

## Abstracts

ignored. While all VL cases should start antiretroviral treatment (ART), studies on ART uptake are missing. A complementary strategy to decrease VL-HIV burden/mortality entails preventing VL in HIV patients living in VL-endemic regions. However, we lack data on how common VL is observed in individuals enrolled in HIV care.

**AIM** (1) Document the proportion of VL diagnoses occurring in previously diagnosed HIV-patients - versus VL/HIV diagnosed concurrently; (2) For both groups: uptake of ART and cotrimoxazole secondary prophylaxis (CPT).

**METHODS** We conducted a retrospective cohort study including all VL-HIV coinfecting adults at the Leishmania center at a referral hospital (2010–2015) and at a district hospital (2010–2014) in North-West Ethiopia.

**RESULTS** We included 112 patients at the referral hospital and 58 at the district hospital. The median age was 30 years, 98% were male. The proportion of VL-HIV coinfecting patients with VL diagnosed while in HIV care was 56% (63/112) and 19% (11/58) at the referral/district hospital respectively; with a median CD4 count at VL diagnosis of 45 cells/ $\mu$ L and 248 cells/ $\mu$ L at the referral/ district hospital respectively. 76% (56/44) were on ART at VL diagnosis. Ten (13%) patients died during admission. Uptake of ART and CPT was high.

The remaining 96 (56%) patients had both infections diagnosed concurrently, with a median CD4 count at VL diagnosis of 56 cells/ $\mu$ L and 143 cells/ $\mu$ L at the referral/district hospital respectively. Nineteen (20%) patients died during admission. Amongst cured patients, CPT uptake was 89% and 72% at the at the referral/district hospital, respectively; documented ART uptake was 67% and 36% at the referral/district hospital respectively. For the entire group ( $n = 96$ ), ART uptake was 61% and 28% at the referral/district hospital respectively. At the district hospital, documented uptake was especially low in referrals.

**CONCLUSIONS** A substantial proportion of VL-HIV cases occur amongst patients in HIV care, requiring further evaluation of preventive strategies. Amongst newly diagnosed VL-HIV coinfecting patients, documented ART initiation was low, especially at district level. The reasons, including poor data collection/referral systems, should be assessed.

## 3S10.1

### Comparison of single Kato-Katz, duplicate Kato-Katz, mini-FLOTAC and FECPAK<sup>G2</sup> for the assessment of anthelmintic efficacy of single dose albendazole

P. Cools<sup>1</sup>, J. Vlaminc<sup>1</sup>, M. Albonico<sup>2</sup>, S. Ame<sup>3</sup>, M. Ayana<sup>4</sup>, J. Keiser<sup>5</sup>, Z. Mekonnen<sup>4</sup>, A. Montresor<sup>2</sup>, S. Sayasone<sup>6</sup>, J. Verweij<sup>7</sup>, J. Vercruysse<sup>1</sup> and B. Levecke<sup>1</sup>

<sup>1</sup>Laboratory of Parasitology, Department Virology, Parasitology, Immunology, Merelbeke, Belgium; <sup>2</sup>Department of Control of Neglected Tropical Diseases, World Health Organization, Geneva, Switzerland; <sup>3</sup>Public Health Laboratory-Ivo de Carneri, Chake Chake, United Republic of Tanzania; <sup>4</sup>Department of Medical Laboratory Sciences and Pathology, College of Public Health and Medical Sciences, Jimma University, Jimma, Ethiopia; <sup>5</sup>Department of Medical Parasitology and Infection Biology, Swiss Tropical and Public Health Institute, Basel, Switzerland; <sup>6</sup>National Institute of Public Health, Ministry of Health, Vientiane, Lao People's Democratic Republic; <sup>7</sup>St. Elisabeth Hospital, The Netherlands

**INTRODUCTION** Soil-transmitted helminths (STHs; *Ascaris*, *Trichuris*, hookworm) are responsible for the highest burden among all neglected tropical diseases. Mass drug administration (MDA) programs, in which a single-oral dose of albendazole or

mebendazole are periodically administered to (pre)school-aged children are the main strategy to control for STHs. This drug pressure makes MDA programs highly vulnerable to the development of anthelmintic resistance (AR), as has been described in veterinary medicine. This necessitates thoroughly designed surveillance systems that allow detection of any changes in anthelmintic drug efficacy that may arise through the evolution of AR. We aimed to assess the performance of new diagnostic tools to monitor the efficacy of anthelmintic drugs.

**METHODOLOGY** In Tanzania, Ethiopia and Laos, stool specimens from school-aged children (5–14 years) were collected during a baseline visit, where children received a single dose of albendazole. Stool specimens were analyzed for the presence of *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm using different microscopic techniques (single Kato-Katz, duplicate Kato-Katz, Mini-FLOTAC and FECPAK<sup>G2</sup>). A follow-up stool sample was collected within two to three weeks for each child positive at baseline for at least one STH with at least one technique. A predefined number of 110 completed cases of *Ascaris* and *Trichuris*, and of 100 cases of hookworm, were included, for each site. DNA extraction of ethanol-preserved stool and qPCR assays for *A. lumbricoides*, *T. trichiura*, *Necator americanus* and *Ancylostoma duodenale* were performed. Egg-reduction rates (ERR) were calculated for the different STHs using the different techniques. The time needed to process and analyze the samples using each microscopic technique was recorded.

**RESULTS** ERR for *Ascaris* and hookworm were comparable for each microscopic technique but differed markedly for *Trichuris*. Single Kato-Katz was the fastest technique in all settings. Overall, FECPAK<sup>G2</sup> had the lowest sensitivity of the microscopic techniques.

*qPCR assays and analysis are currently performed and will also be presented.*

**CONCLUSIONS** The choice of diagnostic techniques to monitor drug efficacy will depend on both the species present in endemic regions and the intensity of infection.

## 3S10.2

### Egg excretion indicators for the measurement of soil-transmitted helminth response to treatment

P. Olliaro<sup>1</sup>, M. Vaillant<sup>2</sup>, A. Diawara<sup>3</sup>, E. K. N'Goran<sup>4</sup>, S. Ame<sup>5</sup>, B. Speich<sup>6</sup>, S. Knopp<sup>6</sup>, P. Steinmann<sup>6</sup>, P. Yap<sup>6</sup>, X.-N. Zhou<sup>7</sup>, M. Albonico<sup>8</sup>, J. Utzinger<sup>6</sup> and J. Keiser<sup>6</sup>

<sup>1</sup>Special Programme for Research and Training in Tropical Diseases (WHO/TDR), Geneva, Switzerland; <sup>2</sup>Luxembourg Institute of Health (LIH), Luxembourg; <sup>3</sup>Biology program, Division of Science and Mathematics, New York University Abu Dhabi (NYUAD), United Arab Emirates; <sup>4</sup>Université Félix Houphouët-Boigny de Cocody-Abidjan, Abidjan, Côte d'Ivoire; <sup>5</sup>Centre for Tropical Diseases, Negrar, Verona, Italy; <sup>6</sup>Swiss Tropical and Public Health Institute, Basel, Switzerland; <sup>7</sup>National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention, Shanghai, China

**INTRODUCTION** Soil-transmitted helminths (STHs: *Ascaris lumbricoides* (Al) *Trichuris trichiura* (Tt) and hookworm (Hw)), affect more than a billion people, especially school-aged children in low- and middle-income countries, who are targeted for preventive chemotherapy with albendazole and mebendazole. However, treatment efficacy varies with the STH species, location and time, and questions remain as to how best express treatment outcomes.

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**AIM** To investigate egg excretion indicators that are best adapted to measure treatment outcomes for STH and detect treatment failures and resistance development.

**METHODS** An individual participant-level database built from 12 treatment clinical trials, classed as albendazole and mebendazole (alone and combinations), and other treatments, including placebo. Only subjects infected with one or several species of STHs and with pre- and post-treatment data, and diagnosed using the Kato-Katz method, were included in the analysis. Baseline infection intensities were expressed as eggs per gram of faeces (EPG); treatment outcomes were expressed as egg reduction rates using arithmetic means (ERRam) and as distribution of individual-participant ERR.

**RESULTS** A total of 4981 patients were diagnosed with 9525 infections overall with one (35%) or several STH species (65%): *Al* 21%, *Tt* 45% and *Hw* 34%. Baseline infection intensity was significantly higher for each STH species in co-infections than mono-infections. The ERRam met the WHO minimal efficacy criteria of  $\geq 95\%$  for *Al*,  $\geq 50\%$  for *Tt* and  $\geq 90\%$  or  $\geq 70\%$  for *Hw* in just 55% of studies of albendazole and mebendazole alone or in combination, independent of whether mono- or multiple-infections. Considering individual responses, placebo achieved 100% ERR (hence cure) in 19% of *Al* and 11% of *Tt* and *Hw* infections. Albendazole alone gave ERR=0 in 1%, 27% and 8% of *Al*, *Tt* and *Hw* infections, and ERR=100% in 79%, 52% and 45%, respectively. The equivalent figures for mebendazole are 2%, 22% and 26%; and 93%, 25% and 21%. All treatments were compared through network meta-analysis.

**CONCLUSION** Co-infections were frequent and had higher infection intensities, but did not influence treatment performance. Just over half of treatments meet the WHO minimal efficacy criteria. Individual ERR response distributions allow identifying the proportions of suboptimal responders and comparing treatment performances.

## 3S10.3

### Landscape of studies generating individual participant data on the efficacy of drugs for treating soil-transmitted helminthiasis and the case for data sharing

J. B. Halder<sup>1</sup>, J. Benton<sup>2</sup>, A. M. Jule<sup>3</sup>, P. J. Guérin<sup>3,4</sup>, M.-G. Basáñez<sup>1</sup>, P. L. Olliaro<sup>3,5</sup> and M. Walker<sup>1,6</sup>

<sup>1</sup>Department of Infectious Disease Epidemiology and London Centre for Neglected Tropical Disease Research, Imperial College London, UK;

<sup>2</sup>Independent Researcher; <sup>3</sup>Centre for Global Health and Tropical Medicine, Nuffield Department of Medicine, University of Oxford, Oxford, UK; <sup>4</sup>Infectious Diseases Data Observatory (IDDO); <sup>5</sup>World Health Organization Special Programme on Research and Training in Tropical Diseases (TDR), Geneva, Switzerland; <sup>6</sup>Department of Pathobiology and Population Sciences and London Centre for Neglected Tropical Disease Research, Royal Veterinary College, Hatfield, UK

**INTRODUCTION** Preventive chemotherapy by mass drug administration is the cornerstone of the World Health Organization (WHO)'s policy to control soil-transmitted helminthiasis (STH) caused by *Ascaris lumbricoides* (roundworm), *Trichuris trichiura* (whipworm) and hookworm species. These neglected tropical diseases (NTDs) affect over 1 billion people globally and, in 2015 alone, over 560 million children were treated with benzimidazoles, a number which is likely to rise year-on-year towards the WHO's 2020 targets. Despite consensus that drug efficacies should be monitored for signs of decline that could jeopardise the long-term effectiveness of preventive chemotherapy, it is difficult to derive clear

information from currently available data. Drug trials primarily estimate efficacies as averages in groups of participants, but heterogeneities in trial design and reporting complicate classical meta-analyses based on aggregate data. Analysis of individual participant data (IPD) circumvent many of the problems associated with trial heterogeneity and permit more detailed powerful analysis of individual drug responses, offering a more sensitive means to identify atypical responses potentially caused by emerging drug resistance.

**AIM** To quantify the volume and characteristics of IPD generated from studies which may be used to estimate the efficacy of the drugs used to treat STH.

**METHODS** We performed a systematic review and identified studies which generated relevant IPD since 2000. We standardised the extraction of variables describing locations, sample sizes, trial designs, participant characteristics and other aspects of these studies to create an overview of the trial landscape.

**RESULTS** We estimate that there exist data on approximately 35 000 participants from 129 trials conducted in 39 countries, including 34 out of 103 countries where preventive chemotherapy is recommended. We present data on trialled drug regimens, reporting methods and key participant demographic information, such as cohorts including pre-school age children and pregnant women.

**CONCLUSION** We argue that establishing a global IPD repository would greatly improve the capacity of the global health community to monitor and evaluate the efficacy of anthelmintic drugs, respond to changes and safeguard the ongoing effectiveness of preventive chemotherapy. Establishing a fair and transparent data governance policy will be key for the engagement of the STH community in this global effort.

## 3S10.4

### Evolution of anthelmintic resistance in the era of preventive chemotherapy

L. E. Coffeng, W. A. Stolk and S. J. de Vlas

Department of Public Health, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands

**INTRODUCTION** Current control strategies for onchocerciasis, lymphatic filariasis, schistosomiasis and soil-transmitted helminths (STH) rely heavily on mass administration of a limited number of drugs. Although not (yet) widely observed, the development of anthelmintic resistance presents a severe threat to the effectiveness of control programs. Mathematical models allow us to synthesise current knowledge and understand the dynamics of the evolution of drug resistance under current and potential alternative intervention strategies, including those related to programmatic shifts from control to elimination. **AIM** Characterise and compare the evolution dynamics of potential polygenic drug resistance in the four major anthroponotic helminth species under various transmission and intervention scenarios.

**METHODS** We performed forward-simulation using a stochastic, individual-based model for transmission and control of helminth infections in humans, and use the quantitative trait model to simulate inheritance of polygenic drug resistance.

**RESULTS** The risk of polygenic drug resistance is generally highest in highly endemic settings, in highly aggregated parasite populations, and during deworming programmes implemented at high coverage and/or frequency. The risk of drug resistance emerging before interruption of transmission is relatively low for