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| **DEPARTMENT OF REPRODUCTIVE HEALTH  AND RESEARCH DEPARTMENT OF HIV** | | |
| **Application of the Spectrum-STI estimation model estimating**  **STI prevalence and time trends**  **Collating Syphilis Prevalence Data for WHO/ UNAIDS Workshops in Spring 2019**  **Version 06 February 2019** | | |
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**1. Introduction**

Spectrum-STI is an epidemiological model developed to estimate and project national adult prevalence levels and time trends in active syphilis, gonorrhea and chlamydia. The model is embedded in the Spectrum suite of modelling tools and is integrated with existing standard estimation and impact modelling tools for family planning and HIV/AIDS.

The tool is ready for application in all low- and middle-income countries, with the user interface pre-loaded with data reported by countries through the Global AIDS Monitoring (GAM, formerly GARPR) system and data collected earlier for the WHO’s global and regional STI burden estimates.

The focus of the multi-country workshops will be on generating trend estimates for active syphilis. This is the infection with the most data available and with the most overlap with HIV as testing for HIV is also done on blood specimens.

**2. Background: Syphilis**

Syphilis is a sexually transmitted infection caused by the bacterium *Treponema pallidum* subspecies pallidum. Syphilis is most commonly spread through sexual activity.  It may also be transmitted from mother to baby during pregnancy or at birth, resulting in congenital syphilis.

Syphilis in adults develops in stages that can last for weeks, months, or even years. The stages may be separated by long periods of apparent good health. Syphilis usually starts with a small, painless sore, called a chancre, on the genitals, anus, or mouth. In the next stage, you may have flu-like symptoms and/or a rash. Later stages of syphilis can damage the brain, heart, and other organs.

Spectrum generates estimates for active syphilis. Active syphilis is defined as concurrent positivity on both nontreponemal and treponemal tests. This definition is also used for regional and global estimates of syphilis in adults.

***2.1 Diagnostic tests for syphilis***

Syphilis tests are used to screen for and diagnose syphilis. There are two types of tests both of which can be done on blood samples (see Annex 1 for more information).

1. Nontreponemal tests: detect biomarkers released during cellular damage that occurs from the syphilis spirochete. Common examples:

* RPR: Rapid Plasma Reagin test
* VDRL: Venereal Disease Research Laboratory test

1. Treponemal tests: detect antibodies that are a direct result of the infection. Common examples:

* TPHA: Treponema pallidum haemagglutination test
* TPPA: Treponema pallidum particle agglutination assay
* FTA-ABS: Fluorescent treponemal antibody absorption test
* EIA: Enzyme immunoassay test

Nontreponemal tests are simple and inexpensive and have been used widely as screening tests. Ideally, however, they should be confirmed by treponemal tests, as false positive reactions can occur due to other viral and bacterial infections, connective tissue diseases, recent vaccinations, or pregnancy. Treponemal tests, that detect antibodies to the Treponema spirochete that causes syphilis, are more specific, but are not able to discriminate between active infection, and treated, cured or past infection.

In addition, there are a number of rapid syphilis point of care tests that are being used. These are treponemal based tests. These can be either a syphilis test only (e.g., SD Bioline Syphilis 3.0) or combined with HIV or Hepatitis C (e.g., Chembio DPP® HIV/ Syphilis Confirm).

In Spectrum-STI Prevalence data are adjusted according to the type of diagnostic test used. The five categories are:

* Nontreponemal test only (e.g., RPR or VDRL only)
* Treponemal test only (e.g., TPHA or TPPA only)
* Dual, Nontreponemal test and Treponemal test- usually blood is screened with a non-treponemal test

and positive tests are confirmed by a treponemal test – or the reverse.

* Rapid test (treponemal based)
* Unknown

**3. Syphilis Prevalence data**

Country data have been preloaded into the Spectrum suite. These data are not comprehensive but are a starting point for generating country estimates. All of these data should be checked again to make sure that they have been transcribed and interpreted correctly. The pre-loaded data were drawn from:

***3.1 Global AIDS Monitoring Data:***

Data reported by countries through the Global AIDS Monitoring (GAM, formerly GARPR) system as of June 2016. The data currently entered are for syphilis in ANC women and include data from both routine screening and periodic sentinel surveys:

*Routine ANC syphilis screening:*

* Number of pregnant women screened for syphilis in ANC, from routine screening services
* Number of pregnant women found syphilis-infected, during routine ANC screening
* Number of pregnant women eligible for ANC-based syphilis screening, i.e. the number of women who attend ANC

*Periodic sentinel surveys in ANC women:*

* Number of pregnant women screened for syphilis in ANC, from routine screening services
* Number of pregnant women found syphilis-infected, during routine ANC screening
* Number of sites (e.g. provinces) included in the sentinel surveys – this is used to determine the statistical weight of the data point

***3.2 Data collected for WHO global and regional STI burden estimates:***

Population prevalence data for chlamydia and gonorrhea collected for the 2005, 2008 and 2012 WHO estimates have been included. These data are based on information collated from a variety of sources including PubMed literature searches (last search conducted on January 30, 2015) (Newman-L et al. 2015) and requests to the WHO regional STI advisors and other leading experts in the field. Inclusion criteria for this studies included: sample size of at least 100; population could be considered representative of the general population (study populations included pregnant women, women at delivery, women attending family planning clinics, military recruits, or individuals selected for participation in a Demographic and Health Survey); and study used an internationally recognised diagnostic test with adequate performance characteristics on urine, urethral, or cervico-vaginal specimens. For studies where the data were published in more than one paper the paper with most information was included in the database.

***3.3 Other data***

In addition, any data points that the Spectrum Implementation team (Avenir Health & international STI surveillance experts) have come across have been included. This could be from country searches, communication with colleagues, etc.

***3.4 Expanding the national data file***

The more country data and the longer the time period covered, the better the Spectrum estimates will be. For the first round of Spectrum data estimates the focus is on data collected in **1990 or later**.

Table 1 summarize the types of prevalence and case reporting data that should be collected for syphilis.

These data can be found in a range of places including:

* Annual HIV/STI program report;
* Annual Maternal and child health program reports;
* Reports of IBBS, Second-Generation Surveillance, or HIV/STI sentinel surveillance;
* Recent evaluations of the HIV/STI program and/or its surveillance system.

Data can be submitted in any language to the Spectrum-STI implementation team; although a translation of the relevant sections into English, French or Spanish would be helpful. Please send electronic copies of all relevant reports to Dr. Eline Korenromp, Avenir Health ([ekorenromp@avenirhealth.org](mailto:ekorenromp@avenirhealth.org)).

For prevalence studies the data inputted into the Spectrum country data file are summarized in Box 1. If submitting data to the Spectrum-STI implementation team please include as much of this information as possible. Data should, where appropriate, be broken down by gender and if available by age.

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| **Table 1: Syphilis** | |
| ***Prevalence*** | |
| Pregnant women | * Sentinel surveys * Routine programmatic screening of women attending ANC   + first visit   + any visit * Other surveys |
| Blood donors | * Routine programmatic screening * Other surveys |
| Population-based surveys | * Demographic and Health Surveys (DHS) * AIDS Indicator Surveys (AIS) * Population-based HIV Impact Assessment (PHIA) * Other surveys |
| Key population surveys  (sex workers, MSMs, etc.,) | * Integrated Bio-Behavioural Surveys * Second-generation Sentinel Surveillance * Other surveys/ studies |
| Other surveys | There are a range of different population groups that data may be available for such as:   * Family planning clinic attendees * Abortion seekers * Students * Workers * Military / military recruits * Blood donors   Please include any data that you find. |
| ***Case reports*** | |
| Adults | * Case reports, by stage and gender, and for women pregnancy status |

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| **Box 1: Data inputted into the Spectrum-STI Prevalence country data file**   * Sample size; * Number of people infected i.e. number of people test-positive; * Clinical specimen tested (e.g. genital fluid, or urine); * Diagnostic test used; * Calendar year(s) of data collection; * Population sampled: for example women attending ANC care, family planning clients, army recruits * Location: for example [CAPITAL CITY name] or ‘2 rural villages’, or simply ‘urban’ or ‘rural’; * Official reference of the data source: Authors, title, publication date, journal title or report number, URL if available. |

**4. Interpreting country estimates and trends: Background information**

In order to interpret the country estimates it would be helpful if you could include a brief summary of current STI policies and practices for the three infections. This is important information for understanding and interpreting the data. Table 2 provides a list of the type of information that would be useful to have. In addition to a summary of the current status of these activities any information you can provide on significant changes that have occurred since 1990 would be helpful for interpreting changes over time.

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| **Table 2: Programmatic information** | |
| Syphilis in pregnant women | * Short summary of how the ANC screening & treatment programme is structured and information on current practice including tests, drugs, algorithms, flow charts) for diagnosis and treatment. * Any data (not already included in the country data file since 1990 on:   + Coverage of routine syphilis screening among women presenting for first ANC visit (or, if first visit not available, any ANC visit), among pregnant women attending for first ANC visit,   + The number of women screened for syphilis at first ANC visit |
| Syphilis in adults | * Short summary of ongoing syphilis prevention and screening activities in other population groups e.g., blood donors, pre-marital, army recruits, FSW, MSM |
| All three infections in adults – case reporting | * Short summary of case reporting system and estimates of reporting completeness. * Short summary of access to health care services and the use of public and private services by symptomatic individuals |

**Annex 1: Laboratory based syphilis serological tests**

In Spectrum-STI there are 6 drop down menus for entering syphilis diagnostic tests. These are detailed in Table A1. Box A1. Records some of the more common treponemal, non-treponemal and rapid tests.

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| **Table A1** | |
| *Spectrum-STI drop down menu* | *What to include* |
| TPHA in ANC or FP population | Any study in ANC or FP populations where only a treponemal test was used |
| TPHA in non-ANC non-FP population | Any study in non-ANC or non-FP populations where only a treponemal test was used |
| RPR/ VDRL | Any study where only a non-treponemal test was used |
| RPR (any titer) & TPHA, or SNTTP\* | Any study where both a treponemal and non-treponemal test were used |
| Rapid test | Any study using one of the rapid tests detailed in Box A1 |
| Unknown | Any study where no data on the type of test is provided or you are not certain |

\* SNTTP stands for serology non-treponemal and *Treponemal pallidum*

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| **Box A1: Treponemal, non-treponemal and rapid tests for syphilis.**  Treponemal specific tests:   * TPHA: *Treponema pallidum* haemagglutination assay * TPPA: *Treponema pallidum* particle agglutination assay * FTA-Abs: Fluorescent treponemal antibody absorption test (FTA-Abs) * CLIA: *Treponema pallidum* chemiluminescent immunoassay (CLIA) * EIA: *Treponema pallidum* enzyme immunoassay (EIA) (includes EIA-IgG or IgM) – e.g. ACON Labs * ELISA : enzyme-linked immunosorbent assay * chromatographic immunoassay - e.g., Syphilis Ultra Rapid Test Device (ulti med Products))   Non-treponemal   * RPR: Rapid plasma reagin * VDRL: Venereal disease research laboratory * TRUST: toluidine red unheated serum test   Rapid tests   * Alere Determine™ Syphilis TP (Abbott Diagnostics) * SD Bioline Syphilis 3.0 (Abbott Diagnostics) * SyphiCheck® WB (Qualpro Diagnostics) * VisiTect® Syphilis (Omega Diagnostics) * Syphilis Health Check™ (Trinity Biotech) * Chembio DPP® Syphilis Screen & Confirm (Chembio Diagnostic Systems) * SD Bioline HIV/ Syphilis Duo (Abbott Diagnostics) * Chembio DPP® HIV/ Syphilis Confirm (Chembio Diagnostic Systems, USA) * Multiplo rapid TP/HIV antibody test (MedMira) |