Syphilis prevalence in Bangladesh, 2000-2019: Spectrum-STI estimates for 8 adult population groups

Final Technical Report, based on an STI/HIV surveillance workshop in Dhaka, October 2019

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- Eline Korenromp designed and implemented the estimations and wrote the report.
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SUMMARY

The Spectrum-STI estimation model was used during and after a UNAIDS/WHO HIV/STI surveillance workshop in Dhaka, Bangladesh, 6-10 October 2019, to estimate the national historic trend in active syphilis in 15 to 49-year-old adults.

Syphilis prevalence data from female and male sex workers (FSW and MSW), men who have sex with men (MSM), people who inject drugs (PWID), transgenders (TG) and lower-risk women and men in Bangladesh were collated by local surveillance experts. Sources included surveys, studies and program screening results from antenatal care clinics, blood donors, representative community and household samples, as well as national HIV/STI integrated bio-behavioural and serological surveys (IBBS) conducted in higher-risk populations.

Data were adjusted for diagnostic definitions, to reflect prevalence of the international gold standard, dual positivity on TPHA and RPR, without titer thresholds.

The 2019 syphilis prevalence estimates were: Low-risk women 0.31% (95% confidence interval: 0-1.2%), FSW 3.5% (0.9-16.2%), female PWID 16.2% (4.8-36.2%), Low-risk men 0.17% (0.12-0.23%), MSM 3.0% (0.9-7.8%), male PWID 8.6% (5.7-13.9%), MSW 7.2% (3.6-12%) and Transgenders 4.0% (1.3-8.5%). In 2019, women, men and TG accounted for 62%, 38% and 0.2% of prevalent cases, respectively; FSW, MSM, MSW and female and male PWIDs covered 2%, 2%, 1%, 0.1% and 1.5% of the overall total, respectively.

For all populations, the 2019 estimates were below the 2000 estimates. For FSW, TG, MSW and Low-risk men, the respective 95% confidence intervals at these two time points did not overlap, suggesting that the decline was statistically significant. For the other 4 groups, the 95% confidence intervals overlapped, indicating that the decline from 2000 to 2019 was not statistically significant, but might represent a chance finding reflecting mere fluctuations in the data.

These estimates show modest to strong declines in the prevalence of syphilis in the last two decades across several higher-risk groups. Prevalence, however, is still relatively high, and its level trend in the general heterosexual population is not well known. Expanding syphilis screening, treatment and prevention services beyond known key populations may be necessary to drive down the burden of adult and congenital syphilis.

INTRODUCTION

Information on the prevalence of STIs is important for health care planning and informing treatment protocols. In Bangladesh, STI cases are managed syndromically (particularly among key populations) and there is no routine systems for reporting STI cases. Prevalence data, however, are available from a long series of national HIV sero-surveillance rounds and IBBS surveys carried out every two years in a number of high-risk and lower-risk sentinel populations across the country [1-11].

Bangladesh formulated its national AIDS Committee (NAC) in 1985, and in 1997 developed a National Policy on HIV and STD, a first National Strategic Plan for AIDS prevention and control, and a national control program. Under a comprehensive policy on HIV/AIDS; early on it implement behavioural prevention education and condom distribution targeted to key groups, resulting in rapid reductions in risk behaviours [1-11]. Support from the Global Fund, since 2004, helped to scale-up HIV treatment and care, and maintain targeted prevention services.

Spectrum-STI is a statistical trend-fitting model designed for countries to estimate national trends over time in the prevalence and incidence of three sexually transmitted infections (STIs): syphilis (etiologic agent: *Treponema pallidum* subspecies *pallidum*); gonorrhea (*Neisseria gonorrhoeae*); and chlamydia (*Chlamydia trachomatis*) from available prevalence data, standardized for diagnostic test, location and age and weighted to reflect representativeness. The programme builds on the Spectrum suite of health policy planning and surveillance models developed by Avenir Health [12]. Spectrum-STI, since 2018, allows for estimates to be generated for different key and non-key groups and for these to be combined to form an overall adult population estimate. Estimation for two higher-risk groups, female sex workers (FSW) and Men who have sex with men (MSM), alongside lower-risk men and women, was piloted first in Yunnan province of China, in 2018 [13].

This report presents adult prevalence trend estimates for syphilis for Bangladesh, based on a national HIV/STI surveillance workshop held in Dhaka in October 2019, and data collection efforts following the workshop, for 8 population groups in Bangladesh: Lower-risk women, Lower-risk men, FSW, male sex workers (MSW), MSM, male and female people who inject drugs (PWID), and transgenders (TG). These 8 estimates were then combined into provincial syphilis estimates for all 15-49 year old women and men. Findings are discussed with a view to how Spectrum-STI can be used by the national HIV/STI program to inform program surveillance, evaluation and strategic and operational planning.

METHODS

STI prevalence data

Prevalence data were identified through a PubMed search of studies published in 1990 or later with the key words Bangladesh AND ('sexually transmitted infection' OR 'sexually transmitted disease' OR 'syphilis'), and back-tracking references of relevant English language articles (see Table 2). These data were supplemented by published and unpublished data identified by STI experts during the October 2019 workshop in Dhaka.

Data were eligible from the following population, sample and study types:

- Lower-risk women: ANC routine screening, ANC sentinel surveillance, community surveys, obstetrics & gynaecology patients, ANC attendees, female workers;
- Lower-risk men: Community surveys, blood donor screening;

- FSW, MSW, MSM, PWIDs and TG: Sentinel surveillance surveys, small-scale studies. Data from FSWs and MSW seeking care in STD clinics were not included.

For the 6 higher-risk key populations (FSW, MSW, MSM, male and female PWIDs and TG) we did not adopt special definitions; operationally, these groups were chosen and defined based on available national and subnational survey and surveillance data assigned to each group, with their corresponding population sizes inferred from pre-existing HIV estimations that distinguished these same key populations (see Population size estimates, below).

In this analysis, we classified as Lower-risk women and Lower-risk men for those adults who are not part of any of 6 key populations (FSW, MSW, MSM, male and female PWIDs and TG) estimated separately.

Spectrum-STI model

Spectrum-STI is a statistical model that fits time trends in national adult STI prevalence and incidence, based on local STI prevalence data [14,15]. Bangladesh' estimations were performed in versions 5.77 beta 47, which is freely available online (https://avenirhealth.org/software-spectrum.php).

Population size estimates

To generate national overall adult estimates, the prevalence estimates for the 8 populations were combined based on their respective contribution to the national population. The overall adult (15-49 years) female and male population sizes were taken from UN Population Division projections (2017 round; medium-growth variant)[16].

Sizes of the higher-risk sub-populations were based on national size estimates and/or estimates documented and used by the national HIV program in their HIV estimations using the *AIDS Epidemic Model* (AEM), September 2019 version.

Table 1a summarizes available earlier population size estimates, including (for reference) those by UNAIDS for the Asian region [17-19]. Table 1b summarizes the size estimates as used in the syphilis estimation. Where possible, we based these on the national size estimates in 2015, keeping the proportional size estimate as at 2015 constant over time. In other words, all 8 subpopulations were assumed to have grown at the same annual rate – as also assumed in HIV/AEM modelling.

Table 1a. Overview of pre-existing population group size estimates for Bangladesh, national and UNAIDS/Asia regional, used to benchmark the sizes used in the STI estimates

	Pre-1997	2009	2015	2015	2015
All women 15-49 years			**44.94M**	**56.5M (15+)**	NA (Asia-Pacific regional estimate)
All men 15-49 years			**44.95M**	**57.0M (15+)**	
Lower-risk Women			44.80M	56.4M	
Female sex workers	50,000-100,000	63,600-74,300 (0.19-0.22%)	139,961 (0.31%)	98,495 (0.17% of 15+)	0.35%
Lower-risk Men, excluding FSW clients			44.85M	50.227M	
Male FSW clients		2.7-3.7M (8-11%)		6.538M (11.5% of 15+)[20]	

	Pre-1997	2009	2015	2015	2015
MSM			101,695 (0.23%)	152,460 (0.27% of 15+)	1.69%
Male Sex Workers				29,777	
Transgenders				10,200 (0.018%)	0.02%
Male PWID	20,000-40,000 [21]	21,800-23,800 (0.06-0.07%)		32,021 (0.06% of 15+)	0.06%
Female PWID			1,045 (0.002% of 15+) of whom 346 are FSW		0.06%
Source	[22,23]	[24]	[25]	AIDS Epidemic Model (AEM) 2019	UNAIDS [17-19]

Note to Table 1a: Unless indicated, population sizes are for 15-49 years old, and percentages are percentage of 15-49 year-olds of the respective gender. Percentages of FSW are relative to the adult female population; for MSM are relative to the adult male population. M = million. For indicators not provided by the source stated in the last row, the cell is left empty.

Table 1b. Modelled population sub-group sizes, in Bangladesh' overall 15-49 year national population, as used in Spectrum-STI estimations

Population	2,000	2,019	Share in M or F population
Total population, women 15-49 years	**31,793,920**	**45,864,614**	**100.0%**
Total population, men 15-49 years	**33,731,020**	**45,911,364**	**100.0%**
Low-risk Women	31,721,066	45,759,517	99.8%
Female Sex Workers	72,094	104,000	0.23%
PWID-Female	760	1,097	0.002%
Low-risk Men	33,552,560	45,668,461	99.5%
Men who have sex with men	117,651	160,135	0.35%
PWID-Male	29,224	39,777	0.09%
Male Sex Workers	23,713	32,276	0.07%
Trans-Genders	7,872	10,715	0.02%

Table 2. Prevalence data from Bangladesh, 1995 to 2019

See XLS.
References: [23,26-55]

& the first ten rounds of national serological & behavioural HIV/STI surveillance:

- 1st round: [1]
- 2nd round: [2]
- 3rd round: [3]
- 4th round: [4]
- 5th round: [5,56]
- 6th round: [6]
- 7th round: [7]
- 8th round: [8]

- 9th round: [9]
- 10th round: [10,11]

Blood donor data over 2019 were unpublished (personal communication of Dr. Alauddin Chowdhury, October 2019).

Diagnostic test adjustments on prevalence data

Prevalence data were adjusted for diagnostic test performance using the same approach and parameters as the WHO 2016 STI estimates [57] for studies that recorded treponemal (e.g. TPPHA or TPHA) + Non-treponemal (RPR or VDRL) dual positivity without RPR threshold titers (the WHO gold standard definition for Active syphilis), or Treponemal alone or Non-treponemal alone. The standard correction factors are: both reactive non-treponemal and reactive tests 1.0 i.e. no adjustment; reactive non-treponemal test without non-treponemal confirmation 0.53; reactive treponemal test without non-treponemal confirmation 0.53; rapid treponemal-based tests 0.70, and test type unknown 0.75.

The majority of Bangladesh IBBS data (for the 6 higher risk groups), however, uses thresholds for RPR – and for a person to be recorded as syphilis positive the TPHA test had to be positive and the RPR above a threshold titer of ≥1:8. Prevalence data in this latter category were adjusted to the WHO and Spectrum-STI default standard definition of RPR+TPHA without thresholds, by multiplying the observed prevalence by 4.0. This value reflected the typical difference in prevalence between the 2 alternative definitions, across Bangladesh data points that reported on both the definitions (Figure 1; best estimate in a linear regression with intercept 0.0 was 4.36) which covered the majority of IBBS data on higher-risk populations (Table 2).

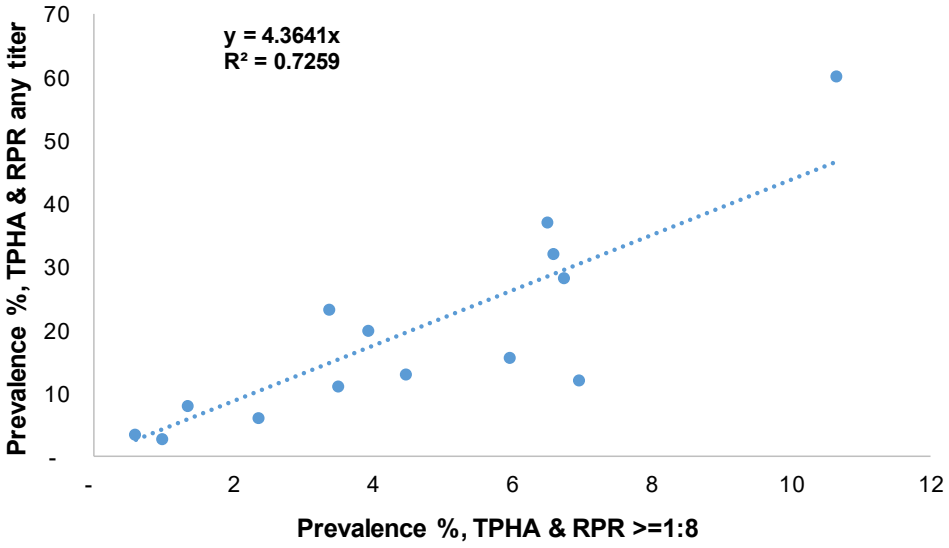
Some survey results had the prevalence reported both for TPHA and RPR dual positivity and both with and without RPR threshold; from these the estimation used the result according to the international gold standard definition, without titer threshold.

Weighting prevalence data

In the statistical trend estimation, within each of the 8 groups estimated, each study was assigned a weight reflecting how representative it was of the particular population group (Table 2).

Lower-risk women: **ANC surveys were weighted** at 100% in years with most sites (e.g. provinces) sampled (in Bangladesh, in the 2008 survey that sampled 26 regions) and proportionally reduced for years with fewer sites (surveys in 2000 and 2007).

Figure 1. Correlation between prevalence defined as TPHA + RPR dual positivity without threshold (x-axis and predictor variable in linear regression) and TPHA + RPR with RPR threshold ≥1:8, in Bangladesh populations



Note to Figure 1. Data sources: Bangladesh national IBBS on FSW, MSM and PWID, Round 1 [1], Round 2 [2], other surveys of high-risk populations [33,34,36,46,47,58], and one survey in lower-risk men [27], between 1995 and 2014. The statistics note the coefficients and correlation coefficient of a linear regression, with intercept set at 0.

Routine ANC programmatic screening data were weighted by their estimated *national* ANC screening coverage. Routine data from 2013 and 2014 were from 3 hospitals in 3 regions that were pioneering PMTCT services at the time. These were assigned a weight of 1%, reflecting that these represent only a very small and not representative proportion of the country. From the same three hospitals, data from years 2015-2018 were not included, because these measured implausibly low prevalence, which probably related to the hospitals being special, tertiary care PMTCT hospitals, where syphilis was only tested if the women requested and paid it, whereas most of these pregnant women – generally from the upper class -- would have been syphilis-tested already at their primary ANC center.

Data from **community surveys** of women (regardless of pregnancy status) were weighted by the regional coverage, at 100% if the study had sampled ≥20 sites or all provinces of the country.

Lower-risk heterosexual men: Prevalence data from large community surveys in general rural population were assigned a 50% weight, so as to represent the large rural population. We also identified several studies in sub-populations of men who are probably at medium-risk: urban slum dwellers, truck drivers, rickshaw pullers, dock workers, launch workers, and youth visiting hotel-based FSW. These were assigned a 5% weight in default/sensitivity analysis, to reflect that these were small studies and/or small sub-populations. In addition, blood donor screening data for men and women were assigned a weight of 50% in the male estimate (2012-2017, 5 annual rounds, each at 50% weight), reflecting that these were considered representative of the broader national population. In contrast, these sex-aggregate data were not used in the female estimation, since the majority of blood donors typically are men. Two data points from 'babus' i.e. boyfriends of FSW, sampled in the 2002

and 2003-04 IBBS rounds [8], were not included in the default estimation but included in a sensitivity analysis.

Higher risk populations: Most of the higher-risk population data came from the periodic HIV sero-surveillance, conducted over 1998 to 2016 in multiple sites (up to 24 for some populations in some years) around the country. These sero-surveys had taken sample sizes based on the past prevalence of HIV and the level of statistical precision and confidence desired for next HIV estimates. When generating the trend estimates, the HIV sero-surveillance and/or IBBS data for a specific population and year were pooled across all sites and assigned a weight of 100%, such that within each year and each sub-population, the data weights summed to 100%. For FSW, data from IBBS that sampled specific subgroups (brothel-based, street-based/floating, hotel-based and casual) were also pooled in the estimation as the IBBS sample sizes were designed to reflect relative sub-population group sizes.

In the case of men, some IBBS data for some sites and years combined MSM and MSW data and it was not possible to disaggregate them; in the default estimate these data were treated as MSW (see Table 2 and Figure 2d). Each pooled data point was given a weight of 20-30%, slightly lower than the group-specific data points, to reflect uncertainty in which specific group these concerned. Alternatives, e.g. excluding the combined MSM and MSW data or treating them as MSM are explored in the sensitivity analysis.

Syphilis trend estimates

Prevalence trends were estimated for each population group by fitting the standardized and weighted prevalence data using logistic regression. Logistic regression was used for all 8 population groups estimated. Logistic regression is the default option in Spectrum -STI, and is appropriate for populations with moderate numbers of data points, and when there is no clear evidence or there have been no a series of policy changes to suggest repeatedly reversing trends within that group [13,59].

Prevalence estimates and the upper-bound of the 95% confidence interval were capped at a maximum value, which was held constant over time. The maximum values, which were Spectrum-STI global defaults, based on global meta-analysis of prevalence data from multiple countries, were: Low-risk women and men 20%, High-risk women 60% and High-risk men 35%. Trend estimates were in a particular population were extrapolated one year before the first data point and one year after the last data point and then assumed to be constant.

For each population group, the estimated prevalence trend was extrapolated for 1 year after the last year with prevalence data for the given group and then held constant at that level for all next years. Similarly, the estimated trend was extrapolated 1 year before the first year with prevalence data for the given group, and then held constant at that level for all earlier years.

Uncertainty intervals

Uncertainty bounds on prevalence for each population group were calculated by bootstrapping [14]. When combining the results to generate national estimates, we assumed that there was no uncertainty in population sizes. Differences between 2000 and 2019 were considered statistically significant if the respective 95% confidence intervals did not overlap.

Sensitivity Analysis

General assumptions underlying the Spectrum-STI model have been addressed in sensitivity analyses in earlier country and global applications and reports [14,15,60]. These analyses have highlighted the

importance of the types of data included, notably how sub-populations are estimated either independently or in aggregation. For the current Bangladesh estimations we therefore undertook several univariate sensitivity analyses that explored how estimations changed depending on how different sub-populations were incorporated in the analysis.

RESULTS

Prevalence data

Table 2 presents the identified data that met the study entry criteria, and the default Spectrum weights assigned to each data point. A total of 105 syphilis data points were used in the estimation. Their data collection periods ranged from 1995 to 2017. Of the 105 data points, 32 were from 2010 or more recent.

Spectrum-estimated prevalence trends

Figure 2 and Table 3 show the Spectrum-STI estimations over the period 2000 to 2019 (with data included shown back to 1995). In 2019, prevalence in lower-risk women was 0.31% (0-1.2%), 3.5% (0.9-16.2%) in FSW and 16.2% (4.8-36.2%) in female PWID . Pooling all 3 women groups, in 2019 the overall estimated female prevalence was 0.32% (0-0.89%), close to that in the low-risk women, who formed by far the largest group.

Among men, prevalence in lower-risk men 0.17% (0.12-0.23%); 3.0% (0.9-7.8%) in MSM, 8.6% (5.7-13.9%) in male PWID, 7.2% (3.6-12%) in MSW and 4.0% (1.3-8.5%) in Transgenders. Pooling all subgroups, the overall male prevalence was 0.19% (0.14-0.25%), close to that in low-risk men who contributed the largest population.

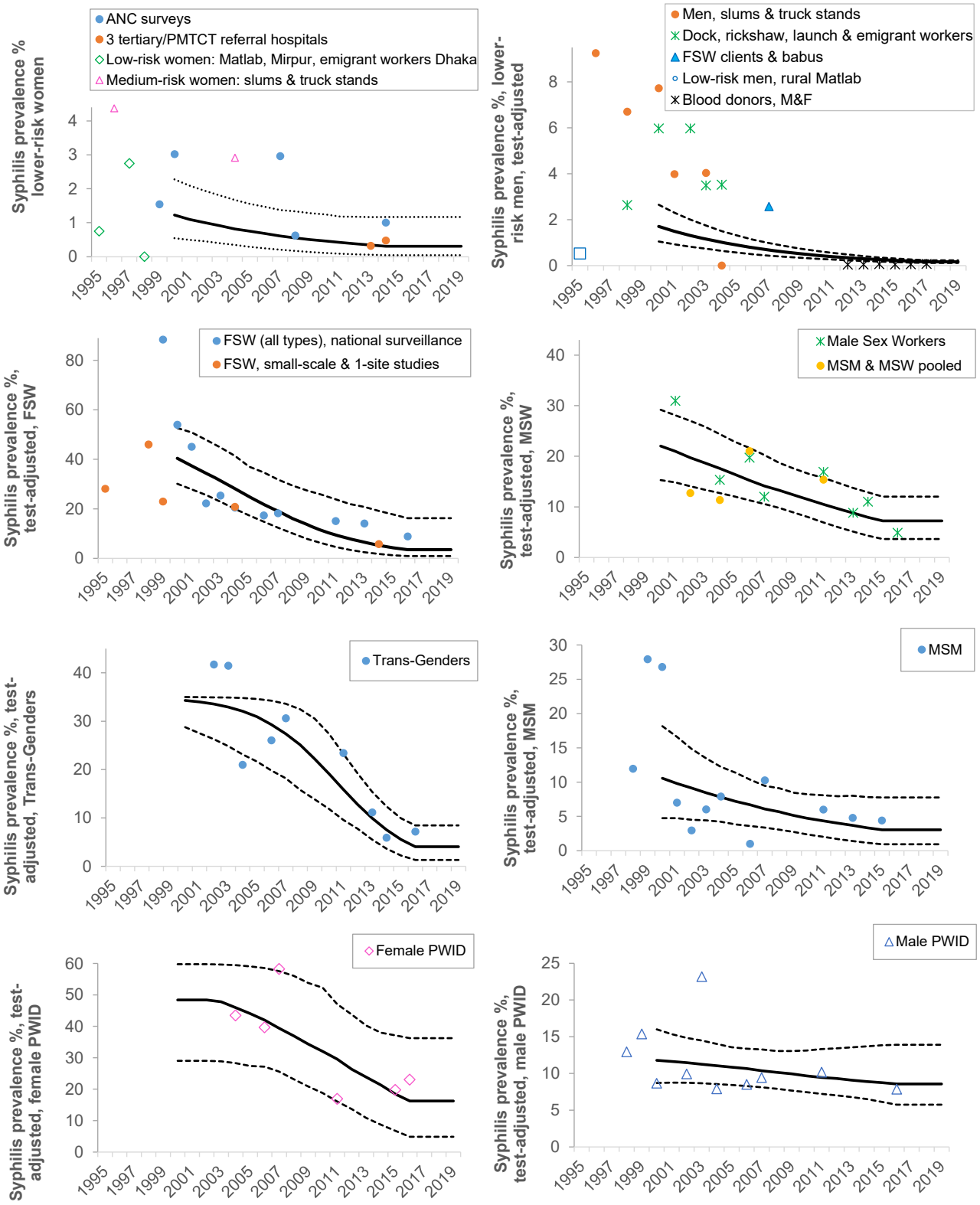
In 2019, women accounted for 62% of prevalent cases, men for 38% and transgenders for 0.2%. In both men and women, the higher-risk groups contributed relatively little to the overall prevalence, due to their small sizes.

Comparing the prevalences in 2000 and 2019, the 2019 estimates were lower than the 2000 estimates for all 8 population groups. For FSW, TG, MSW and Low-risk men, the respective 95% CIs did not overlap, suggesting that the decline was statistically significant. For the other 4 groups the 95% CIs overlapped between 2000 and 2019, which indicating that the decline from 2000 to 2019 was not statistically significant, but might represent a chance finding reflecting mere fluctuations in the data.

Table 3. Estimates of prevalence of active syphilis, and shares in national prevalent cases, for 8 adult (15-49 years) sub-populations in Bangladesh, 2000 and 2019

	Prevalence						Prevalent cases		Share in prevalent cases					
	2000			2019					Women		Men		Women & men	
Population (15-49 years)	Best estimate	Lower bound	Upper bound	Best estimate	Lower bound	Upper bound	2000	2019	2000	2019	2000	2019	2000	2019
All women	**1.3%**	**0%**	**3.7%**	**0.32%**	**0%**	**0.89%**	**418,439**	**145,245**	**100%**	**100%**			**100%**	**100%**
All men	**1.8%**	**1.2%**	**2.3%**	**0.19%**	**0.14%**	**0.25%**	**596,217**	**89,292**			**100%**	**100%**		
Low-risk Women	1.2%	0.54%	2.3%	0.31%	0.0%	1.2%	388,954	141,438	93%	97%			38%	60%
Female Sex Workers	40.4%	30.1%	52.7%	3.5%	0.9%	16.2%	29,117	3,629	7%	2.5%			2.9%	1.5%
Female PWID	48.4%	29.0%	59.7%	16.2%	4.8%	36.2%	368	178	0.1%	0.1%			0.04%	0.08%
Low-risk Men	1.7%	1.1%	2.7%	0.17%	0.12%	0.23%	572,417	78,244			96%	88%	56%	33%
Men who have sex with men	10.6%	4.8%	18.2%	3.0%	0.9%	7.8%	12,441	4,872			2.1%	5.5%	1.2%	2.1%
Male PWID	11.8%	8.7%	16.0%	8.6%	5.7%	13.9%	3,442	3,408			0.6%	3.8%	0.3%	1.5%
Male Sex Workers	22.0%	15.3%	29.2%	7.2%	3.6%	12.0%	5,220	2,335			0.9%	2.6%	0.5%	1.0%
Trans-Genders	34.3%	28.8%	35.0%	4.0%	1.3%	8.5%	2,698	432			0.5%	0.5%	0.3%	0.2%

Figure 2. Syphilis prevalence data and Spectrum-STI trend estimate for: (a/top-left) lower-risk women; (b/top right) lower-risk men; (c/upper-mid left) FSW; (d/upper-mid-right) MSM; (e/lower-mid left) Transgenders; (f/lower mid-right) MSW; (g/bottom left) female PWID; h/bottom right) male PWID.



Notes to Figure 2: Data weights used in the estimation, and sources of data points, are listed in Table 2.
data are shown as colored dots/symbols; the Spectrum estimate as black lines (solid lines is best estimate; dashed lighter lines are the upper- and lower-bounds of the 95% confidence interval. One small-scale survey of high-risk women residing in a slum encircling Tejgaon truck stand of Dhaka, was taken to be FSW, and (for visibility on the graph) shown as 1999 but the data were collected in 1998 and used in estimation for 1998. Unless indicated, for the 6 high-risk groups data come from national surveillance/IBBS. All prevalence data and estimates shown were adjusted for diagnostic test type.

Estimated syphilis incidence rates and incident case numbers

Annual incidence was derived by dividing the estimated prevalence by the average duration of infection [61] using the 2012 WHO average durations of infection values for countries with low treatment access. This duration was estimated by the WHO as an average of 5.16 years for syphilis, considering that on average 60% of syphilis episodes are symptomatic, and of symptomatic episodes, in low-treatment access countries including Bangladesh on average 35% would get treated – in both men and women.

Applying these duration assumptions (across all groups, and throughout 2000 to 2019) to the Spectrum-estimated prevalence, the corresponding incidence was 28,148 and 17,305 new cases in 2019 alone in women and men, respectively – with the male-to-female distribution and change from 2000 to 2019 proportionally to the respective differences in syphilis prevalence (Table 4). Across sub-populations, the distribution in syphilis incidence would also be proportional to that in prevalence, in this calculation which assumes equal duration across all groups.

Table 4. Estimated new syphilis case incidence, based on Spectrum-Sti estimates of the prevalence of active syphilis, Bangladeshi adults (15-49 years)

Indicator	Incidence rate per 1000 population		Incident cases	
Year	**2000**	**2019**	**2000**	**2019**
F	2.6	0.61	81,093	28,148
M	3.4	0.38	115,546	17,305
F+M	**3.0**	**0.50**	**196,639**	**45,453**

Sensitivity analysis

Four alternative estimation 'scenarios' looking at how estimated prevalence in 2000 and 2019 changed when altering group assignment of some data points (scenarios 1 and 4; weights attached to data (scenario 2) or relative population sizes of different subpopulations (scenario 3). The resulting changes to the estimation result are summarized in Table 5.

In the first alternative scenario, the MSM+MSW pooled data (4 data points) were used in the MSM estimation, instead of in the MSW estimation. This slightly increased the prevalence estimates in 2000 and 2019, and decreased the estimate for MSW in year 2019 but had no effect on the MSW 2000 value. The overall adult male estimate did not materially change.

In the second alternative scenario, data from medium-risk individuals (2 female [31,45] and 11 male data points [3-6,27,31,36,45] were excluded from the lower-risk group (male and female) estimations. This

decreased the estimate for the male lower-risk group, throughout 2000, and so did the corresponding overall male estimates.

In the third alternative scenario, the size of the key populations (FSW, MSM, TG and PWID) was taken from UNAIDS' estimates for South-East Asia as a region (Table 1a [17-19]), rather than the AEM model data for Bangladesh. UNAIDS estimated larger proportional group sizes for all higher-risk groups, and as a result, the overall prevalence for men increased, from the default of 0.19% to 0.23% in 2019. For women, the corresponding increase was negligible (from 0.32% to 0.33%).

In the fourth alternative scenario Lower-risk men were split into two groups – Low-risk men and FSW clients – using the sub-population size estimates from the AEM HIV model. Two data points from babus (sampled in the 2002 and 2003-4 [8] IBBS) that were excluded from the default estimation were combined with the 11 male data points from medium-risk men to form the new group FSW clients. The estimate for this new population was 10.7% in 2000 and 8.9% in 2019 and the estimate for lower-risk men in 2019 fell from 0.17% to 0.06%. Combining all male groups increased the overall estimate for men to 2.0% in 2000 and 1.1% in 2019 owing to the large size of the FSW clients group (11.5% of all men 15-49 years; Table 1a). This scenario suggests that the pooling of medium-risk people data into the lower-risk estimation may have over-simplified the gradients of risk existing within the general, lower-risk population. By consequence, the default estimates may be too low for men, and the decline in prevalence for men in the general heterosexual population over-estimated.

Table 5. Sensitivity analysis: effect of varying assumptions and data types included for each population group estimated, on estimated syphilis prevalence in 2000 and 2019

Scenario number	**0**		**1**		**2**		**3**		**4**	
Scenario description	**Default/Best**		**Pool MSM+MSW data into MSM instead of into MSW**		**Exclude data from medium-risk groups, from lower-risk estimation**		**MSM, FSW, PWID and TG group sizes as South-East Asia average**		**Split Lower-risk men into Low-risk versus FSW clients**	
Population	**2000**	**2019**	**2000**	**2019**	**2000**	**2019**	**2000**	**2019**	**2000**	**2019**
All women 15-49 years	**1.32%**	**0.32%**	**Unchanged**		**1.33%**	**0.38%**	**1.39%**	**0.33%**	**Unchanged**	
All men 15-49 years	**1.77%**	**0.19%**	**1.77%**	**0.20%**	**0.48%**	**0.06%**	**1.88%**	**0.23%**	**2.03%**	**1.09%**
Low-risk Women	1.23%	0.31%	Unchanged		1.24%	0.37%	Unchanged		Unchanged	
Female Sex Workers	40.4%	3.5%	Unchanged		Unchanged		Unchanged		Unchanged	
Female PWID	48.4%	16.2%	Unchanged		Unchanged		Unchanged		Unchanged	
Lower-risk men	1.71%	0.17%	Unchanged		0.42%	0.04%	Unchanged		0.82%	0.06%
Male FSW clients	NA	NA	NA		NA		NA		10.73%	8.86%
Men who have sex with men	10.6%	3.0%	10.8%	3.5%	Unchanged		Unchanged		Unchanged	
Male PWID	11.8%	8.6%	Unchanged		Unchanged		Unchanged		Unchanged	
Male Sex Workers	22.0%	7.2%	25.1%	6.0%	Unchanged		Unchanged		Unchanged	
Trans-Genders	34.3%	4.0%	Unchanged		Unchanged		Unchanged		Unchanged	
Sub-Population sizes used in sensitivity analysis/scenario 4, splitting Lower-risk men into 2 groups:										
Low-risk men (not FSW client)									29,694,015	40,416,588
FSW clients									3,858,544	5,251,873
Total population, lower-risk men									**33,552,560**	**45,668,461**

Note to Table 5. The 4th sensitivity analysis/scenario moved 11 datapoints, from FSW clients [27] and other medium-risk groups [3,5,6,31,36,45,56] from the Low-risk men dataset into the FSW client dataset, and added two data points from babus (2002 and 2003; 4th and 5th rounds of IBBS [8]) to the latter. All other lower-risk male data remained with the low-risk men estimation.

DISCUSSION

The 2019 syphilis prevalence estimate in Bangladesh for women 15 to 49 years was 0.26% (0-0.68%) and for men 0.14% (0.09-0.18%). These levels are low compared to other East and Central Asia countries [13,60], compared to middle-income countries in the Western Pacific [62], and compared to low-income countries in Africa [14]. The estimates for all 8 population groups were lower in 2019 than in 2000 – and for four of the groups (FSW, TG, MSW and Low-risk men) the 95% CIs did not overlap. Although the statistical trend estimates based on surveillance data are not an analysis of cause and effect, the estimated trends are consistent with Bangladesh's national HIV/ STI response having been effective at reducing the prevalence of syphilis over the last two decades.

Bangladesh has a wealth of syphilis prevalence data from IBBS. There are data from 10 rounds (from 1998 to 2016) and from over 10 different population groups sampled from over 25 different locations.

Syphilis shares its behavioural risk factors (notably, unsafe sex) as well as protective factors (e.g. condom usage) with HIV/AIDS, for which Bangladesh has conducted national estimations in several rounds, using the AEM model. To explore the broad consistency of the syphilis estimates, we compared the 2019 distribution of syphilis case load by sub-population in 2019 (default scenario) with the 2019 AEM model estimates of HIV incidence and prevalence, that used very similar population size estimates (Figure 3).

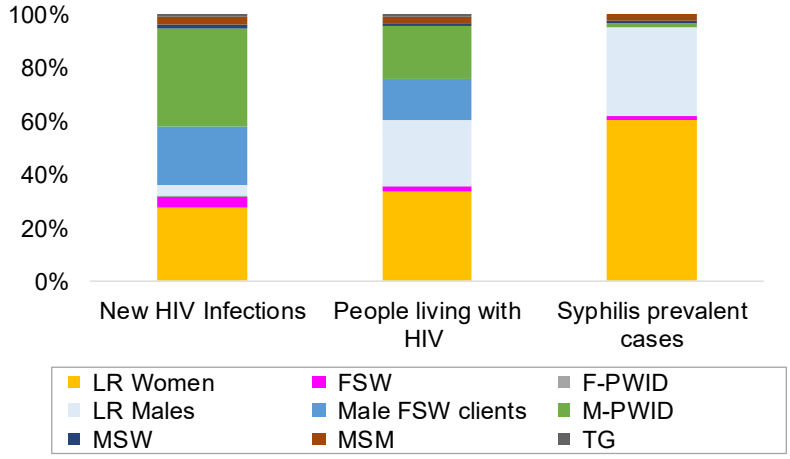
Given the longer average duration of HIV infection compared to syphilis, syphilis case load might be expected to correlate more with HIV incidence than with HIV prevalence. Nevertheless, the population distribution of syphilis cases is closer to the distribution in HIV prevalence than that in HIV incidence, with the largest share born by the large groups of low-risk women and secondly low-risk men (including FSW clients) and much smaller contributions from PWID, Transgenders and MSW.

In the syphilis estimations, low-risk populations have a larger share in national burden than for HIV. This difference is particularly pronounced for PWID, reflecting that HIV is spread primarily through shared needles rather than sexual intercourse. The differences between the relative contribution of the different populations to the burden of syphilis and HIV furthermore reflect the respective probabilities of transmission, access to treatment and prevention services (e.g. treatment of syphilis among diagnosed PLWHIV may have lowered the relative syphilis burden in higher-risk groups).

It should be noted that whilst key populations, such as FSW and MSM, may account for only a small proportion of syphilis and HIV cases, they do play a role in the spread of infection to the more general population. Syphilis and HIV infections among apparently "lower-risk" adults often still have their origins in contacts between and with members of key populations. Men who are or were clients of FSW premaritally or extramaritally can acquire the infection and pass it on to their wives later, even if they have currently ceased to engage in higher-risk behaviors. MSM are often in opposite-sex relationships due to social pressures to marry and social sanctions on same-sex behaviours, creating opportunities for transmission to women. Current and former PWID can transmit syphilis or HIV through needle sharing and sometimes engage in higher risk sexual behaviours, explaining their elevated syphilis rates. They too, can place their current and future spouses or regular sexual partners at risk. While these former key population members and the spouses of current and former key population members are often classified as "lower-risk" based on their "perceived" risk at present, in

reality, the past or present behavior of them or their spouses actually places both at high-risk for incidence and prevalence of either pathogen [63]. Therefore, key populations, even if small in the national syphilis disease burden remain priority groups for targeted interventions to bring down their disproportionately high HIV and syphilis rates and associated transmission potential.

Figure 3. Distribution between risk groups in Bangladesh, in prevalent and incident HIV infections, and prevalent syphilis cases



Notes to Figure 3: HIV numbers from the AEM model, for 2018; syphilis from Spectrum-Sti estimations presented in this study, 2019. For syphilis, male FSW clients were not distinguished, but rather included with lower-risk men.

Limitations

As any prevalence or burden estimation, this study has some important limitations. First, results are very dependent on the underlying national prevalence data, which varied in representativeness and – probably – in quality. The sensitivity analysis highlighted how estimated trends depend on data types included, and how these were combined or separated out.

Importantly, for lower-risk men our default estimate was below that for women, and men also had a lower estimated share in overall prevalent and incident syphilis cases. However, the sensitivity analysis (Scenario 4) highlighted that pooling data between low-risk and (suspected or known) medium-risk populations such as FSW clients and truck drivers may over-simplify the gradients of risk existing within a population.

Within the estimated groups of FSW, MSM and PWID, there are sub-groups with different risk profile and prevalence. Several of Bangladesh' IBBS rounds recognized sampled and reported sub-groups of FSW individually; however available data varied in groups and sub-groups considered across sites and years. Therefore, and considering that for some sub-populations the relative sizes were unknown (e.g. brothel-based versus hotel-based, street-based and casual FSWs), further disaggregation was not deemed feasible.

Of note, some groups sampled in IBBS – for example STI patients, and partners of transgenders – were not included in our estimation, as we did not know their population size, or the extent to which they are also represented within the general population surveys that the estimations did include. The

exclusion or under-sampling of such higher-risk group may have caused our overall estimate to be too low.

Similarly, the IBBS data as recorded included single-site results for some sites, populations and rounds – which our estimation pooled (into 1 aggregated IBBS data point per population per year/round). Since sites varied over the subsequent rounds, and prevalence appeared consistently higher in some sites, this simplification may have biased the actual time trend. However, earlier descriptive analysis of these data (without a modelling synthesis) generally concluded on similar trends – of declines within 2000-2016 notably among FSW and MSM – as our combined analysis.

Recommendations for STI surveillance and programming

Bangladesh' draft 2019-2027 STI strategy includes among its milestones: *Have regular STI surveillance systems in place … report prevalence of infection by Ng, TP, HPV and Ct in general population. Syphilis (unlike the other infections mentioned) has the luxury within the surveillance system of periodic prevalence measurements in many groups, through the two-yearly national IBBS surveillance.* Between 1998 and 2016, ten rounds of IBBS have collection of substantial data on various and varying medium- and higher-risk populations, which provide a solid indication of overall time trends in syphilis and a basis for evaluating programmatic impact. However the size of some of these groups (e.g. male dock workers, launch workers, rickshaw pullers) is not well known, and therefore their role in the overall national adult epidemic is less clear and more difficult to model as well. What Bangladesh lacks is recent and periodic data on the general adult population. Notably for ANC women, there was only one nation-wide sentinel surveys (in 2008) and smaller-scale surveys in 2000 and 2007, and ANC women are not sampled in IBBS.

The absence of data from 'routine' ANC-based screening in part reflects that this service – while being rolled out, using VDRL testing – is not yet available nation-wide. Monitoring and realizing progress towards EMTCT of congenital syphilis, will require universal syphilis screening – whose results would be of great value for STI surveillance too. With an overall adult prevalence estimated at just below 0.5% Bangladesh has the potential to reach the threshold for EMTCT of a CS rate below 50/100,000 [64] – if it can reach and proof having 95% coverage of three essential services: ANC-1 attendance (at least 1 ANC visit per pregnancy), ANC-based syphilis screening and treatment of women diagnosed during ANC.

As an interim measure, the planned **2020 IBBS round** might consider to sample selected ANC sites (including some district and 'upazila' clinics rurally)– and/or groups of heterosexual men in the general population, such as FSW clients, truck drivers and other mobile workers. Interpretation of IBBS data in an international context, where most surveys in other countries do not constrain prevalence by high-titer RPR, may be to report prevalence not only for Bangladesh' definition of TPHA with high-titer RPR but also, alongside, for the international WHO standard definition including TPHA with RPR in any titer.

Besides the IBBS, the pending **STI surveillance 2019-2020**, coordinated by IEDCR, may provide a chance for small-scale prevalence assessments. Building on past sample surveillance rounds, these may complement ongoing surveillance by sampling lower-risk populations, through drop-in centers for key populations, gynaecology clinics in medical colleges, and primary ANC clinics. These may cover not only syphilis, but also gonorrhea, chlamydia and even antimicrobial-resistant *N. gonorrhea*, another indicator requested by the WHO for annual reporting through the GAM system . The usefulness of such small-scale assessments will depend on the representativeness. Clear articulating of

sampling criteria and methods, and the resulting population represented, is critical. Given the low expected prevalence, a fairly large sample size may be needed: as an example, if prevalence is 0.20% in ANC, then sampling 1,000 women sampled would on average yield 2 positive tests per site; thus a 1,000 sample size may be the very minimum.

Blood donor screening is a source of surveillance data ready to be exploited, if requested from blood banks annually. Ideally, screening results are segregated between men and women. Blood donors may or not be representative of the overall population; typically paid donors may be relatively high risk for being poor and/or being PWID; but relatives of patients or voluntary donors more representative. Among any type of donor, repeat donors will have lower-prevalence than candidates first presenting for blood donation, as those candidates found with any blood-transmittable infection will be screened out; therefore the ideal data are by type of donor, and limited to the subset of first-ever screenings/donors.

In terms of **programming and targeting services**, key populations clearly remain a priority in syphilis control, for two reasons. First, key populations probably have a larger share in incident cases than in prevalent cases, as their syphilis treatment coverage may be higher/better, if they received more regular syphilis screening than lower-risk populations. Increased treatment coverage reduces the average episode duration, so that key populations may have a higher incidence for a given prevalence, compared to lower-risk populations who benefit less from periodic syphilis screening and treatment. Second, the share in prevalent or incident burden does not indicate the share in onward transmission of infections. By having more partners, key populations have a larger contribution to ongoing transmission, than lower-risk populations with fewer partners.

The presented estimations furthermore highlighted that syphilis burden may be quite high in the general, heterosexual male population – depending on the size of intermediate risk sub-groups such as FSW clients. These sub-groups, if reachable, may be another priority target for outreach STI screening and control activities.

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