co-infection. There was, however, significant variability due to five studies having no co-infected subjects. Three studies, from China (Ruan et al., 2004), Russia (Rhodes et al., 2006;Platt et al., 2007), and Uzbekistan (Kurbanov et al., 2003), (173 total subjects) found co-infection rates of 30.2%, 14.3%, and 22.4%, respectively (see Table 2).

Among the studies reporting syphilis rates by gender, prevalence among men (N=11 studies, 3,570 subjects) ranged from 0.7% to 13.0%, with a median of 4.0% (interquartile range: 3.4% to 6.6%); prevalence among women (N=6 studies, 1313 subjects) ranged from 9.1% to 60.3%, with a median of 19.9% (interquartile range: 11.4% to 36.0%; see Table 3). Of the mixed gender studies, most included only a small proportion of women (Azim et al., 2006;de Carvalho et al.,

1996;Dowe et al., 2001;Frost et al., 2007;Karapetyan et al 2002;Panda et al., 2002;Panda et al., 2007). A study from Brazil reported a two-fold higher syphilis seroprevalence for women (OR: 2.44, 95% CI: 1.28–4.76; de Carvalho et al., 1996) and a study from Russia reported a 9-fold higher seroprevalence (OR: 9.4, 95% CI: 5.7–15.5; Karapetyan et al., 2002). Additionally, studies from Bangladesh and Russia found a significantly higher rate of syphilis among women sex workers compared to women non-sex workers (Azim et al., 2006;Karapetyan et al., 2002). There was a strong relation (r= 0.68) between overall syphilis prevalence and the proportion of women.

Twenty-three studies reported one or more sexual-risk factors. 84.6% of subjects in 15 studies reported ever having sex. Among 11 studies (N=5,355 subjects), 59.2% reported multiple sexual partners over various time frames (‘currently’ to ‘past 10 years’), and in 5 studies (N=1,016 subjects) the mean age of sexual debut was 16.1 years (range 14.0–19.0). The frequency of men who have sex with men was reported in six studies, ranging from 1.7% in a mixed IDU/NIDU study in India (Carey et al., 2006) to 51.2% in an IDU study in Brazil (de Carvalho et al., 1996).

Use of condoms was reported in 21 studies, using variable time frames from ‘last sex’ to the ‘last six months’ and variable categories including steady partners and paid partners. One Chinese study (Ruan et al., 2004) found that the majority of subjects reported never using a condom with a primary sex partner (88.2%) or with non-primary sex partners (62.9%) in the last month. The frequency of “some” condom use (N=15 studies) ranged from 9.3% in Pakistani IDUs to 100% in Nepalese IDUs. Reports of “always” using condoms (N=8 studies) ranged from 1.0% in Nepalese IDUs to 32.7% in Russian IDU. Five studies presented syphilis rates by frequency of condom use: prevalence among subjects “always” using condoms ranged from 0% to 4.2%, among those reporting “some” condom use ranged from 4.5% to 27.3%, and among those who “never” used condoms was 11.8%.

One Russian study (Karapetyan et al., 2002) found that 22% of syphilis positive respondents reported that they would have unprotected sex even if they knew they had syphilis. Further, 86% of those subjects who reported having sex without a condom while knowing they had syphilis were sex workers. One Pakistani study found that syphilis positive IDUs were more likely to have paid for sex and had a younger age of first sexual intercourse (Altaf et al., 2007).

Thirteen studies reported if subjects had ever worked as a sex worker. Reports of sex work ranged from 1.3% in a mixed gender study in Thailand to 100% in a study of women in China. Three studies reported overall syphilis prevalence among sex workers: 15.0% (Azim et al., 2006), 15.5% (Carey et al., 2006), and 64.7% (Rhodes et al., 2006/Platt et al., 2007). Seventeen studies reported if subjects had ever had sex with a sex worker, using variable time frames from ‘last month’ to ‘ever’. Reports of sex with sex workers ranged from 71.8% in study of IDU men in India to 14.7% in a mixed gender IDU study in Russia. Two studies reported syphilis prevalence among subjects who had sex with sex workers: 10.8% (Carey et al. 2006) and 19.1% (Altaf et al., 2007).

Discussion

Our review identified 32 published studies from LMI countries reporting syphilis prevalence and sexual risk factors in drug users. The prevalence of overall lifetime syphilis ranged from 0.3% to 60.3% in studies from 14 LMI countries. High-risk sexual behaviors are prevalent among drug users and awareness of transmission risks is low (Altaf et al., 2007; Platt et al., 2007; Azim et al., 2006; Liu et al., 2006; Rhodes et al., 2006; Panda et al., 1998; Wai et al., 1996). High rates of sex work, sex with sex workers and MSM coupled with variable but

generally low rates of condom use among illicit drug users could contribute to the high syphilis prevalence in LMI countries.

Women surveyed were more likely both to have syphilis and to trade sex for money. The higher syphilis estimate among women is consistent with other studies illustrating a greater likelihood of syphilis infection among women drug users. This is especially true among women drug users exchanging sex for money and/or drugs (Watters et al., 1994; Platt et al., 2007) who may not perceive themselves to be at high risk of STI infection and transmission (Liu et al, 2006). Lacking awareness of infection status, transmission routes and/or prevention methods, women may continue to practice risky behaviors with their sex and drug partners.

The high-risk group of women sex workers using drugs may “bridge” the population of drug users to non-injecting populations that use the services of sex workers (Strathdee et al., 2008; Liu et al., 2006; Ruan et al., 2006; Karapetyan et al., 2002). One study from Mexico (Strathdee et al., 2008) found that women IDUs often used drugs in a sexual relationship with a drug using male partner, suggesting greater overlap in sexual and drug use networks for women relative to men. This study further demonstrated risky patterns of sexual behavior among women sex workers who injected drugs compared to non-IDUs; IDUs were seven times more likely to use drugs before sex than non-IDUs, a behavior known to lead to lower rates of condom use and reduced condom negotiation skills. Continued studies targeting the risks of women, including larger samples of women drug users, are needed.

Syphilis facilitates the transmission of HIV infection (Lyles et al., 2007; Buchacz et al., 2005; Phipps et al., 2005; Browne et al., 2003; Harrell et al., 2003; Kalichman et al., 2000; Greenblatt et al., 1988). Additionally, syphilis in HIV infected patients is associated with a significant decrease in CD4 cell counts and an increase in HIV viral load (Palacios et al., 2007). The elevated HIV viral load does not consistently decrease after syphilis treatment, likely due to persistent immune activation (Palacios et al., 2007). This may increase both the risk of disease progression in the individual and of disease transmission in the community, illustrating the importance of preventing new syphilis infections in the setting of HIV.

Our results are subject to a number of limitations. Studies reviewed varied substantially in target population, methodology and data coding. Studies defined drug users with varying criteria, which may have affected the estimated prevalence rates. Studies recruited from a variety of settings (prisons, rehabilitation facilities, job seekers, and syringe exchange programs) making it difficult to generalize prevalence rates. Syphilis prevalences were never reported by specific drug type and infrequently by sex-and drug-related risk factors, thus limiting summary results. Many studies focused on HIV or other illnesses, with syphilis as a secondary research objective, often requiring calculations to estimate syphilis prevalence or limiting the details of active versus lifetime rates. The variation between studies and the frequent availability of a single study in certain countries make regional prevalence estimates imperfect. Finally, we accessed only studies with English-language text or abstracts.

The observed rates of syphilis, although highly variable, were higher than those of general population rates in all regions. The variation between studies and the frequent availability of only one study per country limits the reliability of prevalence estimates. Our analysis demonstrates an association between drug use and syphilis, but confirms neither an independent association nor a direct causal relationship between drug use and syphilis. The association of syphilis and drug use is likely due to a convergence of independent, individual and environmental level risk factors. Nonetheless, the increased prevalence of syphilis and the fact that syphilis facilitates the transmission of HIV infection reinforces the need for integrated health care models addressing both issues.

Interventions for HIV prevention among drug users have historically centered on efforts to reduce syringe mediated transmission through reducing behaviors such as front and back loading and syringe sharing through education, syringe exchange and other harm reduction techniques, such as syringe bleaching. Other interventions for STI prevention thus far have included condom promotion and improved diagnosis and treatment with clinic services directed at communities such as fishermen, migrant laborers, truck drivers and street-based sex workers (Abdala, et al 2003; Panda et al., 2002; Karapetyan et al., 2002; Panda et al., 1997; Wai et al., 1996). As prevention efforts for drug users have had an impact in certain areas, it has become clear that drug users retain significant ongoing sexual risk for STI transmission (Des Jarlais et al, 2007a; Des Jarlais 2007b; Kral et al., 2001). The overlap between HIV and TB epidemics have highlighted the limitations of relying entirely on vertical health care programs, which address these related infections separately, highlighting the need for integrated models of care. Similarly, the often high prevalence of syphilis and other STIs found among drug using populations in LMI countries, as well as high income countries, further highlights the need for HIV prevention efforts to address issues both of drug related risks, and of sexual health, among drug using populations in these settings. This reinforces the importance of integrated (or horizontal) health care models and points towards the need for global models of primary health care.

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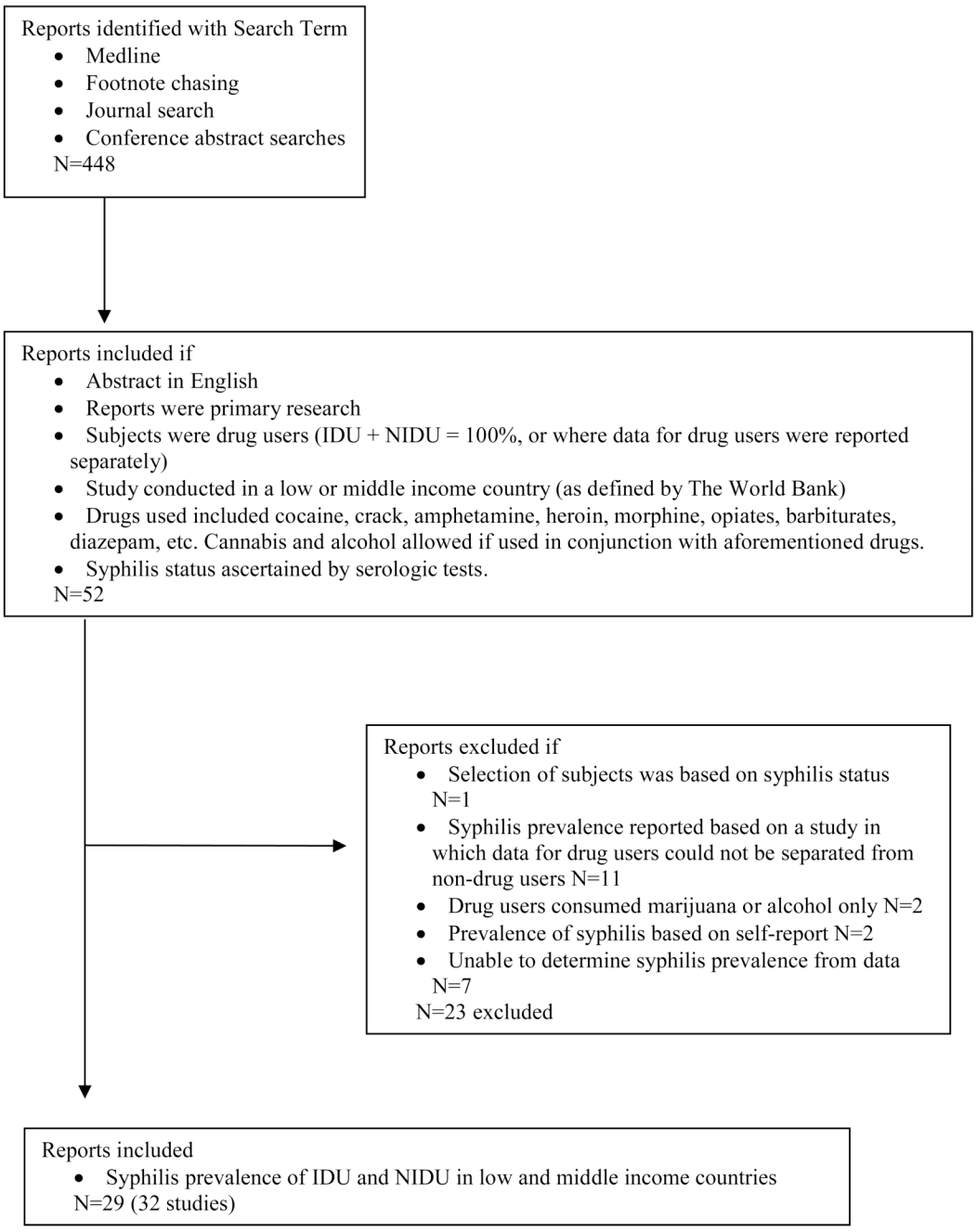

Figure 1.
Decision Tree Used to Retrieve and Select Papers

Table 1

Estimated new cases of syphilis (in million) among adults, 1995 and 1999 (Adapted from World Health Organization, 2001)

Region	1995			1999		
	Male	Female	Total	Male	Female	Total
North America	0.07	0.07	**0.14**	0.054	0.053	**0.107**
Western Europe	0.10	0.10	**0.20**	0.069	0.066	**0.136**
North Africa & Middle East	0.28	0.33	**0.62**	0.167	0.197	**0.364**
Eastern Europe & Central Asia	0.05	0.05	**0.10**	0.053	0.052	**0.105**
Sub Saharan Africa	1.56	1.97	**3.53**	1.683	2.144	**3.828**
South and South East Asia	2.66	3.13	**5.79**	1.851	2.187	**4.038**
East Asia & Pacific	0.26	0.30	**0.56**	0.112	0.132	**0.244**
Australia & New Zealand	0.01	0.01	**0.01**	0.004	0.004	**0.008**
Latin America & Caribbean	0.56	0.70	**1.26**	1.294	1.634	**2.928**
Total	**5.55**	**6.67**	**12.22**	**5.29**	**6.47**	**11.76**

Table 2

Characteristics of drug users studies in our systematic review (n=32)

Citation	Location	Enrollment Date	Recruitment Setting	Sample (Drug users)	Female % (n)	Active Syphilis % (n)	Unspecified Syphilis % (n)	Total Syphilis % (n)	Diagnostic Test	HIV % (n)	Syphilis/ HIV co-infection % (n)
Abdala et al (2003)	St. Petersburg, Russia	June 2000 – Aug 2000	SEP	101	38.6 (39)	-	6.9 (7)	6.9 (7)	TREP-CHEK anti-Trep EIA (detects IgG antibodies)	10.9 (11)	0.0 (0 of 11)
Altaf et al (2007)	Karachi, Pakistan	Oct 2003 – Nov 2003	SEP	161	0.0 (0)	13.0 (21)	-	13.0 (21)	RPR, confirmed with TPHA	0.6 (1)	-
Azim et al (2000)	Bangladesh (4 regions)	June 1998 – March 1999	Drug treatment	402	0.3 (1)	4.5 (18)	12.9 (52)	17.4 (70)	RPR, TPHA	2.5 (10)	-
Azim et al (2002)	Bangladesh (4 regions)	June 1999 – June 2000	SEP, Drug treatment	1236	0.4 (5)	5.8 (72)	15.4 (190)	21.2 (262)	RPR, TPHA	0.6 (7)	-
Azim et al (2004)	Bangladesh (4 regions)	2001	SEP	1015	-	2.2 (22)	13.1 (133)	15.3 (155)	RPR, TPHA	0.7 (7)	-
Azim et al (2004)	Bangladesh (4 regions)	2002	SEP	1008	-	2.5 (25)	13.7 (138)	16.2 (163)	RPR+ & TPHA+ (represents non-active), TPHA & RPR titer of >=8 (represents reactive)	1.6 (16)	-
Azim et al (2006)	Dhaka, Bangladesh	Dec 2004 – May 2005	Street outreach	121	100 (121)	9.1 (11)	51.2 (62)	60.3 (73)	RPR, TPPA (lifetime RPR titer <1:8), active RPR titer >= 1:8)	0.0 (0)	0.0 (0 of 0)
Baqi et al (1998)	Karachi, Pakistan	Apr 1994 – July 1994	Drug treatment	474 (272 tested for syphilis)	0.0 (0)	6.6 (18 of 272)	-	6.6 (18 of 272)	VDRL, confirmed with FTA-ABS	0.0 (0 of 316)	0.0 (0 of 0)
Beyrer et al (2004)	Mae Rim, Thailand	Feb 1999 – Jan 2000	Drug treatment	1865	10.7 (200)	-	2.2 (41)	2.2 (41)	RPR, followed by Serodia-TP-PA for antibody confirmation	10.3 (192)	-

Citation	Location	Enrollment Date	Recruitment Setting	Sample (Drug users)	Female % (n)	Active Syphilis % (n)	Unspecified Syphilis % (n)	Total Syphilis % (n)	Diagnostic Test	HIV % (n)	Syphilis/ HIV co-infection % (n)
Carey et al (2006)	Bangalore, India	Apr 2001 – Oct 2001	Drug ftreatment	356	2.0 (7)	-	12.9 (46)	12.9 (46)	T. pallidum antibodies	1.1 (4)	-
Chen et al (2005)	Yunnan, China	Nov 1999 – May 2000	Drug treatment, Medical setting	292	100 (292)	11.3 (33)	-	11.3 (33)	RPR, confirmed with TPHA	17.8 (52)	-
De Carvalho et al (1996)	Santos, Sao Paulo, Brazil	Oct 1990 – Dec 1992	Drug Treatment Street outreach	220 (197 tested for syphilis)	41.6 (89)	-	34.0 (67 of 197)	34.0 (67 of 197)	FTA-abs	57.0 (122 of 214)	-
Dowe et al (2001)	Jamaica, West Indies	1994 – 1999	Drug treatment	301	9.0 (27)	-	6.3 (19)	6.3 (19)	VDRL, FTA-ab	2.7 (8)	-
El Ghazzawi et al (1995)	Alexandria, Egypt	June 1989 – Nov 1991	Drug treatment	100	0.0 (0)	-	3.0 (3)	3.0 (3)	VDRL, MHA-TP	0.0 (0)	0.0 (0 of 0)
Frost et al (2007)	Tijuana and Ciudad Juarez, Mexico	Feb 2005 – April 2005	Community setting/ street outreach	428 (413 tested for syphilis)	8.2 (35)	-	9.2 (38 of 413)	9.2 (38 of 413)	RPR	3.3 (14)	-
Go et al (2006)	Northern Vietnam	Aug 2003 – Sept 2003	Street outreach	309	3.6 (11)	-	1.0 (3)	1.0 (3)	RPR, TPHA	-	-
Karapetyan et al (2002)	St. Petersburg, Russia	Apr 1998 – Dec 1998	Storefront/ street outreach (Mobile van)	910	31.3 (285)	-	11.5 (105)	11.5 (105)	microprecipitation reaction w/ cardiolipid antigen, confirmation w/IFA (indirect fluorescent antibodies)	0.0 (0)	0.0 (0 of 0)
Kurbanov et al (2003)	Uzbekistan	April 1999 – March 2000	Medical Settings	18	11.1 (2)	-	22.2 (4)	22.2 (4)	TP Ab test	100 (18)	22.2 (4 of 18)
Liu et al (2006)	Anhui Province, China	2003	Drug treatment	312	38.8 (121)	-	11.2 (35)	11.2 (35)	TRUST followed by TP-PA for confirmation	0.3 (1)	-
Ostrovskii et al (1999)	St. Petersburg, Russia	-	Storefront/ street outreach (Mobile van)	900	-	-	11.0 (99)	11.0 (99)	-	0.1 (1)	-
Panda et al (1997)	Calcutta, India	Nov 1994 – Feb 1995	drug treatment, jails	111	0.0 (0)	-	6.3 (7)	6.3 (7)	VDRL	0.9 (1)	-
Panda et al (1998)	Calcutta, India	July 1996 – Sept 1996	Street outreach	103 (91 tested for syphilis)	0.0 (0)	-	4.4 (4 of 91)	4.4 (4 of 91)	VDRL (1/8 dilution)	1.1 (1 of 91)	-

Citation	Location	Enrollment Date	Recruitment Setting	Sample (Drug users)	Female % (n)	Active Syphilis % (n)	Unspecified Syphilis % (n)	Total Syphilis % (n)	Diagnostic Test	HIV % (n)	Syphilis/ HIV co-infection % (n)
Panda et al (2002)	Kolkata, India	Dec 1999 – June 2000	Street outreach	249	0.0 (0)	0.0 (0)	6.8 (17)	6.8 (17)	VDRL (active), TPHA (lifetime)	1.2 (3)	-
Panda et al (2007)	Chennai, India	Apr 2003 – July 2003	Street outreach	211	0.0 (0)	0.9 (2)	-	0.9 (2)	RPR, TPHA (said active)	0.0 (0)	-
Peak et al (1995)	Kathmandu, Nepal	1991	Storefront/ Street outreach	127	10.2 (13)	-	14.2 (18)	14.2 (18)	VDRL	1.6 (2)	-
Peak et al (1995)	Kathmandu, Nepal	1992	Storefront/ Street outreach	39	7.7 (3)	-	10.3 (4)	10.3 (4)	VDRL	2.6 (1)	-
Peak et al (1995)	Kathmandu, Nepal	1993	Storefront/ Street outreach	141	5.0 (7)	-	14.2 (20)	14.2 (20)	VDRL	0.0 (0)	-
Peak et al (1995)	Kathmandu, Nepal	1994	Storefront/ Street outreach	117	3.4 (4)	-	5.1 (6)	5.1 (6)	VDRL	0.0 (0)	-
Rhodes et al (2006)/ Platt et al (2007)	Moscow, Volgogradand Barnaul, Russia	Sept 2003 – Nov 2003	Community setting/ Street outreach	1473	29.4 (433)	-	10.7 (157)	10.7 (157)	TP Ab test (ICE Syphilis, anenzyme immunoas say (EIA) modified for use with oral fluid)	7.6 (112)	14.3 (16 of 112)
Ruan et al (2004)	Sichuan province, China	Nov 2002 – Nov 2004	Community setting	379	17.4 (66)	15.3 (58)	-	15.3 (58)	ELISA Ab, confirmed with TPPA	11.3 (43)	30.2 (13 of 43)
Rumi et al (2000)	Bangladesh	Aug 1994 – May 1996	Medical setting	198	0.0 (0)	-	5.1 (10)	5.1 (10)	PRP, TPHA	1.0 (2)	-
Wai et al (1996)	Kelantan, Malaysia	-	Drug treatment	171	100 (171)	-	38.6 (66)	38.6 (66)	VDRL, TPHA	8.2 (14)	-

Table 3

Syphilis and HIV prevalence among drug users

		Number of Studies	Number of Subjects Tested for Syphilis	Range	Median	Unweighted Interquartile Range of Proportions (1st to 3rd Quartiles)
Overall Syphilis Prevalence	all	32	13,596	1.0% to 60.3%	11.1%	6.3% –15.3%
	men	11	3570	0.7% to 13.0%	4.0%	3.4% – 6.6%
	women	6	1313	9.1% to 60.3%	19.9%	11.4% – 36.0%
Active Syphilis Prevalence		11	5054	0.0% to 15.3%	6.2%	3.0% – 10.8%
Unspecified Syphilis Prevalence		27	12,281	1.0% to 51.2%	11.0%	6.3% – 13.9%
HIV Prevalence		31	13,358	0.0% to 100%	1.1%	0.2% – 5.5%