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Estimating the public health burden associated with adverse pregnancy outcomes resulting from syphilis infection across 43 countries in sub-Saharan Africa

Andreas Kuznik, PhD^{1,2}, Abdulrazaq G. Habib, FRCP³, Yukari C. Manabe, MD^{1,4}, and Mohammed Lamorde, PhD¹

¹Infectious Diseases Institute, Makerere University College of Health Sciences, Kampala, Uganda

²Celgene Corporation, Summit, NJ, USA ³Infectious and Tropical Diseases Unit, Bayero University, Kano, Nigeria ⁴Division of Infectious Diseases, Department of Medicine, Johns Hopkins School of Medicine, Baltimore, Maryland, USA

Abstract

Background—Untreated syphilis in pregnancy is associated with adverse clinical outcomes to the infant. The study aimed to estimate the public health burden resulting from adverse pregnancy outcomes due to syphilis infection among pregnant women not screened for syphilis in 43 countries in sub-Saharan Africa (SSA).

Methods—Estimated country-specific incidence of syphilis was generated from annual number of live births, the proportion of women with 1 antenatal care (ANC) visit, the syphilis prevalence rate, and the proportion of women screened for syphilis during ANC. Adverse pregnancy outcome data (stillbirth, neonatal death, low birth weight, and congenital syphilis) were obtained from published sources. Disability-adjusted life year (DALY) estimates were calculated using undiscounted local life expectancy, the neonatal standard loss function and relevant disability weights. The model assessed the potential impact of raising antenatal care coverage to 95% and syphilis screening to 95% (WHO targets).

Results—For all 43 SSA countries, the estimated incidence of adverse pregnancy outcomes was 205,901 (95% CI: 113,256–383,051) per year, including stillbirth: 88,376 (95% CI: 60,854–121,713), neonatal death: 34,959 (95% CI: 23,330–50,076), low birth weight: 22,483 (95% CI: 0–98,847), and congenital syphilis: 60,084 (95% CI: 29,073–112,414), resulting in approximately 12.5 million DALYs. Countries with the greatest burden are (in DALYs, millions) Democratic Republic of the Congo: 1.809, Nigeria: 1.598, Ethiopia: 1.466, and Tanzania: 0.961. Attaining WHO targets could reduce the burden by 8.5 million DALYs.

Conclusions—Substantial infant mortality and morbidity results from maternal syphilis infection concentrated in countries with low access to ANC or low rates of syphilis screening.

Corresponding author: Dr. Mohammed Lamorde, Research Department, Infectious Diseases Institute, Makerere University College of Health Sciences; P.O. Box 22418, Kampala, Uganda, Telephone: +256-414-307291; Fax: +256-41-307290; mlamorde@idi.co.ug.

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Keywords

Treponema pallidum; developing countries; Illness Burden; Maternal-Fetal Infection Transmission

Introduction

Syphilis infection is an important public health problem causing significant perinatal morbidity and mortality in sub-Saharan Africa (SSA).^{1,2} An estimated 2.7% (0.1% – 10.3%) of pregnant women in SSA are infected with syphilis, representing more than 900,000 pregnancies at risk each year.² Syphilis is a sexually transmitted disease caused by the spirochete, *Treponema pallidum*, and it is of particular concern in pregnancy because of the risk of transmission to the fetus. In a recent meta-analysis, untreated maternal syphilis conferred a risk of adverse pregnancy outcomes in 53.4–81.8% of women with syphilis versus 10.2–20.8% among women without syphilis.³ Neonates surviving congenital syphilis remain at risk for serious complications including low birth weight, premature delivery, congenital anomalies, active syphilis in the infant, and longer-term sequelae such as deafness and neurologic impairment.⁴

Non-treponemal screening tests and more specific treponemal tests have been used to support a diagnosis of syphilis. Recently, rapid, reliable and inexpensive immunochromatographic point-of-care tests were introduced that are reported to be highly cost-effective within antenatal care (ANC) settings.^{5,6} A study in Tanzania reported no increased risk for adverse pregnancy outcomes among seropositive pregnant women that were treated with a single dose of intramuscular benzathine penicillin.⁷ A meta-analysis of interventional studies concluded that adverse pregnancy outcomes can be prevented if infected mothers are identified and treated prior to the third trimester of pregnancy.⁸ In SSA, women may attend only one ANC visit during pregnancy and using these tests, syphilis detection and treatment can be offered on the same day.⁹ This approach is considered feasible on a large scale,¹⁰ and widespread implementation of this strategy may support global initiatives by the World Health Organization (WHO) to eliminate congenital syphilis and considerably reduce associated adverse pregnancy outcomes.

Newman *et al.*¹¹ reported an estimate of 220,000 adverse pregnancy outcomes among women with probable syphilis infection aggregated for all African countries. However, country-specific data is vital because health care policy is generally set at the national level and comparisons of the public health burden across disease states are important to define priorities for individual countries. Country-specific data on adverse pregnancy outcomes resulting from syphilis and standard measures of disease burden (e.g. Disability Adjusted Life Years, or DALYs) associated with this condition are needed to facilitate prioritization and optimal resource allocation to the countries with the greatest disease burden. Here, we report on the public health burden resulting from adverse pregnancy outcomes due to syphilis infection in 43 countries in SSA.

Methods

This study aimed to assess the public health burden, in terms of adverse pregnancy outcomes and DALYs, associated with unrecognized maternal syphilis infection for 43 countries in SSA. We assumed active syphilis infection would go unrecognized if women do not access antenatal care or get screened for syphilis during an ANC visit. To define the size of these two populations, we first collected data on the annual number of births in each of the 43 countries of interest and estimated in how many cases women did, or did not, have access to at least one ANC visit preceding birth. National estimates on the proportion of ANC attendees tested for syphilis were used to estimate the total number of women likely to be screened, or not screened, for syphilis infection.² We applied the local antenatal syphilis prevalence rate to the total number of women that either do not access ANC [annual number of live births x (1–proportion of women with at least one ANC visit)], or are not screened for syphilis during ANC [annual number of live births x proportion of women with at least one ANC visit x (1–syphilis screening rate)], to generate an estimate of the number of syphilis seropositive pregnant women in each of the 43 SSA countries. From previous research, an adjustment factor of 65% was applied to convert number of seropositive cases to probable active syphilis infections.¹¹

Next, the incremental impact attributable to probable syphilis infection on four adverse pregnancy outcomes was assessed. The four outcomes of interest were stillbirth (stillbirth plus early fetal death), neonatal death (death within 28 days after delivery), prematurity or low birth weight, and congenital syphilis.¹¹ For each of these four outcomes, the rate of adverse pregnancy outcomes among the general population was subtracted from the rate observed in syphilis-infected women to estimate the incremental number of adverse outcomes associated with maternal syphilis infection.¹¹ The sum of these four mutually exclusive events was defined as the total number of adverse pregnancy outcomes.¹¹

We translated the estimated number of adverse pregnancy outcomes into DALYs by following the methodology outlined in the 2013 Global Health Estimates (GHE) published by the WHO.¹² To capture the years of life lost (YLL) due to stillbirth or neonatal death, we multiplied the neonatal standard loss function of 91.93 years by the number of incremental events calculated by our model. Similarly, to estimate the years of life lived with disability (YLD), we applied the reported disability weights for the outcomes of low birth weight (all sequelae) and congenital syphilis to the average duration of the case, e.g. the local life expectancy at birth, and multiplied the YLD by the number of incremental events. Total DALYs were defined as the sum of YLL and YLD. Last, the WHO has recently begun an initiative to eliminate the mother-to-child transmission of syphilis, with a goal of fewer than 50 cases of congenital syphilis per 100,000 live births and targets of ANC coverage of 95%, syphilis screening of 95%, and syphilis treatment of 95%.¹³ We explored the impact of a hypothetical scenario in which we increased ANC coverage rates and syphilis screening rates to match the targets outlined in the WHO global guidance to estimate the potential reduction in adverse pregnancy outcomes and DALYs.

Data Inputs

Country-specific inputs are displayed in Table 1. Annual number of live births was based on a 2012 data reported by UNICEF.¹ The proportion of women with at least one ANC visit was also based on 2012 data.¹ For 37 out of the 43 countries in the sample, the proportion of women screened for syphilis in the ANC setting was reported by the WHO for the latest year that this data was available for, generally between 2010 to 2012, although in six cases it dated back to 2008.² For the remaining 6, we assumed this rate to be equivalent to the weighted average of the 37 countries with available data (39.5%), which was similar to a previously published estimate of 38%.¹⁴ The prevalence of syphilis infection in the ANC setting was also reported in the epidemiologic report published by the World Health Organization and was based on data reported in the years 2010 to 2012.² Where no WHO prevalence estimates were available, the analysis relied on prevalence data published in the scientific literature (Table 1, column 5), which were less current and dated back to the years 2001 to 2004.

For women with probable active syphilis, the rates of stillbirth, neonatal death, low birth weight and congenital syphilis were reported at 25.6% (95% CI: 18.5%–34.2), 12.3% (95% CI: 9.3%–16.2%), 12.1% (95% CI: 3.9%–31.8%), and 15.5 % (95% CI: 7.5%–29.0%), respectively based on a meta-analysis of adverse pregnancy outcomes in untreated syphilis-infected mothers.³ In that publication, to estimate the incremental impact of infection for uninfected women, the rate of low birth weight of 6.3% was subtracted from the rate in infected women. The published rates of stillbirth and neonatal death among the general population^{15,16} were subtracted from the syphilis-infected population in our analysis. Furthermore, the disability weights applied to low birth weight (0.106) and congenital syphilis (0.315) were based on the 2004 Global Burden of Disease Update.¹⁷ When calculating the reduction in DALYs that could be achieved by increasing ANC coverage rates to at least 95% and the rate of syphilis screening to at least 95%, we estimated how many additional women would likely be treated for an active syphilis infection and then assumed an effectiveness of penicillin therapy in reducing the incidence of stillbirth by 82% (95% CI: 67%–90%), the incidence of neonatal death by 80% (95% CI: 68%–87%), the incidence of pre-term delivery or low birth weight by 64% (95% CI: 53%–73%), and the incidence of congenital syphilis by 97% (95% CI: 93%–98%).⁸ Furthermore, the proportion of women tested positive for syphilis who receive treatment is only available for 11 out of the 43 countries in our panel, but since their weighted average estimate was relatively high (93.7%), we made the simplifying assumption that all seroprevalent cases would receive treatment. Finally, we used the lower and upper ranges of the 95% confidence intervals reported in the literature to in order to estimate confidence intervals around our base case estimates.^{3,8}

Results

Country-specific model results are displayed in Table 2. An estimated 387,636 pregnancies are expected to occur annually in women with probable syphilis infection in SSA who are not tested or treated for syphilis. Approximately 265,426 of these cases (68%) occur among women who access ANC at least once but are not screened for syphilis during pregnancy.

Across the 43 countries, 205,901 (95% CI: 113,256–383,051) additional syphilis-related adverse pregnancy outcomes are estimated to occur, comprised of 88,376 (95% CI: 60,854–121,713), stillbirths, 34,959 (95% CI: 23,330–50,076) neonatal deaths, 22,483 (95% CI: 0–98,847) low birth weight infants and 60,084 (95% CI: 29,073–112,414) cases of congenital syphilis. Almost half of all events are expected to occur in only four countries: DR Congo, Nigeria, Ethiopia, and Tanzania. Table 3 shows the public health burden associated with adverse pregnancy outcomes due to syphilis infection. We estimate that the 205,901 syphilis-related adverse pregnancy outcomes translate into 12,532,253 DALYs (95% CI: 8,252,867–18,363,948). The specific breakdown of DALYs by outcome (% of total) is stillbirth: 8,124,424 (95% CI: 5,594,314–11,189,064) DALYs (64.9%), neonatal death: 3,213,749 (95% CI: 2,144,689–4,603,528) DALYs (25.6%), low birth weight: 133,542 (95% CI: 0–587,124) DALYs (1.1%), and congenital syphilis: 1,060,538 (95% CI: 513,164–1,984,232) DALYs (8.5%). The greatest burden is estimated for the Democratic Republic of the Congo (1,809,177 DALYs; 95% CI: 1,173,634–2,667,308), followed by Nigeria (1,597,870 DALYs; 95% CI: 1,021,325–2,379,122), Ethiopia (1,466,399 DALYs; 95% CI: 969,794–2,149,390), and Tanzania (960,569 DALYs; 95% CI: 643,088–1,395,997). The lowest public health burden is estimated for Comoros (0 DALYs; 95% CI: 0–0), Cape Verde (170 DALYs; 95% CI: 116–245), Burundi (736 DALYs; 95% CI: 483–1,079) and Benin (1,125 DALYs; 95% CI: 749–1,639). The greatest relative share of the public health burden that is due to a lack of screening within the ANC setting is observed for Ghana and Malawi, where 94% of the public health burden is expected to occur in women who have at least one ANC visit. Conversely, in Niger, 96% of the burden is occurring among women with no access to ANC.

Our results suggest that increasing ANC coverage rate to at least 95% and the syphilis screening rate to at least 95% among these countries could potentially reduce the disease burden by 8,573,350 (95% CI: 6,202,785–10,421,600) DALYs annually. The potential annual reduction exceeded 100,000 DALYs in 16 countries and exceeded 1,000,000 DALYs in three cases: Nigeria, DR Congo and Ethiopia.

Discussion

This analysis estimated the annual public health burden associated with adverse pregnancy outcomes resulting from maternal syphilis infection for 43 countries in SSA. Our aggregate finding of approximately 206,000 adverse pregnancy outcomes is similar to a recently published work reporting the aggregate of the same four adverse pregnancy outcomes in SSA at approximately 220,000 per year.¹¹ The minor difference between these two point estimates is not due to methodological differences, but likely driven by the fact that syphilis prevalence estimates in Newman et al. were based on data reported through the WHO HIV Universal Access Reporting System for 2008, whereas our analysis was based on more recent data published in the 2013 WHO report on global STD infection surveillance. In this report, the most current prevalence estimates are reported by country, and generally range from 2008–2012 (see Table 1). The contribution of the present study is twofold.

First, country-specific estimates reported in this work demonstrate significant heterogeneity with much of the burden is concentrated among a few high population SSA countries with

either a relatively small proportion of women that access ANC, or a relatively low rate of syphilis screening within the ANC setting, or both. One noteworthy exception among high population countries is South Africa, where 97% of pregnant women have access to at least one ANC visit and 74.5% of those are also screened for syphilis infection, resulting in approximately 110,000 DALYs due to adverse pregnancy outcomes resulting from maternal syphilis infection. This compares to Sudan, which has a similar number of live births and only a slightly higher syphilis prevalence rate, yet because proportionately fewer women access ANC and only 3.4% are reported to be screened for syphilis infection, the public health burden in Sudan is almost six times larger. In addition, we find that the DALY estimates for countries with high rates of syphilis prevalence such as Gambia, Liberia, Madagascar and Mozambique are disproportionately high compared to the observed annual number of live births.

Second, we express the disease burden not only in terms of adverse pregnancy outcomes, but also convert the roughly 206,000 outcomes into 12.5 million DALYs. In the 2013 GHE, the disease burden associated with syphilis infection for the African region in 2011 was reported at 5.2 million DALYs.¹² This discrepancy is largely explained by the fact that the GHE estimate excludes stillbirth as an outcome in assessing the disease burden, essentially implying that human life begins exactly at birth. However, this notion is challenged by the brain-life theory, which postulates that a human being should be defined by the presence of an active human brain.¹⁸ By this definition, no distinction would exist between stillbirth and neonatal death. In fact, a recent bioethical assessment concluded that it would be ethically preferable to include stillbirths in burden of disease estimates,¹⁹ such as the GHE, and several cost-effectiveness analyses focused on maternal health have included stillbirth in their DALY estimates.^{5,20,21} In our model, stillbirths associated with maternal syphilis infection account for almost two-thirds of the disease burden (8.1 million DALYs). In fact, the burden associated with syphilis-related stillbirths is slightly below the public health burden associated with tuberculosis in the African region (9.4 million DALYs in 2011).¹² If included, the public health burden associated with adverse pregnancy outcomes resulting from maternal syphilis infection in SSA would be comparable to that of combined childhood cluster diseases (whooping cough, diphtheria, measles, and tetanus: 12.5 million DALYs) or neonatal sepsis and infections (12.6 million DALYs).¹² Such re-assessment may elevate the recognition of maternal syphilis as a public health priority.

Maternal syphilis infection may go unrecognized when there is no access to ANC, no screening for syphilis, or poor results reporting within the ANC setting. In our study, over two-thirds of all cases are missed among women who attend an ANC facility at least once, but are not screened for syphilis during their visit. Out of the 37 countries in SSA that publish such data, a screening rate below 5% is reported for 8 countries: the Democratic Republic of the Congo, Eritrea, Ethiopia, Guinea Bissau, Mali, Sierra Leone, Sudan and Togo. A national effort to increase the screening rate, particularly in countries with low screening rates, constitutes a logical first step to reduce the public health burden associated with maternal syphilis infection. The case examples of Benin, Burkina Faso, Burundi, and Chad, which all report screening rates of 100% – demonstrate that national coverage may be feasible in SSA when it is prioritized.

However, merely raising the syphilis screening rate in ANC is not sufficient given that approximately three out of ten adverse pregnancy outcomes occur in women who do not access ANC facilities, which is particularly pronounced in Chad, Ethiopia, Niger, Nigeria, and Sudan. In these countries, syphilis screening could be preceded by broader public health programs to increase access to ANC and create community-level demand for diagnosis and treatment. Alternatively, syphilis screening could be integrated with ongoing community-based campaigns for HIV screening in populations that traditionally do not seek out ANC. With the increasing emphasis on prevention of mother-to-child transmission of HIV and decentralized care, integration of syphilis testing would require relatively few additional human resources. Its feasibility and acceptability was demonstrated in Uganda and Zambia where significant increases in syphilis testing using a point-of-care test and subsequent treatment were achieved without a negative impact on HIV service delivery.⁹ Ultimately, improved access to ANC services plus improved rates of syphilis screening and subsequent antibiotic treatment is likely to have the most significant public health impact, with over 8 million DALYs potentially averted annually across SSA if the recent WHO targets were met by all countries.¹³

Globally, penicillin is recommended for syphilis treatment. United States guidelines recommend administering one single dose injection of 2.4 million units of benzathine penicillin intramuscularly for infections acquired within the previous 12 months and three doses for a total of 7.2 million units for infections of longer or unknown duration.^{22,23} A meta-analysis of birth outcomes in syphilis-infected pregnant women in resource-limited settings reported penicillin therapy reduced incidence of stillbirth and neonatal death by 80% and congenital syphilis by 97%.⁸ Using point-of-care tests and benzathine penicillin, a recent cost-effectiveness analysis found antenatal syphilis screening in SSA to be highly cost-effective in all 43 SSA countries at an average cost of \$11 per DALY averted.⁵

Similar to a previous study,¹¹ we incorporated a 65% adjustment factor to translate the seroprevalence data reported by the various epidemiologic surveillance reports into cases of probable active syphilis. This estimate was derived from RPR (non-treponemal) screening followed by treponemal test confirmation in three studies in resource-limited settings.^{7,24,25} With treponemal point-of-care testing, these biologic false positives with RPR will be eliminated such that higher estimates may be more applicable. Greatest gains will be achieved in countries where screening is limited by poor laboratory infrastructure and older tests. If the 65% adjustment factor proves conservative to estimate cases of probable active syphilis, e.g. true adjustment factor between 65%–100%, the predicted number of adverse pregnancy outcomes and DALYs would increase proportionately and may reach up to 317,000 adverse pregnancy outcomes, or 19.2 million DALYs (individual country estimates not shown). However, the relative ranking of individual countries would not change.

Our modelling approach is subject to various limitations. We used a weighted average of the remaining 39.5% for the 6 countries with no syphilis screening data. However, the actual screening rate in those 6 countries may differ from this point estimate. Our population-level estimate of the total number pregnancies was based on live births, and was not adjusted for early fetal loss or stillbirth. Furthermore, we restricted the assessment of adverse pregnancy outcomes to women who either do not access ANC or are not screened for syphilis during

ANC, although additional adverse pregnancy outcomes may occur in those women that are currently screened and treated. Also, we assumed that all seroprevalent cases are treated, but that may not always be the case. However, due to reliable data on treatment rates across the 43 countries in our analysis, it was not possible to adjust for this parameter in the calculation and, as a result, the true public health burden may be under-estimated in our calculations. Moreover, when treatment is administered, its effectiveness may not be sufficient to completely eliminate all incremental risk to the infant due to non-adherence to injection regimens or when therapy is initiated close to delivery. Consequently, our estimates likely under-represent the true public health burden by not including untreated and unsuccessfully treated cases. In addition, our assessment of the potential public health improvement associated with the WHO target levels¹³ assumes that these ambitious targets are in fact achievable, which in the case of countries with weak health care systems may not be realistic. Finally, syphilis seroprevalence in the ANC setting is not routinely reported across SSA and whenever national prevalence data was not available from the WHO reports, we looked to studies in the scientific literature for these estimates, which may not have been nationally representative. In that context, we rely on the validity of data from the WHO reports and should these contain any inaccuracies, we would carry them forward into our estimates.

Conclusion

Maternal syphilis infection is associated with substantial mortality and morbidity in infants across SSA. Notwithstanding population size and prevalence rate, the public health burden tends to be more pronounced in countries with low access to ANC or low syphilis screening rates among ANC attendees, but could be substantially reduced if countries were able to meet the WHO antenatal care and syphilis screening targets. There is an urgent need to strengthen antenatal syphilis screening programs in SSA.

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SHORT SUMMARY

Findings from a model to calculate disease burden suggest that substantial infant morbidity and mortality arises from maternal syphilis infection in sub-Saharan Africa.

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TABLE 1

Data Inputs

Country	Annual Number of Births (2012) ¹	At least 1 Antenatal Care Visit (2012) ¹	ANC Syphilis Screening Rate ²	Syphilis Prevalence (Reporting Year) ²	Estimated Active Syphilis Infection [Prevalence x 65%]	Stillbirth Rate (2009) ¹⁵	Neonatal Mortality Rate (2012) ¹
Angola	934,100	747,280	39.5% ^a	5.2% ²⁶⁽²⁰⁰²⁾	3.4%	2.5%	4.0%
Benin	371,000	319,060	100.0% (2011)	0.1% (2011)	0.1%	2.4%	3.1%
Botswana	47,700	44,838	39.5% ^a	1.3% (2010)	0.8%	1.6%	3.7%
Burkina Faso	682,700	641,738	100.0% (2011)	1.9% (2011)	1.2%	2.6%	2.5%
Burundi	443,400	438,966	100.0% (2010)	0.8% (2010)	0.5%	2.8%	2.8%
Cameroon	820,000	697,000	39.5% ^a	0.6% (2010)	0.4%	2.6%	3.2%
Cape Verde	10,100	9,898	95.0% (2012)	1.0% (2012)	0.7%	1.6%	0.8%
Central African Republic	156,300	106,284	82.6% (2011)	7.6% (2011)	4.9%	2.4%	3.8%
Chad	579,200	306,976	100.0% (2012)	4.7% (2012)	3.1%	2.9%	2.9%
Comoros	25,700	19,275	95.0% (2008)	0.0% (2010)	0.0%	2.7%	2.2%
Côte d'Ivoire	730,800	665,028	92.1% (2008)	0.2% (2010)	0.1%	2.7%	4.4%
DR Congo	2,839,500	2,527,155	4.2% (2011)	3.3% (2010)	2.1%	2.9%	3.5%
Djibouti	23,900	21,988	11.5% (2010)	8.1% (2010)	5.3%	3.4%	2.9%
Equatorial Guinea	26,400	22,704	75.8% (2012)	6.8% (2012)	4.4%	1.7%	3.0%
Eritrea	229,500	160,650	0.0% (2010)	1.1% (2008)	0.7%	2.1%	1.9%
Ethiopia	3,084,200	1,326,206	0.0% (2010)	2.2% (2010)	1.4%	2.6%	3.8%
Gabon	52,700	49,538	61.4% (2012)	2.2% (2012)	1.4%	1.7%	2.7%
Gambia	77,200	75,656	41.5% (2012)	7.0% ²⁶⁽²⁰⁰²⁾	4.6%	2.6%	3.7%
Ghana	794,300	762,528	30.8% (2008)	1.5% (2012)	1.0%	2.2%	2.6%
Guinea	427,900	376,552	30.8% (2008)	1.5% (2009)	1.0%	2.4%	3.8%
Guinea Bissau	63,100	58,683	0.4% (2008)	1.1% (2010)	0.7%	3.0%	3.6%
Kenya	1,534,900	1,412,108	71.8% (2012)	1.3% (2012)	0.8%	2.2%	2.4%
Lesotho	56,800	52,256	70.0% (2012)	2.9% (2012)	1.9%	2.5%	2.1%
Liberia	150,000	118,500	10.9% (2010)	10.3% (2012)	6.7%	2.7%	4.8%

Country	Annual Number of Births (2012) ¹	At least 1 Antenatal Care Visit (2012) ¹	ANC Syphilis Screening Rate ²	Syphilis Prevalence (Reporting Year) ²	Estimated Active Syphilis Infection [Prevalence x 65%]	Stillbirth Rate (2009) ¹⁵	Neonatal Mortality Rate (2012) ¹
Madagascar	780,500	671,230	37.7% (2012)	5.9% (2012)	3.8%	2.1%	2.4%
Malawi	638,900	606,955	23.0% (2012)	2.1% (2012)	1.4%	2.4%	3.0%
Mali	705,000	493,500	4.8% (2008)	2.4% (2010)	1.6%	2.3%	4.0%
Mauritania	130,900	98,175	4.9% (2012)	2.4% <i>b</i> (2010)	1.6%	2.7%	5.2%
Mozambique	994,700	915,124	36.8% (2012)	6.4% (2012)	4.2%	2.8%	3.5%
Namibia	59,700	56,715	93.8% (2010)	1.9% (2012)	1.2%	1.5%	2.1%
Niger	858,400	394,864	95.0% (2011)	2.6% (2009)	1.7%	2.3%	2.6%
Nigeria	7,028,000	4,076,240	39.5% <i>a</i>	1.5% (2005)	1.0%	4.2%	4.0%
Rwanda	410,100	401,898	72.3% (2012)	2.7% (2011)	1.8%	2.3%	3.5%
Senegal	524,400	487,692	39.5% <i>a</i>	0.6% ²⁷ (2001)	0.4%	3.4%	2.2%
Sierra Leone	222,500	206,925	0.0% (2010)	1.4% (2010)	0.9%	3.0%	4.2%
South Africa	1,102,300	1,069,231	74.5% (2010)	1.6% (2011)	1.0%	2.0%	1.5%
Sudan	1,263,400	707,504	3.4% (2010)	2.2% (2009)	1.4%	2.4%	2.0%
Swaziland	37,100	35,987	34.8% (2010)	8.3% (2010)	5.4%	1.8%	/A8%
Tanzania	1,898,300	1,670,504	44.9% (2010)	3.8% (2010)	2.5%	2.6%	3.2%
Togo	245,100	176,472	4.6% (2010)	1.2% (2011)	0.8%	2.5%	3.3%
Uganda	1,590,900	1,479,537	39.5% <i>a</i>	3.0% ²⁸ (2004)	2.0%	2.5%	2.5%
Zambia	608,000	571,520	27.6% (2012)	4.7% (2012)	3.1%	2.6%	2.6%
Zimbabwe	439,500	395,550	95.7% (2012)	1.9% (2012)	1.2%	2.0%	2.7%
Sum/Weighted Average	33,699,100	25,476,490	39.5%	2.7%	1.7%	2.9%	3.2%

^aThe rate of syphilis screening was not reported for 6 countries. In these cases, the weighted average of the remaining 37 countries of 39.5% was used as a proxy.

^bUsed neighbouring Mali as a proxy.

^cThe syphilis prevalence estimate of 3.0% was reported for the general female population of child-bearing age in the 2007 HIV/AIDS surveillance update by the WHO.²⁸ For this specific country, syphilis prevalence data from the antenatal care setting were not available, neither in one of the WHO reports nor in the scientific literature.

Estimated Missed Cases of Probable Active Syphilis Infection and Associated Adverse Pregnancy Outcomes

TABLE 2

Country	Stillbirth (95% CI)	Neonatal Death (95% CI)	Low Birth Weight (95% CI)	Congenital Syphilis (95% CI)	All Adverse Pregnancy Outcomes (95% CI)
Angola	4,986 (3,453–6,842)	1,684 (1,036–2,525)	1,252 (0–5,504)	3,346 (1,619–6,259)	11,267 (6,108–21,131)
Benin	8 (5–11)	3 (2–5)	2 (0–9)	5 (3–10)	18 (10–34)
Botswana	61 (43–83)	24 (16–34)	15 (0–65)	39 (19–73)	139 (78–254)
Burkina Faso	116 (80–160)	48 (33–68)	29 (0–129)	78 (38–147)	272 (151–503)
Burundi	5 (4–7)	2 (1–3)	1 (0–6)	4 (2–7)	12 (7–23)
Cameroon	488 (338–671)	223 (159–306)	123 (0–541)	329 (159–616)	1,163 (656–2,134)
Cape Verde	1 (1–1)	1 (0–1)	0 (0–1)	1 (0–1)	3 (2–5)
Central Afr. Republic	785 (545–1,076)	278 (176–410)	196 (0–863)	525 (254–981)	1,784 (975–3,330)
Chad	1,888 (1,297–2,603)	690 (441–1,015)	482 (0–2,121)	1,289 (624–2,412)	4,349 (2,362–8,150)
Comoros	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Côte d'Ivoire	35 (24–48)	13 (8–19)	9 (0–39)	24 (12–45)	81 (44–151)
DR Congo	13,309 (9,146–18,351)	4,632 (2,873–6,918)	3,401 (0–14,951)	9,088 (4,397–17,003)	30,429 (16,417–57,223)
Djibouti	250 (170–347)	104 (70–147)	65 (0–287)	174 (84–326)	593 (324–1,107)
Equatorial Guinea	97 (68–132)	36 (24–52)	24 (0–104)	63 (30–118)	220 (123–405)
Eritrea	386 (269–527)	172 (123–236)	95 (0–418)	254 (123–476)	907 (515–1,657)
Ethiopia	10,144 (7,013–13,937)	4,146 (2,823–5,866)	2,558 (0–11,247)	6,836 (3,308–12,790)	23,684 (13,143–43,839)
Gabon	76 (54–104)	31 (22–44)	18 (0–81)	49 (24–92)	175 (99–321)
Gambia	479 (331–659)	198 (135–279)	121 (0–531)	323 (156–604)	1,121 (623–2,074)
Ghana	1,276 (889–1,745)	518 (355–731)	316 (0–1,391)	845 (409–1,582)	2,956 (1,653–5,449)
Guinea	706 (490–967)	271 (179–389)	176 (0–776)	471 (228–882)	1,624 (897–3,014)
Guinea Bissau	102 (70–140)	35 (21–52)	26 (0–115)	70 (34–130)	232 (125–437)
Kenya	1,030 (718–1,409)	423 (291–594)	255 (0–1,123)	682 (330–1,277)	2,391 (1,338–4,403)
Lesotho	88 (61–121)	30 (18–45)	22 (0–97)	59 (29–111)	199 (108–373)
Liberia	2,102 (1,450–2,891)	881 (606–1,239)	532 (0–2,340)	1,423 (688–2,662)	4,938 (2,744–9,132)
Madagascar	4,753 (3,317–6,493)	2,043 (1,436–2,832)	1,173 (0–5,158)	3,135 (1,517–5,866)	11,105 (6,271–20,349)
Malawi	1,581 (1,097–2,167)	675 (470–941)	395 (0–1,738)	1,056 (511–1,976)	3,708 (2,079–6,822)
Mali	2,476 (1,722–3,390)	861 (542–1,275)	616 (0–2,710)	1,647 (797–3,082)	5,601 (3,061–10,458)

Country	Stillbirth (95% CI)	Neonatal Death (95% CI)	Low Birth Weight (95% CI)	Congenital Syphilis (95% CI)	All Adverse Pregnancy Outcomes (95% CI)
Mauritania	450 (311–620)	175 (116–252)	114 (0–502)	305 (148–570)	1,044 (574–1,943)
Mozambique	6,240 (4,297–8,594)	2,545 (1,724–3,613)	1,587 (0–6,979)	4,242 (2,053–7,937)	14,616 (8,074–27,124)
Namibia	19 (14–26)	8 (6–12)	5 (0–20)	12 (6–23)	45 (26–82)
Niger	1,903 (1,323–2,605)	776 (531–1,094)	474 (0–2,083)	1,266 (613–2,369)	4,419 (2,467–8,151)
Nigeria	11,300 (7,551–15,842)	4,436 (2,852–6,495)	3,063 (0–13,466)	8,185 (3,960–15,314)	26,984 (14,363–51,116)
Rwanda	489 (340–669)	214 (151–296)	122 (0–535)	325 (157–608)	1,150 (648–2,108)
Senegal	287 (195–398)	128 (89–178)	75 (0–330)	200 (97–375)	690 (381–1,281)
Sierra Leone	458 (314–632)	148 (87–227)	117 (0–516)	314 (152–587)	1,037 (553–1,962)
South Africa	750 (525–1,024)	343 (248–467)	184 (0–811)	493 (238–922)	1,771 (1,011–3,224)
Sudan	4,112 (2,853–5,636)	1,666 (1,134–2,357)	1,028 (0–4,519)	2,747 (1,329–5,140)	9,552 (5,317–17,652)
Swaziland	316 (221–430)	123 (84–175)	77 (0–338)	206 (99–385)	721 (404–1,327)
Tanzania	6,523 (4,509–8,962)	2,893 (2,042–3,999)	1,645 (0–7,232)	4,396 (2,127–8,225)	15,457 (8,679–28,418)
Togo	427 (296–586)	166 (111–238)	107 (0–471)	287 (139–536)	987 (545–1,832)
Uganda	4,531 (3,138–6,217)	1,961 (1,373–2,726)	1,138 (0–5,001)	3,040 (1,471–5,688)	10,670 (5,982–19,633)
Zambia	3,164 (2,187–4,347)	1,293 (880–1,829)	798 (0–3,508)	2,132 (1,032–3,989)	7,387 (4,099–13,673)
Zimbabwe	178 (124–242)	63 (41–93)	44 (0–192)	117 (56–218)	401 (221–745)
Sum	88,376 (60,854–121,713)	34,959 (23,330–50,076)	22,483 (0–98,847)	60,084 (29,073–112,414)	205,901 (113,256–383,051)

^a All adverse pregnancy outcomes defined as the sum of stillbirth + neonatal death + low birth weight + congenital syphilis

TABLE 3

Public Health Impact in terms of Disability-adjusted Life Years (DALYs)

Country	Total DALYs Associated with Adverse Pregnancy Outcomes Due to Syphilis Infection (95% CI) ^a	DALY Burden under 95% ANC and 95% Syphilis Screening Rate	DALY Reduction Achievable with Improved Antenatal Care
Angola	674,229 (438,978–992,738)	222,198 (115,098–442,970)	452,031 (323,880–549,768)
Benin	1,125 (749–1,639)	551 (329–943)	574 (420–697)
Botswana	8,432 (5,707–12,100)	2,760 (1,492–5,342)	5,672 (4,215–6,759)
Burkina Faso	16,669 (11,085–24,275)	14,467 (9,477–21,611)	2,202 (1,608–2,664)
Burundi	736 (483–1,079)	736 (483–1,079)	0 (0–0)
Cameroon	73,738 (49,261–107,772)	23,387 (12,390–46,136)	50,351 (36,871–61,637)
Cape Verde	170 (116–245)	170 (116–245)	0 (0–0)
Central Afr. Republic	106,903 (70,227–156,415)	41,670 (23,083–77,534)	65,232 (47,144–78,882)
Chad	260,184 (169,748–382,485)	78,259 (39,135–161,591)	181,924 (130,613–220,894)
Comoros	0 (0–0)	0 (0–0)	0 (0–0)
Côte d'Ivoire	4,838 (3,166–7,096)	3,330 (2,081–5,269)	1,508 (1,086–1,828)
DR Congo	1,809,177 (1,173,634–2,667,308)	541,513 (268,285–1,126,083)	1,267,664 (905,349–1,541,225)
Djibouti	36,272 (23,662–53,575)	10,843 (5,428–22,387)	25,429 (18,234–31,188)
Equatorial Guinea	13,423 (8,982–19,446)	5,753 (3,345–10,216)	7,670 (5,636–9,230)
Eritrea	56,909 (38,468–82,247)	15,732 (7,959–32,493)	41,177 (30,510–49,754)
Ethiopia	1,466,399 (969,794–2,149,390)	416,856 (207,674–867,995)	1,049,543 (762,120–1,281,395)
Gabon	10,977 (7,388–15,914)	4,218 (2,400–7,726)	6,759 (4,988–8,188)
Gambia	68,978 (45,800–100,670)	20,645 (10,556–41,992)	48,334 (35,244–58,678)
Ghana	183,264 (122,188–267,041)	54,895 (28,251–111,152)	127,582 (93,362–154,933)
Guinea	99,091 (65,524–144,818)	31,267 (16,242–62,533)	67,824 (49,282–82,286)
Guinea Bissau	13,857 (8,921–20,564)	4,124 (2,024–8,640)	9,733 (6,898–11,924)
Kenya	148,346 (99,036–215,992)	64,166 (37,362–113,816)	84,180 (61,674–102,176)
Lesotho	11,852 (7,729–17,414)	5,127 (2,901–9,261)	6,725 (4,827–8,153)
Liberia	304,578 (202,044–445,074)	88,768 (44,844–182,593)	215,811 (157,200–262,482)
Madagascar	696,298 (467,715–1,011,208)	219,698 (116,682–432,720)	476,600 (351,032–578,487)
Malawi	227,918 (152,929–329,918)	69,182 (36,009–138,747)	158,735 (116,920–191,170)
Mali	338,703 (221,827–497,634)	99,437 (49,500–206,497)	239,266 (172,327–291,136)
Mauritania	64,142 (42,092–94,403)	18,640 (9,283–38,737)	45,502 (32,809–55,666)
Mozambique	882,758 (585,815–1,283,874)	288,831 (152,525–568,465)	593,927 (433,289–715,409)
Namibia	2,836 (1,930–4,085)	2,597 (1,752–3,796)	239 (178–288)
Niger	272,269 (181,611–396,107)	93,408 (50,626–179,539)	178,861 (130,984–216,569)
Nigeria	1,597,870 (1,021,325–2,379,122)	516,480 (260,063–1,052,817)	1,081,390 (761,262–1,326,305)
Rwanda	71,936 (48,277–104,501)	28,053 (15,980–51,246)	43,884 (32,297–53,255)
Senegal	42,655 (28,084–62,703)	14,105 (7,439–27,767)	28,550 (20,645–34,936)
Sierra Leone	60,697 (39,022–89,779)	18,295 (8,982–38,262)	42,402 (30,039–51,518)

Country	Total DALYs Associated with Adverse Pregnancy Outcomes Due to Syphilis Infection (95% CI) ^a	DALY Burden under 95% ANC and 95% Syphilis Screening Rate	DALY Reduction Achievable with Improved Antenatal Care
South Africa	110,389 (75,256–158,276)	46,837 (27,771–82,167)	63,553 (47,485–76,109)
Sudan	591,440 (392,497–864,654)	168,503 (84,363–349,576)	422,937 (308,134–515,079)
Swaziland	43,910 (29,567–63,257)	13,145 (6,817–26,463)	30,765 (22,749–36,794)
Tanzania	960,569 (643,088–1,395,997)	318,223 (171,244–617,439)	642,345 (471,844–778,558)
Togo	60,258 (39,839–88,086)	17,444 (8,735–36,125)	42,814 (31,103–51,961)
Uganda	660,093 (441,897–958,472)	215,506 (115,258–420,630)	444,588 (326,639–537,842)
Zambia	452,813 (300,516–660,595)	141,367 (73,476–282,961)	311,446 (227,040–377,634)
Zimbabwe	24,551 (16,190–35,976)	16,930 (11,342–27,832)	7,622 (4,848–8,143)
<u>Sum</u>	12,532,253 (8,252,167–18,363,948)	3,958,904 (2,049,382–7,942,348)	8,573,350 (6,202,785–10,421,600)

^aTo estimate the DALY burden without the impact of stillbirth, multiply the country estimate by 35%.