COMPARISON OF ONE-STOP VERSUS
CONVENTIONAL SERVICE ON ANTENATAL
SYPHILIS SCREENING IN ULAANBAATAR,
MONGOLIA

BAYALAG MUNKHUU

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Author: Bayalag Munkhuu

Program: Epidemiology

Supervising committee: 

Examining committee:
This is to certify that the work here submitted is the result of the candidate’s own investigations. Due acknowledgement has been made of any assistance received.

Associate Professor

Tippawan Liabsuetrakul M.D., Ph.D.

Principle supervisor

Bayalag Munkhuu M.D., M.Sc

Candidate
I hereby certify that this work has not already been accepted in substance for any degree, and is not being concurrently submitted in candidate for any degree.

Bayalag Munkhuu M.D., M.Sc.

Candidate
ABSTRACT

Background: Congenital syphilis can be prevented by antenatal syphilis screening; however, complexity in the delivery of conventional service facilitates low screening, less treatment and thus prevention. One-stop antenatal syphilis screening service, which includes rapid testing and case management, is the proposed method to overcome the problems inherent with conventional services. This cluster randomized trial was performed to test whether one-stop service would be better at preventing congenital syphilis than the conventional antenatal screening service in Ulaanbaatar, Mongolia. The feasibility of the one-stop service on antenatal syphilis screening was also assessed.
Methods: Out of 14 antenatal clinics in 6 districts of Ulaanbaatar, 7 were randomly selected for the one-stop service and the remaining for the conventional service. Intervention clinics provided onsite rapid syphilis testing and immediate treatment for positive cases and their partners. The control clinics provided conventional syphilis screening services with routine offsite rapid plasma regain testing followed by case management. Analysis was performed on an intention to treat basis. For the feasibility part of the study, opinions and level of satisfaction from antenatal women and their providers regarding the one-stop service at two antenatal clinics were assessed during the run-in period of the trial.

Results: Of 3,850 antenatal women recruited in each group, the proportions of syphilis testing at the first antenatal visit and the third trimester were over 99% in the intervention group compared to 79.6% and 61.5% in the control group, respectively (p<0.001 for both periods). Correspondingly, syphilis cases detected in the intervention group were 73 (1.9%) and 20 (0.5%), significantly higher than 27 (0.9%) and 2 (0.08%) in the control group. Eventually, 98.9% (92/93) of the detected cases in the intervention and 89.6% (26/29) in the control group were adequately treated (p=0.02). The corresponding treatment rates of the sexual partners were 94.6% versus 55.2% (p<0.001). Only one congenital syphilis case out of 3,632 deliveries in the intervention group versus 15 out of 3,552 in the control group was
ascertained at the end, a reduction of 93.5% (95% confidence interval 66.0% to 98.6%).

The feasibility study found that the majority of 246 women interviewed were satisfied with the one-stop service. All women accepted the one-stop service and tested for syphilis. The husbands of four women with positive rapid tests their husbands were treated. The mean aggregate satisfaction score derived from 11 questions on specific aspects of satisfaction was 3.2 (range 2.6-3.8). The providers were also satisfied and most of them reported that they did not encounter any significant problems to either delay or hamper the other routine services. However, all providers agreed that the one-stop service was time consuming, resulting in high staff workloads and the need for good clinical management. In addition, they preferred to treat husbands presumptively in order to avoid the possibility of diagnosing couples with discordant syphilis, which may lead to possible domestic violence.

**Conclusion and Recommendations:** The one-stop service of antenatal syphilis screening is feasible and did not face any critical obstacles in terms of women and providers’ perspectives. The one-stop service on antenatal syphilis screening implemented in antenatal clinics was more effective for prevention of congenital syphilis than conventional service & could have a large impact on congenital syphilis prevention. Implementation of one-stop service can be considered to improve overall access to interventions to eliminate congenital syphilis as a public health problem.
Key words: antenatal syphilis screening, cluster randomized trial, congenital syphilis, feasibility, one-stop service, Mongolia
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First and foremost, I would like to thank my supervisor Associate Professor Dr Tippawan Liabsuetrakul, under whose supervision I chose this topic and began the thesis, and whose thoughtful advice often served to give me a sense of direction during my studies.

This work would not have been possible without the support and encouragement of the head of Epidemiology unit Professor Dr Virasakdi Chongsuvivatwong who shared with me a lot of his expertise.

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Bayalag Munkhuu
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<th>Description</th>
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<tbody>
<tr>
<td>ANC</td>
<td>Antenatal Care</td>
</tr>
<tr>
<td>ASYS</td>
<td>Antenatal Syphilis Screening</td>
</tr>
<tr>
<td>DALY</td>
<td>Disability-adjusted life years</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>MCH Centre</td>
<td>State Research Centre on Maternal and Child Health</td>
</tr>
<tr>
<td>NCCD</td>
<td>National Centre of Communicable Diseases</td>
</tr>
<tr>
<td>OB-GYN</td>
<td>Obstetrician-Gynecologist</td>
</tr>
<tr>
<td>OR</td>
<td>Odds Ratio</td>
</tr>
<tr>
<td>RPR</td>
<td>Rapid Plasma Reagin</td>
</tr>
<tr>
<td>TPHA</td>
<td><em>Treponema pallidum</em> Hemoagglutination</td>
</tr>
<tr>
<td>STI</td>
<td>Sexually Transmitted Infection</td>
</tr>
<tr>
<td>T. Pallidum</td>
<td><em>Treponema Pallidum</em></td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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CHAPTER 1

INTRODUCTION

1. BACKGROUND

The first chapter covers the overview of maternal and congenital syphilis at global and local level. It also introduces the socio-demographic characteristics and health delivery system regarding sexually transmitted infections in Mongolia.

1.1 Study background

Syphilis is a sexually transmitted infection (STI). If it is not treated in its early stages, the infection spreads through the body, causing permanent damage to the main organs, such as the nervous and cardiovascular systems. If a syphilis infected woman becomes pregnant or a pregnant woman becomes infected, she can pass the infection to her unborn baby regardless of the syphilis stage. Untreated maternal syphilis can lead to serious complications, such as spontaneous abortion, preterm birth, stillbirth and congenital infection in the neonate at birth.1-2

In 1999, the World Health Organization (WHO) reported that at least half a million infants are born with congenital syphilis annually. In addition, maternal syphilis causes another half
a million adverse pregnancy outcomes, such as stillbirths and miscarriages. Currently, WHO estimates that up to 1.4 million cases of congenital syphilis occur worldwide each year and over 90% of them take place in developing countries. Over the past few decades, congenital syphilis has become a public health concern in many developing and former socialist countries.

Congenital syphilis is a serious but preventable disease. Early detection and treatment of syphilis in pregnant women is a standard measure for preventing congenital syphilis. With this noble purpose, ASYS on the first day of antenatal care (ANC) registration of a pregnant woman is a mandatory procedure. Now there is new evidence and recommendations that routine testing should be repeated in the third trimester of gestation, even in low prevalence areas. Many countries have policies providing for universal screening of syphilis in pregnant women. However, for various reasons, in many developing countries the policies are not systematically implemented, resulting in failure of the syphilis seropositive women to receive treatment during the course of their pregnancy.

1.2 Study setting background

1.2.1 Socio-demographic characteristics of Mongolia

Mongolia is a landlocked country in central Asia, bordered by Russia to the north and China, to the south. According to the 2000
census, Mongolia has a population of 2.6 million with an annual population growth rate of 1.4% and a population density of 1-2 person/km². Almost 60% of the population is aged below 35 years with a sex ratio of approximately 1:1 (50.7% female versus 49.3% male). The crude birth rate is 1.8 per 1000 population and the infant mortality rate was 17.8/1,000 in 2007. The life expectancy at birth is 66 years. The adult literacy rate is 98%. About one half of the population live in urban areas with approximately 25% residing in the capital city Ulaanbaatar.

Over the past few decades, Mongolia has developed a socialist social service infrastructure that achieved a high level of literacy and equity of basic education and health service accessibility. Due to the collapse of the Soviet Union in the 1990s, the underlying weaknesses of the country’s socialist economy became more and more apparent. Therefore, Mongolia experienced reforms towards a more democratic government and a market-oriented economy. The sudden breakup of the socialist regime and rapid transition to an open market system led to changes in the social, economic and cultural landscape. The biggest impacts have been the adverse socioeconomic and political changes, the increasing number of prostitutes, street children, runaway adolescents, unemployed and the apparent growing prevalence of STIs. According to the Household Budget Survey data in 2000, poverty has increased in Mongolia from 14.5% in 1990 to 36.0% in 1996. In 1997, the number of children living on the
streets was estimated at about 4,000 of which 60% were in Ulaanbaatar and 30% were girls.\textsuperscript{13}

The proportion of women who engage in sexual activities before marriage has been increasing and the age at first intercourse has decreased. In 1995, an adolescent reproductive health survey found that 26% of teenagers aged 17-18 years had had sexual intercourse. This figure rose to 35% in 1999.\textsuperscript{14} In Mongolian society, homosexuality and bisexuality are viewed as aberrant behaviors which are discouraged. The status of transsexuals and substance/drug users is therefore unclear.

\textbf{1.2.2 Health delivery system regarding STI in Mongolia}

The National Centre of Communicable Diseases (NCCD) in Ulaanbaatar is responsible for STIs diagnosis and case management. Patients presenting to a public system suspected of having STIs are referred to specialized venereology services at the centre or special STI cabinets of district general hospitals, which diagnose and treat the patients. In Mongolia, a syndromic approach, as advocated by WHO, is the alternative care when a laboratory test for a particular disease is inaccessible. The syndromic management of STI involves an immediate treatment of patients according to those pathogens which are most commonly associated with each clinical syndrome.

Maternal and congenital syphilis in Mongolia has recently re-emerged as a public health threat. Prior to 1990, the number of
maternal and congenital syphilis cases reported annually in Mongolia was very low. During this socialist period, the problem of venereal disease, as well as syphilis infection, seemed distant with respect to the given context of tight governmental and police controls related to prostitution and STIs, and the conservative values concerning sexuality. Infectious diseases were controlled by routine active detection of cases and their hospitalization until cure, compulsory notification and treatment of sexual partners. During the 1990s economic constraints forced STI services to rationalize their extensive diagnostic testing and screening activities. Patients themselves increasingly avoided the stigma and sanctions associated with public venereology clinics and found more convenient alternatives in the emerging official and unofficial private sectors. Nowadays, patients are charged for any STI blood testing and treatment even in the public system and specialized venereology clinic of the National Centre of Communicable Diseases. However, antenatal syphilis testing, as well as Human Immunodeficiency Virus (HIV) testing, is free of charge.

1.2.3 Syphilis during pregnancy in Ulaanbaatar

Ulaanbaatar is the capital city of Mongolia. According to the 2000 census, the population of the city was 691,000. The crude annual birth rate is 25.4 per 1,000 population. In six districts of Ulaanbaatar, approximately 11,000 live births occur annually and 99% of all deliveries occur in 3 maternity hospitals and the State
Research Centre on Maternal and Child Health (MCH Centre). The ANC coverage was 98%, according to the health statistics in 2007. Six district general hospitals, each covering 2-4 antenatal clinics and 15-20 family units, provide the ANC services. The MCH centre is responsible for ANC services for the whole country. There are approximately 700 ANC providers (around 3-6 OB-GYNs in each antenatal clinic and 5-10 family doctors in each family unit). According to the national policy, the Rapid Plasma Reagin (RPR) test is used as a screening test free of charge during pregnancy at the first antenatal visit and the third trimesters of gestation with confirmation of Treponema Pallidum Haemagglutination Assay (TPHA). Women testing positive, along with sexual partner(s), are treated with three weekly doses of 2.4 million units of benzathine penicillin.

Maternal syphilis at delivery has increased from no reported cases in 1988 to 21 cases in 1999, 26 cases in 2000 and 32 cases in 2006 in the MCH centre, while the number of deliveries has decreased. Congenital syphilis was recorded in 2 new case reports in 1995 and increased to 51 new cases in 2006 (Figure 1). This reflects the rapidly increasing number of active adult syphilis cases during past decades owing to social and behavioral changes, such as poverty, unemployment, internal and external migration and prostitution. Since the 1990s, the number of patients with active syphilis has been rising in Ulaanbaatar. In the city, the number of active syphilis cases almost doubled from 1995 to 2000,
reaching 730 cases in 1995, 1,647 cases in 2000 and 2,387 cases in 2005. Likewise, the incidence of active syphilis in Mongolia has increased from 18/100,000 in 1993 to 32/100,000 population in 1995. The data suggested a 1.5-3 fold higher rate of syphilis for people aged 15-24 years than for any other age group.

Figure 1. Reported congenital syphilis cases and birth rates in Mongolia
2. LITERATURE REVIEW

The contents were chosen based on a relevance of the scope of the study. This review includes 1) Cause and transmission of syphilis, 2) Maternal and congenital syphilis, 3) Congenital syphilis prevention, 4) Missed opportunity of antenatal syphilis screening, 5) Interventions for antenatal syphilis screening, and 6) Evaluation of the antenatal syphilis screening coverage and system in Ulaanbaatar, Mongolia.

2.1 Cause and transmission of syphilis

Syphilis is highly transmissible, bacterial disease caused by the spirochaete, Treponema pallidum (*T. pallidum*) and is almost always transmitted by sexual contact with an infected person. Syphilis is divided into four stages: primary, secondary, latent and tertiary. However, for purpose of treatment, syphilis is also divided into early syphilis (less than one year’s duration) and late syphilis (more than one year’s duration).16

**Primary stage:** This stage generally starts 21 days (range: 10–90 days) following infection. It is characterized by a painless genital ulcer (chancre) at the site of inoculation, which is often found on the genitalia, and less frequently on the rectum, tongue, lips or other parts of the body. Because the ulcer may be painless and may occur inside the body, the infected person might not notice it for a number of days. The bacterium spreads from the ulcer to the skin or mucous membranes of the genital area, mouth
or anus of an infected sexual partner in this period. The ulcer lasts 2–6 weeks with spontaneous resolution whether or not a person is treated.

**Secondary stage:** This stage lasts 2–6 weeks and the infected person develops a skin rash over the whole body, often with fever and muscle pain. Because active bacteria are present in the rash, condyloma and body fluids, the infected person may also spread the infection at this stage.

**Latent stage:** Secondary stage is followed by a latent stage of many years, during which there are no signs or symptoms. The latency is subdivided into early (1 year or less from the onset of the infection) and late (more than 1 year) latent stage. However, even the infected person seems normal in this phase; *T. pallidum* may circulate in the blood resulting in spread of the infection through the body of the infected person and is therefore considered infectious syphilis.

**Tertiary stage:** If the infected person is untreated, tertiary syphilis or neuro-syphilis occurs after many years or decades after the infection. In this stage the brain or spinal cord are usually affected and cardiovascular syphilis involving the aorta and heart, or late benign syphilis involving primarily the skin may occur. Nowadays, the occurrence of tertiary syphilis is less common due to widespread use of antibiotics.¹⁶

Mother to baby transmission can occur throughout early syphilis in the mother, which is called congenitally transmissible syphilis.
The mother can transmit the infection through the placenta to the fetus or during passage through the birth canal by contact of the newborn with a genital lesion.\textsuperscript{2,5,16,17}

\subsection*{2.2 Maternal and congenital syphilis}

The distribution of maternal syphilis varies widely by country and by time. An earlier review showed a wide range on the prevalence of seropositivity among pregnant women varying from 0.03\% in Scotland to 16.0\% in Brazil.\textsuperscript{18} In 2004, an unpublished report by Mullick et al.\textsuperscript{18} reviewed 215 published studies and identified the prevalence of syphilis in pregnant women varying from 0.09\% in Guatemala to 8.4\% in South Africa. However, syphilis prevalence in pregnancy is lower in developed countries ranging from 0.02\% in Europe to 4.5\% in parts of the United States.\textsuperscript{19} In contrast, in developing areas, such as Africa and Latin America, syphilis is still endemic, and the incidence is high.\textsuperscript{20-21} The high rates of seropositive syphilis have consistently been reported among pregnant women in Africa, ranging from 3\% to 18\%.\textsuperscript{20} Over the past few decades, there has been a dramatic increase in the incidence of syphilis in pregnant women in Eastern Europe and Central Asia in the aftermath of the sudden breakup of the socialist regime and rapid political and economic changes.\textsuperscript{22-24}

The vertical transmission of the syphilis infection results in spontaneous abortion, stillbirth, prematurity, low birth weight and the classical clinical syndrome of congenital syphilis, which itself carries a high risk of neonatal death.\textsuperscript{25-30} The risks of the
vertical transmission and fetal diseases are directly related to the stage of maternal syphilis during pregnancy. Women who are in the first two years of syphilis infection (primary, secondary and latent syphilis) have highest plasma concentration of *T. pallidum* and are most likely to transmit the infection to their fetuses. The timing of syphilis transmission (regarding the gestational age) is variable. Although pregnant women can transmit the infection to the fetus as early as nine weeks of gestation, most transmission occurs between 16 and 28 weeks of gestation. Thus, diagnosing and treating women in the first trimester is the preferred strategy for preventing intrauterine transmission of *T. pallidum*.

The risk of an infected untreated pregnant woman transmitting *T. pallidum* is high. Estimated morbidity and mortality among fetuses and neonates is estimated to range as high as 75% (Table 1).

**Table 1. Rates of adverse outcomes of untreated maternal syphilis**

<table>
<thead>
<tr>
<th>Pregnancy outcome</th>
<th>Harman&lt;sup&gt;29&lt;/sup&gt;</th>
<th>Igraham&lt;sup&gt;31&lt;/sup&gt;</th>
<th>Schultz&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Hira&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Watson-Jones&lt;sup&gt;30&lt;/sup&gt;</th>
<th>WHO&lt;sup&gt;37&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stillbirth/spontaneous abortion</td>
<td>17%</td>
<td>22%</td>
<td>30-40%</td>
<td>22%</td>
<td>25%</td>
<td>20%</td>
</tr>
</tbody>
</table>
Studies

<table>
<thead>
<tr>
<th>Pregnancy outcome</th>
<th>Harman\textsuperscript{29}</th>
<th>Igraham\textsuperscript{31}</th>
<th>Schultz\textsuperscript{a}</th>
<th>Hira\textsuperscript{b}</th>
<th>Watson-Jones\textsuperscript{c,d}</th>
<th>WHO\textsuperscript{37}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infected infant</td>
<td>21%</td>
<td>33%</td>
<td>10-20%</td>
<td>2%</td>
<td>No data</td>
<td>20%</td>
</tr>
<tr>
<td>Prematurity or low birth weight</td>
<td>No data</td>
<td>No data</td>
<td>No data</td>
<td>33%</td>
<td>25%</td>
<td>20%</td>
</tr>
<tr>
<td>Any adverse outcome</td>
<td>61%</td>
<td>67%</td>
<td>50-80%</td>
<td>57%</td>
<td>49%</td>
<td>75%</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Estimates from a mathematical model.

\textsuperscript{b} This study underestimated neonatal infection, since all babies of seropositive mothers were treated at birth.

\textsuperscript{c} This study was restricted to high-titer seropositive mothers (RPR 1:8), who accounted for 73% of all women with active syphilis.

Congenital syphilis is one of the main causes of perinatal death. A wide spectrum of severity of the in utero infection with \textit{T. pallidum} exists, and only severe cases are clinically apparent at birth. An infant with congenital syphilis may have signs such as hepatosplenomegaly, rash, condyloma lata, snuffles, jaundice, pseudo-paralysis, anemia, or edema (nephrotic syndrome and/or malnutrition). An older child may have stigmata (e.g.,
interstitial keratitis, nerve deafness, anterior bowing of shins, frontal bossing, mulberry molars, Hutchinson teeth, saddle nose, rhagades, or Clutton joints).6, 38-41

According to the Centre of Disease Control and Prevention, USA guideline6, diagnostic classifications of congenital syphilis are divided into two main cases: confirmed and compatible. If T. pallidum is identified by appropriate methods, such as darkfield microscopy in specimens from lesions, autopsy material, placenta, or umbilical cord, it is considered as a confirmed case. If one of the following criteria is met, it is considered as a compatible case:

i) a positive serological test for syphilis in a stillborn;

ii) a positive serological test for syphilis in an infant whose mother had syphilis during pregnancy and was not adequately treated, regardless of symptoms in the infant;

iii) a positive non-treponemal test of cerebrospinal fluid;

iv) a positive serological test for syphilis in an infant with any of the following signs: snuffles, condyloma lata, osteitis, periostitis or osteochondritis, ascites, skin and mucous membrane lesions, hepatitis, hepatomegaly, splenomegaly, nephrosis, nephritis, or hemolytic anemia;

v) fourfold or greater rise in titers or non-treponemal tests than mothers and a confirmed fluorescent treponemal
antibody absorption or microhemagglutination assay for antibody to *T. pallidum* over a 3-month period;

vi) a positive treponemal test or non-treponemal test that does not revert to negative in 6 months.

Although the rate of congenital syphilis is lower than the syphilis rate in pregnant women, it is closely parallel since neonates can get infected from their infected mothers. Although congenital syphilis is a preventable disease and there is a wide availability of health services, it continues to be one of the main causes of perinatal morbidity and mortality worldwide. WHO estimates that worldwide, 750,000 to 1,500,000 congenital syphilis cases occur annually, which is comparable to the incidence of perinatal HIV infection. According to the 2006 birth cohort of 133,201,704 live births, this number represents between 0.54% and 1.18% of the pregnancies carried to term annually worldwide.18,42,43

The congenital syphilis burden is greatest in certain African nations where 5% to 8% of pregnant women may be infected with syphilis.20,44,45 The burden is also high in Latin America21,46 and other regions around the world in which universal maternal syphilis screening and treatment of positive cases does not occur routinely.47,48 In contrast, relatively few maternal syphilis cases have resulted in congenital syphilis owing to access to adequate ANC and ASYS.49
2.3 Congenital syphilis prevention

The prevention of congenital syphilis can be achieved by primary preventive interventions which identify the women with a disease who are non-pregnant or who may become pregnant and treated before the disease affects.\textsuperscript{50} If an infected woman becomes pregnant, or a pregnant woman becomes infected, only ASYS can prevent the effects of maternal infection on fetus. Therefore, early detection and treatment of syphilis in pregnant women through universal antenatal screening is a standard measure for preventing congenital syphilis.\textsuperscript{5,6} The screening can be done once during pregnancy, ideally in the first trimester, but recently acquired syphilis infection requires between 10 and 45 days post-infection to be detectable by blood tests and so may be missed if the test is performed too soon after infection. Moreover, women who are negative in the first trimester, or even positive and receiving treatment, can acquire syphilis later in the pregnancy. For this reason, WHO has recommended screening for syphilis preferably before 16 weeks of gestation and again in the third trimester. If the woman was not tested during pregnancy, syphilis screening should be offered after delivery.\textsuperscript{7}

Pregnant women who are seropositive for syphilis should be treated as soon as they know the results of the test at their first antenatal visit and should be counseled extensively about the infection, impact on the pregnancy, the importance of adequate treatment and appropriate follow-up. The management of partners is
important to prevent not only the spread of the infection in the society, but also re-infection of the pregnant women.6,7

Simple and effective serological tests are available for the ASYS or diagnosis of maternal syphilis.51,52 Traditional laboratory diagnosis for ASYS is based on initial use of a non-treponemal screening test, such as Venereal Disease Research Laboratory test and the RPR test. However, these tests are not specific for T. pallidum. With non-treponemal tests, false positive reactions can occur because of pregnancy and some diseases such as, autoimmune disorders and viral infections. Therefore, a confirmatory treponemal test, such as TPHA and T. pallidum particle agglutination assay, are essential for positive results by the non-treponemal test.51,52 The non-treponemal test is inexpensive and sensitive (especially in early infection) and especially the RPR test can be done rather quickly. However, these tests have disadvantages, such as it cannot be done on whole blood, they require a microscope or rotator for processing, and misinterpretation is common by inexperienced laboratory staff because reading of the result is subjective.51,52

Treponemal tests are more specific than non-treponemal tests. However, they are expensive and require laboratory equipment and therefore usually reference laboratories perform the tests. Another disadvantage of the treponemal test is that it may give false-positive results, since treponemal antibodies persist for years. The treponemal test result will be positive in both cases
of individuals with active (untreated) syphilis and those who have previously been successfully treated for infection. Non-treponemal tests, on the other hand, can distinguish current or recent infections from old, treated infections. A combination of the two types of tests is therefore recommended.\(^{51,52}\)

Recently, simple, rapid treponemal tests, which use whole blood, require minimal training, no equipment or special storage conditions, have become widely available. These tests allow testing by health providers on the spot of primary health care services where laboratories are not available. The most rapid tests have sensitivities of 85–98% and specificities of 92–98% compared with standard treponemal assays. However, since the rapid tests are treponemal tests, similarly it cannot distinguish active infection from past treated infection.\(^{51,53}\)

Syphilis in pregnant women is easily cured using inexpensive treatment with penicillin and can prevent vertical transmission of the infection.\(^{2,6,7,54-56}\) Depending on the stage of infection, treatment may consist of as little as a single dose of penicillin, which is widely available in primary care settings. When provided early in pregnancy, treatment of the mother effectively prevents infection in the fetus.\(^2\) Even in women with syphilis of long duration, who themselves would benefit from three weekly doses of penicillin, a single dose of penicillin can prevent infection in the fetus.\(^{55}\) Birth outcomes for such women are similar to those for women without syphilis.\(^{30}\)
2.4 Cost-effectiveness of antenatal syphilis screening

Antenatal syphilis screening is cost-effective because the medical costs of managing a case of congenital syphilis are usually high compared to the costs of antenatal syphilis screening. Data in 2001 showed that the costs of averting one case of congenital syphilis was 86$–177$ USD (86$ USD at a prevalence of 6.5% and 177$ USD at a prevalence of 3.4%) in Table 2. The cost per Disability Adjusted Life Years (DALY) saved for congenital syphilis ranged from 3.97$ to 10.56$ USD. These costs are extremely low in comparison with other widely implemented interventions, making congenital syphilis prevention one of the most cost-effective interventions available.

Table 2. Cost-effectiveness of ASYS (in USD at 2001 prices)

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<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Cost per woman screened</td>
<td>0.93</td>
<td>1.96</td>
<td>1.24</td>
</tr>
<tr>
<td>Cost per woman treated</td>
<td>22.11</td>
<td>34.26</td>
<td>40.32</td>
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<tr>
<td>Cost per person treated</td>
<td>11.93</td>
<td>21.82</td>
<td>26.27</td>
</tr>
<tr>
<td>Type of cost</td>
<td>Hira\textsuperscript{17} et al, 1990</td>
<td>Jenniskens\textsuperscript{72} et al, 1995</td>
<td>Fonck\textsuperscript{69} et al, 2001</td>
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<td>-------------------------------------</td>
</tr>
<tr>
<td>Cost per congenital syphilis averted</td>
<td>158</td>
<td>86</td>
<td>177</td>
</tr>
<tr>
<td>Cost per DALY saved</td>
<td>3.97</td>
<td>9.84</td>
<td>9.57</td>
</tr>
</tbody>
</table>

2.5 Missed opportunity of antenatal syphilis screening

Nowadays, most countries have policies providing for universal screening for syphilis in pregnant women. However, for various reasons, in many developing countries the policies are not systematically implemented, resulting in failure of the syphilis seropositive couples to receive treatment during the course of the pregnancy\textsuperscript{3,9,11}. A recent review of ASYS in 13 countries revealed that the actual coverage varied widely. The proportions of pregnant women screened were 17\%-88\% in Bolivia, 64\%-79\% in Brazil, 51\%-81\% in Kenya, 43\% in Malawi, <5\%-40\% in Mozambique, 83\% in the United Republic of Tanzania and 32\%-83\% in the USA\textsuperscript{11}.

In both developed and developing countries, the lack of adequate ANC and ASYS are the major contributing factors for congenital syphilis\textsuperscript{57-66}. In developing countries, ANC coverage is only around 68\% and, among these, the average time of the first antenatal
visit is 20 to 24 weeks of gestation.\textsuperscript{60} However when ANC is accessed, the antenatal screening for syphilis is not usually provided to women who received ANC on time.\textsuperscript{21,23,61,62} A review of 22 sub-Saharan countries documented that antenatal syphilis screening was not provided to all pregnant women despite the fact that they came for ANC early enough and the main obstacles to syphilis screening were the problems of organizing services and costs.\textsuperscript{20} Three-quarters of the countries had a national policy of ASYS but it was not routinely implemented. Also, the review reported that fewer than 1 in 10 potentially infected women were adequately treated.\textsuperscript{20}

Furthermore, other studies have reported that when women’s blood was collected at community clinics and transported to reference laboratories and syphilis infected women were treated at a follow-up visit, the centralized ASYS service failed.\textsuperscript{17,66} The findings from a survey from Botswana indicated that most primary health care units do not have any laboratory facilities or do not perform any of the blood tests as recommended by WHO. Clinical staff at the antenatal clinic with available antibiotics used the syndromic approach for the syphilis treatment. The woman’s partner was notified but did not come to the facility to get treatment for syphilis.\textsuperscript{64} Another cross-sectional study from Bolivia showed that only a minority of women had documented screening for syphilis and treatment during pregnancy, although the majority of the participating mothers received ANC.\textsuperscript{21}
Once the syphilis infected pregnant women are diagnosed, early adequate treatment of the infection is important since the women often do not return to health centers for results.\textsuperscript{26} In Botswana, among 546 women coming for a repeat antenatal care visit, 71 (13\%) had not been screened for syphilis. Late testing for syphilis in pregnancy and delayed treatment were other identified obstacles to the effective prevention of congenital syphilis.\textsuperscript{64} Another case study in South Africa in 2002 found that health providers gave minimal information and counseling on syphilis and failed to stress the importance of treatment to syphilis-infected pregnant women and their partners.\textsuperscript{66}

\subsection*{2.6 Interventions for antenatal syphilis screening}

Since ANC services often provide the only opportunity to screen pregnant women for syphilis, the ASYS should be available and accessible at primary health care settings or antenatal clinics. Availability can be reached by decentralization of syphilis testing or onsite testing, which is effective and cost-effective.\textsuperscript{68-71} Accessibility can be addressed by free antenatal syphilis testing and treatment of detected cases and their sexual partners.\textsuperscript{20} Thus nowadays many efforts to address the availability and accessibility of the ASYS are considered for improving the antenatal syphilis screening. Among the published papers on the one-stop service the most relevant regarding these studies are reviewed.\textsuperscript{17,62,67,68,72-77}
Onsite antenatal syphilis screening (decentralized ASYS) with both non-treponemal RPR and treponemal rapid tests and immediate treatment of positive cases at the primary health care settings were the main objectives of the reviewed studies to show whether the intervention was appropriate or helpful to increase the antenatal syphilis testing rates, case detection and their treatment rates and to reduce the incidence of congenital syphilis or adverse pregnancy outcomes. The summaries of the 7 relevant studies on interventions are shown in Table 3. Out of the 7 studies reviewed, 3 were intervention studies 17, 67, 74, 2 were operational researches 72, 77, one was a descriptive study 75 and one was a cluster randomized trial 76.

The studies that used onsite RPR syphilis testing and treatment of positive cases in the antenatal clinics documented that the intervention was potential to increase the screening coverage and reduce maternal syphilis at delivery and the perinatal death rate due to syphilis. For example: An intervention study in Mozambique (2000) showed that perinatal mortality was significantly higher in the control group than in the intervention group, 3.4% versus 1.3% (p=0.030). The enrolled women in the intervention group had significantly more negative RPR results; 40.9% versus 24.4% (p<0.001) at delivery. 74 However, a cluster randomized trial in South Africa (2003) could not find any benefit of intervention over the control group in terms of the proportion of women with adequate treatment or perinatal loss due to maternal syphilis. The explanations of these results were 1) the onsite RPR test faced
many logistical and technical obstacles in performing and reading the tests, 2) insufficient power of the trial for perinatal death or adequate treatment outcomes, and 3) failure of treatment in the intervention group.\textsuperscript{76}

Bronzan et al, in 2007 compared 3 different screening strategies at rural clinics in South Africa.\textsuperscript{67} The study found that an onsite rapid treponemal test had high sensitivity (89.4\%) and specificity (92.9\%) compared to the onsite RPR test. The onsite rapid treponemal test resulted in the highest percentage of pregnant women correctly diagnosed and treated for syphilis (onsite rapid test-89.4\%, onsite RPR-63.9\% and offsite RPR/TPHA-60.8\%). The providers of the onsite RPR test faced many problems with performing the more technically demanding test. Also offsite RPR resulted in high rates of non-compliance at follow-up and lost opportunities for treatment. Because the rapid test cannot differentiate between past and current infections, one percent of women screened with the rapid treponemal test received penicillin unnecessarily but there were no adverse treatment outcomes presented.\textsuperscript{67}

The cost-effectiveness of the decentralized syphilis screening program with onsite rapid has been well introduced.\textsuperscript{70,71} A decision analysis to estimate the incremental cost-effectiveness of two onsite ASYS methods (onsite RPR and onsite rapid test) to avert congenital syphilis compared to the control (offsite RPR/TPHA) was used in South Africa. The analysis found that with antenatal
active syphilis prevalence of 6.3%, the incremental cost-effectiveness of onsite rapid test in averting congenital syphilis was estimated to be US$ 104, averting 82% of cases. The incremental cost-effectiveness of offsite RPR/TPHA was US$ 82 but would avert only 55% of congenital syphilis cases. Likewise, a study conducted in Bolivia and Mozambique was aimed to compare the costs of ASYS with onsite RPR and onsite rapid test. The study findings showed that in Mozambique, the average cost per woman screened was US$ 0.91 and US$ 1.05 for onsite RPR and onsite rapid test, respectively. In Bolivia, the average cost of screening was US$ 1.48 and US$ 1.91 for onsite RPR and onsite rapid test, respectively. These data suggested the cost of onsite rapid test is similar to that of onsite RPR testing.

In 1999, a study in Mozambique has shown that an intervention with onsite syphilis testing could increase screening coverage percentage over 90%. After adding a free treatment into the intervention, both the testing and treatment percentages were consistently over 90%. A recent study in Bolivia in 2007 reported that onsite antenatal syphilis testing with rapid treponemal test could reach universal screening and treatment (93.2%) in both rural and urban areas. In addition, they were also able to identify high rates of male partners and 76.9% of them presented for treatment. The success of the intervention was providing the solution of the disassociation between testing and administering treatment. However, the study had no control group and did not follow-up antenatal women after delivery.
<table>
<thead>
<tr>
<th>Studies</th>
<th>Objective</th>
<th>Arm</th>
<th>Sample</th>
<th>ASYS</th>
<th>Main findings</th>
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<tr>
<td></td>
<td>To compare adverse pregnancy outcomes (abortion, stillbirth, preterm, LBW, CS)</td>
<td>Intervention</td>
<td>806 antenatal women in 3 suburban clinics</td>
<td>-Onsite RPR</td>
<td>-Prompt treatment, Partner treatment</td>
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<td></td>
<td>Control</td>
<td>1274 antenatal women in 3 suburban clinics</td>
<td>-Offsite RPR</td>
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<td>(1)</td>
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<tr>
<td><strong>Intervention</strong> study</td>
<td><strong>Control</strong> study</td>
<td><strong>Intervention</strong> study</td>
<td><strong>Control</strong> study</td>
<td><strong>Intervention</strong> study</td>
<td><strong>Control</strong> study</td>
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<tr>
<td>Bique74, 2000, Mozambique</td>
<td>To compare adverse pregnancy outcomes (abortion, perinatal and neonatal death)</td>
<td>453 RPR+ women in 2 antenatal clinics</td>
<td>-Onsite RPR -Prompt treatment -Partner treatment</td>
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<td>Bronzan67, 2007, South Africa</td>
<td>To compare effectiveness (diagnosis &amp; treating) active syphilis overtreatment (resulting from previously treated infections)</td>
<td>476 RPR+ women in 2 antenatal clinics</td>
<td>-Offsite RPR</td>
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<td></td>
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<td>555 antenatal women in onsite RPR in 4 clinics and 695 antenatal women in onsite rapid test in 4 clinics</td>
<td>-Onsite RPR -Onsite rapid test -Prompt treatment -Partner treatment</td>
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<td></td>
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<td>1,456 antenatal women in off-site RPR 8 clinics</td>
<td>-Offsite treatment</td>
<td>-</td>
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<td>(1)</td>
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<td>Jenniskens, 1995</td>
<td>Kenya</td>
<td>Operational study</td>
<td>To establish and implement decentralized syphilis control program in pregnant women</td>
<td>13,131 antenatal women in 9 ANC clinics</td>
<td>-Onsite RPR</td>
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<tr>
<td>Control</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Garcia, 2007</td>
<td>Bolivia</td>
<td>Operational study</td>
<td>To introduce rapid treponemal test into ANC settings in Bolivia and evaluate its feasibility</td>
<td>11,618 antenatal women in 4 urban, 37 rural clinics</td>
<td>-Onsite rapid testing</td>
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<tr>
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<tr>
<td>Majoko75, 2003, Zimbabwe</td>
<td>Descriptive study</td>
<td>To determine coverage for ASYS in rural areas and evaluate the accuracy of onsite RPR tests performed by nurse-midwives</td>
<td>800 antenatal women in 23 rural clinics</td>
<td>Onsite RPR</td>
<td>85</td>
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<tr>
<td>Myer76, 2003, South Africa, Cluster randomized trial</td>
<td>Intervention</td>
<td>To compare impact of onsite RPR in treatment delays &amp; rate, perinatal mortality</td>
<td>5,201 antenatal women in 7 primary care level</td>
<td>Onsite RPR</td>
<td>91</td>
</tr>
<tr>
<td>(1)</td>
<td>(2)</td>
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<tr>
<td>2,417 antenatal women in 7 primary care levels</td>
<td>-Offsite RPR</td>
<td>98</td>
<td>-</td>
<td>7**</td>
<td>69**</td>
</tr>
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</table>

"**" significant, "***" non-significant, "-" not reported, "NA" not applicable
2.7 Evaluation of the antenatal syphilis screening coverage and system in Ulaanbaatar, Mongolia

The following details show how routine syphilis testing of pregnant women in Mongolia is managed. Family doctors at family units send pregnant women coming for their first antenatal visits to OB-GYNs at antenatal clinics. Then the OB-GYNs send the women to laboratories at district general hospitals or the venereology clinic of National Center of Communicable Diseases for syphilis testing. In the district general hospitals, that do not perform the syphilis test, only women’s blood will be drawn. The blood samples are transported to the venereology clinic’s laboratory to have RPR tests done. The women have to return 1-7 days later to the district general hospital or the venereology clinic to obtain their results, and then return with their results to the OB-GYNs. Women with positive results are then referred to a venereologist at the district general hospitals or venereology clinic for confirmation, appropriate treatment, contact tracing and follow-up of serological controls, as shown in Figure 2. During and after the treatment of syphilis, the OB-GYNs will continue the antenatal services instead of the family doctors, who take care of the pregnant women with negative results until 32 weeks of gestation.
Figure 2. Diagram of the system of ANC with ASYS in Ulaanbaatar

National Centre of Communicable Diseases
- RPR test
- Confirmatory TPHA
- Case management
- Follow-up: control

District general hospitals that perform syphilis test
- RPR test
- Case management
- Follow-up control

District general hospital that do not perform syphilis test
- Blood drawn
- Case management
- Follow-up control

OB-GYNs in ANC clinics
- ANC for complicated pregnancy
- Normal pregnancy after 32 weeks of gestation

Family doctors in family units
ANC for normal pregnancy after OB-GYNs’ conclusion until 32 weeks of gestation
According to the national policy, congenital syphilis is reported when neonates are symptomatic and have persistent serologic abnormalities. Congenital syphilis is usually diagnosed by a neonatologist with a venereologist’s confirmation. The treatment of congenital syphilis is benzathine penicillin G 50,000 units/kg of body weight intramuscularly per day for 10 days. Asymptomatic neonates as well as stillborns of inadequately treated or untreated mothers are usually not reported although asymptomatic neonates should receive benzathine penicillin 50,000 units/kg intramuscularly in a single prophylactic dose, according to the national guideline.

Although syphilis screening for pregnant women is usually provided free of charge in ANC services, only a fraction are actually screened in Mongolia. In 2007, the ASYS coverage was 60.9% nationally; however, this rate is less than 50% among those who live in rural regions or among nomadic women. Even in Ulaanbaatar, the capital city, although the ANC coverage is relatively high (98%) and syphilis screening for pregnant women is usually provided free of charge in antenatal services, ASYS is not routine.

In 2004, a cross-sectional study was conducted to assess the antenatal syphilis control program in Mongolia. According to the study findings, among 3,519 antenatal records, the coverage of syphilis screening was only 77.7%. Of 2,735 screened women, 54
(2.0%) had positive serological results and subsequently received treatment. Four women who arrived late for ANC delivered infants with congenital syphilis. The main reasons leading to failure of universal ASYS were either the burden with access of ASYS or ignorance of both mothers and doctors. Being unscreened was significantly associated with late ANC (odds ratio OR=2.6), lack of knowledge (OR=5.5), history of previous STI (OR=3.7), and living far from screening services (OR=4.9). In Ulaanbaatar, the concentration of ASYS service in the few laboratory facilities exclusively results in inconvenience to pregnant women, long travels and discourages them from actively participating in the prevention of congenital syphilis policy.

3. RATIONALE

The concept of ASYS is simple and well-known globally. Nowadays, the offsite RPR/TPHA strategy is used for ASYS in many settings. However, it causes client return visit problems in both developed and developing countries. To address this problem, onsite RPR has been practiced. However, the onsite RPR is relatively complex because the RPR test requires basic laboratory equipment and experienced laboratory staff to perform the test and interpret results. In addition, the onsite RPR showed no improvement in the syphilis screening in pregnancy and the perinatal loss rate. Some logistical and technical problems, such as electricity shortage in the conduct of the onsite RPR test, were also reported. Therefore, an alternative, more effective approach is needed to
prevent congenital syphilis. It was evident that rapid treponemal test could improve the screening and treatment coverage. However, the studies were non-randomized studies and had no control group. Therefore, a well-designed randomized controlled trial is needed.

In Mongolia, congenital syphilis is a reflection of the lack of a screening system in the country where almost all pregnant women receive antenatal care services at least once during their pregnancy. Despite the existence of a national policy regarding antenatal syphilis control and free RPR syphilis testing for pregnant women in the country, the coverage of ASYS is relatively low.

Current regulations regarding ASYS in Mongolia stipulate that only a few specialized laboratories for STIs are allowed to perform the syphilis screening tests and only venereologists are authorized to treat syphilis-infected pregnant women and undertake contact tracing. Therefore, most antenatal clinics rely on syphilis testing using RPR with TPHA confirmation at referral laboratories. This requires antenatal clients to make extra return visits, which may lead to long distance travel in order to be tested for syphilis or to obtain their test results, thus missing the opportunity for ASYS. The complexity of the existing ASYS service is one of the obstacles to universal coverage of ASYS and maybe to prevention of congenital syphilis. In addition, it is questionable whether this current system of screening is still
practical in the presence of which the risks of infected syphilis in pregnant women have been rising.

To overcome the need of reducing the missed opportunities for ASYS, more efficient and client-friendly services, such as a one-stop antenatal syphilis screening service, are needed. The one-stop service, which includes standard ANC service, onsite treponemal rapid syphilis test, prompt case management and counseling (given in the same visit and setting), could provide a solution of the disassociation between ANC and ASYS services and testing and administering treatment. In Ulaanbaatar, almost all pregnant women obtain ANC service at least once during their pregnancy, thus pregnant women have a chance to receive ASYS at the first day of ANC booking.

Syphilis testing by rapid treponemal test and case management are not complicated.\textsuperscript{6,7,53} Rapid test is a simple test, which can be performed without any equipment by any trained and motivated general practitioner or nurse.\textsuperscript{53} Thus, there are anticipated efficiencies of the one-stop service because of existing sufficient number of health personnel and facilities in every antenatal clinic. In addition, since the treatment method of syphilis is a standard routine\textsuperscript{6,7,54}, the question might be raised of why the venereologists should do it exclusively. Since the one-stop service is a new policy which needs efforts of ANC providers, the effectiveness of the one-stop service should be evaluated by a cluster randomized trial. Furthermore, feasibility of the one-stop
service is needed to ensure whether the one-stop service is accepted by the women and providers.

4. RESEARCH QUESTIONS

1. Is the one-stop service on antenatal syphilis screening in Ulaanbaatar feasible and accepted by the antenatal women and providers?

2. Is the one-stop service more effective than the conventional service on antenatal syphilis screening in Ulaanbaatar?

5. OBJECTIVES

5.1 General objectives

The overall objectives are to test whether one-stop service could better prevent congenital syphilis than the conventional antenatal screening service in Ulaanbaatar, Mongolia.
5.2 Specific objectives

The specific objectives are:

1. To assess the feasibility on satisfaction and practicability of one-stop service on antenatal syphilis screening in Ulaanbaatar in terms of women’s and providers’ perspectives.

2. To compare the effectiveness of one-stop versus conventional service on antenatal syphilis screening in Ulaanbaatar.
CHAPTER 2

METHODS

6. CONCEPTUAL FRAMEWORK

Congenital syphilis prevention consists of main four interlinked components: (i) Routine syphilis testing on all women receiving ANC, (ii) Early detection of syphilis infected antenatal women, (iii) Adequate treatment of the detected cases and (iv) Prevention of re-infection of the treated antenatal women. The routine syphilis testing of all pregnant women can detect syphilis infected antenatal women at their first antenatal visits and the third trimester of gestation. The detected cases should be treated as soon as they are diagnosed and re-infection should be prevented before delivery.

An onsite rapid treponemal test may achieve a universal syphilis screening thus may detect more syphilis cases. Because of the immediate access to the test results, infected women may be able to receive prompt treatment while they are still in the antenatal clinics. The prompt treatments of cases have important impacts on adequate and complete treatment before delivery and effective partner treatment will prevent re-infection of the women.
Counseling is a supportive procedure which helps on encouraging the pregnant women and their partners to accept the tests and treatment. To achieve the congenital syphilis prevention goal, one-stop service with the onsite syphilis testing by rapid treponemal tests, immediate treatment of positive cases and their sexual partners and active counseling at the antenatal clinics is the proposed new method.

The one-stop service is a new policy which needs the effort of ANC providers. Thus to ensure whether or not the one-stop service works well and is needed to be modified for appropriateness, the feasibility is assessed and evaluated through the feasibility study (Part I) in the one-month run-in period of the study. The feasibility is measured by antenatal women and providers’ satisfaction and opinions on practicability of the service using described study. To test the effectiveness of the new approach or the one-stop service on ASYS, a cluster randomized trial was conducted (Part II).
Congenital syphilis prevention

Adequate treatment of detected women

Prevention of reinfection of women

Feasibility of one-stop service (Part I)

Effectiveness of one-stop service (Part II)

Figure 3. Diagram of conceptual framework
7. METHODOLOGY PART I: Feasibility study

To serve the first objective: To assess the feasibility on satisfaction and practicability of one-stop service on antenatal syphilis screening in Ulaanbaatar in terms of women's and providers’ perspectives.

7.1 Study design

A cross-sectional survey was conducted in the one-month run-in period of the main cluster randomized controlled trial. A combination of quantitative (for antenatal women) and qualitative (for providers) approaches was used.

7.2 Study setting

Two of the seven antenatal clinics from the intervention group were randomly selected to be the study setting for feasibility. Only two were chosen due to the limited number of rapid syphilis tests.

7.3 Study samples

1. All antenatal women requiring the one-stop service on ASYS at the first antenatal visit and the third trimester of gestation during the run-in period from mid July to mid August 2007 in the two clinics.
2. All available ANC providers who managed women receiving the one-stop service on ASYS from mid July 2007 to mid August 2007.

7.4 Sample size and sampling method

For clinic sampling, the 7 intervention clinics were divided into two groups depending on their geographical locations (downtown or remote), and then one clinic from each group was randomly selected.

For women, the sample size was calculated based on an estimated 80% of feasibility and satisfaction of one-stop services with a precision of 5% using a survey formula in the R software. A total of 246 eligible consenting women (123 women in each clinic) were recruited into the study.

For providers, all available 13 ANC providers at the two selected antenatal clinics were interviewed.

7.5 Study variables

For women

Outcome variable: women’s overall satisfaction score

Independent variables: age, education, marital status, current employment status, residency, history of previous pregnancy, history of previous induced abortion, adverse pregnancy outcome, gestational age at the first antenatal visit and history of STIs.
For providers

**Outcome variable:** Providers' opinions on one-stop service, challenges/problems experienced by the providers and acceptance in offering one-stop service.

**Independent variables:** age, profession, position, year of service and ANC experiences.

### 7.6 Definitions and measurement of outcomes

#### For antenatal women

1. Women’s opinions and satisfaction was assessed using a 4-point scale rating ("1" for “strong disagreement” and “4” for “strong agreement” in positive aspects and reverse scoring as “1” for “strong agreement” and “4” for “strong disagreement” in negative aspects on testing, counseling, treatment and waiting time. The overall satisfaction score was calculated by averaging the score of 11 opinion questions.

2. Providers’ opinions on one-stop service, challenges/problems which needed to be reorganized and the acceptance of providers in offering the services were measured.

### 7.7 Data collection

1. All ANC providers were trained in the workshop on the interventions.
2. Necessary supplies were provided to the clinics.

3. All pregnant women receiving the first antenatal visit and in the third trimester were approached and invited to participate in the study then signed the consent form (Appendix 1).

4. After eligible pregnant women had experienced the one-stop services, the women were interviewed using a self-administered questionnaire (Appendix 2.1).

5. At the same time, the providers were invited to participate in the study. They were then interviewed using the in-depth interview guideline by the principal investigator. Each interview took about one hour to complete.

7.8 Data collection instruments

1. Self-administered questionnaire (Appendix 2.1)

2. Interview guideline (Appendix 2.2)

3. Tape recorder

4. Note writing

5. Code mapping
7.9 Data management and analysis

Data were coded and entered twice to verify accuracy of the entry using Epidata (The EpiData Association Odense, Denmark) and analyzed using R software (The R foundation for Statistical Computing, Vienna, Austria). Descriptive statistics were used for demographic characteristics and satisfaction scores. To assess the associations between clients’ characteristics and overall satisfaction scores, independent sample t-test and one-way analysis of variance were used. Multiple linear regression models with stepwise method were used to ascertain which factors were independently associated with the overall satisfaction score. Data from in-depth interview were audio recorded and transcribed verbatim and the contents analyzed by code mapping and described qualitatively in the text.
8. METHODOLOGY PART II: Cluster randomized trial

To serve the second objective: to compare the effectiveness of one-stop versus conventional service on antenatal syphilis screening in Ulaanbaatar

8.1 Study design

A cluster randomized trial was conducted and since the intervention was based on practices, rather than individuals, it was considered impossible to randomize individual patients into two screening options in the same clinic.

8.2 Study sites

Fourteen antenatal clinics in six districts of Ulaanbaatar served as the study sites. Figure 4 shows locations of the 14 antenatal clinics and the National Center of Communicable Diseases in Ulaanbaatar. The identification of the intervention and control groups is not shown and kept anonymously due to ethical issues.
Figure 4. Map of 6 districts of Ulaanbaatar and study sites
8.3 Study population

**First level:** All antenatal clinics which provide ANC services in six districts of Ulaanbaatar.

**Second level:** All antenatal women requiring ASYS services.

8.4 Study samples

**First level:** All antenatal clinics which had sufficient numbers of antenatal visits (at least five new antenatal visits a day) between August 2007 and September 2008 in the six study districts of Ulaanbaatar.

**Second level:** All pregnant women attending one of the antenatal clinics above who were eligible for the study. Pre-defined exclusion criteria were: women with multiple pregnancy, women known to be unable to return for the scheduled antenatal visit during the study period, living outside Ulaanbaatar, unwilling to give informed consent and absence of a willing guardian for under-aged, illiterate, women and women unable to make a decision, such as those with a mental illness.

8.5 Sample size and sampling method

**First level:** Of the 14 selected antenatal clinics, seven were randomly assigned into the intervention group, and seven were assigned to the conventional service group (Figure 5). The
allocation into intervention and control arms was achieved by computer-generated randomization. The MCH Centre was excluded from the sampling because the centre is responsible for the whole country, while two of the 16 antenatal clinics were also excluded due to a very small attendance.

Figure 5. Study overview and sampling
**Second level:** For the cluster randomized trial, the required sample size, \( n \), was calculated using the following formula:

\[
\frac{{\{Z_{\alpha/2}\sqrt{2P(1-P)} + Z_{1-\beta}\sqrt{1(1-P_1) + P2(1-P_2)}\}^2}}{(P_1 - P_2)^2}
\]

\( n \) Number of pregnant women attending ANC service per group

\( Z_{\alpha/2} \) Type I error of 5\%

\( Z_{1-\beta} \) Type II error of 20\%

\( P_1 \) Estimated prevalence of the congenital syphilis in the control group (0.006)

\( P_2 \) Anticipated prevalence of congenital syphilis in the intervention group (0.001)

\( P \) \((P_1 + P_2)/2\)

Most recently, 51 cases of congenital syphilis were diagnosed in 2006 in Ulaanbaatar.\(^{12}\) Without an intervention or with conventional screening, the incidence of congenital syphilis was estimated at 6/1,000 and the aim of the intervention was to reduce this number to below 1/1,000. Using a significance level of 5\%, a power of 80\%,
and assuming that the intra-class correlation is 0.001, as shown in a previous study, the required sample was calculated to be 3,183 per group (2-sided test) or 455 subjects per clinic.

After adjusting for an expected loss to follow-up rate of 20%, 550 subjects per clinic, (a total of 3,850 subjects) were required and recruited in each group.

8.6 Variables

8.6.1 Primary outcome variables

1. Coverage of ASYS at the first antenatal visit and the third trimester of gestation

2. Congenital syphilis cases

8.6.2 Secondary outcome variables

1. Syphilis cases

2. Adequate treatment

3. Partner treatment

8.6.3 Independent variables

Data on women’s age, education level, marital status, current employment status, residency, history of previous pregnancy, history of previous induced abortion, adverse pregnancy outcome,
gestational age at the first antenatal visit and history of STIs were collected.

8.7 Definitions and measurements

8.7.1 Primary outcome variables

1. Coverage of ASYS at the first antenatal visit and the third trimester of gestation – Number of antenatal women being tested coverage of syphilis testing at the first antenatal visit and the third trimester per number of women enrolled.

2. Congenital syphilis cases – Number of congenital syphilis cases per number of women tested at delivery.

Adopting WHO’s and CDC’s criteria, congenital syphilis was defined if any the following existed: (i) neonate manifesting classic signs of congenital syphilis, such as hepatosplenomegaly, rash, condyloma lata and snuffles; (ii) neonate whose mothers have a syphilitic lesion at delivery; (iii) neonate born to mother with positive RPR and TPHA who are untreated or inadequately treated at delivery (if mothers received non-penicillin therapy, or penicillin administered <30 days before the delivery), regardless of signs in the infant; (iv) neonate born to mother with positive RPR and TPHA whose serological response to penicillin was not documented or was equivocal (the definition of appropriate response for primary or secondary syphilis is a fourfold decline in non-treponemal titers by 3 months and for early latent syphilis
is a fourfold decline in non-treponemal titers by 6 months); (v) neonate with RPR titers fourfold or greater than the mother’s titer; and (vi) Treponemas seen in autopsy material by silver stain or darkfield in stillborns born to mother with positive RPR and TPHA.

### 8.7.2 Secondary outcome variables

1. Syphilis cases – Number of antenatal women with positive RPR and TPHA results per number of women tested for syphilis.

2. Adequate treatment of cases – Number of women with positive RPR and TPHA results who completing three doses of benzathine penicillin before delivery per number of women with positive RPR and TPHA results.

3. Partner treatment – Number of treated partner of syphilis cases per number of women with positive RPR and TPHA results.

### 8.7.3 Syphilis case reporting

In the study, syphilis cases are defined as the women attending for ANC who had positive rapid treponemal tests confirmed by RPR and TPHA in the intervention group or who had positive RPR confirmed by TPHA in the control group. At the second syphilis testing (at the third trimester) and third syphilis testing (after delivery), only new syphilis cases were reported.
8.8 Data collection process

8.8.1 Preparatory phase

ANC providers in both intervention and control clinics received training but the contents provided were different. Two separate workshops for the intervention and control groups were organized.

In the intervention clinics, the first two-day workshop was held for OB-GYNs and nurses. The main agendas included highlighting the importance of decentralizing the ASYS service, logistics, the organization of the one-stop service and case reporting. The second two-day workshop was also held for OB-GYNs and covered the specific knowledge on maternal and congenital syphilis, case detection and management, counseling and contact tracing. A manual of the test reading was distributed to all relevant providers in order to assure a correct and reliable interpretation of the rapid syphilis test results. The intervention clinics were supplied with the necessary materials, such as lancets, rapid syphilis tests and benzathine penicillin injectable sets.

In the control clinics, ANC providers (nurses and OB-GYNs) in the control clinics participated in a two-day training workshop on the project overview, logistics of the project and case reporting. The OB-GYNs received refresher training on the same topics as the intervention group to reduce the bias of training effect on our main outcomes. As with the intervention group, treatment of syphilis cases and their partners was given free of charge.
Benzathine penicillin was supplied for treatment but not facilities for serological tests.

8.8.2 Implementation phase

In both intervention and control clinics, all pregnant women presenting to the antenatal clinics had their eligibility for entering the study checked by the nurses. All eligible subjects were then approached, given information about the study and asked to join. Subjects who agreed were asked to give informed consent to participate in the study (Appendix 1). The syphilis tests were done twice during pregnancy at the first antenatal visit and the third trimester of gestation. The third syphilis testing was provided immediately after delivery among the women who had been seronegative during ANC. Regardless of the group randomized to, all syphilis cases received three doses of benzathine penicillin on a weekly basis. Neonates of seropositive women were then examined and positive cases given and injection of benzathine penicillin following the WHO guideline.

ASYS in the intervention clinics

The one-stop service included the following elements (i) onsite screening for syphilis using rapid treponemal syphilis tests at the first antenatal visit and the third trimester of gestation; (ii) immediate onsite treatment for seropositive women and their sexual partners with benzathine penicillin; and (iii) pre- and
post-test counseling (Figure 6). Pre-test counseling and interviews were carried out in a private counseling room.

After the interview, 20 µl of whole blood from all consenting new attendees was collected by finger prick. The onsite rapid test was assayed with SD Bioline Syphilis 3.0 (Standard Diagnostics Inc., Kyunggi-do, Korea) according to the manufacturer’s specifications. The presence of only one band within the result window indicates a negative result, in contrast, the presence of two colour bands ("T" and "C") within the result window, no matter which band appears first, indicates a positive result for TP antibodies. If the purple colour band is not visible within the result window after performing the test, the result is considered invalid.

The results were available in 10-15 minutes. Women testing negative on the rapid assays were provided with post-test counseling by ANC providers and invited for a second test during the third trimester of pregnancy. Women testing positive by the rapid test had their venous blood further collected and sent to the reference laboratory. Women without a history of drug allergy were initially treated free of charge with initial dose of benzathine penicillin G 2.4 million units intramuscular. The confirmation test at the reference laboratory was carried out using RPR titer (Omega Immutrep-RPR, Omega Diagnostics, Alva, United Kingdom) and the positive samples were further tested TPHA (Immutrep TPHA, Omega Diagnostics, Alva, United Kingdom). Women who tested positive on both RPR and TPHA tests were subsequently
given two doses of benzathine penicillin at weekly intervals. The contact tracing was based on a voluntary agreement between the woman and the OB-GYN. The husbands/sexual partners were invited to come at their earliest convenience to the clinics for treatment free of charge. For quality control reasons, 10% of the sera negative samples and all positive sera were sent to the reference laboratory where the test was redone without awareness of the initial test results.
First ANC attendee

History, examination and counselling

RT+

RT-

Repeat RT at 3rd trimester

Benzathine penicillin 2.4m IM

Take blood for RPR and TPHA

RPR+, TPHA+

RPR titer control: three times on monthly intervals decreased 4 folds

RPR titer decreased 4 folds

Yes

No

One dose of benzathine penicillin

RT- Repeat test at delivery

RT+

RPR-, TPHA-

RT- Repeat test at delivery

RT+

Figure 6. Diagram of the one-stop screening service
**ASYS in the control clinics**

After being admitted to the antenatal clinic, a pregnant woman could visit any district general hospital or the venereology clinic for free initial testing with RPR and, where necessary, TPHA confirmation test. The test result is normally collected by the woman and brought to the ANC service. Women testing positive for syphilis were sent to a venereologist for appropriate case management and follow-up control, including contact tracing and counseling. Routine treatment is three weekly doses (2.4 million international unit) of benzathine penicillin and this is given free of charge.

After intervention and control groups were assigned, the services in both groups were compared as shown in Table 4.

**Table 4. Comparison of ANC/ASYS service between control and intervention groups**

<table>
<thead>
<tr>
<th>Picture of ANC/ASYS service</th>
<th>Control groups</th>
<th>Intervention groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANC service provider</strong></td>
<td>OB-GYNs of antenatal clinics</td>
<td>OB-GYNs of antenatal clinics</td>
</tr>
<tr>
<td><strong>ANC visits examination</strong></td>
<td>According to norm</td>
<td>According to norm</td>
</tr>
<tr>
<td><strong>Syphilis screening tests</strong></td>
<td>Offsite RPR with TPHA confirmation (free)</td>
<td>Onsite rapid treponemal test with RPR and TPHA confirmation (free)</td>
</tr>
<tr>
<td><strong>Place performed</strong></td>
<td>District general hospitals and or venereology clinic</td>
<td>Antenatal clinics</td>
</tr>
<tr>
<td>---------------------</td>
<td>------------------------------------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td><strong>Laboratory staff</strong></td>
<td>Specialized lab/staff staff</td>
<td>Nurses of antenatal clinic</td>
</tr>
<tr>
<td><strong>Time test performed</strong></td>
<td>1&lt;sup&gt;st&lt;/sup&gt; and 3&lt;sup&gt;rd&lt;/sup&gt; trimesters of gestation</td>
<td>-1&lt;sup&gt;st&lt;/sup&gt; visit clients -Repeat test at 3&lt;sup&gt;rd&lt;/sup&gt; trimester if patient tested negative</td>
</tr>
<tr>
<td><strong>Case treatment</strong></td>
<td>Venereologists</td>
<td>OB-GYNs of antenatal clinics</td>
</tr>
<tr>
<td><strong>Payment for treatment</strong></td>
<td>Free of charge</td>
<td>Free of charge</td>
</tr>
<tr>
<td><strong>Contact tracing &amp; Partner treatment</strong></td>
<td>Venereologists</td>
<td>OB-GYNs</td>
</tr>
<tr>
<td><strong>Counseling</strong></td>
<td>Venereologists</td>
<td>OB-GYNs or nurses</td>
</tr>
<tr>
<td><strong>RPR testing and case management at delivery</strong></td>
<td>Same procedures as intervention clinics</td>
<td>-Repeat test at delivery if patient always tested negative to detect any late infection. -Free treatment for seropositives and neonates -Free partner treatment</td>
</tr>
</tbody>
</table>
8.9 Data collection instruments

1. Admission questionnaire for women (Appendix 3.1)
2. Admission form (Appendix 3.2)
3. Follow-up 1 form at the third trimester (Appendix 3.3)
4. Follow-up 2 form at delivery (Appendix 3.4)

8.10 Data collection techniques

The process of data collection is illustrated in Figure 7. The data collection consisted of 3 visits: the first antenatal visit, the third trimester of gestation and at delivery in both arms.

8.10.1 At the first antenatal visit

Medical records: Antenatal women’s pregnancy and STI related variables were extracted from medical records, including previous pregnancy and induced abortion, adverse pregnancy outcomes, gestational age at the first antenatal visit and previous history of STIs.

Questionnaire: An admission questionnaire taking 10 minutes to complete was given to the women to obtain information, such as age, marital status, residence, education level, current employment status and number of sexual partners (no, sigle, >single).
Physical examination: Apart from the normal routine ANC examination, a special examination was performed by an OB-GYN to detect syphilitic lesions.

First blood testing for syphilis: In the intervention clinics, 20 µl of whole blood was collected from all women by finger prick. The onsite rapid test was assayed with SD Bioline Syphilis 3.0 (Standard Diagnostics Inc., Kyunggi-do, Korea) according to the manufacturer’s specifications (Appendix 4). The results were available in 5-20 minutes. Women testing positive by the rapid tests had their venous blood further collected and sent to the reference laboratory. The confirmation test at the reference laboratory was carried out using RPR titer (Omega Immutrep-RPR, Omega Diagnostics, Alva, United Kingdom) and the positive samples were further tested TPHA (Immutrep TPHA, Omega Diagnostics, Alva, United Kingdom).

In the control clinics, RPR test with TPHA confirmation was done by specialized laboratory technicians either at district general hospitals or the venereology clinic of National Center of Communicable Diseases. A 10 ml venous blood sample was collected into a plain vacutainer and centrifuged. A standard RPR test (Omega Diagnostics, Alva, United Kingdom) and TPHA assay (Immutrep TPHA, Omega Diagnostics, Alva, United Kingdom) was performed on all RPR positive sera.
Admission form: All data on the syphilis test results and cases and treatment of their sexual partner at the first antenatal visit were noted on the admission form by the nurses.

8.10.2 Follow-up visit 1 at the third trimester of gestation

The same procedures as the first antenatal visit were conducted at the first follow-up visit (at the third trimester of gestation). In the intervention clinics, all pregnant women who were seronegative at the first antenatal visit were retested by the rapid treponemal test at the third trimester of gestation. Those women, who were seropositive at the first antenatal visit, were retested by only RPR to detect possible re-infection. In the control clinics, offsite RPR with TPHA confirmation was repeated. All information regarding the first follow-up visit were documented in the Follow-up 1 form by nurses in both control and intervention clinics.

8.10.3 Follow-up visit 2 at delivery

A third syphilis test (with TPHA confirmation of positives) was repeated in all subjects admitted for delivery and RPR and TPHA positives were treated free of charge. Midwives/nurses at all three maternity hospitals and the MCH centre collected blood specimens from mothers and the blood samples were sent to the reference laboratory for RPR with TPHA confirmation. Results were known after one day after testing. The nurses filled the Follow-up 2 form in both groups.
**Infant management:** Every baby that was born to a woman who tested positive for syphilis was physically examined by a neonatologist immediately after delivery to detect signs of congenital syphilis. Mothers and infants with signs of syphilitic lesions would be examined by specialized laboratory staff using a darkfield microscope to detect *T. pallidum*. The treatment and follow-up of infants born to mothers with positive RPR tests will follow WHO guidelines (Appendix 5).

**Partner management:** The plan for contact tracing and notification of partner was followed according to current WHO guidelines as described above.
Figure 7. Data collection

At the first antenatal visit
- Medical records
- Questionnaire
- Physical examination
- 1st blood test
  - if seroreactive: Case management
  - Admission form

At the third trimester
- Medical records
- Physical examination
- 2nd blood test
  - if seroreactive: Case management
  - Follow-up 1 form

At delivery
- Medical records
- Physical examination
- 3rd blood test
  - If seropositive: Case management
  - Infant management
  - Follow-up 2 form
8.11 Quality assurance of data and syphilis test

In order to assure a correct and reliable reading of the test, a manual was distributed to ensure standardization of readings to all the relevant health personnel of the antenatal clinics. During the run-in period, every week the trainers from the reference laboratory visited each antenatal clinic to supervise the performing of rapid test and ensure its quality. During the data collection period, the supervision was done every month.

All positive sera and 10% random sample of negative sera were sent to the reference laboratory for quality control. The sera received from the intervention clinics were retested using rapid treponemal test and qualitative and quantitative RPR. TPHA assay was performed on all RPR positive sera and also on all negative sera. Laboratory technicians were not aware of the RPR results of the intervention clinics.

8.12 Data management and analysis

Data were coded and entered twice to verify accuracy of the entry using Epidata (The EpiData Association Odense, Denmark) and analyzed using R software (The R foundation for Statistical Computing, Vienna, Austria).

The analysis was undertaken on an intention to treat basis. Differences in the proportions of syphilis testing at the first antenatal visit and at the third trimester of gestation, number of
detected syphilis cases during pregnancy, adequate treatment, treated partners and congenital syphilis were compared. Since the main outcomes were nested within clinics, Rao and Scott’s chi-square test in “survey” package was used in the univariate analysis. For multivariate analysis, a multilevel analysis was carried out having individual women at the first (lower level) and the clinic at the second level (higher) using the “lme4” package. Women’s characteristics were independent, explanatory variables.

9. ETHICAL CONSIDERATIONS

The study protocol was reviewed and approved by the Institutional Ethics Committee of Mongolia, the corresponding health authorities where the trial was implemented, the Scientific and Ethical Review Croup of the Special Programme of Research, Development and Research Training in Human Reproduction and Ethics Review Committee, WHO, the Institute Ethics Committee of Faculty of Medicine, Prince of Songkla University, Thailand.
CHAPTER 3

RESULTS

The findings in this study were divided into three main parts: the feasibility study, the cluster randomized controlled trial and subsidiary results.

1. Feasibility of the one-stop service

1.1 Syphilis test results and case management

A total of 246 women were eligible for ASYS services at their first antenatal visit or at the third trimester of gestation at two antenatal clinics during the run-in period. Table 5 shows background characteristics of the participating women. The age of the women ranged from 17 to 44 years (mean ± sd 27.3 ± 5.9).

All antenatal women accepted the one-stop service and tested for syphilis by rapid test. All women received their results and counseling from ANC providers. Most (242/246) of the women tested negative with the rapid test. The four positive cases all accepted their test results with counseling and received single dose of benzathine penicillin.
The sera of these four women were retested by RPR and TPHA titers and all returned for their confirmatory test results on the next day. Three women’s infections were subsequently confirmed and one was found to be a false positive because she had tested positive for syphilis before her pregnancy but did not inform the provider during her counseling. All sexual partners of women having positive results received treatment. Follow-up RPR titer control and subsequent two doses of penicillin were given to the three women and their husbands with weekly doses.

### Table 5. Background characteristics of the participating women

<table>
<thead>
<tr>
<th>Women characteristics</th>
<th>Subjects (n=246)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
</tr>
<tr>
<td>Education level achieved</td>
<td></td>
</tr>
<tr>
<td>never attended school/primary</td>
<td>2</td>
</tr>
<tr>
<td>secondary and/or technical college</td>
<td>166</td>
</tr>
<tr>
<td>university and/or equivalent</td>
<td>78</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>married/cohabiting</td>
<td>211</td>
</tr>
<tr>
<td>single/widow/separated</td>
<td>35</td>
</tr>
</tbody>
</table>
Subjects (n=246)

<table>
<thead>
<tr>
<th>Women characteristics</th>
<th>Subjects (n=246)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
</tr>
<tr>
<td>Residency</td>
<td></td>
</tr>
<tr>
<td>Ulaanbaatar city</td>
<td>106</td>
</tr>
<tr>
<td>registered migrant</td>
<td>118</td>
</tr>
<tr>
<td>unregistered migrant</td>
<td>22</td>
</tr>
<tr>
<td>Having previous pregnancy</td>
<td>162</td>
</tr>
<tr>
<td>&gt;2</td>
<td>46</td>
</tr>
<tr>
<td>Mean gestational age at first ANC (sd)</td>
<td>12.1 (4.4)</td>
</tr>
<tr>
<td>Previous STI</td>
<td>22</td>
</tr>
<tr>
<td>History of previous miscarriage, preterm</td>
<td></td>
</tr>
<tr>
<td>birth, stillbirth and or early neonatal death</td>
<td>6</td>
</tr>
<tr>
<td>Syphilis test performed at 3rd trimester</td>
<td>107</td>
</tr>
</tbody>
</table>

1.2 Survey with antenatal women on satisfaction level

The satisfaction level of women regarding one-stop service according to agreement or disagreement on 11 opinion statements is summarized in Table 6. All women preferred receiving results on
the same day and were satisfied with the rapid test. All questions had an average satisfaction score above 2.5 (range 2.6 to 3.8). The mean of the aggregate satisfaction scores of respondents was 3.2 with a standard deviation of 0.3, indicating that women were well satisfied with the rapid test.

One hundred and sixty-three women gave answers to the open-ended question on the reasons of their satisfaction. The most frequent four answers were: reduction of extra travel, time and expenses related to transportation (87.8%), painless testing and rapid available result (76.7%), received information (41.8%) and being able to discuss their problems with the providers or counseling (36.8%).

Table 6. Women’s satisfaction level

<table>
<thead>
<tr>
<th>Positive opinions</th>
<th>No. (%) of women (n = 246)</th>
<th>Mean score (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Strongly agree</td>
<td>Agree</td>
</tr>
<tr>
<td>I prefer receiving syphilis testing the same place as ANC visit</td>
<td>211 (85.8)</td>
<td>32 (13.0)</td>
</tr>
<tr>
<td>I prefer receiving my results the same day</td>
<td>196 (79.7)</td>
<td>45 (18.3)</td>
</tr>
<tr>
<td>I prefer receiving counselling from ANC providers</td>
<td>76 (30.9)</td>
<td>150 (61.0)</td>
</tr>
<tr>
<td>Positive opinions</td>
<td>No. (%)</td>
<td>Mean score</td>
</tr>
<tr>
<td>----------------------------------------------------------------------------------</td>
<td>---------</td>
<td>------------</td>
</tr>
<tr>
<td></td>
<td>of women</td>
<td>(SD)</td>
</tr>
<tr>
<td></td>
<td>(n = 246)</td>
<td></td>
</tr>
<tr>
<td>I prefer receiving syphilis treatment at the ANC clinics</td>
<td>67</td>
<td>147</td>
</tr>
<tr>
<td></td>
<td>(27.2)</td>
<td>(59.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(SD)</td>
</tr>
<tr>
<td>I understand the result of my rapid test.</td>
<td>100</td>
<td>130</td>
</tr>
<tr>
<td></td>
<td>(40.7)</td>
<td>(52.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(SD)</td>
</tr>
<tr>
<td>I would recommend one-stop service to a friend</td>
<td>91</td>
<td>142</td>
</tr>
<tr>
<td></td>
<td>(37.0)</td>
<td>(57.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(SD)</td>
</tr>
<tr>
<td>I am satisfied with the one-stop service</td>
<td>118</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>(48.0)</td>
<td>(39.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(SD)</td>
</tr>
<tr>
<td>Negative opinions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I spent long time in the service room*</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>(0.0)</td>
<td>(5.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(SD)</td>
</tr>
<tr>
<td>I found the rapid testing stressful and less confidential*</td>
<td>34</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>(13.8)</td>
<td>(24.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(SD)</td>
</tr>
</tbody>
</table>

Satisfaction score: ranges 1-4, * reverse scaling
From the univariate analysis of the effect of women’s background characteristics on overall satisfaction, older age (p<0.001), higher education level (p<0.001), being married (p=0.001), being employed (p=0.012) and history of previous pregnancy (p<0.001) were associated with a higher score of satisfaction. No association with residency, history of previous induced abortion, adverse pregnancy outcome, gestational age at the first antenatal visit and history of STIs was detected.

In the multiple linear regression analysis, those with higher level of education (p<0.001), married (p<0.001) and history of previous pregnancy (p<0.001) showed higher overall satisfaction scores. (Table 7)

Table 7. Final model of multiple regression analysis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Coefficient*</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Education level (ref=non/primary)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>secondary and or technical</td>
<td>0.152</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>university and or equivalent</td>
<td>0.776</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Marital status (ref=married)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>single/widowed/separated/divorced</td>
<td>-0.052</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>No previous pregnancy</strong></td>
<td>-0.174</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*adjusted for independent variables: women’s age, employment status, residency, history of induced abortion, adverse pregnancy outcomes, gestational age at 1st ANC visit and history of STIs
1.3 In-depth interviews with providers

All 13 providers, including six OB-GYNs and seven nurses in the study settings, agreed to participate in the interview. The OB-GYNs working experience ranged from 5 to 25 years (median 11 years) while that of the nurses ranged from 2 to 16 years (median 6 years). The ANC experience of OB-GYNs ranged from 2 to 20 years (median 12 years) while that of nurses ranged from 2 to 12 years (median 5 years). Providers' opinions on one-stop service in antenatal clinic were categorized into 3 main areas: one-stop service, challenges/problems experienced by the providers and acceptance in offering the one-stop service.

1.3.1 Opinions on the one-stop service

All providers agreed that ASYS must be an integral part of ANC and other maternal and newborn health services. They also agreed that linking ASYS with ANC services, as well as other reproductive health initiatives, was essential for controlling maternal syphilis at delivery as well as congenital syphilis.

All providers supported the one-stop service with the reason that women would suffer with an additional journey to STI laboratories for testing. They quoted that "We usually advise antenatal women to have the test, but they are reluctant because it is far, they say if it (the testing) was here they could have done it", "In the remote areas women have time and travel difficulties getting to the STI laboratories and easily delay or ignore it" or "Of course, for pregnant women who have to attend another clinic again for testing, results clarification or treatment undoubtedly it is
inconvenient, especially for the women where geographic barriers are present.”

Most providers highlighted that the introduction of the one-stop service into antenatal clinics would not create any significant change in the existing infrastructure of services and procedures would not face major problems. For example, one OB-GYN said “Since Mongolian antenatal clinics are well organized with good facilities and sufficient number of providers the introduction of the new service should be straightforward”.

1.3.2 Challenges/problems experienced by the providers

The majority of providers reported they did not encounter significant problems to either delay or hamper their routine services. In addition, no extra space was needed for the one-stop service. However, most providers agreed that the one-stop service was time consuming and needs good organizational management. According to one OB-GYN: “Each woman needs at least 40-60 minutes inclusive of pre-test counseling, testing, results, examination and post-test counseling for the one-stop service. For positive cases of course it will take longer. However, if we can arrange the service as is one part of the standard ANC procedures, it will be a good solution.”

Most providers agreed that the one-stop service had a high workload, although the benefits far outweighed any disadvantages. “There is more work now because the person managing the one-stop service is still expected to have other duties in the clinic” quoted by an OB-GYN, while a nurse said “It has affected the
services because sometimes it causes delays in serving other patients since I’m the only nurse in the procedures room” or “After starting this service, it has made my work beyond the normal ...However, I am happy that none of my patients will be missed for syphilis testing and treatment” quoted by an OB-GYN.

One nurse at the clinic reported that there were occasions where extra nursing staff were required to meet the one-stop service pledge (same visit service) as “It was felt that the trend of one-stop service would face manpower problems if the number of antenatal clients increase in the future”.

All providers were concerned about the supplies of one-stop service in the future. “The supplies this time are provided through your project thus we had no problem with the shortages of essential supplies, such as rapid tests, lancets and penicillin. If we will extend the one-stop service in the future, who will provide the supplies? We do not want the one-stop service to be only a one-time study”.

1.3.3 Acceptance in offering one-stop service

All providers agreed that the rapid test was very easy to use. The technique required to use the rapid test was straightforward, the time needed minimal, and would not be a concern for them. The four women who tested positive by rapid test during the study period had been well prepared to accept a positive status. All OB-GYNs agreed that the extra workload required, due to counseling, performing clinical examination and interpretation of test results, was no more complicated than their routine work. All
nurses also reported that offering the rapid test was a satisfying experience for them. A nurse quoted that "The whole procedure of counseling and testing by rapid test was conducted by one single ANC provider who therefore could provide a comprehensive package of service to individual woman from pre-test through post-test counseling. Also, the women have a chance to receive information and counseling again from OB-GYNs. This significantly facilitated connection building between the women and the providers".

The majority of the providers said that contact tracing by ANC doctors are better than by others because antenatal women trust antenatal doctors more and usually they come with their husbands for ANC. According to an OB-GYN: "Contact tracing of positive cases would be the best choice since most husbands of our clients wait for them in the clinic". However, some providers expressed concern regarding testing the husbands of positive cases. "If there is suddenly discordance between the syphilis test result of women and husbands, then what should we do? I felt it was difficult to explain clearly the implications to the clients. Positive test results could easily fuel family quarrels and even lead to domestic violence, so it may be better to ask the husband first to receive treatment without doing any tests".

All providers expressed confidence in offering one-stop service in the antenatal clinic setting. They also felt confident if they were asked to train other providers to offer one-stop service. The issues that concern themselves were case management, counseling skills, and performing the tests.
2. Cluster randomized trial: Effectiveness of the one-stop service on antenatal syphilis screening

Recruitment started in August 2007 and all follow-up data was completed in August 2008. Figure 8 shows the flow of study clusters and eligible women throughout the trial. We collected follow-up data on 94.3% of enrollees at delivery in the intervention and 92.6% in the control. The proportion of overall lost to follow-up did not vary between the groups (p=0.1).
14 antenatal clinics

7 allocated to intervention
7 allocated to control

4284 new attendees eligible
4277 new attendees eligible

434 excluded
- 327 not meet inclusion criteria
- 107 refused to participate

427 excluded
- 210 not meet inclusion criteria
- 217 refused to participate

At 1st antenatal visit
3850 received one-stop service

At 1st antenatal visit
3850 received routine screening service

At 3rd trimester
3756 followed up
94 lost to follow-up

At 3rd trimester
3823 followed up
27 lost to follow-up

At delivery
3632 followed up
218 lost to follow-up

At delivery
3564 followed up
286 lost to follow-up

Figure 8. Trial profile
The distributions of baseline characteristics of both groups were well-balanced, such as mean age, education and marital status; however, significant differences were observed for gestational age at the first antenatal visit and multiple sexual partners (Table 8).

**Table 8. Baseline characteristics of participants**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
<td>26.9 (5.5)</td>
<td>27 (7.5)</td>
</tr>
<tr>
<td>Education level (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>never attended school/primary</td>
<td>81 (2.1)</td>
<td>73 (1.9)</td>
</tr>
<tr>
<td>secondary and/or technical</td>
<td>2,560 (66.5)</td>
<td>2,619 (68)</td>
</tr>
<tr>
<td>university and/or equivalent</td>
<td>1,209 (31.4)</td>
<td>1,158 (30.1)</td>
</tr>
<tr>
<td>Marital status (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>married/cohabiting</td>
<td>3,496 (90.8)</td>
<td>3,456 (89.8)</td>
</tr>
<tr>
<td>single/widowed/separated</td>
<td>354 (9.2)</td>
<td>394 (10.2)</td>
</tr>
<tr>
<td>Residency (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulaanbaatar</td>
<td>1,618 (42.0)</td>
<td>1,641 (42.6)</td>
</tr>
<tr>
<td>registered migrant</td>
<td>1,816 (47.2)</td>
<td>1,787 (46.4)</td>
</tr>
<tr>
<td>unregistered migrant</td>
<td>416 (10.8)</td>
<td>422 (11.0)</td>
</tr>
</tbody>
</table>
### Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control (n=3850)</th>
<th>Intervention (n=3850)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous pregnancy (%)</td>
<td>2,465 (64.0)</td>
<td>2,503 (65.0)</td>
</tr>
<tr>
<td>Mean gestational age at the first ANC (SD)</td>
<td>14.1 (6.6)</td>
<td>12.0 (4.8)</td>
</tr>
<tr>
<td>Previous STI (%)</td>
<td>352 (9.1)</td>
<td>324 (8.4)</td>
</tr>
<tr>
<td>Any adverse pregnancy outcome (%)</td>
<td>222 (9.0)</td>
<td>221 (8.8)</td>
</tr>
<tr>
<td>Any multiple sexual partners (%)</td>
<td>450 (11.7)</td>
<td>365 (9.4)</td>
</tr>
</tbody>
</table>

SD-standard deviation, ANC-antenatal care, STI-sexually transmitted disease

Of 3,850 pregnant women recruited in each group, the proportion of syphilis testing at the first antenatal visit was over 99% in the intervention group and 79.6% in the control group (p<0.001) as shown in Figure 9. In the third trimester, 94 (2.4%) and 27 (0.7%) women in the respective groups were lost to follow-up, all of whom had had a negative test at the first antenatal visit. Of the remaining 3,683 and 3,796 (not included previous seropositives at the first antenatal visit) who revisited at the third trimester, 99.7% and 62.1% had the second test (p<0.001) in the intervention and control groups, respectively. In the corresponding two periods, 73 (1.9%) and 20 (0.5%) cases of syphilis were detected in the intervention group and 27 (0.9%) and 2 (0.08%) were
detected in the control group (p<0.001 for first test and p=0.01 for second test). Eventually, 98.9% (92/93) of the overall detected cases in the intervention group and 89.6% (26/29) in the control group were adequately treated (p=0.02). The corresponding overall treatment rates of the sexual partners was 92.5% versus 55.2% (p<0.001). Only one congenital syphilis case out of 3,632 deliveries in the intervention group versus 15 out of 3,552 in the control (p=0.002) were ascertained at the end of the study, a reduction of 93.5% (95% CI 66.0% - 98.6%). The only case of congenital syphilis in the intervention group was born to a woman who arrived late for the antenatal visit (38 weeks of gestation), and who had been seropositive in the first antenatal visit, and had received only single injection of benzathine penicillin and did not return until delivery.
Figure 9. Primary and secondary outcomes at intervention and control
Multilevel analysis was separately computed for the main outcomes with the same set of independent variables that were significant in the univariate analysis. After adjustment, the primary and secondary outcomes were all significantly associated with the intervention except adequate treatment of positive cases. (Table 9)

Table 9. Associations between the main outcomes and significant independent variables obtained from multilevel logistic regression model

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>Adjusted OR*</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N (%)</td>
<td>n/N (%)</td>
<td>(95% CI)</td>
<td></td>
</tr>
<tr>
<td>Primary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital syphilis</td>
<td>1/3632 (0.03)</td>
<td>15/3564 (0.42)</td>
<td>0.09 (0.01-0.67)</td>
<td>0.019</td>
</tr>
<tr>
<td>Coverage at 1st visit</td>
<td>3849/3850 (99.9)</td>
<td>3065/3850 (79.6)</td>
<td>989.84 (129.42-7570.46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coverage at 3rd trimester</td>
<td>3670/3683 (97.7)</td>
<td>2357/3796 (62.1)</td>
<td>617.88 (123.91-3081.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Intervention</td>
<td>Control</td>
<td>Adjusted OR* (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>--------------------------</td>
<td>--------------</td>
<td>---------</td>
<td>-----------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Syphilis case at 3rd trimester</td>
<td>20/3670 (0.5)</td>
<td>2/2357 (0.08)</td>
<td>6.27 (1.46-26.87)</td>
<td>0.013</td>
</tr>
<tr>
<td>Adequate treatment</td>
<td>92/93 (98.9)</td>
<td>26/29 (89.6)</td>
<td>10.44 (0.94-116.28)</td>
<td>0.06</td>
</tr>
<tr>
<td>Partner treatment</td>
<td>88/93 (94.6)</td>
<td>16/29 (55.2)</td>
<td>18.17 (4.16-79.35)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

OR - odds ratio, CI- confidence interval

* adjusted for significant independent variables such as gestational age at 1st antenatal visit and multiple sexual partners with a random effect for antenatal clinics
3. Subsidiary results

In this section, some important subsidiary results are described, including treatment of rapid test positive cases, diagnostic accuracy of the rapid treponemal test conducted at the antenatal clinics and characteristics of syphilis infected women.

3.1 Treatment of rapid test positive women

The 81 women testing positive by the rapid test at the first antenatal visit and 23 women testing positive by the rapid test at the third trimester received immediate treatment of benzathine penicillin G (2.4 million units intramuscular). There were no penicillin-allergic cases and no complications related to penicillin treatment. All 91 women with RPR/TPHA confirmed syphilis received second and third doses of benzathine penicillin at weekly intervals except one late comer who gave birth to a baby with congenital syphilis. The 13 women who had false positive test results at the first antenatal visit and the third trimester of gestation were over-treated. Ten of them were diagnosed and treated at pregnancy but the history was obtained later. The two cases who were detected during the retesting of negative cases also received 3 doses of penicillin.

3.2 Rapid treponemal test results

Out of the 3849 women who were tested by the rapid test at the first antenatal visit and the 3670 women who were tested by the
rapid test at the third trimester, 81 positive cases and 23 positive cases were detected, respectively. The remaining women tested negative by the rapid test (Figure 10). Three of 3,849 (0.08%) showed no valid results during the first testing. The rapid testing was repeated in the 3 cases and all three were negative.

All rapid test positive sera and 10% of the negative sera were randomly selected to be tested by qualitative and quantitative RPR/TPHA run at the reference laboratory.

At the first antenatal visit, all the 81 positive sera and 389 negative sera were retested. Of the 81 positive sera, 72 (83.7%) had confirmed syphilis, of which high-titer (titer ≥1:8) syphilis presented in 69 sera and low-titer (titer <1:8) syphilis diagnosed in 3 sera. Of the 389 negative sera, 1 woman showed positive with the RPR/TPHA but low titer of 1:2 was detected. At the third trimester, of 3850 enrolled women, 94 were lost to follow-up and 13 were unscreened at the third trimester of gestation. All 23 positive sera and 394 negative sera were retested. Of the 23 positive sera, 19 women (82.6%) had confirmed syphilis of which 17 had high-titer (titer ≥1:8) syphilis and 2 had low-titer (titer <1:8) syphilis. Of the 394 negative sera, one showed positive by the RPR/TPHA but low titer of 1:2 was detected.

At both of the points of syphilis testing, 887 sera were retested by the RPR/TPHA confirmation. It showed high accuracy in 98.3% with a false positive rate of 1.5% and false negative rate in
0.2%. High titer of syphilis could be detected by rapid test in 100% but in only 71.4% of women with low-titer syphilis.

**Figure 10. Onsite rapid syphilis test results**
At delivery all available 3,632 women were retested by RPR and all were seronegative.

3.3 Characteristics of syphilis infected women

Totally, 136 syphilis infected women were detected during pregnancy (at the first antenatal visit and the third trimester) and/or at delivery. The mean age of the women with syphilis was 26.9 years (range, 18–41 years) and there was no significant difference in mean age between the uninfected (26.2 years) and infected (26.9 years) women. Univariate comparisons of demographic and reproductive characteristics of uninfected and infected women are displayed in Table 10. The syphilis infected group was significantly more likely to be unmarried, have a lower education level, to be an unregistered rural migrant, to be unemployed, to have a previous STI, to have multiple sexual partners and previous adverse pregnancy outcomes. However, the mean gestational age at first antenatal visit and previous pregnancy were not significantly different.
Table 10. Demographic and reproductive characteristics of syphilis infected and uninfected pregnant women

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Uninfected women n=7564</th>
<th>Syphilis-infected women n=136</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD)</td>
<td>26.9 (5.5)</td>
<td>26.2 (5.5)</td>
<td>0.08</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>married/cohabiting</td>
<td>6,851 (90.6)</td>
<td>101 (74.3)</td>
<td></td>
</tr>
<tr>
<td>widowed/separated/divorce</td>
<td>713 (9.4)</td>
<td>35 (25.7)</td>
<td></td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>never attended school</td>
<td>138 (1.8)</td>
<td>16 (11.8)</td>
<td></td>
</tr>
<tr>
<td>secondary and/technical</td>
<td>5,085 (67.2)</td>
<td>94 (69.1)</td>
<td></td>
</tr>
<tr>
<td>university and/equivalent</td>
<td>2,341 (31.0)</td>
<td>26 (19.1)</td>
<td></td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ulaanbaatar</td>
<td>3,222 (42.6)</td>
<td>37 (27.2)</td>
<td></td>
</tr>
<tr>
<td>Registered rural migrant</td>
<td>3,549 (46.9)</td>
<td>54 (39.7)</td>
<td></td>
</tr>
<tr>
<td>Unregistered rural migrant</td>
<td>793 (10.5)</td>
<td>45 (33.1)</td>
<td></td>
</tr>
</tbody>
</table>
Table 11 summarizes the independent factors for being syphilis infected during pregnancy using multivariate logistic regression analysis. The odds of being infected were increased significantly in women reporting being single/widowed/separated (adjusted OR=2.16, 95% CI=1.2-3.91). Higher education level, having no adverse pregnancy outcomes and no multiple sexual partners were protective factors for syphilis infection during pregnancy.
Table 11. Independent factors for being syphilis infected during pregnancy using multivariate logistic regression analysis

<table>
<thead>
<tr>
<th></th>
<th>Crude OR(95%CI)</th>
<th>adj. OR(95%CI)</th>
<th>P (Wald's test)</th>
<th>P (LR-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Education level</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(ref=never attended school/primary)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>secondary</td>
<td>0.08 (0.04,0.16)</td>
<td>0.11 (0.05,0.23)</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>university and/technical</td>
<td>0.05 (0.03,0.11)</td>
<td>0.08 (0.03,0.18)</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(ref=married/cohabiting)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>single/widowed/divorced</td>
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CHAPTER 4

DISCUSSION AND RECOMMENDATIONS

The theme of the discussion refers to the conceptual framework which emphasizes on feasibility and effectiveness of the one-stop service for ASYS and congenital syphilis prevention. The subsidiary results as mentioned on the objective part are concluded separately. A discussion on the strengths and weaknesses of the project and the main recommendations are also given at the end of this chapter.

1. Summary of findings

1.1 Feasibility of the one-stop service

The feasibility study conducted on 246 antenatal women in two antenatal clinics showed that the all women accepted the one-stop service and tested for syphilis. All women received their results and counseling from ANC providers. The majority were satisfied with the on-stop service.
The mean aggregate satisfaction score derived from 11 questions on specific aspects of satisfaction was 3.2 (range 2.6 to 3.4) from a possible 1 to 4, where 1=very dissatisfied and 4=very satisfied. The providers were also satisfied and most of them reported that they did not encounter any significant problems to either delay or hamper the other routine services. However, all providers agreed that the one-stop service is time consuming and leads to high staff workloads and needs good clinical management. In addition, they preferred to treat husbands presumptively to avoid the possibility of diagnosing couples with discordant syphilis, which may lead to possible violence. In summary, the study results showed that one-stop service with rapid onsite syphilis testing, prompt treatment of syphilis cases, contact tracing and counseling by ANC providers at antenatal clinics in Ulaanbaatar, Mongolia was feasible and well accepted among both women and providers according to their perspectives.

1.2 Effectiveness of one-stop service for antenatal syphilis screening

The cluster randomized trial provides solid evidence that the one-stop service on ASYS implemented in antenatal clinics was more effective for the prevention of congenital syphilis. Almost all antenatal clients in the intervention clinics tested for syphilis at both time points of testing (over 99%), resulting in more seropositive cases detected (73 [1.9%] and 20 [0.5%] for the first and second testing, respectively, versus 27 [0.9%] and 2 [0.08%])
in the control group). A higher proportion of the seropsitive women (98.9% versus 89.6%) in the control group were adequately treated and their sexual partners (92.5% versus 55.2%) were completely treated. Finally, the intervention resulted in a significantly lower number of congenital syphilis cases than the control group (a reduction of 93.5%).

1.3 Subsidiary results

Onsite screening for syphilis at antenatal clinics is a practicable and effective means of diagnosing and treating maternal syphilis. The onsite rapid treponemal test absolutely reassured the diagnosis of syphilis in women with high titer and low false negative results. The test gave only a few false positive results and thus only a few women received unnecessary penicillin treatment; however, no penicillin-allergic cases and no complications related to the penicillin treatment occurred.

Women infected with syphilis detected during pregnancy (at the first antenatal visit and the third trimester) and at delivery were most likely to be unmarried, have a low education and have multiple sexual partners.
2. Discussion

2.1 Feasibility of the one-stop service

Overall, the feasibility study results showed that one-stop service with rapid onsite syphilis testing, prompt treatment of syphilis cases, contact tracing and counseling by ANC providers at antenatal clinics in Ulaanbaatar, Mongolia, were practical and would not face any critical obstacles regarding their clients’ and providers’ perspectives. This is an important finding of the study because the antenatal care clients and ANC providers’ perspectives can strongly influence daily performance and acceptance of a new regulation or policy.85

In developing countries, one of the greatest gaps of syphilis control in pregnant women and congenital syphilis prevention is that the women coming for ANC remain unscreened for syphilis, thus remain untreated.11 To address this challenge, an alternative integrated ASYS model that includes onsite syphilis screening, treatment and counseling was introduced in some developing countries. To examine the effectiveness of this model, several studies with different designs were carried out and they have shown that the model can dramatically improve the screening coverage and consequently reduce the risk of congenital syphilis.67,68,77,78 However, these studies did not focus on the perspectives and level of satisfaction from both the antenatal women and providers on the new model. Therefore, direct
comparisons of our results with the previous studies are difficult.

Some studies reported a number of logistical problems with the decentralized model, such as complexity of the onsite RPR syphilis testing, difficulty reading the test results and women leaving before receiving their results. In contrast, in our study we used rapid treponemal tests where results are obtained within 10-15 minutes. In a Bolivian study, where the rapid syphilis test was used for the ASYS, the new model (one-stop service) was not only an effective intervention for detection and treatment of syphilis cases but also feasible in terms of acceptance by providers and women.

In our study, the findings of the women’s satisfaction survey were very encouraging by the reasons that the one-stop service reduced extra travel, time and expenses related to transportation. This was in accordance with our previous study which revealed that the distance from home to laboratory was a barrier of universal ASYS coverage. Moreover, the same preferences of collection of blood by finger prick than venipuncture were also reported in a study by Liu et al, (2003).

Apart from client satisfaction, good acceptance on the side of care providers also supports the use of a one-stop service at ANC clinics. The challenge of logistic arrangements on offering one-stop service, such as extra time required and increased staff workloads, is consistent with other studies. However, the
providers in our study accepted the challenges and offered some ideas for overcoming these challenges. Some providers suggested we modify the contact tracing plan to treat males presumptively for ethical reasons to avoid the possibility of diagnosing couples with discordant syphilis results in order to avoid possible conflicts since it may lead to domestic violence.88

2.2 Effectiveness of the one-stop service

Our study provides evidence that one-stop service on ASYS implemented in antenatal clinics was more effective for the prevention of congenital syphilis than conventional service. Almost all antenatal clients in the intervention clinics tested for syphilis at both time points of testing, resulting in more seropositive cases detected. A higher proportion of the syphilis infected women and their sexual partners were completely treated. Finally, the intervention resulted in a significantly lower number of congenital syphilis cases than the control group.

The need for a more effective alternative approach to ASYS is obvious since in many developing countries antenatal women remain unscreened for syphilis, thus remain untreated.11 To address the challenge to detect and treat syphilis infected antenatal women at their first antenatal visit, an intervention on decentralized ASYS was developed and assessed in studies from some developing countries.67,70,74,76,77,89 The findings of the studies showed that the decentralized service of ASYS could detect and treat more maternal syphilis in pregnancy or could reduce congenital syphilis.67,70,77,89
One African study in 2003 documented a 75% decrease in rates of congenital syphilis after allowing for decentralized screening of maternal syphilis.\textsuperscript{89} Another South African study using decision-analytic cost-effectiveness modelling demonstrated that onsite rapid testing prevented over 80% of predicted cases of congenital syphilis.\textsuperscript{70}

Our randomized study demonstrates that one-stop service with onsite rapid treponemal syphilis test with treatment and counselling is able to increase the coverage of screening and improve the rate of case detection in women and their partners as well as facilitate completion of treatment and thus dramatically reduce the incidence of congenital syphilis. There were two previous randomized controlled trials to evaluate the one-stop service on ASYS; however, the findings of these studies could not be compared directly to our findings because the onsite syphilis tests were different. In a study of Bique et al., onsite RPR was compared to centralized RPR and showed a significant improvement of perinatal mortality in the onsite RPR arm.\textsuperscript{74} In contrast, the comparison of onsite and centralized RPR did not show an improvement in either the proportion receiving adequate follow-up or the perinatal loss rate in a study of Myer et al.\textsuperscript{76}

There are several reasons to explain how the one-stop service has played an important role in reducing the rates of congenital syphilis. Firstly, onsite testing is convenient to women, resulting in universal ASYS coverage at both time points of
testing. Conventional centralized services for ASYS in Mongolia require women to have at least one extra visit in order to be fully tested for syphilis and to make return visits to get their test results. This inconvenience leads to delay or loss of contacts and subsequently leaves a number of syphilis cases undetected and untreated. A study in Mozambique reported that the similar intervention could increase the antenatal syphilis testing by over 90%.

Secondly, once substantially increased syphilis screening coverage the intervention could detect a significant number of syphilis cases among women attending antenatal clients. Besides demonstrating the success of detection rate in the intervention group, the study confirmed the previously reported comparatively high rates of syphilis among pregnant women in the country and the necessity of universal antenatal syphilis screening. The 20 incident cases identified would have been undetected and untreated if screening test at the third trimester had not been performed in the intervention clinics. Conversely, in control clinics coverage of syphilis testing at the third trimester was only 68.9% and could detect only 2 cases of active syphilis. This data support the necessity of performing syphilis testing also at the third trimester of gestation. Moreover, our data support the recommendation that syphilis testing should be performed on all women at the time of delivery if they were not tested for syphilis during pregnancy. Had it not been done, 15 seropositive women in the control group would have been missed during their delivery.
Thirdly, the one-stop services for ASYS allowed prompt treatment of seropositive cases which resulted in a higher proportion of adequately treated women before delivery in the intervention group than the control group. A similar success rate was reported by a Bolivian study in 2007. Using the onsite rapid syphilis testing the study detected more active syphilis cases among pregnant women and over 80% of those who tested positive received all three recommended doses of penicillin before delivery. The treatment success can be explained by the immediate access to the test results, for example women receive their test results while they are still in the antenatal clinics. In fact, a high proportion of patients do not return for collecting their test results in many countries, and this results in delay of early treatment or no treatment at all. One study found that only 24.5% of women with syphilis were attended the referral clinics for treatment.

Fourthly, notification and treatment of sexual partners at the one-stop service can be implemented. Similarly, the Bolivian study also reported that over three quarters (498/577) of the male partners were identified at the time of testing and most of them (383/498) presented for treatment. The increase in percentage of partner notification and treatment could be explained by active counseling provided by ANC doctors. Diaz-Olavarrieta et al suggested that screening for domestic violence and counseling about partner notification should be integrated into screening programs, since women who do not fear their partner's reactions
were more likely to notify them of their infection status.\textsuperscript{17} Notification to male partners is not only important to their own health, but is critical in preventing re-infection of women. Emphasis on notification of partners of pregnant women with syphilis has been associated with a threefold improvement in pregnancy outcome.\textsuperscript{88}

Finally, one-stop service is effective in preventing of congenital syphilis. A 93.5\% case reduction would mean significant relief of this health burden since several complications are well known to occur in congenital syphilis, such as miscarriages, stillbirths and early neonatal deaths.\textsuperscript{3}

Our study did not look at the reasons of the low syphilis screening coverage in the control group. However, our previous study in 2006 showed that late ANC visit, lack of knowledge on the importance of ASYS and awareness of the infection, travelling long distances to ASYS service, overcrowding at STI laboratories and living far from service spot were related to unscreened cases in routine syphilis screening in Ulaanbaatar.\textsuperscript{79}

With these results, the current one-stop service could still be improved. One seropositive woman received inadequate treatment due to arriving late for ANC resulting in congenital syphilis. Although the husband/sexual partner treatment percentage was significantly higher in the intervention group than control group, five sex partners remained untreated, thus the women had a high chance of being re-infected.
2.3 Subsidiary results

2.3.1 Onsite rapid test results

Although the conventional RPR test is inexpensive and easy to perform, it is not effective when used for onsite antenatal syphilis screening and the sensitivity and specificity of the test are highly user-dependent.\textsuperscript{73,74,76,86,92,93} The rapid treponemal test is simpler to use thus it may be suitable for onsite testing at the primary health care level. The rapid syphilis tests have demonstrated high sensitivity and specificity when studied in a variety of populations, including pregnant women, demonstrating 85-98% sensitivity and 93-98% specificity in most studies.\textsuperscript{55,92} In a trial that included 1,250 pregnant women in field settings in South Africa, onsite rapid treponemal tests performed by trained nurses resulted in the highest percentage of pregnant women correctly diagnosed and treated for syphilis (89.4% ICS, 63.9% onsite RPR and 60.8% offsite RPR/TPHA).\textsuperscript{67}

In our study, comparisons of test performance are not possible since all sera were not tested by the same three tests (the rapid test, RPR and TPHA). All positive sera and 10% of negative sera from rapid tests were retested with RPR and only positive RPR sera were confirmed by TPHA. Therefore, sensitivity and specificity of the onsite rapid test for antenatal syphilis screening was not determined. Only overall accuracy, false positive and negative rates were presented to assure the performance validation of rapid
tests and showed a high detection rate with low false positive and negative rates.

Rapid syphilis tests or treponemal tests, while theoretically more specific than non-treponemal tests, may also give false positive results. Moreover, they can not differentiate between individuals with active (untreated) syphilis and those who have previously been successfully treated for the infection. In both cases, the test result will be positive because the antibodies are long-lived in the human body for a life. In our case, there were 13 women who tested positive by rapid test assays during pregnancy, yet were negative at confirmation and 10 of them had previously treated syphilis. Thus, to be at all useful the results of confirmatory tests should be available promptly.

Although rapid tests are simple to perform and easy to interpret, in our study, two negative samples from antenatal clinics were judged as positive when read by experts at the reference laboratory. In fact, the two samples had low RPR titers and the positive test lines were faint and the line became clearer if the time to reading was increased to 15 minutes. This finding demonstrates that ANC staff do require appropriate training with regular updates and lab quality control is important. Also the South African study showed the necessity of additional refresher training of the testing personnel.
2.3.2 Treatment of rapid test positive women

The 13 women whose initial rapid test results were later confirmed as false positives received their first dose of penicillin at the antenatal clinic. Fortunately, usually single dose penicillin has not been associated with adverse sequels.\textsuperscript{2,54,62,67,68,76} Similarly, in the South African study, reported that one percent of antenatal women screened with the rapid test may have received penicillin unnecessarily due to false positive results and none developed any adverse treatment outcomes.\textsuperscript{67}

The rate of over-treatment usually depends on the overall prevalence of syphilis (TPHA-positive women) and on the relative proportion of active versus previously treated syphilis in different settings (proportion of RPR-positive versus RPR-negative women among those with a positive TPHA).\textsuperscript{52,55} Over time, the proportion of women who were once infected but have been appropriately treated will increase. These women may still be diagnosed as positive by the rapid treponemal test, and thus the rate of women receiving unnecessary penicillin treatment will increase if they are repeatedly tested using the rapid test without their history taken. On the other hand, it is possible that negative confirmatory RPR represents early infection rather than actual false positive. Therefore, it would be preferable to treat women who test positive rather than risk missing a maternal syphilis.
2.3.3 Characteristics of syphilis infected women

The prevalence of syphilis in pregnant women from our study (1.7%) likely underestimates the true prevalence of syphilis in pregnant women, because women with early miscarriages resulting from syphilis never present for antenatal care and the control group had a high percentage of women who were unscreened and lost to follow-up.

In our study, the pregnant women who had syphilis were most likely to be unmarried, have a low education and having multiple sexual partners. Most of them were unregistered rural migrants. These characteristics were similar to those previously reported in studies from other countries. These women generally had little education, had very poor knowledge of the prevention of STIs, had multiple sexual partners and had little contact with the health care, making them at high risk of STIs. Thus, these people are a very important target population for correcting the problem.

Early ANC and ASYS are essential. Women who first come to antenatal clinics in the last trimester of their pregnancies, or at the time of delivery, have a fetus that is already infected with syphilis. Further study is required to determine the reasons for the late antenatal care, and thus determine potential ways to encourage early antenatal care and screening.
3. Strengths and limitations of the study

3.1 Strengths

This is the first cluster randomized trial on one-stop antenatal syphilis screening service ever implemented. The study offered an opportunity to assess the introduction of the one-stop service for antenatal syphilis screening and prevention of congenital syphilis in antenatal clinics in Ulaanbaatar using the research design of a cluster randomized controlled trial.

In addition, our study can influence the national policy regarding antenatal syphilis screening. As a result of this study, the Mongolian government has significantly invested on this policy, with a specific interest about the syphilis screening in rural areas.

3.2 Limitations

The limitations of the feasibility study were the fact that there were no control findings of conventional ASYS, small sample size of positive cases and a short period of evaluation. While the present study aims to describe the feasibility of one-stop service, the lack of control subjects did not allow us to compare the satisfaction of the conventional service. However, we interviewed both women and providers after experiencing the one-stop services. Another limitation is the short time period for offering the one-stop service in the two clinics, thus the
providers did not gain enough experience. However, we could interview all eligible women and providers, including nurses in both clinics, to gather their opinion during the study period and some ideas were obtained through this study.

There were some limitations of the randomized trial. First, incomplete follow up was still detected in our study, however the number was small (5.7%). Although these women were initially seronegative, their final status and that of their newborns were unknown. Second, since the all women testing positive by the rapid test received immediate treatment, some women had unnecessarily received first dose of penicillin because the rapid treponemal tests cannot differentiate between women with current infection and those who have previously been treated for syphilis. However, this condition could be avoided if they were interviewed on their previous history of diagnosis and treatment. Lastly, the syphilis tests were supplied to the intervention arm but not in the control arm. It is known that logistical supply issues are at the core of failure in some programs and this may result in an advantage of the intervention arm. However, there were no shortages of routine RPR in the control arm during the study period.

4. Conclusion and recommendations

Prevention of congenital syphilis has become a global priority in public health, and through our project, we demonstrated that the one-stop service for antenatal syphilis screening increased the detection rate of syphilis, treated more positive women and their
partners and effectively reduced the incidence of congenital syphilis. In addition, the one-stop service of antenatal syphilis screening is feasible and did not face any critical obstacles in terms of antenatal women or providers’ perspectives. Implementation of one-stop service can be considered to improve overall access to interventions to eliminate congenital syphilis as a public health problem.
REFERENCES


110


76. Myer L, Wilkinson D, Lombard C, Zuma K, Rotchford K, Karim SS. Impact of on-site testing for maternal syphilis on


for Partner Notification and Universal Screening. Sex Transm Dis 2007; 34:S42-S46.


APPENDICES
Appendix 1: Informed consent forms

1.1 Informed consent form (For women, one-stop service)

Introduction: I am ………………from the …………………. I would like to introduce our study on syphilis.

Syphilis in pregnancy is harmful for both mothers and unborn babies. The screening services through blood testing for syphilis among pregnant women have been available free in Mongolia but the use of the screening services remains low.

Purpose of the research: The main purpose of the study is to test the way receiving the syphilis screening and antenatal care services in the same clinic (one-stop service) would be helpful to improve the coverage of antenatal syphilis screening and maybe to prevention of syphilis in the mother at delivery and baby’s infection in the mother's womb or at delivery.

Procedures: You will be asked questions about your background by a trained nurse. The interview will last about 5-10 minutes. In addition, about 1 drop blood will be collected by finger prick at your first visit to the antenatal clinic and at the about 28 weeks of gestation. The blood will be tested if there is the infection present. You will be informed about the results within 5-20 minutes while you are in the clinic.
If an infection is found then a free treatment will be given to you immediately by your antenatal doctor and you will be followed up until cure. In order to prevent re-infection we would like to treat your husband/sexual partner. However, your partner/spouse/husband notification will be done on your voluntary basis and will be conducted in such way that all information remains confidential. If you agree with, your husband/sexual partner(s) will be invited to come any time as soon as possible to the clinic for free syphilis testing and will receive also free treatment. Depending on your wish the notification will be by your referral or by your antenatal doctor’s referral. The doctor will explain the reasons for testing, the likely results and the possibility of treatment based on the results.

After delivery, the doctor will perform a routine post delivery examination. Your blood will be tested again to detect any late infection. A trained midwife of the Maternity hospital will collect your blood. The blood results will come after one day while you are in the Maternity hospital. The baby will also be examined. Also your baby’s blood will be examined.

The samples that are taken are part of the routine care during pregnancy and delivery and will not be stored for future use.

If an infection is found after delivery then you will be treated free of charge at the Maternity hospital. As described above, your husband/sexual partner will receive free treatment to prevent your re-infection. We would like to remember again, the notification
will be based on your voluntary basis and all information will remain confidential.

If an infection in the baby (congenital infection) is confirmed (if your infection is confirmed and/or presence of specific signs of the infection in the baby and your baby’s blood test is positive) then your baby will be treated for 10 days free of charge. Although your baby might have no any signs of the infection (even your infection was confirmed) at delivery, he/she will receive a single injection treatment and will be followed up for at least 6 months by a children’s doctor free of charge.

**Risks and Discomforts:** There is a slight risk that you may share some personal or confidential information by chance or that you may feel uncomfortable talking about some of the topics. However, we do not wish this to happen, and you may refuse to answer any question or not take part in a portion of the interview if you feel the question(s) are personal or if talking about them makes you uncomfortable.

**Benefits:** You will receive information and counseling about the early detection of the infection. This study is beneficial for you and your baby if the infection will be defined and the treatment will be given without charge. In addition, your participation is likely to help us find out more about how to increase access to the syphilis screening services. We hope that this will help reduce maternal syphilis at delivery and unborn baby’s infection.
Compensation: You will be provided a small gift as a token of appreciation for taking part in the study.

Confidentiality: We will give you a personal number, which will be used when filling in this study forms. This ensures all information including the laboratory test results will be kept strictly confidential and only medical staff directly involved in this study will have access to the clinical and laboratory notes and records. These records will be destroyed five years after the completion of the study by the investigators.

Right to refuse or withdraw: You do not have to take part in this research if you do not wish to do so, and refusing to participate will not affect your future medical care at the antenatal clinic here in any way. You may stop participating in the interview at any time that you wish. Your partner/spouse/husband notification will be based on your voluntary basis. If you have any questions you may ask those now or later. If you wish to ask questions later, you may contact with:

Dr Bayalag Munkhuu (Principal investigator)

Tel: 99088562    Email address: baymun2001@yahoo.com

Certificate of Consent for Interview of Women

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any
questions I have been asked have been answered to my satisfaction. I consent voluntarily to be a participant in this study and understand that I have the right to withdraw from the study at any time without in any way affecting my medical care.

Print Name of Respondent       Date and Signature

_________________________       __________________________

If illiterate or underage

Print Name of Independent Witness       Date and Signature

_________________________       _________________________

(if possible, this person should be selected by the participant and should have no connection to the research team)

_________________________       _________________________

Print Name of Researcher       Date and Signature

_________________________       ___________________________
1.2 Informed consent form (For women, control clinic)

**Introduction:** I am ................. from the ................. I would like to introduce our study on syphilis.

Syphilis in pregnancy is harmful for both mothers and unborn babies. The screening services through blood testing for syphilis among pregnant women have been available free in Mongolia but the use of the screening services remains low.

**Purpose of the research:** The main purpose of the study is to test the way receiving the syphilis screening and antenatal care services in the same clinic (one-stop service) would be helpful to improve the coverage of antenatal syphilis screening and maybe to prevention of syphilis in the mother (maternal syphilis) at delivery and baby’s infection in the mother's womb or at delivery (congenital infection). In order to test the one-stop service we need compare the service with the usual/conventional service.

**Procedures:** You are being asked to participate in the study and you will receive the routine syphilis screening service. If you agree to participate, the nurse will register you and interview using a short questionnaire about your pregnancy etc. The interview will last about 10 minutes. During your antenatal visits the nurse will note about your syphilis testing results. If an infection is found during pregnancy then you will receive treatment.
After delivery, the doctor will perform a routine delivery examination and your blood will be tested again to detect any late infection. A trained midwife of the Maternity home will collect your blood. The blood results will come after one day while you are in the Maternity home. The baby will also be examined and also your baby’s blood will be examined.

The samples that are taken are part of the routine care during pregnancy and delivery and will not be stored for future use.

If an infection is found after delivery then you will be treated at the Maternity home. We would like to remember again, the notification will be based on your voluntary basis and all information will remain confidential. If an infection in the baby (congenital infection) is confirmed (if your infection is confirmed and/or presence of specific signs of the infection in the baby and your baby’s blood test is positive) then your baby will be treated for 10 days free of charge. Although your baby might have no signs of the infection (even your infection was confirmed) at delivery, he/she will receive a single injection treatment and will be followed up for at least 6 months by a children’s doctor.

**Risks and Discomforts:** There is a slight risk that you may share some personal or confidential information by chance or that you may feel uncomfortable talking about some of the topics. However, we do not wish this to happen, and you may refuse to answer any question or not take part in a portion of the interview if you
feel the question(s) are personal or if talking about them makes you uncomfortable.

**Benefits:** Your participation is likely to help us find out more about how to increase access to the syphilis screening services.

**Confidentiality:** We will give you a personal number, which will be used when filling in this study forms. This ensures all information including the laboratory test results will be kept strictly confidential and only medical staff directly involved in this study will have access to the clinical and laboratory notes and records. These records will be destroyed five years after the completion of the study by the investigators.

**Right to refuse or withdraw:** You do not have to take part in this research if you do not wish to do so, and refusing to participate will not affect your future medical care at the antenatal clinic here in any way. You may stop participating in the interview at any time that you wish. If you have any questions you may ask those now or later. If you wish to ask questions later, you may contact with:

**Dr Bayalag Munkhuu (Principal investigator)**

Tel: 362886 or 99176551  Email address: baymun2001@yahoo.com
Certificate of Consent for Interview of Women

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions I have been asked have been answered to my satisfaction. I consent voluntarily to be a participant in this study and understand that I have the right to withdraw from the study at any time without in any way affecting my medical care.

Print Name of Respondent                   Date and Signature

_________________________________________________________________________

If illiterate or underage

Print Name of Independent Witness          Date and Signature

(if possible, this person should be selected by the participant and should have no connection to the research team)

_________________________________________________________________________

Print Name of Researcher                   Date and Signature

_________________________________________________________________________
### Appendix 2: Feasibility study data collection form

#### 2.1 Satisfaction survey questionnaire for one-stop service

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Comparison of “one-stop” versus “conventional” service on antenatal syphilis screening in Ulaanbaatar, Mongolia

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<td>1. yes 2. no</td>
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</tr>
</tbody>
</table>

**MEDICAL INFORMATION**

<table>
<thead>
<tr>
<th>7. Has subject ever been pregnant before?</th>
<th>[ ]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. yes 2. no</td>
<td>[ ]</td>
</tr>
<tr>
<td>If no, go to q10</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>8. Total number of live births</th>
<th>[ ]</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>9. Has subject ever had any adverse pregnancy outcome (miscarriage, stillbirth, preterm birth etc)</th>
<th>[ ]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. yes 2. no</td>
<td>[ ]</td>
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<table>
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<tr>
<th>10. Gestational age at the first ANC (by ultrasound examination)</th>
<th>[ ]</th>
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<tbody>
<tr>
<td>........................weeks</td>
<td>[ ]</td>
</tr>
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<table>
<thead>
<tr>
<th>11. Previous STI history?</th>
<th>[ ]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. yes 2. no</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>12. Any multiple sexual partner?</th>
<th>[ ]</th>
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</thead>
<tbody>
<tr>
<td>1. yes 2. no</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

**TEST RESULTS**

<p>| 13. Rapid test result | [ ] |</p>
<table>
<thead>
<tr>
<th></th>
<th>positive</th>
<th>negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>14. If positive, did she receive the 1st dose of penicillin?</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>15. If positive, was the infection confirmed with RPR/TPHA?</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>confirmed</td>
<td>not confirmed</td>
</tr>
<tr>
<td>16. If confirmed, did she receive adequate treatment?</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>17. Did the partner receive treatment?</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Investigator’s name</td>
<td>Signature</td>
<td>Date</td>
</tr>
<tr>
<td></td>
<td>Question</td>
<td>Options</td>
</tr>
<tr>
<td>---</td>
<td>-------------------------------------------------------------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>2.</td>
<td>I refer receiving my results the same day</td>
<td>[ ] strongly agree 2.agree 3.disagree 4.strongly disagree</td>
</tr>
<tr>
<td>3.</td>
<td>I prefer receiving counseling from ANC providers</td>
<td>[ ] strongly agree 2.agree 3.disagree 4.strongly disagree</td>
</tr>
<tr>
<td>4.</td>
<td>I prefer receiving syphilis treatment at antenatal clinics</td>
<td>[ ] strongly agree 2.agree 3.disagree 4.strongly disagree</td>
</tr>
<tr>
<td>5.</td>
<td>I satisfied with information provided on syphilis testing</td>
<td>[ ] strongly agree 2.agree 3.disagree 4.strongly disagree</td>
</tr>
<tr>
<td>6.</td>
<td>I would rather have my finger stuck than have blood drawn from my vein</td>
<td>[ ] strongly agree 2.agree 3.disagree 4.strongly disagree</td>
</tr>
<tr>
<td>7.</td>
<td>I understand the result of my syphilis test</td>
<td>[ ] strongly agree 2.agree 3.disagree 4.strongly disagree</td>
</tr>
<tr>
<td>8.</td>
<td>I would recommend one-stop service to a friend</td>
<td>[ ] strongly agree 2.agree 3.disagree 4.strongly disagree</td>
</tr>
<tr>
<td>9.</td>
<td>I am satisfied with the one-stop service</td>
<td>[ ] strongly agree 2.agree 3.disagree 4.strongly disagree</td>
</tr>
<tr>
<td>10.</td>
<td>I spent long time in the service room</td>
<td>[ ] strongly agree 2.agree 3.disagree 4.strongly disagree</td>
</tr>
<tr>
<td>11.</td>
<td>I found the rapid testing less confidential</td>
<td>[ ] strongly agree 2.agree 3.disagree 4.strongly disagree</td>
</tr>
<tr>
<td>Question</td>
<td>Answer</td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>--------</td>
<td></td>
</tr>
<tr>
<td>12. What did find most satisfied/dissatisfied</td>
<td>[ ][ ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. What is the main reason?</td>
<td>[ ][ ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THANK YOU</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.2 Guiding questions of the provider’s In-depth interviews

1. Greeting

2. Introduction (interviewer, research, rationale, objectives, methods, confidentiality, rights, consent)

3. Background information (age, gender, occupation, place of work/position)

4. Working experience (as an ANC provider)

5. What is your opinion on the one-stop service on antenatal syphilis screening in Ulaanbaatar?

6. Did you have any challenges/problems with one-stop service on antenatal syphilis screening while you carried out it?

7. How do you feel about one-stop service on ASYS during the intervention?

8. Do you have any suggestion on “one-stop” service on ASS?
Appendix 3: Randomized trial data collection forms

3.1 Questionnaire for women

Comparison of "one-stop" versus "conventional" service on antenatal syphilis screening in Ulaanbaatar, Mongolia

<table>
<thead>
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<th></th>
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<td>ANC clinic number</td>
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</tr>
<tr>
<td>Subject number</td>
<td>[ ][ ][ ][ ][ ]</td>
</tr>
<tr>
<td>Group:</td>
<td>1.Intervention</td>
</tr>
<tr>
<td></td>
<td>2.Control</td>
</tr>
<tr>
<td></td>
<td>[ ]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PERSONAL INFORMATION</th>
<th></th>
</tr>
</thead>
</table>
| 1. Date of admission (day, month, year) | [ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][][ ]
5. Residency

<table>
<thead>
<tr>
<th>Option</th>
<th>[ ]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ulaanbaatar</td>
<td></td>
</tr>
<tr>
<td>2. registered rural migrant</td>
<td></td>
</tr>
<tr>
<td>3. unregistered rural migrant</td>
<td></td>
</tr>
</tbody>
</table>

6. Current employment status

<table>
<thead>
<tr>
<th>Option</th>
<th>[ ]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. yes</td>
<td>2. no</td>
</tr>
</tbody>
</table>

**MEDICAL INFORMATION**

7. Has subject ever been pregnant before?

<table>
<thead>
<tr>
<th>Option</th>
<th>[ ]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. yes</td>
<td>2. no</td>
</tr>
</tbody>
</table>

If no, go to q10

8. Total number of live births

| [ ] [ ] |

9. Has subject ever had any adverse pregnancy outcome (miscarriage, stillbirth, preterm birth etc)

<table>
<thead>
<tr>
<th>Option</th>
<th>[ ]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. yes</td>
<td>2. no</td>
</tr>
</tbody>
</table>

10. Gestational age at the first ANC (by ultrasound examination)  

| [ ] [ ] |

weeks

11. Previous STI history?

<table>
<thead>
<tr>
<th>Option</th>
<th>[ ]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. yes</td>
<td>2. no</td>
</tr>
</tbody>
</table>

12. Any multiple sexual partner?

<table>
<thead>
<tr>
<th>Option</th>
<th>[ ]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. yes</td>
<td>2. no</td>
</tr>
</tbody>
</table>

Investigator’s name  __________  Signature  __________

Date  ________________
### 3.2 Admission form

Comparison of “one-stop” versus “conventional” service on antenatal syphilis screening in Ulaanbaatar, Mongolia

<table>
<thead>
<tr>
<th>IDENTIFICATION</th>
<th>[ ][ ]</th>
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<tr>
<td>ANC clinic number</td>
<td>[ ][ ]</td>
</tr>
<tr>
<td>Subject number</td>
<td>[ ][ ][ ][ ]</td>
</tr>
<tr>
<td>Group: 1.Intervention 2.Control</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TEST RESULTS</th>
<th>[ ]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Syphilis testing at 1st visit:</td>
<td>[ ]</td>
</tr>
<tr>
<td>1. yes 2. no</td>
<td></td>
</tr>
<tr>
<td>2. Rapid (if control RPR) test result</td>
<td>[ ]</td>
</tr>
<tr>
<td>1. positive 2. negative</td>
<td></td>
</tr>
</tbody>
</table>

**If negative go to q12**

| 3. If positive, did she receive the 1st dose of | [ ] |
| penicillin? | |
| 1. yes 2. no | |
| 4. If positive, was the infection confirmed with | [ ] |
| RPR/TPHA? | |
| 1. confirmed 2. not confirmed | |
5. If confirmed, RPR titer:  1:__________________  1:[ ][ ]

6. If confirmed, did she receive adequate treatment?
   1. yes    2. no

7. Did the partner receive treatment?  [ ]
   1. yes    2. no

**Follow-up control**

8. Follow-up1 RPR titer:  1:__________________  1:[ ][ ]

9. Did she receive additional treatment?  [ ]
   1. yes    2. no

10. Follow-up2 RPR titer:  1:__________________  1:[ ][ ]

11. Did she receive additional treatment?  [ ]
    1. yes    2. no

12. **Was the sample sent to ref/lab for quality control?**  
    1. yes    2. no

13. If yes, RPR/TPHA test result

    1. positive    2. negative

14. If yes, RPR titer:  1:__________________  1:[ ][ ]

Investigator’s name ________  Signature ________
Date ________________
### 3.3 Follow-up 1 form at the third trimester

**STATE RESEARCH CENTRE ON MATERNAL AND CHILD HEALTH AND HUMAN REPRODUCTION ULAANBAATAR, MONGOLIA**

**Comparison of “one-stop” versus “conventional” service on antenatal syphilis screening in Ulaanbaatar, Mongolia**

<table>
<thead>
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<td>ANC clinic number</td>
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<tr>
<td>Subject number</td>
</tr>
<tr>
<td>Group:</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>TEST RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Gestational age at second testing: weeks</td>
</tr>
<tr>
<td>2. Syphilis testing at 3rd trimester:</td>
</tr>
<tr>
<td>2.1. yes</td>
</tr>
<tr>
<td>3. Rapid (if control RPR) test result</td>
</tr>
<tr>
<td>3.1. positive</td>
</tr>
</tbody>
</table>

*If negative go to q13*

<table>
<thead>
<tr>
<th>4. If positive, did she receive the 1st dose of penicillin?</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1. yes</td>
</tr>
</tbody>
</table>
5. If positive, was the infection confirmed with [ ]
   RPR/TPHA?
   1.confirmed  2.not confirmed

6. If confirmed, RPR titer:  1:…………………..  1:[ ][ ]

7. If confirmed, did she receive adequate [ ]
   treatment?  1.yes  2.no

8. Did the partner receive treatment?  [ ]
   1.yes  2.no

Follow-up control

9. Follow-up1 RPR titer:  1:…………………..  1:[ ][ ]

10. Did she receive additional treatment?  [ ]
    1.yes  2.no

11. Follow-up2 RPR titer:  1:…………………..  1:[ ][ ]

12. Did she receive additional treatment?  [ ]
    1.yes  2.no

13. Was the sample sent to ref/lab for quality
    control?  1.yes  2.no

14. If yes, RPR/TPHA test result
    1.positive  2.negative

15. If yes, RPR titer:  1:…………………..  1:[ ][ ]

Investigator’s name  _________  Signature  _________
Date  ________________
3.4 Follow-up 2 form at delivery

Comparison of “one-stop” versus “conventional” service on antenatal syphilis screening in Ulaanbaatar, Mongolia

<table>
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<th>FOLLOW UP 2 FORM</th>
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<td>[ ] [ ]</td>
</tr>
<tr>
<td>Subject number</td>
<td>[ ][ ][ ][ ]</td>
</tr>
<tr>
<td>Group: 1.Intervention 2.Control</td>
<td>[ ]</td>
</tr>
<tr>
<td>Delivery clinic:</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TEST RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Gestational age at delivery: .......... weeks</td>
</tr>
<tr>
<td>2. Syphilis testing at delivery:</td>
</tr>
<tr>
<td>1. yes 2. no</td>
</tr>
<tr>
<td>3. RPR test result</td>
</tr>
<tr>
<td>1. positive 2. negative</td>
</tr>
</tbody>
</table>

If negative go to q13

4. If positive, was the infection confirmed with [ ] RPR/TPHA?

1. confirmed 2. not confirmed
5. If confirmed, RPR titer: 1: ............ 1:[ ][ ]
6. If confirmed, did she receive treatment? [ ]
   1. yes 2. no
7. Did the partner receive treatment? [ ]
   1. yes 2. no
8. Infant status
   1. normal
   2. with low birth weight
   3. preterm
   4. stillbirth
   5. neonatal death
   6. others, specify ________________
9. Confirmed congenital syphilis:
   1. yes 2. no
10. Did the baby receive adequate treatment?
    1. yes 2. no

Investigator’s name __________ Signature __________
Date ________________
Appendix 4: Laboratory tests

Standard Operating Procedure of Standard SD Bioline Syphilis 3.0

1. Remove the test from the foil pouch and place on a flat dry surface
2. Slowly add 20 µl of whole blood to the sample well
3. Add 3 drops of assay diluents to the sample well
4. Read the test at 5-20 minutes as follows:

Negative result

The presence of only one band within the result window indicates a negative result

Positive result

The presence of two colour bands ("T" and "C") within the result window, no matter which band appears first, indicates a positive result for TP antibodies.

Invalid result

If the purple colour band is not visible within the result window after performing the test, the result is considered invalid.
**RPR test:** A 10 ml venous blood sample was collected into a plain vacuntainer and centrifuged for 10 minutes at 2000g. A standard RPR 18 mm circle card test (Omega Diagnostics, Alva, United Kingdom) was carried out, mixing one drop of serum with one drop of RPR reagent, mixing on a shaker for 8 minutes, and read in the best available light. Positive and negative control sera were included in each day’s testing. All positive RPR sera were further analyzed by serial twofold dilutions of serum in physiological saline up to 1:1024. The highest dilution showing flocculation was reported. To determine the serum end point titers to the haemagglutination assay, all sera positive in the qualitative assay were quantitatively tested in twofold dilutions (1:80 up to 1:5160) in absorbing diluents (a mixture of sonicated cell membranes from sheep erythrocytes, normal rabbit testicular extract, sonicated Reiter treponemes, and normal rabbit serum). Results were reported as the highest dilution giving haemaglutination.

**TPHA test:** TPHA assay (Omega Diagnostics, Alva, United Kingdom) was performed on all RPR positive sera. The sera were diluted to 1/160 and mixed with sensitized and unsensitized red blood cells. This was read after 1 hour at room temperature. Sera were considered positive if agglutination occurred with sensitized cells only. Samples will be considered void if agglutination occurred with unsensitized cells.
Appendix 5: Treatment of neonatal syphilis

Treatment of neonatal syphilis

(Sexually Transmitted and other Reproductive Tract Infections: A Guide to Essential Practice WHO RHR-2005, pages 90-91)

Mother's VDRL status - positive

Infant with signs of congenital syphilis

- Aqueous crystalline penicillin benzyl penicillin 100,000-150,000 units/kg of body weight per day, administered as 50,000 units/kg of body weight, intramuscularly or intravenously, every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days.

OR

- Procaine benzyl penicillin 50,000 units/kg of body weight, intramuscularly in a single dose for 10 days.

Infant without signs of congenital syphilis

Benzathine benzyl penicillin 50,000 units/kg of body weight, intramuscularly in a single dose.
Appendix 6: Manuscripts

Manuscript I: Feasibility of one-stop antenatal syphilis screening in Ulaanbaatar, Mongolia: women and providers perspectives.

(This manuscript has been accepted for publication in the Southeast Asian Journal of Tropical Disease and Public Health.)

Bayalag Munkhuu, MD, MSc1, Tippawan Liabsuetrakul, MD, PhD2, Edward McNeil, MSc3, Radnaabazar Janchiv MD, PhD4

1, 4 Department of Human Reproduction and Medical Genetics, State Research Center on MCH, Ulaanbaatar, Mongolia

2, 3 Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand

Correspondence: Bayalag Munkhuu, MD, MSc.

Department of Medical Genetics and Human Reproduction, State Research Center on Maternal and Child Health
Amarsanaa Street, Bayangol District, Ulaanbaatar, Mongolia PO box 24/677
Tel: +976 99088562, Fax: +976 11 362886,
E-mail address: baymun2001@yahoo.com
Abstract

Congenital syphilis can be prevented by antenatal syphilis screening; however, complexity in the delivery of service facilitates low screening, treatment and thus prevention. One-stop antenatal syphilis screening service, which includes rapid testing and case management, is the proposed method to overcome this problem; however, its feasibility needs to be tested in accordance with the effectiveness. In the study, opinions and level of satisfaction from antenatal women and their providers regarding the one-stop service at two antenatal clinics in Ulaanbaatar, Mongolia were assessed. The study found that the majority of 246 women were satisfied on the service. The mean aggregate satisfaction score derived from 11 questions on specific aspects of satisfaction was 3.2. The providers were also satisfied and most of them reported that they did not encounter any significant problems to either delay or hamper the other routine services. However, all providers agreed that the one-stop service is time consuming and leads to high staff workloads and needs good clinical management. In addition, they preferred to treat husbands presumptively to avoid the possibility of diagnosing couples with discordant syphilis, which may lead to possible violence. One-stop service is feasible in Ulaanbaatar, Mongolia in the women or providers' perspectives.

Key words: antenatal syphilis screening, feasibility, Mongolia, one-stop service, satisfaction
INTRODUCTION

Early detection and treatment of syphilis in pregnant women through universal antenatal screening is a standard measure for preventing congenital syphilis (WHO, 2001; WHO, 2007). Although the conventional non-treponemal rapid plasma regain (RPR) test has been used successfully, it requires appropriate equipment and regimen storage, well trained laboratory staff, followed by confirmatory Treponema pallidum hemagglutination assay (TPHA) for a reactive sample, the results of which are not immediately available. Therefore, the conventional tests are not suitable for primary care and their use is largely limited to referral laboratories (Peeling and Ye, 2004).

Despite the existence of a national policy regarding antenatal syphilis control and free RPR syphilis testing for pregnant women in Mongolia, the coverage of antenatal syphilis screening (ASYS) is relatively low (Ministry of Health Mongolia, 2008, Munkhuu et al, 2006a). Congenital syphilis is a reflection of the lack of a screening system in the country where almost all pregnant women receive antenatal care (ANC) services at least once during their pregnancy period. Congenital syphilis was recorded in 2 new case reports in 1995 and has continuously increased to 51 new case reports in 2006 (Ministry of Health, Mongolia, 2008). Current regulations regarding ASYS in Mongolia, stipulate that only a few specialized laboratories for sexually transmitted infections (STIs) are allowed to perform the syphilis screening
tests and only venereologists are authorized to treat syphilis-infected pregnant women and undertake contact tracing. Therefore, most ANC clinics rely on syphilis testing using RPR with TPHA confirmation at referral laboratories. This requires antenatal clients to make extra return visits, which may lead to long distance travel in order to be tested for syphilis or to obtain their test results, thus missing the opportunity for ASYS (Munkhuu et al, 2006b). To overcome the need of a return visit, more efficient and client friendly services, such as a one-stop antenatal syphilis screening service, are needed.

The one-stop service, which includes standard ANC service, on-site rapid syphilis test, prompt case management and counseling (given in the same visit and setting), provides a solution of the disassociation between ANC and ASYS services and testing and administering treatment. In some countries, on-site rapid syphilis tests increased the coverage of screening among pregnant women, consequently reducing risks of congenital syphilis (Bronzan et al, 2007; Garcia et al, 2007; Montoya et al, 2006). The effectiveness of the one-stop service should be evaluated by a cluster randomized trial; however, the one-stop service is a new policy which needs efforts of ANC providers. Thus the feasibility of this new policy needs to be evaluated. This feasibility paper is a part of the main trial on one-stop service for antenatal syphilis screening and prevention of congenital syphilis in Ulaanbaatar, Mongolia to ensure whether the one-stop service is feasible and accepted by the women and providers.
MATERIALS AND METHODS

The feasibility study was part of the cluster randomized controlled trial on comparing the effectiveness of one-stop versus conventional services on ASYS in Ulaanbaatar, Mongolia (Munkhuu et al, 2009). To ensure that the one-stop service is accepted by both antenatal women and providers, or needs to be modified for appropriateness, the feasibility was assessed and evaluated in the one-month run-in period of the aforementioned trial. The study is an explorative study and not designed to test hypotheses; rather it is intended to describe the perspectives of women and providers, including their opinions, problems and satisfaction on the one-stop service. This study used a combination of quantitative and qualitative approaches and was conducted at the two antenatal clinics in Ulaanbaatar, Mongolia. The sample size was calculated based on an estimated 80% of feasibility and satisfaction of one-stop services with a precision of 5%. All providers were interviewed. All antenatal women requiring ASYS services at the first ANC visit and third trimester of gestation during the run-in period of July to August 2007 were approached to participate. A total of 246 eligible consenting (written) women were recruited into the study.

Preparatory phase

A two-day training workshop for the obstetrician-gynecologists (OB-GYNs) and nurses of both clinics was arranged focusing on the importance of decentralizing the ASYS service, and
conducting the one-stop services, such as the on-site rapid syphilis test, reading the test results, ethical issues, counseling, data collection and filling forms. Another two-day refresher training workshop for particular OB-GYNs was arranged emphasizing maternal and congenital syphilis and physical examinations and case management of syphilis positive cases, including treatment, counseling and contact tracing. In order to assure a correct and reliable reading of the test, a manual was distributed to ensure standardization of readings to all the trained ANC providers. Both clinics were supplied with necessary supplies and regimens, such as lancets, rapid tests and benzathine penicillin.

**Data collection**

The one-stop service comprised (i) on-site testing for syphilis using rapid treponemal syphilis test; (ii) immediate treatment for women testing positive and their sexual partners; and (iii) pre-test and post-test counseling. After informed consent, pre-test counseling was provided to rapid test when the women attended for ANC service at their first visit and third trimester of gestation. Blood for the rapid test was collected by finger prick and tested with SD Bioline Syphilis 3.0 (Standard Diagnostics Inc., Kyunggi-do, Korea) according to the manufacturer’s specifications, with results known in 10-15 minutes. Women testing positive by RT had blood collected by venipuncture and sent to the reference laboratory (STI Center’s
laboratory) for confirmation by RPR titer (Omega Immutrep-RPR, Omega Diagnostics, Alva, UK). Reactive samples were confirmed by TPHA (Immutrep TPHA®, Omega Diagnostics, Alva, UK). Positive RPR and TPHA tests were gold standard for diagnosis of syphilis. All women diagnosed with syphilis, without a history of drug allergy, were treated free of charge with benzathine penicillin G 2.4 million units intramuscular in a single dose immediately. If RPR and TPHA were confirmed, the women were given the subsequent two doses of penicillin at weekly intervals. Otherwise, no additional doses were given. Although contact tracing is mandatory in Mongolia, the contact tracing was based on voluntary basis of the infected women and the agreement between women and doctor’s preferences. The women’s partners were invited to come any time as soon as possible to the clinics for free testing and treatment.

A self-administered satisfaction survey on the one-stop service was done after post-test counseling using a questionnaire for women with positive and negative test results. Women were asked about their opinions and satisfaction with the one-stop service using 4 point score (1 point for “strong disagreement” and 4 points for “strong agreement” or for reverse scoring i.e. 1 represented “strong agreement” with the statement and 4 represented “strong disagreement”). Also women were asked about their opinion using open-ended questions “What do you find most satisfied with and what is the main reason?”.
In-depth interviews on the one-stop service among all available providers were carried out to identify the types of challenges/problems which needed to be re-organized and the acceptance of providers in offering the service. Providers’ year of service and ANC experiences and approximate number of one-stop services were collected.

**Data analysis**

The quantitative data were entered into a computer using Epidata 2.0 (The EpiData Association Odense, Denmark) and analyzed with R 2.8.0 (The R foundation for Statistical Computing, Vienna, Austria). Descriptive statistics was used for demographic characteristics and satisfaction scores. To assess the associations between clients’ characteristics and overall satisfaction scores, independent sample t-test and one-way analysis of variance were used. Multiple linear regression models with stepwise method were used to ascertain which factors were independently associated with the overall satisfaction score. Data from in-depth interview were audio recorded and transcribed verbatim then the contents analyzed by code mapping and described qualitatively in the text.

The main trial was reviewed and approved by the Institutional Ethics Committee of Mongolia, the corresponding health authorities where the trial was implemented, the Scientific and Ethical Review Group of the Special Programme of Research, Development and Research Training in Human Reproduction and Ethics
Review Committee, World Health Organization (WHO), the Institute Ethics Committee of Faculty of Medicine, Prince of Songkla University, Thailand.
RESULTS

A total of 246 women were eligible for ASYS services at their first ANC visit or third trimester of gestation at two ANC clinics during the run-in period. Table 1 shows background characteristics of the participating women. The age of the women ranged from 17 to 44 years old (mean ± SD 27.3 ± 5.9). The all antenatal women accepted the one-stop service and tested for syphilis. All women received their results and counseling from ANC providers. Most (242/246) of the women tested negative with the rapid test. The four positive cases all accepted their test results with counseling and received single dose of benzathine penicillin. The sera of four women were retested by RPR and TPHA titers and all returned for their confirmatory test results on the next day. Three women’s infections were subsequently confirmed and one found to be a false positive because she had been tested syphilis positive before pregnancy but did not inform the provider during counseling. All sexual partners of women having positive results received treatment. Follow-up RPR titer control and subsequent two doses of penicillin were given to the three women and their husbands on weekly doses.

Client satisfaction on the one-stop service

Women’s satisfaction level of providing one-stop service according to agreement or disagreement to 11 opinion statements is summarized in Table 2. All women preferred receiving results in
the same day and were satisfied with the rapid test. All questions had an average satisfaction score above 2.5 (range 2.6 to 3.8). The mean of the aggregate satisfaction scores of respondents was 3.2 with a standard deviation of 0.3, indicating that women were well satisfied with the rapid test.

From univariate analysis of the effect of women’s background characteristics on overall satisfaction, older age (p<0.001), higher education level (p<0.001), married (p=0.001), employed (p=0.012) and history of previous pregnancy (p<0.001) were associated with a higher score of satisfaction. No association with residency, history of previous induced abortion, adverse pregnancy outcome, gestational age at 1st ANC visit and STIs was detected. In multiple regression analysis, those with higher level of education (p<0.001) and history of previous pregnancy (p<0.001) showed higher overall satisfaction scores.

One hundred and sixty-three women gave answers to the open-ended question on the reasons of their satisfaction. The most frequent four answers were: reduction of extra travel, time and expenses related to transportation (87.8%), painless testing and rapid available result (76.7%), providers’ counseling (41.8%) and being able to discuss their problems with the providers or counseling (36.8%).
In-depth interviews with providers on one-stop service

All 13 providers, including six OB-GYNs and seven nurses in the study settings, agreed to participate. The OB-GYNs working experience ranged from 5 to 25 years (median 11 years) while the nurses ranged from 2 to 16 years (median 6 years). The ANC experience of OB-GYNs ranged from 2 to 20 years (median 12 years) while those of nurses ranged 2 to 12 years (median 5 years). Providers’ opinions on one-stop service in ANC clinic were categorized into 3 main areas: one-stop service, challenges/problems experienced by the providers and acceptance in offering one-stop service.

One-stop service

All providers agreed that ASYS must be an integral part of ANC and other maternal and newborn health services. They also agreed that linking ASYS with ANC service, as well as other reproductive health initiatives, was essential to controlling maternal syphilis at delivery as well as congenital syphilis.

All providers supported one-stop service with the reason that women would suffer with an additional journey to STI laboratories for testing. They quoted that “We usually advise antenatal women to go for the test, but they are reluctant because it is far, they say if it (the testing) was here they could have done it”, “In the remote areas women have time and travel difficulties getting to the STI laboratories and easily delay or
ignore it” or “Of course, for pregnant women who have to attend another clinic again for testing, results clarification or treatment undoubtedly it is inconvenient especially for the women where geographic barriers are present”

Most providers highlighted that the introduction of the one-stop service into ANC clinics would not create any significant change in the existing infrastructure of services and procedures would not face major problems. For example, one OB-GYN said “Since Mongolian antenatal clinics are well organized with good facilities and sufficient number of providers the introduction of the new service should be straightforward”.

Challenges/problems experienced by the providers

The majority of providers reported they did not encounter significant problems to either delay or hamper their routine services. In addition, no new space was needed for the one-stop service. However, most providers agreed that the one-stop service was time consuming and needs good clinical management. According to one OB-GYN, she mentioned that “Each woman needs at least 40-60 minutes inclusive of pre-test counseling, testing, results, examination and post-test counseling for the one-stop service. For positive cases of course it will take longer. However, if we can arrange the service as is one part of the standard ANC procedures, it will be good solution.”
Most providers agreed that the one-stop service had high workloads, although it’s the benefits far outweighed any disadvantages. They referred to “There is more work now because the person managing the one-stop service is still expected to have other duties in the clinic” quoted by an OB-GYN, while a nurse said “It has affected the services because sometimes it causes delays in serving other patients since I’m the only nurse in the procedures room” or “After starting this service, it has made my work beyond the normal ... However, I am happy that none of my patients will be missed for syphilis testing and treatment” quoted by an OB-GYN.

One nurse at the clinic reported that there were occasions where extra nursing staff were required to meet the one-stop service pledge (same visit service) as “It was felt that the trend of one-stop service would face manpower problems if antenatal clients will be more than now in the future”. Another nurse concerned if the room where the rapid test was placed for result turnover should be left open where the result of the test might be read by people passing by.

All providers were concerned about the supplies of one-stop service in the future. The example of one statement mentioned by an OB-GYN is “The supplies this time are provided through your project thus we had no problem with the shortages of essential supplies, such as rapid tests, lancets and penicillin. If we will extend the one-stop service in the future, who will provide the
supplies? We do not want the one-stop service to be only a [one-time] study“.

Acceptance in offering one-stop service

All providers agreed that the rapid test was very easy to use. The technique required to use the rapid test was straightforward, the time needed minimal, and would not be a concern for them. The four women who tested positive by rapid test during the study period had been well prepared to accept a positive status. All OB-GYNs agreed that the extra workload that is offering of counseling, performing clinical examination and interpretation of test results was no more complicated than their routine work. All nurses also reported that offering the rapid test was a satisfying experience for them. A nurse quoted that “The whole procedure of counseling and testing by rapid test was conducted by one single ANC provider who therefore could provide a comprehensive package of service to individual woman from pre-test through post-test counseling. Also, the women have a chance to receive information and counseling again from OB-GYNs. This significantly facilitated connection building between the women and the providers”.

The majority of the providers said that contact tracing by ANC doctors are better than others because antenatal women trust antenatal doctors more and usually they come with their husbands for ANC: according to an OB-GYN “Contact tracing of positive cases would be the best choice since most husbands of our clients wait
for them in the clinic”. However, some providers expressed concern regarding testing the husbands of positive cases. As they said “If there is suddenly discordance between the women and husbands syphilis test result, then what should we do? I felt it was difficult to explain clearly the implications to the clients. Positive test results could easily fuel family quarrels and even lead to violence, so it may be better to ask the husband first for treatment without doing any prior tests”.

All providers expressed confidence in offering one-stop service in the ANC clinic setting. They also felt confident if they were asked to train other providers to offer one-stop service. The issues that concern themselves were case management, counseling skills, and performing the tests.
Overall, the study results showed that one-stop service with rapid on-site syphilis testing, prompt treatment of syphilis cases, contact tracing and counseling by ANC providers at ANC clinics in Ulaanbaatar, Mongolia were feasible and well accepted among both women and providers.

In developing countries, one of the greatest gaps of syphilis control in pregnant women and congenital syphilis prevention is the women coming for ANC remain unscreened for syphilis, thus remain untreated (Hossain, 2007). To address this challenge, an alternative integrated ASYS model that includes on-site syphilis screening, treatment and counseling was introduced. To examine the effectiveness of this model, several studies with different designs were carried out and they have shown that the model can dramatically improve the screening coverage and consequently reduce the risk of congenital syphilis (Bronzan et al, 2007; Garcia et al, 2007; Gloyd et al, 2007; Montoya et al, 2006). However, these studies did not focus on the perspectives and level of satisfaction from both the antenatal women and providers on the new model. Therefore, direct comparisons of our results with the previous studies are difficult.

Some studies reported a number of logistical problems with the decentralized model, such as complexity of the on-site RPR syphilis testing, difficulty reading the test results and women leaving before receiving their results (Fonck et al, 2001;
Jenniskens et al, 1995; Myer et al, 2003; Patel et al, 2001). In contrast, in our study we used rapid treponemal tests where results are obtained within 10-15 minutes. In a Bolivian study, where the rapid syphilis test was used for the ASYS, the new model (one-stop service) was not only an effective intervention for detection and treatment of syphilis cases but also feasible in terms of acceptance by providers and women (Garcia et al, 2007).

In our study, the findings of the women’s satisfaction survey were very encouraging by the reasons that the one-stop service reduced extra travel, time and expenses related to transportation. This was in accordance with our previous study which revealed that the distance from home to laboratory was a barrier of universal ASYS coverage (Munkhuu et al, 2006a). Moreover, the same preferences of collection of blood by finger prick than venipuncture were also reported in a study by Liu et al, (2003).

Apart from client satisfaction, good acceptance on the side of care providers also supports the use of a one-stop service at ANC clinics. The challenge of logistic arrangements on offering one-stop service, such as extra time required and increased staff workloads, is consistent with other studies (Deperthes et al, 2004; Gloyd et al, 2007). However, the providers in our study accepted the challenges and offered some ideas for overcoming these challenges. Some providers suggested we modify the contact tracing plan to treat males presumptively for ethical reasons to
avoid the possibility of diagnosing couples with discordant syphilis results in order to avoid possible conflicts since it leads to violence (Díaz-Olavarrieta et al, 2007).

The limitations of this study were the fact that there were no control findings of conventional ASYS, small sample size of positive cases and a short period of evaluation. While the present study aims to describe the feasibility of one-stop service, the lack of control subjects did not allow us to compare the satisfaction of the conventional service. However, we interviewed both women and providers after experiencing the one-stop services. Another limitation is the short time period for offering the one-stop service in the two clinics, thus the providers did not gain enough experience. However we could interview all eligible women and providers, including nurses in the both clinics, to gather their opinion during the study period and some ideas were obtained through this study.

In conclusion, one-stop service of ASYS is feasible and would not face any critical obstacles in Ulaanbaatar, Mongolia in terms of women or providers' perspectives and their satisfactions. The logistical arrangements such as time and manpower challenges and contact tracing plan should be considered in the cluster randomized trial.
ACKNOWLEDGMENTS

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REFERENCES


Montoya PJ, Lukehart SA, Brentlinger PE et al. Comparison of the diagnostic accuracy of a rapid immunochromatographic test and


### Table 1. Background characteristics of the participating women

<table>
<thead>
<tr>
<th>Women characteristics</th>
<th>Subjects (n=246)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td><strong>Education level</strong></td>
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<td></td>
</tr>
<tr>
<td>never attended school/primary</td>
<td>2</td>
<td>0.8</td>
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<tr>
<td>secondary and/or technical</td>
<td>166</td>
<td>67.5</td>
</tr>
<tr>
<td>university and/or equivalent</td>
<td>78</td>
<td>31.7</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>married/cohabiting</td>
<td>211</td>
<td>85.8</td>
</tr>
<tr>
<td>single/widow/separated</td>
<td>35</td>
<td>14.2</td>
</tr>
<tr>
<td><strong>Residency</strong></td>
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<td></td>
</tr>
<tr>
<td>Ulaanbaatar city</td>
<td>106</td>
<td>43.1</td>
</tr>
<tr>
<td>registered migrant</td>
<td>118</td>
<td>48.0</td>
</tr>
<tr>
<td>unregistered migrant</td>
<td>22</td>
<td>8.9</td>
</tr>
<tr>
<td><strong>Employed</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>92</td>
<td>37.4</td>
</tr>
<tr>
<td><strong>Having previous pregnancy</strong></td>
<td>162</td>
<td>65.9</td>
</tr>
<tr>
<td><strong>Number of live births</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>96</td>
<td>59.3</td>
</tr>
<tr>
<td>&gt;2</td>
<td>46</td>
<td>40.7</td>
</tr>
<tr>
<td><strong>Mean gestational age at first ANC (SD)</strong></td>
<td>12.1 (4.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Previous STIs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>8.9</td>
</tr>
<tr>
<td><strong>History of previous miscarriage, preterm birth, stillbirth and early neonatal death</strong></td>
<td>6</td>
<td>3.7</td>
</tr>
<tr>
<td><strong>Syphilis test performed at 3rd trimester</strong></td>
<td>107</td>
<td>43.5</td>
</tr>
</tbody>
</table>
Table 2. Women’s satisfaction level

<table>
<thead>
<tr>
<th>No. (%) of women (n = 246)</th>
<th>Mean score (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strongly agree</strong></td>
<td><strong>Agree</strong></td>
</tr>
<tr>
<td>Positive opinions</td>
<td></td>
</tr>
<tr>
<td>I prefer receiving syphilis testing the same place as ANC visit</td>
<td>211 (85.8)</td>
</tr>
<tr>
<td>I prefer receiving my results the same day</td>
<td>196 (79.7)</td>
</tr>
<tr>
<td>I prefer receiving counseling from ANC providers</td>
<td>76 (30.9)</td>
</tr>
<tr>
<td>I prefer receiving syphilis treatment at the ANC clinics</td>
<td>67 (27.2)</td>
</tr>
<tr>
<td>I satisfied with information provided on syphilis testing</td>
<td>55 (22.4)</td>
</tr>
<tr>
<td>I would rather have my finger stuck than have blood drawn from my vein.</td>
<td>43 (17.5)</td>
</tr>
<tr>
<td></td>
<td>No. (%) of women (n = 246)</td>
</tr>
<tr>
<td>-----------------------------------------------------------------</td>
<td>----------------------------</td>
</tr>
<tr>
<td></td>
<td>Strongly agree</td>
</tr>
<tr>
<td>I understand the result of my rapid test.</td>
<td>100 (40.7)</td>
</tr>
<tr>
<td>I would recommend one-stop service to a friend</td>
<td>91 (37.0)</td>
</tr>
<tr>
<td>I am satisfied with the one-stop service</td>
<td>118 (48.0)</td>
</tr>
</tbody>
</table>

**Negative opinions**

<p>| | | | | | |</p>
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<tbody>
<tr>
<td></td>
<td>Strongly agree</td>
<td>Agree</td>
<td>Disagree</td>
<td>Strongly disagree</td>
<td></td>
</tr>
<tr>
<td>I spent long time in the service room*</td>
<td>0 (0.0)</td>
<td>13 (5.0)</td>
<td>149 (50.2)</td>
<td>84 (43.9)</td>
<td>3.2 (0.6)</td>
</tr>
<tr>
<td>I found the rapid testing stressful and less confidential*</td>
<td>34 (13.8)</td>
<td>61 (24.8)</td>
<td>126 (51.2)</td>
<td>25 (10.2)</td>
<td>2.6 (0.8)</td>
</tr>
</tbody>
</table>

Satisfaction score: ranges 1-4, * reverse scaling
Manuscript II: One-stop service for antenatal syphilis screening and prevention congenital syphilis in Ulaanbaatar, Mongolia: a cluster randomized trial

(This manuscript has been accepted for publication in the Sexually Transmitted Disease Journal.)

Bayalag Munkhuu MD, MSc*, Tippawan Liabsuetrakul MD, PhD†, Virasakdi Chongsuvivatwong MD, PhD’, Edward McNeil MSc†, Radnaabazar Janchiv MD, PhD*

* Department of Human Reproduction and Medical Genetics, State Research Center on Maternal and Child Health, Ulaanbaatar, Mongolia
† Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90112, Thailand

Correspondence to: Bayalag Munkhuu MD, MSc
Department of Medical Genetics and Human Reproduction, State Research Center on Maternal and Child Health, Amarsanaa Street, Bayangol District, Ulaanbaatar, Mongolia
Tel:+ 976-99088562, Fax:+976-11-362886
E-mail address: baymun2001@yahoo.com

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**Short summary:** One-stop services increased the detection rate of syphilis, treated more syphilis infected antenatal women and their partners and effectively reduced that rate of congenital syphilis.
Abstract

Background: This cluster randomized trial was performed to test whether one-stop service could better prevent congenital syphilis than the conventional antenatal screening service in Mongolia.

Methods: Out of 14 antenatal clinics in 6 districts of Ulaanbaatar, 7 were randomly selected for the one-stop service and the remaining for the conventional service. Intervention clinics provided on-site rapid syphilis testing and immediate treatment for positive cases and their partners. In control clinics, syphilis screening services with routine off-site rapid plasma regain testing and case management were followed. Analysis was intention to treat.

Results: Of 3,850 antenatal women recruited in each group, the proportion of syphilis testing at the 1st visit and 3rd trimester was over 99% in the intervention group and 79.6% and 61.5% in the control group, respectively (p<0.001 for both periods). Correspondingly, syphilis cases detected in the intervention group was 73 (1.9%) and 20 (0.5%) for the 1st visit and 3rd trimester, respectively, and 27 (0.9%) and 2 (0.08%) in the control group and 98.9% (92/93) of the detected cases in the intervention group and 89.6% (26/29) in the control group were adequately treated (p=0.02). The corresponding treatment rates for sexual partners were 94.6% and 55.2% (p<0.001). One congenital syphilis case out of 3,632 deliveries in the intervention group, compared to 15 out
of 3,552 in the control group, was diagnosed, a reduction of 93.5% (95% confidence interval 66.0% to 98.6%).

Conclusions: One-stop services increased the detection rate of syphilis, treated more positive women and their partners and effectively reduced the rate of congenital syphilis.

Key words: antenatal syphilis screening, cluster randomized trial, congenital syphilis, one-stop service, Mongolia
Introduction

Congenital syphilis is a serious but preventable disease. Antenatal syphilis screening (ASYS) is one of the most effective ways for prevention and most countries do have policies providing for universal screening for syphilis in pregnant women. However, for various reasons, in many developing countries the policies are not systematically implemented, resulting in failure of the syphilis seropositive couples to receive treatment during the course of the pregnancy.1-3

The rapid increase in number of cases of active syphilis, as well as other sexually transmitted infections (STIs), among adults during the past decades can be attributed to the rapid social, economical and behavioral changes in the country.4,5 As a result, the incidence of congenital syphilis has been increasing and consequently is raising a public health concern in Mongolia. Congenital syphilis was recorded in 2 new case reports in 1995 and has continuously increased to 51 new cases in 2006.4 The actual number was likely to be much higher since the diagnosis was based on clinical criteria only. Adverse pregnancy outcomes, such as miscarriages and stillbirths due to maternal syphilis, are usually not diagnosed and thus underreported.

The current resurgence of congenital syphilis is an indication of the difficulties experienced by basic services of antenatal care (ANC) and ASYS in Mongolia. There are approximately 55,000 births reported annually and about 98% of pregnant women
attend antenatal services. Although syphilis screening for pregnant women is usually provided free of charge in ANC services, only a fraction is actually screened. In 2006, the ASYS coverage was reported in 77% in Ulaanbaatar, the capital city of Mongolia, and 60.9% nationally; however, this rate was less than 50% among those who live in rural remote regions or among nomadic women.

Routine ASYS regulations in the country stipulate that only a few specialized laboratories for STIs are allowed to perform syphilis tests and only venereologists are authorized to treat syphilis infected pregnant women and undertake contact tracing. This organization of the services has led to antenatal women needing to travel to the laboratories, situated at the District General Hospitals or at the National Center of Communicable Diseases (NCCD). The tests are done in batches, resulting in delay of diagnosis and treatment and inconvenience to the clients discouraging them from actively participating in the prevention of congenital syphilis policy.

Although the ANC coverage is high and ASYS is provided free of charge, around a quarter of pregnant women were not tested and thus missed being treated. This indicates a need to improve the services of which the complexity of ASYS was mainly hypothesized. A one-stop service for antenatal syphilis screening with on-site rapid syphilis test, prompt treatment of syphilis cases and their sexual partners and counseling at the same place or antenatal clinics was therefore planned. The aim of this trial was to test
whether the one-stop service could better prevent congenital syphilis than the conventional antenatal syphilis screening service in Ulaanbaatar, Mongolia.

Materials and methods

Study design

Since the intervention was based on practices, rather than individuals, it was considered impossible to randomize the individual patients into two screening options in the same clinics. A cluster randomized trial was thus applied.

The study protocol was reviewed and approved by the Institutional Ethics Committee of Mongolia, the corresponding health authorities where the trial was implemented, the Scientific and Ethical Review Group of the Special Programme of Research, Development and Research Training in Human Reproduction and Ethics Review Committee, World Health Organization (WHO), the Institute Ethics Committee of Faculty of Medicine, Prince of Songkla University, Thailand.

Study areas and participants

There are approximately 11,000 live births per year in Ulaanbaatar, and 99% of these occur in 3 maternity hospitals and the State Research Centre on Maternal and Child Health (MCH Center). ANC services are provided by 16 antenatal clinics linked to six district general hospitals and MCH Center. The MCH Center
was excluded from sampling because the centre is responsible for the whole country, while two of the 16 antenatal clinics were also excluded due to a small attendance. Of the remaining 14 antenatal clinics, seven were randomly assigned into the intervention group. The rest were assigned to the conventional service group. Figure 1 shows locations of the 14 antenatal clinics and NCID in Ulaanbaatar. The identification of the intervention or control group was not shown and kept anonymously due to ethical issues.

All new ANC attendees with a single pregnancy were eligible for the study. Pre-defined exclusion criteria were: women known to be unable to return for the scheduled antenatal visit during the study period, living outside Ulaanbaatar, unwilling to give informed consent and absence of a willing guardian for underaged women.

**Preparatory phase**

ANC providers in both intervention and control clinics received training but the contents provided were different. Two separate workshops for the intervention and control groups were organized.

In the intervention clinics, the first two-day workshop was held for obstetrician-gynecologists (OB-GYNs) and nurses. The main agendas included highlighting the importance of decentralizing the ASYS service, logistics, the organization of the one-stop service
and case reporting. The second two-day workshop was also held for OB-GYNs and covered the specific knowledge on maternal and congenital syphilis, case detection and management, counseling and contact tracing. A manual of the test reading was distributed to all relevant providers in order to assure a correct and reliable interpretation of the rapid syphilis test results. The intervention clinics were supplied with the necessary materials, such as lancet, rapid syphilis tests and benzathine penicillin injectable sets.

In the control clinics, ANC providers (nurses and OB-GYNs) in the control clinics participated in a two-day training workshop on the project overview, logistics of the project and case reporting. The OB-GYNs received refresher training on the same topics as the intervention group to reduce the bias of training effect on our main outcomes. As with the intervention group, treatment of syphilis cases and their partners was given free of charge. Benzathine penicillin was supplied for treatment but not facilities for serological tests.

**Implementation phase**

In both intervention and control clinics, all pregnant women presenting to the antenatal clinics were checked by the nurses on their eligibility for entering the study. All eligible subjects were then approached, given information about the study and asked to join. Subjects who agreed were then asked to give informed consent to participate in the study. The syphilis tests were done
twice during pregnancy at the 1st antenatal visit and at the 3rd trimester of gestation. The third syphilis testing was provided immediately after delivery among the women who had been seronegative during ANC. Regardless of the group randomized to, all syphilis cases received three doses of benzathine penicillin on a weekly basis. Neonates of seropositive women were then examined and positive cases given and injection of benzathine penicillin following the WHO guidelines.

**ASYS in the intervention clinics**

The one-stop service included the following elements (i) on-site screening for syphilis using rapid treponemal syphilis tests at the 1st antenatal visit and at the 3rd trimester of gestation; (ii) immediate on-site treatment for seropositive women and their sexual partners with benzathine penicillin; and (iii) pre and posttest counseling.

Pretest counseling and interviews were carried out in a private counseling room. After the interview, about 10 µl of whole blood from all consenting new attendees was collected by finger prick. The on-site rapid test was assayed with SD Bioline Syphilis 3.0 (Standard Diagnostics Inc., Kyunggi-do, Korea) according to the manufacturer’s specifications. The results were available in 10-15 minutes. Women testing negative on the rapid assays were provided with posttest counseling by ANC providers and invited for second testing during the 3rd trimester of pregnancy. Women testing positive by the rapid test had their venous blood further
collected and sent to the reference laboratory. Women without a history of drug allergy were initially treated free of charge with initial dose of benzathine penicillin G 2.4 million units intramuscular. The confirmation test at the reference laboratory was carried out using Rapid Plasma Regain (RPR) titre (Omega Immunrep-RPR, Omega Diagnostics, Alva, United Kingdom) and the positive samples were further tested Treponema Pallidum Hemagglutination (TPHA) (Immutrep TPHA, Omega Diagnostics, Alva, United Kingdom). Women who tested positive on both RPR and TPHA tests were subsequently given two doses of benzathine penicillin at weekly intervals. The contact tracing was based on a voluntary agreement between the woman and the OB-GYN. The husbands/sexual partners were invited to come at their earliest convenience to the clinics for free treatment.

All women attending for ANC who had been seronegative at the first visit were retested by the rapid treponemal test at the 3rd trimester of gestation. Those women who were seropositive at the first visit, were retested by only RPR to detect possible re-infection. For quality control reasons, 10% of the sera negative samples and all positive sera were sent to the reference laboratory where the test was redone without awareness of the initial test results.

Asys in the control clinics

After being admitted to the antenatal clinic, a pregnant woman could visit any District General Hospital or the NCID for
free initial testing with RPR and, where necessary, TPHA confirmation test. The test result is normally collected by the woman and brought to the ANC service. Women testing positive for syphilis are sent to a venereologist for appropriate case management and follow-up control, including contact tracing and counseling. Routine treatment is three weekly doses (2.4 million international unit) of benzathine penicillin and this is given free of charge.

**Outcome assessments and case reporting**

The primary outcome of the study was (1) utilization of ASYS at the 1st antenatal visit and at the 3rd trimester of gestation; and (2) number of congenital syphilis cases. Adopting WHO’s criteria, congenital syphilis was defined if any the following existed: (i) neonate manifesting classic signs of congenital syphilis, such as hepatosplenomegaly, rash, condyloma lata and snuffles; (ii) neonate whose mothers have a syphilitic lesion at delivery; (iii) neonate born to mother with positive RPR and TPHA who are untreated or inadequately treated at delivery (if mothers received nonpenicillin therapy, or penicillin administered <30 days before the delivery), regardless of signs in the infant; (iv) neonate born to mother with positive RPR and TPHA whose serological response to penicillin was not documented or was equivocal (the definition of appropriate response for primary or secondary syphilis is a fourfold decline in non-treponemal titres by 3 months and for early latent syphilis is a fourfold decline in
non-treponemal titers by 6 months); (v) neonate with RPR titers fourfold or greater than the mother’s titer; and (vi) Treponemas seen in autopsy material by silver stain or darkfield in stillborns born to mother with positive RPR and TPHA.

The secondary outcome set included (1) detected syphilis cases; (2) adequate treatment (percentage of sero-positive cases completing three doses of benzathine penicillin before delivery) and (3) percentage of completely treated husbands/sexual partners of seropositive women.

In the study, syphilis cases are defined as the women attending for ANC who had positive rapid treponemal tests confirmed by RPR and TPHA in the intervention group or who had positive RPR confirmed by TPHA in the control group. At the second syphilis testing (at 3rd trimester) and third syphilis testing (after delivery), only new syphilis cases were reported.

**Statistical Analysis**

Most recently, 51 cases of congenital syphilis were diagnosed in 2006 in Ulaanbaatar. Without an intervention, the incidence of congenital syphilis was estimated at 6/1,000 and the aim of the intervention was to reduce this number to below 1/1,000. Using a significance level of 5%, a power of 80%, and assuming that the intra-class correlation is 0.001, as shown in a previous study, the required sample was calculated to be 3,183 per group (2-sided test) or 455 subjects per clinic. After
adjusting for an expected loss to follow-up rate of 20%, 550 subjects per clinic, a total of 3,850 subjects were required and recruited in each group.

Data were computerized using EpiData (The EpiData Association Odense, Denmark) and analyzed using R software (The R foundation for Statistical Computing, Vienna, Austria). The analysis was undertaken as intention to treat. Differences in the proportions of syphilis testing at the 1st antenatal visit and at the 3rd trimester of gestation, number of detected syphilis cases during the pregnancy, adequate treatment, treated partners and congenital syphilis were compared. Since the main outcomes were nested within clinics, Rao and Scott’s chi-square test in “survey” package was used in the univariate analysis. For multivariate analysis, a multilevel analysis was carried out having individual women at the first (lower level) and the clinic at the second level (higher) using the “lme4” package. Women’s characteristics were independent, explanatory variables.
Results

Recruitment started in August 2007 and all follow-up data was completed in August 2008. Figure 2 shows the flow of study clusters and eligible women throughout the trial. We collected follow-up data on 94.3% of enrollees at delivery in the intervention and 92.6% in the control. The proportion of overall missing did not vary between the groups (p=0.1). The study groups were well balanced for distribution of baseline characteristics, such as mean age, education and marital status; although significant differences were observed for gestational age at first ANC and multiple sexual partners (Table 1).

As shown in Figure 3, of 3,850 pregnant recruited in each group, the proportion of syphilis testing at the 1st visit were over 99% in the intervention and 79.6% in the control group (p<0.001). In the 3rd trimester, 94 (2.4%) and 27 (0.7%) women in the respective groups were lost to follow-up, all of whom had had a negative test at the first visit. Of the remaining 3,683 and 3,796 (not included previous seropositives at the 1st visit) who revisited at the 3rd trimester, 99.7% and 62.1% had the second test (p<0.001) in the intervention and control groups, respectively. In the corresponding two periods, 73 (1.9%) and 20 (0.5%) cases of syphilis were detected in the intervention group and 27 (0.9%) and 2 (0.08%) were in the control group (p<0.001 for first test and p=0.01 for second test).
Eventually, 98.9% (92/93) of the overall detected cases in the intervention and 89.6% (26/29) in the control group were adequately treated (p=0.02). The corresponding overall treatment rates of the sexual partners was 94.6% versus 55.2% (p<0.001). Only one congenital syphilis case out of 3,632 deliveries in the intervention group versus 15 out of 3,552 in the control (p=0.002) were ascertained at the end, a reduction of 93.5% (95% CI 66.0% - 98.6%). The only case of congenital syphilis in the intervention group was born to a late ANC (38 weeks of gestation) comer, a woman who had been seropositive in the 1st visit, and had received only single injection of benzathine penicillin and did not return until delivery. Thirteen women who tested positive by the rapid test assays during pregnancy, yet were negative at confirmation had unnecessarily received the first dose of penicillin at the antenatal clinics. Ten of them revealed that they had previously been treated for syphilis but the information was not obtained before RPR results were available.

Multilevel analysis was separately computed for main outcomes with the same set of independent variables that were significant with the univariate analysis. After adjustment, the primary and secondary outcomes were all significantly associated with the intervention except adequate treatment of positive cases. (Table 2)
Discussion

Our study provides evidence that one-stop service on ASYS implemented in antenatal clinics was more effective for the prevention of congenital syphilis. Almost all antenatal clients in the intervention clinics tested for syphilis at both time points of testing, resulting in more seropositive cases detected. A higher proportion of the syphilis infected women and their sexual partners were completely treated. Finally, the intervention resulted in a markedly lower number of congenital syphilis cases than the control group.

The need for a more effective alternative approach to ASYS is obvious since in many developing countries antenatal women remain unscreened for syphilis, thus remain untreated. To address the challenge to detect and treat syphilis infected antenatal women at their first ANC visit, an intervention on decentralized ASYS was developed and assessed in studies from some developing countries. The findings of the studies showed that the decentralized service of ASYS could detect and treat more maternal syphilis in pregnancy or could reduce congenital syphilis. One African study in 2003 documented a 75% decrease in rates of congenital syphilis after allowing for decentralized screening of maternal syphilis. Another South African study using decision-analytic cost-effectiveness modeling demonstrated that on-site rapid testing prevented over 80% of predicted cases of congenital syphilis.
Our randomized study demonstrates that one-stop service with on-site rapid treponemal syphilis test with treatment and counseling is able to increase the coverage of screening and improve the rate of case detection in women and their partners as well as facilitate completion of treatment and dramatically reduce the incidence of congenital syphilis. There were two previous randomized controlled trials to evaluate the one-stop service on ASYS; however, the findings of these studies could not be compared directly to our findings because the on-site syphilis tests were different. In a study of Bique et al., on-site RPR was compared to centralized RPR and showed a significant improvement of perinatal mortality in the on-site RPR arm. In contrast, the comparison of on-site and centralized RPR did not show an improvement in either the proportion receiving adequate follow-up or the perinatal loss rate in a study of Myer et al.

There are several reasons to explain how the one-stop service has played an important role in the reducing rates of congenital syphilis in the study. Firstly, on-site testing is convenient to women, resulting in universal ASYS coverage at both time points of testing. Conventional centralized services for ASYS in Mongolia require women to have at least one extra visit in order to be fully tested for syphilis and to make return visits to get their test results. This inconvenience leads to delay or loss of contacts and subsequently leaves a number of syphilis cases undetected and untreated. A study in Mozambique reported that the
similar intervention could increase the antenatal syphilis testing by over 90\%."\(^{16}\)

Secondly, once substantially increased syphilis screening coverage the intervention could detect a significant number of syphilis cases among antenatal clients. Besides demonstrating the success of detection rate in the intervention the study confirmed the previously reported comparatively high rates of syphilis among pregnant women in the country and the necessity of universal antenatal syphilis screening.\(^4,6\) The 20 incident cases identified would have been undetected and untreated if screening test at the 3\(^{rd}\) trimester had not been performed in the intervention clinics. Conversely, in control clinics coverage of syphilis testing at the 3\(^{rd}\) trimester was only 68.9\% and could detect only 2 cases of active syphilis. This data support the necessity of performing syphilis testing also at the 3\(^{rd}\) trimester of gestation.\(^{17}\) Moreover, our data support the recommendation that syphilis testing should be performed on all women at the time of delivery if they were not tested for syphilis during pregnancy.\(^{17}\) Had it not been done, 15 seropositive women in the control group would have been missed during the delivery.

Thirdly, the one-stop services for ASYS allowed prompt treatment of seropositive cases which resulted in a higher proportion of adequately treated women before delivery in the intervention than the control group. A similar success rate was reported by a Bolivian study in 2007. Using the on-site rapid
syphilis testing the study detected more active syphilis cases among pregnant women and over 80% of those who tested positive received all three recommended doses of penicillin before delivery. The treatment success can be explained by the immediate access to the test results, for example women receive their test results while they are still in the antenatal clinics. In fact, high rates of patients do not return for collecting test results in many countries, and this results in delay of early treatment or no treatment at all. One study found that only 24.5% of women with syphilis were treated when they were sent to the referral clinics for syphilis therapy.

Fourthly, notification and treatment of sexual partners at the one-stop service can be implemented. Similarly, the Bolivian project also reported that over three quarters (498/577) of the male partners were identified at the time of testing and most of them (383/498) presented for treatment. The increase in percentage of partner notification and treatment could be explained by active counseling provided by ANC doctors. A recent Bolivian study findings suggested that screening for domestic violence and counseling about partner notification should be integrated into screening programs, since women who do not fear their partner's reactions were more likely to notify them of their infection status. Notification to male partners is not only important to their own health, but is critical in preventing re-infection of women. Emphasis on notification of partners of
pregnant women with syphilis has been associated with a threefold improvement in pregnancy outcome.\textsuperscript{21}

Finally, one-stop service is effective in prevention of congenital syphilis. A 93.5\% case reduction would mean significant relief of this health burden since several complications are well known to occur in congenital syphilis, such as miscarriages, stillbirths and early neonatal deaths.\textsuperscript{2}

Our study did not look at the reasons of low syphilis screening coverage in the control group. However, our previous study in 2006 showed that late ANC visit, lack of knowledge on the importance of ASYS and awareness of the infection, long travel to ASYS service, overcrowding at STI laboratories and living far from service spot were related to unscreened in routine syphilis screening in Ulaanbaatar.\textsuperscript{6}

With these good results, the current one-stop service is still not perfect. One seropositive woman received inadequate treatment due to late ANC resulting in congenital syphilis. Although the male partner treatment percentage was significantly higher in the intervention than control group, five sex partners remained untreated, thus the women could be re-infected. There were some limitations of this study. First, incomplete follow up was still detected in our study but the figure was small (5.7\%). Although they were initially seronegative, the final status of the women and their newborns were unknown. Second, since the all women testing positive by the rapid test received immediate treatment,
some women had unnecessarily received first dose of penicillin because the rapid treponemal tests can not differentiate between women with current infection and those who have previously treated for the infection. However, this condition could be avoided mostly if they were interviewed on their previous history of diagnosis and treatment. Last, the syphilis tests were supplied to the intervention arm but not in the control arm. Since it is known that logistical supply issues are at the core of why some programs fail and this may result in an advantage of intervention arm. However, there were no any shortages of routine RPR at the control arm during the study period.

In conclusion, one-stop services increased the detection rate of syphilis, treated more syphilis infected women and their partners and effectively reduced congenital syphilis. In addition, the one-stop service of antenatal syphilis screening is feasible and did not face any critical obstacles in terms of women and providers’ perspectives. Implementation of one-stop service can be considered to improve overall access to interventions to eliminate congenital syphilis as a public health problem.
Acknowledgments

We would like to thank the staff of the intervention and control clinics, the district health supervisors of the 6 participating district general hospitals (Dr Panzila, Dr Ariumaa, Dr Tsetsegmaa, Dr Davaasuren, Dr Sainbuyan and Dr Erdenechimeg) and all the participating women. This trial received financial support from the Special Programme of Research, Development and Research Training in Human Reproduction, WHO, through a re-entry grant awarded to the first author.

Abbreviations

ASYS	Antenatal Syphilis Screening
ANC	Antenatal Care
MCH Center	State Research Center on Maternal and Child Health
NCCD	National Center of Communicable Diseases
OB-GYN	Obstetrician-Gynecologist
RPR	Rapid Plasma Reagin
STI	Sexually Transmitted Infection
TPHA	Treponema Pallidum Haemagglutination Assay
WHO	World Health Organization
References


Figure 1 Study settings
14 antenatal clinics

7 allocated to intervention

7 allocated to control

4,284 new attendees

4,277 new attendees

434 excluded
- 327 not meet inclusion criteria
- 107 refused to participate

427 excluded
- 210 not meet inclusion criteria
- 217 refused to participate

At 1st antenatal visit
3,850 received one-stop service

At 1st antenatal visit
3,850 received routine screening service

At 3rd trimester
3,756 followed up
94 lost to follow-up

At 3rd trimester
3,823 followed up
27 lost to follow-up

At delivery
3,632 followed up
218 lost to follow-up

At delivery
3,564 followed up
286 lost to follow-up

Figure 2 Trial profile
Table 1 Baseline characteristics of participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=3,850)</td>
<td>(n=3,850)</td>
</tr>
<tr>
<td>Mean age, years (SD)</td>
<td>26.9 (5.5)</td>
<td>27 (7.5)</td>
</tr>
<tr>
<td>Education level (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>never attended school/primary</td>
<td>81 (2.1)</td>
<td>73 (1.9)</td>
</tr>
<tr>
<td>secondary and/or technical</td>
<td>2,560 (66.5)</td>
<td>2,619 (68)</td>
</tr>
<tr>
<td>university and/or equivalent</td>
<td>1,209 (31.4)</td>
<td>1,158 (30.1)</td>
</tr>
<tr>
<td>Marital status (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>married/cohabiting</td>
<td>3,496 (90.8)</td>
<td>3,456 (89.8)</td>
</tr>
<tr>
<td>single/widowed/separated</td>
<td>354 (9.2)</td>
<td>394 (10.2)</td>
</tr>
<tr>
<td>Residency (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulaanbaatar</td>
<td>1,618 (42.0)</td>
<td>1,641 (42.6)</td>
</tr>
<tr>
<td>registered migrant</td>
<td>1,816 (47.2)</td>
<td>1,787 (46.4)</td>
</tr>
<tr>
<td>unregistered migrant</td>
<td>416 (10.8)</td>
<td>422 (11.0)</td>
</tr>
<tr>
<td>Currently employed (%)</td>
<td>1,279 (33.2)</td>
<td>1,309 (34.0)</td>
</tr>
<tr>
<td>Previous pregnancy (%)</td>
<td>2,465 (64.0)</td>
<td>2,503 (65.0)</td>
</tr>
<tr>
<td>Characteristics</td>
<td>Control</td>
<td>Intervention</td>
</tr>
<tr>
<td>-----------------------------------------------------</td>
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</tr>
<tr>
<td>Mean gestational age at the first ANC (SD)</td>
<td>14.1 (6.6)</td>
<td>12.0 (4.8)</td>
</tr>
<tr>
<td>Previous STI (%)</td>
<td>352 (9.1)</td>
<td>324 (8.4)</td>
</tr>
<tr>
<td>Any adverse pregnancy outcome (%)</td>
<td>222 (9.0)</td>
<td>221 (8.8)</td>
</tr>
<tr>
<td>Any multiple sexual partners (%)</td>
<td>450 (11.7)</td>
<td>365 (9.4)</td>
</tr>
</tbody>
</table>

SD - standard deviation, ANC - antenatal care, STI - sexually transmitted disease
Figure 11. Primary and secondary outcomes at intervention and control

**Intervention - At 1st antenatal visit: 3850**

- Screened: 3849 (99.9%)
  - Syphilis: 73 (1.9%)
  - Adequately treated: 72 (98.6%)

**Control - At 1st antenatal visit: 3850**

- Screened: 3065 (79.6%)
  - Syphilis: 27 (0.9%)
  - Adequately treated: 24 (88.9%)

**At 3rd trimester of gestation: 3756 (97.6%)**

- Screened: 3670 (99.7%)
  - Syphilis: 20 (0.5%)
  - Adequately treated: 20

- At delivery: 3632 (94.3%)
  - Congenital syphilis: 1

**At 3rd trimester of gestation: 3823 (99.3%)**

- Screened: 2357 (62.1%)
  - Syphilis: 2 (0.08%)
  - Adequately treated: 2

- At delivery: 3564 (92.6%)
  - Congenital syphilis: 15
Table 2. Associations between the main outcomes and significant independent variables obtained from multilevel logistic regression model

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>Adjusted OR* (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N (%)</td>
<td>n/N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Primary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital syphilis</td>
<td>1/3632 (0.03)</td>
<td>15/3564 (0.42)</td>
<td>0.09 (0.01-0.67)</td>
<td>0.019</td>
</tr>
<tr>
<td>Coverage at 1st visit</td>
<td>3849/3850 (99.9)</td>
<td>3065/3850 (79.6)</td>
<td>989.84 (129.42-7,570.46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coverage at 3rd trimester</td>
<td>3670/3683 (97.7)</td>
<td>2357/3796 (62.1)</td>
<td>617.88 (123.91-3,081.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syphilis case at 1st visit</td>
<td>73/3,849 (1.9)</td>
<td>27/3,065 (0.9)</td>
<td>2.45 (1.55-3.88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Syphilis case at 3rd trimester</td>
<td>20/3,670 (0.5)</td>
<td>2/2,357 (0.08)</td>
<td>6.27 (1.46-26.87)</td>
<td>0.013</td>
</tr>
<tr>
<td>Intervention</td>
<td>Control</td>
<td>Adjusted OR*(95% CI)</td>
<td>p value</td>
<td></td>
</tr>
<tr>
<td>--------------</td>
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<td></td>
</tr>
<tr>
<td>Adequate treatment</td>
<td>92/93 (98.9)</td>
<td>26/29 (89.6)</td>
<td>10.44 (0.94-116.28)</td>
<td>0.06</td>
</tr>
<tr>
<td>Partner treatment</td>
<td>88/93 (94.6)</td>
<td>16/29 (55.2)</td>
<td>18.17 (4.16-79.35)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

OR - odds ratio, CI- confidence interval

* adjusted for significant independent variables such as gestational age at 1st antenatal visit and multiple sexual partners with a random effect for antenatal clinics