INTRODUCTION TO GERMS-SA CLINIC BASED SURVEILLANCE FOR TB, HIV AND OTHER STIS AND RELATED DRUG RESISTANCE

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Introduction

The NICD surveillance platform, GERMS-SA, has been in existence for more than a decade. Originally, GERMS included laboratory based surveillance where a surveillance officer (SO), alerted to a predetermined test result of a confirmed pathogen related disease (e.g. invasive pneumococcal disease) by NHLS laboratory staff, traced hospital based patients and gathered additional information on risk factors through patient interview and review of medical records. However, the platform did not include surveillance for tuberculosis (TB), human immunodeficiency virus (HIV) infection or sexually transmitted infections (STI). In 2012, following the introduction of Xpert MTB/RIF technology in South Africa, surveillance of rifampicin-resistant tuberculosis (TB) was included in the GERMS-SA programme and enhanced surveillance was expanded to include selected clinics as well as hospital based patients. Additional sputum samples were collected for drug susceptibility testing and genotyping at the National Institute for Communicable Diseases (NICD).

In 2014, a decision was made to further expand GERMS -SA to include clinic based surveillance, initially at one clinic per province in South Africa. The entry point for clinic based surveillance is patients presenting with a positive result for TB, HIV or STI which would then lead to further monitoring for related drug resistance. For this, protocols were developed and ethics approval obtained from the University of the Witwatersrand, local ethics boards and provincial approval bodies as required.

Integrated TB/HIV clinic based surveillance

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In 2011, the National Department of Health began a phased implementation of Xpert MTB/RIF (Xpert) rapid testing for all TB suspects. This test is used to diagnose TB infection and assess rifampicin (Rif) resistance, but cannot test for isoniazid (INH) resistance. Isoniazid mono-resistance is more common than multi-drug resistant TB (MDR-TB) or rifampicin mono- resistant TB. The 2001/2002 South African Drug Resistance Tuberculosis survey reported INH resistance in 5.7% of new patients and in 11.8% of previously treated patients, with mono-resistance to INH present in 2.6% (new) and 2.9% (re-treatment) patients respectively. Thus, surveillance for INH and other first line resistance has been identified as a priority need in the national TB control program. In addition, understanding risk factors and microbiological characteristics (e.g. strain type, minimum inhibitory concentration changes etc.) related to this group are important for designing appropriate control strategies and are therefore also included in the surveillance programme.

South Africa has over 6 million HIV infected individuals with ~2.6 million people receiving antiretroviral therapy (ART), making this HIV control programme the largest in the world. Routine testing for HIV drug resistance (HIVDR) is offered to patients failing protease inhibitor-based ART only in terms of providing access to third-line antiretroviral options. Surveillance of HIVDR in patients

initiating therapy with or without prior exposure to ART is limited globally. However, as higher levels of HIVDR are expected in those with prior ARV exposure (for example women exposed to PMTCT, or patients returning to care after >3 months), these populations would be expected to contribute disproportionally to levels of observed resistance. It is necessary to differentiate these groups as changes in public health policy may warrant different first-line regimens for these different subgroups.

District and site/clinic selection for the surveillance programme was influenced by burden of disease, National Health Insurance status and in some instances, logistics as well as inputs from provincial Departments of Health. Surveillance officers have been placed at selected clinics and their brief is to work together with facility staff to identify eligible participants for surveillance. This includes all newly diagnosed rifampicin susceptible TB patients, all HIV positive patients older than 15 years of age initiating ART, a specified number of patients presenting with STIs and individuals presenting at family planning clinics. After obtaining informed consent, an SO administers a questionnaire including demographic features, risk factors for TB or HIV drug resistance and socio-economic status. Two blood specimens on ART initiators and one sputum specimen for TB patients are collected and sent to the NICD for HIV and TB drug resistance testing respectively. Clinic data regarding the numbers of patients tested for TB and HIV, rates of co-infection and other aspects of the TB-HIV treatment cascade are also monitored. Specimens are also collected for the STI component of the surveillance and a short questionnaire is completed.

This surveillance programme provides a unique national platform to understand, characterize and track the dual TB/HIV epidemic in an operational setting using a standardised approach across all provinces, and creates an opportunity to better understand the TB-HIV treatment cascade and associated challenges in a real life clinical setting. Both the HIV and TB treatment programmes use a public health approach with empiric regimens, which require on-going surveillance to monitor whether they remain appropriate over time. For TB, on-going enhanced surveillance will be needed to monitor emerging trends for INH resistance and resistance to other TB drugs, and will help to identify and study the risk factors for INH resistance. For HIVDR, the findings of this surveillance programme will inform the burden and extent of existing drug mutations (previous ART and unexposed to ART), support optimal regimen selection and inform strategic planning of ART programmes countrywide.

In addition, the objectives of this surveillance programme are to measure key components of the TB-HIV treatment cascade or continuum of care. This will help to better understand points of losses and determinants thereof within the South African TB-HIV continuum of care process. This data will inform strategies for strengthening current systems supporting TB-HIV care. Lessons learned during implementation and findings from this surveillance can potentially be used to inform larger representative cross-sectional studies where indicated.

Sentinel surveillance of sexually transmitted infection syndrome aetiologies, gonococcal antimicrobial resistance and HPV genotypes among patients attending public healthcare facilities in South Africa

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Sexually transmitted infections (STIs) continue to be highly prevalent among individuals of reproductive age within South Africa. STIs have been treated using the syndromic management approach since the late 1990s.

The WHO recommends that periodic assessments of aetiologies of STI syndromes ((e.g. male urethritis syndrome (MUS), vaginal discharge syndrome (VDS), genital ulceration syndrome (GUS)) should be a core STI surveillance activity, especially in countries where STI syndromic management and case reporting are routinely undertaken. The numbers of total STI syndrome episodes and new episodes of MUS are recorded at all public sector primary health care facilities within South Africa. However, no data are routinely recorded for other STI syndromes, including VDS and GUS.

In the past five years, several antimicrobial resistance surveys and research studies undertaken in eastern and southern Africa have reported an unacceptably high prevalence of fluoroquinolone resistant *Neisseria gonorrhoeae* isolates. In response, South Africa has moved to replace fluoroquinolones with single dose oral cefixime. The first *N. gonorrhoeae* isolates demonstrating decreased susceptibility or resistance to oral extended spectrum cephalosporins (ESCs), in one case associated with cefixime treatment failure, were reported in South Africa among men-who-have-sex-with-men residing in Johannesburg in 2013.

HPV is the most common STI. Specific types of "high-risk" HPV can cause cervical cancer. The current vaccines, Cervarix and Gardasil, vaccinate against HPV-16 and HPV-18, the two major HPV types that cause cervical cancer, and also provide cross-protection against some of the other high-risk HPV types. In addition, Gardasil protects against HPV-6 and 11, which cause anogenital warts.

This surveillance programme will provide aetiological STI data on each of the three major STI syndromes (MUS, VDS and GUS) that present to South African primary healthcare clinics (PHC), at 9 sentinel public sector healthcare facility sites (1 site/province). The prevalence of HIV, HSV-2, hepatitis B and syphilis co-infections will be determined among patients with MUS, VDS and GUS. These data will additionally be analyzed by province and, for HSV-2, hepatitis and syphilis co-infections, by HIV status. Urethral discharge samples will be collected from a minimum of 150 men per province with MUS for gonococcal culture. All gonococcal strains that are isolated will be tested for antimicrobial susceptibility. In order to determine HPV prevalence among young sexually-active women, HPV surveillance will be conducted among 900 eighteen to twenty year old women attending family planning clinics within the same nine primary health care clinics. HPV prevalence and genotype data will provide important pre-vaccination data and will enable future monitoring of trends in both the prevalence of HPV detection and the relative prevalence of vaccine-related HPV genotypes once HPV vaccine is fully introduced into South Africa.

Progress to date

Clinic based surveillance sites have been established in the Eastern Cape (Nelson Mandela Bay) and North West provinces (Kenneth Kaunda) and in a small rural clinic in Mpumalanga Province. The KwaZulu-Natal (Umgungundlovu) and Mpumalanga (Ehlanzeni) sites are expected to be established by June or July 2015 and the Gauteng (City of Johannesburg) site before the end of 2015.

Reference

1. WHO HIV drug resistance report 2012. http://www.who.int/hiv/pub/drugresistance/report2012/en/