Scaling up syphilis testing in China: implementation beyond the clinic

Joseph D Tucker,[a] Sarah J Hawkes,[b] Yue-Pin Yin,[c] Rosanna W Peeling,[d] Myron S Cohen[e] & Xiang-Sheng Chen[c]

Abstract China is experiencing a syphilis epidemic of enormous proportions. The regions most heavily affected by syphilis correspond to regions where sexually transmitted HIV infection is also a major public health threat. Many high-risk patients in China fail to receive routine syphilis screening. This missed public health opportunity stems from both a failure of many high-risk individuals to seek clinical care and a disconnect between policy and practice. New point-of-care syphilis testing enables screening in non-traditional settings such as community organizations or sex venues. This paper describes the current Chinese syphilis policies, suggests a spatiotemporal framework (based on targeting high-risk times and places) to improve screening and care practices, and emphasizes a syphilis control policy extending beyond the clinical setting.

Une traduction en français de ce résumé figure à la fin de l'article. *Al final del artículo se facilita una traducción al español.* الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

In 2008, China had 278 215 officially reported syphilis cases – a threefold rise in the number of reported cases compared to 2004 and a tenfold increase over the past decade.[1] The majority of syphilis cases are in regions of China that also have a substantial burden of sexually transmitted HIV infection, highlighting the importance of effective syphilis control efforts.[1] Technical advances in syphilis diagnostics now permit onsite identification of syphilis cases using sensitive and specific treponemal tests,[2] thus enabling programmes to plan for syphilis testing outside traditional clinical settings.[3] Although validated point-of-care syphilis tests are available at prices negotiated by the World Health Organization (WHO), successful pilot programmes have been implemented in high burden areas, and policy latitude for screening and scale-up already exist, routine syphilis screening has not been widely implemented in China.[4]

Public health authorities keep records of syphilis testing and treatment since syphilis cases cluster and re-infection rates are high.[5] Coordination of clinical and public health functions is no small task, and this is why developing rationale syphilis policy is very important. Syphilis case reporting to local public health departments allows partner notification and treatment, which are both centrally important in syphilis control programmes.

This paper reviews the current Chinese syphilis policy and introduces a theoretical framework for syphilis screening based on high-risk times and places (i.e. spatiotemporal). The WHO syphilis programme shows how onsite rapid syphilis testing enhances syphilis control using this framework. Finally we propose a comprehensive plan to improve the quality of syphilis screening and control programmes in China.

Current syphilis policy

Since syphilis re-emerged in China as a major sexually transmitted infection,[1] the national response has focused on prompt and effective clinical services for high-risk patients.[6] China's national syphilis policy recommends screening for individuals who have multiple sex partners, unprotected sex or partners with a history of sexually transmitted infection (STI). This clinic-focused syphilis policy is similar to practice guidelines from Canada,[7] the Russian Federation,[8] the United Kingdom of Great Britain and Northern Ireland,[8] and the newly independent states of eastern Europe and central Asia.[9] Despite these recommendations, a large number of high-risk patients in many regions of the world fail to receive regular syphilis screening. Incomplete syphilis screening in China relates to two linked problems: (i) limitations of traditional STI clinical services in reaching high-risk groups, and (ii) a failure to implement effective interventions. Unsafe commercial sex and unsafe homosexual sex are major drivers of the resurgent syphilis epidemic,[10] but there is ample data suggesting that neither sex workers nor homosexual men attend clinics in great numbers.[11,12] When these high-risk individuals do attend public clinics in China, there is often no record of their detailed sexual history, which is not in line with official guidelines.[13] There is no tradition of secondary case finding or partner notification in China (or in many low-income nations), so all related infections remain untreated. In addition, the lack of laboratory facilities to perform standard diagnostic tests in some parts of China has led to the use of syndromic STI management, an approach with poor sensitivity for the detection of syphilis infection.[14]

Several aspects of the Chinese syphilis epidemic make a spatiotemporal framework for screening particularly important. China has an estimated 4–6 million sex workers[15] and the commercial sex industry has rapidly expanded during the past 10 years.[16] A population-based study of sexual health in China suggested that commercial sex is more important than casual sex in spreading STIs.[15] The prominence of the commercial sex industry in the spread of syphilis creates opportunities for targeted interventions at sex venues, community organizations

[a] Massachusetts General Hospital, 100 Blossom Street, Boston, MA, 02114, United States of America (USA).
[b] University College London, London, England.
[c] National Center for STD Control, Chinese Academy of Medical Sciences and Peking Union Medical College Institute of Dermatology, Nanjing, China.
[d] London School of Hygiene and Tropical Medicine, London, England.
[e] University of North Carolina School of Medicine, Chapel Hill, USA.
Correspondence to Joseph D Tucker (e-mail: jtucker4@partners.org).
(*Submitted: 29 July 2009 – Revised version received: 12 October 2009 – Accepted: 13 October 2009*)

Table 1. **Comparison of traditional syphilis control efforts in China and non-traditional spatiotemporal approaches**

Variable	Traditional syphilis control (current Chinese policy)	Spatiotemporal syphilis control
Key organizational unit	Individual STI clinics	STI clinics in cooperation with local public health bureaus
Optimal times to position syphilis screening	No changes in syphilis based on time	Rural-to-urban migration, marriage, pregnancy
Optimal places to position syphilis screening	No specific locations for testing outside clinics	Entertainment centres, venues frequented by MSM and related locales may be feasible
Partner notification and treatment	Mentioned in guidelines, but not routinely implemented	Potential for enhanced partner notification programmes in places/ times with higher syphilis prevalence

MSM, men who have sex with men; STI, sexually transmitted infection

and similar non-traditional sites. While China's sex industry is found in many locations, data from sex workers can be useful to establish place-based syphilis testing, counselling and referral.[17,18]

A spatiotemporal framework

The known variation in syphilis incidence related to high-risk times and places provides the template for a spatiotemporal screening framework. Spatial syphilis incidence variation includes two separate but complementary notions related to the spread of syphilis – local syphilis prevalence variation within a city (e.g. comparing sex venues with entertainment centres) and regional syphilis surveillance variation (e.g. comparing reported cases in cities or counties). Novel point-of-care syphilis tests have been validated in low-income areas including China,[3,19] providing opportunities to expand testing at "non-traditional" sites (Table 1). Location-focused syphilis testing avoids much of the stigma associated with STI clinics. The China Health and Family Life Survey, a national stratified probability sample of 3426 individuals, found that among those Chinese who had symptoms consistent with an STI, only 23% presented to a formal public clinic, 8% attended a private clinic, 15% directly purchased medicine and 52% did nothing.[15] These data are consistent with the national Chinese census in the year 2000, which found that many Chinese people with STIs never present to public STI clinics.[12] STI epidemiology and prevention initiatives at specific local sites have proved useful in several different settings, and these may be enhanced by the introduction of point-of-care syphilis tests.[20,21]

In addition to considering the local variation in syphilis burden, regional syphilis variation can be used as a tool to target syphilis screening programmes. Syphilis cases are more spatially clustered than other STIs.[22] In 2006, all of the country's primary and secondary syphilis cases were found in just 24.8% of counties in the United States of America (USA).[23] Chinese epidemiology data also suggests that syphilis is mainly found in a relatively small number of areas. Cities along the south-eastern coast report higher numbers of syphilis cases consistent with hyperendemic phase spread.[1] The increasing focus on regional syphilis incidence variation is reflected in national policy documents, including those of the USA. The 2006 plan to eliminate syphilis in the USA allocated resources for local syphilis control programmes based on reported primary and secondary syphilis cases, and also differentiated support based on epidemic phase.[24]

Temporal variation in syphilis incidence is also important, and empirical evidence shows that temporal clustering of syphilis cases may increase HIV acquisition risk during specific periods which have greater acute HIV infections (JD Tucker, X Gao, HC Wang, unpublished data, 2009). This is also supported by recurrent seasonal patterns in reported syphilis cases.[25] Seasonal changes in reported STI cases have been noted elsewhere,[26,27] but very few programmes have taken advantage of these temporal changes.

Implementing syphilis control programmes at specific times and places can help focus public health programmes. The Chinese context offers several settings and times to target syphilis screening (Table 2): potential entry points for expanded syphilis screening include several different time periods (marriage, migration, pregnancy) and settings (entertainment centres, prisons, detention centres). The following are examples of spatially and temporally focused syphilis screening.

Time-focused screening

Prenatal syphilis screening programmes have proved successful and cost-effective for women in several settings.[34–37] The largest Chinese experience with syphilis screening tested nearly half a million pregnant women at antenatal clinics in a city over a three-year period, using government funded syphilis tests. They found 0.5% of women had a positive rapid plasma reagin (RPR) and *Treponema pallidum* particle agglutination assay (TPPA), and thus successfully treated 1855 pregnant women with syphilis infection.[35] A cost-effectiveness analysis of this massive screening programme found that one disability-adjusted life year could be saved for the cost of US$ 215, and it cost US$ 770 to find one mother with syphilis infection.[37] The same study found that local variation in syphilis prevalence was a key variable in determining the cost-to-benefit ratio. Identification of pregnant women with syphilis must also be used to direct partner-management efforts. In light of the potential public health benefit, scalability and large target population in some regions, this approach may hold great promise for congenital syphilis prevention. WHO recommends syphilis screening (and treatment as appropriate) for pregnant women to reduce the burden of congenital syphilis.[38]

Focusing syphilis screening at pregnancy using a spatiotemporal approach represents a marked departure from current Chinese syphilis screening policy in two important ways. First, current Chinese syphilis policy fails to differentiate between regions in China with hyperendemic spread and other regions, despite the well known substantial spatial variation in reported congenital syphilis cases.[1] A spatiotemporal syphilis screening programme focused at pregnancy could help mobilize resources for screening to regions with greater congenital syphilis burden. Second, Chinese syphilis policy focuses on diagnosis in clinical settings without acknowledging existing non-traditional testing sites. Some regions

Table 2. **Overview of potential syphilis screening entry points (times or places) in China**

Screening entry point	1998 STI asymptomatic screening	2008 STI asymptomatic screening	Estimated syphilis prevalence[a]	Estimated target population size[b]	Scalability[c]
Time					
Marriage	Yes	Limited	ca. 0.1–0.6%	8.3 million[28]	No
Pregnancy	No	Limited	ca. 0.1–0.45%	ca. 31 million[d]	Yes
Rural-to-urban migration	No	Limited	ca. 0.4–1.0%[e]	ca. 79 million[29]	Variable
Place					
Entertainment centres (including venues frequented by MSM)	No	Variable	ca. 0.5–18%	Tens of millions	Variable
Prisons	No	No	Unknown	ca. 1.6 million	Yes
IDU, CSW, detention centres	Variable	Limited	IDU ca. 6%, CSW ca. 12%	ca. hundreds of thousands	Yes

CSW, commercial sex worker; IDU, injecting drug users; MSM, men who have sex with men; STI, sexually transmitted infection

[a] Estimations based on data from the National Center for STI Control (Chinese Centers for Disease Control and Prevention) and the systematic review of syphilis seroprevalence among various groups,[10] but included with ranges due to limited syphilis data in China.[30]

[b] Population statistics from the *China Population Yearbook 2006* unless otherwise noted.

[c] The term "scalability" has been used in the public health literature to describe the ability of an innovation to be expanded in different contexts.[31] In this case, it refers to the potential for the syphilis screening to be effectively scaled up to the entire estimated population.

[d] Total pregnant women in China estimated from the total number of births, stillbirths and miscarriages in China.

[e] The estimate for rural-to-urban migrants is based on two cross-sectional studies from eastern China.[32,33]

of south China already have routine prenatal testing in community settings, providing an organizational structure for onsite rapid syphilis testing and spatially focused syphilis screening.

Location-focused screening

Commercial sex in China thrives in several entertainment venues, including karaoke bars, clubs, hotels and resorts. Several epidemiology studies in China have suggested a link between entertainment centres and STI risk,[13,39,40] and a systematic review found a syphilis prevalence of ca. 0.8% among women at entertainment sites.[10] Regional differences in sex work could impact the effectiveness of this kind of screening programme since some regions have more easily identifiable venues frequented by men who have sex with men (MSM), sex venues or other locations where people meet new sex partners. Using entertainment centres for syphilis screening in China shows how a spatiotemporal approach can focus otherwise unrealistic public health strategies. Instead of providing rapid syphilis tests at all of the tens of millions of entertainment centres in China, consolidating syphilis screening campaigns in regions with a higher burden of syphilis would expand the public health impact.

A WHO pilot programme in south China demonstrates how a spatiotemporal framework can help focus syphilis screening at sex venues. Local public health officials at the WHO rapid syphilis test site in Guangdong Province noticed that sex workers infrequently attended the local public STI clinic, so they formed small outreach teams to provide free onsite rapid syphilis testing. The outreach team includes a physician, a nurse and a volunteer from a nongovernmental organization to provide voluntary counselling and testing.

Typically the outreach team gives a general talk about the importance of routine STI screening, followed by voluntary rapid syphilis testing in a separate enclosed room. Rapid syphilis test results are available within 30 minutes, and all patients who have a positive rapid treponemal test then require nontreponemal testing at the local clinic. A positive treponemal rapid syphilis test must be followed by a nontreponemal test to differentiate early syphilis infection, previous treated syphilis or false positive. Nontreponemal tests are performed at the local STI clinic laboratory and the results are telephoned to patients. A systematic analysis of rapid syphilis test characteristics found a high sensitivity and high specificity.[4] Local prevalence of syphilis infection will determine whether treatment is onsite or at an STI clinic. The preliminary experience of this WHO pilot in south China suggests that rapid syphilis testing is feasible and may help reach a subsection of sex workers and MSM who would otherwise be unlikely to attend traditional clinical services.

A comprehensive response

Expanding syphilis screening is a key first step for syphilis control, but subsequent steps in testing, partner notification and linkage to care are also integral to a comprehensive response. Although syphilis partner notification is not widely practiced in the Chinese public health system, if it were focused on entertainment venues, this might circumvent some of the stigma and distrust in the clinic system that have limited the expansion of this traditional pillar of syphilis control. Sex workers and MSM may be more willing to provide their social and sexual contacts outside public clinic settings, as demonstrated in an MSM sexual network project that successfully used MSM entertainment venues.[41] Small studies of entertainment establishment managers in south China suggest that there is willingness to prevent HIV/STI and provide a positive structural environment that promotes sex worker health.[17,42] The WHO pilot programme in south China has shown that, once STI patients are diagnosed with syphilis, effective and timely treatment and follow up are feasible.[43] More work needs to be done with partner notification programmes in China to evaluate their efficacy and sustainability.

Conclusion

Accelerating syphilis screening and treatment in China is a new public health imperative, driven by sustained increases in reported cases and an increasingly responsive government policy environment. A rapid point-of-care syphilis test can help move beyond the traditional behaviour-based framework to focus on settings and times, allowing interventions specific to epidemic phases and promoting integrated systems of testing, treatment and referral. Syphilis testing at high-risk places and times independent of individual-reported behaviour can help improve syphilis control programmes. At the same time, the addition of a single syphilis test is not a panacea for the looming syphilis threat. More data regarding provider behaviours and testing incentives, local human resource capacity, patient preferences, cost-effectiveness and organizational structures will be needed to ensure sustainable systems of syphilis diagnosis, treatment and referral.

In light of the scalability and potential public health impact, expanding syphilis testing for pregnant women in high-burden regions should be a key priority for the Chinese syphilis response. Cost-effectiveness analyses of antenatal syphilis screening have been conducted in several countries,[34,37,44,45] including China.[37] Preliminary data from both national government programmes and WHO pilot programmes suggest that routine syphilis screening for pregnant women is feasible, but more work and operational research are needed to ensure sustainability, especially as international programmes are completed and routine services resume.

In China's market-based, largely fee-for-service, health-care environment, determining who will pay for testing and how to incentivize testing at the patient and provider levels are not trivial issues. They will have important implications for the sustainability of any comprehensive intervention. With the help of a spatiotemporal framework, China's scale-up can focus on the times and locations where widespread syphilis testing provides the greatest impact. ■

Acknowledgements:

Joseph Tucker is also affiliated with the University of North Carolina at Chapel Hill, USA.

We thank the China Syphilis Working Group, the University of North Carolina Fogarty AIDS International Research and Training Program (NIH FIC D43 TW01039), the University of North Carolina Social Science Research on HIV/AIDS in China (NIH NICHD R24 HD056670–01), the WHO Rapid Syphilis Test Project (WHO OD/TS-08–00088), the Harvard Initiative for Global Health, the American Society of Tropical Medicine and Hygiene and the United States National Institutes of Health Fogarty International Center International Clinical Fellowship. We also thank Peter Leone for helpful discussions.

Competing interests: None declared.

الملخص

الارتقاء بالاختبارات لكشف الزهري في الصين: التنفيذ خارج نطاق العيادات

تعاني الصين من وباء الزهري بأعداد كبيرة. والمناطق الأكثر تعرُّضاً للزهري هي نفسها المناطق التي تشكل فيها العدوى بفيروس الإيدز تهديداً خطيراً للصحة العمومية. وليس بمقدور الكثير من المرضى المعرّضين لخطر مرتفع في الصين الاستفادة من التحري الروتيني لكشف الزهري، وينجم فقدان هذه الفرصة التي تقدمها الصحة العمومية عن عدم قدرة الكثير من المعرّضين لخطر مرتفع التماس الرعاية الطبية، وعن فقدان الترابط بين السياسات وبين الممارسات. إن النقاط الجديدة للرعاية التي يُجرى فيها اختبار الكشف عن الزهري تتيح التحري عن الزهري في مواقع غير تقليدية مثل المنظمات الاجتماعية وأماكن البغاء. وتصف هذه الورقة السياسات الصينية المعمول بها حالياً حول الزهري، وتقترح إنشاء إطار زماني ومكاني (يرتكز على استهداف الأوقات والأماكن العالية الخطورة)، لتحسين ممارسات التحري وتقديم الرعاية، وللتأكيد على سياسات لمكافحة الزهري تتجاوز المواقع السريرية.

Résumé

Étendre le dépistage de la syphilis en Chine au-delà des dispensaires

La Chine vit une épidémie de syphilis qui prend d'énormes proportions. Les régions les plus lourdement touchées par cette maladie correspondent à celles où le VIH/sida, en tant que maladie sexuellement transmissible, constitue déjà une menace importante pour la santé publique. En Chine, de nombreux individus à haut risque ne bénéficient pas d'un dépistage systématique de la syphilis. Les raisons de cette opportunité manquée pour la santé publique tiennent à la fois à l'absence de demande de soins cliniques par de nombreux individus à haut risque et à la déconnection entre politique et pratique. Le dépistage de la syphilis au niveau de nouveaux points de soins permet de dépister cette maladie dans des contextes moins classiques tels que des organisations communautaires ou des établissements sexuels. L'article décrit les politiques actuellement appliquées par la Chine contre la syphilis, propose un cadre spatiotemporel (reposant sur le ciblage des moments et des endroits à haut risque) pour l'amélioration du dépistage et des pratiques de soins et met l'accent sur une politique de lutte contre cette maladie sortant du cadre des dispensaires.

Resumen

Expansión de las pruebas de la sífilis fuera del ámbito de los dispensarios en China

China está sufriendo una epidemia de sífilis de enormes proporciones. Las regiones más afectadas por esa enfermedad coinciden con aquellas donde la infección por VIH de transmisión sexual constituye también una grave amenaza para la salud pública. Muchos pacientes de alto riesgo del país no se benefician del cribado sistemático de la sífilis. Esta oportunidad perdida para la salud pública se debe tanto al hecho de que muchas personas de alto riesgo no buscan atención clínica como a la desconexión existente entre la política y la práctica. Una nueva prueba de la sífilis en el lugar de consulta permite hacer cribados en entornos no tradicionales, como por ejemplo organizaciones comunitarias o locales de sexo. En este artículo se describen las políticas aplicadas actualmente contra la sífilis en China, se sugiere un marco espaciotemporal (basado en focalizar la acción en momentos y lugares de alto riesgo) para mejorar las prácticas de cribado y atención, y se hace hincapié en una política de control de la sífilis que trascienda el ámbito de los dispensarios.

References

1. Chen ZQ, Zhang GC, Gong XD, Lin C, Gao X, Liang GJ et al. Syphilis in China: results of a national surveillance programme. *Lancet* 2007;369:132–8. doi:10.1016/S0140-6736(07)60074-9 PMID:17223476
2. Tucker JD, Chen XS, Peeling RW. Syphilis and social upheaval in China. *N Engl J Med* 2010. In press
3. Mabey D, Peeling RW, Ballard R, Benzaken AS, Galbán E, Changalucha J et al. Prospective, multi-centre clinic-based evaluation of four rapid diagnostic tests for syphilis. *Sex Transm Infect* 2006;82(Suppl 5):v13–6. doi:10.1136/sti.2006.022467 PMID:17215274
4. Tucker JD, Bu J, Brown LB, Yin YP, Chen XS, Cohen M. Accelerating global syphilis control through novel rapid syphilis testing: a systematic review. *Lancet Infect Dis* 2010. In press
5. Mandell GL, Bennett JE, Dolin R. *Mandell, Douglas, and Bennett's principles and practice of infectious diseases.* 7th edn. Philadelphia: Churchill Livingstone/Elsevier; 2010.
6. *National standard of the People's Republic of China: diagnostic criteria and management of syphilis* (GB 15974-1995). Beijing; Ministry of Health: 1996.
7. Kropp RY, Latham-Carmanico C, Steben M, Wong T, Duarte-Franco E. What's new in management of sexually transmitted infections? Canadian Guidelines on Sexually Transmitted Infections, 2006 Edition. *Can Fam Physician* 2007;53:1739–41. PMID:17934039
8. Renton AM, Borisenko KK, Tichonova LI, Akovbian VA. The control and management of the sexually transmitted diseases: a comparison of the United Kingdom and the Russian Federation. *Int J STD AIDS* 1999;10:659–64. doi:10.1258/0956462991913231 PMID:10582633
9. Radcliffe K. Developing evidence-based guidelines for the management of sexually transmitted diseases in former Soviet Union countries. *Int J STD AIDS* 2005;16:589–93. doi:10.1258/0956462054944525 PMID:16176622
10. Lin CC, Gao X, Chen XS, Chen Q, Cohen MS. China's syphilis epidemic: a systematic review of seroprevalence studies. *Sex Transm Dis* 2006;33:726–36. doi:10.1097/01.olq.0000222703.12018.58 PMID:16755273
11. Ma W, Detels R, Feng Y, Wu Z, Shen L, Li Y et al. Acceptance of and barriers to voluntary HIV counselling and testing among adults in Guizhou province, China. *AIDS* 2007;21(Suppl 8):S129–35. doi:10.1097/01.aids.0000304708.64294.3f PMID:18172381
12. Ma JM, Liu N, Chen AP, Yang GH. Study on knowledge, attitudes and behaviors regarding infectious diseases among Chinese people in 2002 *Zhonghua Liu Xing Bing Xue Za Zhi* 2005;26:389–93. PMID:16185442
13. Chen XS, Yin YP, Tucker JD, Gao X, Cheng F, Wang TF et al. Detection of acute and established HIV infections in sexually transmitted disease clinics in Guangxi, China: implications for screening and prevention of HIV infection. *J Infect Dis* 2007;196:1654–61. doi:10.1086/522008 PMID:18008249
14. Yin YP, Wu Z, Lin C, Guan J, Wen Y, Li L et al.; NIMH Collaborative HIV/STD Prevention Trial Group. Syndromic and laboratory diagnosis of sexually transmitted infection: a comparative study in China. *Int J STD AIDS* 2008;19:381–4. PMID:18595875
15. Parish WL, Laumann EO, Cohen MS, Pan S, Zheng H, Hoffman I et al. Population-based study of chlamydial infection in China: a hidden epidemic. *JAMA* 2003;289:1265–73. doi:10.1001/jama.289.10.1265 PMID:12633188
16. Tucker JD, Henderson GE, Wang TF, Huang YY, Parish W, Pan SM et al. Surplus men, sex work, and the spread of HIV in China. *AIDS* 2005;19:539–47. doi:10.1097/01.aids.0000163929.84154.87 PMID:15802971
17. Huang Y, Henderson GE, Pan S, Cohen MS. HIV/AIDS risk among brothel-based female sex workers in China: assessing the terms, content, and knowledge of sex work. *Sex Transm Dis* 2004;31:695–700. doi:10.1097/01.olq.0000143107.06988.ea PMID:15502679
18. Xia G, Yang X. Risky sexual behavior among female entertainment workers in China: implications for HIV/STD prevention intervention. *AIDS Educ Prev* 2005;17:143–56. doi:10.1521/aeap.17.3.143.62904 PMID:15899752
19. Herring AJ, Ballard RC, Pope V, Adegbola RA, Changalucha J, Fitzgerald DW et al. A multi-centre evaluation of nine rapid, point-of-care syphilis tests using archived sera. *Sex Transm Infect* 2006;82(Suppl 5):v7–12. doi:10.1136/sti.2006.022707 PMID:17118953
20. Michaud JM, Ellen J, Johnson SM, Rompalo A. Responding to a community outbreak of syphilis by targeting sex partner meeting location: an example of a risk-space intervention. *Sex Transm Dis* 2003;30:533–8. doi:10.1097/00007435-200307000-00001 PMID:12838079
21. Weir SS, Figueroa JP, Byfield L, Hall A, Cummings S, Suchindran C. Randomized controlled trial to investigate impact of site-based safer sex programmes in Kingston, Jamaica: trial design, methods and baseline findings. *Trop Med Int Health* 2008;13:801–13. PMID:18482079
22. Kerani RP, Handcock MS, Handsfield HH, Holmes KK. Comparative geographic concentrations of 4 sexually transmitted infections. *Am J Public Health* 2005;95:324–30. doi:10.2105/AJPH.2003.029413 PMID:15671471
23. Weinstock H. Primary and secondary syphilis in the United States: epidemiology and emerging issues [abstract A6b]. In: *2008 National STD Prevention Conference, Chicago, 10–13 March 2008.*
24. *The national plan to eliminate syphilis from the United States.* Atlanta: Centers for Disease Control; 2006.
25. Bu J, Tucker JD, Chen XS. *STD situational briefing.* Beijing: China Centers for Disease Control; 2009.
26. Wellings K, Macdowall W, Catchpole M, Goodrich J. Seasonal variations in sexual activity and their implications for sexual health promotion. *J R Soc Med* 1999;92:60–4. PMID:10450213
27. Shah AP, Smolensky MH, Burau KD, Cech IM, Lai D. Recent change in the annual pattern of sexually transmitted diseases in the United States. *Chronobiol Int* 2007;24:947–60. doi:10.1080/07420520701648325 PMID:17994348
28. China's divorce rate up 21.2 percent in 2004. *Xinhua News*, 1 March 2005.
29. Liang Z, Ma Z. China's floating population: new evidence from the 2000 Census. *Popul Dev Rev* 2004;30:467–88. doi:10.1111/j.1728-4457.2004.00024.x

30. Yin L, Qin GM, Ruan YH, Zhang L, Hao QN, Chen XH et al. A prospective cohort study on human immunodeficiency virus and syphilis seroconversion among injecting drug users *Zhonghua Liu Xing Bing Xue Za Zhi* 2006;27:293–7. PMID:16875529
31. Simmons R, Fajans P, Ghiron L, eds. *Scaling up health service delivery: from pilot innovations to policies and programmes*. Geneva: World Health Organization; 2007. Available at: http://whqlibdoc.who.int/publications/2007/9789241563512_eng.pdf [accessed 22 April 2010].
32. Hesketh T, Li L, Ye X, Wang H, Jiang M, Tomkins A. HIV and syphilis in migrant workers in eastern China. *Sex Transm Infect* 2006;82:11–4. doi:10.1136/sti.2004.014043 PMID:16461594
33. He N, Detels R, Zhu J, Jiang Q, Chen Z, Fang Y et al. Characteristics and sexually transmitted diseases of male rural migrants in a metropolitan area of Eastern China. *Sex Transm Dis* 2005;32:286–92. doi:10.1097/01.olq.0000152219.58592.9b PMID:15849529
34. Schackman BR, Neukermans CP, Fontain SN, Nolte C, Joseph P, Pape JW et al. Cost-effectiveness of rapid syphilis screening in prenatal HIV testing programs in Haiti. *PLoS Med* 2007;4:e183. doi:10.1371/journal.pmed.0040183 PMID:17535105
35. Cheng JQ, Zhou H, Hong FC, Zhang D, Zhang YJ, Pan P et al. Syphilis screening and intervention in 500,000 pregnant women in Shenzhen, the People's Republic of China. *Sex Transm Infect* 2007;83:347–50. doi:10.1136/sti.2006.023655 PMID:17693449
36. Schmid GP, Stoner BP, Hawkes S, Broutet N. The need and plan for global elimination of congenital syphilis. *Sex Transm Dis* 2007;34(Suppl):S5–10. doi:10.1097/01.olq.0000261456.09797.1b PMID:17592390
37. Hong FC, Liu JB, Feng TJ, Liu XL, Pan P, Zhou H et al. Congenital syphilis: an economic evaluation of a prevention program in China. *Sex Transm Dis* 2009;37:26–31.
38. Hossain M, Broutet N, Hawkes S. The elimination of congenital syphilis: a comparison of the proposed World Health Organization action plan for the elimination of congenital syphilis with existing national maternal and congenital syphilis policies. *Sex Transm Dis* 2007;34(Suppl):S22–30. doi:10.1097/01.olq.0000261049.84824.40 PMID:17592387
39. Li L, Wu Z, Rotheram-Borus MJ, Guan J, Yin Y, Detels R et al.; NIMH Collaborative HIV/STD Prevention Trial Group. Visiting entertainment venues and sexual health in China. *Arch Sex Behav* 2009;38:814–20. doi:10.1007/s10508-008-9311-7 PMID:18256918
40. Li L, Wu Z, Rotheram-Borus MJ, Guan J, Yin Y, Detels R et al.; NIMH Collaborative HIV/STD Prevention Trial Group. Visiting entertainment venues and sexual health in China. *Arch Sex Behav* 2009;38:814–20. doi:10.1007/s10508-008-9311-7 PMID:18256918
41. Choi KH, Ning Z, Gregorich SE, Pan QC. The influence of social and sexual networks in the spread of HIV and syphilis among men who have sex with men in Shanghai, China. *J Acquir Immune Defic Syndr* 2007;45:77–84. doi:10.1097/QAI.0b013e3180415dd7 PMID:17325608
42. Yang H, Li X, Stanton B, Fang X, Zhao R, Dong B et al. Condom use among female sex workers in China: role of gatekeepers. *Sex Transm Dis* 2005;32:572–80. doi:10.1097/01.olq.0000175418.48665.95 PMID:16118607
43. Tucker JD, Yang LG, Zhu ZJ, Yang B, Yin YP, Cohen MS et al. Integrated syphilis/HIV screening in China: a qualitative analysis. *BMC Health Serv Res* 2010;10:58. doi:10.1186/1472-6963-10-58 PMID:20205942
44. Rydzak CE, Goldie SJ. Cost-effectiveness of rapid point-of-care prenatal syphilis screening in sub-Saharan Africa. *Sex Transm Dis* 2008;35:775–84. doi:10.1097/OLQ.0b013e318176196d PMID:18607319
45. Adam T, Lim SS, Mehta S, Bhutta ZA, Fogstad H, Mathai M et al. Cost effectiveness analysis of strategies for maternal and neonatal health in developing countries. *BMJ* 2005;331:1107. doi:10.1136/bmj.331.7525.1107 PMID:16282407