Is it possible to reduce syphilis and gonorrhoea incidence by 90%? A review of STI control in the WHO South-East Asia Region with an eye on 2030 global targets

Tjandra Yoga Aditama, Bharat Bhushan Rewari, Mukta Sharma, Prasad Turlapati, Gina Dallabetta, Richard Steen

Abstract (346 words)

The WHO has set targets for 90% reductions of syphilis and gonorrhoea incidence by 2030. We review STI trends and country experience in the WHO South-East Asia Region (SEAR) to assess current status of STI control and feasibility of reaching global targets. Methods include literature review, trend analysis of routine data and structured interviews with programme managers.

The proportion of new STI cases estimated for SEAR has declined from a third of the total global estimate in the 1990s to 11% in 2012. Three countries – Sri Lanka, Thailand, Myanmar – have reported 90% or greater reductions in syphilis and/or gonorrhoea at some point between 1975-2010. Evidence from multiple sources suggest that smaller STI reductions over India's large population have driven regional declines. In the other seven countries, STI trends remain high, are increasing, or data are not reliable enough to measure change. Most countries in the region, however, including those with good control, have seen some evidence of STI resurgence during the past decade.

STI programme structure, resources and performance also vary greatly across the region, with strong, multi-pronged programmes in Sri Lanka and Thailand, and targeted STI control efforts at scale in Myanmar and India. In other countries, limited STI activities are often subsumed by AIDS programmes, where programme managers report low priority and limited resources for STIs. A consistent programme component in countries with documented STI reductions is a focused approach to condoms and STIs among key populations. At national and sub-national levels, data show rapid STI declines when targeted STI services are scaled up to reach sex workers in large numbers, particularly where peers and communities are actively involved in implementation. The converse also appears to be true as STI outbreaks in underserved MSM networks are linked to rebounding STI trends.

The regional approach for SEAR prioritises 'reducing STI transmission in highest transmission networks', while also supporting progress towards universal access and reliable STI surveillance as endorsed in the global STI strategy. Regional experience argues that the former may be the critical link to achieving global STI control targets.

Corresponding author

Richard Steen (steenr7@gmail.com)

Word count: 3328

Short abstract (249 words)

The WHO has set targets for 90% reductions of syphilis and gonorrhoea incidence by 2030. We review STI trends and country experience in the WHO South-East Asia Region (SEAR) to assess current status of STI control and feasibility of reaching global targets.

STI estimates for SEAR have declined from a third of the global total in the 1990s to 11% in 2012. Sri Lanka, Thailand and Myanmar have reported 90% or greater reductions in syphilis and/or gonorrhoea between 1975-2010. Evidence suggest that smaller STI reductions over India's large population have driven regional declines. In other countries, STI trends remain high, are increasing, or data are not reliable enough to measure change. Most countries in the region, including those with good control, have seen evidence of STI resurgence during the past decade.

STI programme structure, resources and performance also vary greatly across the region, with strong programmes in Sri Lanka and Thailand, and targeted control efforts at scale in Myanmar and India. In other countries, limited STI activities are subsumed by AIDS programmes, where programme managers report low priority and limited resources for STIs.

Key populations appear to be critical. At national and sub-national levels, data show rapid STI declines when targeted condom and STI services are scaled up to reach sex workers in large numbers, particularly where peers and communities are actively involved in implementation. The converse also appears to be true as STI outbreaks in underserved MSM networks are linked to rebounding STI trends.

Background

The World Health Organization (WHO) has set global targets calling for 90% reductions in the incidence of *Treponema pallidum* (Tp/syphilis) and *Neisseria gonorrhoeae* (Ng/gonorrhoea) by 2030. [1] We review sexually transmitted infection (STI) trends and country experience in the WHO South-East Asia Region (SEAR) to assess the current status of STI control and feasibility of reaching global targets. The primary focus is on control of common curable STIs – syphilis, gonorrhoea, chlamydia, chancroid and trichomoniasis.

Historically, STIs have been among the most serious public health problems in SEAR, with high associated morbidity, mortality, disability and adverse pregnancy outcomes. [2-4] The incidence and prevalence of curable STIs were extremely high in urban areas, along migrant and trucking routes, and closely linked – particularly ulcerative chancroid and syphilis – to rapid early spread of HIV. However, large-scale interventions to improve conditions and increase condom use in sex work led to large STI declines and slowing of HIV epidemics in several countries during the 1990s and early 2000s.

Recent reports of rising syphilis and gonorrhoea incidence raise concerns about the adequacy of current STI prevention efforts as programmes focus increasingly on HIV-specific interventions such as antiretroviral therapy (ART) and pre-exposure prophylaxis (PrEP). [5-7] Declining condom use and behavioural risk compensation, particularly within key population networks, may facilitate resurgent STI transmission at a time when resources are insuffient for condom programmes and basic STI services.

This review aims to assess current STI epidemiology and control in SEAR with attention to recent trends and regional heterogeneity both across and within countries. Where STI control has improved, we look for evidence of what constitutes an effective response.

Methods

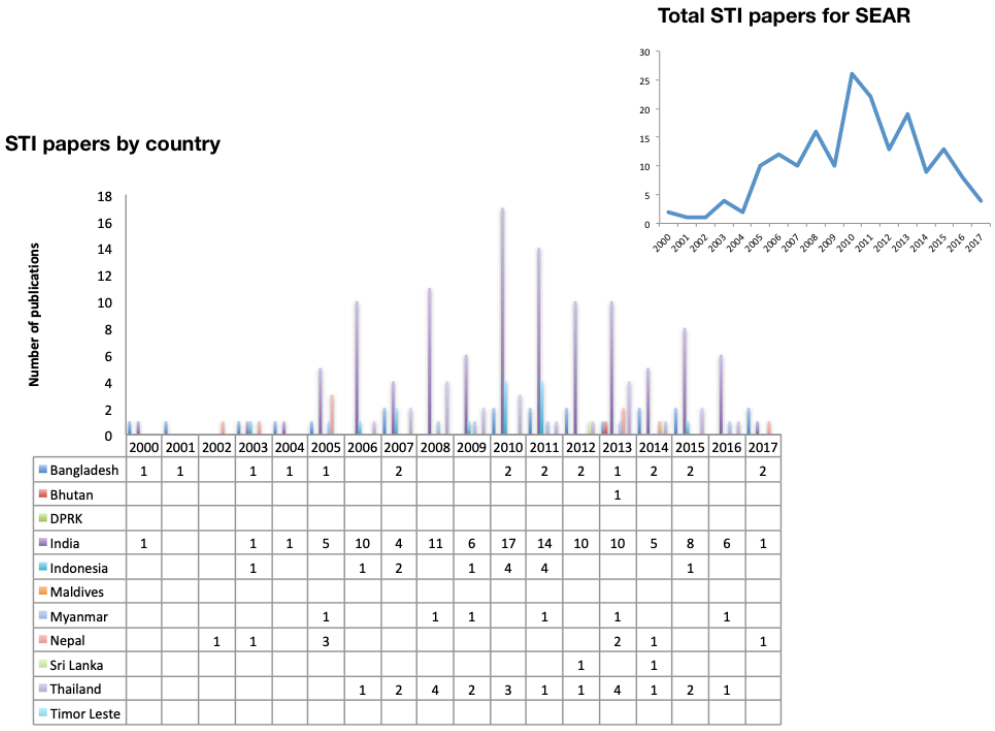
This review of the STI situation in SEAR comprises a broad assessment of available regional data, national STI programme capacity and performance, and sub-national examples. It was conducted in April-May 2018 using multiple methods including literature review, interviews and analysis of available country data (updated in July 2019). Interviews using a structured set of questions involved programme managers and WHO country focal points responsible for STI activities.

We examined trends in the published literature to see if publication bias might be a factor in assessing STI epidemiology and programme factors in SEAR countries. WHO global STI estimates are based mainly on review of prevalence studies reported in the published literature. [8-11] The WHO uses these methods for STI estimation partly due to a lack of reliable routine STI reporting from countries (this is only partially true for SEAR, as discussed below).

However, the publication of papers with an STI focus has fluctuated widely over past decades. Figure 1 summarises the number of papers from SEAR sites mentioning STIs as a main topic since 2000. The number of studies peaked from about 2005 to 2013, a period when donor

investment in STI control (including the large Avahan India AIDS Initiative) was highest. Studies reporting data on STI incidence or prevalence are a subset of the total and follow a similar pattern. [11]

Figure 1. STI literature – number of papers with STI as a major focus



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Bangladesh	1	1		1	1	1		2			2	2	2	1	2	2		2
Bhutan														1				
DPRK																		
India	1			1	1	5	10	4	11	6	17	14	10	10	5	8	6	1
Indonesia				1			1	2		1	4	4				1		
Maldives																		
Myanmar						1			1	1		1		1			1	
Nepal			1	1		3								2	1			1
Sri Lanka													1		1			
Thailand							1	2	4	2	3	1	1	4	1	2	1	
Timor Leste																		

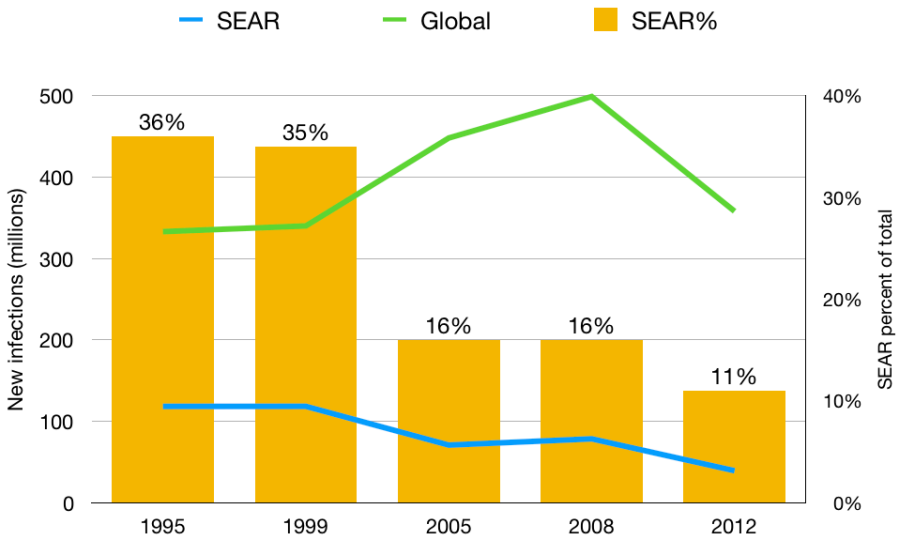
Several limitations are apparent when estimating STI burden and trends from the literature. The number and distribution of studies with population-based prevalence data are few and poorly represent regional diversity. In addition, given fluctuations over time, the likelihood of publication bias is high, particularly as sites with donor-supported interventions (and related publications) may achieve better STI control than those without resources. Most published STI prevalence data in SEAR come from key populations (KP), male bridge groups or clinic-based samples, which are informative for those sub-populations but cannot be directly extrapolated to derive general population estimates.

Several countries in the region routinely monitor STI trends through national STI surveillance systems. In Thailand, Sri Lanka and Myanmar, surveillance data were assessed to be complete enough to permit analysis of STI trends at national level. Incomplete reporting in other countries precluded similar analysis.

Findings

WHO global estimates for four common curable STIs – syphilis, gonorrhoea, chlamydia and trichomoniasis – have shown little change over three decades. Yet, the proportion of new cases estimated for SEAR has declined from a third of the total global estimate in the 1990s to 11% in 2012. Despite limitations of methods used, such a large magnitude of change begs further analysis. An important possibility is that STIs have indeed declined dramatically in SEAR, more so than in other regions. Evidence for and against this hypothesis is examined from national and sub-national data, with special attention to the most populous countries, which have disproportionate influence on regional trends.[1]

Figure 1. Global STI trends and proportion estimated for SEAR



Reported STI declines, routinely reported data from programmes

Routinely reported STI surveillance data vary greatly in completeness and reliability across the region. Yet, such data from several countries is sufficiently robust to examine long-term trends in common curable STIs. Table 1 summarises data from Sri Lanka, Thailand and Myanmar, which show >90% reduction in incidence or prevalence of select STIs over different but overlapping time periods. These data demonstrate the feasibility of achieving greater than 90% reductions in syphilis, gonorrhoea and chancroid.

[1] Any regional trends in SEAR are driven strongly by events in India, which accounts for about 68% of the region's population.

Table 1. Reported country-level reductions in common curable STIs in SEAR since 1975

Country	STI	Interval	Pre	Post	Reduction	Rate
Sri Lanka	Gonorrhoea	1975-2000	61.6	3.5	94.3%	Cases per 100,000 population
	Syphilis	1975-2000	21.5	1.4	93.5%	Cases per 100,000 population
Thailand	Gonorrhoea	1985-2005	445	7	98.4%	Cases per 100,000 population
	Syphilis	1985-2005	32	2.1	93.4%	Cases per 100,000 population
	Chancroid	1985-2005	93	0.4	99.6%	Cases per 100,000 population
Myanmar	Gonorrhoea	1985-2005	15.4	1.4	90.6%	Cases per 10,000 male population
	Syphilis	1996-2016	4.2	0.3	92.9%	Prevalence ANC screening
	Chancroid	1985-2005	7.5	0.4	94.5%	Cases per 10,000 male population

Figures 2 and 3 show more detail on these declining STI trends in Sri Lanka and Thailand. Both countries have detected increases in syphilis and gonorrhoea during recent years through routine surveillance, and have used such data to inform and strengthen control efforts.

Figure 2. STI trends Sri Lanka, 1952-2016

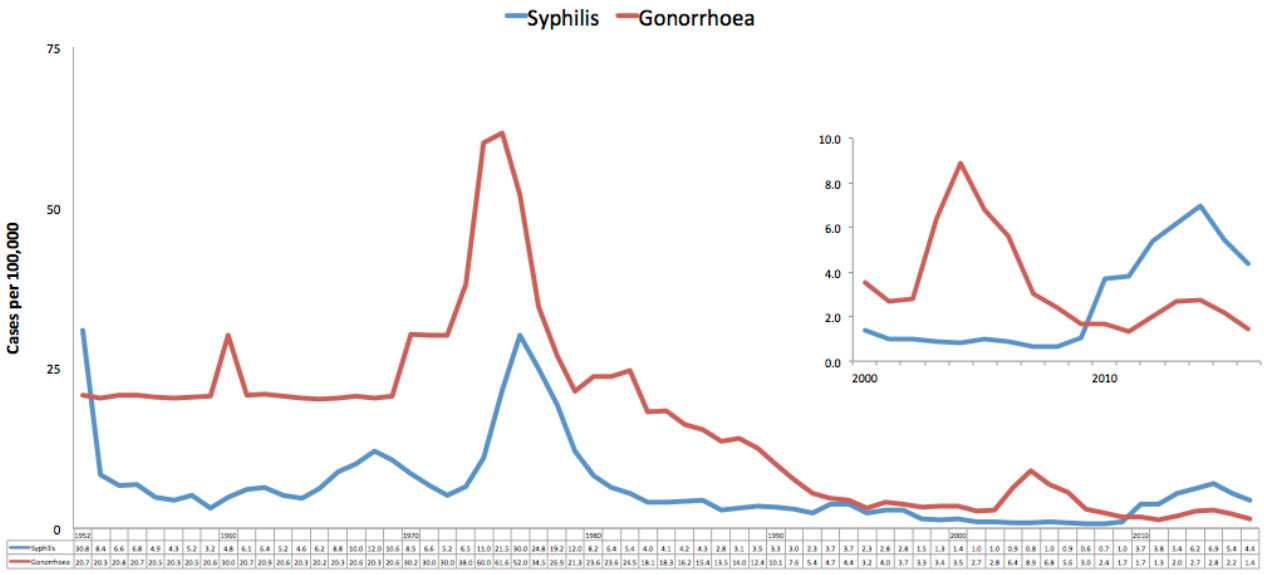
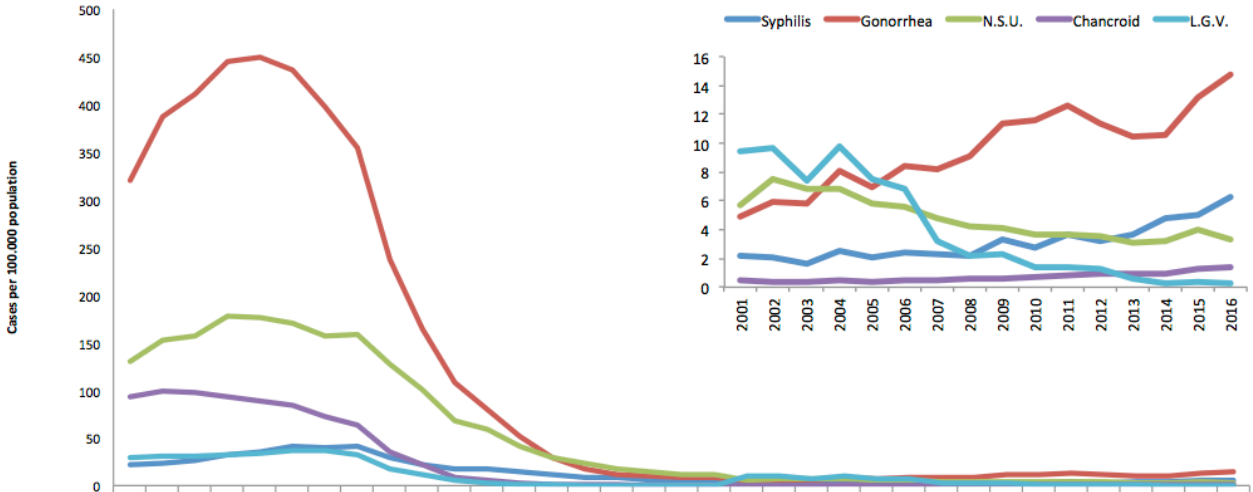


Figure 3. STI trends Thailand, 1982-2016



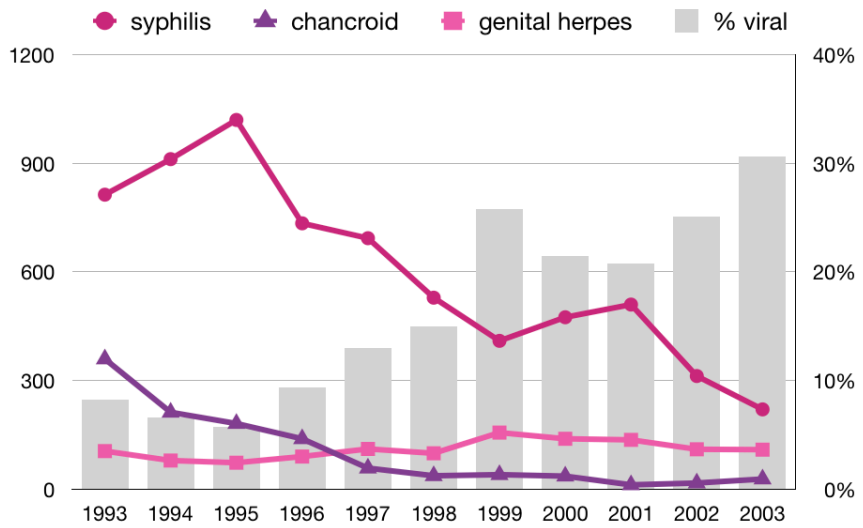
	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Syphilis	22	23	26	32	36	41	40	41	30	22	17	17	15	11	8	8	6	5	5	2.2	2.1	1.6	2.5	2.1	2.4	2.3	2.1	3.3	2.8	3.6	3.2	3.7	4.8	5.1	6.2
Gonorrhea	320	387	411	445	450	436	397	355	237	164	108	80	52	30	18	12	10	9	9	4.9	5.9	5.8	8.1	7.0	8.4	8.1	9.1	11.3	11.6	12.6	11.4	10.4	10.6	13.1	14.7
N.S.U.	131	153	157	178	176	170	157	159	128	101	68	59	42	30	23	17	15	11	12	5.7	7.5	6.8	6.9	5.8	5.6	4.8	4.2	4.1	3.6	3.6	3.5	3.1	3.2	3.9	3.3
Chancroid	93	99	98	93	89	85	73	63	35	22	9	5	3	1	1	1	0	0	0	0.4	0.4	0.3	0.5	0.4	0.5	0.5	0.6	0.6	0.7	0.8	0.9	0.9	1.0	1.2	1.4
L.G.V.	29	31	31	32	34	37	37	32	18	12	5	3	1	1	0	0	0	0	0	9.4	9.7	7.4	9.8	7.5	6.8	3.2	2.2	2.3	1.4	1.4	1.2	0.5	0.3	0.4	0.3

Evidence of STI declines in India

India is the largest country in the region, accounting for over two-thirds of SEAR's population. Geographically large and diverse, it has also demonstrated a large degree of heterogeneity in STI epidemiology and control over the years. [3,4] Historically, STI transmission, including the early AIDS epidemic, followed migrant pathways to large cities such as Mumbai, Delhi, Kolkata and Chennai, and early control efforts focused on large metropolitan areas. From about 2004 onwards, large-scale efforts were made to scale up interventions and services for KP, first in high-prevalence states and along major highways (Avahan), then nationwide (NACO). [12,13] STI prevention, screening and treatment were major programme components.

India lacks reliable national-level STI incidence or prevalence data. However, numerous epidemiological studies illustrate changing trends and patterns over several decades. Those from the 1990s describe similar patterns of poor control – high prevalence rates of bacterial, and particularly ulcerative STIs including chancroid, which were closely associated with HIV transmission in largely urban settings characterised by high vulnerability, migration and population mobility. [14-23] Later studies show very different epidemiological trends and patterns particularly after about 2005. Compared to studies from the 1990s, STI rates are commonly lower, with significant aetiological shifts from bacterial and ulcerative infections to chronic viral STIs. Figure 3 shows how this trend progressed for genital ulcers in Chennai with 73-92% declines in syphilis and chancroid over ten years. These patterns continued elsewhere during the first decade of the millennium [24-41] with data closely linked to ongoing intervention efforts. [13,35-41]

Fig 3. Genital ulcer trends, Madras Medical College STD Clinic 1993-2003 [42]



Among the earliest and largest declines were reported among female sex workers in Kolkata following implementation of targeted condom and STI interventions with active community involvement. Syphilis prevalence, assessed by sentinel surveillance, declined by more than 99%, from 25% in 1992 to 0.2% in 2005. [24] Another community-led intervention project in two districts of Karnataka reported significant reductions in prevalence of syphilis (45%), gonorrhoea (83%) and chlamydia (63%) between the start of the intervention in 2004 and 2009. with more recent routine clinic data showing near elimination of several common STIs. [25,26] Increasing condom use and significant STI/HIV declines were reported in surveys from several other districts in Karnataka. [27] In Tamil Nadu, genital ulcers declined two-thirds among FSW, from 13.1% in 1997 to 4.5% in 2008 ($p<0.001$). [28]

Among MSM in Maharashtra, reactive syphilis declined from 8.8% in 2004 to 1.1% in 2008. [29] Syphilis also declined significantly in Tamil Nadu among both high-risk MSM (14.3 percent to 6.8 percent) and transgenders (16.6 percent to 4.2 percent) [30] Significantly decreased STI incidence (p-value for trend<0.001) between 2005 and 2008 was also reported from a study of Bangalore STI clinics. [31] The association of STI declines and Avahan scale-up between 2004 and 2009 is supported by studies in different states (Table 2). During this period, KP outreach and service provision increased rapidly, and a study of STI service quality indicators reported three- to seven-fold improvement. [13,32]

Strikingly different STI patterns were being reported for symptomatic men seeking care from STI clinics compared to the 1990s. Among 121 men with laboratory-confirmed GUD from 8 STI clinics in 4 states, 48% were found to have HSV-2, 23% syphilis with only one case of chancroid. [33] In a busy Mumbai STI clinic, 53% of STIs seen in 1994 were assessed to be bacterial, dropping to 28% in 2006. [34] HSV-2 was the most commonly identified pathogen among adult males and females presenting with genital ulcer disease at clinics in Karnataka. [35] This aetiologic shift from bacterial to viral STIs was also reported in a general population sample from Andhra Pradesh where sero-incidence of HSV-2 was estimated to be 25.6 per 1000 person-years, while only 3.0 for syphilis. [36]

In many cases, papers reported STI reductions linked to large-scale intervention efforts that were being implemented, particularly in four large southern states which account for almost a third of India's population (see Table 2). [36-45]

Table 2. Reported large-scale (state-level or higher) STI reductions in India under Avahan 2004-2009

State(s)	STI	Interval	Pre	Post	% decline	Notes	Reference
Andhra Pradesh	Syphilis	2006-2009	10.8	6.1	44%	Consistent condom use increased with regular (63.6% to 83.4%; p<0.001) and occasional clients (70.8% to 83.7%; p<0.001). The prevalence of lifetime syphilis decreased (10.8% to 6.1%; AOR=0.39; p<0.001)	Rachakulla [37]
Karnataka	Syphilis (high titre)	2004-2009	5.9	3.4	42%	Over 85% of FSW reported contact by a peer educator and having visited a project STI clinic. Reductions in prevalence of high-titre syphilis (5.9% vs 3.4%, p=0.001); and chlamydia and/or gonorrhoea (8.9% vs 7.0%, p=0.02).	Ramesh [43] Ramakrishnan [44]
	Ng and/or Ct		8.9	7.0	21%		
Maharashtra	Syphilis	2004-2007				Among FSW, the FPP intervention was significantly correlated with lower probability of STI seropositivity.	Gutierrez [41]
Tamil Nadu	Syphilis	2006-2009	9.7	2.2	77%	Reactive syphilis declined significantly (p=0.001) as programme coverage and consistent condom use rose with occasional (72% to 93%; p=0.001) and regular clients (68% to 89%; p=0.001).	Thilakavathi [38]
Avahan (6 intervention states)	STI syndromes	2005-2009	39	11	72%	Proportion of STI syndromes diagnosed amongst female sex workers as proportion seeking regular STI check-ups increased.	Gurung [39]
			12	3	75%	Proportion of STI syndromes diagnosed amongst high-risk MSM as proportion seeking regular STI check-ups increased)	
Avahan (highway intervention areas)	Syphilis	2007-2010	3.2	1.7	47%	With increased exposure to interventions and consistent condom use with paid female partners, proportion testing positive for syphilis reduced from 3.2% to 1.7% (p<0.05).	Pandey [40]
Avahan (4 intervention states - Andhra Pradesh, Karnataka, Maharashtra, Tamil Nadu)	Syphilis	2006-2008	4.8	2.6	46%	Clients of sex workers significant decrease p<0.001. Increased FSW coverage associated with reduced incidence of syphilis.	Rajaram [45]

Large changes were also reported among lower-risk populations. Syphilis prevalence among pregnant women declines steadily from 3% in 1995 to 0.8% in 2005. [46] In Mysore district in Karnataka, where STIs were virtually eliminated among female, male and transgender sex workers, and an eight-fold reduction in HIV prevalence was measured among pregnant women. [26]

Table 3. Other sub-national STI declines reported from India

Location	STI	Interval	Pre	Post	% decline	Notes	Reference
Kolkata	Syphilis	1992-2005	25	0.2	99%	Prevalence FSW	Jana [24]
Mysore	Syphilis	2004-2009	24.9	13.6	45%	Prevalence FSW	Isac [25]
	Gonorrhoea		5.4	0.9	83%		
	Chlamydia		10.8	4.0	63%		
	Several STIs	2006-2014	586.0	5.0	99%	Routine STI clinic screening data (cases detected)	Reza-Paul [26]
Karnataka	District surveys					Increasing condom use and significant STI/HIV declines	Boily [27]
Tamil Nadu	Genital ulcers	1997-2008	13.1	4.5	66%	FSW (p<0.001)	Charles [28]
Maharashtra	Reactive syphilis	2004-2008	8.8	1.1	87%	MSM	Ramanathan [29]
Tamil Nadu	Syphilis		14.3	6.8	52%	MSM significant decline	Subramanian [30]
			16.6	4.2	75%	Transgender significant decline	
Bangalore STI clinics		2005-2008				Significantly decreased STI incidence (p-value for trend<0.001)	Souverein [31]
Chandigarh hospital	Syphilis	1996-2005	3.0	0.8	72%		Sethi [46]
Madras Medical College STD Clinic	Syphilis	1993-2003	813	221	73%	Genital ulcer trends, STI clinic (cases detected)	Usman [42]
	Chancroid		360	29	92%		

Data on STI epidemiology elsewhere in the region

Among the remaining seven countries in the region, Bangladesh, Indonesia and Nepal have medium to large-sized populations and documented STI epidemics. However, routine STI surveillance is neither complete nor reliable enough to assess trends, and few studies are reported in the literature. Table 4 summarises the limited regional data in the published literature for countries other than India.

Table 4. Sub-national STI declines reported elsewhere in region (apart from India)

Country	STI	Interval	Pre	Post	% decline	Notes	
Bangladesh	Gonorrhoea and/or chlamdyia	9 months	41	7	83%	FSW intervention trial in Dacca hotels following PPT/ ESM intervention	McCormick [47]
Indonesia	Gonorrhoea and/or chlamydia	15 months (March 2008 to June 2009)	36.1	7.6	79%	Decreased prevalence among sex workers in Bintan (both p<0.01). Consistent condom use doubled to 40% (p<0.01). Prevalence lower among those who received PPT (p<0.01).	Bollen [48]
	Chlamydia		33.7	10.2	70%		
	Prevalence of active syphilis (RPR≥1:8)		6.0	3.9	35%	Prevalence lower among those who received at least one dose of PPT (3.9% vs 6.0%; p=0.008)	Majid [49]

Where STI declines have been documented in a few specific locations, these are linked to programmes that have increased condom use in sex work while improving STI clinical services. STI declines are also associated with specific STI interventions such as periodic presumptive treatment (PPT). [47-49]

Programme response and challenges

The programme response to STIs varies greatly across the region, from highly effective to almost non-existent. Many countries are struggling to scale up outreach to key populations, support basic clinical services, maintain stocks of effective STI treatments, conduct STI surveillance and monitor antibiotic resistance. On the other hand, Thailand and Sri Lanka have maintained strong commitment and funding for STI control over many years, and have documented high levels of control over STI/HIV transmission. Thailand and Maldives have recently been certified as having eliminated mother-to-child transmission of both syphilis and HIV, while Sri Lanka is undergoing validation for the same.

Several reasons for this diversity in STI programme capacity and response across the region are evident from review of programme reports and interviews with programme managers. In many countries, STI and HIV programmes merged in the 1990s for greater efficiency, and to leverage higher levels of funding for HIV. In a few countries like Thailand and Sri Lanka, high levels of support for STI control activities were maintained. In most others, attention to scale-up of HIV testing, ART and other HIV-specific services increasingly consumed most human and financial resources. Little or no funding or personnel were left for STI diagnostics, treatment and related control activities such as contact tracing and surveillance. Even basic STI services such as routine syphilis screening in pregnancy were interrupted or abandoned in some countries due to lack of basic commodities, including test reagents and benzathine penicillin. Meanwhile, pre-exposure prophylaxis (PrEP) absorbs a greater share of prevention resources, yet has been associated with behavioural risk compensation and increasing STI trends. [50]

One indirect way of assessing STI programmes is through GARPR/GAM reporting. From 2009 through 2016, only three SEAR countries reported over 90% ANC syphilis screening during any one year, three others reported almost no ANC screening and the remaining five countries ranged from about ten to seventy percent. Reporting itself was sporadic, with only about a third of countries on average reporting on this indicator each year.

Multiple gaps in STI control efforts in the region were identified through questionnaires and interviews with programme managers. Perhaps most significant is the lack of an identifiable STI control 'programme' in several countries. With the merging of HIV and STI programmes, and increasing focus on HIV-specific activities, attention to a number of key STI prevention and control activities has been diluted or lost. Strategic and operational planning in most countries is dominated by HIV priorities and targets, with staff and resources allocated accordingly. Low perceived priority and programme funding were cited by most countries as the main reasons for declining attention to STI control and surveillance. Important gaps in core STI control programme activities were identified (Table 5).

Table 5. Common STI programming gaps

Programmatic area	Status	Gaps/constraints
Strategic planning	National strategic plans (NSP) for HIV/ STI programmes increasingly oriented towards HIV-specific targets, with little attention to STI control.	STI generally low priority, may include some provision for STI treatment services. Recent interest in 'Triple Elimination' may be opportunity to improve ANC syphilis screening.
Resources	Resource allocation aligned to NSP, including for GFATM and other donors, few resources for STI activities.	Budgets lack separate line items for core STI control activities.
Staffing	Few or no staff with STI-specific responsibilities in many countries.	Often lacking STI programme manager and staff with responsibility for even basic clinical services and surveillance.
Commodities	Condom promotion and distribution for HIV also work for STIs, yet resources for condom programming diminishing. STI drugs and diagnostics often overlooked.	Gaps include reliable supply of condoms, STI diagnostics and treatment, logistics and supply management to avoid stock-outs.
Outreach	Outreach to KP and bridge groups works for both HIV and other STIs, yet programming support limited.	Outreach with single focus (ie HTC only) misses opportunities for broader STI prevention and risks alienating KP.
Clinical service delivery	Variable attention across countries.	Variable, often lacking monitoring, supervision, refresher training, etc.
Contact tracing	Neglected in most countries.	Lacking dedicated staff to follow up contacts of index cases.
Guidelines development, training, supervision	Some countries have not updated STI case management guidelines in last 5 years.	Guidelines updates, training and supervision required to maintain effective STI case management.
STI surveillance	Neglected in most countries.	Requires dedicated staff to ensure complete, accurate and timely reporting, analyse and disseminate data, etc.
Anti-microbial resistance (AMR) monitoring	Neglected in most countries.	Requires planning, funding and technical assistance for periodic AMR surveys.

Discussion

The proportion of new STI cases estimated for SEAR has declined from more than a third of the total global estimate in the 1990s to 11% in 2012. Global estimates, however, are based on a small and decreasing number of published STI prevalence studies, which poorly capture regional heterogeneity and fail to reflect trends over time. Yet, these same limitations and biases pertain to other regions as well, prompting further questions. Why has the proportion of incident STIs from SEAR fallen more than three times relative to other regions? Are these relative STI declines plausible? Do they point to successful STI control programmes that can inform action towards reaching global targets elsewhere?

In fact, three regional countries – Sri Lanka, Thailand, Myanmar – have reported 90% or greater reductions in syphilis and/or gonorrhoea during the period 1975 to 2010. The routine reporting data supporting these declines is robust, and more geographically representative and timely than information from the published literature. In absolute terms, syphilis and gonorrhoea incidence reported from Thailand and Sri Lanka are comparable to those reported from western Europe (2012 ECDC reported 4.5 syphilis cases per 100,000 population. Thailand reported 3.2 and Sri Lanka 5.4 cases per 100,000). With respect to the two primary global STI targets – 90% reductions in syphilis and gonorrhoea incidence – these examples provide solid evidence of feasibility.

Evidence from multiple sources suggest that smaller STI reductions over India's large population – more than two-thirds of the region's total – have driven regional declines. Yet, STI reporting on a national level in India is neither reliable nor consistent enough to discern trends as in Sri Lanka, Thailand or Myanmar. Evidence for large STI declines from the 1990s to 2010 comes instead from a large number of surveys conducted across India, which report STI prevalence among key populations, male bridge groups and pregnant women. Taken together, these studies suggest declining prevalence trends, as well as a marked epidemiological transition from predominately bacterial to viral STIs. The strongest intervention-linked data documents STI declines of at least 21-77% across several large Indian states between approximately 2004 and 2010.

In the other seven regional countries, STI trends remain high, are increasing, or data are simply inadequate to detect change. Without reliable routine STI reporting – and with fewer than ten papers per country reporting STI prevalence data since 2000 – it remains difficult to characterise STI epidemiology or describe trends over time.

Current STI programme structure, resources and performance also vary greatly across the region, with well-staffed, multi-pronged programmes in Sri Lanka and Thailand, and targeted STI control efforts at scale in Myanmar and India. Elsewhere, national STI responses vary greatly, with many countries struggling to support basic clinical services, maintain stocks of effective STI treatments, conduct outreach to key populations, maintain basic STI surveillance and monitor antibiotic resistance. Limited STI activities are often subsumed by HIV programmes, where programme managers report low priority and limited resources for STIs. As national programmes and donors increasingly promote HIV-specific services like ART and PrEP, there is growing risk of behavioural

disinhibition, erosion of condom use and rebounding STI transmission. Unfortunately, in many countries STI surveillance is not sufficiently operational or reliable to detect increasing trends, when and where they may occur. To a large extent, STIs other than HIV have fallen off the radar. Echoing this, programme managers described multiple gaps and constraints related to STI control and surveillance, mainly linked to low perceived priority and insufficient resources.

What then are the most important programme components in countries that have documented STI reductions? At national and sub-national levels, data show rapid STI declines when targeted condom and STI services are scaled up to reach sex workers and other key populations in large numbers, particularly where peers and communities are actively involved in implementation. The converse also appears to be true as recent STI outbreaks in underserved MSM networks are linked to rebounding STI trends.

In fact, evidence of STI declines at sub-national level points to similar interventions that drove national declines in Sri Lanka, Thailand, India and Myanmar. Evidence strongly supports attribution to programmes that have increased condom use in sex work, while maintaining good clinical services – for both key populations and the general population – and reliable STI surveillance. STI services specific to key populations – including quarterly medical checkups, presumptive treatment for asymptomatic infections and regular syphilis screening – have resulted in rapid STI declines in diverse settings. [26,47-49]

Yet, a high degree of heterogeneity in STI control, particularly in large countries like India, Indonesia and Bangladesh, hamper national STI control efforts. Without a scaled-up response and reliable data, STI control remains an elusive target for many countries.

With this in mind, and in light of global targets, several opportunities can be seen moving forward. Regional experience shows that 90% global targets are feasible, particularly for syphilis, for several reasons. Data on syphilis declines are more available and reliable than for other STIs, and useful as markers of sexual transmission trends in general. Evidence of declining syphilis, as well as progress in eliminating mother-to-child transmission (eMTCT) in some countries, supports the feasibility of regional elimination of syphilis as a public health problem. Weak STI surveillance and limited syphilis screening among key populations and pregnant women are current barriers to regional elimination. Recent increases in syphilis among MSM in several countries underline the importance of routinely screening key populations for syphilis, and monitoring prevalence trends.

Data on other STIs are less reliable but combinations of syndromic and aetiologic reporting, that have proven useful in guiding control efforts in several countries, can be adapted elsewhere. Reliable data on gonorrhoea are routinely reported from Sri Lanka and Thailand, which use affordable microscopy with Gram stain to distinguish gonococcal from non-gonococcal infections.

Despite these opportunities, recent reports and surveillance data raise concerns. Most countries in the region, including those with good control, have seen some evidence of STI resurgence during the past decade. STI control is volatile, with evidence of increasing syphilis and gonorrhoea mirroring global trends. Such outbreaks and rebounding trends pose new challenges for countries aiming to reach global STI elimination targets.

References

1. WHO. Global health sector strategy on sexually transmitted infections 2016–2021. Geneva 2016. WHA69/2016/REC/1
2. Ruxrungtham K, Brown T, Phanuphak P. HIV/AIDS in Asia. Lancet 2004;364(9428):69–82.
3. Garg R, Yu D, Narain JP. Epidemiology and transmission dynamics. In: Three Decades of HIV/AIDS in Asia. Narain JP (Ed). Sage publications, New Delhi (2012).
4. Steen R, Zhao PF, Wi TE, Punchihewa N, Abeyewickreme I, Lo Y-R. Halting and reversing HIV epidemics in Asia by interrupting transmission in sex work: experience and outcomes from ten countries. Expert review of anti-infective therapy 2013;11(10):999-1015.
5. Kukanok S, Kiertiburanakul S. Prevalence of positive syphilis serology among HIV-infected patients: role for routine screening in Thailand. Southeast Asian J Trop Med Public Health. 2014;45(2):435-41. PubMed PMID: 24968686.
6. Centers for Disease Control and Prevention (CDC). HIV and syphilis infection among men who have sex with men--Bangkok, Thailand, 2005-2011. MMWR Morb Mortal Wkly Rep. 2013 Jun 28;62(25):518-20. Erratum in: MMWR Morb Mortal Wkly Rep. 2013;62(27):558. PubMed PMID: 23803960; PubMed Central PMCID: PMC4604950.
7. Ahn JY, Boettiger D, Kiertiburanakul S, Merati TP, Huy BV, Wong WW, et al. Incidence of syphilis seroconversion among HIV-infected persons in Asia: results from the TREAT Asia HIV Observational Database. J Int AIDS Soc. 2016;19(1):20965. doi: 10.7448/IAS.19.1.20965. eCollection 2016.
8. WHO. Global prevalence and Incidence of selected curable sexually transmitted infections: overview and estimates. Geneva 2001. WHO/HIV_AIDS/2001.02 WHO/CDS/CSR/EDC/2001.10
9. WHO. Prevalence and incidence of selected sexually transmitted infections, Chlamydia trachomatis, Neisseria gonorrhoeae, syphilis and Trichomonas vaginalis: methods and results used by WHO to generate 2005 estimates. Geneva 2011. ISBN 978 92 4 150245 0
10. WHO. Global incidence and prevalence of selected curable sexually transmitted infections - 2008. Geneva 2011. ISBN 978 92 4 150383 9
11. Newman L, Rowley J, Vander Hoorn S, Wijesooriya NS, Unemo M, Low N, et al. (2015) Global Estimates of the Prevalence and Incidence of Four Curable Sexually Transmitted Infections in 2012 Based on Systematic Review and Global Reporting. PLoS ONE 10(12):e0143304. doi: 10.1371/journal. pone.0143304
12. Chandrasekaran P, Dallabetta G, Loo V, et al. Containing HIV/AIDS in India: the unfinished agenda. Lancet Infect. Dis. 2006;6(8):508–521.
13. Steen R, Mogasale V, Wi T, et al. Pursuing scale and quality in STI interventions with sex workers: initial results from Avahan India AIDS Initiative. Sex. Transm. Infect 2006;82:381–385
14. Kamat HA, Banker DD. Human immunodeficiency virus-1 infection among patients with sexually transmitted diseases in Bombay. Natl Med. J. India 1993;6(1):11–13.

15. Bhave G, Lindan CP, Hudes ES et al. Impact of an intervention on HIV, sexually transmitted diseases, and condom use among sex workers in Bombay, India. AIDS 1995;9(S1):S21–S30.
16. Kura MM, Hira S, Kohli M, Dalal PJ, Ramnani VK, Jagtap MR. High occurrence of HBV among STD clinic attenders in Bombay, India. Int. J. STD. AIDS 1998;9(4):231–233.
17. Rodrigues JJ, Mehendale SM, Shepherd ME et al. Risk factors for HIV infection in people attending clinics for sexually transmitted diseases in India. BMJ 1995;311(7000):283–286.
18. Risbud A, Chan-Tack K, Gadkari D et al. The etiology of genital ulcer disease by multiplex polymerase chain reaction and relationship to HIV infection among patients attending sexually transmitted disease clinics in Pune. India. Sex. Transm. Dis. 1999;26(1):55–62.
19. Gangakhedkar RR, Bentley ME, Divekar AD et al. Spread of HIV infection in married monogamous women in India. JAMA 1997;278(23):2090–2092.
20. Gadkari DA, Quinn TC, Gangakhedkar RR et al. HIV-1 DNA shedding in genital ulcers and its associated risk factors in Pune, India. J. Acquir. Immune Defic. Syndr. 1998;18(3):277–281.
21. Bollinger RC, Brookmeyer RS, Mehendale SM et al. Risk factors and clinical presentation of acute primary HIV infection in India. JAMA 1997;278(23):2085–2089.
22. Mehendale SM, Rodrigues JJ, Brookmeyer RS et al. Incidence and predictors of human immunodeficiency virus type 1 seroconversion in patients attending sexually transmitted disease clinics in India. J. Infect. Dis. 1995;172(6):1486–1491.
23. Narain JP (ed). Three Decades of HIV/AIDS in Asia. Sage publications, New Delhi (2012).
24. Jana S, Dey B, Reza-Paul S, Steen R. Combating Human Trafficking in the Sex Trade: Can Sex Workers Do It Better? J Public Health (Oxf). 2014;36(4):622-8. doi: 10.1093/pubmed/fdt095.
25. Isac S, Ramesh BM, Rajaram S, et al. Changes in HIV and syphilis prevalence among female sex workers from three serial cross- sectional surveys in Karnataka state, South India. BMJ Open. 2015;5(3):e007106. doi: 10.1136/bmjopen-2014-007106.
26. Reza-Paul S, Steen R, Maiya R, Lorway R, Wi T, Wheeler T, Dallabetta G. Sex Worker Community-led Interventions Interrupt Sexually Transmitted Infection/Human Immunodeficiency Virus Transmission and Improve Human Immunodeficiency Virus Cascade Outcomes: A Program Review from South India. Sex transm dis. 2019;46:556-562. 10.1097/OLQ.0000000000001020.
27. Boily MC, Pickles M, Lowndes CM, Ramesh BM, Washington R, Moses S, et al. Positive impact of a large-scale HIV prevention programme among female sex workers and clients in South India. AIDS. 2013;27:1449-60.
28. Charles B, Jeyaseelan L, Edwin Sam A, Kumar Pandian A, Thenmozhi M, Jeyaseelan V. Trends in risk behaviors among female sex workers in south India: priorities for sustaining the reversal of HIV epidemic. AIDS Care. 2013;25:1129-37.
29. Ramanathan S, Deshpande S, Gautam A, Pardeshi DB, Ramakrishnan L, Goswami P, et al. Increase in condom use and decline in prevalence of sexually transmitted infections among

high-risk men who have sex with men and transgender persons in Maharashtra, India: Avahan, the India AIDS Initiative. BMC Public Health. 2014;14:784.

30. Subramanian T, Ramakrishnan L, Aridoss S, Goswami P, Kanguswami B, Shajan M, et al. Increasing condom use and declining STI prevalence in high-risk MSM and TGs: evaluation of a large-scale prevention program in Tamil Nadu, India. BMC Public Health. 2013;13:857.
31. Souverein D, Euser SM, Ramaiah R, Narayana Gowda PR, Shekhar Gowda C, Grootendorst DC, et al. Reduction in STIs in an empowerment intervention programme for female sex workers in Bangalore, India: the Pragati programme. Glob Health Action. 2013;6:22943.
32. Mogasale V, Wi TC, Das A, Kane S, Singh AK, George B, Steen R. Quality assurance and quality improvement using supportive supervision in a large-scale STI intervention with sex workers, men who have sex with men/transgenders and injecting-drug users in India. Sex Transm Infect. 2010;86 Suppl 1:i83-8.
33. Prabhakar P, Narayanan P, Deshpande GR, Das A, Neilsen G, Mehendale S, Risbud A. Genital ulcer disease in India: etiologies and performance of current syndrome guidelines. Sex Transm Dis. 2012;39:906-10.
34. Setia MS, Jerajani HR, Brassard P, Boivin JF. Clinical and demographic trends in a sexually transmitted infection clinic in Mumbai (1994-2006): an epidemiologic analysis. Indian J Dermatol Venereol Leprol. 2010;76:387-92.
35. Becker M, Stephen J, Moses S, Washington R, Maclean I, Cheang M, et al. Etiology and determinants of sexually transmitted infections in Karnataka state, south India. Sex Transm Dis. 2010;37:159-64.
36. Hochberg CH, Schneider JA, Dandona R, Lakshmi V, Kumar GA, Sudha T, et al. Population and dyadic-based seroincidence of herpes simplex virus-2 and syphilis in southern India. Sex Transm Infect. 2015;91:375-82.
37. Rachakulla HK, Kodavalla V, Rajkumar H, Prasad SP, Kallam S, Goswami P, et al. Condom use and prevalence of syphilis and HIV among female sex workers in Andhra Pradesh, India - following a large-scale HIV prevention intervention. BMC Public Health. 2011;11 Suppl 6:S1.
38. Thilakavathi S, Boopathi K, Girish Kumar CP, Santhakumar A, Senthilkumar R, Eswaramurthy C, et al. Assessment of the scale, coverage and outcomes of the Avahan HIV prevention program for female sex workers in Tamil Nadu, India: is there evidence of an effect? BMC Public Health. 2011;11 Suppl 6:S3.
39. Gurung A, Narayanan P, Prabhakar P, Das A, Ranebennur V, Tucker S, et al. Large-scale STI services in Avahan improve utilization and treatment seeking behaviour amongst high-risk groups in India: an analysis of clinical records from six states. BMC Public Health. 2011;11 Suppl 6:S10.
40. Pandey A, Mishra RM, Sahu D, Benara SK, Sengupta U, Paranjape RS, et al. Heading towards the Safer Highways: an assessment of the Avahan prevention programme among long distance truck drivers in India. BMC Public Health. 2011;11 Suppl 6:S15.

41. Gutierrez JP, McPherson S, Fakoya A, Matheou A, Bertozzi SM. Community-based prevention leads to an increase in condom use and a reduction in sexually transmitted infections (STIs) among men who have sex with men (MSM) and female sex workers (FSW): the Frontiers Prevention Project (FPP) evaluation results. BMC Public Health. 2010;10:497.
42. Personal communication; Dr Usman, Madras Medical College.
43. Ramesh BM, Beattie TS, Shajy I, Washington R, Jagannathan L, Reza-Paul S, et al. Changes in risk behaviours and prevalence of sexually transmitted infections following HIV preventive interventions among female sex workers in five districts in Karnataka state, south India. Sex Transm Infect. 2010;86 Suppl 1:i17-24.
44. Ramakrishnan L, Gautam A, Goswami P, Kallam S, Adhikary R, Mainkar MK, et al. Programme coverage, condom use and STI treatment among FSWs in a large-scale HIV prevention programme: results from cross-sectional surveys in 22 districts in southern India. Sex Transm Infect. 2010;86 Suppl 1:i62-8.
45. Rajaram SP, Banandur P, Thammattoor UK, et al. Two cross-sectional studies in south India assessing the effect of an HIV prevention programme for female sex workers on reducing syphilis among their clients. Sex Transm Infect 2014;90: 556–562.
46. Sethi S, Sharma K, Dhaliwal LK, Banga SS, Sharma M. Declining trends in syphilis prevalence among antenatal women in northern India: a 10-year analysis from a tertiary healthcare centre. Sex Transm Infect 2007;83:592
47. McCormick DF, Rahman M, Zadrozny S, Alam A, Ashraf L, Neilsen GA, et al. Prevention and control of sexually transmissible infections among hotel-based female sex workers in Dhaka, Bangladesh. Sex Health 2013;10(6):478-86
48. Bollen LJ, Anartati AS, Morineau G, Sulami S, Prabawanti C, Silfanus FJ, et al. Addressing the high prevalence of gonorrhoea and chlamydia among female sex workers in Indonesia: results of an enhanced, comprehensive intervention. Sex Transm Infect 2010; 86:61–65.
49. Majid N, Bollen L, Morineau G, Daily SF, Mustikawati DE, Agus N, et al. Syphilis among female sex workers in Indonesia: need and opportunity for intervention. Sex Transm Infect 2010; 86:377–383.
50. Werner RN, Gaskins M, Nast A, Dressler C. Incidence of sexually transmitted infections in men who have sex with men and who are at substantial risk of HIV infection – a meta-analysis of data from trials and observational studies of pre-exposure prophylaxis. PLoS ONE 13(12):e0208107. doi: 10.1371/journal.pone.0208107.
51. WHO/SEARO. Regional strategy for the prevention and control of sexually transmitted infections, 2007–2015. New Delhi 2007. ISBN 978-92-9022-295-8