NATIONAL INSTITUTE FOR MEDICAL RESEARCH
HEALTH RESEARCH SUMMARIES 2019

The following are research summaries of various journal publications from NIMR Scientists in 2019:

1.0 MALARIA

1. **Bacterial larvicides used for malaria vector control in sub-Saharan Africa : review of their effectiveness and operational feasibility.**
   By Derua YA, Kweka EJ, Kisinza WN, Githeko AK, Mosha FW. Parasite and Vectors, 2019;12:426.

   Introduction: Several studies have outlined the potential role of larviciding for malaria control in sub-Saharan Africa (SSA) to supplement the core indoor insecticide-based interventions. It has been argued that widespread use of long-lasting insecticide-treated nets and indoor residual spraying interventions in many parts of Africa result in many new areas with low and focal malaria transmission that can be targeted with larvicides. As some countries in SSA are making good progress in malaria control, application of bacterial larvicides, could be included in the list of viable options to maintain the gains achieved. **Methods:** We conducted a review of published literature that investigated the application of *Bacillus thuringiensis* var. *israelensis* (*Bti*) and/or *Bacillus sphaericus* (*Bs*) for malaria vector control in SSA. Data for the review were identified through PubMed, files of the authors and reference lists of articles retrieved. **Findings and conclusions:** A total of 56 studies were identified and included in the review. The findings indicated that, at low application rates, bacterial larvicide products based on *Bti* and/or *Bs* were effective in controlling malaria vectors. The larvicide interventions were found to be feasible, accepted by the general community, safe to the non-target organisms and the costs compared fairly well with those of other vector control measures practiced in SSA. Our review suggests that larviciding should gain more ground due to the decline in malaria which creates more appropriate conditions for the intervention and to the recognition of limitations of insecticide-based vector control tools. The advancement of technology for mapping landscapes could moreover facilitate identification and targeting of the numerous larval habitats preferred by the African malaria vectors. To build sustainable anti-larval measures in SSA, there is a great need to build capacity in relevant specialties and develop

organizational structures for governance and management of larval source management programmes.

2. **Susceptibility of *Anopheles gambiae* complex mosquitoes to microbial larvicides in diverse ecological settings in western Kenya.**
By Derua YA, Kahindi SC, Mosha FW, Kweka EJ, Atieli HE, Zhou G, Lee MC, Githeko AK, Yan G. Medical and Veterinary Entomology. 2019; 33:220-227.

Introduction: Bacterial larvicides *Bacillus thuringiensis israelensis* (*Bti*) and *Bacillus sphaericus* (*Bs*) are well-known for their efficacy and safety for control of malaria mosquitoes. As a background for assessing their potential value for future mosquito control in western Kenya, the current study tested the susceptibility of five populations of *Anopheles gambiae* complex, collected from five diverse ecological settings in this area, to *Bti* and *Bs* under laboratory conditions. The sites included an area known for pyrethroid resistance, a rice agricultural ecosystem, an area with indoor insecticide and microbial larvicide use, an area without history of microbial larvicide use and a semi-urban area predisposed to urban pollutants. **Methods:** From each population, bioassays were conducted with eight concentrations of larvicides (*Bti*/*Bs*) in four replicates, and experiments were repeated on three separate days. Larvae mortality was recorded at 24 or 48 hours after application of larvicide and subjected to Probit analysis. **Results and conclusion:** A total of 2400 larvae of *An. gambiae* complex from each population were tested for their susceptibility to *Bti* and *Bs*. *Bti* mean lethal concentration values for 50 and 95% larvae mortality (LC_{50} and LC_{95}) for the five populations were 0.062 mg/l and 0.797 mg/l respectively, while the corresponding values for *Bs* were 0.058 mg/l and 0.451 mg/l. Statistical analysis indicated that the five populations of *An. gambiae* complex tested were fully susceptible to *Bti* and *Bs*, and there was no significant variation in susceptibility between the tested populations.

3. **Improved spatial ecological sampling using open data and standardization: an example from malaria mosquito surveillance.**
By Luigi Sedda, Eric R. Lucas, Luc S. Djogbe´nou, Ako V. C. Edi, Alexander Egyir-Yawson, Bilali I. Kabula, Janet Midega, Eric Ochomo, David Weetman and Martin J. Donnelly. J. R. Soc. Interface 16: 20180941. http://dx.doi.org/10.1098/rsif.2018.0941

Introduction: Vector-borne disease control relies on efficient vector surveillance, mostly carried out using traps whose number and locations are often determined by

expert opinion rather than a rigorous quantitative sampling design. **Methods:** In this work we propose to establish a framework for ecological sampling design which in its preliminary stages can take into account environmental conditions obtained from open data (i.e. remote sensing and meteorological stations) not necessarily designed for ecological analysis. These environmental data are used to delimit the area into ecologically homogeneous strata. We employed the Bayesian statistics within a model-based sampling design, deploy traps among the strata using a mixture of random and grid locations which allows balancing predictions and model-fitting accuracies. Sample sizes and the effect of ecological strata on sample sizes are estimated from previous mosquito sampling campaigns open data. **Results and Conclusion**: Notably, we found that a configuration of 30 locations with four households each (120 samples) will have a similar accuracy in the predictions of mosquito abundance as 200 random samples. In addition, we show that random sampling independently from ecological strata, produces biased estimates of the mosquito abundance. Finally, we propose standardizing reporting of sampling designs to allow transparency and repetition/re-use in subsequent sampling campaigns.

4. Reduction of malaria prevalence after introduction of artemisinin-combination-therapy in Mbeya Region, Tanzania: results from a cohort study with 6773 participants.
   Authors: Froeschl, Guenter, Elmar Saathoff, Inge Kroidl, Nicole Berens-Riha, Petra Clowes, Leonard Maboko, Weston Assisya, Wolfram Mwalongo, Martina Gerhardt, Elias Nyanda Ntinginya and Michael Hoelscher.

   Background: A marked decline in malaria morbidity and mortality has been reported after the introduction of artemisinin-based combination therapy (ACT) in high malaria prevalence countries in Africa. Data on the impact of ACT and on the prevalence of malaria has so far been scarce for Southwest Tanzania. **Methods:** Between 2005 and 2011, a large general population cohort in the Mbeya Region in the south-west of Tanzania has been surveyed within the EMINI-study (Evaluation and Monitoring of the Impact of New Interventions). Participants were examined once per year, including rapid diagnostic testing for malaria. ACT was introduced in the region according to national guidelines in the time period 2006/2007, replacing sulfadoxine/pyrimethamine as first-line therapy. In four study sites, 6773 individuals who participated in the first two of three consecutive survey visits in the period from 2006 to 2009 were included in this analysis. The burden of *Plasmodium* infection prior to and after the introduction of ACT was compared with consideration of climatic variability, age, sex, socio-

economic status and bed net use as potential factors which may have hidden effect on the outcome. **Results:** A significant reduction over time in the prevalence of *Plasmodium falciparum* infection from 2.5 to 0.3% was shown across the four study sites. The decline was not explained by other factors included in the analysis; therefore, the decline over time most likely reflects the impact of introduction of ACT in the study area. **Conclusions:** The longitudinal study showed a significant and relevant decline in the burden of *P. falciparum* infection after introduction of ACT, which could not be explained by potential confounders. The data suggests that artemisinin-based combinations are not only an effective instrument for reduction of immediate morbidity and mortality, but also for reduction of transmission rates.

5. **Emerging implications of policies on malaria treatment: genetic changes in the *Pfmdr-1* gene affecting susceptibility to artemether-lumefantrine and artesunate-amodiaquine in Africa.**

   Okell LC, Reiter LM, Ebbe LS, Baraka V, Bisanzio D, Watson OJ, Bennett A, Verity R, Gething P, Roper C, Alifrangis M. BMJ Glob Health. 2018 Oct 19;3(5):e000999. doi: 10.1136/bmjgh-2018-000999. eCollection 2018.

   Background. Artemether-lumefantrine (AL) and artesunate-amodiaquine (AS-AQ) are the most commonly used artemisinin-based combination therapies (ACT) for treatment of Plasmodium falciparum in Africa. Both treatments remain efficacious, but genetic changes (SNPs) in the Plasmodium falciparum multidrug resistance 1 (Pfmdr1) gene may compromise sensitivity. AL and AS-AQ exert opposing selective pressures.

   Methods. Through a systematic review, we identified 397 surveys measuring the prevalence of Pfmdr1 polymorphisms at positions 86 184 or 1246 in 30 countries in Africa. Temporal trends in SNP frequencies after introduction of AL or AS-AQ as first-line treatment were analysed in 32 locations, and selection coefficients estimated. We examined associations between antimalarial policies, consumption, transmission intensity and rate of SNP selection. **Results.** 1246Y frequency decreased on average more rapidly in locations where national policy recommended AL (median selection coefficient(s) of -0.083), compared with policies of AS-AQ or both AL and AS-AQ (median s=-0.035 and 0.021, $p<0.001$ respectively). 86Y frequency declined markedly after ACT policy introduction, with a borderline significant trend for a more rapid decline in countries with AL policies ($p=0.055$). However, these trends could also be explained by a difference in initial SNP frequencies at the time of ACT introduction. There were non-significant trends for faster selection of N86 and D1246 in areas with higher AL consumption and no trend with transmission intensity. Recorded

consumption of AS-AQ was low in the locations and times Pfmdr1 data were collected. **Conclusion:** SNP trends in countries with AL policies suggest a broad increase in sensitivity of parasites to AS-AQ, by 7-10 years after AL introduction. Observed rates of selection have implications for planning strategies to cycle drugs or use multiple first-line therapies to maintain drug efficacy.

6. **High efficacy of artemether–lumefantrine and dihydroartemisinin–piperaquine for the treatment of uncomplicated falciparum malaria in Muheza and Kigoma Districts, Tanzania.**
Celine I. Mandara, Reginald A. Kavishe, Samuel Gesase, Janneth Mghamba, Esther Ngadaya, Peter Mmbuji, Sigsbert Mkude, Renata Mandike, Ritha Njau, Ally Mohamed, Martha M. Lemnge, Marian Warsame and Deus S. Ishengoma.

Background: Artemether–lumefantrine (AL) is the recommended first-line artemisinin-based combination therapy (ACT) for the treatment of uncomplicated falciparum malaria in most of the malaria-endemic countries, including Tanzania. Recently, dihydroartemisinin–piperaquine (DP) has been recommended as the alternative anti-malarial to ensure effective case management in Tanzania. This study assessed the parasite clearance rate and efficacy of AL and DP among patients aged 6 months to 10 years with uncomplicated falciparum malaria in two sites with different malaria transmission intensity. **Methods:** This trial was conducted at two sites of Muheza Designated District Hospital in Tanga and Ujiji Health Centre in Kigoma region. Patients were treated with either AL or DP and followed up for 28 (extended to 42) and 42 (63) days for AL and DP, respectively. Parasite clearance time was monitored in the first 72 h post treatment. The primary outcome was parasitological cure on days 28 and 42 for AL and DP, respectively. Secondary outcome was extended parasitological cure on days 42 and 63 for AL and DP, respectively. **Results:** Of the 509 children enrolled (192 at Muheza and 317 at Ujiji), there was no early treatment failure. PCR uncorrected cure rates on day 28 in AL group was 77.2% in Muheza and 71.2% at Ujiji. In the DP arm, the PCR uncorrected cure rate on day 42 was 73.6% at Muheza and 72.5% at Ujiji. With extended follow-up (up to day 42 for AL and 63 for DP) cure rates were lower at Ujiji compared to Muheza (AL: 60.2 vs. 46.1%; DP: 57.6 vs. 40.3% in Muheza and Ujiji, respectively). The PCR corrected cure rate ranged from 94.6 to 100% for all the treatment groups at both sites. **Conclusion:** These findings confirm high efficacy of the first and the newly recommended alternative ACT for treatments for uncomplicated falciparum malaria in Tanzania. The high parasite clearance rate suggests absence of suspected artemisinin resistance, defined as delayed parasite clearance.

7. **High cure rates and tolerability of artesunate–amodiaquine and dihydroartemisinin–piperaquine for the treatment of uncomplicated falciparum malaria in Kibaha and Kigoma, Tanzania.**

Celine I. Mandara, Filbert Francis, Mercy G. Chiduo, Billy Ngasala, Renata Mandike, Sigsbert Mkude, Frank Chacky, Fabrizio Molteni, Ritha Njau, Ally Mohamed, Marian Warsame7, and Deus S. Ishengoma.

Background: The Tanzanian National Malaria Control Programme and its partners have been implementing regular therapeutic efficacy studies to monitor the performance of different drugs used or with potential use in Tanzania. This study was conducted at two sites (Kibaha, Pwani and Ujiji, Kigoma) to assess the efficacy and safety of artesunate–amodiaquine (ASAQ) and dihydroartemisinin–piperaquine (DP), which are the current alternative artemisinin-based combinations in Tanzania. **Methods:** This was a prospective study to evaluate clinical and parasitological responses of ASAQ and DP for treatment of uncomplicated falciparum malaria. Children aged 6 months to 10 years were enrolled and treated with either ASAQ or DP. Follow-up was done for 28 days (ASAQ) and 42 days (DP) to determine the cure rate while observing reinfection using PCR. We also observed the occurrence of adverse events (AEs) or serious adverse events (SAEs). **Results:** Of the 724 patients screened at both sites, 333 (46.0%) were enrolled and 326 (97.9%) were followed up properly. Before correction for re-infection (PCR) adequate clinical and parasitological response for DP on day 42 was 98.8% and 75.9% at Kibaha and Ujiji, respectively. After correction for reinfection (PCR), DP's ACPR was 100% for both drugs at both sites. Of the patients recruited (n=333), 175 (52.6%) had AEs with 223 episodes (at both sites) in the two treatment groups. There was no SAE and the commonly reported AE episodes (with>5%) included, cough, running nose, abdominal pain, diarrhoea and fever. **Conclusion:** Both artemisinin-based combinations had high cure rates (100%) after PCR. The two drugs had adequate safety with no SAE and all AEs were mild, and not associated with the anti-malarials. Continued TES is critical to monitor the performance of nationally recommended artemisinin-based combination therapy and supporting evidence-based review of malaria treatment policies.

8. **Safety profile of the RTS,S/AS01 malaria vaccine in infants and children: additional data from a phase III randomized controlled trial in sub-Saharan Africa**

Yolanda Guerra Mendoza, Elodie Garric, Amanda Leach, Marc Lievens,Opokua Ofori-Anyinam, Jean-Yves Pirçon, Jens-Ulrich Stegmann, Pascale Vandoolaeghe, LucasOtieno, Walter Otieno, Seth Owusu-Agyei, Jahit Sacarlal, Nahya Salim Masoud, Hermann Sorgho,Marcel Tanner, Halidou Tinto, Innocent Valea, Ali Takadir Mtoro, Patricia Njuguna, Martina Oneko,Godfrey Allan Otieno, Kephas Otieno, Samwel Gesase, Mary J Hamel, Irving Hoffman, SeyramKaali, Portia Kamthunzi, Peter Kremsner, Miguel Lanaspa, Bertrand Lell, ***John Lusingu, Anangisye Malabeja,*** *Pedro Aide, Pauline Akoo, Daniel Ansong, Kwaku Poku Asante, James A Berkley,Samuel Adjei, Tsiri Agbenyega, Selidji Todagbe Agnandji & Lode Schuerman*

Introduction: The widespread implementation of malaria prevention and control measures, such as the use of insecticide-treated nets, improved diagnosis, and artemisinin combination therapy, has led to considerable gains in the control of malaria. Nevertheless, malaria remains a major public health threat, especially in young children in sub-Saharan Africa (SSA). In 2017, an estimated 219 million cases of malaria occurred worldwide, resulting in 435,000 deaths, of which 93% occurred in Africa. About 61% of all malaria deaths were estimated to occur in children younger than 5 years. The development of an effective malaria vaccine is a further important step towards reducing the disease burden. RTS,S/AS01 is a malaria vaccine candidate has proven efficacy in clinical trials. **Method:** 8922 children (enrolled at 5–17 months) and 6537 infants (enrolled at 6–12 weeks) were divided into three groups to receive 4 doses of malaria vaccine or non-malaria control vaccine and were followed for 48 and 38 months respectively. **Results:** The trial demonstrated vaccine efficacy (VE) against clinical malaria of 36.3% in children and 25.9% in infants, VE against severe malaria was 32.2% in children and 17.3% in infants. Serious adverse event (SAE) and fatal SAE incidences throughout the study were 24.2%–28.4% and 1.5%–2.5%, respectively across groups; 0.0%–0.3% of participants reported vaccination-related SAEs. The most frequently reported SAEs were malaria (9.9%–14.2%; 8.3%–10.7%). A statistically significant numerical imbalance was observed for meningitis cases in children but not in infants. **Discussion:** The malaria vaccine candidate RTS,S/AS01 is safe and warrant further evaluation in phase IV studies and WHO-led pilot implementation programs to establish the RTS,S/AS01 benefit-risk profile in real-life.

2.0. NEGLECTED TROPICAL DISEASES

1. **Lymphatic filariasis transmission in Rufiji District, southeastern Tanzania : infection status of the human population and mosquito vectors after twelve rounds of mass drug administration.**
   By Jones C, Ngasala B, Derua YA, Tarimo D, Reimer L, Bockarie M, Malecela MN. Parasite and Vectors, 2018; 11:588.

   Introduction: Control of lymphatic filariasis (LF) in most sub-Saharan Africa is based on annual mass drug administration (MDA) using a combination of ivermectin and albendazole. Monitoring the impact MDA is crucial for measuring the success of the LF control programmes. This study assessed the status of LF infection in Rufiji district, south eastern Tanzania after twelve rounds of MDA. **Methods:** Community members aged ≥ 5 years were examined for *Wuchereria bancrofti* circulating filarial antigens (CFA) and antigen positive individuals were screened for microfilaraemia. All study participants were furthermore examined for LF clinical manifestations and interviewed with respect to drug uptake during MDAs. Moreover, filarial mosquito vectors were collected indoor and outdoor and examined for infection with *W. bancrofti*. **Results and implications:** Out of 854 participants tested, 9 (1.1%) were positive for CFA and one (0.1%) was found to be microfilaraemic. The prevalence of hydrocele and elephantiasis was 4.8% and 2.9%, respectively. Surveyed drug uptake rates were relatively high, with 70.5% of the respondents reported to have swallowed the drugs in 2014. Eighty three percent of the respondents reported to have swallowed the drugs at least once since inception of the MDA intervention. Of 1,054 filarial vectors caught indoors and dissected for infection with *W. bancrofti*, none was found to be infected. Analysis by quantitative polymerase chain reaction (qPCR) of 1092 pools of gravid *Culex quinquefasciatus* collected outdoor resulted in an estimated infection rate of 0.1%. None of the filarial vector tested with qPCR were found infective, suggesting cessation of local transmission. **Conclusion:** Analysis of LF infection in human and mosquito vectors indicated a substantial decline in prevalence of LF in the study areas. We recommend a formal transmission assessment survey (TAS) in the study areas to make an informed decision on whether MDA can be stopped in Rufiji district.

2. ***Wuchereria bancrofti* infection is linked to systemic activation of CD4 and CD8 T cells**

Authors: Inge Kroidl Mkunde Chachage, Jonathan Mnkai, Anthony Nsojo, Myrna Berninghoff, Jaco J. Verweij, Lucas Maganga, Nyanda E. Ntinginya, Leonard Maboko, Petra Clowes, Michael Hoelscher, Elmar Saathoff, Christof Geldmacher

Introduction: CD4 T cells of the immune system especially those that have been **activated** to fight an infectious agent are predominantly targeted for HIV infection and have been linked to HIV susceptibility. In this study, we described an activation state of CD4 T cells in the blood of individual infected with a worm (*Wuchereria bancrofti*) that causes lymphatic filariasis (LF). We did this research because, we have recently observed and reported an increase in HIV new infections in people infected with *LF worm* compared to uninfected individuals from the same area and thus wanted to investigate the reasons/mechanism for such an observation. **Methods:** 235 HIV negative adults with or without LF worm infection were included in the study, whereby samples including blood was collected for measurement of activated CD4 T cells by using a cell measurement machine. **Findings:** This study revealed an increased proportion of activated CD4 T cells in LF worm infected volunteers compared to their uninfected counterparts. **Conclusion:** Indeed, such an elevation of activated CD4 T cells may contribute to the increased risk of HIV infection in individuals infected with LF worm.

3. **Prevalence of *Wuchereria bancrofti* Infection in Mosquitoes from Pangani District, Northeastern Tanzania**

Author: Godlisten S. Materu

Background: *Wuchereria bancrofti* is the most widely distributed of the 3 nematodes known to cause lymphatic filariasis, the other 2 being *Brugia malayi* and *Brugia timori*. *Anopheles gambiae* and *Anopheles funestus* are the main vectors. However, the relative contributions of mosquito vectors to disease burden and infectivity are becoming increasingly important in coastal East Africa, and this is particularly true in the urban and semi-urban areas of Pangani District, Tanzania. **Methods:** Mosquitoes were sampled from 5 randomly selected villages of Pangani District, namely, Bweni, Madanga, Meka, Msaraza, and Pangani West. Sampling of mosquitoes was done using standard Centers for Disease Control light traps with incandescent light bulbs. The presence of W. bancrofti in mosquitoes was determined via polymerase chain reaction (PCR) assays using NV1 and NV2 primers, and PoolScreen 2 software was used to

determine the estimated rate of W. bancrofti infection in mosquitoes. **Results:** A total of 951 mosquitoes were collected, of which 99.36% were *Culex quinquefasciatus,* 0.32% were Anopheles gambiae, and 0.32% other Culex species. The estimated rate of W. bancrofti infection among these mosquitoes was 3.3%. **Conclusion:** This was the first study employing the use of PoolScreen PCR to detect W. bancrofti circulating in mosquito vectors in Pangani District, northeastern Tanzania. The presence of W. bancrofti infection suggests the possibility of infected humans in the area. The high abundance of *Cx. quinquefasciatus* calls for integrated mosquito control interventions to minimise the risk of W. bancrofti transmission to humans. Further research is required to gain an in-depth understanding the W. bancrofti larval stages in mosquitoes, their drug sensitivity and susceptibility profiles, and their fecundity.

4. **Community knowledge, perceptions and water contact practices associated with transmission of urinary schistosomiasis in an endemic region: a qualitative cross-sectional study.**

   Teckla Angelo, Joseph R. Mwanga, Safari M. Kinung'hi [BMC Public Health (2019) 19:703]

   Background: In an effort to complement the current chemotherapy-based schistosomiasis control interventions in Shinyanga district, community knowledge, perceptions and water contact practices were qualitatively assessed using focus group discussions and semi structured interviews involving 271 participants in one S. haematobium prevalent community of Ikingwamanoti village, Shinyanga district, Northwestern, Tanzania. **Methods:** In October, 2016 we conducted 29 parent semi structured interviews and 16 focus group discussions with a total of 168 parent informants. Adult participants were conveniently selected from three sub-villages of Butini, Miyu, and Bomani of Ikingwamanoti village, Shinyanga district. In March, 2017, a total of 103 children informants participated in 10 focus group discussions and 20 semi structured interviews, administered to children from standard four, five, six and seven attending Ikingwamanoti Primary School. Note taking and digital recorders were used to collect narrative data for thematic analysis of emergent themes. **Results:** Among participants, 75% parents and 50% children considered urinary schistosomiasis as a low priority health problem. Of the informants, 70% children and 48.3% parents had misconceptions about the cause, modes of transmission and control of schistosomiasis demonstrating gaps in their biomedical knowledge of the disease. Assessment of treatment seeking behaviour for urinary schistosomiasis revealed a combination of traditional and modern health care sectors. However, modern medicines were considered effective in the treatment of urinary schistosomiasis. Lack of alternative

sources of water for domestic and recreational activities and unhygienic water use habits exposed community members to high risk of acquiring urinary schistosomiasis. **Conclusion:** Use of Schistosoma haematobium contaminated water sources for daily domestic and recreational use facilitated contraction of urinary schistosomiasis among community members in Shinyanga district. People's perceptions of urinary schistosomiasis as a less priority health problem promoted persistence of the disease. Future efforts to control urinary schistosomiasis should take into account integrated approaches combining water, sanitation and hygiene, health education, alternative sources of clean and safe water to facilitate behaviour change.

5. **Village response to mass drug administration (MDA) for control of schistosomiasis in Mwanza region, Tanzania: Are we missing the socio-economic, cultural and political dimensions?**

Safari Kinung'hi, Justina Mosha, Teckla Angelo, Jane Maganga, Joseph Mwanga

Introduction: The reasons for villages or communities being a persistent hotspot are not well understood. It is likely that some villages have higher reinfection rates due to a greater force of transmission, which in turn could be the result of poor sanitation, use of open water sources, and abundance of vector snails and other contextual factors including socio-economic, cultural and political. The SCORE project has undertaken comparative studies between persistent hot spot (PHS) and responding (RES) villages in Tanzania in efforts to identify village characteristics that correlate with being a RES or a PHS village. The **study objectives** were to understand the behavioural attributes of water usage, water contact and open defecation and to assess the level of sanitation within schools and households within the study villages which influence a village being a PHS or a RES. **Methods**: Qualitative studies were conducted to examine factors that might differentiate villages which did not show substantial decrease in *Schistosoma mansoni* prevalence despite repeated, high treatment coverage PHS villages', from villages which showed a substantial decrease in prevalence, RES villages. The study was conducted in 8 villages in Mwanza region. Four villages included in the study were responding villages while the other four were persistent hotspot villages (PHS). Structured questionnaires were used to collect data on Water, Sanitation and hygiene (WASH) in these villages targeting the school children, household heads and head teachers of the primary schools. In addition, urine and stool sample were collected from fifty 9-12-year-old children and 50 household adults in the community. A convenient sample of adults was drawn from these eight

villages. Thirty-nine key informants were interviewed, and sixteen focus group discussion sessions were held with a total of 123 participants. The focus of this study was on the following variables: perceptions on common illnesses, village structure, socio-economic status, village and school leadership quality; migration, community engagement, and motivation and commitment to schistosomiasis control interventions. **Results and Conclusion**: from this study show that the baseline prevalence of *S. mansoni* by Kato-Katz was 43.6% (range 34-54%) in PHS villages compared to 21.5% (range 12-30%) in the RES villages. RES villages were more likely to have hand washing facilities in schools compared to PHS villages, though the difference was not significant (p=0.157).The proportion of school children always using a toilet was higher in RES villages (90%) compared to PHS villages (81%) (p<0.001). Further, the proportion of people using surface water sources for bathing was higher in PHS villages (76.4%) compared to RES village (65.5%) (p<0.016). For both PHS and RES villages, the proportion of households owning a latrine/toilet was high (>80%) while the proportion of households practicing open defecation was relatively low (<20%), but without significant differences between PHS and RES villages (p>0.05). The factors contributing to sustained high schistosomiasis prevalence among PHS villages were identified to be of socio-economic, cultural and political in nature and included poor leadership style, lack of or insufficient social engagement**, l**ittle or lack of genuine community participation and little motivation and commitment to schistosomiasis control programmes. There were no differences in terms of perceptions on common illnesses between PHS and RES villages. In both sets of villages, schistosomiasis was not given priority as an important health problem compared to acute illnesses such as malaria. Immigrants was reported in both PHS and RES villages whereby immigrants came from other areas around Lake Victoria such as Kagera, Geita, Mara, Shinyanga and Simiyu regions and sometimes from other East African countries such as Rwanda and Burundi. We do concur with scholars who have suggested that factors responsible for persistence of high prevalence of schistosomiasis in PHS villages should therefore be addressed by adopting a biosocial approach at the local level that link biological and social factors focusing on the inter-connection between biological and social aspects of life. [Am. J. Trop. Med. Hyg, Submitted]

6. **Comparison of the Impact of Different Mass Drug Administration Strategies on Infection with Schistosoma mansoni in Mwanza Region, Tanzania—A Cluster-Randomized Controlled Trial.**
Safari Kinung'hi [Am. J. Trop. Med. Hyg., 99 (6), 2018, pp. 1573–1579].

Introduction: Annual school-based mass drug administration with praziquantel has been widely implemented to control schistosomiasis, but other treatment strategies could have a different impact. The **aim** of this study was to investigate the impact of six different treatment strategies on *Schistosoma mansoni* infection in a cluster-randomized controlled trial in schoolchildren, in a high transmission area of the Mwanza Region, Tanzania. **Methods:** A total of 150 villages were randomized into six arms with 25 villages in each arm. In each village, approximately 100 schoolchildren aged 9–12 years were randomly selected each year and investigated for *S. mansoni* prevalence and intensity based on three consecutive stool samples using the duplicate Kato–Katz technique. Four years of community-wide treatment (CWT) was the most intensive treatment strategy, whereas 2 years of school-based treatment (SBT) combined with 2 years without treatment (holiday) was the least intensive treatment. The remaining strategies constituted different combinations of CWT, SBT, and holiday years. **Results:** Baseline results on *S. mansoni* infection were obtained from 14,620 schoolchildren from 148 villages, and mean prevalence and mean intensity among infected were 48.6–60.6% and 130.5–229.8 eggs per gram, respectively. Over the years, mean prevalence and mean intensities declined in all arms, but when comparing year 5 mean prevalence and mean intensity, there were no statistically significant differences between treatment arms. Thus, measured in a random selection of schoolchildren aged 9–12 years, four times CWT was not superior to four times SBT, while 2 years of treatment holiday combined with 2 years of SBT had the same impact as 4 years of SBT.

7. **Persistent Hotspots in Schistosomiasis Consortium for Operational Research and Evaluation Studies for Gaining and Sustaining Control of Schistosomiasis after Four Years of Mass Drug Administration of Praziquantel.**
Safari Kinung'hi [Am J Trop Med Hyg. 2019 Sep;101 (3):617-627].

Control of schistosomiasis presently relies largely on preventive chemotherapy with praziquantel through mass drug administration (MDA) programs. The Schistosomiasis Consortium for Operational Research and Evaluation has concluded five studies in four countries (Côte d'Ivoire, Kenya, Mozambique, and Tanzania) to evaluate alternative

approaches to MDA. Studies involved four intervention years, with final evaluation in the fifth year. Mass drug administration given annually or twice over 4 years reduced average prevalence and intensity of schistosome infections, but not all villages that were treated in the same way responded similarly. There are multiple ways by which responsiveness to MDA, or the lack thereof, could be measured. In the analyses presented here, we defined persistent hotspots (PHS) as villages that achieved less than 35% reduction in prevalence and/or less than 50% reduction in infection intensity after 4 years of either school-based or community-wide MDA, either annually or twice in 4 years. By this definition, at least 30% of villages in each of the five studies were PHSs. We found no consistent relationship between PHSs and the type or frequency of intervention, adequacy of reported MDA coverage, and prevalence or intensity of infection at baseline. New research is warranted to identify PHSs after just one or a few rounds of MDA, and new adaptive strategies need to be advanced and validated for turning PHSs into responder villages

8. **High prevalence of epilepsy in two rural onchocerciasis endemic villages in the Mahenge area, Tanzania, after 20 years of community directed treatment with ivermectin.**

Mmbando BP, Suykerbuyk P, Mnacho M, Kakorozya A, Matuja W, Hendy A, Greter H, Makunde WH, Colebunders R.

Background: Epilepsy is a neurological disorder with a multitude of underlying causes, which may include infection with *Onchocerca volvulus*, the parasitic worm that causes human onchocerciasis. A survey carried out in 1989 revealed a high prevalence of epilepsy (1.02% overall, ranging from 0.51 to 3.71% in ten villages) in the Mahenge area of Ulanga district, an onchocerciasis endemic region in south eastern Tanzania. This study aimed to determine the prevalence and incidence of epilepsy following 20 years of onchocerciasis control through annual community directed treatment with ivermectin (CDTI). **Methods:** The study was conducted in January 2017 in two suburban and two rural villages in the Mahenge area. Door-to-door household visits were carried out by trained community health workers and data assistants to screen for persons suspected of having epilepsy, using a standardised questionnaire. Persons with suspected epilepsy were then interviewed and examined by a neurologist for case verification. Onchocerciasis associated epilepsy was defined as epilepsy without

an obvious cause, with an onset of seizures between the ages of 3-18 years in previously healthy children. In each village, fifty males aged ≥20 years were tested for onchocerciasis antibodies using an OV16 rapid test and were examined for presence of onchocerciasis nodules. Children aged 6-10 years were also tested using OV16 tests. **Results:** 5117 individuals (median age 18.5 years, 53.2% female) from 1168 households were screened. 244 (4.8%) were suspected of having epilepsy and invited for neurological assessment. Prevalence of epilepsy was 2.5%, with the rural villages having the highest rate (3.5% vs 1.5%). Prevalence of OV16 antibodies in children 6-10 years old was higher in rural villages (42.6%) than in suburban (4.7%) villages. **Conclusions:** This survey revealed a high prevalence of epilepsy in two rural onchocerciasis endemic villages in the Mahenge area. Despite 20 years of CDTI, a high prevalence of OV16 antibodies in children aged 6-10 years suggests on-going O. volvulus transmission. Reasons for the persistence of on-going parasite transmission in the Mahenge area need to be investigated.

3.0. REPRODUCTIVE, MATERNAL, NEWBORN, CHILD AND ADOLESCENT HEALTH

1. **Patterns and causes of hospital maternal mortality in Tanzania: A 10-year retrospective analysis.**
   By Veneranda M Bwana, Susan F Rumisha, Irene R Mremi, Emanuel P Lyimo and Leonard E. G. Mboera, Published at Plos One Journal 2019.

   Introduction: Maternal mortality is among the most important public health concerns in Sub-Saharan Africa. There is limited data on hospital-based maternal mortality in Tanzania. The objective of this study was to determine the causes and maternal mortality trends in public hospitals of Tanzania from 2006–2015. **Methods:** This study was conducted between July and December 2016 and involved 34 public hospitals in Tanzania. Information on causes of deaths due to pregnancy and delivery complications among women of child-bearing age (15–49 years old) was extracted from inpatient and death registers and International Classification of Disease (ICD)-10 report forms. Maternal deaths were classified based on case definition by ICD 10 and categorized as direct and indirect causes. **Findings:** Out of 40,052 deaths of women of child-bearing age, 1,987 (5.0%) were attributed to maternal deaths. Two thirds of the deaths affected women aged 20–34 years old. Hospital-based maternal mortality ratio increased from 40.24 (2006) to 57.94 deaths per 100000 births in 2015 during the ten-

year period. Of the 1,987 deaths, 83.8% were due to direct causes and 16.2% were due to indirect causes. Major direct causes were eclampsia (34.0%), obstetric haemorrhage (24.6%) and maternal sepsis (16.7%). Anaemia (14.9%) and cardiovascular disorders (14.0%) were the main indirect causes. While there was a decline in the number of deaths due to eclampsia and abortion, those due to haemorrhage and cardiovascular disorders increased during the period. **Discussion:** Several factors have been identified to be responsible for the high maternal deaths among young women. These include biological, economic, and cultural factors, malnutrition, immature reproductive tract, child marriage, and gender inequities. It is important therefore that reproductive health programmes provide education, family planning services, and pre- and post-natal care services to reduce mortality among young women. In our study major indirect causes were attributed to anaemia, cardiovascular disorders, malaria, HIV/AIDS and meningitis. Despite this contribution, indirect causes they have received little attention as most national and international efforts are directed toward direct causes of maternal deaths–focusing on emergency obstetric care. It is important that studies are designed to focus on these indirect causes of death are carried out to provide evidence to develop appropriate interventions to holistically reduce maternal mortality. **Conclusions:** During the ten-year period (2006–2015), there was an increase in the number of hospital maternal deaths in public hospitals in Tanzania. Most maternal deaths were due to direct causes including eclampsia, haemorrhage and sepsis. The findings of this study provide evidence for better planning and policy formulation for reproductive health programmes to reduce maternal deaths in Tanzania.

2. **Fostering, children's education, and work in north-western Tanzania**
   Author: Mark Urassa [Demographic Research, Volume 41, Article 10, Pages 263-292. July, 2019].

   Background: Fostering, raising children that are not one's biological children, is common in many societies worldwide. Despite predicted lower investment in non-biological offspring, numerous studies report no obvious well-being penalty for fostered children. Building on prior research, we suggest that fostering is incentivized by close relatedness between foster child and caregivers and that children's work contributions can offset their costs to fostering households. **Method:** We used multilevel logistic and fractional multinomial regression analyses to investigate the association between fostering, educational investment, and time allocation in a sample of 1,273 Sukuma children (aged 7–19) from north-western Tanzania, where

fostering is traditionally common. **Results:** Twenty-six per cent of children are fostered, with most having at least one living parent. Children fostered by close kin have similar educational outcomes to those living with both biological parents, though their grade for age is lower, perhaps reflecting differences in timing rather than overall level of investment. Those fostered by distant kin are less likely to be enrolled or to progress to secondary school. Overall, fostered children are more likely to do farm work; however, on weekdays when work conflicts with school, differences in time allocation to work activities are not pronounced. We further find that orphans are generally not particularly disadvantaged compared to other fostered children. **Conclusion:** Being fostered by close kin does not appear to disadvantage children, and buffers orphans from parental death. Fostered children may offset some of their costs through increased farm work.

3. **FOETAL for NCD-FOetal Exposure and Epidemiological Transitions: the role of Anaemia in early Life for Non-Communicable Diseases in later life: a prospective preconception study in rural Tanzania.**
Hjort L, Lykke Møller S, Minja D, Msemo O, Nielsen BB, Lund Christensen D, Theander T, Nielsen K, Larsen LG, Grunnet LG, Groop L, Prasad R, Lusingu J, Schmiegelow C, Bygbjerg IC.

Background: Low-income and middle-income countries such as Tanzania experience a high prevalence of non-communicable diseases (NCDs), including anaemia. Studying if and how anaemia affects growth, placenta development, epigenetic patterns and newborns' risk of NCDs may provide approaches to prevent NCDs. **Participants**: The FOETALforNCD (FOetal Exposure and Epidemiological Transitions: the role of Anaemia in early Life for Non-Communicable Diseases in later life) study involved women of reproductive age in Korogwe and Handeni Districts of north-eastern Tanzania in which first group included 1415 women of reproductive age were enrolled before pregnant and upon conception followed throughout pregnancy until conception. The second group included 583 pregnant women enrolled during early in pregnancy and followed throughout pregnancy until delivery. During follow up period the following data were collected: Body mass index, haemoglobin and micronutrients levels, HIV, malaria and reproductive tract infections, blood pressure and glucose level. Foetal growth and placental blood flow patterns were assessed every after three moths using ultrasound and Doppler studies. Soon after delivery and one month later , the babies' weight, length, chest and mid upper arm circumferences as well as skinfold thickness were assessed. In order to determine alterations in placental vascularization placenta and

umbilical cord were collected and analysed. Furthermore, umbilical cord and placental blood were collected to explore various genetic alterations and markers that shows increased risk of newborn susceptibility to NCDs later in their adult life following exposure to maternal anaemia. Findings to Date: Before conception over one third (31.4%) of women were either overweight or obese (body mass index ≥25kg/m2) or 36.7% had anaemia of which 6.1% had severe anaemia before conception. Anaemia increased to 66.7% during pregnancy. Approximately 60% of anaemia was due to iron deficiency. 27.6% of anaemic and 26.7% of iron deficient women were found to be either overweight or obesity. **Future Plans**: Data analysis is ongoing but preliminary results shows that babies born to moderate to severely anaemic mothers were delivered earlier and had significant lower birth weight compared to their healthy counterparts. Analysis of foetal genetic alterations will provide new knowledge on how health of the mother, even before conception, might modify foetal growth and influence the risk of developing NCDs and how to promote better health during pregnancy. The present project ended data collection 1 month after giving birth, but follow-up is continuing through regular monitoring of growth and development and health events according to the National Road Map Strategic Plan in Tanzania. This data will link foetal adverse event to childhood development, and depending on further grant allocation, throughout their life course.

4. **Anthropometric measurements can identify small for gestational age newborns: a cohort study in rural Tanzania.**
Paulsen CB, Nielsen BB, Msemo OA, Møller SL, Ekmann JR, Theander TG, Bygbjerg IC, Lusingu JPA, Minja DTR, Schmiegelow C.

Background: Small-for-gestational-age (SGA) is associated with increased neonatal mortality and morbidity. In low- and middle-income countries an accurate gestational age is often not known, making the identification of SGA newborns difficult. Measuring foot length, chest circumference and mid upper arm circumference (MUAC) of the newborn have been previously shown to be reasonable methods for detecting low birth weight (< 2500 g) and prematurity. The aim of this study was to investigate if the three measurements could also correctly identify SGA newborns in Tanzania. **Methods**: In the current study from a rural village in Korogwe and Handeni districts, north-eastern Tanzania, 376 live newborns had foot length, chest circumference, and MUAC measured within 24 h of birth. Gestational age was estimated by transabdominal ultrasound in early pregnancy and SGA was diagnosed using a sex-specific weight

reference chart previously developed in the study area. The ability of each measurement in detecting SGA infants were tested and compared. **Results:** Of the 376 newborns, 68 (18.4%) were SGA. Foot length, chest circumference and mid upper arm circumference (MUAC) correctly identified 78%, 88% and 85% of SGA infants, respectively. **Conclusion**: In a setting in which is it difficult to precisely determine gestational age, all three methods had a high ability to identify SGA infants. Overall, chest circumference was the best method compared to foot length and MUAC.

5. **Anemia in late pregnancy induces an adaptive response in fetoplacental vascularization.**

Moeller SL, Schmiegelow C, Larsen LG, Nielsen K, Msemo OA, Lusingu JPA, Minja DTR, Theander TG, Bygbjerg IC, Nyengaard JR (Placenta, 2019).

Introduction: Anemia during pregnancy may compromise fetal and newborn's health, however, little is known about how and when the alterations in placental blood vessels development and birth weight are most vulnerable to maternal anemia. **Methods**: Placental samples from women who haemoglobin concentrations were measured throughout pregnancy were randomly collected from 189 women in a rural setting in Korogwe and Handeni Districts of north-eastern Tanzania. The vascularization patterns in terms of were assessed and vessel length, surface area, diffusion distance as well as villi volume calculated and compared to birth weight. **Results**: From a gestational age of 23 weeks maternal anaemia significantly increased the placental transport surface and diffusion area, volume, and diameters. Furthermore, all the placental vascular parameters were affected the birth weight. **Conclusion**: Altered placental vascularization in relation to anaemia after gestational age of 23 weeks together with the association birth weight suggest that the timing of anaemia determines placental vascularization patterns and underscores the clinical relevance for proper development of placental vasculature. Similarly, alterations in placental vasculature affected birth weight.

6. **Marked reduction in fertility among African women with urogenital infections: A prospective cohort study.**
Perslev K, Msemo OA, Minja DTR, Møller SL, Theander TG, Lusingu JPA, Bygbjerg IC, Nielsen BB, Schmiegelow C. (PLoS One, 2019).

Background: There is paucity of data on risk factors for reduced fertility in low-income countries. **Objective**: To investigate factors associated with fertility among women in rural north eastern Tanzania. **Subjects and Methods**: A group of 1248 non-pregnant women was followed with by testing urine for pregnancy every after three months or if they reported a missed menstrual period and pregnancy confirmed using abdominal ultrasound. Information regarding general health, socioeconomic status and history of the health of reproductive system were collected and scientific analysis performed on the factors associated with the ability of the woman to conceive within six months (180 days). **Results**: Among the 1248 women, 736 were followed for 180 days and 209 of these had an ultrasound confirmed pregnancy. During the follow-up period, 169/736 women were diagnosed with urogenital infections, including suspected sexually transmitted or reproductive tract infections, urinary tract infection, and vaginal candidiasis. Urogenital infections were associated 80% reduced ability to conceive. Similarly, age above 30 years was associated with 45% reduction in the ability to conceive within six months. On the other hand, women who recently stopped using modern contraceptives (implants or oral contraceptives) were nearly three times more likely and those with low socioeconomic status twice more likely to become pregnant within six months. **Conclusion**: Urogenital infection seems to be a major health problem in this setting and a risk factor for reduced ability to conceive. Considering the availability of effective treatment options for these diseases, health authorities should increase awareness of diagnostic tools in settings with limited resources in order to improve fertility.

4.0: ONE HEALTH

1. **Enhancing One Health Surveillance systems**.
Karimuribo E.D, Sindato C, Mboera L.E.G and Beda E (2019).

Introduction: The challenges faced by the event-based surveillance (EBS) in Tanzania include inadequate engagement of community, untimely capturing and submission of reports on health events from the primary sources, lack of feedback and difficulty in

contact tracing. Most vulnerable communities are located in hard to reach areas with poor infrastructure, which motivated us to think about fit-for-purpose innovative approaches to strengthen EBS. **Methods:** The National Institute for Medical Research in collaboration with Sokoine with University of Agriculture through SACIDS Foundation for One Health has designed and developed a digital tool branded *AfyaData* to support Event-based surveillance (EBS) in human and animal populations. **Results and discussion:** *AfyaData* (http://afyadata.sacids.org/) is an open source digital disease surveillance tool that eases collection, analysis, visualization, documentation and feedback of public/animal health events, storing/hosting and management. It collects georeferenced data to enhance contact tracing. It can integrate data from multiple sources and is enhanced with an early warning short message service for notification to decision makers on health events through their mobile phones. *AfyaData* is powered by One Health Knowledge Repository, which is a decision-making system that helps to support the prediction of likely disease conditions based on the reported signs and symptoms. It can be used for sample tracking and communication of test results between different points/sections of health care delivery system using barcode feature. It supports multiple languages and can be customized based on different clients' needs. It has been deployed in Ngorongoro, Kilosa, Malinyi, Ulanga, Mvomero, Gairo, Ngara and Wete districts of Tanzania. There are currently over 700 users of *AfyaData* at community level in Tanzania. **Conclusion:** Preliminary findings show that *AfyaData* has been found useful to enhance timely capture and reporting of health events .

2. **Is Tanzania prepared to respond to and prevent Ebola Outbreak?**

Rogath Saika Kishimba, Janneth Mghamba, Mohamed Ally Mohamed, Leonard Subi, Elias Kwesi, Charles Massambu, Amalberga Kasangala, Khalid Massa, Nyambura Moremi, Ndekya Oriyo, Mary Kitambi, Faraja Fred, Jacob Lusekelo, Remidius Kakulu, Mtoroki Majaliwa, Catherine Sungura, George Cosmas, Azma Simba, Neema Camara, Solomoni Moshi, Senga Sembuche, Julius Massaga, Grace Saguti, Mary Mataka, Ahmed Abade, Ali Nyanga, Mohammad Bakari. Tanzania Public Health Bulletin Volume 1, No 1 (Issue 1).

Introduction: An Ebola Virus Disease (EVD) outbreak is an existent public health threat to Tanzania due to the Ebola outbreak in the neighboring Democratic Republic of Congo (DRC). It is evidenced that Ebola outbreak can be contained if the country is prepared and the conventional epidemiological measures are instituted immediately. Therefore, we present how Tanzania, through the Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC), is operationally prepared to respond to and prevent an

EVD outbreak in the country. **Actions Taken:** After receiving notification of the Ebola outbreak in the DRC, the MoHCDGEC notified all administrative levels, activated the Public Health Emergency Operation at level one, and conducted a risk assessment. The assessment identified priority regions (i.e., regions bordering DRC with high numbers of visitors from DRC) and assessed the status of preparedness in the identified high-risk regions with the assistance of an external evaluator using the World Health Organization (WHO) Ebola Virus Disease Consolidated Preparedness Checklist (WHO Checklist). The WHO Checklist assessed the existence of coordination, trained Rapid Response Team (RRT), infection prevention and control (IPC), public awareness and community engagement, case management including safe dignified burial, epidemiological surveillance, and contact tracing. **Outcome:** Eight regions were selected as priority regions, these included Kigoma, Kagera, Mwanza, Songwe, Katavi, Mbeya, Rukwa and Dar es Salaam. Generally, the WHO Checklist scores indicated that priority regions needed to improve their preparedness status. Scores were below 24%. As a result, a total of 438 health care workers (HCWs) were trained; 190 on RRT, 106 on case management and over 142 on event-based surveillance and contact tracing. Also, 122 community health workers were also trained on event-based surveillance and contact tracing. Risk communication guidelines were developed and distributed to all priority regions. Medical equipment and supplies, personal protective equipment (PPE), standard case definitions (SCD), factsheets, and laboratory standard operating procedures (SOPs) on Ebola sample collection, storage, and transportation were also distributed to priority regions. Trainings in Ebola detection, prevention and response were conducted among health workers, the media, musicians, and community groups. Public awareness creation and sensitization campaigns were implemented through media, social networks and Ebola National Walk campaigns. **Conclusions:** With the existence of porous borders and constant movement of travelers from DRC to Tanzania, the likelihood of having an EVD outbreak in the country is high. Based on this situation, and actions taken by the government, we are pleased to inform the public that Tanzania is on high alert and is operationally prepared to respond to and prevent an EVD outbreak in the country.

5: TUBERCULOSIS

1. **Effect of Xpert MTB/RIF on clinical outcomes in routine care settings: individual patient data meta-analysis**

   Authors: Di Tanna L.G., Khaki R.A., Theron G., McCarthy K., Cox H., Mupfumi L., Trajman A., Zijenah S.L., Mason P., Bandason T., Durovni B., Bara W., Hoelscher W., Clowes P., Mangu C.,

Chanda D., Pym A., Mwaba P., Cobelens F., Nicol P.M., Dheda K., Churchyard G., Fielding K., and Metcalfe Z.J.

Introduction: Xpert MTB/RIF, the most widely used automated nucleic acid amplification test for tuberculosis, is available in more than 130 countries. Although diagnostic accuracy is well documented, anticipated improvements in patient outcomes have not been clearly identified. We performed an individual patient data meta-analysis to examine improvements in patient outcomes associated with Xpert MTB/RIF. **Methods:** We searched PubMed, Embase, ClinicalTrials.gov, and the Pan African Clinical Trials Registry from inception to Feb 1, 2018, for randomised controlled trials (RCTs) comparing the use of Xpert MTB/RIF with sputum smear microscopy as tests for tuberculosis diagnosis in adults (aged 18 years or older). We excluded studies of patients with extrapulmonary tuberculosis, and studies in which mortality was not assessed. We used a two-stage approach for our primary analysis and a one-stage approach for the sensitivity analysis. To assess the primary outcome after 6-month which was deaths from all causes, we performed logistic regression models for each trial, and then pooled the odds ratio (OR) estimates by either by measuring effects that do not vary among TB patients and those that vary (fixed- vs random-effects) adjusting for age and gender, and stratified by HIV status and previous tuberculosis-treatment history. **Results:** Our search identified 387 studies, of which five RCTs were eligible for analysis. 8567 adult clinic attendees (4490 [63·5%] of 7074 participants for whom data were available were HIV-positive) were tested for tuberculosis with Xpert MTB/RIF (Xpert group) versus sputum smear microscopy (sputum smear group), across five low-income and middle-income countries (South Africa, Brazil, Zimbabwe, Zambia, and Tanzania). The primary outcome (reported in three studies) occurred in 182 (4·5%) of 4050 patients in the Xpert group and 217 (5·3%) of 4093 patients in the smear group (pooled adjusted OR 0·88, 95% CI 0·68–1·14 [p=0·34]; for HIV-positive individuals OR 0·83, 0·65–1·05 [p=0·12]). By Kaplan-Meier estimates there was lower rate of death (12·73 per 100 person-years in the Xpert group vs 16·38 per 100 person-years in the sputum smear group) for HIV-positive patients and the risk of death was lowered by 24% in HIV patients who had Xpert used. **Conclusion:** Despite individual patient data analysis from five RCTs, we were unable to confidently rule in nor rule out an Xpert MTB/RIF-associated reduction in mortality among outpatients tested for tuberculosis. Reduction in mortality among HIV-positive patients in a secondary analysis suggests the possibility of population-level impact.

2. **Xpert MTB/RIF Ultra assay for the diagnosis of pulmonary tuberculosis in children: a multicentre comparative accuracy study.**

Authors: Sabi, Issa, Andrea Rachow, Daniel Mapamba, Petra Clowes, Nyanda E Ntinginya, Mohamed Sasamalo, Lujeko Kamwela, Frederick Haraka, Michael Hoelscher, Daniel H Paris, Elmar Saathof and Klaus Reither

Introduction: It is difficulty to diagnosis TB in children compared to adults. The main challenges of TB diagnosis in children are the difficulties of obtaining sputum (a mixture of saliva and mucus coughed up from the respiratory tract) for testing and poor performance of available diagnostics (tests). **Methods:** We evaluated the diagnostic performance of the novel next-generation Xpert MTB/RIF Ultra (Xpert Ultra) in comparison to Xpert MTB/RIF (Xpert) assay for the detection of paediatric pulmonary tuberculosis in high burden settings.**Findings:** From May 2011 to September 2012, children with suspected pulmonary tuberculosis were enrolled at the Mbeya site of the National Institute for Medical Research (NIMR) and at the Ifakara Health Institute (IHI). Sputum samples were examined using sputum smear, Xpert and culture. Xpert Ultra was tested between January and June 2017 using sputum pellets, which had been stored at -80°C. The diagnostic accuracy of Ultra versus Xpert was determined using well-defined case definitions as reference standard. In total, 215 children were included. The median age was 5.4 years, the HIV prevalence was 52% and 13% had culture-confirmed pulmonary tuberculosis. When only the first available sample of each patient was analysed, the sensitivity of Xpert Ultra was 64.3 % while that of Xpert was 53.6%. The specificity of Xpert Ultra based on analysis of all available samples was 98.1%, that of Xpert was 100%. **Conclusion:** Xpert Ultra was found to have a higher sensitivity, compared to Xpert in detecting pulmonary tuberculosis in children.

3. **Phenotypic Changes on Mycobacterium Tuberculosis-Specific CD4 T Cells as Surrogate Markers for Tuberculosis Treatment Efficacy**

Authors: Mohamed I. M. Ahmed, Nyanda E. Ntinginya, Gibson Kibiki, Bariki A Mtafya, Hadija Semvua, Stellah Mpagama, Charles Mtabho, Elmar Saathoff, Kathrin Held, Rebecca Loose, Inge Kroidl, Mkunde Chachage, Ulrich von Both, Antelmo Haule, Anna-Maria Mekota, Martin J. Boeree, Stephen H. Gillespie, Michael Hoelscher, Norbert Heinrich and Christof Geldmacher on behalf of the Pan African Consortium for the Evaluation of Anti-tuberculosis Antibiotics (PanACEA)

Introduction: Diagnosis and treatment monitoring of active tuberculosis (TB) disease by existing tools/methods have a lot of limitations including methodological problems and insufficient ability to accurately identify diseased and treated persons. These shortcomings in the currently used methods can impede accurate detection of people with an active TB disease and monitoring of their treatment response. Thus, novel

diagnostic and treatment tools are urgently needed to achieve a WHO target of a World free of TB by 2030. A method that utilizes changes that happen on blood immune cells which target TB causing bacteria in the course of TB infection, is a promising approach for diagnosis and monitoring treatment success of TB disease. Using this method, we have previously shown a high specific detection of active TB disease in children when compared to the gold-standard method of detection of TB bacteria in the sputum. Herein, we studied the ability of this novel tool to be used in monitoring of TB treatment response. **Method:** blood and sputum samples from 55 volunteers with or without active TB infection was collected at the initiation of TB treatment, weeks 9, 12 and 26 (end of treatment). Collected blood was then analysed for changes in different markers on immune cells targeting TB bacteria after simulation of TB infection in the lab. Concurrently, TB bacteria was also examined in the collected sputum. **Findings:** We found that TB treatment induced certain changes on immune cells targeting TB bacteria during the course of treatment in a manner that coincided with the gold standard method. **Conclusion**: Such changes could thus be potentially used as a method of accurately discriminating a diseased TB patient from a successfully treated/cured one.

4. Molecular Bacterial Load Assay Concurs with Culture on NaOH-Induced Loss of *Mycobacterium tuberculosis* Viability

   Authors: Bariki Mtafya, Wilber Sabiiti , Issa Sabi, Joseph John, Emanuel Sichone , Nyanda E. Ntinginya , Stephen H. Gillespie

   Introduction: Effective methods to detect viable *Mycobacterium tuberculosis (Mtb)*, the main causative agent of tuberculosis (TB), are urgently needed. Currently, cultivation of *Mtb* is the gold standard, which depends on initial sample processing with N-acetyl-L-cysteine–sodium hydroxide (NALC-NaOH), chemicals that compromise *Mtb* viability and performance of downstream tests. **Methods:** We applied culture and the novel molecular bacterial load assay (MBLA) to measure the loss of *Mtb* viability following NALC-NaOH treatment of *Mtb* H37Rv pure culture and clinical sputum samples from pulmonary TB patients. **Results:** Compared to the bacterial loads of untreated controls, NALC-NaOH treatment of *Mtb* reduced the MBLA-detectable bacillary load (estimated number of CFU [eCFU] per milliliter) by 0.66±0.21 $\log_{10}$ at 23°C (P=0.018) and 0.72±0.08 $\log_{10}$ at 30°C (P=0.013). Likewise, NALC-NaOH treatment reduced the viable count on solid culture by 0.84±0.02 $\log_{10}$ CFU/ml at 23°C (P=0.001) and 0.85±0.01 $\log_{10}$ CFU/ml at 30°C (P=0.001), respectively. The reduction in the viable count was reflected by a corresponding increase in the time to positivity of the mycobacterial growth indicator tube (MGIT) liquid culture: 1.2days at 23°C (P=0.001) and 1.1days at 30°C (P=0.001). This NaOH-induced *Mtb* viability

loss was replicated in clinical sputum samples, with the bacterial load dropping by 0.65±0.17 log_{10} from 5.36±0.24 log_{10} eCFU/ml to 4.71±0.16 log_{10} eCFU/ml for untreated and treated sputa, respectively. Applying the model of Bowness et al. (*R. Bowness, M. J. Boeree, R. Aarnoutse, R. Dawson, et al., J Antimicrob Chemother 70:448–455, 2015, https://doi .org/10.1093/jac/dku415*) revealed that the treated MGIT time to culture positivity of 142 ± 7.02 h was equivalent to 4.86±0.28 log_{10} CFU, consistent with the MBLA measured bacterial load. **Conclusion:** Our study confirms the contribution of NALC-NaOH treatment to the loss of viable bacterial counts. Tests that obviate the need for decontamination may offer an alternative option for the accurate detection of viable *Mtb* and treatment response monitoring.

6: HUMAN IMMUNODEFICIENCY VIRUS (HIV)

1. Operational evaluation of HIV Point of Care tests for very early infant HIV diagnostics in infants born from HIV infected mothers in Mbeya, Tanzania

   Authors: Sabi, Issa, Hellen Mahiga, Jimson Mgaya, Otto Geisenberger, Sabine Kastner, Willyhelmina Olomi, Elmar Saathoff, Lilian Njovu, Cornelia Lueer, John France Leonard Maboko, Nyanda Elias Ntinginya, Michael Hoelscher, Arne Kroidl

   Introduction: HIV in infants is mainly vertically transmitted by HIV infected mothers and is associated with high mortality rates if no antiretroviral treatment is provided. Accurate HIV diagnosis in infants is only feasible by detection of HIV nucleic acid (HIV RNA or DNA) and therefore HIV early infant diagnostic (EID) screening is routinely performed at the age of 6 weeks from dried blood samples requiring specialized laboratory facilities and multiple step linkage procedures for result dissemination. Point-of-care (PoC) systems for early infant diagnosis (EID) may improve timely infant HIV management. **Methods:** We evaluated the operational feasibility as well as specificity, sensitivity and predictive values of the Cepheid Xpert HIV-1 (Xpert PoC) to detect infant HIV infection at birth, weeks 1, 2, 3 and 6. In this study Xpert PoC tests were performed by nurses and midwives at the health facilities. The possibility of infant HIV diagnosis as early as the time of birth opens the possibility for earlier infant antiretroviral treatment initiation resulting into a possible further reduction of HIV related infant mortality/morbidity. **Results:** From June 2015 to November 2016, 614 neonates from 606 mothers were enrolled. At week 6, 15 (2.5%) infants were diagnosed with HIV; 10 (66.7%) of them at birth. The Xpert-PoC correctly identified all HIV infection in neonates. In total 2736 tests were performed by nurses at the obstetric health facilities with very good performance overall. Problems were reported in 183 (6.7%) of Xpert-PoC tests, mostly related to power cuts.

Conclusion: We demonstrated excellent Xpert HIV-1 Qual performance and good operational feasibility for PoC-EID testing at obstetric health facilities.

2. **HIV-sero-conversion among HIV-1 sero-discordant married couples in Tanzania: a cohort study.**
Mark Urassa, Julius Mngara [BMC Infectious Diseases (2019) 19:518]

Background: Heterosexual transmission is the main driver of the HIV epidemic in Tanzania. Only one estimate of the incidence rate of intra-marital HIV sero-conversion in Tanzania has been reported and was derived from data collected between 1991 and 1995. Moreover, little is known about the specific risk factors for intra-marital sero-conversion in Tanzania. Improved evidence around factors that increase the risk of HIV transmission to a sero-discordant spouse is needed to develop and improve evidence-based interventions. We sought to investigate the rate of intra-marital HIV sero-conversion among HIV sero-discordant couples in Tanzania as well as its associated risk factors. **Methods:** We identified all HIV positive individuals in the TAZAMA HIV-sero survey cohort and followed up their Sero-discordant spouse from 2006 to 2016. The rate of sero-conversion was analyzed by survival analysis using nonparametric regressions with exponential distribution. **Results:** We found 105 sero-discordant couples, 14 of which had a sero-converting spouse. The overall HIV-1 incidence rate among spouses of people with HIV-1 infection was 38.0 per 1000 person/years. Notably, the HIV-1 incidence rate among HIV-1 sero-negative male spouses was 6.7 per 1000 person/years, compared to 59.3 per 1000 person/years among female spouses. Sex of the sero-discordant spouse was the only significant variable, even after adjusting for other variables. **Conclusions:** Our study suggests that rates of HIV-1 sero-conversion of sero-discordant partners are much higher within marriage than in the general population in Tanzania. The major risk factor for HIV-1 sero-conversion is sex of the sero-discordant spouse, with female spouses being at very high risk of acquiring HIV infection. This suggests that future programs that target sero-discordant couples could be a novel and effective means of preventing HIV-1 transmission in Tanzania.

3. Hepatitis E virus epidemiology among HIV-infected women in an urban area in Tanzania

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Introduction: Hepatitis E virus (HEV) is probably the most common agent causing acute viral hepatitis in the world. HEV can cause self-limiting hepatitis with mortality rates varying from 0.2% to 4%. However, considerably higher mortality rates (15–25%) are reported among pregnant women. The reported prevalence of HEV antibodies varies regionally: among pregnant women in African countries, the rate differs from 0% in Southern Tanzania to 84% in Egypt. The prevalence of HIV among pregnant women in sub-Saharan countries is high, and there is limited knowledge of HEV co-infection rates in this group of susceptible patients and no studies from Tanzania. The aim of this study was to determine the seroprevalence and incidence rates of HEV infection among HIV-infected women during pregnancy and post-partum in a cohort study of women from Tanga, Tanzania. **Methods:** HIV-infected women participating in a study on antiretroviral therapy for the prevention of mother-to-child HIV transmission between 2006 and 2011, were tested retrospectively for anti-HEV immunoglobulin G (IgG) in plasma samples at 9 months post-partum. Anti-HEV IgG-positive patients were tested for anti-HEV IgG and immunoglobulin M (IgM) in samples from enrolment, and seroconverting women were tested for HEV RNA. **Findings:** A total of 16 out of 184 women were anti-HEV IgG-positive, two of whom had seroconverted between enrolment and 9 months post-partum, with no detection of anti-HEV IgM or HEV RNA, yielding an HEV seroprevalence of 8.0% and an annual incidence rate of 1.0%. CD4 cell counts were relatively high and was not significant difference between women with and without serological signs of HEV. **Discussion and Conclusions:** An annual HEV infection incidence rate of 1% strongly indicates ongoing transmission of HEV in Tanzania and should be kept in mind for pregnant women presenting with signs of acute hepatitis. Therefore, testing of pregnant women should be considered to avoid complications resulting from HEV infection

7.0: HEALTH DEMOGRAPHICS

1. **Point-of-contact Interactive Record Linkage (PIRL): A software tool to prospectively link demographic surveillance and health facility data.**

   Mark Urassa, Richard Machemba, Baltazar Mtenga, Denna Michael [Gates Open Research 2018, 1:8].

   Introduction: Linking a health and demographic surveillance system (HDSS) to data from a health facility that serves the HDSS population generates a research infrastructure for directly observed data on access to and utilization of health facility services. Many HDSS sites, however, are in areas that lack unique national identifiers or suffer from data quality issues, such as incomplete records, spelling errors, and name and residence changes, all of which complicate record linkage approaches when applied retrospectively. **Methods:** We developed Point-of-contact Interactive Record Linkage (PIRL) software that is used to prospectively link health records from a local health facility to an HDSS in rural Tanzania. This prospective approach to record linkage is carried out in the presence of the individual whose records are being linked, which has the advantage that any uncertainty surrounding their identity can be resolved during a brief interaction, whereby extraneous information (e.g., household membership) can be referred to as an additional criterion to adjudicate between multiple potential matches. Our software uses a probabilistic record linkage algorithm based on the Fellegi-Sunter model to search and rank potential matches in the HDSS data source. Key advantages of this software are its ability to perform multiple searches for the same individual and save patient-specific notes that are retrieved during subsequent clinic visits. **Results:** In this setting, a purely automated retrospective approach to record linkage would have only correctly identified about half of the true matches and resulted in high linkage errors; identified about half of the true matches and resulted in high linkage errors; therefore highlighting immediate benefit of conducting interactive record linkage using the PIRL software.

8.0: SICKLE CELL DISEASE

1. **A ten-year review of the sickle cell program in Muhimbili National Hospital, Tanzania.**
   Makani J, Tluway F, Makubi A, Soka D, Nkya S, Sangeda R, Mgaya J, Rwezaula S, Kirkham FJ, Kindole C, Osati E, Meda E, Snow RW, Newton CR, Roberts D, Aboud M, Thein SL, Cox SE, Luzzatto L, Mmbando BP.

   Background: Africa has the highest burden of Sickle cell disease (SCD) but there are few large, systematic studies providing reliable descriptions of the disease spectrum. Tanzania, with 11,000 SCD births annually, established the Muhimbili Sickle Cell program aiming to improve understanding of SCD in Africa. We report the profile of SCD seen in the first 10 years at Muhimbili National Hospital (MNH). **Methods:** Individuals seen at MNH known or suspected to have SCD were enrolled at clinic and laboratory testing for SCD, haematological and biochemical analyses done. Ethnicity was self-reported. Clinical and laboratory features of SCD were documented. **Results:** From 2004 to 2013, 6397 individuals, 3751 (58.6%) SCD patients, were enrolled, the majority (47.4%) in age group 5-17 years. There was variation in the geographical distribution of SCD with regions around the lake zone and the Indian Ocean been mostly affected. The main causes of hospitalization for SCD were pain for adults, and fever and severe anaemia for children. **Conclusion:** This report confirms that the wide spectrum of clinical expression of SCD observed elsewhere is also present in Tanzania, with non-uniform geographical distribution across the country.