

Investment case for eliminating mother-to-child transmission of syphilis

Promoting better
maternal and child health
and stronger health systems



World Health
Organization

initiative for the global elimination of congenital syphilis

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WHO Library Cataloguing-in-Publication Data

Investment case for eliminating mother-to-child transmission of syphilis: promoting better maternal and child health and stronger health systems.

1.Syphilis – transmission. 2.Syphilis – prevention and control. 3.Syphilis, Congenital. 4.Infectious Disease Transmission, Vertical. 5.Infant, Newborn, Diseases. I.World Health Organization.

ISBN 978 92 4 150434 8

(NLM classification: WC 161)

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Printed by the WHO Document Production Services, Geneva, Switzerland

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Abbreviations and acronyms

ANC	antenatal care
BASTA	Battling Against Syphilis – a Team Approach
CDC	Centers for Disease Control and Prevention (USA)
DALY	disability-adjusted life year
DSTDP	Division of STD Prevention
MCA	WHO Department of Maternal, Child and Adolescent Health
MCH	maternal and child health
MDG	millennium development goal
MTCT	mother-to-child transmission (of syphilis and/or HIV)
NGO	nongovernmental organization
PAHO	Pan American Health Organization
PGT	programme guidance tool
PMTCT	prevention of mother-to-child transmission (of HIV)
RHR	WHO Department of Reproductive Health and Research
RPR	rapid plasma reagin
RTI	reproductive tract infection
STI	sexually transmitted infection
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNFPA	United Nations Population Fund
UNICEF	United Nations Children’s Fund
USA	United States of America
VDRL	venereal disease research laboratory
WHO	World Health Organization

Executive summary

Nearly 1.5 million pregnant women are infected with probable active syphilis each year, and approximately half of infected pregnant women who are untreated, will experience adverse outcomes due to syphilis, such as early fetal loss and stillbirth, neonatal death, low-birth-weight infants, and infants with clinical evidence of infection. It is estimated that in 2008, syphilis in pregnancy contributed to 305 000 stillbirths and fetal and neonatal deaths, and an additional 215 000 infants at increased risk of dying from low birth weight, prematurity or complications of infection related to syphilis.

Mother-to-child transmission (MTCT) of syphilis (commonly referred to as “congenital syphilis”) is relatively simple to eliminate and it is inexpensive to detect and treat, making it a possible “easy win” in terms of cost, feasibility and speed of scale-up. Investing in screening and treatment for syphilis in pregnant women ranks as one of the most cost-effective antenatal interventions. Screening all pregnant women, using simple and low-cost technologies, is feasible, even in low-resource settings. Syphilis is easily cured with penicillin, and MTCT of syphilis is easily prevented when pregnant mothers with syphilis infection are identified early and treated promptly. Penicillin is off patent, widely available, on the World Health Organization (WHO) list of essential medicines and, above all, inexpensive.

Moreover, a number of factors make this the ideal time to invest, specifically: the strong political will on the part of many governments in high-burden countries to support the *Global strategy for women’s and children’s health*; the resources and attention being devoted to achieving the Millennium Development Goals (MDGs), particularly HIV, reproductive, maternal, newborn and child health objectives (MDGs 4, 5 and 6); the push for dual elimination of MTCT of HIV and syphilis; the increased availability and use of antenatal care (ANC) in many countries; and technological advances in screening for syphilis in low-resource settings.

This investment case outlines why and how an investment of US\$17 million over 4 years can:

- reduce adverse outcomes of syphilis in pregnancy by 2015 through intensified support to 12 high-burden countries, and develop a stronger global network to eliminate MTCT of syphilis in other countries;
- strengthen sexual and reproductive health services, as well as maternal and child health services, to ensure dual elimination of MTCT of HIV and syphilis;
- improve collaboration among, and capacity of, stakeholders engaged in activities aimed at reducing the overall burden of adult syphilis.

Through a series of national, regional and international consultations, it is clear that a number of countries are committed to syphilis elimination. These countries have established ANC, prevention of MTCT of HIV, and other programmes, which are funded through various sources. Countries have asked for technical support to prioritize and scale up interventions for MTCT of syphilis in a way that builds upon existing investments in maternal and child health services. The investment case is not intended to provide resources for routine programme management and operations at the country level, but rather to assist countries in identifying how to incorporate antenatal syphilis testing and treatment into routine national health plans and expenditure for ANC.

Despite its devastating impact, MTCT of syphilis is preventable and curable. And now – more than ever before – is the right time to address it with a coordinated, strategic global initiative. Investment in the elimination of MTCT of syphilis will contribute significantly to improved maternal and child health around the world, including achievement of MDGs 4, 5 and 6, while also strengthening underlying health systems.

1. The case for investment

1.1 Mother-to-child transmission of syphilis: a continuing public health burden

An estimated 11 million people acquire new syphilis infections annually (1). This is despite the fact that a successful test for syphilis has been available since the early 1900s and effective treatment (penicillin) has been widely available since the 1940s.

In 2009, there were approximately 2.6 million stillbirths and an additional 3.1 million infants died within the first month of life (2, 3). In 2004, the World Health Organization (WHO) global burden of disease estimate of deaths due to syphilis among children aged 0–4 years was approximately 64 000 deaths, or 0.6% of all deaths in children aged under 5 years (4). However, it is widely felt that syphilis is underdiagnosed as a cause of death in death registries and verbal autopsies, and estimates in some developing countries have suggested that mother-to-child transmission (MTCT) of syphilis contributes to up to one quarter of all stillbirths and 11% of neonatal deaths (4–6).

This document uses the term **mother-to-child transmission (MTCT) of syphilis** throughout, but it should be noted that most of the related literature to date uses the term **congenital syphilis**. The term MTCT is preferred, as it better reflects the range of adverse outcomes that occur when syphilis is transmitted from mother to child. MTCT of syphilis is any adverse outcome in a fetus or neonate associated with syphilis infection in a pregnant woman. Adverse outcomes include early fetal loss, stillbirth, neonatal death, prematurity, low birth weight and clinical evidence of syphilis in a neonate.

Untreated maternal syphilis results in MTCT of syphilis (see text box) in over half of affected pregnancies (see Table 1.1). A recent meta-analysis of syphilis-associated pregnancy outcomes found a profound impact: stillbirth and late fetal loss in 21% and neonatal death in 9% of untreated infections (7). Additionally, untreated maternal syphilis contributes

Table 1.1
Estimated proportion of adverse outcomes in untreated pregnancies affected by syphilis, and number of adverse outcomes in 2008 taking into account existing services^a

Outcome	Estimated % of adverse outcomes in untreated pregnancies affected by syphilis	Estimated number of adverse outcomes in 2008
Early fetal loss/stillbirth	21	215 000
Neonatal death	9	90 000
Prematurity or low birth weight	6	65 000
Clinical evidence of syphilis in newborn	16	150 000
Any adverse outcome	52	520 000

^a Adverse outcomes estimates = % of pregnancies affected in syphilis seropositive women minus the % of pregnancies affected in syphilis seronegative women. This methodology thus accounts for background morbidity and mortality not attributable to syphilis.

to serious neonatal complications such as premature and low-birth-weight infants (6%) and infants with clinical evidence of syphilis (16%) – who are then at higher risk of ill health. Estimates for 2008 suggest that globally there are nearly 1.5 million pregnant women infected with probable active syphilis each year (8). Although there is wide variation in antenatal care (ANC) practices globally, the vast majority of pregnant women with syphilis are not identified and treated early enough to avoid the adverse effects of infection on their pregnancy. Thus, assuming that 30–70% (depending on region) of all pregnant women with syphilis were tested and treated early enough to avert an adverse outcome, in 2008 there were an estimated 520 000 pregnancies and neonates adversely affected by syphilis, including 215 000 early fetal losses and stillbirths and 90 000 neonatal deaths.

1.2 Addressing syphilis in pregnant women: a feasible solution

Adverse pregnancy outcomes caused by untreated maternal syphilis are preventable and curable, and interventions to improve screening and treatment for syphilis in pregnancy can substantially reduce the current global burden of preventable perinatal mortality and morbidity (9). Detection and treatment of syphilis has been identified as being one of the most effective and cost-effective interventions to prevent stillbirths and neonatal deaths (10). Screening all pregnant women, using simple and low-cost technologies, is feasible, even in low-resource settings.

All pregnant women should be tested for syphilis, not just those perceived as being “high risk”.

New point-of-care tests, which can use whole-blood samples from a finger prick, provide results and allow for treatment at a single visit. They can be used in all health-care settings, even in the face of limited electricity, refrigeration or skilled laboratory staff. Existing tests (rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL)) can also be used successfully in settings with

sufficient laboratory capacity and minimal quality-control processes. With a combination of these two diagnostic options, programmes can achieve universal access to syphilis screening in pregnant women. If syphilis is diagnosed early and treated promptly, penicillin is highly effective in treating maternal infection and preventing MTCT of syphilis (11). Penicillin is off patent, widely available, on the WHO list of essential medicines (12) and, above all, inexpensive. Moreover, *Treponema pallidum*, the bacterium causing syphilis, has not developed resistance to penicillin.

1.3 Why now is the time to invest in elimination of mother-to-child transmission of syphilis

More than ever before, elimination of MTCT of syphilis as a public health problem is feasible, achievable and affordable.

The Millennium Development Goal “window of opportunity”

As we near the 2015 deadline for achieving the Millennium Development Goals (MDGs), there is increased global commitment and attention to improving child and maternal health (MDGs 4 and 5). This paves the way for tackling MTCT of syphilis as an important contributor to maternal and infant morbidity and mortality.

Elimination of MTCT of syphilis will contribute to MDGs 4 (reduce child mortality), 5 (improve maternal health) and 6 (combat HIV/AIDS, malaria and other diseases).

Addressing MTCT of syphilis through an initiative that strengthens ANC services as well as existing infrastructure and programmes can contribute to reductions in other preventable infections affecting pregnancy, including perinatal malaria, maternal and neonatal tetanus, and HIV transmission to neonates, and can improve maternal health. This will bolster efforts to achieve MDGs 4, 5 and 6 (combat HIV/AIDS, malaria and other diseases), as highlighted in the 2009 United Nations (UN) MDG report (13).

MDG 4: reduce child mortality

Infant and child mortality have declined globally, but the pace of progress is uneven. In 2010, an estimated 8 million children died before their fifth birthday – mainly from preventable causes. MTCT of syphilis is a preventable cause of low birth weight, neonatal death, stillbirth and congenital infection (3). The UN MDG report states that “many countries, particularly in sub-Saharan Africa and southern Asia, have made little or no progress at all [towards MDG 4]” (13) (see Box 1.1). An emphasis on strengthening health systems to provide ANC, which includes screening for MTCT of syphilis, will help to address this public health tragedy.

MDG 5: improve maternal health

ANC is a core component of comprehensive maternal health care. The UN MDG report emphasizes that “many health problems among pregnant women are preventable, detectable or treatable through visits with trained health workers before birth” (13). In all regions, progress has been made on ensuring that more women reach and receive at least one ANC visit in their pregnancy – thus providing more opportunities for women to be screened for syphilis and other

conditions during pregnancy. Through the initiative outlined in this document, maternal health will be improved as a result of earlier ANC and fewer spontaneous abortions and stillbirths. In addition, the simultaneous implementation of interventions to eliminate MTCT of syphilis, and efforts to control sexually transmitted infections (STIs) in the general adult population, will also reduce the incidence and prevalence of syphilis in pregnant women.

MDG 6: combat HIV/AIDS, malaria and other diseases

It is estimated that women account for about half of all people living with HIV infection, and that the vast majority of HIV-infected women live in developing countries. Given the common mode of sexual transmission, coinfection of HIV and syphilis is not uncommon. Syphilis infection is a recognized cofactor for increased risk of HIV transmission and acquisition, and maternal syphilis infection has even been associated with increased risk of MTCT of HIV (15, 16).

WHO recognizes that HIV services should be integrated within a package of core interventions for maternal, newborn and child health that includes

Box 1.1 Avoiding HIV but dying of syphilis

An HIV-positive mother in Haiti successfully completes therapy for prevention of mother-to-child-transmission (PMTCT) of HIV, but her baby dies at 3 weeks from congenital syphilis [mother-to-child transmission of syphilis]. This is not an isolated case.

Large investments in PMTCT of HIV have been one of the big successes of recent years. But too many of the babies born HIV free tragically die of syphilis. This is despite the fact that it is feasible and cheap to add screening for syphilis to existing antenatal and PMTCT programmes.

Even in countries with clear policy recommendations on syphilis screening, congenital syphilis still poses a major threat to both women and infants. For example, only about one third of women attending antenatal clinics in 22 sub-Saharan African countries were reported to have been tested for syphilis, despite 17 of these countries having explicit policy recommendations mandating syphilis screening. This shows a clear disconnect between policy and implementation.

There is an opportunity for policy-makers and the donor community to recognize the importance of integration of programmes at the local level, and to capitalize on new opportunities to enhance health systems.

A concerted effort can avert the tragedy of babies avoiding HIV but dying of syphilis, and help to realize the goal to reduce childhood mortality.

Source: Peeling R et al. Avoiding HIV and dying of syphilis. *The Lancet*, 2004, 364:1561–1563 (14).

syphilis screening and care (17). Systematic screening of women for syphilis in programmes for PMTCT of HIV will allow mothers and infants to be tested and, where necessary, treated for both HIV infection and syphilis, thereby reducing fetal and infant deaths. Treating maternal syphilis infections also improves maternal and neonatal health. Moreover, the Joint United Nations Programme on HIV/AIDS (UNAIDS) recognizes testing and treatment of syphilis in pregnant women as an indicator of quality ANC services in the context of HIV prevention (18).

Global momentum to eliminate new HIV infections among children

The global call to eliminate new HIV infections among children by 2015 and keep their mothers alive specifically notes the importance of HIV programmes working together with maternal, newborn and child health programmes to lead to improved health outcomes (17, 19). Three WHO regions (Region of the Americas, South-East Asia Region, and Western Pacific Region) have launched elimination of MTCT of HIV as a *dual* elimination initiative with MTCT of syphilis, and the African Region includes elimination of MTCT of syphilis within its strategy for elimination of MTCT of HIV (20–22). Such dual-elimination initiatives strive to promote synergies for overall strengthening of the perinatal health-system platform.

Elimination of mother-to-child transmission of syphilis supports the global strategy for women's and children's health

With just a short amount of time left to achieve the MDGs, the UN Secretary-General launched the *Global strategy for women's and children's health* (23). This strategy calls for all partners to unite to enhance financing, strengthen policy and improve service delivery of proven interventions. As a result, many countries have committed to improve coordination around maternal and neonatal health issues and create platforms for integration. Bringing ministries of health and partners together to provide universal coverage of antenatal syphilis screening, and ensuring treatment of all pregnant women with syphilis, is a specific example of an activity called for within the global strategy.

More availability and utilization of antenatal care than ever before

The relatively high utilization of ANC by pregnant women in many countries makes this service an ideal venue to implement population-based interventions. Although women often delay seeking care until later in pregnancy, an estimated 82% of pregnant women have at least one ANC visit (24).

An important component of the initiative proposed in this investment case will be to promote sufficiently early ANC, which maximizes the benefits of maternal syphilis screening when universally provided to women at low or no cost, as part of an integrated service package of proven-effective antenatal interventions. Early ANC also improves the effectiveness of other antenatal interventions, including prevention of HIV and malaria.

Important technological advances

Existing screening for syphilis (i.e. RPR testing) is simple and cheap, but requires a basic laboratory capacity and quality control that may not be available at many antenatal facilities, particularly in remote settings or in resource-poor settings with limited infrastructure. However, syphilis screening has evolved over the past 10 years. On-site diagnosis of syphilis and prompt treatment of women who screen positive is increasingly possible, even in remote settings, with rapid point-of-care diagnostics. These new diagnostics allow syphilis-infected women to be diagnosed and treated in a single antenatal visit. Extensive research has helped greatly in our understanding of more effective diagnostic tools, algorithms and approaches in specific settings, and has ensured availability of high-performing point-of-care syphilis tests to low- and middle-income countries at affordable prices (i.e. at less than US\$1 per test).

1.4 Why the problem persists

In theory, it is easy and cheap to prevent and treat MTCT of syphilis. In practice, however, there have been a number of barriers to elimination. Chief among these is a general lack of awareness of the true impact of MTCT of syphilis and the extent of the problem. Without diagnostic testing,

syphilis-associated fetal loss and stillbirth, neonatal deaths and premature births are not recognized as being caused by syphilis or as being preventable. Lack of awareness about the true toll of maternal syphilis is a significant barrier at all levels – in communities, among service providers and programme managers, and among policy-makers and decision-makers (25). In many countries, a lack of clarity regarding roles, responsibilities and accountability for measures to control MTCT of syphilis is a problem, since efforts involve both STI and maternal and child health (MCH) programmes. In addition, many existing ANC programmes do not have the information, training and technology they need to incorporate maternal syphilis screening and treatment into their health-care systems.

Other key barriers are outlined in Table 1.2.

1.5 The strong economic case for syphilis elimination

Economic costs of mother-to-child transmission of syphilis

The direct medical costs of MTCT of syphilis are substantial, because of the infection's high prevalence and high rate of complications. However, the true economic burden of any disease, including syphilis, includes more than just direct medical costs. It involves indirect costs, such as lost productivity, and other non-medical costs, such as special educational needs and the emotional impact of having a disabled child, which are extremely difficult to quantify.

Although the full economic cost of MTCT of syphilis has not been definitively determined, available estimates of the direct medical costs can provide a glimpse of the true cost to individuals, families and

Table 1.2
Barriers to the elimination of mother-to-child transmission of syphilis

Setting	Barriers
In local communities	<ul style="list-style-type: none"> • The problem is not seen as important • Women do not seek ANC early enough or at all, or do not seek care from trained providers • Stigma associated with STIs • Costs associated with detection and treatment, whether direct, indirect, opportunity related or stigma related
Among health-care service providers	<ul style="list-style-type: none"> • Lack of awareness of or training in the appropriate intervention • Lack of commodities appropriate to the setting • Insufficient logistical support for the intervention • No financial incentives to screen for syphilis (especially among private providers)
Among programme managers	<ul style="list-style-type: none"> • Syphilis accorded a low priority compared with other health problems • Lack of resources for effective interventions • Lack of clarity regarding roles, responsibilities and accountability • Poor planning, coordination and monitoring of programmes
Among policy-makers and decision-makers	<ul style="list-style-type: none"> • Lack of awareness of true disease burden • Lack of awareness of the cost effectiveness of the intervention • Little external pressure to adopt or implement policies • Few apparent political rewards for action

health systems. For example, in the United States of America (USA), the hospital cost per newborn infant with congenital syphilis (MTCT of syphilis) was estimated to be almost US\$5000 higher than the cost per uninfected infant (26). In South Africa, hospital-based treatment of congenital syphilis (MTCT of syphilis) was estimated at US\$638 per case (27). Globally, the annual direct medical costs of addressing the adverse outcomes associated with syphilis in pregnant women are calculated to be US\$309 million (see Table 1.3).

MTCT of syphilis, tetanus, malaria, hypertension and HIV are all important contributors to disease burden in pregnant women.

Although the direct medical costs of MTCT of syphilis are estimated to be lower than those of some other perinatal infections, such as vertically transmitted HIV (estimated to be US\$3520 million), the current global burden of disease attributable to MTCT of syphilis as measured in disability-adjusted years (DALYs) is enormous, at approximately 3.6 million. A DALY is a time-based measure of the burden of disease that combines years of life lost due to premature mortality with the time lived in a state of less than full health. Table 1.3 outlines several conditions affecting pregnancy that could

be prevented or treated through improving current ANC programmes. For each ill-health outcome, the economic cost and the health burden (in actual numbers of cases, deaths and DALYs) are presented. These estimates are based on current levels of programme coverage – which is higher for some programmes (e.g. neonatal tetanus) than others (e.g. MTCT of syphilis). Because different conditions cause different types of outcomes, and estimates are not available for all potential outcomes (e.g. stillbirth associated with HIV), death estimates are not directly comparable.

Cost effectiveness of syphilis-elimination programmes

We have conducted an analysis of the additional cost, health impact and cost-effectiveness of implementing syphilis programmes in existing ANC screening programmes in eight different country case scenarios, which vary in terms of syphilis testing and treatment coverage (high (70%) or low (20%)), syphilis ANC prevalence (high (3%) or low (0.5%)), and country cost of health services (high or low). For each of the eight different country scenarios, the cost analysis assesses the cost of the intervention (i.e. implementing testing and treatment of syphilis in pregnancy), while the health-impact analysis estimates the health benefits of the intervention in terms of DALYs averted.

Table 1.3
Disease burden in pregnant women, associated perinatal deaths, DALYs and direct medical costs for syphilis, tetanus, malaria, hypertension and HIV

	Clinical cases	Deaths	DALYs	Direct medical costs (US\$)
Syphilis	1 360 000 pregnant women (8)	305 000 fetal, stillbirth, neonatal (8)	3.6 million ^a	309 million ^b
Tetanus	187 000 children aged 0–4 years (28)	187 000 children aged 0–4 years ^c (27)	5.1 million (28)	No data available
Malaria	No data available	563 300 children aged <5 years (29)	No data available	No data available
Hypertension	No data available	71 000 maternal (28)	1.9 million (28)	No data available
HIV	440 000 new infections in children (30)	440 000 new infections in children	6.2 million (31)	3520 million (31)

^a DALYs for syphilis also include low-birth-weight and syphilis-infected infants.

^b Assumes a 50:50 share of less- and more-expensive country settings.

^c Tetanus deaths include the age group 0–4 years (excludes stillbirths); expert opinion is that 90% of deaths are neonatal.

Table 1.4
Estimated net cost (in US\$) over 4 years, number of DALYs averted over 4 years and cost per DALY averted for eight country scenarios varying by burden of disease, syphilis testing and treatment coverage, and health-care costs^a

Country scenario	Prevalence of syphilis in pregnant women	Proportion of all pregnant women tested and treated	Health-care cost structure	Net cost (savings) of intervention (4 years) (cost of intervention minus disease costs averted), US\$	Number of DALYs averted (4 years)	Cost per DALY averted, US\$
A	High	Low	Low	(1 943 017)	106 042	Cost saving ^b
B	High	Low	High	(12 261 250)	106 042	Cost saving
C	High	High	Low	(765 563)	39 155	Cost saving
D	High	High	High	(4 587 778)	39 155	Cost saving
E	Low	Low	Low	1 736 807	17 678	98.25
F	Low	Low	High	543 472	17 678	30.74
G	Low	High	Low	593 188	6527	90.88
H	Low	High	High	140 282	6527	21.49

a Classifications used for this exercise are: prevalence of syphilis = high (3%) or low (0.5%), proportion of all pregnant women tested and treated = high (70%) or low (20%), health-care cost structure = high (1) or low (0.25), based on WHO CHOICE (CHoosing Interventions that are Cost Effective) data (32).

b The cost per DALY averted ratio is not calculated when the intervention is “cost saving” – i.e. reduces DALYs and saves money.

The cost-effectiveness analysis combines this information into an estimate of the “cost per DALY averted”, taking into account the medical costs saved by the intervention. An intervention is said to be “cost-saving” if it pays for itself in terms of offset medical costs. In such instances, the cost per DALY averted is <US\$0. The key inputs and results are presented in Table 1.4 for each of the eight different country case scenarios, and described in greater detail in Appendix 1. Although the data presented are calculated as a ratio per 1 million pregnancies, the results should scale (i.e. the costs and the health outcomes would change similarly for smaller or larger populations), thus leaving the cost per DALY unchanged for countries of different sizes.

The costs of controlling MTCT of syphilis are outweighed by the money saved in nearly all scenarios.

We found that controlling MTCT of syphilis would be a “cost-saving” intervention in four of the eight country scenarios examined – i.e. the intervention will “pay for itself” in offset medical costs. In the other four scenarios, the cost per DALY averted is between US\$20 and US\$100, far below the annual

gross domestic product per capita in any country, the WHO criterion for “very cost effective”.

1.6 Who should invest in the elimination of mother-to-child transmission of syphilis?

Efforts to improve maternal and child health, and specifically to eliminate MTCT of syphilis, can be considered to constitute a global public good, defined as multicountry policies, programmes and initiatives having a positive impact on health that extends beyond the borders of any specific country (33). However, even with widespread consensus around the financial and social benefits of procuring a global public good, achieving these benefits requires the involvement and commitment of a wide range of actors and stakeholders.

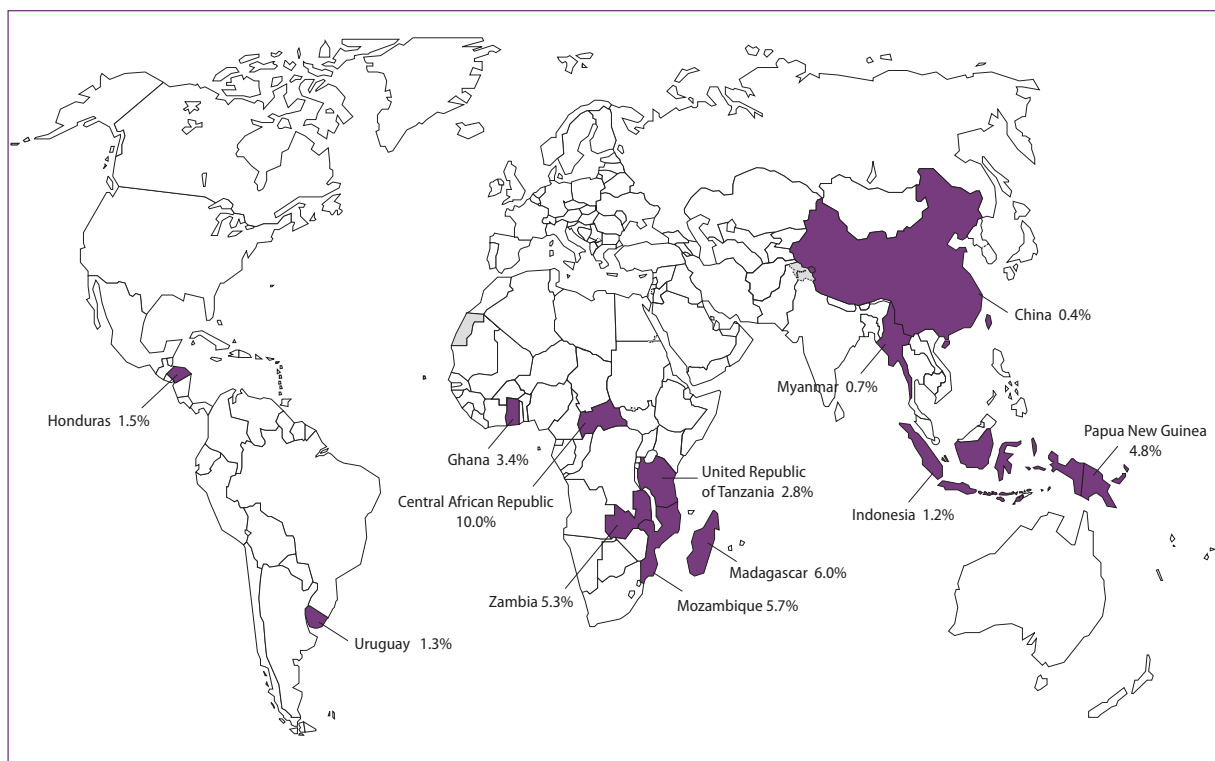
- **Those interested in reducing neonatal and infant mortality should invest** because untreated maternal syphilis contributes to nearly a quarter of a million stillbirths each year – an especially high proportion of all stillbirths in developing countries. In addition, in 2008, MTCT of syphilis contributed to approximately 90 000 neonatal deaths, 65 000 low-birth-weight or premature babies and 150 000 babies born with syphilis infection – almost all preventable.

- **Those interested in promoting maternal health should invest** because improving screening in ANC is an opportunity to identify women at risk of pregnancy complications and adverse outcomes of pregnancy.
- **Those interested in reducing STIs should invest** because this initiative will reduce the overall burden of STIs. It will also increase countries' abilities to identify pregnant women with syphilis, which can facilitate partner notification, thus strengthening overall syphilis control in high-burden countries.
- **Those interested in HIV should invest** because integration of syphilis screening with HIV screening in pregnancy is a low-cost intervention that contributes to dual elimination of MTCT of HIV and syphilis and makes HIV services more comprehensive.
- **Those interested in strengthening health services to deliver integrated sexual and reproductive health care should invest** because this initiative represents a vital step towards integration of STI prevention and care into maternal health services.

1.7 How much and what sort of investment is needed?

We are seeking an investment of US\$17 million over 4 years (see budget in Appendix 2), which will facilitate the implementation of the initiative to eliminate MTCT of syphilis in up to 12 "intensified support" countries (see Fig. 1.1). We estimate that this level of implementation will reduce cases of MTCT of syphilis by 80% in these countries by the end of 2015. In 2008, the estimated burden of disease in the proposed 12 countries accounted for 33% of the global burden of pregnancies and neonates affected by syphilis. The funding will also enable WHO to provide technical support at a global and regional level to other countries working towards the elimination of MTCT of syphilis ("general support" countries).

Fig. 1.1
Reported syphilis prevalence for 2010 (2009 for Indonesia) in intensified support countries for the investment case for eliminating mother-to-child transmission of syphilis^a



^a Source: Data for Papua New Guinea are from the National Department of Health, STI, HIV and AIDS Surveillance Unit: The 2010 STI, HIV and AIDS Annual Surveillance Report. Data for Indonesia available at: <http://www.who.int/hiv/pub/2010progressreport/en/index.html>. Data for all other countries available at: http://www.who.int/hiv/pub/progress_report2011/en/.

2. Details of the initiative: objectives, activities and stakeholders

The overall goal of the initiative is global elimination of MTCT of syphilis as a public health problem (34).

The specific goals of this elimination effort are to prevent transmission of syphilis from mother to child through ensuring that:

- at least 90% of pregnant women are screened for syphilis;
- at least 90% of pregnant women who are positive for syphilis are treated appropriately.

Given the difficulties in diagnosing and reporting MTCT of syphilis consistently throughout the world, a specific global target for a case rate for MTCT of syphilis has not been set. However, countries and regions are encouraged to identify country- or region-specific goals and targets to measure the impact of elimination efforts. The Region of the Americas, South-East Asia Region, and Western Pacific Region have defined elimination of congenital syphilis (MTCT of syphilis) as corresponding to an incidence of 0.5 cases or fewer per 1000 births (including stillbirths) (21, 22). However, this specific threshold was established for these regions and may not be appropriate for the rest of the world.

Elimination can be achieved by strengthening reproductive and sexual health programmes to ensure:

- the unmet need for family planning is met, thus helping women to avoid unintended pregnancy;
- early ANC, including syphilis screening for all pregnant women, and prompt treatment of those infected;
- treatment of all sexual partners of infected women, promotion of condom use during pregnancy and counselling of all women on how to prevent infection;
- all neonates born to syphilis-positive mothers are given penicillin as presumptive treatment.

There are three primary objectives for the investment case:

- **reduce adverse outcomes of pregnancy due to MTCT of syphilis through intensified support in 12 focus countries by 2015:** achieved by scaling up early maternal syphilis screening for all pregnant women and ensuring prompt treatment for women with positive tests;
- **strengthen sexual and reproductive health services, including family planning, maternal and child health services:** this will involve ensuring that activities aimed at elimination of MTCT of syphilis are integrated into existing health systems, commodities distribution and monitoring and evaluation systems;
- **promote collaboration among different stakeholders working to reduce the overall the burden of syphilis:** this will include building on synergies and forging partnerships among different groups and agencies that address adult syphilis.

To realize these objectives, specific activities will be carried out in 12 intensified support countries and at regional and global levels. In addition, the support network created by the investment case will provide general support to other high-burden countries requesting technical assistance to eliminate MTCT of syphilis.

2.1 Choosing 12 intensified support countries

The 12 intensified support countries were selected by the WHO regional offices from among those countries with available data demonstrating a high burden of disease. In addition, selection of countries was determined by level of interest and commitment to implementation of the 4-year plan through improved maternal and child health services. The full selection criteria included:

- demonstrable burden of syphilis in pregnancy or its adverse consequences;
- interest in integration of initiative activities into existing national maternal and child health frameworks;
- commitment to attaining high coverage of ANC services;

- initiation of collection of indicators for national and global monitoring, including some form of stillbirth surveillance;
- designation of at least one person to coordinate and monitor congenital syphilis (MTCT of syphilis) activities;
- desire by regional offices to strive for subregional diversity and representativeness.

All of the countries selected for intensified support have made significant investments in establishing effective ANC programmes, and their participation in the initiative should strengthen these investments over the medium and long term.

It is recognized that many of the countries with the highest burden of disease may not have data available and that data on burden of disease change over time. However, other countries will receive general support through the network established with the funding of the investment case, in particular for monitoring and evaluation. In addition, once activities in the 12 intensified support countries are under way, a phased approach to supporting other high-burden countries in future phases of the investment case will be discussed and developed.

2.2 Activities

While the initiative is designed to bring about a major reduction in cases of MTCT of syphilis in 12 intensified support countries, investment case funds are not primarily intended for routine programme expenses. Instead, investment case funds are sought to provide assistance with integrating syphilis interventions into existing programmes, and ensuring and sustaining the effectiveness of these interventions. To this end, funding for the initiative will be devoted to three activity streams:

1. **gathering evidence** to assess the current situation and needs in each country in relation to MTCT of syphilis, to determine the most effective approach to elimination;
2. **building capacity for the development and implementation of national plans** to scale up the coverage and quality of maternal,

newborn and child health services that support elimination of MTCT of syphilis, in addition to other perinatal and maternal health outcomes;

3. **monitoring and evaluation** of interventions related to MTCT of syphilis through strengthened existing systems, within each of the countries as well as at global and regional levels.

Activity stream 1: gathering evidence to guide best practice

Much about MTCT of syphilis is well understood, but additional evidence in certain areas – particularly practical operational research – is needed to strengthen the implementation and effectiveness of country plans for eliminating the condition. Proposed research areas are not stand-alone activities, but exist to strengthen the implementation of feasible, high-quality, cost-effective and sustainable interventions to eliminate MTCT of syphilis.

Table 2.1 outlines some of the areas of research necessary to support the implementation and evaluation of interventions to eliminate MTCT of syphilis, which is a vital element of the initiative. Each country has its own need for filling evidence gaps; therefore, research priorities will be set locally – and may be drawn from this indicative list, or from elsewhere. It is expected that countries will also leverage additional funds to support evidence gathering locally.

Activity stream 2: building capacity for the development and implementation of national plans

While each country has its own unique issues regarding elimination of MTCT of syphilis, this initiative will help national health ministries to identify the best means to address issues specific to their country, and will promote clarification of the roles and responsibilities within the context of existing programmes.

Table 2.1

Key research areas for efforts for elimination of mother-to-child transmission of syphilis

Evidence needed	Where can evidence be gathered?
<p>Who is at risk of syphilis in pregnancy? Aim of research – to understand epidemiological and demographic features associated with the risk of syphilis in pregnancy</p>	Country- and subnational-level research – primary data collection
<p>What is the impact of syphilis in pregnancy? Aim of research – to further explore the impact of MTCT of syphilis (particularly stillbirths, neonatal and infant deaths) in a wider variety of settings (e.g. extent of infant death (>28 days) related to maternal syphilis, impact of stillbirth in low-income settings)</p>	Multicountry studies, possibly linking to existing national surveys Modelling studies at global/national levels
<p>What are the most effective models for delivering the intervention? Aim of research – to identify different models for delivering syphilis screening and treatment for pregnant women, e.g. how to increase early ANC attendance; how to engage communities in increasing ANC attendance</p>	Country-level studies of health systems
<p>What are the resource requirements for delivering the intervention? Aim of research – to quantify levels of resources (human, financial, logistic, policy) needed to achieve elimination in different settings. What additional data are needed to support inclusion of MTCT of syphilis as a contributor to infant mortality for major global initiatives?</p>	Country-level studies focusing on the level of service delivery
<p>How can the effectiveness of screening and treatment be improved? Aim of research – to maximize the potential of interventions (screening and treatment) in different settings. Also, to address issues such as the best methods of partner services, timing of screening/treatment, algorithms for use of enzyme-linked immunoassay tests, increasing availability of penicillin at lower-level facilities, etc.</p>	Country-level studies of health systems and on the level of service delivery
<p>Monitoring and evaluation issues Aim of research – to identify feasible and appropriate indicators for monitoring and evaluation at multiple levels (e.g. use of stillbirth as an impact measure). How to interpret data with increased use of treponemal rapid testing. What are appropriate criteria for certification and maintenance of elimination?</p>	Studies at country, regional and global levels
<p>What is the evidence for integrated interventions? Aim of the research – to understand the benefits and risks of integrated screening efforts (e.g. with PMTCT or malaria prevention in pregnancy). What is the field performance of dual HIV/syphilis point-of-care tests?</p>	Country-level studies; literature reviews

Intensified support countries will receive technical support to develop their own national plans through the following processes:

- consultations between WHO regional offices and country ministries of health to gauge interest in each country (in process);
- regional-level meetings involving participants from interested countries (already held in some regions);
- country development of plans and strategies for elimination of MTCT of syphilis, with global and regional support, assistance and capacity building, to:
 - strengthen and expand coverage of early maternal screening and prompt treatment of individuals who test positive;
 - integrate global indicators of elimination of MTCT of syphilis into existing maternal, newborn and child health monitoring and evaluation systems (in process).

Countries are encouraged to identify opportunities to develop integrated plans or plans that take other programmes into account, such as the dual initiatives in the three WHO regions to eliminate MTCT of HIV and syphilis (see Section 1.3) (21, 22). Once plans have been developed, each country will be encouraged and supported to follow a step-by-step approach to implementation, such as that based on WHO's programme guidance tool for reproductive tract infection (RTI)/STI programmes (PGT) (see Box 2.1) (35). The PGT, along with a number of other guidelines and tools, are available

to support implementation of the country plans (see Appendix 3). The tools and technical support provided by the initiative partners can assist countries to set their own priorities for syphilis elimination and improvement of ANC. The process is intended to increase the likelihood that all stakeholders will buy into the priorities set for the initiative, thereby strengthening sustainability and the potential for success.

Intensified support countries will be asked to make a commitment to ensuring that their existing workforce involved with maternal, newborn and child health systems will carry out the country plans for the elimination of MTCT of syphilis. Furthermore, over the course of the 4 years of funding, we will work with intensified support countries to obtain future funding or justify the reallocation of existing health-care budgets to ensure the sustainability of the intervention.

Activity stream 3: monitoring and evaluation

Monitoring and evaluation are critical components of the initiative at multiple levels. At national, subnational and local levels, the collected data will be used to ensure that programmes have sufficient coverage and quality to meet the initiative's goal, and that key subpopulations are targeted appropriately. It will also serve as vital evidence for advocacy and resource mobilization around the elimination of MTCT of syphilis, which can ensure programme continuity and sustainability.

Box 2.1

Programme guidance tool for reproductive tract infection/sexually transmitted infection programmes

The PGT facilitates an action-oriented process that can be used by decision-makers to set goals and directions and to prioritize interventions for addressing the problem of RTIs, including STIs. It takes into account the full range of contextual factors that can influence the ability of a health system to set priorities and deliver effective interventions, recognizing that appropriate decisions about policy and programme development should not only be based on disease epidemiology. The PGT recognizes the importance of relationships between the community, service clients, the service-delivery system, and the mix of interventions and services provided, taking into account how these interactions are influenced by the broader sociocultural, economic and political context.

The PGT approach consists of 10 steps. The first eight steps amount to a strategic assessment of the current situation, on the basis of which strategic recommendations can be made. In step 9, the strategic recommendations are implemented, and in step 10, those recommendations found to be effective are implemented on an expanded scale.

At the regional level, monitoring and evaluation data will enable countries with similar policy- and systems-level issues (e.g. distribution; health services coverage; surveillance and data systems; maternal, newborn and child health programme integration) to learn from each other.

At the global level, impact indicators will be used to monitor global programme impact, while the tools developed and lessons learnt through this initiative will contribute to scale-up in other countries in the future.

A broad range of activities are planned to monitor and evaluate the initiative, including:

- global collaboration with stakeholders to assist initiative partners in defining how indicators should be measured;
- development of tools to assist with collection of high-quality data, analysis that provides informative data to guide the programme, and dissemination of findings;
- regional consultations to define criteria and processes for validation of elimination of MTCT of both syphilis and HIV;
- national-level collaborative efforts to adapt existing national indicators to WHO recommendations where possible, outline definitive plans for monitoring and evaluation of MTCT of syphilis, and determine how indicators

should be integrated into existing data-monitoring systems;

- regular collection and analysis of monitoring reports at all levels, with prompt feedback to programmes;
- development of sustainable mechanisms for providing ongoing support for in-country monitoring and evaluation of the adverse outcomes of pregnancy that result from syphilis infection.

Indicators and targets for the elimination of mother-to-child transmission of syphilis

Extensive consultations with a wide range of stakeholders have identified a limited number of indicators and targets to measure progress towards the goal of eliminating MTCT of syphilis, which can be feasibly incorporated into existing maternal, newborn and child health data systems (36). These include core indicators from WHO-recommended indicators for measuring universal access to reproductive health, as well as universal access to HIV interventions; impact indicators (congenital syphilis rates and the proportion of stillbirths attributable to syphilis in the mother); and a summary process indicator to estimate overall programme effectiveness. Furthermore, additional indicators may be necessary at the global, regional and national level, to provide a more comprehensive picture of initiative progress. Indicators are summarized in Box 2.2.

Box 2.2

Indicators for the elimination of mother-to-child transmission of syphilis

Core process indicators – routine

Testing of ANC attendees for syphilis at first visit (*global target >90% by 2015*)

Positive syphilis serology in pregnant women (*country-specific target*)

Treatment of syphilis-seropositive pregnant women (*global target >90% by 2015*)

Additional indicators – as able

Congenital syphilis rate (country- or region-specific target)

Estimated proportion of all syphilis-infected pregnant women who receive treatment by 24 weeks' gestation (*proposed target > 80%*)

Proportion of stillbirths attributable to syphilis in the mother (*proposed target <2%*)

2.3 Key initiative partners

National-level country teams

In-country activities for intensified support countries will be led by a programme coordinator working with a **country team**, made up of key stakeholders such as representatives from involved health programmes (maternal and child health, STI/HIV etc.), WHO country offices, representatives of civil society, representatives of primary stakeholder groups, donors, multilaterals, bilaterals, nongovernmental organizations (NGOs), research investigators and communications specialists.

The World Health Organization

The WHO Department of Reproductive Health and Research (RHR), with the assistance of the Departments of Maternal, Child and Adolescent Health (MCA) and HIV/AIDS, will coordinate global leadership and implementation of the initiative, provide technical support, and promote improvement of the evidence base for interventions. In addition, WHO regional advisers covering one or more of the areas of STI, HIV, reproductive health and MCH will provide similar functions at the regional level.

The mission of RHR is to help people to lead healthy sexual and reproductive lives. In pursuit of this mission, the department endeavours to strengthen the capacity of countries to enable people to promote and protect their own sexual and reproductive health and that of their partners, and to have access to, and receive, high-quality sexual and reproductive health services when needed.

MCA works to strengthen WHO capacity to support countries' efforts to improve maternal, newborn and child health and reduce maternal, perinatal and child mortality. The department aims to reinforce advocacy, technical support, monitoring and evaluation, and partnerships in countries, to ensure that WHO can provide the most up-to-date information and guidance on maternal, newborn and child health, including issues related to MTCT of syphilis.

Staff of the Department of HIV/AIDS collaborate with other UN agencies, ministries of health, development agencies, NGOs, health-services providers, health-care institutions, people living with HIV and other partners. The aim is to strengthen all aspects of the health sector, in order to deliver much-needed HIV services. WHO provides technical support and develops evidence-based norms and standards to help transform the goal of universal access to HIV care into a reality. An important aspect of universal access to HIV is to strengthen and expand health systems, including those for prevention and treatment of MTCT of syphilis.

WHO will manage the technical, programmatic and resource-building functions of the initiative. It will also appoint seven full-time staff at the global and regional level: a programme director, a laboratory quality assurance/procurement officer, an advocacy/communications/fundraising officer, an assistant/fiscal programme officer and three regional officers. Funds channelled through WHO would also be used at the global, regional and country levels to promote advocacy, strengthen policy, develop guidelines, scale up programmes, and support essential research to support elimination of MTCT of syphilis. Funds channelled through WHO are not intended for routine programme costs.

United Nations agency partners

The United Nations Population Fund (UNFPA) is an international development agency that promotes the right of every woman, man and child to enjoy a life of health and equal opportunity. UNFPA supports countries in using population data for policies and programmes to reduce poverty and to ensure that every pregnancy is wanted, every birth is safe, every young person is free of HIV/AIDS, and every girl and woman is treated with dignity and respect. For the initiative for the elimination of MTCT of syphilis, UNFPA plans to support introductory activities, implementation and upscaling, as well as capacity building and logistics management. In addition, UNFPA can facilitate pooled procurement and support countries to integrate adequate programmes in their national budget.

The United Nations Children’s Fund (UNICEF), is the leading UN agency tasked to advocate for children. The heart of UNICEF’s work is in the field. Each country office carries out UNICEF’s mission through a unique programme of cooperation developed with the host government. Regional offices guide this work and provide technical assistance to country offices as needed. For the initiative for the elimination of MTCT of syphilis, UNICEF plans to support implementation and scale-up, as well as logistics and supplies.

The Joint United Nations Programme on HIV/AIDS (UNAIDS) is an innovative joint venture of the UN family, bringing together the efforts and resources of 10 UN system organizations in the AIDS response, to help the world prevent new HIV infections, care for people living with HIV, and mitigate the impact of the epidemic. The UNAIDS Secretariat works on the ground in more than 80 countries worldwide. Coherent action on AIDS by the UN system is coordinated in countries through the UN theme groups, and the joint programmes on AIDS. For the initiative for the elimination of MTCT of syphilis, UNAIDS plans to support advocacy on HIV-infected women, and linkages between HIV programmes, STI control programmes and sexual and reproductive health programmes.

United States of America Centers for Disease Control and Prevention

The Centers for Disease Control and Prevention (CDC) is the agency of the Department of Health and Human Services in the USA that focuses on public health and prevention. With a mission of collaborating to create the expertise, information and tools that people and communities need to protect their health, CDC works with global partners on specific global goals, including public health programmes aimed at reducing infant mortality. The Division of STD [Sexually Transmitted Disease] Prevention (DSTDP) in the National Center for HIV, Viral Hepatitis, STD and TB Prevention is CDC’s component agency supporting the global elimination of MTCT of syphilis. In the initiative for the elimination of MTCT of syphilis, DSTDP will

provide technical support for the surveillance, monitoring and evaluation framework for the global initiative, as well as quality assurance of laboratory and health services.

Battling Against Syphilis – a Team Approach (BASTA)

An informal collaboration of key partners interested in eliminating MTCT of syphilis was created by WHO and CDC approximately 5 years ago, called “BASTA”: Battling Against Syphilis – a Team Approach. There are over 100 BASTA collaborators, who share ideas and information on efforts to eliminate MTCT of syphilis. BASTA collaborators work around the world in bilaterals, NGOs, academic centres, professional organizations and civil society (see Appendix 4). BASTA has been instrumental in the development of the investment case and research agenda outlined in this document, and has promoted and supported collaborative efforts, including dissemination of information (publications, symposium, etc.), development of tools, research in key areas, provision of technical expertise to countries, and integration of elimination of MTCT of syphilis into their respective work agendas.

In March 2012, several BASTA collaborators created the Global Congenital Syphilis Partnership, hosted in the London School of Hygiene and Tropical Medicine. WHO looks forward to collaborating with the newly formed partnership, in particular to:

- heighten public and professional awareness, and sense of urgency, on maternal syphilis and MTCT of infection;
- mobilize global commitment and action to scale up knowledge transfer and capacity building to accelerate the elimination of MTCT of syphilis;
- optimize the use of available tools in the fight against MTCT of syphilis, and enhance delivery of syphilis diagnosis and treatment, especially in pregnant women.

2.4 Management structure

WHO will coordinate the activities of each of the main partners involved in the initiative, as well

as donor inputs and reporting requirements, and a global fundraising and advocacy campaign. Initiative partners will also be responsible for disseminating outputs (e.g. at national and international meetings), updating and reviewing existing guidelines, and disseminating recommendations to both intensified and general support countries.

These activities will be undertaken through a close collaboration between staff at global and regional levels who are dedicated to work on this elimination initiative, as well as staff working for allied programmes that are fundamental to the success of the initiative (e.g. staff working on maternal child health, and those working on STI control and HIV programmes).

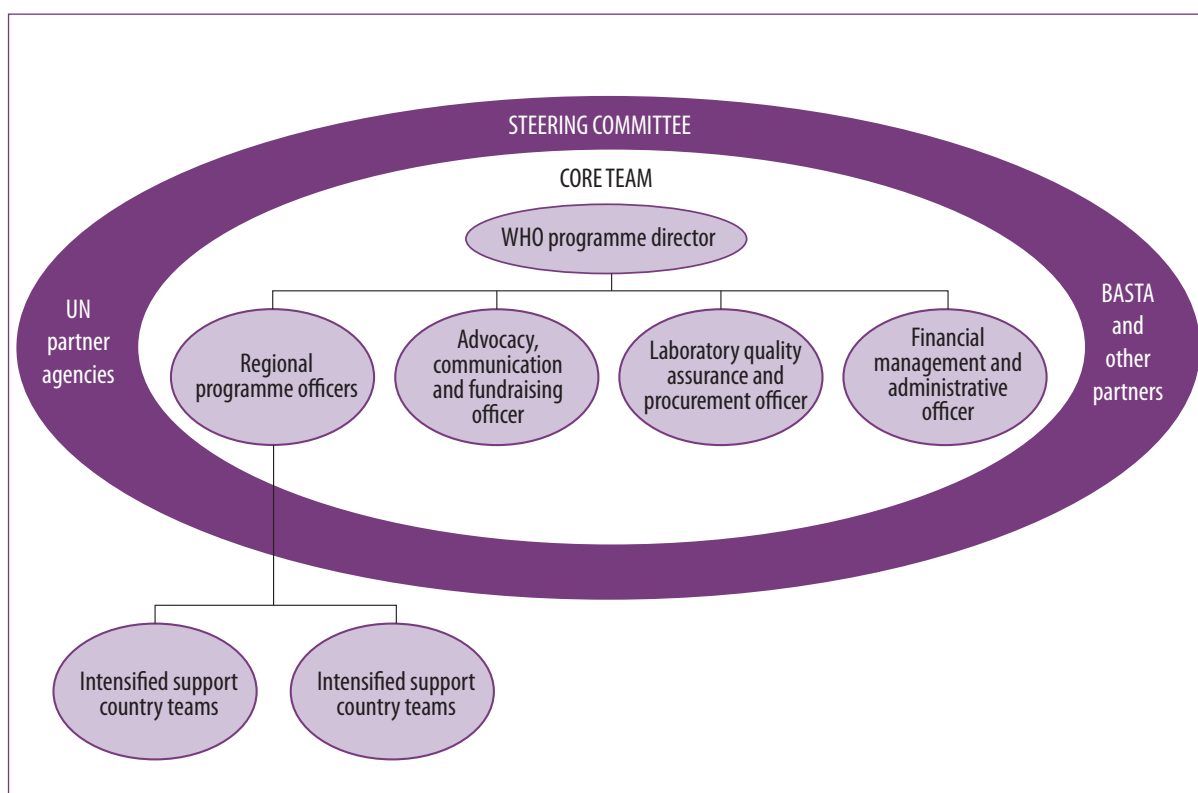
Fig. 2.1 is a graphical representation of the overall management structure for implementing the initiative. The roles and responsibilities of the major players are described next.

The **core team** will be composed of the WHO programme director, the regional programme officers (who will represent the intensified support country teams), the advocacy/communication/fundraising officer, the laboratory quality assurance and procurement officer, and the financial management/administrative officer. The core team will report to the steering committee. The **steering committee** will be composed of the core team, as well as representatives of key UN partner agencies and other partners. The core team and the steering committee will need to be financially and logistically supported to achieve their mandates.

The role of the core team is to ensure coordination at all levels, in both intensified and general support countries:

- **the programme director**, based at WHO headquarters, will act on behalf of the steering committee to oversee the core team. This person will have primary responsibility for programme implementation, coordination of the programme and with partners, and achievement of

Fig. 2.1
Management structure of the initiative for the global elimination of mother-to-child transmission of syphilis



objectives. In addition, the programme director will oversee operational research, monitoring and evaluation activities;

- **regional officers** will be placed in three of the WHO regions to aid in full implementation of activities, and to promote the initiative to intensified and general support countries in their region. These regional officers will also serve as technical officers, responsible for monitoring and evaluation for their region. The regional officers will help to coordinate activities across the range of programmes involved in delivering the goals of the initiative (ANC, STI control, prevention of MTCT of HIV, etc.).
- **an advocacy, communication and fundraising officer** will be hired and deployed at WHO headquarters to lead an advocacy/communication/fundraising technical group. This person will have primary responsibility for advocacy, donor coordination, and communication. This officer will provide fundraising and strategic guidance to fund and launch the initiative, and ensure active communication between the core team, the steering committee and other partners;
- **a laboratory quality assurance and procurement officer** will be hired and deployed at WHO headquarters to work closely with the WHO Essential Medicines Programme Department to develop and support global, regional and national laboratory quality assurance systems, support the steps necessary for prequalification of diagnostics, and work to improve the stability of procurement of essential diagnostics and medications by countries;

- **a financial and administrative officer** will be hired and deployed at WHO headquarters. Her/his primary responsibilities will be to lead the financial management technical group, develop a fiscal reporting system that will be used by all funds' recipients, and track all funds held and deployed in the field for specific activities;

The role of the **steering committee** will be to:

- determine the overall strategic plan for the global initiative;
- direct policy and guide the overall trajectory of the initiative;
- review narrative and financial reports;
- be responsible for the overall accountability of the resources;
- champion the global elimination initiative in the international arena;
- review and approve the annual programme of work to ensure that activities in intensified support countries are in line with the vision and goals;
- review, discuss and provide input on funding proposals;
- support intensified-support-country-level programme coordinators to develop national plans;
- coordinate overall monitoring and evaluation;
- review annual programme results and overall progress towards achievement of the global elimination initiative.

3. The strength of this initiative

3.1 Leveraging existing investments in maternal and child health

This initiative will build on investments in maternal and child health services that have already been made by governments and donors in developing countries. It works through, and therefore inevitably strengthens, national health systems, particularly antenatal and other reproductive and sexual health-care programmes.

Today, over three quarters of all pregnant women receive at least one ANC visit (24). This is an indication that programmes and infrastructure exist in many countries, and that there is widespread awareness and acceptance of ANC by pregnant women.

This initiative will help to maximize the ability of these existing programmes to improve maternal health and reduce infant mortality. It will harness new technological developments and strengthen existing services to promote early ANC for all pregnant women and ensure that they receive testing (and, where indicated) treatment for syphilis at their first antenatal clinic visit. We support a simple, integrated and effective ANC approach that can provide sustainable services within the broad context of strengthening primary health care, while concentrating on this prevalent, high-burden and neglected disease.

The focus on early access to services and the quality of comprehensive ANC will strengthen synergistic efforts to reduce the burdens of HIV, malaria, tetanus, parasites and accompanying anaemia, as well as MTCT of syphilis. As such, it will promote synergies by supporting:

- ongoing community mobilization programmes (to encourage women to seek and access ANC early in pregnancy);
- existing efforts to improve the quality of ANC;

- health-system initiatives to promote integrated comprehensive sexual and reproductive health care.

In addition, it is recognized that the elimination of MTCT of syphilis is likely to be more achievable if syphilis screening and treatment activities are also included in the existing health initiatives (such as elimination of MTCT of HIV). Therefore, combining syphilis interventions with basic ANC programmes as well as prevention of MTCT programmes makes medical, economic and political sense (37).

Recent efforts by WHO have simplified ANC and provided norms to encourage health-care workers to emphasize a few essential components of care (38, 39). This initiative will build on these norms and provide support for health-services evaluation that can jump-start feasible and efficient management and data-collection systems around integrated ANC. It will also build capacity that supports all ANC – even beyond elimination of MTCT of syphilis.

3.2 Supporting country-level impact through global coordination

The initiative outlined in this investment case does seek a limited amount of funding for country-level programme implementation. Countries identified for intensified support – which all have a high burden of MTCT of syphilis – will already be committed to syphilis elimination and have ANC programmes in place, backed by other sources of funding. They also may already be receiving substantial financial support for HIV, tuberculosis and malaria prevention (e.g. The Global Fund to Fight AIDS, Tuberculosis and Malaria). It is hoped that the funding for country-level programme implementation from this initiative can be used to integrate components of elimination of MTCT of syphilis into existing ministry of health programmes to ensure sustainable and strengthened health systems.

Through a series of global, regional and national consultations, countries have indicated that they need technical assistance to learn how to integrate and scale up syphilis screening and treatment into existing programmes and to monitor these interventions. Countries have also indicated a need to bring more attention to the burden of MTCT of syphilis at all levels, which will help to prioritize the issue on national and international health agendas.

To this end, the initiative will mobilize regional and global stakeholders into a network that can deliver rapid, targeted technical assistance to intensified support countries to work alongside national counterparts to fully and effectively integrate syphilis interventions into existing ANC and PMTCT of HIV programmes. This initiative will also dedicate human and financial resources at the regional and global levels, to work with national colleagues to monitor the scale-up of country-level syphilis-elimination interventions. Although prioritization of resources will be aimed at the intensified support countries, it is anticipated that the network created by the investment case will also be able to provide general support for other countries as needed.

3.3 Investing in surveillance, monitoring and evaluation

Previous WHO/CDC technical consultations have recommended the development of a monitoring system based upon already-established national systems for ANC. Such an approach supports overall health-systems infrastructure and a quality package of antenatal and perinatal preventive services. Through these consultations, a list of the critical benchmarks was proposed for appropriate local programmes within each country, with annual measurement recommended. Some have already been tried out in local settings; others need further evaluation for feasibility. Investment in this initiative will support local and national-level research needed to solidify the critical programme benchmarks that will be adopted globally.

Adverse pregnancy outcomes are the critical public health problem associated with maternal syphilis infection. The congenital syphilis case rate is the most widely recognized measure of the impact of elimination efforts. Unfortunately, global surveillance of MTCT of syphilis is challenging, since there is no single test or combination of laboratory tests to definitively diagnose an infected infant. As a result, a case definition for congenital syphilis must rely on clinical history and examination. Thus, case definitions vary widely by country, and a globally accepted surveillance case definition is still under development.

Maternal syphilis infection also contributes substantially to rates of stillbirth, though this outcome is often underreported in many settings. Nonetheless, despite the current lack of universal measuring of stillbirth rates, we are proposing this as a potentially sensitive and specific measure of the impact of elimination of MTCT of syphilis efforts. Promoting the monitoring and measurement of stillbirth rates will not only allow us to assess the impact of this initiative, it will also help support and strengthen reproductive health surveillance programmes more generally.

In addition, discussions at a regional and global level are under way to identify criteria and processes for validation of elimination. Given that there are several countries that may actually have eliminated MTCT of syphilis already, establishment of such a process is critical for recognizing this achievement, as well as is providing recommendations on how to maintain elimination. In addition, validation may be an important motivator to engage countries in elimination, and encourage countries to go the last distance to provide services for even the most difficult-to-reach populations. The validation process is being undertaken jointly with the global programme to eliminate MTCT of HIV, given the commonalities of the initiatives and programme platforms.

3.4 Implementing knowledge and best practices

This investment case represents a new direction for WHO and its partners in their goal of eliminating MTCT of syphilis, but it also builds upon many years of experience and evidence gathering. In recent years, several state-of-the-art reviews on maternal and congenital syphilis (MTCT of syphilis) have been published to highlight the problem and advocate action for its elimination (40). These reviews provide empirical evidence of the burden of MTCT of syphilis globally and information on experiences of programmes attempting to intervene and address this burden.

At regional level, some longstanding efforts to eliminate MTCT of syphilis have made great progress, but still need assistance to reach the last distance. For example, the Pan American Health Organization (PAHO) has developed several tools to assist countries with development of policy, clinical guidance, and monitoring and evaluation (41). See also Box 3.1. However, PAHO needs additional support to provide technical assistance to countries and strengthen monitoring and evaluation systems. In the WHO South-East Asia and Western Pacific Regions, the Asia Pacific Task Force (which includes WHO, UNAIDS, UNICEF and UNFPA) has also made great strides in outlining a strategy for dual elimination of MTCT of HIV and syphilis, including indicators for monitoring and evaluation, and a

costing, too, for example (42). The next step for the South-East Asia and Western Pacific Regions, however, is to identify resources to work with countries to establish integrated policies and ensure clinical guidelines and monitoring systems support these policies. The African Region is currently developing a regional framework for elimination of MTCT of HIV, which includes the strengthening of related MCH services such as the elimination of MTCT of syphilis (22).

In all of these regions, scaling-up of use of point-of-care rapid testing has been identified as critical for expanding testing to pregnant women seen in peripheral health settings. All regions have also expressed the need to establish criteria and a process for validation of elimination that is integrated with that for MTCT of HIV. Thus, it is crucial that WHO works closely with the regions to facilitate interregional collaboration and establish credible, sustainable processes for validation of elimination globally and regionally.

There is also much work being done in the area of improving best practices for syphilis testing. WHO and other partners also support the elimination of MTCT of syphilis through work on improved rapid syphilis diagnostic tests applicable for resource-limited settings, including development of rapid point-of-care tests that use whole blood (e.g. finger prick) samples that can be used by health-care

Box 3.1

PAHO Regional Initiative to Eliminate Vertical Transmission of HIV and Syphilis

Since 1995 PAHO has strived to eliminate MTCT of syphilis in the Americas. In 2009, PAHO countries, in collaboration with WHO, UNICEF and others, agreed to a goal of dual elimination MTCT of HIV and congenital syphilis (MTCT of syphilis) by 2015.

The PAHO initiative aims to reduce MTCT of HIV to 2% or less and reduce congenital syphilis (including stillbirths) to 0.5 cases per 1000 live births or fewer. In addition, the regional initiative seeks to ensure that at least 95% of pregnant women receive early ANC that includes screening for both HIV and syphilis.

The initiative intends to attain these goals through scaling up services for primary prevention of HIV and syphilis and strengthening of health systems for maternal and child health services, surveillance, monitoring and evaluation.

providers at the lowest level of health care. However, the syphilis point-of-care tests currently available commercially are treponemal, meaning that they can only measure a lifetime history of syphilis exposure. Thus, additional support is needed for WHO to encourage development and field testing of nontreponemal tests to measure current syphilis infection, as well as bundled diagnostics that allow concomitant testing for syphilis, HIV, hepatitis B, etc. The development of such tests is critical for minimizing the burden of primary care health workers to provide quality, integrated care.

These are just a few examples of the efforts and advances that this initiative will build upon and help to advance. Now – more than ever before – is the right time to address MTCT of syphilis with a large-scale, global initiative. Investment today will contribute significantly to maternal and child health improvements around the world, including achievement of the MDGs.

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Appendix 1: economic analysis and disability-adjusted life years calculations

Methods

We conducted an illustrative analysis of the 4-year cost, health impact, and cost-effectiveness of syphilis programmes in eight hypothetical country case scenarios. These country scenarios vary in terms of current syphilis testing and treatment coverage of all pregnant women (high (70%) or low (20%)), syphilis ANC prevalence (high (3%) or low (0.5%)), and country cost of health services (high or low, based on WHO CHOICE (Choosing Interventions that are Cost Effective) unit cost data).

The cost analysis assessed the cost of the intervention – implementing expanded testing and treatment of syphilis in pregnancy. The health-impact analysis translated increased testing and treatment into adverse outcomes averted, and the associated averted disability adjusted life years (DALYs). The cost-effectiveness analysis adjusted for offsetting savings due to averted adverse outcomes, and if there was still a net cost, that cost was divided by the DALYs averted. The key inputs, assumptions and rationale for the calculations of the costs and DALYS results are presented in Table A.1.

Our key cost assumption concerned the cost of implementing testing and treatment. This was derived from several sources. Key commodity prices (e.g. rapid plasma reagin (RPR) tests and penicillin doses) were determined from the World Health Organization (WHO) bulk procurement system, with allowances for delivery costs. The costs of labour and of adverse outcomes were derived from an analysis using South Africa costs (43). The overall cost of testing was US\$1.83–2.30 per woman and of treatment with three doses of penicillin was US\$3.72–3.79.

We assumed, based on published evidence, that treatment was 90% effective, that coverage depends on the current proportion tested and treated: 70–95% of women are in antenatal care (ANC), of whom 80–90% are tested, and 90–95% of test-positive women are treated. The adverse outcomes averted were stillbirth/early fetal losses, 20.9%; early neonatal deaths, 9.3%; prematurity or low birth weight, 5.8%; and infants with clinical evidence of syphilis, 15.5%. These rates derived from a systematic search and abstraction of studies of untreated syphilis.

We also assumed that treating syphilis reduced the horizontal spread of syphilis and had a modest (20%) effect in reducing the effect of syphilis as a cofactor for transmission of HIV. The DALYs averted per adverse event averted were derived from estimates in the *Global burden of disease* (44). All long-term outcomes were discounted, but the analysis did not discount over the 4 years of initiative implementation. Further details (including sensitivity analyses) are available in a technical supplement on request.

Results

We found that controlling mother-to-child transmission (MTCT) of syphilis appears to save more than it costs in four of the eight country scenarios we examined. The initiative was cost saving in these four countries, even when excluding the benefits of reducing the horizontal spread of syphilis, and excluding syphilis-attributable HIV. Results by scenario are presented Table 1.4.

Table A.1
Inputs and assumptions for illustrative analysis of the 4-year cost, health impact, and cost-effectiveness of syphilis programmes in 8 hypothetical country case scenarios

Parameter	Value or range ^a	Source/notes
Adverse event rate		
Stillbirth/early fetal loss	0.209	Synthesis of research findings (Table 1.1)
Early neonatal death	0.093	Synthesis of research findings (Table 1.1)
Infected infant	0.155	Synthesis of research findings (Table 1.1)
Prematurity or low birth weight	0.058	Synthesis of research findings (Table 1.1)
Costs, US\$		
Stillbirth / spontaneous abortion	(0)–(1)	Per Rydzak and Goldie 2008 (43), delivery of healthy infant = US\$58
Perinatal death	893–3571	Per Rydzak and Goldie, 2008 (43), adjusted per WHO CHOICE inpatient unit costs
Infected infant	182–243	Per Blandford et al, 2007 (27), and Rydzak and Goldie, 2008 (43), includes adjustment for 30% discovery rate, adjusted per WHO CHOICE outpatient unit costs
Prematurity or low birth weight	366–1464	Per Rydzak and Goldie, 2008 (43), adjusted per WHO CHOICE inpatient unit costs
Primary syphilis	15	Estimate based on single visit, test, penicillin
Secondary and early latent syphilis	15	Same as primary
Late latent and tertiary syphilis	500–2000	Based on Chesson et al, 2004 (45) estimates for USA,, adjusted for lower price and lower incidental treatment in developing countries and WHO CHOICE inpatient unit costs
HIV infection	6500 (28)	
Syphilis test, test + labour/supplies	1.83–2.30	Based on WHO Bulk Procurement estimates (WHO, unpublished data, 2012)
Course of benzathine benzylpenicillin (3 doses)	3.72–3.79	Based on WHO Bulk Procurement estimates (WHO, unpublished data, 2012)

^a Values in parentheses indicate negative values.

Appendix 2: proposed budget for the initiative for the global elimination of mother-to-child transmission of syphilis

5-year budget summary in US\$	Year 1	Year 2	Year 3	Year 4	4-year total
Global support					
1 P5, programme director, Geneva	330 000	330 000	330 000	330 000	1 320 000
1 P4, laboratory quality assurance and procurement officer, Geneva	285 000	285 000	285 000	285 000	1 140 000
1 P3, advocacy, communications, and fundraising officer, Geneva	230 000	230 000	230 000	230 000	920 000
1 G5, financial and administrative officer, Geneva	170 000	170 000	170 000	170 000	680 000
Advocacy efforts	50 000	50 000	50 000	50 000	200 000
Technical and strategic support to regions and countries	100 000	100 000	100 000	100 000	400 000
International meetings	150 000	150 000	150 000	150 000	600 000
<i>Subtotal global support</i>	<i>1 315 000</i>	<i>1 315 000</i>	<i>1 315 000</i>	<i>1 315 000</i>	<i>5 260 000</i>
Regional support					
1 P3, regional officer	230 000	230 000	230 000	230 000	920 000
1 P3, regional officer	230 000	230 000	230 000	230 000	920 000
1 P3, regional officer	230 000	230 000	230 000	230 000	920 000
Technical and strategic support to countries	150 000	150 000	150 000	150 000	600 000
Regional meetings	120 000	120 000	120 000	120 000	480 000
<i>Subtotal regional support</i>	<i>960 000</i>	<i>960 000</i>	<i>960 000</i>	<i>960 000</i>	<i>3 840 000</i>
Country support					
Programme supervision	400 000	400 000	400 000	400 000	1 600 000
Advocacy and policy development	150 000	150 000	150 000	150 000	600 000
Evidence-based guideline development, training and dissemination	300 000	300 000	300 000	300 000	1 200 000
Evaluation of indicators and impact	200 000	200 000	200 000	200 000	800 000
Strengthening of laboratory quality assurance and test procurement	300 000	300 000	300 000	300 000	1 200 000
Policy, implementation barriers and operational research	200 000	200 000	200 000		600 000
Research on social sciences or partner management		150 000	150 000		300 000
<i>Subtotal country support</i>	<i>1 550 000</i>	<i>1 700 000</i>	<i>1 700 000</i>	<i>1 350 000</i>	<i>6 300 000</i>
<i>Subtotal</i>					<i>15 400 000</i>
Administrative support (13%)					2 002 000
<i>Grand total</i>	<i>3 825 000</i>	<i>3 975 000</i>	<i>3 975 000</i>	<i>3 625 000</i>	<i>17 402 000</i>

Appendix 3: list of tools available for country-level activities

Advocacy and programme tools

The global elimination of congenital syphilis: rationale and strategy for action

- Description: document outlining strategies for elimination that can be used for advocacy and implementation
- Available at: <http://www.who.int/reproductivehealth/publications/rtis/9789241595858/en/index.html>

A strategic approach to strengthening control of reproductive tract and sexually transmitted infections

- Description: programme manager tool based on stepwise and comprehensive approach to integrate interventions in existing programmes or to strengthen health programmes
- Available at: <http://www.who.int/reproductivehealth/publications/rtis/9789241598569/en/index.html>

Methods for surveillance and monitoring of congenital syphilis elimination within existing systems

- Description: tool for regional and national programme managers on the core indicators for elimination of congenital syphilis (MTCT of syphilis) efforts that are harmonized with and integrated into existing data-collection systems
- Available at: <http://www.who.int/reproductivehealth/publications/rtis/9789241503020/en/index.html>

Global strategy for the prevention and control of STIs: 2006–2015. Breaking the chain of transmission

- Description: a technical and advocacy document intended to offer guidance on how to improve sexually transmitted infection (STI) control programmes
- Available at: <http://www.who.int/reproductivehealth/publications/rtis/9789241563475/en/>

Nine steps for developing a scaling-up strategy

- Description: a guide for programme managers and technical support agencies to facilitate systematic planning for scaling up
- Available at: <http://www.expandnet.net/PDFs/ExpandNet-WHO%20Nine%20Step%20Guide%20published.pdf>

Clinical guidelines

Sexually transmitted and other reproductive tract infections: a guide to essential practice

- Description: a reference manual developed for health-care workers and programme managers on STI/reproductive tract infection (RTI) control and management in reproductive health settings (family planning and maternal and child health clinics as well as primary health care)
- Available at: <http://www.who.int/reproductivehealth/publications/rtis/9241592656/en/index.html>

Standards for maternal and neonatal care: prevention of mother-to-child transmission of syphilis

- Description: World Health Organization (WHO) recommendations on essential care for women and their babies
- Available at: http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/prevention_mtct_syphilis.pdf

Regional and national treatment/management guidelines

- Description: Expert recommendations on clinical management of syphilis and MTCT of syphilis that is locally relevant. Most nations have this information in national treatment guidelines

The use of rapid syphilis tests

- Description: information for health-care workers and laboratory technicians on the use and interpretation of rapid plasma reagin (RPR) and point-of-care rapid treponemal syphilis tests
- Available at: http://www.who.int/reproductivehealth/publications/rtis/TDR_SDI_06_1/en/index.html

Appendix 4: Battling Syphilis – a Team Approach (BASTA) participant affiliations

Alberta Health Services of Canada	National Center for STD Control, China
Amsterdam institute for Global Health and Development (AIGHD)	National Coalition of STD, United States (NCSD)
Brazil Ministry of Health	Norwegian Agency for Development Cooperation (Norad)
CDC Foundation	PATH
Centers for Disease Control and Prevention, United States (CDC)	The Population Council
Centro Internacional de Entrenamiento e Investigaciones Médicas (CIDEIM)	Public Health Agency of Canada
Centro Latinoamericano de Perinatología (CLAP)	United Nations Population Fund (UNFPA)
Children's Investment Fund Foundation (CIFF)	United Nations Children's Fund (UNICEF)
Cornell University	United States Office of the US Global AIDS Coordinator (OGAC)
Elizabeth Glaser Pediatric AIDS Foundation (EGPAF)	United States Agency for International Development (USAID)
Engenderhealth	Universidad Peruana Cayetano Heredia
FHI360	University of Alabama Birmingham
The Global Fund	University of Antwerp
Harvard University	University of Barcelona
Health Alliance International	University of California Los Angeles
Imperial College London	University of California San Francisco
Institute of Development Studies	University College London
Jhpiego	University of Gent
Johns Hopkins University	University of North Carolina
Joint United Nations Programme on HIV/AIDS (UNAIDS)	University of Victoria
London School of Hygiene and Tropical Medicine (LSHTM)	University of Washington
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