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Research Unit on AIDS

## MRC/UVRI MONTHLY PUBLICATIONS DIGEST – JUNE 2015

Zacchaeus Anywaine, Andrew Abaasa, Jonathan Levin, Ronnie Kasirye, Anatoli Kamali, Heiner Grosskurth, Paula Munderi, Andrew Nunn; Safety of discontinuing Cotrimoxazole prophylaxis among HIV infected adults on anti-retroviral therapy in Uganda (COSTOP Trial): Design. *Contemporary Clinical trials journal* 2015 May 22; 43:100-104. doi: 10.1016/j.cct.2015.05.015.

### INTRODUCTION:

Cotrimoxazole (CTX) prophylaxis is recommended by the World Health Organisation for HIV infected persons. However, once HIV infected patients have commenced ART in resource limited settings, the benefits of continued CTX prophylaxis are not known. The few studies that investigated the safety of discontinuing CTX prophylaxis in these settings had limitations due to their design.

### MATERIALS AND METHODS:

COSTOP is a randomised double blind placebo controlled non-inferiority trial among HIV infected Ugandan adults stabilised on anti-retroviral treatment (ART). Participants with CD4 count of 250 or more cells/mm<sup>3</sup> are randomised to two arms: the intervention arm in which CTX is discontinued and the control arm in which CTX prophylaxis is continued. The study aims to assess whether the intervention regimen is not inferior, with respect to the incidence of pre-defined CTX-preventable events, to the control regimen and superior with respect to the incidence of haematological adverse events.

### DISCUSSION:

Studies that have previously evaluated the safety of discontinuing CTX prophylaxis among HIV infected adults in resource limited settings have provided moderate to low quality evidence owing in part to methodological limitations. COSTOP is designed and conducted with sufficient rigour to answer this question. The results of the trial will assist in guiding policy recommendations.

### CONCLUSION:

This paper describes the design and methodological considerations important for the conduct of CTX cessation studies.

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Kavishe B, Biraro S, Baisley K, Vanobberghen F, Kapiga S, Munderi P, Smeeth L, Peck R, Mghamba J, Mutungi G, Ikoona E, Levin J, Plus AB, Katende D, Kisanga E, Hayes R, Grosskurth H. High prevalence of hypertension and of risk factors for non-communicable diseases (NCDs): a population based cross-sectional survey of NCDs and HIV infection in Northwestern Tanzania and Southern Uganda. *BMC Med.* 2015 May 9;13(1):126.

### BACKGROUND:

The burden of non-communicable diseases (NCDs) is increasing in sub-Saharan Africa, but data available for intervention planning are inadequate. We determined the prevalence of selected NCDs and HIV infection, and NCD risk factors in north western Tanzania and southern Uganda.

### METHODS:

A population-based cross-sectional survey was conducted, enrolling households using multistage sampling with five strata per country (one municipality, two towns, two rural areas). Consenting adults (≥18 years) were interviewed using the WHO STEPS survey instrument, examined, and tested for HIV and diabetes mellitus (DM). Adjusting for survey design, we estimated population prevalences

of hypertension, DM, obstructive pulmonary disease, cardiac failure, epilepsy and HIV, and investigated factors associated with hypertension using logistic regression.

### RESULTS:

Across strata, hypertension prevalence ranged from 16 % (95 % confidence interval (CI): 12 % to 22 %) to 17 % (CI: 14 % to 22 %) in Tanzania, and from 19 % (CI: 14 % to 26 %) to 26 % (CI: 23 % to 30 %) in Uganda. It was high in both urban and rural areas, affecting many young participants. The prevalence of DM (1 % to 4 %) and other NCDs was generally low. HIV prevalence ranged from 6 % to 10 % in Tanzania, and 6 % to 12 % in Uganda. Current smoking was reported by 12 % to 23 % of men in different strata, and 1 % to 3 % of women. Problem drinking (defined by Alcohol Use Disorder Identification Test criteria) affected 6 % to 15 % men and 1 % to 6 % women. Up to 46 % of participants were overweight, affecting women more than men and urban more than rural areas. Most patients with hypertension and other NCDs were unaware of their condition, and hypertension in treated patients was mostly uncontrolled. Hypertension was associated with older age, male sex, being divorced/widowed, lower education, higher BMI and, inversely, with smoking.

### CONCLUSIONS:

The high prevalence of NCD risk factors and unrecognized and untreated hypertension represent major problems. The low prevalence of DM and other preventable NCDs provides an opportunity for prevention. HIV prevalence was in line with national data. In Tanzania, Uganda and probably elsewhere in Africa, major efforts are needed to strengthen health services for the PREVENTION, early detection and treatment of chronic diseases.

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**Mawa PA, Nkurunungi G, Egesa M, Webb EL, Smith S, Kizindo R, Akello M, Lule SA, Muwanga M, Dockrell HM, Cose SC, Elliott AM. The impact of maternal infection with *Mycobacterium tuberculosis* on the infant response to BCG immunization. *Phil Trans Roy Soc B*. 2015 Jun 19;370(1671). pii: 20140137. doi: 10.1098/rstb.2014.0137.**

Bacille Calmette-Guérin (BCG) immunization provides variable protection against tuberculosis. Prenatal antigen exposure may have lifelong effects on responses to related antigens and pathogens. We therefore hypothesized that maternal latent *Mycobacterium tuberculosis* infection (LTBI) influences infant responses to BCG immunization at birth. We measured antibody ( $n = 53$ ) and cellular ( $n = 31$ ) responses to *M. tuberculosis* purified protein derivative (PPD) in infants of mothers with and without LTBI, in cord blood and at one and six weeks after BCG. The concentrations of PPD-specific antibodies declined between birth (median [interquartile range (IQR)]) 5600 ng ml<sup>-1</sup> [3300-11 050] in cord blood) and six weeks (0.00 ng ml<sup>-1</sup> [0-288]). Frequencies of PPD-specific IFN- $\gamma$ -expressing CD4(+)T cells increased at one week and declined between one and six weeks ( $p = 0.031$ ). Frequencies of IL-2- and TNF- $\alpha$ -expressing PPD-specific CD4(+)T cells increased between one and six weeks ( $p = 0.019$ ,  $p = 0.009$ , respectively). At one week, the frequency of PPD-specific CD4(+)T cells expressing any of the three cytokines, combined, was lower among infants of mothers with LTBI, in crude analyses ( $p = 0.002$ ) and after adjusting for confounders (mean difference, 95% CI -0.041% (-0.082, -0.001)). In conclusion, maternal LTBI was associated with lower infant anti-mycobacterial T-cell responses immediately following BCG immunization. These findings are being explored further in a larger study.

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**Ssetaala A, Nakiyingi-Miiró J, Asiki G, Kyakuwa N, Mpendo J, van Dam GJ, Corstjens PL, Pala P, Nielsen L, de Bont J, Pantaleo G, Kiwanuka N, Kaleebu P, Elliott AM. *Schistosoma mansoni* and HIV acquisition in fishing communities of Lake Victoria, Uganda: a nested case control study. *Tropical Medicine and International Health*. 2015 May 5. doi: 10.1111/tmi.12531.**

### OBJECTIVE:

It has been suggested that *Schistosoma mansoni*, which is endemic in African fishing communities, might increase susceptibility to human immunodeficiency virus (HIV) acquisition. If confirmed, this would be of great public health importance in these high HIV-risk communities. This study was undertaken to determine whether *S. mansoni* infection is a risk factor for HIV infection among

the fishing communities of Lake Victoria, Uganda. We conducted a matched case-control study, nested within a prospective HIV incidence cohort, including 50 HIV seroconverters (cases) and 150 controls during 2009-2011.

#### **METHODS:**

*S. mansoni* infection prior to HIV seroconversion was determined by measuring serum circulating anodic antigen (CAA) in stored serum. HIV testing was carried out using the Determine rapid test and infection confirmed by enzyme-linked immunosorbent assays.

#### **RESULTS:**

About 49% of cases and 52% of controls had *S. mansoni* infection prior to HIV seroconversion (or at the time of a similar study visit, for controls): odds ratio, adjusting for ethnicity, religion, marital status, education, occupation, frequency of alcohol consumption in previous 3 months, number of sexual partners while drunk, duration of stay in the community, and history of schistosomiasis treatment in the past 2 years was 1.23 (95% CI 0.3-5.7)  $P = 0.79$ . *S. mansoni* infections were chronic (with little change in status between enrolment and HIV seroconversion), and there was no difference in median CAA concentration between cases and controls.

#### **CONCLUSIONS:**

These results do not support the hypothesis that *S. mansoni* infection promotes HIV acquisition.

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**Richard E Sanya, Lawrence Muhangi, Margaret Nampijja, Victoria Nannozi, Proscovia Kabubi, Elson Abayo, Emily L Webb, Alison M Elliott for the LaVIISWA study team. Association between *Schistosoma mansoni* and HIV infection in a Ugandan population with high HIV and helminth prevalence. Tropical Medicine and International Health. 2015 May 15. doi: 10.1111/tmi.12545.**

Recent reports suggest that *Schistosoma* infection may increase the risk of acquiring human immunodeficiency virus (HIV). We used data from a large cross-sectional study to investigate whether *Schistosoma mansoni* infection is associated with increased HIV prevalence.

#### **METHODS:**

We conducted a household survey of residents in island fishing communities in Mukono district, Uganda, between October 2012 and July 2013. HIV status was assessed using rapid test kits. Kato-Katz (KK) stool tests and urine-circulating cathodic antigen (CCA) were used to test for *Schistosoma* infection. Multivariable logistic regression, allowing for the survey design, was used to investigate the association between *S. mansoni* infection and HIV infection.

#### **RESULTS:**

Data from 1412 participants aged 13 years and older were analysed (mean age 30.3 years, 45% female). The prevalence of HIV was 17.3%. Using the stool Kato-Katz technique on a single sample, *S. mansoni* infection was detected in 57.2% (719/1257) of participants; urine CCA was positive in 73.8% (478/650) of those tested. *S. mansoni* infection was not associated with HIV infection. [KK (aOR = 1.04; 95% CI: 0.74-1.47,  $P = 0.81$ ), CCA (aOR = 1.53; 95% CI: 0.78-3.00,  $P = 0.19$ )]. The median *S. mansoni* egg count per gram was lower in the HIV-positive participants ( $P = 0.005$ ).

#### **CONCLUSIONS:**

These results add to the evidence that *S. mansoni* has little effect on HIV transmission, but may influence egg excretion.

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**Alison Elliott, Barbara Nerima, Bernard Bagaya, Andrew Kambugu, Moses Joloba, Stephen Cose, Guiseppe Pantaleo, Maria Yazdanbakhsh, David Mabey, David Dunne, Ashley Moffett, Eli Katunguka Rwakishaya, Pontiano Kaleebu, Edward Katongole Mbidde Capacity for science in Africa. Lancet. A commentary**