Cost-effectiveness of Integrated Routine Offering of Prenatal HIV and Syphilis Screening in China

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Background: In China, recent rises in syphilis and HIV cases have increased the focus on preventing mother-to-child transmission of these infections. We assess the health and economic outcomes of different strategies of prenatal HIV and syphilis screening from the local health department's perspective.

Methods: A Markov cohort decision analysis model was used to estimate the health and economic outcomes of pregnancy using disease prevalence and cost data from local sources and, if unavailable, from published literature. Adverse pregnancy outcomes included induced abortion, stillbirth, low birth weight, neonatal death, congenital syphilis in live-born infants, and perinatal HIV infection. We examined 4 screening strategies: no screening, screening for HIV only, for syphilis only, and for both HIV and syphilis. We estimated disability-adjusted life years (DALYs) for each health outcome using life expectancies and infections for mothers and newborns.

Results: For a simulated cohort of 10,000 pregnant women (0.07% prevalence for HIV and 0.25% for syphilis; 10% of HIV-positives were coinfected with syphilis), the estimated costs per DALY prevented were as follows: syphilis-only, $168; HIV-and-syphilis, $359; and HIV-only, $5636. The estimated incremental cost-effectiveness ratio if an existing HIV-only strategy added syphilis screening (i.e., move from the HIV-only strategy to the HIV-and-syphilis strategy) was $140 per additional DALY prevented.

Conclusions: Given the increasing prevalence of syphilis and HIV among pregnant women in China, prenatal HIV screening programs that also include syphilis screening are likely to be substantially more cost-effective than HIV screening alone and prevent many more adverse pregnancy outcomes.

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Acknowledgments: Staff of the National Center for HIV/STD Prevention and Control and the National Center for Women and Children's Health of the China CDC were helpful in the conduct of this analysis. The authors also thank UNICEF-China and WHO-China for the encouragement. The authors are particularly grateful to Professor Gui Xien of Wuhan University for helpful discussions. In addition, Chin-Yih Ou, Sujian Situ, and Christine Korhonen at the CDC Global AIDS Program in China provided useful suggestions on an earlier draft.

Conflict of interest statements: None.

Funding: None.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the United States Centers for Disease Control and Prevention (CDC). Mention of company names or products does not imply endorsement by CDC.

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Received for publication May 7, 2013, and accepted December 2, 2013.
DOI: 10.1097/OLQ.0000000000000085

Prevention of mother-to-child transmission (PMTCT) of HIV is a global health focus in most parts of the world, including Asia.[1] Effective PMTCT requires prenatal HIV screening and, for women testing positive, administration of one of several effective antiretroviral (ARV) therapy regimens.[2] Depending on the ARV regimen chosen, vertical transmission of HIV can be virtually eliminated, as is already the case in most of the developed regions of the world.[3] In 2011, the joint United Nations Programme on HIV/AIDS identified preventing HIV-associated maternal and infant mortality as a global priority in the new "PMTCT strategic vision 2010–2015: preventing MTCT of HIV to reach the UNGASS and Millennium Development Goals."[1] Toward this end, in 2010 the World Health Organization (WHO) published its strategy to support country-level and global efforts to scale up PMTCT services and to integrate such services into maternal, newborn, and child health programs.[1]

In China, the HIV epidemic seems to be shifting toward women in the childbearing age group, implying that more infants will be at risk for MTCT of HIV.[4] In 2005, the Ministry of Health reported that an estimated 9000 infants were infected with HIV.[5] Current HIV prenatal screening policies in China require HIV testing for all pregnant women and aim to reach at least 80% coverage nationwide by 2015.[2] Newly released PMTCT guidelines in early 2011 recommend triple ARV prophylaxis for all HIV-infected pregnant women identified.[6]

Maternal syphilis infection can cause substantial perinatal morbidity and mortality. Left untreated, maternal syphilis results in adverse pregnancy outcomes (APOs) such as stillbirth (SB), neonatal death (ND), and congenital syphilis in newborns (CSN) in as high as 80% of affected pregnancies.[7] Thus, current global guidelines include maternal syphilis screening as part of the basic package of antenatal services and recommend universal syphilis screening for all pregnant women and prompt treatment for women testing positive. A single dose of intramuscular benzathine penicillin is highly effective in preventing congenital syphilis in the unborn infant.[8] Studies have demonstrated that preventing MTCT of syphilis through prenatal screening and treatment for infected mothers is cost-effective in most cases (and can be cost-saving in high prevalence regions).[9,10] In 2007, WHO and other multinational and bilateral partners launched the global elimination of congenital syphilis.[11] In 2011, the nations included in the Asia and Pacific regions (including China) launched a dual campaign toward eliminating both congenital syphilis and MTCT of HIV.[12]

Routine syphilis screening for pregnant women was discontinued in China in 1964, after mass screening and treatment and closure of brothels virtually eliminated the disease in the 1950s.[13] Despite the resurgence of syphilis cases since the late 1980s, most pregnant women are not currently tested for

syphilis, particularly in rural and poorer areas of China.[12] Thus, although HIV prenatal screening has rapidly expanded in recent years in China, many infants continue to be congenitally exposed to syphilis infection and its serious health complications.

Owing to the potential APOs attributable to syphilis infection among pregnant women, preventing MTCT of syphilis has emerged as a vital part of syphilis prevention efforts in China.[14] Furthermore, preventing MTCT of both HIV and syphilis through integrated prenatal HIV and syphilis screening of pregnant women followed by treatment for those infected has increased in some parts of China,[15] and the demand for these services continues to grow.[14] A recent qualitative study of the status and prospects of integrated HIV and syphilis screening in China concluded that substantial potential for expansion of integrated HIV and syphilis services exists, and the authors recommended that more studies be conducted to guide decision making regarding scaling up these efforts.[15]

Any provision (or scaling up) of preventive perinatal services in China requires substantial commitment of resources (due to the >17 million births annually[16]), and studies that provide estimates on the health and economic outcomes of such interventions, such as cost-effectiveness analyses, are important in informing policy decision making. However, published cost-effectiveness analyses of HIV, syphilis, and integrated HIV and syphilis screening for pregnant women in China are limited. In this study, we estimate the cost-effectiveness of prenatal HIV and syphilis screening interventions in China using local data and estimates from published literature.

METHODS

We used a Markov cohort decision analysis to estimate pregnancy outcomes for 10,000 pregnant women aged 26 years (the average age of the women at pregnancy in China[17]), assuming a single fetus for each pregnancy. We focused on the common APOs caused by untreated HIV and syphilis in pregnancy, including SB, low birth weight (LBW), ND, CSN, and HIV in a newborn (HIV). We also included the possibility of induced abortion (IA) for syphilis and/or HIV-infected mothers.

We examined 4 antenatal HIV and syphilis screening strategies for pregnant women from the Chinese national health departments' perspective:

1. no-prenatal-screening, in which neither HIV nor syphilis testing was offered (this was used as the baseline for costs and APOs);
2. HIV-only, in which only HIV testing was offered, and women who accepted and tested positive were treated to prevent MTCT of HIV;
3. syphilis-only, in which only syphilis testing was offered, and those who accepted the test and tested positive were treated for syphilis; and
4. HIV-and-syphilis, in which both HIV and syphilis testing were offered, and women who accepted both tests and tested positive for either infection were treated accordingly.

Screening coverage for each strategy was based on the product of the probability of being insured (90%), the probability of accessing prenatal care (84% for the insured; 55% for the uninsured), and the probability of accepting tests (92%).[18,19]

Based on Global Diseases Burden (GBD) measurement methods, we estimated disability-adjusted life years (DALYs) lost for all adverse health outcomes for both mother and newborn using HIV- and syphilis-related disability weights.[20] The life expectancies for newborns (74 years) and for 26-year-old mothers (49 years) were based on life table values for China.[17] We repeated our analyses using standard life expectancy values from Japan (highest life expectancy[17]). Owing to the controversy surrounding age weighting, we did not adjust for age in our DALY calculations.[21]

To keep the analysis simple, we assumed 4 disease states for HIV (i.e., healthy, HIV, AIDS, and death) and syphilis (i.e., healthy, early [i.e., primary or secondary syphilis]/latent syphilis, tertiary syphilis, and death) infections of the mother. Schematics of the Markov progression showing the simplified health states used to determine the DALYs lost for syphilis[9] and HIV-syphilis coinfections are presented in Figure 1A and B.

Based on unpublished local data, we assumed that syphilis infections were at the early (i.e., primary or secondary; 25%) or latent (75%) stages. We also assumed that 10% of those infected with HIV were also infected with syphilis, and the DALY weight for coinfection was computed as follows: DALY weight 1 + DALY weight 2 * (1 − DALY weight 1).

As an example, for a pregnant woman with HIV (DALY weight, 0.135[20]) and tertiary syphilis (DALY weight, 0.283[20]), the combined DALY weight was 0.38. We repeated our analyses using only the DALY value for the disease with the higher

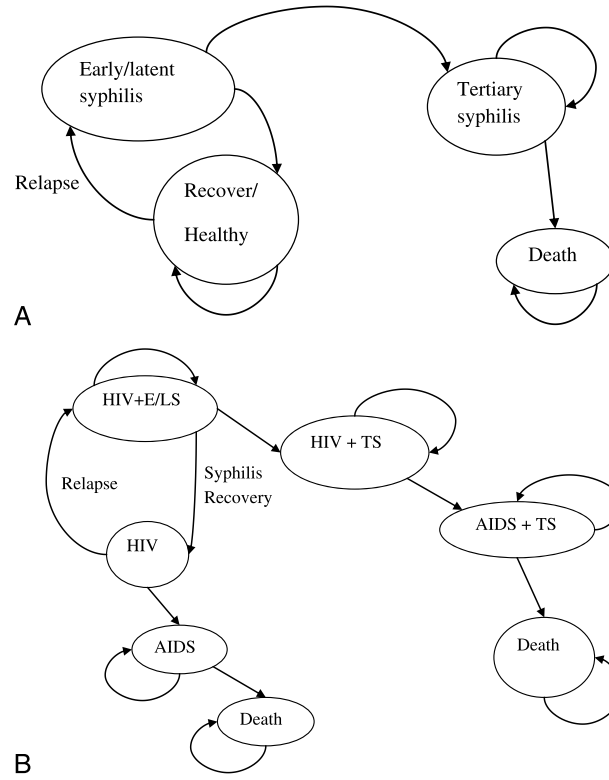

Figure 1. A, A schematic of the Markov progression states used to estimate the DALYs for the mothers—adopted from a previous study.[9] Syphilis-infected pregnant women were in the early/latent syphilis states at the time of screening. State transition probabilities were obtained from the literature (see Table 1). B, A schematic of the Markov progression states used to estimate the DALYs for the mothers with HIV and syphilis coinfection. Syphilis-infected pregnant women were in the early latent syphilis stage at screening. State transition probabilities were obtained from the literature. E/LS indicates early/latent syphilis; TS, tertiary syphilis.

weight. This was done because previous reports have suggested that DALYs cannot be adjusted to account for comorbidities.[22] Finally, if the mother was coinfected, the resulting probability of aborting was computed in a similar way as described above—0.7 (i.e., 0.5 + 0.4 * (1 − 0.5)).

Cost of APOs

The treatment cost of HIV-infected infants (first-line ARV treatment) was used as the direct cost of HIV-related APO (i.e., MTCT of HIV). Our literature search for the direct costs of syphilis-related APOs (i.e., congenital syphilis, LBW, and ND) in China yielded no results. Consequently, to estimate direct costs, we adjusted the costs found in a recent economic evaluation study that estimated the total cost incurred to prevent each of the APOs from a prevention program in China.[23] In that study, the estimated costs to prevent each of the APOs were approximately $5300 for congenital syphilis, $6100 for LBW, and $8500 for ND (adjusted to 2010 US dollars).[23] These costs included direct institutional costs (such as cost of syphilis screening and diagnosis, CSN treatment and personnel), and individual/private direct (such as transportation and medical expenses paid by patient or family members) and indirect costs (such as lost income due to missed work time).[23] The relative magnitude of the costs was consistent with cost values used in previous studies.[9,10] Following previous studies, the cost of SB was assumed to be the same as the cost of delivery.[9,10]

The cost data in the above-mentioned study came from one of the most developed regions of China (i.e., Shenzhen). Second, a substantial portion (>50%) of the cost was from individual/private expenses.[23] Thus, using them as reported may overestimate the cost-effectiveness of prenatal screening from the national health department's perspective. Consequently, we used very conservative values by assuming that the costs elsewhere in China were 25% of the costs in Shenzhen (i.e., reducing them by 75%). Specifically, we adjusted the numbers by multiplying them by 0.25 for our base case cost and varied the multiplier from 0.1 to 0.4. In addition, given the uncertainty surrounding the costs of these APOs and the substantial influence those costs could have on the final results, we conducted a separate sensitivity analysis using a wider range of costs by increasing the APO cost multiplier from 0.1 to 3. This cost multiplier allowed us to vary the cost of APOs simultaneously in a single 1-way sensitivity analysis. Thus, in the separate sensitivity analyses on combined cost of APOs, the costs increased from $530 to $15,900 for CSN, $610 to $18,300 for LBW, and $850 to $25,500 for ND, as the APOs cost multiplier increased from 0.1 to 3.

The expected APOs attributable to syphilis infection of the mother were obtained from a WHO-funded meta-analysis reviewing expected MTCT of syphilis in untreated infections that accounted for background cases.[24] To be consistent with the expected APOs estimated in that study, we adjusted the probability of fetal transmission in our model. A comprehensive list of the parameter values obtained from local data, model assumptions, and published literature is presented in Table 1.

We computed cost as the net cost (total cost of the strategy [i.e., HIV-only, syphilis-only, and HIV-and-syphilis) minus the total cost of the no-prenatal-screening strategy). We conducted 1-way sensitivity analyses on all of the variables using the ranges specified in Table 1. However, because of the large number of variables, we focused the discussion of the 1-way sensitivity analyses on the burden of the 2 infections (i.e., the prevalence of HIV and syphilis) and the cost of the APOs. In addition, we conducted a probabilistic sensitivity analysis (Monte Carlo simulation) in which we included all the variables and the ranges specified in Table 1 by assuming triangular distributions.

We used TreeAge Pro version 2011 (TreeAge Software, Williamstown, MA) to construct the decision tree and conduct the comprehensive sensitivity analyses. Microsoft Excel, version 2010 (Microsoft Corporation, Redmond, WA) was used for summary analyses and presentation of results. All costs were adjusted to 2010 US dollars using the medical care component of the Consumer Price Index for All Urban Consumers.

RESULTS

A summary of the estimated APOs, associated costs, and DALYs lost is presented in Table 2. Based on our assumptions, our results indicated that for a cohort of 10,000 pregnant women (0.07% prevalence for HIV and 0.25% for syphilis; 10% of HIV positives were infected with syphilis), the HIV-only strategy prevented 2 cases of MTCT of HIV and 3 IAs compared with no program; the syphilis-only strategy prevented 3 SBs, 3 cases of congenital syphilis in live-born infants, 1 ND, 1 case of LBW, and 8 IAs compared with no program (see Table 2). The HIV-and-syphilis strategy prevented the sum of the APOs prevented by the HIV-only and syphilis-only strategies, except for the number of IAs, which were 10. Estimated costs per DALY prevented were as follows: syphilis-only, $168; HIV-and-syphilis, $359; HIV-only, $5,636. The estimated incremental cost-effectiveness ratio (ICER) when an existing HIV-only strategy included syphilis screening (i.e., move from the HIV-only strategy to the HIV-and-syphilis strategy) was $140 per additional DALY prevented.

When we used the standard life expectancy values (i.e., from Japan) and did not account for comorbidity in the DALY calculations, the estimated summary results decreased by less than 3% (syphilis-only, $162; HIV-and-syphilis, $349; HIV-only, $5,602; the ICER was $134).

One-Way Sensitivity Analysis on Prevalence of HIV and Syphilis

When we increased the prevalence of syphilis from 0.001 to 0.005,[25] the net cost per DALY prevented for the HIV-and-syphilis strategy declined from $890 to $170, whereas the net cost per DALY prevented for the syphilis-only strategy declined from $440 to $70 (see Fig. 2) and the net cost per DALY prevented for the HIV-only strategy remained unchanged (not shown). The net cost per DALY prevented declined from $33,000 to $4000 for the HIV-only strategy as we increased HIV prevalence from 0.0001 to 0.001, whereas the net cost per DALY prevented for the syphilis-only strategy remained unchanged. However, the net cost per DALY prevented for the HIV-and-syphilis strategy decreased slightly from $380 to $350.

One-Way Sensitivity Analysis on Cost of APOs

A summary of the range of estimated total cost for each strategy as we increased the APOs cost is shown in Figure 3; we adjusted the multiplier from 0.1 to 3 (this increased the cost of CSN from $530 to $15,900, the cost of LBW from $610 to $18,300, and the cost of ND from $850 to $25,500 simultaneously). When the cost multiplier was greater than 1.58 (i.e., when the cost of CSN was at least $8400, the cost of LBW was at least $9600, and the cost of ND was at least $13,400), the HIV-and-syphilis strategy was less expensive than the HIV-only option (see point a in Fig. 3). When the cost multiplier was greater than 1.86 (i.e., when the cost of CSN was at least $9900, the cost of LBW was at least $11,300, and the cost of ND was at least $15,800), the syphilis-only strategy was cost-saving compared with no program (see point b in Fig. 3).

TABLE 1. Description, Point Values, Range and Sources for All Variables Used in the Model to Assess the Health and Economic Outcomes of Prenatal HIV, Syphilis, and integrated HIV/Syphilis Screening in China

Variable	Value	Low	High	Source
Disease burden				
Prevalence of HIV	0.0007	0.0004	0.0010	*
Prevalence of syphilis	0.0025	0.001	0.005	[25]
Proportion of early syphilis infections (primary and secondary)	0.25	0.10	0.40	*
Prevalence overlap, HIV and syphilis	0.1	0.05	0.15	*
Probability of fetal transmission				
HIV, no treatment, breast-feeding	0.30	0.20	0.40	[6]
HIV, with treatment, no breast-feeding	0.01	0.0050	0.015	[6]
HIV, postnatal via breast-feeding, no treatment	0.162	0.081	0.243	[27]
HIV, postnatal via breast-feeding, with treatment	0.118	0.059	0.177	[27]
Syphilis, early syphilis	0.7	0.6	0.8	*
Syphilis, latent syphilis	0.5	0.25	0.75	*
Probability of syphilis APOs given fetal transmission				
SB†	0.21	0.11	0.32	[24]
Congenital syphilis	0.19	0.10	0.29	[24]
ND	0.09	0.05	0.14	[24]
LBW	0.06	0.03	0.09	[24]
Intervention details				
Proportion insured	0.90	0.80	1	*
Proportion who get prenatal care, insured	0.84	0.60	1	[18,19]
Proportion who get prenatal care, not insured	0.55	0.275	0.83	[18,19]
Probability of hospital delivery, insured	0.88	0.80	0.96	[18,19]
Probability of hospital delivery, not insured	0.4	0.2	0.60	[18,19]
Probability of accepting test	0.92	0.85	1	*
Probability of aborting if infected with syphilis	0.4	0.2	0.60	[30]*
Probability of aborting if HIV positive	0.5	0.25	0.75	[30]*
Probability of breast-feeding	0.95	0.90	1	*
Probability of breast-feeding if HIV positive	0.10	0.05	0.15	*
Test sensitivity				
Initial HIV test (EIA)	0.988	0.95	1	[27]
Confirmatory HIV test (Western blot)	0.99	0.98	1	[27]
RPR, latent syphilis	0.9	0.80	1	[9,10]
RPR, primary and secondary syphilis	0.9	0.80	1	[9,10]
TPHA, latent syphilis	0.97	0.95	1	[9,10]
TPHA, primary and secondary syphilis	0.87	0.80	1	[9,10]
Test specificity				
Initial HIV test (EIA)	0.989	0.98	1	[27]
Confirmatory HIV test (Western blot)	0.9999	0.98	1	[27]
RPR	0.957	0.90	1	[9,10]
TPHA	0.99	0.98	1	[9,10]
Costs, $				
Initial syphilis test (RPR)	3	1.5	4.5	*
Confirmatory syphilis test (TPHA)	6	3	9	*
Initial HIV test (EIA)	3	1.5	4.5	*
Confirmatory HIV test (Western blot)	30	15	45	*
Treatment, primary and secondary syphilis	26	13	39	*
Treatment, latent syphilis	44	22	66	*
First-line ARV treatment, mother	200	100	300	*
Second-line ARV treatment, mother	1200	800	1600	*
IA	80	40	120	*
Prenatal care (exclusive of testing)	50	25	75	*
Hospital delivery (exclusive of testing)	350	175	525	*
Home delivery	50	25	75	*
Cost of APOs, $				
First-line ARV treatment, infants	1470	735	2205	*
Congenital syphilis	1325	530	2120	[23]‡
LBW	1525	610	2440	[23]‡
ND	2125	850	3400	[23]‡
SB	§	§	§	Model assumption
DALY weights				
Early/Latent syphilis	0.015	0.0075	0.0225	[20]
Tertiary syphilis	0.283	0.1415	0.4245	[20]
Congenital syphilis (3 y)	0.315	0.1575	0.47	[20]
LBW (1 y)	0.106	0.053	0.159	[20]
SB	1	—	—	[20]

(Continued on next page)

TABLE 1. *(Continued)*

Variable	Value	Low	High	Source
Death	1	—	—	[20]
IA	0	—	—	[20]
HIV	0.135	0.0675	0.2025	[20]
AIDS, no treatment	0.505	0.2525	0.8	[20]
AIDS, with treatment	0.167	0.0835	0.2505	[20]
Life expectancy and duration of infection, y				
Newborn, healthy	74	70	83	[17]
Mother (age at pregnancy, 26 y)	49	45	60	[17]
Duration of HIV with treatment, newborn	15	7.5	22.5	[27]
Duration of HIV without treatment, newborn	2	1	3	[27]
Duration of AIDS with treatment, child	5	2.5	7.5	[27]
Duration of AIDS without treatment, child	1	0.5	1.5	[27]
Annual disease progression rate (mother)				
HIV to AIDS, no treatment	0.06	0.03	0.09	[31]
HIV to AIDS, with treatment	0.0060	0.0030	0.01	[31]
AIDS to death	0.03	0.015	0.045	[31]
Early/Latent syphilis to tertiary syphilis	0.33	0.165	0.495	[9,10]
Tertiary syphilis to death	0.11	0.055	0.165	[9,10]
Relapse from healthy to early/latent syphilis	0.236	0.118	0.354	[9,10]
Other				
Probability of treatment success, syphilis	0.95	0.90	1	Model assumption
Discount rate	0.03	0.01	0.05	Model assumption
APOs cost multiplier	0.25	0.1	0.4	Model assumption

EIA indicates enzyme immunoassays; TPHA, *Treponema pallidum* hemagglutination assay.
*Estimated from unpublished local data.
†Includes fetal loss due to syphilis infection.
‡Costs reported in this study were adjusted using the APOs cost multiplier.
§Same as the cost of delivery.

Multiway Sensitivity Analysis (Monte Carlo Simulation)

A summary of the probabilistic sensitivity analysis for 1000 simulations showing the estimated total costs and DALYs lost for each strategy is presented in Figure 4. Based on the ranges used, the estimated total costs were between $3.9 million and $10.5 million for all the strategies examined (see Fig. 4). However, the DALYs lost were substantially lower if the strategy included syphilis screening—more than 90% of estimated DALYs lost for the HIV-and-syphilis and syphilis-only strategies were between 45 and 300, whereas more than 90% of the DALYs lost for the HIV-only and no-screening-program were higher than 400 (see Fig. 4). Thus, although there is a substantial difference in the estimated health outcomes as measured by the total DALYs lost (i.e., for the strategies that included syphilis screening vs. the no-screening-program and HIV-only strategy), the estimated cost outcomes did not vary as much between the different strategies in the same simulation as the strategies varied among themselves between different simulations.

The summary statistics of the estimated total costs and DALYs lost from the 1000 simulations were as follows: no-screening-program (average total cost [ATC], $6.784 million [95% confidence interval {CI}, $4.522–$9.248; average DALYs lost, 497 [CI, 149–997]), HIV-only (ATC, $6.845 million [CI, $4.580–$9.325]; average DALYs lost, 485 [CI, 136–980]), syphilis-only (ATC, $6.823 million [CI, $4.551–$9.303]; average DALYs lost, 223 [CI, 77–449]), and HIV-and-syphilis (ATC, $6.881 million [CI, $4.603–$9.365]; average DALYs lost, 215 [CI, 71–444]). Based on the estimated ATCs and DALYs lost obtained from the 1000 simulations, the estimated CERs were as follows: HIV-only, $5,489; syphilis-only, $159; and HIV-and-syphilis, $346. Finally, the estimated ICER was $134 per additional DALY prevented if one changed from the HIV-only strategy to the HIV-and-syphilis strategy.

DISCUSSION

Our study has demonstrated that with conservative cost estimates for APOs, integrated HIV and syphilis testing in

TABLE 2. Summary Results From the Cohort Decision Model Comparing the Health and Economic Outcomes of Prenatal HIV, Syphilis, and integrated HIV and Syphilis Screening for 10,000 Pregnant Women Aged 26 Years in China

	APOs						Cost-Effectiveness Summary					
Screening Strategy	SB	CSN	ND	LBW	MTCT (HIV)	IA	Total Cost (million)	DALYs Lost	Net Cost	DALYs Prevented	CER	ICER
No-screening-program	5	5	2	1	3	0	6.814	476	—	—	—	—
HIV-only	5	5	2	1	1	3	6.876	465	62,000	11	5636	—
Syphilis-only	2	2	1	0	3	8	6.859	208	45,000	268	168	—
HIV-and-syphilis	2	2	1	0	1	10	6.913	200	99,000	276	359	140

All costs are in 2010 US dollars.
CER indicates cost-effectiveness ratio.

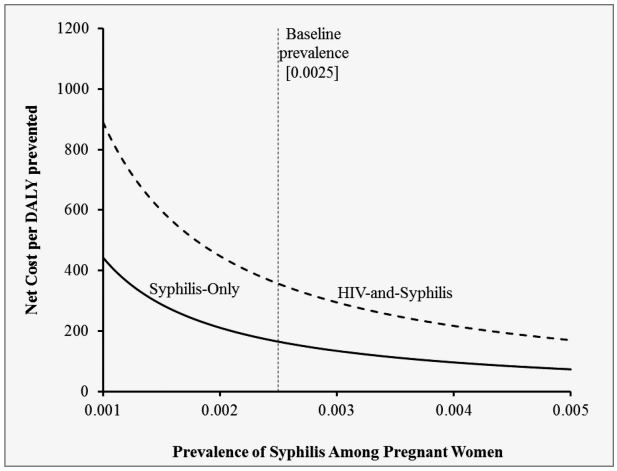

Figure 2. One-way sensitivity analysis for the prevalence of syphilis among 10,000 pregnant women showing the net total costs for the HIV-and-syphilis and syphilis-only prenatal screening strategies to prevent APOs in China.

prenatal care was substantially more cost-effective than HIV screening only—the estimated cost-effectiveness ratio was more than 15 times lower ($359 vs. $5636). In addition, this study has shown that adding syphilis screening to an existing prenatal HIV screening program was substantially more cost-effective (i.e., $140 per additional DALY prevented) than HIV screening alone.

The estimated relative APOs found in this study were slightly different from what has been reported in previous studies that examined pregnancy outcomes in other settings for syphilis screening, which reported a relatively higher proportion of CS than we found.[9,10,26] This is because we used different values obtained from a more recent comprehensive meta-analysis study.[24] However, there was no substantial difference in the relative magnitude of the CER estimates when we used the distribution of APOs reported in the previous studies. We are not aware of any published studies (in the English literature) that examined prenatal HIV, syphilis, or integrated HIV and syphilis screening in China, so comparison of the estimated APOs prevented (and the associated CERs) is not possible.

The substantially lower CER we found for the strategies that included syphilis screening (i.e., HIV-and-syphilis and syphilis-only) compared with HIV-only screening was largely due to the following reasons. First, among pregnant women in China, the prevalence of syphilis is now substantially higher (>3-fold) than the prevalence of HIV. Second, although HIV disease is not curable, syphilis is easily curable with relatively inexpensive antibiotic treatment. Early and even late stages of syphilis are far less costly to treat than HIV. Finally (and most important for congenital morbidity and mortality), the likelihood of MTCT without any intervention is higher for syphilis than for HIV/AIDS (0.55 on average for syphilis[24] vs. around 0.3 for HIV[27]). Thus, including syphilis screening results in high incremental health benefit at very low costs, as was depicted in the Monte Carlo simulation results shown in Figure 4. In fact, previously published studies that examined the health and economic outcomes in settings with high syphilis prevalence (such as in Sub-Saharan Africa) found prenatal syphilis screening to be cost-saving.[9,10,28]

Our study has a number of limitations. First, our results are from a model that is a simplification of real-world events. Thus, all limitations associated with models are applicable. Second, there are limited data on health and economic outcomes of syphilis and HIV specifically from China, particularly for costs of the APOs and the probability of abortion if the pregnant woman is infected with HIV and syphilis. Nonetheless, the

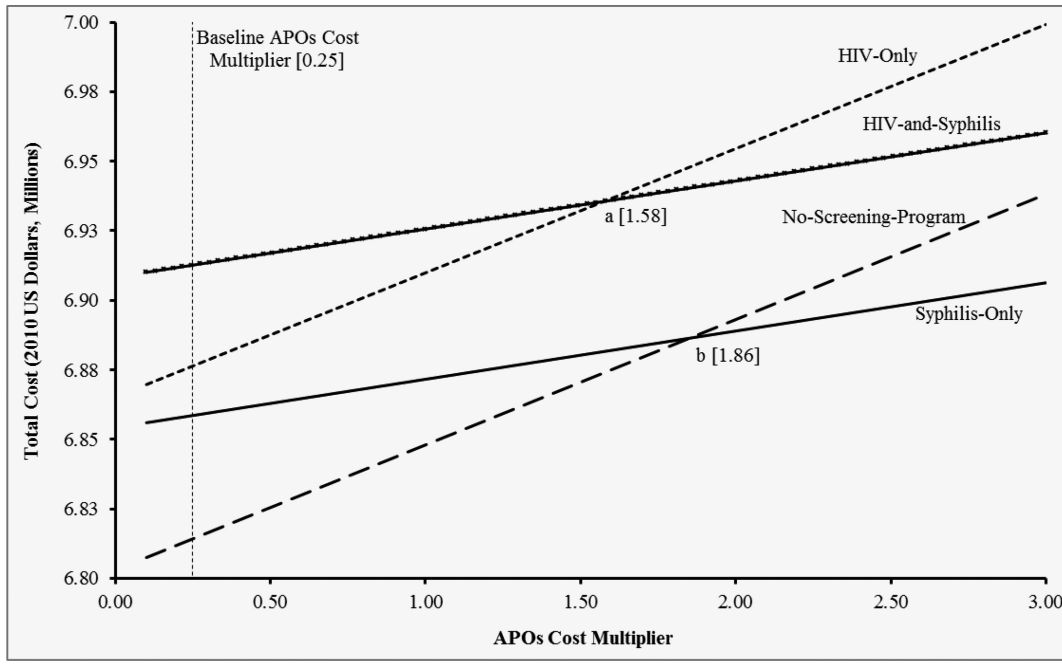

Figure 3. Combined 1-way sensitivity analysis for the cost of APOs (i.e., CSN, LBW, and ND) showing the total costs for all 4 prenatal screening strategies (i.e., no-screening-program, HIV-only, syphilis-only, and HIV-and-syphilis) to prevent APOs among 10,000 pregnant women in China.

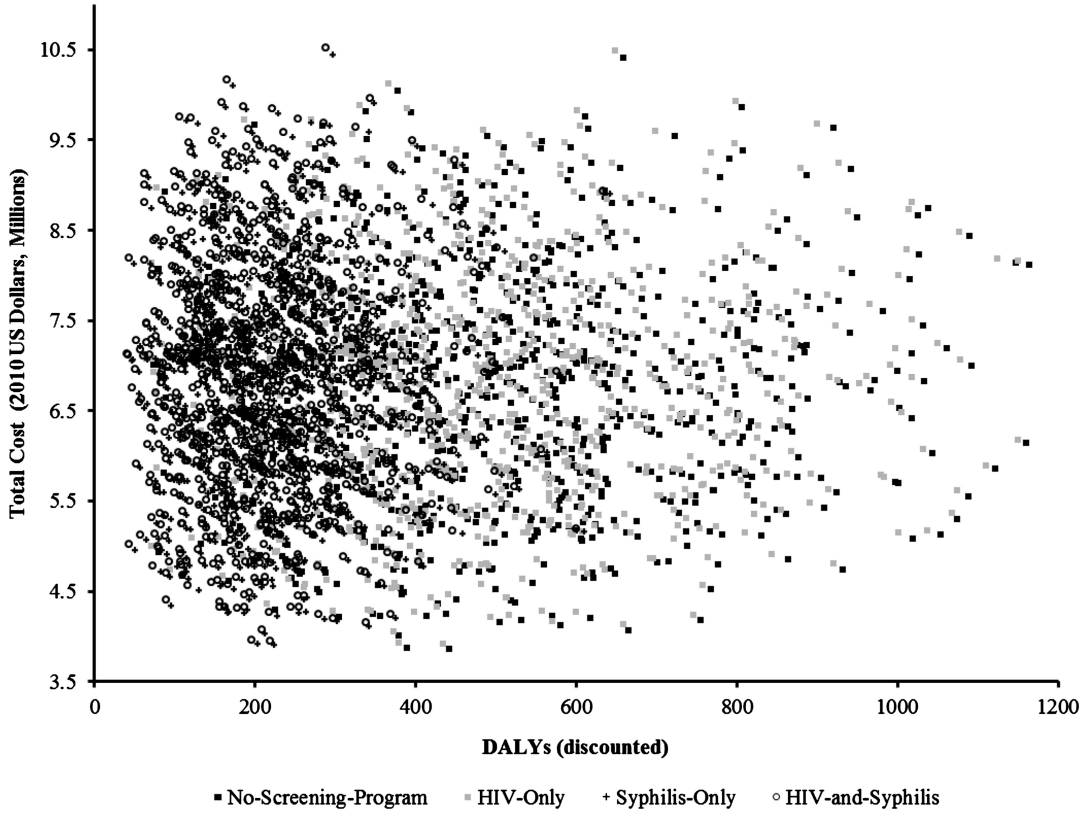

Figure 4. A summary scatter diagram of the results of the probabilistic sensitivity analysis of 1000 simulations showing the estimated total costs and DALYs lost for the 4 prenatal screening strategies examined (i.e., no-screening-program, HIV-only, syphilis-only, and HIV-and-syphilis).

comprehensive sensitivity analyses we conducted on all the parameter values as well as the separate sensitivity analysis specifically on the costs of APOs provide additional information that readers can use to judge the effects of our assumptions on our findings. Our findings may not be generalizable to other countries, where the cost structure, ability to deliver antenatal care, and percentage of the population with prior syphilis (and thus reactive to rapid plasma reagin [RPR] testing without active infections) might be different.

Most pregnant women have latent syphilis and are not infectious to sexual partners, although they are capable of transmitting to the fetus. In addition, although a few women may have had primary or secondary infection, it is likely that their sexual activity and concurrent partnerships were somewhat reduced during the time of pregnancy.[9] Our model did not account for ongoing transmission of HIV and/or syphilis in the community because we do not believe that pregnant women play an important role in the overall transmission of these infections within the community.

Owing to lack of data, the costs of AIDS and advanced stages of syphilis were not included in this analysis. Including the cost of AIDS and advanced stages of syphilis would have made the prenatal screening strategies even more cost-effective. We did not account for potential differences (or changes over time) in test acceptance rate for the strategies we examined owing to the lack of data. We examined one age cohort of pregnant women (instead of a distribution of ages) because the available data on the risk of APOs are not age based. Consequently, our results do not reflect age-based differences in the health (APOs) and economic outcomes. Based on a recent study,[4] we assumed that all patients with confirmed positive test results received treatment (ignoring those who were not treated because of concerns of adverse effects). Had we used a treatment rate lower than 100% (either because of inadequacies on the part of the health facilities or because the patient simply refused/failed to present for treatment), our cost-effectiveness estimates for the screening strategies would have been higher (less favorable). Finally, we may have underestimated the potential APOs attributable to HIV infection of the mother (such as sepsis or LBW[29]). Including the other HIV-related APOs would have made the screening strategies that included HIV screening more cost-effective.

Despite the limitations discussed above, our study has 2 major strengths. First, our search of the literature revealed no other published study that examined the cost-effectiveness of both HIV and syphilis screening of pregnant women in China. Second, our study has demonstrated that including syphilis screening in prenatal HIV screening programs to prevent or reduce APOs is substantially cost-effective in China and may be cost-saving in areas within China with relatively high syphilis prevalence.[4] In areas where prenatal HIV screening programs exist, adding syphilis screening can yield greater health and economic returns from efforts to prevent APOs. In addition, given the magnitude of the annual number of births in China (>17 million[16]), including syphilis screening can prevent a large number of APOs and improve the lives of several million infants overtime. Owing to the relative lack of medical cost data from China, future studies should estimate costs associated with APOs as well as HIV- and syphilis-related morbidity and mortality.

REFERENCES

1. New WHO strategy calls for elimination of HIV in children by 2015. 2010. Available at: http://www.unaids.org/en/resources/presscentre/featurestories/2010/april/20100421whostrategypmtct/. Accessed April 12, 2012.
2. Korhonen C, Wang L, Wang L, et al. Breastfeeding and HIV infection in China. In: Kourtis AP, Bulterys M, eds. Human Immunodefi ciency Virus Type 1 (HIV-1) and Breastfeeding: Science, Research Advances, and Policy. New York, NY: Springer, 2012:237–245.
3. Cooper ER, Charurat M, Mofenson L, et al. Combination antiretroviral strategies for the treatment of pregnant HIV-1–infected women and prevention of perinatal HIV-1 transmission. J Acquir Immune Defic Syndr 2002; 29:484–494.
4. Ministry of Health, People's Republic of China, Joint United Nations Programme on HIV/AIDS, World Health Organization. 2005 Update on the HIV/AIDS epidemic and response in China. Beijing, People's Republic of China; 2006.
5. Cheng JQ, Zhou H, Hong FC, et al. Syphilis screening and intervention in 500,000 pregnant women in Shenzhen, the People's Republic of China. Sex Transm Infect 2007; 83:347–350.
6. Fowler MG, Kourtis AP, Aizire J, Onyango-Makumbi C, Bulterys M. Breastfeeding and Transmission of HIV-1: Epidemiology and global magnitude. In: Kourtis AP, Bulterys M, eds. Human Immunodeficiency Virus Type 1 (HIV-1) and Breastfeeding: Science, Research Advances, and Policy. New York, NY: Springer, 2012:3–25.
7. Walker GJA, Walker DG. Congenital syphilis: A continuing but neglected problem. Semin Fetal Neonatal Med 2007; 12:198–206.
8. Darville T. Syphilis. Pediatr Rev 1999; 20:160–164, quiz 165.
9. Owusu-Edusei K Jr, Gift TL, Ballard RC. Cost-effectiveness of a dual non-treponemal/treponemal syphilis point-of-care test to prevent adverse pregnancy outcomes in sub-Saharan Africa. Sex Transm Dis 2011; 38:997–1003.
10. Owusu-Edusei K, Koski KA, Ballard RC. The tale of two serologic tests to screen for syphilis-treponemal and nontreponemal: Does the order matter? Sex Transm Dis 2011; 38:448–456.
11. Yang L-G, Tucker JD, Wang C, et al. Syphilis test availability and uptake at medical facilities in southern China. Bull World Health Organ 2011; 89:798–805.
12. UNAIDS, UNICEF, UNFPA, WHO. Towards eliminating new HIV infections in children and congenital syphilis in Asia-Pacific: Report from the 8th Meeting of the Asia-Pacific UN Task Force for the Prevention of Parents-to-Child Transmission of HIV. Bangkok, Thailand: UNICEF East Asia and Pacific Regional Office; 2011.
13. Cohen MS, Henderson GE, Aiello P, et al. Successful eradication of sexually transmitted diseases in the People's Republic of China: Implications for the 21st century. J Infect Dis 1996; 174:S223–229.
14. Tucker JD, Hawkes SJ, Yin YP, et al. Scaling up syphilis testing in China: Implementation beyond the clinic. Bull World Health Organ 2010; 88:452–457.
15. Tucker JD, Yang LG, Zhu ZJ, et al. Integrated syphilis/HIV screening in China: A qualitative analysis. BMC Health Serv Res 2010; 10:58.
16. China—Statistics. UNICEF, 2010. Available at: http://www.unicef.org/infobycountry/china_statistics.html. Accessed May 1, 2012.
17. Global health observatory data repository—life tables, China. World Health Organization, 2006. Available at: http://apps.who.int/ghodata/?vid=720. Accessed December 20, 2011.
18. Bogg L, Dong HJ, Keli W, et al. The cost of coverage: rural health insurance in China. Health Policy Plann 1996; 11:238–252.
19. Long Q, Zhang Y, Raven J, et al. Giving birth at a health-care facility in rural China: Is it affordable for the poor? Bull World Health Organ 2011; 89:144–152.
20. World Health Organization. The Global Burden of Disease: 2004 Update. Geneva: WHO, 2004.
21. Anand S, Hanson K. Disability-adjusted life years: A critical review. J Health Econ 1997; 16:685–702.
22. Gold MR, Stevenson D, Fryback DG. HALYS and QALYS and DALYS, Oh My: Similarities and differences in summary measures of population Health. Annu Rev Public Health 2002; 23:115–134.
23. Hong FC, Liu JB, Feng TJ, et al. Congenital syphilis: An economic evaluation of a prevention program in China. Sex Transm Dis 2010; 37:26–31.
24. Gomez GB, Kamb ML, Newman LM, et al. Untreated maternal syphilis and adverse outcomes of pregnancy: A systematic literature review and meta-analysis. Bull World Health Organ 2013; 91: 217–226.
25. Chen ZQ, Zhang GC, Gong XD, et al. Syphilis in China: Results of a national surveillance programme. Lancet 2007; 369:132–138.
26. Bronzan RN, Mwesigwa-Kayongo DC, Narkunas D, et al. Onsite rapid antenatal syphilis screening with an immunochromatographic Strip improves case detection and treatment in rural south African clinics. Sex Transm Dis 2007; 34:S55–S60.
27. Soorapanth S, Sansom S, Bulterys M, et al. Cost-effectiveness of HIV rescreening during late pregnancy to prevent mother-to-child HIV transmission in South Africa and other resource-limited settings. J Acquir Immune Defic Syndr 2006; 42:213–221.
28. Rydzak CE, Goldie SJ. Cost-effectiveness of rapid point-of-care prenatal syphilis screening in sub-Saharan Africa. Sex Transm Dis 2008; 35:775–784.
29. Rollins NC, Coovadia HM, Bland RM, et al. Pregnancy outcomes in HIV-infected and uninfected women in rural and urban South Africa. J Acquir Immune Defic Syndr 2007; 44:321–328.
30. Liang K, Meyers K, Zeng W, et al. Predictors of elective pregnancy termination among women diagnosed with HIV during pregnancy in two regions of China, 2004–2010. Int J Obstet Gynaecol 2013; 120:1207–1214.
31. Sanders GD, Bayoumi AM, Sundaram V, et al. Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy. N Engl J Med 2005; 352:570–585.