S03.2 GLOBAL AND REGIONAL ESTIMATES OF HSV2, HSV1 AND NEONATAL HERPES FOR 2012

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Background Genital infection with herpes simplex virus type 2 (HSV-2) is the most common cause of genital ulcer disease worldwide and increases susceptibility to, and transmissibility of, HIV. HSV type 1 (HSV-1) can also cause genital herpes, but most HSV-1 infection is oro-labial ("cold sores") and acquired during childhood. Neonatal herpes, acquired during delivery from mothers with genital herpes, is rare but has high rates of mortality and lifelong disability. The global burden of HSV-2 infection was last estimated for 2003. The global burden of HSV-1 infection, and of neonatal herpes, has never been estimated to our knowledge.
Aim To present, for 2012, new global HSV-2 estimates for females and males aged 15–49 years, first global HSV-1 estimates for females and males aged 0–49 years, and first global estimates of neonatal herpes cases.
Methods Literature review of recent HSV-1 and HSV-2 prevalence studies world-wide, followed by fitting of a model with constant incidence by age to pooled prevalence values by HSV type, WHO region, age and sex. Prevalence values were adjusted for test sensitivity and specificity. Published risks of neonatal herpes transmission were applied to maternal infections to estimate neonatal herpes cases.
Results We estimate that in 2012, 417 million people aged 15–49 years (range: 274–678 million) had existing HSV-2 infection world-wide: a global prevalence of 11.3%. Of those infected, 267 million were women. Also in 2012, we estimate that 19.2 million (range: 13.0–28.6 million) individuals aged 15–49 years were newly-infected with HSV-2: 0.5% of all individuals globally. Prevalence was highest in Africa (31.5%), followed by the Americas (14.4%). Burden of numbers infected was highest in Africa. However, despite lower prevalence, South-East Asia and Western Pacific regions also contributed large numbers to the global totals because of large population sizes. Estimates for HSV-1 and neonatal herpes will be presented at the conference.
Conclusions The global burden of HSV infection is large. This highlights the critical need for development of vaccines, microbicides and other prevention strategies against HSV.

S03.3 STI ESTIMATES WITHIN THE INSTITUTE FOR HEALTH METRICS AND EVALUATION GLOBAL BURDEN OF DISEASE PROCESS

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Introduction Sexually-transmitted infections (STIs) are an important cause of acute illness, disability and death throughout the world. In this study, we used GBD 2013 systematic approach to analyze levels and trends in health loss due to STI for the years 1990 to 2013, for 188 countries, both sexes, and 20 separate age groups. We separately estimated deaths, years of life lost (YLLs), prevalence, incidence and years of life lived with disability (YLDs) for five different infections: gonorrhea (*Neisseria gonorrhea*), chlamydia (*Chlamydia trachomatis*), trichomoniasis (*Trichomonas vaginalis*), syphilis (*Treponema pallidum*), genital herpes due to herpes simplex virus 2 (HSV-2), and the residual category of "other" STI.
Methods Age- and sex-specific mortality due to all STI in ages 10 and over was estimated using cause-of-death ensemble modeling (CODEm). Syphilis deaths in ages 0 to 9 used a natural history model combining data on syphilis prevalence in pregnancy, live births, antenatal care coverage, routine antenatal syphilis testing, and excess neonatal mortality rates in those infected with syphilis. Years of life lost (YLL) were calculated by multiplying age-specific deaths with life expectancy at time of death. We estimated non-fatal STI burden consequent to acute, recurrent, and chronic infection as well as pelvic inflammatory disease (PID) and infertility. Our dataset was developed via systematic literature review, supplemented with national reports and hospital datasets. We modeled the epidemiology of each condition using DisMod-MR 2.0, a Bayesian meta-regression tool developed for GBD 201313, thereby generating age- and sex-specific prevalence and incidence estimates for each condition. Years of life lived with disability (YLD) were calculated by pairing symptomatic case numbers with corresponding disability weights (DW).
Results Global STI deaths decreased from 257,648 (95% UI: 154,732 to 396,443) in 1990 to 142,017 (87,589 to 213,920) in 2013. Most deaths were due to congenital syphilis which was the dominant driver of YLLs. Over 99% of all STI deaths occurred in developing countries, including 32.9% in eastern sub-Saharan Africa alone. Annualised rate of change (ARC) of age-standardized death rates globally was -3.0%, with 38 countries exceeding -5.0%. New cases of chlamydia, gonorrhea, trichomoniasis and genital herpes all increased between 1990 and 2013 and were amongst the top 25 most common acute conditions. North Africa and the Middle East saw the biggest percentage increase, driven mostly by population growth. Peak ages for incident infection in each STI were between 20 and 25 years and largely unchanged from 1990 to 2013. The most common acute STI in females was trichomoniasis whereas it was chlamydia in males. Genital herpes was by far the most common chronic infection in both sexes. In females, chlamydia and gonorrhea were the dominant driver of YLDs, mostly due to PID and infertility, whereas genital herpes was the biggest cause of disability due to STI in males.
Discussion Despite significant improvement in congenital syphilis mortality from 1990 to 2013, STI remain a significant cause of acute infection and disability throughout much of the world, even increasing in many locations. Surveillance and treatment programs for STI should remain a priority.

S03.4 FUTURE DIRECTIONS FOR GLOBAL STI ESTIMATES

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Background Estimating STI prevalence and incidence are important for programming and advocacy. Current global and regional estimates are based on meta-analysis of prevalence data of gonorrhoea, chlamydia and trichomoniasis among low-risk populations, and on national surveillance of syphilis sero-prevalence among antenatal care attendees, with adjustment for laboratory test types, geography and age. The precision and utility of these estimates is limited by insufficient, varying, and uncertain data availability and quality, notably on duration of infection and symptoms, representativeness of survey samples, etc. Current

estimation methods are not able to incorporate data from high risk populations and are not able to generate national STI estimates.

The Spectrum suite of estimation and program planning tools has been developed to support estimation of burdens, trends, service needs and program impact for family planning, HIV/AIDS, tuberculosis and other diseases. The HIV/AIDS, Spectrum is used by over 120 countries every two years to estimate their burden of HIV/AIDS, antiretroviral treatment need and other services.

Next generation of estimating STIs A module for estimating burdens and trends of STIs in the Spectrum suite of health modelling tools is being developed, initially for gonorrhoea and syphilis, for which relatively good and abundant country data are available. The Spectrum module will fit STI burdens and trends using standard STI indicators collected routinely by countries and reported annually to the WHO and UNAIDS through the Global AIDS Response Progress Reporting (GARPR) system and STI data on general populations from peer-reviewed literature.

By building onto the HIV/AIDS model within Spectrum, the STI estimation tool will benefit from efficiency, expertise, coherence and consistency with estimations of HIV/AIDS.

Next steps The development and piloting of the Spectrum STI module is a first phase towards supporting country-level STI estimation and program planning. The STI module will be implemented in selected countries in. two-yearly cycle of country consultations tagged into the UNAIDS HIV/AIDS estimation. A companion module for strategic STI intervention modelling, program planning and costing – as an extension to Spectrum's current One Health Tool representation of MNCH, family planning and HIV primary/behavioural prevention programs will be designed and developed.

S04 - Revealed: Neglected and emerging STIs

S04.1 *HAEMOPHILUS DUCREYI* IN "YAWS" ULCERS IN PAPUA NEW GUINEA

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Skin infections with ulceration are a major health problem in the South Pacific countries. Yaws, diagnosed by the presence of cutaneous ulcers (CU) and a reactive syphilis serology, is one important cause, but this can be confused clinically with ulcers due to other aetiologies. In a prospective cohort study in yaws-endemic villages of a Papua New Guinean (PNG) island we showed that *Haemophilus ducreyi* is the leading cause of chronic CU in children; nearly 60% of patients with ulcers had detectable lesional *H. ducreyi* DNA, while 35% were *Treponema pallidum* subsp. pertenue positive. Similar findings were reported from yaws endemic communities in the Solomon Islands, Vanuatu and Ghana. Unlike yaws, *H. ducreyi* lesions appear to be restricted to the skin and, if left untreated, do not result in inflammatory lesions of the bones. Whole-genome sequencing studies have shown that CU strains of *H. ducreyi* are remarkably similar to class I genital ulcer (GU) strains with an overall sequence similarity of 99.98%, and that CU strains diverged from class I strains ≈0.18mya which supports the idea that CU with *H. ducreyi* preceded syndromic management of GU. A single oral dose of azithromcycin (AZ, 30 mg/Kg) is effective for treatment of yaws and, cutaneous strains of *H. ducreyi* have been shown to be susceptible to macrolides. In the context of new efforts to eradicate yaws, the use of mass treatment with azithromycin in PNG reduced the absolute prevalence of yaws CU from 2.4 to 0.3 percent at 12 months after treatment, and *H. ducreyi* CU from 2.7% to 0.6%. The persistence of skin ulcers in the population raises the possibility that the bacteria may exist in an environmental reservoir or are so infectious that MDA at less than 100% above coverage rate fails to eradicate the diseases from a community.

S04.2 NEW DIAGNOSTICS FOR SYPHILIS AND YAWS AND DETECTION OF *HAEMOPHILUS DUCREYI* IN CUTANEOUS LESIONS IN CHILDREN

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Introduction We evaluated a multiplex PCR assay that can distinguish between syphilis and yaws on children with cutaneous lesions. Also, a rapid syphilis test, Chembio DPP Screen and Confirm Assay was evaluated for serological diagnosis of yaws.

Methods Lesions swabs for PCR were obtained from children (5–14 years old) in West Akyem Municipality, Ghana pre- and post-MDA with azithromycin and pre-MDA on Tanna Island, Vanuatu. DPP testing was done on site and blood was collected for serology (RPR and TPPA). Molecular diagnosis and screening for azithromycin resistance markers was done using TaqMan-based real-time multiplex PCR tests. Another duplex PCR test was used to detect *H. ducreyi* and M. ulcerans.

Results Pre-MDA TPPA and RPR dual positivity was 35.8% (63/176) in Vanuatu and 33.6% (109/326) in Ghana and post-MDA was 18.6% (16/43) and 6.5% (3/46), respectively in children with skin lesions. The overall sensitivity and specificity of the DPP treponemal component versus TPPA was 88.2% and 82.7%, and DPP non-treponemal component versus RPR was 84.8% and 94.7%. In children with *T. pertenue* PCR-positive lesions, dual positive DPP had an overall sensitivity and specificity of 86.3% and 78.6%, and a PPV of 44% and a NPV of 96.7%. 14.9% (27/181) of pre-MDA swab samples from Vanuatu and 17.3% (31/179) in Ghana were PCR-positive for *T. pertenue*. None of the 49 samples from Ghana were positive for *T. pertenue* post-MDA. Azithromycin resistance markers were not found in any of the samples. *H. ducreyi* was detected by PCR in 40.3% (73/181) of samples from Vanuatu, and 27.4% (51/208) from Ghana pre-MDA and 28.6% (14/49) in Ghana post-MDA. Six children were co-infected with *T. pertenue* and *H. ducreyi* in Vanuatu and seven in Ghana. M. ulcerans was not detected.

Conclusion The DPP test is a useful screening test to exclude yaws in cases with a high index of suspicion on clinical grounds and the real-time PCR is essential for confirmation of a yaws diagnosis. MDA with oral azithromycin is effective for treatment of yaws but has limited impact on *H. ducreyi*.