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ABSTRACTS OF THE EIGHTH EDCTP FORUM, 6–9 NOVEMBER 2016

Defeating poverty-related and neglected diseases in Africa: harnessing research for evidence-informed policies

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10.1136/bmjgh-2016-000260.1

The Eighth Forum of the European & Developing Countries Clinical Trials Partnership took place in Lusaka, Zambia from 6 to 9 November 2016. The biennial Forum has grown in size and recognition to become one of the largest international conferences for the presentation and discussion of frontier clinical research on poverty-related infectious diseases, as well as capacity development including ethics, regulatory and training initiatives in sub-Saharan Africa. With the support of the European Union, EDCTP member countries and other sponsors, the conference offers scholarships to many early and mid-career researchers especially from sub-Saharan Africa to present results of their studies and meet colleagues from Africa, Europe and beyond. Moreover, the conference provided opportunities for new collaborations with other actors in the field of global health, such as research institutes, international private and public funders, development agencies, product development partnerships and pharmaceutical and biomedical companies. The conference was attended by 434 participants from 48 countries, with scholarships for 120 early career scientists.

The theme of the Eighth Forum was: 'Defeating poverty-related and neglected diseases in Africa: harnessing research for evidence-informed policies' This reflects two specific aspects of the second EDCTP programme (EDCTP2, 2104–2024). The reference to neglected infectious diseases points to the broadening of the scope of the programme. In addition to HIV, tuberculosis and malaria, the scope of EDCTP includes now most neglected infectious diseases, diarrhoeal diseases, lower respiratory tract infections, and emerging or re-emerging infectious diseases of relevance to sub-Saharan Africa. Secondly, the theme refers to the importance of making sure that new scientific results find their way into health care policies and practice.

The Forum offered a comprehensive scientific programme with keynote addresses by prominent speakers from the North and South, oral presentations in plenary and parallel sessions, panel discussions, a collaborative session, scientific symposia, educational workshops, meet-the-expert sessions and poster presentations. In this Supplement to *BMJ Global Health*, the abstracts of the plenary presentations, the oral presentations in the various parallel sessions, and poster presentations are published. The abstracts give a work-in-progress impression of the scope and objectives of the EDCTP programme.

This Forum was officially opened by His Excellency Mr. Edgar Chagwa Lungu, the President of the Republic of Zambia, who is a true advocate for health research capacity development in Africa. Several high-ranking government policy makers including ministers, directors from ministries of health, higher education and science & technology from Zambia and other African countries participated. This was a clear demonstration of the growing interest among African governments to strengthen their collaboration with EDCTP. The EDCTP programme has an added value for all countries in sub-Saharan Africa through its funding strategies and plans.

This general theme of partnership between North and South, between Europe and Africa was taken up again by the new High Representative for the North, Professor Marcel Tanner, in his keynote address to the conference. He reflected on the nature of partnership which should go beyond cooperating on individual projects to programme portfolio level and partnering at a strategic level. 'Mutual learning for change' is a feature of a true partnership in which North and South can learn much from each other.

Partnership was also demonstrated by many stakeholders who enriched the programme by organising workshops, a collaborative meeting and satellite meetings. Moreover, nine symposia were organised as part of the scientific programme by BioVentures for Global Health, Cochrane Centre South Africa, Deutsche Stiftung Weltbevölkerung, European Vaccine Initiative, Medicines for Malaria Ventures with the West African Network for Clinical Trials for Antimalarial Drugs, NWO-WOTRO Science for Global Development, the Pan-African Consortium for the Evaluation of Antituberculosis Antibiotics (PanACEA) consortium, and the University of Tübingen. The Ministry of Health of Zambia organised a symposium on Clinical research in Zambia for effective control programmes and showed further support by co-hosting the Forum.

The Forum, which showcases the tangible results of collaborative research and partnership, was the appropriate setting for the award of four EDCTP 2016 Prizes. EDCTP recognised outstanding individuals and research teams from Africa and Europe who have made significant contributions in their field of research. In addition to their scientific excellence, the awardees made major contributions to the EDCTP objectives of clinical research capacity development in Africa and establishing research networks between North and South as well as within sub-Saharan Africa. The Award for Outstanding Research Team was given to the University of Zambia – University College London Medical School (UNZA-UCLMS) Research & Training Program. Professor Marleen Temmerman (Aga Khan University, Kenya) received the Award for Outstanding Female Scientist. Professor Shabir A. Mahdi (University of the Witwatersrand, South Africa) was given the Award for Scientific Leadership, while Professor Fred Newton Binka (Ghana; currently coordinator of WHO's Emergency Response to Artemisinin Resistance in Phnom Penh, Cambodia) was honoured with the Dr Pascoal Mocumbi Prize in recognition of his outstanding achievements in advancing health research and capacity development in Africa.

We would like to express our sincere thanks to the EDCTP member states and all our sponsors for their generous support. In particular, we extend a special thanks to the Ministry of Health of the Republic of Zambia, an EDCTP member country, for co-hosting the Eighth EDCTP Forum. In conclusion, we would like to thank the EDCTP Organising committee, colleagues and friends for their help, support and advice in planning and implementing the Forum. The members of the Programme committee, i.e. the members of the Scientific Advisory Committee and the EDCTP Project Officers, earned our warm thanks for putting together the Eighth EDCTP Forum Programme.

ABSTRACTS OF PRESENTATIONS IN PLENARY SESSIONS

PS-001 R&D TO TACKLE GLOBAL HEALTH CHALLENGES: ROLES AND RESPONSIBILITIES FOR EDCTP

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As well documented, the diseases of poverty and Neglected Tropical Diseases (NTDs) cost the lives of millions of people worldwide and threaten the health of millions more. More than 200 million health years of life are lost every single year due to mortality, morbidity and disability. This not only represents an unacceptable burden for the populations concerned, mainly the most impoverished segments of a population, but also impairs health development and all our efforts to reach the Sustainable Development Goals. NTDs and diseases of poverty are clearly part of the overall neglect of people and health and social systems.

The high burden of diseases of poverty and NTDs calls for new efforts in developing effective and efficient approaches to control or even eliminate these diseases. This in turn implies that we must aim at new discoveries and innovations and – at the same time – make most effective use of existing tools as well as of innovative partnerships between the public and the private sectors and between different countries; clearly the niche and responsibility of EDCTP.

The presentation will discuss needs and ongoing efforts in diagnosis, drug and vaccine development against diseases of poverty and NTDs and will also discuss (i) obstacles at the level of health and social systems that prevent access of the populations to new and existing efficacious tools as well as (ii) new approaches in R&D to overcome these obstacles and barriers. While there are great hopes and also substantial advances in drug, diagnostics and vaccine development, R&D does not and should not alone focus on developing new tools, but rather on combining existing and new tools for integrated approaches of diseases control and elimination that are tailored to a given endemic setting and are combined with effective capacity building. The outlook and discussion will emphasize the potential, chances and responsibilities of EDCTP to strengthen effective partnership, capacity building and national and global health development.

PS-003 EVIDENCE-INFORMED POLICY MAKING: CHALLENGES AND OPPORTUNITIES

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Evidence-informed health policy making depends on the availability of the results of studies that have assessed what works, what does not work, and what may be harmful. However, even where such evidence exists it will not always be embraced by policy makers or other decision makers.

This presentation begins by discussing the environment in which policy making takes place and identifying the role of players involved, drawing attention to the complexity of the policy making process. It shows how competing forces, such as beliefs, vested interests, values, habits and financial considerations can lead to important evidence being rejected or ignored by national and international policy makers, sometimes with serious consequences.

The talk also explores the role researchers can play in promoting the flow of evidence from research to policy to implementation by focussing on 5 key issues: generating primary research, conducting systematic reviews of evidence, improving access to relevant evidence, enhancing the use of evidence in policy making, and providing information on how best to scale up programmes. Case studies from LMIC settings, relevant to the EDCTP's remit, will be employed to illustrate the various concepts covered in the presentation.

PS-004 REVIEW OF HIV IN SUB-SAHARAN AFRICA: CURRENT SITUATION, OPPORTUNITIES AND CHALLENGES

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10.1136/bmjgh-2016-000260.4

UNAIDS estimates that in 2015, 19 million (17.7–20.5 million) and 6.5 million (5.3–7.8 million) people were living with HIV in Eastern and Southern Africa (ESA) and Western and Central Africa (WCA), respectively. Between 2010 and 2015, new HIV infections declined by 14% in ESA and 8% in WCA, while AIDS-related deaths fell by 38% and 10%, respectively. In ESA, 10.3 million people or 54% (50–58%) of all people living with HIV were accessing antiretroviral therapy (ART), compared to 1.8 million people or 28% (23–34%) of all people living with HIV in WCA. Since 2010, there has been a 66% decline in new HIV infections among children in ESA compared to a 31% decline in WCA.

These striking regional differences mask large discrepancies in country progress, sex differences in ART uptake, and a diversity of micro-epidemics across sub-Saharan Africa. The goal to end AIDS as a public health threat by 2030, the UN-AIDS 90–90–90 treatment cascade goal for 2020, and the WHO recommendation to offer ART when HIV is diagnosed regardless of CD4 count are galvanizing public health and community-based responses in Africa. Despite improvements in ART and new prevention tools, including voluntary medical male circumcision and oral pre-exposure prophylaxis, the goals will not be achieved without new tools, including an HIV vaccine and a cure.

EDCTP has funded high-impact HIV research that has resulted in, among others, policy change; prequalification of new products; improved treatment strategies, including for children; and strategies to prevent mother-to-child transmission, while building research capacity and clinical trial infrastructures. Promoting African country membership and increased financial contributions from African countries, EDCTP2 aims to leverage co-funding from public/private sources for calls for proposals that address important gaps in HIV prevention and treatment science that can be answered through phase I-IV clinical trials in sub-Saharan Africa.

PS-005 POLICY-DRIVEN INTERVENTIONS: TUBERCULOSIS

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Annual tuberculosis (Tb) rates decline by 1.7%, which is inadequate to reach WHO targets. We describe three host-biomarker developments that are entering clinical testing and that could accelerate progress against TB.

Blood mRNA signatures with promising predictive ability for incident TB were recently described in African cohorts. Correlate of risk (COR) positive participants have 7 to 18 times increased risk for progression. A clinical trial is underway in South Africa under leadership of the South African Tuberculosis Vaccine Initiative to evaluate targeted chemoprophylaxis in COR positive people in an area with a very high prevalence of latent TB infection, where untargeted preventative treatment is not practical.

Historical data suggests that 85% of patients are cured after 4 months of TB treatment but attempts to shorten treatment without an unacceptable relapse rate have failed. Treatment shortening criteria based on PET/CT imaging and microbiological criteria were developed. An EDCTP/Bill & Melinda Gates Foundation/NIH co-funded study, led by the Tuberculosis Research Section of the NIH, will start in South Africa and in China in 2017 to evaluate biomarker-driven treatment shortening to 4 months.

To address diagnostic bottlenecks, a blood-based 7-host marker diagnostic signature was recently found with promising screening potential for active TB. An EDCTP-funded project with Africa and EU partners aims to develop a point-of-care, finger stick blood test that can simultaneously measure all 7 markers and rule out 75% of people with symptoms compatible of active TB in whom the diagnosis is subsequently ruled out. Such screening tests could speed up diagnostic work-up and save significant costs. Taken together, biomarker-driven interventions are now being actively tested and hold promise to provide important tools towards the eventual eradication of the TB scourge.

PS-006 MALARIA

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At the beginning of the Roll Back Malaria (RBM) initiative around 2000, sub-Saharan Africa was going through a major malaria epidemic, compounded by the failure of chloroquine and emerging resistance to sulphadoxine-pyremithamine, as the first-line treatments for uncomplicated malaria. The initial call for increased funding through the 2000 Abuja Declaration only began to materialise in 2002 when the Global Fund to Fight AIDS, Tuberculosis and Malaria was established. The scale-up of malaria interventions, especially for vector control, began in earnest in 2004 in sub-Saharan Africa but by 2007 only less than 20% of children in Africa had slept under an insecticide-treated net. In addition, it is only from 2006 that the widespread use of artemesinin combination therapy (ACT) started to occur on a wide scale. By 2015, however, substantial coverage with both vector and treatment interventions had been achieved. Consequently, the malaria burden has decreased across sub-Saharan Africa. Here I review the current malaria situation in sub-Saharan Africa and discuss opportunities and challenges. I discuss some of the analytical work, including mapping that contributed to our understanding of the epidemiology of malaria and progress during the RBM era. I present examples of how this research has led to changes in policy and practice globally and in sub-Saharan Africa. I discuss the current major research needs and policy gaps in the malaria elimination agenda and how these may be applicable to other diseases in the EDCTP remit. I conclude with suggestions on the potential role of EDCTP in supporting clinical trials and capacity strengthening towards malaria elimination.

PS-007 NEGLECTED INFECTIOUS DISEASES

Nathalie Strub-Wourgaft. *DNDi, Switzernad*

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Achievement of the UN's Sustainable Development Goals (SDGs) will only be possible if the burden of neglected tropical diseases (NTDs) is significantly reduced. NTDs have an impact on population health, and are a drain on community resources, hindering economic development. The burden is particularly high in Africa, and urgent action is required on NTDs to enable the attainment of the SDGs.

The World Health Organization has listed 17 NTDs that impact one billion people worldwide and produced overwhelming evidence to show that their impact may be effectively controlled and, in many cases, eliminated or eradicated. The WHO Strategic and Technical Advisory Group for NTDs and partners adopted a roadmap for control, elimination and eradication which set targets for 2012–2020.

In its systematic assessment of the drug and vaccine landscape for neglected diseases up to 2011, DNDi found a persistent insufficiency in drug and vaccine development, and that new therapeutic products urgently need to be developed and delivered to improve control and potentially achieve elimination. It is significant that the second EDCTP programme includes neglected infectious diseases and more trial phases. DNDis focusses on the needs of neglected patients, and is developing treatments for sleeping sickness, leishmaniasis, Chagas disease, filariasis, HCV, paediatric HIV, and Mycetoma. In Africa there is an acute need for treatments for visceral leishmaniasis (VL), HIV-VL coinfection, post kalaazar dermal leishmaniasis, and cutaneous leishmaniasis. Mycetoma was recognized as an NTD by the WHA in 2016; this devastating disease affects remote populations; is poorly understood and lacks effective treatment. In Africa, 115 million people are at risk of onchocerciasis and 410 million people require preventive chemotherapy for lymphatic filariasis; mass administration programs are hampered by drugs that only kill the juvenile form of the worms, leaving only temporarily sterilized adults, requiring repeated administration over a period of decades.

PS-008 INNOVATIVE CLINICAL TRIAL DESIGNS

Patrick Phillips. *MRC Clinical Trials Unit, UCL, United Kingdom*

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Since the middle of the 20th century, randomised controlled trials have provided the strongest level of evidence to inform the treatment of all diseases. In particular, trials in the 1970s and 1980s in Africa led to a highly efficacious 6-month regimen for the treatment of TB; these were followed by trials in the 1990s and 2000s which resulted in today's HAART regimens that are recommended for all patients living with HIV.

These diseases, however, still cause 1.3 million deaths every year in Africa, and further trials are needed to improve treatment and develop control strategies that will ultimately end the epidemics. Furthermore, there are many neglected diseases where few if any trials have been conducted and therefore the evidence base for treatment is extremely weak.

The randomised clinical trial is an indispensable tool for defeating poverty-related and neglected diseases in Africa, but it should not be seen as a static instrument that has remained unchanged since its first introduction in the 1940s. Innovations in clinical trial design can overcome many barriers, facilitating more efficient trials where alternatives are prohibitively long or resource-intensive. For example, adding multiple intervention arms or sequential randomisations allows for more questions being answered in a single trial, and adaptive designs permit modifications to ongoing trials in light of internal or external data, thereby making better use of limited resources.

This presentation covers the opportunities for innovation in clinical trial design in poverty-related and neglected diseases. Recent developments relate to multi-arm multi-stage and other adaptive trial designs, interpretation of non-inferiority trials, choice of comparator arms, the role of pragmatic trials, and treatment strategy trials. Specific examples will be presented, including recent TB, HIV and Ebola trials, in addition to other areas for possible progress, all with the ultimate goal of faster patient benefit.

PS-009 IMPROVING MATERNAL AND CHILD HEALTH THROUGH COMMUNITY ENGAGEMENT IN CLINICAL TRIALS

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Clinical trials contribute to the improvement of health through testing potentially efficacious interventions (e.g. vaccines, drugs, devices, and even behavioural strategies) among selected population segments to provide evidence to support health policy and practice. There are indisputable health benefits, not only to the communities directly involved in the trials but also to the wider population affected by the health problems in question. On the other hand, regardless of the results of the trials, it is assumed that there are immediate benefits disseminated to the whole population of reference resulting from training, resources, services quality, and improvement and local knowledge. Particularly for low-income countries, this assumption is often taken for granted, as the implementation of clinical trials is usually accompanied by infrastructure development, institutional capacity building, and improved standards of care. The actual direct benefit to health and health care delivery, its sustainability, and more importantly, the communities' perceptions of those benefits are seldom measured, because clinical trials often miss the opportunity to evaluate communities' acceptability of the potential intervention, and the extent to which their needs and priorities are met through the trials. Formative research, which must be conducted in advance and during trial implementation, is a valuable approach to address such questions and to recommend appropriate ways of conducting the trials so as to gain optimal synergies with communities' expectations while balancing those with the intended improvement of health. The Manhiça Health research centre takes such approach when implementing complex interventions involving large segments of the population and health services catchment areas, such as entire districts and provinces. This talk focuses on lessons learnt from engaging the community in three different interventions, namely the Malaria Elimination Program in Magude District, the Community Level Interventions for Pre-eclampsia in Maputo and Gaza Provinces, and the Cause of Death Determination using Minimally Invasive Autopsies in Manhiça District, all in Southern Mozambique.

ABSTRACTS OF ORAL PRESENTATIONS

OA-001 THE ADDED VALUE OF A MULTICOUNTRY NETWORK FOR PROMOTING ETHICAL AND REGULATORY STANDARDS IN CLINICAL TRIALS IN LOW- AND MIDDLE-INCOME COUNTRIES: THE EXPERIENCE OF THE 'SWITCHING THE POLES NETWORK'

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10.1136/bmjgh-2016-000260.10

Background In 2008, we created the 'Switching The Poles' Clinical Research Network, by joining the forces of non-commercial clinical research groups in Benin, Burkina Faso, Cambodia, Cuba, the Democratic Republic of Congo, Ethiopia, India, Indonesia, Nepal, Peru, Rwanda, The Gambia and Vietnam. Our aim was to strengthen capacity to conduct non-commercial clinical trials that comply with ethical/regulatory standards.

Methods Our capacity building initiatives were designed to directly benefit the implementation of clinical trials, including various EDCTP-sponsored projects, e.g. 4ABC (7 countries), PREGACT (4), Microbicide Safety Biomarkers (3) and Ring Plus (1). Our training, coaching and networking activities targeted young researchers from the South as well as research professionals who are traditionally 'neglected' in trainings, such as data managers and laboratory staff. There were several thematic packages: Good Clinical Practice (GCP), Good Clinical Laboratory Practice, data management (DM), monitoring, and informed consent.

Results We developed a theoretical and practice-based GCP training that was adopted by WANETAM Plus in 2013, and a set of standardised DM procedures. Data managers used to working on their own, now benefit from an e-platform (admit-network.org) for collaboration and peer advice. We started coaching clinical monitors, for facilitating reciprocal monitoring schemes. We publicly spoke out about ethical issues, e.g. ethical

review of externally-sponsored trials, voluntariness in informed consent in vulnerable populations, and provided recommendations to the International Conference of Harmonization in its revision of GCP Guidelines. The inclusion of partners from so many diverse countries and settings resulted in cross-fertilisation and mutual learning. The Networks' small size facilitated interpersonal collaboration.

Conclusions Our experience shows that a relatively small, but focused international network provides an excellent platform for supporting young researchers across different professional disciplines and helps to strengthen capacity for clinical research. This approach has enabled partners in low- and middle-income countries to successfully conduct harmonised GCP-compliant clinical trials.

OA-002 TRANSLATING ETHICS GUIDELINES ON COMPENSATION FOR RESEARCH-RELATED INJURIES INTO POLICY IN LOW-INCOME COUNTRIES: LESSONS LEARNT FROM MALAWI

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10.1136/bmjgh-2016-000260.11

Background Injury to human participants in biomedical research is a known problem and despite a number of ethical guidelines advocating compensation for research-related injuries (RRIs), African countries do not have a unified approach for compensation. In 2012, Malawi introduced a policy mandating no-fault insurance coverage for RRIs. We conducted this study to explore the challenges associated with the implementation of this policy and what lessons can be learnt from Malawi.

Methods We conducted a qualitative case study through nine in-depth interviews with purposively sampled key stakeholders in research in Malawi: policy-makers, researchers, ethics committee members and insurers. Interviews were conducted by one researcher, recorded using a voice-recorder and later transcribed and verified for consistency. Manual data analysis was done using a word-table and pattern-matching. The study was approved by two ethics committees: in Malawi and South Africa.

Results Participants were in favour of compensation for RRIs through the insurance mechanism of no-fault type, although there was discordance in the understanding of the 'no-fault' principle. Some researchers felt this policy was instituted to punish them and stifle clinical research. In addition, we found that the local insurance industry was not in a position to cover clinical research. This deficiency in local capacity to provide insurance left some researchers feeling that Malawi would lose out by externalising hard-earned resources.

Conclusions All stakeholders in research in Malawi view the policy mandating no-fault insurance cover for RRIs as a positive step in research governance. However, certain challenges need to be addressed, such as the understanding of the concept of no-fault and local capacity to handle clinical trial insurance. Compensation for RRIs through no-fault insurance needs to be tried in other African countries and be adopted by the African Union in order to standardise and enforce compensation in Africa, where it is ethically acceptable based on the African ethic of Ubuntu.

OA-003 IMPROVING THE EFFICIENCY OF AFRICAN RESEARCH ETHICS COMMITTEES AND STANDARDISING ETHICS REVIEW PROCESSES THROUGH AN AUTOMATED REVIEW PLATFORM

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10.1136/bmjgh-2016-000260.12

Background The sheer amount of research being conducted in Africa, the under-resourced research ethics committees (RECs), and the lack of modern review technologies has resulted in unprecedented review timelines – with an estimated 1.5 years to get ethical clearance in many African countries. The Research for Health Innovation Organiser (RHInnO), a cloud-based ethics review platform, has ushered a new frontier of digital ethics review in Africa. It facilitates and manages the entire ethics review process. RHInnO ethics integration is estimated to reduce the review time by 12 months. In 2015, RHInnO ethics was used by 25 RECs in 8 African countries. We evaluated its impact on efficiency, data security and cost.

Methods Qualitative and quantitative data was collected using an online questionnaire administered to REC administrators/chairpersons in user countries.

Results Responses were received from 60% of RECs using RHInnO ethics. Reported areas of high impact (81%-100% of respondents) included: improved protocol submission and distribution process, improved quality of communication between RECs and researchers, improved standardisation of review process and improved data security. Reported areas of medium impact (60%-80% of respondents) included reduced REC administrator's workload and reduced RECs' administrative costs. Improved reviews of multicentre trials were reported as a low impact area by over 60% of respondents. Respondents (20%) who used RHInnO ethics for more than 2 years reported 57% reduction in review time while those who used RHInnO ethics for less than a year, (80%) reported it is too early to see the impact on reduction of review timelines.

Conclusions RHInnO ethics had high impact on data security, submission process, communication, standardisation and cost reduction. However, a long-term evaluation approach is needed to determine impact on review timelines. Integration of new monitoring and evaluation (M&E) indicators on efficiency into the platform would improve RECs capacity to conduct long-term impact analysis.

OA-004 DEVELOPMENT AND EVALUATION OF A MULTIMEDIA TOOL FOR OBTAINING INFORMED CONSENT IN THE GAMBIA: A MIXED METHOD STUDY

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10.1136/bmjgh-2016-000260.13

Background Communicating crucial research information to low-literacy research participants in Africa is highly challenging in the context of several factors which make the participants vulnerable to poor comprehension of consent information. We

previously developed and validated a digitised audio comprehension questionnaire. Here, we report the development and evaluation of a multimedia consent tool amongst low-literacy participants in The Gambia.

Methods Adults eligible for inclusion in a malaria treatment trial (n=311) were randomised to receive information needed for informed consent using either a multimedia tool (intervention arm) or a standard procedure (control arm).

A computerised audio questionnaire was used to assess participants' comprehension of informed consent. This was done immediately after consent had been obtained (at day 0) and at subsequent follow-up visits (days 7, 14, 21 and 28). The acceptability and ease of use of the multimedia tool were assessed in focus groups.

Results On day 0, the median comprehension score in the intervention arm was 64% compared with 40% in the control arm (p=0.042). The difference remained significant at all follow-up visits. Poorer comprehension was independently associated with female sex (odds ratio, OR: 0.29; 95% CI: 0.12 – 0.70) and residing in Jahaly rather than Basse province (OR: 0.33; 95% CI: 0.13–0.82). There was no significant independent association with educational level. The risk that a participant's comprehension score would drop to half of the initial value was lower in the intervention arm (hazard ratio 0.22, 95% CI: 0.16–0.31). Overall, 70% (42/60) of focus group participants from the intervention arm found the multimedia tool clear and easy to understand.

Conclusions A customised multimedia tool significantly improved comprehension and retention of consent information by research participants with low levels of literacy in The Gambia. Further evaluation of the tool is warranted in similar settings.

OA-005 PERFORMANCE OF XPERT MTB/RIF AND DETERMINE LAM IN HIV-INFECTED ADULTS IN PERI-URBAN SITES IN ZAMBIA (CDC OP-X STUDY)

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10.1136/bmjgh-2016-000260.14

Background Tuberculosis (TB) mortality in HIV-infected patients remains high in sub-Saharan Africa. Inadequate diagnostic tools delay time to TB treatment.

Methods A two-phase TB diagnostic study was conducted among HIV-infected adult patients from 2014–2016. Patients underwent history/physical exam, chest x-ray, urine for lipoarabinomannan (LAM), sputum smear and culture. We evaluated sensitivity, specificity and time to appropriate treatment within 14 and 28 days of screening for culture-positive patients, comparing Xpert MTB/RIF assay (GXP), and LAM to standard-of-care (SOC) in 3 peri-urban clinics. chi-square and Wilcoxon Rank-Sum tests were used to test for differences between SOC and GXP for categorical variables and continuous variables, respectively.

Results 1353 patients were enrolled; 755 in the SOC arm and 598 in the GXP arm. Median age was 34.3 and 65.1% were male. TB was diagnosed by any method (smear, clinical, GXP, LAM, culture) in 237 (17.5%) and with positive MTB culture in 152 (11.2%); 84 and 68 in the SOC and GXP arms, respectively. The overall sensitivity and specificity (culture as reference standard) of SOC was 91.7% and 92.9% respectively while GXP was 50.8% and 99.2%, respectively. LAM, when used with SOC, did not improve sensitivity or specificity in any CD4 strata, however when used with GXP increased sensitivity from 20% to 50% at CD4<50. There was a marginally significant difference (p=0.08) at 14-day TB treatment initiation between the GXP and SOC phases but no difference at 28-days. Among those initiating therapy, the median time to TB treatment initiation was shorter for the GXP arm (4 *vs*15 days).

Conclusions GXP did not significantly increase the number or accuracy of TB diagnoses compared to SOC but reduced median number of days to TB treatment by 11 days. GXP and LAM when used together have the potential to rapidly identify TB in patients with advanced HIV disease.

OA-006 COMPARATIVE EVALUATION OF GENOTYPE MTBDRPLUS VERSION 2 AND GENE XPERT MTB/RIF ASSAYS TO DETECT *MYCOBACTERIUM TUBERCULOSIS* AND RESISTANCE GENE PATTERNS IN GABON

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Background Tuberculosis (TB) remains a major cause of morbidity and mortality in Africa. A major challenge of TB diagnosis is slow growth of its causative agent, *Mycobacterium tuberculosis* complex (MTBC). WHO has endorsed the application of molecular methods to rapidly diagnose TB and detect drug resistance mutations in MDR-TB. We hereby evaluate the efficacy of the GenXpert MTB/RIF and the GenoType MTBDRplus, using culture as gold standard.

Methods We applied the GeneXpert MTB/RIF (Cepheid) and the Genotype MTBDRplus (Hain Life Sciences, Germany) to compare between molecular and standard traditional methods (smear microscopy and culture). In total, 246 consecutive sputa samples from suspected TB cases (individuals) in Lambarene and surrounding villages were analysed. The molecular methods confirm MTBC and detect resistant mutations in the rpoB, katG and inh genes corresponding to rifampicin (RIF) and isoniazid (INH), respectively.

Results Of the 193 samples available for analysis, 51 were positive and 142 were negative by culture. The overall sensitivity of GeneXpert compared to culture was 86.3% and the specificity was 93.7%. The sensitivity and specificity of Genotype MTBDRplus compared to culture were 82.5% and 95.8%. Rifampicin-resistant strains determined by standard drug susceptibility testing (DST) were 100% identified by GeneXpert and 83.3% by Genotype MTBDRplus. All the rifampicin-resistant strains were also exhibiting the high level resistance against high-level isoniazid corresponding to katG genes. Genotype MTBDRplus identified two isolates carrying only mutations to low-level isoniazid resistance.

Conclusions This comparative study has established a strong correlation between the GeneXpert and the MTBDRplus assays for the rapid diagnosis of multi-drug resistant TB (MDR-TB); as well as with drug susceptibility testing by standard culture method. Our findings further strengthen the WHO recommendation for the universal implementation of molecular tests in order to enhance the rapid diagnosis of TB and early initiation of treatment in confirmed cases.

OA-007 MOLECULAR BACTERIAL LOAD ASSAY: A FAST AND ACCURATE MEANS FOR MONITORING TUBERCULOSIS TREATMENT RESPONSE

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Background Tuberculosis is a difficult disease to treat. We report a multi-centre performance evaluation of the molecular bacterial load assay (MBLA) that monitors change in patient bacterial load (BL) as they respond to TB therapy.

Methods Smear or Xpert MTB/RIF-positive patients were prospectively monitored for treatment response using MBLA and culture at four sites in Southeast Africa. Treatment response was defined as decline in BL and or rise in time to culture positivity (TTP) or conversion to negative culture status. Positive culture at 5 or 6 months confirmed treatment failure. MBLA-MGIT correlation and association with treatment outcome were determined by Spearman's ρ and logistic regression, respectively.

Results A total of 1764 serial samples from 178 patients were assessed for treatment response of which 91% were treatment success. Of those who failed treatment (n=17), MBLA detected TB in 82% at 2 months of treatment compared to MGIT 24% and LJ 6%. Mean BL at baseline was 6±1.3log10 CFU/ml falling to zero in 59% of the patients by 3 months of treatment. A corresponding rise in MGIT TTP, 5±3 to 22±11 was observed, r=–0.5, p<0.0001. The rate of sputum clearance (SLOPE) was high among high-burden patients – 1.0log10C-FU/ml than low-burden patients, –0.7log10CFU/ml in the first 2 weeks of treatment. Despite higher rates of clearance, high-burden patients were more likely to be TB-positive at 2 months of treatment, p=0.01(OR 2.5). Response was generally slower among the MDR than susceptible TB patients. Time to result was 4h with MBLA and 5–22 days for MGIT. Contamination was 25% in MGIT and 4% on solid culture.

Inter-site testing revealed that MBLA was reproducible, ANOVA p >0.05.

Conclusions MBLA is a contamination-insensitive, reproducible method capable of giving results in real-time. Direct quantification of bacterial load from uncultured sputum demonstrates considerable potential for application in resource-limited settings where TB culture facilities are scarce.

OA-009 DIAGNOSTIC TOOLS FOR HUMAN AFRICAN TRYPANOSOMIASIS ELIMINATION AND CLINICAL TRIALS: THE DITECT-HAT PROJECT

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Background *Trypanosoma brucei gambiense* (Tbg) causes human African trypanosomiasis (HAT), one of the neglected tropical diseases targeted for elimination. Integration of diagnosis and case management into the general health system, sustainable monitoring of eliminated foci and development of safe and efficacious drugs, remain important challenges.

Methods The DiTECT-HAT project tackles these challenges. For passive case detection, we will determine the diagnostic performance and cost of rapid diagnostic tests (RDTs) performed on clinical suspects in peripheral health centres, whether or not combined with serological and/or molecular tests on filter paper done at regional reference centres. Cost-effective diagnostic algorithms with high positive predictive values might allow test-and-treat scenarios without the need for complicated parasitological confirmations. Secondly, health workers performing house to house visits in foci with very low HAT prevalence can easily collect blood on filter paper and send it to regional HAT reference centres for analysis. The feasibility and cost of diagnostic algorithms with RDTs, serological and molecular high-throughput tests for post-elimination monitoring will be determined. An appropriate threshold will be established to trigger active case finding to avoid re-emergence of HAT, without unnecessarily raising the alarm. Finally, the accuracy of neopterin and RNA detection as early test-of-cure will be determined in therapeutic trials.

Earlier treatment outcome assessment will speed up the development of new drugs for HAT, and improve management of relapses in routine care.

Results An update of ongoing and planned activities is given. The passive case detection sub-project is being set up in DR Congo, Côte d'Ivoire and Guinea. The inclusions for the early test-of-cure sub-project are ongoing in DR Congo.

Conclusions The proposed research will provide evidence to support policies for improved HAT diagnosis and patient management within a context of disease elimination, and will contribute to successful and sustainable HAT elimination.

OA-010 PREVALENCE AND CLINICAL SIGNIFICANCE OF SCHISTOSOMIASIS-CHRONIC HEPATITIS B VIRUS CO-INFECTION IN ZAMBIA

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10.1136/bmjgh-2016-000260.18

Background Hepatosplenic schistosomiasis (HSS) and hepatitis B virus (HBV) are both endemic in sub-Saharan Africa but the clinical epidemiology of co-infection is not well-characterised. Within a current HIV cohort study, we assessed the prevalence of HSS and its impact on markers of liver fibrosis in HIV-HBV co-infected individuals.

Methods At two urban HIV care facilities in Zambia's capital Lusaka, we screened for HBV co-infection using a hepatitis B surface antigen (HBsAg) test and for lifetime infection with *Schistosoma mansoni* using an IgG enzyme-linked immunoassay (Abcam, Cambridge, UK). Among HIV-HBV patients, we also performed abdominal ultrasonography. We defined HSS as evidence of periportal hepatic fibrosis on ultrasound regardless of IgG result. Patient characteristics, including liver fibrosis markers (ALT and transient elastography) were measured and stratified by HSS. We used Wilcoxon rank sum test for continuous and chi-square test for categorical comparisons between groups.

Results Among 895 HIV-infected adults, lifetime exposure to *S. mansoni* was observed in 23.3%. Within the cohort 92 HBsAg-positives underwent assessment for HSS. Median age

among these was 34.7 years (interquartile range [IQR], 28.9–39.9), 48% were men, CD4 count was 247 cells/mm3 (IQR, 145–335), HBV viral load was 2.87 (IQR, 1.00–5.18) log10 IU/mL, and liver stiffness was 5.5 kilopascals (IQR, 4.7–6.9).

On ultrasound, 1 patient had cirrhosis and 36 (39.1%) had evidence of HSS. HBV-HSS patients had a non-significant trend toward higher portal vein diameter (8.5 versus 10.2; p=0.15) compared to those without HSS but ALT (18.5 *vs* 20 U/L), and liver stiffness (5.3 *vs* 5.0 kPa) were similar between groups (both p >0.05).

Conclusions Lifetime *S. mansoni* exposure and current HSS were common among HIV-infected patients with HBV co-infection in Zambia. Mild HSS did not appear to alter non-invasive markers of liver fibrosis. Further research on the impact of more advanced HSS on HBV co-infection is needed.

OA-011 THE IMMUNE TRYPANOLYSIS TEST: AN ACCURATE SEROLOGICAL MARKER TO MANAGE ELIMINATION OF *T.B. GAMBIENSE* HUMAN AFRICAN TRYPANOSOMIASIS

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Background Continued post-elimination monitoring is required to ensure sustainability of zero transmission of human African trypanosomosis (HAT) and to avoid re-emergence caused by potential remaining *Trypanosoma brucei gambiense* reservoirs (animal and/or human). Until now, no tool is able to attest or validate elimination. Increasingly, the serological immune trypanolysis test is being implemented in the decision algorithms to characterise parasitological unconfirmed CATT or RDT seropositive subjects. Therefore, we wanted to assess further the high specificity of immune trypanolysis.

Methods We first tested samples from domestic animals from a tsetse-infested area in Ethiopia, a country where no *T. b. gambiense* exists, but where bovine trypanosomosis is prevalent. Then, we tested cattle and human samples from the south-west of Burkina Faso, a historical focus of *gambiense* HAT that still shelters tsetse flies populations and animal trypanosomosis. Lastly, we were interested in testing human samples from active foci in Côte d'Ivoire and Guinea.

Results Our results showed zero trypanolysis-positive animals from Ethiopia while in the historical HAT foci in Burkina Faso, 4.89% (14/286) of cattle were trypanolysis-positive. In humans, zero samples over 729 were trypanolysis-positive in Burkina Faso, while the percentage of positives was 3.77% (44/1166) in Guinea, including 7 new cases diagnosed during the sampling and 1.3% in Côte d'Ivoire (8/598).

Conclusions Considering results from this study, we think that trypanolysis test, confirmed to be a very specific test in human, can be a tool able to certify HAT elimination in a given area. It also suggests that the risk of the reintroduction of *T. b. gambiense* in Burkina Faso is real, especially in the south-west which shelters a high density of tsetse populations, in addition to the possible presence of *T. b. gambiense* in domestic animals. However, further studies on the specificity of the trypanolysis test regarding *T. b. gambiense* in animals should be conducted.

OA-012 PREVALENCE AND RISK FACTORS OF VIROLOGICAL FAILURE AMONG CHILDREN ON ANTIRETROVIRAL THERAPY

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10.1136/bmjgh-2016-000260.20

Background An unprecedented global effort at scaling up universal access to antiretroviral therapy has decreased the progression of HIV. However, due to challenges with supplies and adherence to intermittent antiretroviral therapy (ART) for mothers, infants continue to be infected, some with resistant viruses. Exposure to these resistant strains leads to non-responsiveness to therapy resulting in virological failure. Children are more vulnerable to HIV drug resistance because of their life long treatment, the possible selection of resistant strains as a result of prophylaxis for mothers with HIV enrolled in PMTCT. The objective of the study was to determine the prevalence and risk factors of virological resistance among HIV-1-positive children on antiretroviral therapy.

Methods This was a longitudinal study that was performed at the HIV paediatric clinic of the Komfo Anokye Teaching Hospital, Kumasi, Ghana. Blood samples of children below the age of 18 years who had been on therapy for at least 3 months were analysed for virological load using real-time COBAS AmpliPrep/COBAS Taqman PCR. The samples were analysed at two consecutive time points when they came for their ART refill. Socio-demographic and clinical information was collected from their folders and also from the mother.

Results A total of 188 subjects were enrolled into the study from September 2015 to June 2016. The average duration on ART was 36 months (IQR=12–72 months). Of all subjects recruited, 134 (71.3%) were found to be on regular drug ART. Of these, 21 (15.7%) had virological failure and 102 (76.1%) had virological suppression. A regression analysis showed that subjects whose parents were unemployed had 5.4 (1.4–20.9) chances of virological failure compared to those with parents employed.

Conclusions The risk of virological failure among HIV-positive children is still high. Efforts must be made to further identify the potential causes of virological failure among these children.

OA-013 VIROLOGICAL RESPONSE TO EARLY COMBINED ANTIRETROVIRAL THERAPY IN HIV-INFECTED INFANTS: EVALUATION AFTER TWO YEARS OF TREATMENT IN THE PEDIACAM STUDY

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10.1136/bmjgh-2016-000260.21

Background Little is known about virological responses to early combined antiretroviral therapy (cART) in HIV-infected infants in limited-resource settings. We estimated the probability of achieving viral suppression within two years of cART initiation, and investigated the factors associated with success.

Methods We analysed all 190 infants from the Cameroon PediaCAM study who began free cART before the age of 12 months. The main outcome measure was viral suppression (<1000 cp/mL) on at least one occasion. The other outcome measures considered were viral suppression (<400 copies/ mL) on at least one occasion and confirmed viral suppression (both thresholds) on two consecutive occasions. We used competing-risks regression for a time-to-event analysis to estimate the cumulative incidence of outcomes, and univariate and multivariate models to identify risk factors.

Results During the first 24 months of cART, 20.0% (38) of the infants died, giving a mortality rate of 11.9 deaths per 100 infant-years [95% CI: 8.1–15.7]. The probability of achieving a viral load below 1000 or 400 copies/mL was 80.0% [69.0–81.0] and 78.0% [66.0–79.0], respectively. The probability of virological suppression (with these two thresholds) on two consecutive occasions was 67.0% [56.0–70.0] and 60.0% [49.0–64.0], respectively. Virological success was associated with not having missed any doses of treatment before the visit, but not with socioeconomic and living conditions.

Conclusions The long-term daily administration of drugs to babies seems to be difficult. Mortality remained high despite early cART initiation. Future studies should focus on longer-term treatment outcomes in children still alive after two years of treatment.

OA-014 HIV INFECTION AND CARDIOVASCULAR RISK PROFILE IN A RURAL SOUTH AFRICAN POPULATION: THE NDLOVU COHORT STUDY

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10.1136/bmjgh-2016-000260.22

Background Life expectancy increased in HIV-infected populations due to antiretroviral treatment (ART). Whether HIV-infection and/or ART increase cardiovascular risk against a background of increasing prevalence of obesity, hypertension and diabetes in low- and middle-income countries is not yet clear. To answer this question in a rural South-African population, the Ndlovu Cohort Study was designed. We describe the baseline distribution of cardiovascular risk factors in relation to HIV and ART.

Methods The Ndlovu Cohort Study is a prospective cohort study of 1000 HIV-positive and 1000 HIV-negative adults from the Moutse area, Limpopo, South Africa with an intended follow-up duration of ten years. Information is collected on demographics, anthropometrics, life-style, kidney and liver function, CRP, glucose and proteinuria. Carotid intima-media thickness (CIMT) and pulse wave velocity (PWV) measurements are used to assess subclinical atherosclerosis, respectively arterial stiffness. Cardiovascular risk factors were compared between HIV-negative and HIV – positive participants, whether or not on ART. Data were adjusted for gender and age.

Results By December 2015, 1053 participants were included, 66% women; 345 (32.8%) women were HIV-positive of whom 235 (68.1%) received ART. HIV-infected participants were significantly older (40.0 versus 37.3 years), and mainly women (73%). HIV was associated with a lower body mass index, lower total – and LDL cholesterol and a lower prevalence of hypertension and diabetes. ART was associated with increased HDL and triglyceride levels. Current smoking did not differ between groups (23.6%), HIV and ART were associated with higher CRP values. Framingham risk scores (FRS) did not differ between HIV+/HIV- and/or ART use.

Conclusions HIV infection is accompanied by a lower prevalence of cardiovascular risk factors, although the level of inflammation is increased. So far, we found no evidence that the 10-year cardiovascular disease risk according to FRS is influenced by HIV infection or HIV treatment.

OA-015 PHYLOGENETIC AND DEMOGRAPHIC CHARACTERISATION OF HIV-1 TRANSMISSION NETWORKS IN A GENERAL POPULATION COHORT IN UGANDA

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10.1136/bmjgh-2016-000260.23

Background The General Population Cohort (GPC) in Southwestern Uganda is a low-risk population with low HIV incidence rates (<1%). Despite several interventions for close to 30 years, new cases of HIV continue to emerge. We set out to use phylogenetics and patients' demographic data to understand the HIV transmission dynamics in this population to inform prevention.

Methods A total of 2049 pol sequences of participants diagnosed from 2003–2015 were included in this analysis; pol sequences were from GPC (n=1049), Central Uganda (n=800) and Eastern Uganda (n=200). Phylogenetic analysis was used to identify transmission networks. The demographic and clinical characteristics of the transmission clusters were analysed.

Results The overall subtype distribution was: A (45%), C (3%), D (40%) and others (12%). The subtype distribution by region was for GPC: A (41%), C (2%), D (45%) and others (12%). For Central: A (49%), C (4%), D (35%) and others (12%). Eastern: A (60%), C (3%), D (24%) and others (13%). We identified 233 transmission clusters (cluster size variation 2–10) that comprised of 559 (27%) of the 2049 participants.

The majority of clusters comprised transmission pairs (n=186) and triplets (n=30). The majority (~60%) of the 233 clusters was from the GPC and all 13 large clusters (≥5) were also from the GPC. A significant number of clusters (n=25, 11%) was formed between individuals from different geographic locations. Participants in transmission networks were associated with high-risk sexual behaviour: low condom use, high alcohol use, and partner change even with known HIV-positives.

Conclusions The transmission networks identified among individuals from the GPC and other populations or geographic regions may imply HIV introductions from outside communities. This suggests that HIV introductions into communities are common and account for a substantial number of new infections in the GPC. HIV prevention efforts should therefore target the broader communities beyond the GPC.

OA-016 PREVALENCE AND RISK FACTORS FOR EFAVIRENZ-BASED ANTIRETROVIRAL TREATMENT-ASSOCIATED SEVERE VITAMIN D DEFICIENCY: A PROSPECTIVE COHORT STUDY

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10.1136/bmjgh-2016-000260.24

Background Initiation of efavirenz-based combination antiretroviral therapy (cART) is associated with Vitamin D deficiency, but the risk factors for cART-induced severe vitamin D deficiency (SVDD) and the impact of anti-tuberculosis (TB) co-treatment is not explored well.

Methods Treatment-naïve HIV patients with (n=102) or without (n=89) tuberculosis co-infection were enrolled prospectively and received efavirenz-based cART. In TB-HIV co-infected patients, rifampicin-based TB treatment was initiated. Plasma 25-hydroxyvitamin D (25(OH)D), cholesterol and 4-beta hydroxycholesterol concentrations were measured at baseline, and weeks 4, 16 and 48 of cART. Plasma efavirenz concentrations were determined at week 4 and 16 of cART. Genotyping for CYP2B6, CYP3A5, ABCB1, SLCO1B1, and UGT2B7 were done.

Results TB-HIV patients had significantly lower plasma 25 (OH)D3 levels than HIV-only patients at baseline. TB co-infection, low Karnofsky score, high viral load and high CYP3A activity as measured by plasma 4-beta hydroxycholesterol/ cholesterol ratios were significant predictors of low 25 (OH) D3 levels at baseline. In HIV-only patients, initiation of efavirenz-based cART increased the prevalence of SVVD from 27% at baseline to 76%, 79% and 43% at weeks 4, 16 and 48 of cART, respectively. The median 25(OH)D3 levels declined from baseline by –40%, –50% and –14% at weeks 4, 16 and 48 of cART, respectively. In TB-HIV patients, prior TB therapy had no influence on 25(OH)D3 levels, but the initiation of efavirenz-based cART increased the prevalence of SVDD from 57% at baseline to 70% and 72% at weeks 4 and 16 of cART, respectively. Whereas the median plasma 25(OH)D3 declined from baseline by –17% and –21% at week 4 and 16 of cART, respectively. None of the genotypes were significantly associated with SVDD.

Conclusions Low plasma cholesterol, high CYP3A activity, and high plasma efavirenz concentrations are significant predictors of early efavirenz-based cART-induced SVDD. Low plasma 25 (OH)D3 level at baseline is associated with TB co-infection and HIV diseases progression.

OA-018 THE BURDEN AND FUTURE SCOPE FOR IMPORTANT VIRAL ENTERIC PATHOGENS IN AFRICA

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Background The burden of viral enteric infections in Africa is enormous, although poorly described. Some, such as rotavirus, are well recognized, whereas others including norovirus or enteric adenovirus (EAd), show high burden which is only now being described. Hepatitis E virus (HEV) is a neglected enteric viral infection although is on WHO's radar screen as an important pathogen which needs further evaluation in Africa and Asia. This presentation will focus on these four enteric viral pathogens describing our current understanding of disease burden and the potential for vaccines as potential interventions.

Many countries in Africa have documented the high burden of rotavirus. Almost 30 countries have introduced rotavirus vaccines with or without Gavi support, and recent studies document dramatic reductions in diarrhoeal hospitalizations and diarrhoeal deaths post introduction.

Norovirus is a ubiquitous virus causing diarrhoeal disease in all age ranges, although the incidence is highest in young children. Although a common cause of diarrhoea, norovirus is often associated with asymptomatic shedding making it difficult to ascertain the true burden of the disease. Nevertheless, advances towards understanding the epidemiology and diversity of norovirus in Africa are important to inform future vaccine efforts.

EAds have recently been described as one of the top 5 pathogens associated with acute severe diarrhoea in young children <5 years in Africa and Asia. Coupled with the high prevalence of EAds in HIV-infected children requires more focused research, although there is very limited vaccine development currently.

HEV is associated with water-borne and zoonotic infections, and is reported in large outbreaks. It has high mortality in pregnant women and is associated with high rates of stillbirths. Little is known of the extent of HEV infection in Africa. A Chinese vaccine against HEV has been licensed and WHO has identified gaps in research that are required for future immunization opportunities.

OA-019 NEW POSSIBILITIES FOR THE DEVELOPMENT OF A COMBINED VACCINE AGAINST ETEC AND *SHIGELLA*

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Background Together, enterotoxigenic *Escherichia coli* (ETEC) and *Shigella* contribute greatly to the mortality and the morbidity due to diarrhoeal diseases, including a number of negative lifetime health impacts. Vaccines represent a reasonable option to reduce this burden.

Vaccine candidates PATH has reviewed the landscape of vaccine candidates for these diseases and identified two candidates to be moved towards licensure in the near-term as a combined ETEC and *Shigella* vaccine for use on an Expanded Programme on Immunisation (EPI) schedule.

ETVAX One candidate is a formalin-inactivated ETEC vaccine (ETVAX) consisting of four *E. coli* preparations, each engineered to hyper-produce the CFA/1, CS3, CS5, and CS6 antigens of ETEC. In addition, the vaccine contains a cholera B subunit modified to be more cross-reactive with the B subunit of ETEC. ETVAX is co-administered with a double-mutant of the ETEC heat-labile toxin (dmLT), which serves as a potent mucosal adjuvant.

TSWC The other candidate includes formalin-killed *S. flexneri* 2a and 3a and *S. sonnei* prepared as a trivalent vaccine, called TSWC. A prototype of TSWC, *S. flexneri* 2a, was administered to North American volunteers and found to be safe and immunogenic; it is now currently in a challenge trial.

Looking ahead Early 2017 in a phase I trial, we will test TSWC given alone and co-administered with ETVAX. ETVAX given alone exceeded expectations for immunogenicity in Swedish volunteers and is projected to be evaluated for safety and early efficacy in Finnish travellers to Benin in early 2017. ETVAX is also currently being tested in a descending-age trial in

Bangladesh to determine the optimum safe dose of vaccine and adjuvant to be given to infants as young as 6 to 10 weeks of age. We also hope that the dmLT will have a dose-sparing effect on the vaccine given to this target population.

OA-020 IMPACT OF TARGETED INTERVENTIONS AGAINST DIARRHOEA IN ZAMBIA

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Background Diarrhoea is a leading cause of morbidity and mortality with the brunt of diarrhoea felt most in developing countries like Zambia where 13% of all deaths of children between 1–59 months are attributable to the disease. The Ministry of Health, in partnership with the Centre for Infectious Disease Research in Zambia (CIDRZ) and other stakeholders, implemented the Programme for the Awareness and Elimination of Diarrhoea (PAED) in 2012 to reduce all-cause under-five mortality by 15% in Lusaka Province.
Methods Baseline data were collected in 2012 and endline data were collected 3 years following PAED implementation. The primary outcome of interest was all-cause under-five mortality rate. Additionally, a case-control study to estimate rotavirus vaccine effectiveness (VE) was undertaken.
Results The percentage of children under age 5 who had diarrhoea in the last 2 weeks preceding the survey declined from 15.8% (95% CI: 15.2–16.4%) in 2012 to 12.7% (95% CI: 12.3–13.%) in 2015. Post-neonatal mortality declined by 34%, from an estimated rate of 29 (95% CI: 26–32) to 19 (95% CI: 16–21) deaths per 1000 live births. The adjusted 2-dose VE was 26% (95% CI: 30%–58%) among children ≥6 months of age. VE against hospitalised children ≥6 months of age was 56% (95% CI, – 34%–86%).
Conclusions Well-packaged preventive and treatment interventions against diarrhoea could reduce probability of death among children aged 1–59 months. VE results from Zambia were consistent with others in the region, and while we observed a higher point estimate for VE against increased severity of illness compared with milder disease, the study was not powered to detect a low level of VE against milder disease.

OA-021 POINT-OF-NEED DIAGNOSTICS: BIOSURVEILLANCE WITH A DEVICE2CLOUD CAPABILITY IN SIERRA LEONE

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Background Infectious diseases contribute to a high burden of diseases globally. Surveillance using low-cost technology, combined with cutting edge platforms offers a path for understanding the disease ecology of locations of interest in resource-poor countries. Our goal was to pilot a bio surveillance system comprising of rapid lateral flow immunoassays, rapid PCR and a cloud database.
Methods The study was carried out in Bo, Sierra Leone at the Mercy Hospital. We recruited 1570 subjects over a period of two years. Inclusion criteria for the study were being febrile, being at least five years of age, living within the city of Bo or its neighbouring villages and agreeing to participate in the study. The assays used included a DPP multiplex lateral flow assay for dengue, *Burkholderia pseudomallei*, *Yersinia pestis*, malaria Pf/Pan, a Film Array PCR platform with multiplex Biothreat and SASFI panels that together detect over 30 pathogen targets. We used a Deki Reader to upload lateral flow images to the cloud database. The Deki reader quantitates test results, such that scores at ≥1.75 are considered positive. A special computer program was designed to upload pdf images of PCR results to the cloud database. The cloud database was designed for automated quality assessment and remote monitoring.
Results Preliminary results show that out of 1570 samples processed by DPP, 30(1.9%) were positive for Burkholderia, 41 (2.6%) were positive for Dengue NS1 antigen, 22(1.4%) were positive for *Yesinia pestis* fraction 1 antigen, and 340(21.7%) were positive for malaria. When a cross-section of results obtained by eye was compared with results automatically detected by the D2C platform, there was 95.2% concordance between results obtained by eye and those obtained automatically by the Deki reader to the cloud database.
Conclusions Active disease surveillance and the ability to remotely monitor activities in peripheral health units are critical needs in many poor countries. Our results provide additional perspectives on the twin problem of surveillance and remote quality assessment.

OA-022 SAFETY AND IMMUNOGENICITY OF CO-ADMINISTERED HOOKWORM VACCINE CANDIDATES NA-GST-1 AND NA-APR-1 WITH ALHYDROGEL® AND GLUCOPYRANOSYL-LIPID A IN GABONESE ADULTS: INTERIM RESULTS

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Background Hookworm disease is one of the most prevalent of the neglected tropical diseases. To date, the control of hookworm infection has been limited to mass-administration of anthelminthic drugs. Despite this, the global hookworm prevalence does not decrease, thus there is a need for a vaccine. We evaluated the Na-GST-1 and Na-APR-1 hookworm vaccine candidates simultaneously in a hookworm endemic Gabonese population.
Methods Eligible healthy Gabonese adults aged 18–50 years were enrolled in a randomised, double blind, controlled phase I trial. The first cohort received 30 μg Na-GST-1 co-administered with 30 μg Na-APR-1. The second cohort received 100 μg Na-GST-1 and 100 μg Na-APR-1. All doses were administered after mixing with 5 μg of an aqueous formulation of glucopyranosyl Lipid A (GLA-AF), a Toll-like Receptor-4 agonist. Hepatitis B vaccination (HBV) was administered as a comparator. Study subjects were vaccinated on days 0, 28 and 180 by intramuscular injection. IgG antibody levels were measured by qualified ELISA. This study evaluated the safety, reactogenicity,

and immunogenicity of *Na*-GST-1/Alhydrogel® co-administered with Na-APR-1/Alhydrogel®.

Results Thirty-two study participants were enrolled. No serious adverse events or significant changes in haematological, renal or liver function parameters were observed. Mild-to-moderate injection-site pain, headache and fever were common adverse events. Elevated Na-GST-1 and Na-APR-1 IgG antibody levels were detected on day 194. Significant differences in mean antibody levels were observed between dose groups for Na-APR-1 [30 μg: 18 (50–86.9) *vs* 100 μg: 197 (131– 264); p< 0.0001] but not for Na-GST-1 [30 μg: 338 (213–463) *vs* 100 μg: 402.54 (283.65–521); p=0.5].

Conclusions Co-administration of the hookworm vaccine candidates (Na-GST-1 and Na-APR-1) was safe and well tolerated. In order to achieve optimal antibody levels, a series of three high doses needs to be administered. Additional investigations are necessary to consider this combination as a potential bivalent vaccine candidate.

OA-023 ONE-YEAR SAFETY OF THE RVSVΔG-ZEBOV-GP VACCINE IN ADOLESCENTS AND CHILDREN IN LAMBARENE, GABON

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10.1136/bmjgh-2016-000260.30

Background The rVSVΔG-ZEBOV-GP vaccine was safe and immunogenic in American, European and African adults. Few cases of transient, self-limiting arthritis have been reported in some adult participants in Geneva. We describe one-year safety of a single dose (2×10^7 plaque forming unit (PFU)) of the vaccine administered to adolescents and children living in Lambaréné.

Methods A phase I, open label randomized trial conducted in Lambaréné, Gabon, to assess the clinical safety (adverse events (local/systemic symptoms, and laboratory anomalies)) for 365 days' post injection. The primary objective was to assess the nature, frequency, and severity of adverse events (AEs) and/or serious adverse events (SAEs) associated with the administration of the vaccine.

Results From 08-May 2015 to 07-Jul-2015, a total of 20 adolescents and 20 children aged 13–17 and 6–12 years respectively, were vaccinated with a single intramuscular dose of 2×10^7 PFU rVSVΔG-ZEBOV-GP vaccine. Two serious adverse events (SAE) were reported over one year of follow-up. Two adolescents were hospitalized for *Plasmodium falciparium* malaria and pneumonia infection. Up to 12 months' (6 months of extended follow-up) of both active and passive reporting, the most frequently reported symptoms by vaccinees are classified under the following system organ classes (SOC): Gastrointestinal disorders 30%(6/20) and 40%(8/20), respiratory-thoracic and mediasternal disorders 5%(1/20) and 45%(9/20), and infections/infestations 20%(4/20) and 20%(4/20) for adolescents and children respectively. No case of arthritis was observed, few cases 13%(5/40) of mild to moderate arthralgia, unrelated to the vaccine were reported. No delayed reactogenicity symptoms were reported beyond the already mild to moderate intensity symptoms reported during the first 28 days' post injection. No severe (grade 3) adverse event was reported. Median haematology and biochemistry values were within site normal ranges at month 12.

Conclusion The vaccine dose of 2×10^7 PFU showed an acceptable safety and tolerability profile in our volunteers' age 6–17 years, living in a setting endemic for Ebola virus transmission. This acceptable safety profile seen in adolescents and children is similar to that previously reported in adults.

OA-024 THE ROLE OF CLINICAL TRIALS FOR ELIMINATION OF NEGLECTED INFECTIOUS DISEASES AMENABLE TO MASS DRUG ADMINISTRATION

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10.1136/bmjgh-2016-000260.31

Background In 2012, WHO published a roadmap, for 'Accelerating Work to Overcome the Global Impact of Neglected Tropical Diseases (NTD)', which set out control and elimination targets for five NTDs that were considered tools-ready. Lymphatic filariasis, onchocerciasis, schistosomiasis, trachoma and soil-transmitted helminthiasis are amenable to the preventive chemotherapy (PC) strategy and manageable through the implementation of available diagnostic products, and safe and effective medicines. The optimism for achieving the WHO 2020 targets for control and elimination for these PC NTDs was crystallised by the London Declaration of 2012 – a pledge by leaders of several major global health and development organizations, together with industry partners to unite efforts to achieve the targets by 2020. Clinical research involving human subjects is driven primarily by the need for novel products, devices or interventions. The question remains whether clinical trials have a role in the fight against NTDs that are tools-ready. Can an investment case be made for vaccines or new drugs for the five PC NTDs? Four of the five PC NTDs are vector-borne diseases, but clinical trials are not normally designed to measure vector outcomes and there is little information available for the conduct of clinical trials involving entomological tools and products. Moreover, human and laboratory capabilities for conducting clinical trials in the countries most affected by NTDs in sub-Saharan Africa are limited. Nonetheless, alternative intervention strategies based on new drugs, vaccines and novel devices have been proposed as additional tools that could fast-track the fight against the PC NTDs. The role of clinical trials in defining these new strategies will be discussed.

OA-025 ARTEMISININ-BASED COMBINATION TREATMENTS IN PREGNANT WOMEN IN ZAMBIA: EFFICACY, SAFETY AND RISK OF RECURRENT MALARIA

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10.1136/bmjgh-2016-000260.32

Background In Zambia, malaria is one of the leading causes of morbidity and mortality, especially among under five children and pregnant women. For the latter, WHO recommends the use of Artemisinin-based Combinations Treatments (ACTs) in the

second and third trimester of pregnancy. In a context of limited information on ACTs, the safety and efficacy of three ACTs, namely artemether-lumefantrine (AL), mefloquine-artesunate (MQAS) and dihydroartemisinin-piperaquine (DHAPQ) were assessed in malaria-infected pregnant women.

Methods Trial was carried out between July 2010 and August 2013 in Nchelenge district, Luapula Province, an area of high transmission, as part of multi-centre trial. Women in second or third trimester of pregnancy and with malaria were recruited and randomized to one of three study arms. Women were actively followed up for 63 days, and then at delivery and one year post-delivery.

Results Nine hundred pregnant women were included, 300 per arm. PCR-adjusted treatment failure was 4.7% (12/258) (95% CI:2.7–8.0) for AL, 1.3% (3/235) (95%CI:0.4–3.7) for MQAS and 0.8% (2/236) (95%CI:0.2–3.0) for DHAPQ, with significant risk difference between AL and DHAPQ (p=0.01) and between AL and MQAS (p=0.03) treatments. New infections during follow up were more frequent in AL (Hazard Ratio (HR):4.70; 95%CI:3.18–6.94; p<0.01) and MQAS (HR:1.59; 95%CI:1.02–2.46; p=0.04) arms compared to DHAPQ arm. PCR-adjusted treatment failure was significantly associated with women under 20 years [HR5.35 (95%CI:1.07–26.73; p=0.04)] and higher malaria parasite density [3.23 (95%CI:1.03–10.10; p=0.04)], and still women under 20 years [1.78, (95%CI:1.26–2.52; p<0.01)] had a significantly higher risk of new infections. Unadjusted for treatment, low treatment dosage per kg body weight was significantly associated with the risk of new infections (HR:1.72; 95%CI:1.29–2.28; p<0.01). The three treatments were generally well tolerated. Dizziness, nausea, vomiting, headache and asthenia as Adverse Events (AEs) were more common in MQAS than in AL or DHAPQ (p<0.001). Birth outcomes were not significantly different between treatment arms.

OA-027 MASS DRUG ADMINISTRATION (MDA) INTEGRATED MALARIA ELIMINATION IN A HYPO-ENDEMIC ISLAND IN LAKE VICTORIA, KENYA

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10.1136/bmjgh-2016-000260.33

Background Mass drug administration (MDA) for malaria elimination has been proposed as a feasible weapon especially for low endemicity settings. Nonetheless, the concept has not been tried for hypo-endemic areas of inland Africa. We conducted MDA using artemisinin-piperaquine and low dose primaquine with insecticide-treated bed nets (ITN) in Ngodhe Island, Lake Victoria, Kenya, aiming to reduce prevalence to below 1% in 6 months post MDA.

Methods We conducted 2 rounds of MDA on days 0, 1, 35 and 36. We employed strong community linkages to ensure robust engagement with the community using workshops, feedback sessions and involvement of community health volunteers previously set up by the Ministry of Health and community fieldworkers. The MDA was administered (directly observed) and participants followed up for possible side effects. Participants were not tested for glucose-6-phosphate dehydrogenase deficiency. Malaria infection was determined by microscopy and polymerase chain reaction (PCR).

Results MDA coverage was 90% for round 1 and 89% for round 2, with no major drug side effects or haemolytic emergencies. The mean haemoglobin decrease after MDA was not significant. Prevalence by microscopy decreased from 3.1% on day 0 to 0% on day 8. Prevalence was 1.1% on day 35, and 0.21% on day 120. Importation of malaria was noted to pose a challenge in maintaining malaria freedom.

Conclusions MDA led to a rapid reduction in malaria prevalence in a hypo-endemic setting in Western Kenya demonstrating feasibility when combined with strong community engagement. Primaquine was well tolerated with no haemolytic emergencies. Nonetheless, strategies to mitigate imported malaria need to be developed for long-term sustainability.

OA-028 RANDOMIZED TRIAL TO ASSESS EFFECT OF REPEATED TREATMENT OF DHA-PQ AND AL ON QTC INTERVAL IN PATIENTS PRESENTING WITH UNCOMPLICATED MALARIA IN BOBO-DIOULASSO, BURKINA FASO

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10.1136/bmjgh-2016-000260.34

Background Artemisinin combination therapies (ACTs) are widely used for the management of malaria and even tested for chemoprevention. In single episode efficacy studies, these drugs were clinically well tolerated but cardiac effects over repeated treatment are less investigated.

Methods We conducted a prospective randomised controlled trial in Bobo-Dioulasso from August to October 2013 where patients aged 6 months and over were randomly allocated to receive either dihydroartemisinin-piperaquine (DHAPQ) or artemether-lumefantrine (AL) on first and subsequent episodes. Each participant was screened against inclusion criteria including the ECG which was repeated again 2 hours after the last dose. We considered that a QTc interval more than 30 ms compared to the baseline value is abnormal, but a prolonged QTc interval over 450 ms was reported as adverse event. QTc values were categorised into less or greater or equal to 450 ms. Drug tolerance was compared using Chi-square test, and p-value of less than 0.5 is significant.

Results Patients were randomised to receive DHAPQ (n=224) or AL (n=236). During the 2 years follow-up we observed a total of 130 (in 1173 electrocardiogram performed on day 2 monitoring) prolonged QTc more than 450 ms (96/548 for DHAPQ and 34/625 for AL, p< 0.001). Irrespective of the drug, these proportions of prolonged QTc decreased over the subsequent episodes (50 QTc =450 in episode 1 to 0 in episode 8 up to episode 10).

Conclusions The proportion of prolonged QTc was higher in DHAPQ group compared to the AL group but decreased along with the number of retreatments. Otherwise, DHAPQ and AL were well tolerated despite repeated treatment of malaria, which seemed to improve over consecutive episodes.

OA-029 PATTERNS OF MOLECULAR MARKERS OF RESISTANCE IN 'REAL LIFE' REPETITIVE DIHYDROARTEMISININ-PIPERAQUINE MALARIA TREATMENT: A MOLECULAR ANALYSIS OF THE WANECAM CLINICAL TRIAL PLATFORM OUTPUT

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10.1136/bmjgh-2016-000260.35

Background The pharmacologic characteristic of piperaquine (PPQ), namely its very long half-life, raises concerns on the possibility of relatively rapid rise of resistance. Recent unequivocal reports from SE Asia support this worry. Due to its long half-life, conventional follow-up of up to 63 days in efficacy trials misses the low concentrations of PPQ, prone to select less sensitive parasite sub-populations. The WANECAM clinical trials included a follow-up of two years of the same patients, allowing for the first time the analysis of both, the patterns of selection upon an expected large range of PPQ concentrations and the potential effect of residual levels upon repetitive treatments.
Methods We have successfully determined a random sample of E1 (D0) 151 and 405 (E2-E10) pfcrt K76T genotypes, as well as 151 E1 (D0) and 389 (E2-E10) genotypes for the pfmdr1 E2-E10 episodes. Pfmdr1 N86Y analysis was limited by a large (>90%) prevalence of the 86N allele. Established PCR-RFLP methods were applied, with high precision band analysis being performed through image analysis software (GelEval®). Qui Square and Kruskal Wallis tests were used as applicable.
Results The present data analysis was limited to episodes with an intervening period of<180 days. Preliminary conclusions point to recurrences of pfmdr1 carrying 184Y parasites to emerge earlier as compared with 184F (D78 *vs* D89, Kruskal Wallis test, p< 0.01), corresponding to an expected difference of ca. 20 to 10 nM on PPQ blood levels. No significant differences were detected concerning pfcrt K76T.
Conclusions Long-term analysis of molecular markers throughout repetitive treatments is expected to unveil informative patterns concerning early steps of PPQ resistance development. The complete set of data will be presented and analysed in the context of the recent findings of PPQ resistance in SE Asia. Its relevance for the East African settings will be discussed.

OA-030 IMMUNOGENS DESIGNED FOR TARGETING NEUTRALIZING EPITOPES OF HIV-1 ENVELOPE GLYCOPROTEIN

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10.1136/bmjgh-2016-000260.36

Background Due to its unique challenge of establishing lifelong reservoirs a successful HIV-1 vaccine must elicit protective antibodies responses at the portals of entry. Broadly neutralising antibodies (bnAb) have been demonstrated not only to be therapeutic through suppressing viraemia in HIV-1 infected people but also preventive in blocking HIV-1 infection in animal models. This implies that a desirable HIV-1 vaccine candidate should be able to induce HIV-1 specific bnAb with an extensive ability to neutralise a broad range of HIV-1 isolates. Although several bnAb are known to target conserved regions in the HIV-1 envelope glycoprotein, no vaccination strategy has successfully produced such antibodies. Thus, the ability to optimise and deliver HIV envelope immunogens that can induce bnAb has remained a formidable challenge.
Methods To optimise immunogens for inducing bnAb, our group has pursued two main directions. In the first instance we developed B cell immunogens mimicking the native HIV-1 enveloped gp120 glycoprotein. Supernatants of stably transfected mutant lec1 CHO cells using a flag tag. We next assess antibodies isotypes specific to this immunogen in plasma obtained from antiretroviral naive participants. Secondly, through surface engineering of the evolutionary phage Qbeta we built in several epitopes of bnAbs for effective delivery to the immune system. We next assess in plasma from 648 seropositive participants the abundance of antibody isotypes specific to these B cell immunogens.
Results The results obtained showed that all IgG isotypes were detected for both the manosylated and CHO wild-type expressed gp120. Although all IgG antibody isotypes including IgG1, IgG2, IgG3 and IgG4 were dictated, there was no significant difference between antibody titres directed to manosylated gp120 and wild-type gp120. Well over 87% of seropositive participants showed specific antibody responses to conserved B cell epitopes displayed on the surface of Qbeta phage.
Conclusions These novel immunogens can be used as vaccine candidates.

OA-031 PROGRESS IN THE DEVELOPMENT OF SAFE AND EFFECTIVE TUBERCULOSIS VACCINES

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10.1136/bmjgh-2016-000260.37

Background Tuberculosis (TB) is the largest cause of mortality due to a single infectious agent. There were ~9.6 million cases of TB and ~1.5 million TB deaths in 2014, of which over 80% occurred in low- and middle income countries. In 1993, TB was declared a public health emergency by the World Health Organisation. Multidrug- and extensively drug-resistant TB is becoming increasingly common and adding significantly to the burden of disease. We will not meet the target of the WHO End TB Strategy of TB elimination by 2035 unless new interventions, drugs, diagnostics, and vaccines, become available. Modelling has demonstrated that elimination of TB is most likely to be achieved with new and effective TB vaccines. Effective and safe TB vaccines will also address the global crisis of drug resistant TB. The development of safe and effective TB vaccines is achievable as the human immune response does control TB in some circumstances – the highest risk of TB disease is within two years of skin test conversion, 90% of people with latent TB infection never develop TB disease, and BCG vaccine does provide partial protection. The probability of success is improved by significant progress in the field and the availability of new tools such as the robust use of improved animal models, increased diversity of mechanisms of action, combination vaccines, use of alternative routes of administration and stringent stage gates to concentrate resources of those vaccines most likely to succeed. New tools such as a controlled human infection model are in development, and novel clinical trial designs and use of special populations allow more streamlined studies and potentially earlier proof of concept. Globally, there are currently 13 TB vaccines in various stages of clinical development and efficacy data will be available from some of these candidates within one to three years.

OA-032 COMMUNITY ENGAGEMENT IN TB VACCINE RESEARCH AND DEVELOPMENT IN ZAMBIA

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10.1136/bmjgh-2016-000260.38

Background Community engagement (CE) is an essential component of clinical research. In 2000, the National Institute of General Medical Sciences recommended that researchers obtain community input into all phases of research, respect communities as partners, and establish appropriate community review procedures.
Method: Aeras incorporated CE activities into all its studies and continues to seek input from communities into Aeras-conducted clinical trials.
Results In Zambia, Aeras conducts TB vaccine clinical trials in collaboration with Zambia AIDS Related Tuberculosis (ZAMBART) Project and the Centre for Infectious Disease Research in Zambia (CIDRZ). Through an established CE program communities have received information on, and provided input to, the design and conduct of clinical trials. CE has provided a very useful avenue for communication between communities where clinical trials are being conducted and researchers.
Conclusions The presentation will highlight CE activities related to TB vaccine clinical trials and their impact, and will promote discussion on the utility of CE activities in Zambia and elsewhere. The impact of funding shortfalls for CE will be discussed. As CE is an essential component of clinical trials continuous evaluation, it is important to ensure it remains effective and addresses changing knowledge and beliefs.

OA-033 THE RESULTS OF THE EV06 DNA-PROTEIN COMBINATION TRIAL AND PLANS FOR GREAT, AN EDCTP2-FUNDED CONSERVED-MOSAIC EPITOPE HIV VACCINE TRIAL

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Background These two trials under Europe-Africa collaborations aim at addressing two factors relevant for Africa i.e helminth infections and HIV-1 diversity. EV06 used a novel combination of DNA expressing clade C Env, Gag and Pol-nef co-administered with AIDSVAX®B/E Env protein to study the effect of *S. mansoni* on vaccine responses. GREAT is a recently awarded trial using a 2nd generation improved conserved tHIVConsvX T-cell vaccine candidate combined with bivalent mosaic design to increase breadth and protective epitopes.
Methods EV06 enrolled 72 males and females aged 18–45, half infected with *S. mansoni* (SM+). In each arm 30 received vaccine and 6 placebo at week 0, 4 and 24. Responses were evaluated at week 0, 6, 26 and 36. Humoral responses were measured as binding IgG against a panel of HIV-1 envelope glycoproteins and as neutralizing antibodies (Nabs), using TZM/ bl cells and tier 1 pseudoviruses. Cellular responses were measured as HIV-specific CD4+ and CD8+ T-cell by IFN-γ ELIS-pot and multi-cytokine intracellular staining flow cytometry. GREAT will be a phase IIa trial and preparation for efficacy trials in Kenya, Uganda and Zambia testing ChAdOx1.tHIVconsv5 and ChAdOx1.tHIVconsv6 followed by MVA.tHIVconsv3 and MVA.tHIVconsv4 on week 2 (Arm 1) or week 8 (Arm 2).
Progress Differences in binding IgG response rates were observed in vaccinated participants against the vaccine matched clade C V1V2 (gp70–96ZM651.02 V1V2) at week 6: 56% among SM+ versus 86% among SM – (p=0.039). At week 36, response magnitudes were statistically lower in the SM+ against gp120 and gp140 proteins (p=0.04 for both). SM+ also had lower Nabs and ELISpot responses at various time points. Still blinded data on the first 20 volunteers show 80% responders for CD4 T cell at w26 and 70% CD8 responders at w36. These trials will provide more data on challenges facing HIV vaccine development in Africa.

ABSTRACTS OF POSTER PRESENTATIONS

PA-001 OCCURRENCE OF DAY 3 SUBMICROSCOPIC *PLASMODIUM FALCIPARUM* PARASITAEMIA BEFORE AND AFTER IMPLEMENTATION OF ARTEMETHER-LUMEFANTRINE TREATMENT POLICY IN TANZANIA

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Background Emergence of *Plasmodium falciparum* resistance against artemisinin in Southeast Asia raises a serious concern about the long-term efficacy of artemisinin-based combination therapy (ACT) globally. In Africa, ACT has remained highly efficacious with a microscopy determined asexual parasites clearance occurring within 48 hours post-treatment in most patients. However, submicroscopic parasitaemia has been reported on Day 3 after ACT treatment. We assessed the prevalence of patients with submicroscopic parasitaemia on Day 3 and its associated factors following treatment with artemether-lumefantrine (AL) from 2006 to 2014 in Bagamoyo district, Tanzania.
Methods Cytochrome b-nested polymerase chain reaction (PCR) was used for screening of submicroscopic parasitaemia from blood samples collected on filter paper on Day 3 post-AL treatment for acute uncomplicated *P. falciparum* malaria.

Primary outcome was proportion of patients with submicroscopic parasitaemia on Day 3 from 2006 to 2014. Secondary outcomes included proportional difference in submicroscopic parasitaemia across years, association of pre-treatment characteristics with submicroscopic parasitaemia, and association of submicroscopic parasitaemia with recurrent infection.

Results Only 2/584 (0.34%) of the screened patients had microscopy determined parasitaemia on Day 3, whereas, 256/584 (43.8%) had submicroscopic parasitaemia. Submicroscopic parasitaemia prevalence increased from 28% (14/50) in 2006 to 74.2% (132/178) in 2007–8, and thereafter declined to 36% (50/139) in 2012–13 and 27.6% (60/217) in 2014, with the likelihood of being positive for submicroscopic parasitaemia decreasing by 14.7% (95% CI: 9.5–19.7%, p<0.001) for an increase in year by one. Pre-treatment parasitaemia >100,000/μL, haemoglobin <10 g/dL, fever, being aged <5 years and year of study 2007–8 and 2012–13 were associated with the presence of submicroscopic parasitaemia. There was no association between submicroscopic parasitaemia and recurrent infection.

Conclusions Day 3 submicroscopic parasitaemia was common in patients treated with AL before and after implementation of the policy, and changed considerably across years from 2006 to 2014, however, its presence was associated with pre-treatment characteristics.

PA-002 EVIDENCE OF *PLASMODIUM FALCIPARUM* RESISTANCE TO SULPHADOXINE-PYRIMETHAMINE (SP) IN PREGNANT WOMEN ALONG THE SLOPE OF MOUNT CAMEROON

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Background Malaria in pregnancy (MiP) has debilitating effects for both mother and neonate, with intermittent preventive treatment in pregnancy (IPTp) central to successful malaria control and management in this vulnerable group. However, the effectiveness of IPTp with sulphadoxinepy-rimethamine (SP) is threatened by the emergence of drug resistant *Plasmodium falciparum* parasites vastly documented in some settings but not in south-western Cameroon. This study sought to ascertain the level of resistance of natural parasite populations to SP in this area.

Methods A total of 358 parturients were enrolled through a cross-sectional survey from May to October 2015. Malaria parasitaemia was determined by light microscopy using Giemsa-stained thick and thin smears of the peripheral blood, while DNA was extracted from dried blood spots of *P. falciparum*-positive samples by the Chelex-PBS method. SNPs in *pfdhps* and *pfdhfr* were then genotyped by nested polymerase chain reaction followed by allele-specific restriction analysis (ASRA).

Results A total of 47 women (13.1%) had MiP, with a geometric mean parasitaemia density of 1064 parasites/μl of blood. The weight (p=0.038), gestational age (p=0.001), IPTp-SP usage (p< 0.001) and IPTp-SP dosage (p=0.001) of parturients were identified as risk factors of malaria parasitaemia. Overall, 76.5% (274/358) and 60.3% (216/358) of the women took IPTp-SP and two or more SP doses, respectively. Participants who had taken IPTp-SP (p=0.009) and two or more SP doses (p<0.001) had lower parasite loads compared to non-IPTp-SP users and those who had taken one dose or less, respectively. The Pfdhps K540E substitution was absent in the area, the prevalence of Pfdhfr S108N and Pfdhps A581G was 97.6% and 51.1%, respectively.

Conclusions These results show the value of IPTp-SP usage and dosage in malaria parasitaemia control, in spite of the high prevalence of *P. falciparum* resistance to SP in the area, with implications for the control of malaria in this vulnerable group.

PA-003 CHLOROQUINE-SENSITIVE *PLASMODIUM FALCIPARUM* IN A HIGH-BURDEN MALARIA AREA AFTER OVER A DECADE OF ITS WITHDRAWAL AS FIRST-LINE ANTIMALARIAL MEDICINE: CASE OF NCHELENGE DISTRICT

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Background *Plasmodium falciparum* (*Pf*) resistance to antimalarial drugs remains a major hindrance to malaria control and elimination. *Pf* has developed resistance to nearly all antimalarial drugs including chloroquine, the first most frequently used first-line treatment for uncomplicated malaria. In Zambia, chloroquine was used as treatment for uncomplicated malaria for a long time until *Pf*-developed resistance and rose to as high as 60% in some parts of the country. This prompted the Ministry of Health to effect a drug policy change in 2003. Recent reports have indicated recovery of chloroquine susceptibility in neighbouring like Malawi, Mozambique and Tanzania. To update the information on chloroquine sensitivity in Zambia we conducted a study that assessed the prevalence of mutant *Pf* in Nchelenge district 10 years post chloroquine withdrawal.

Methods Dried blood spots for this study were collected from finger-prick blood of consenting pregnant women. Deoxyribonucleic acid (DNA) was extracted and genotyped for *Pf*crt-76 resistance marker using specific primers in a nested polymerase chain reaction (PCR). The PCR products obtained were then pyrosequenced and read using PyroMarkTM Q96MD software. The wild-type 3D7 and Dd2 were used as wild-type and mutated controls.

Results No chloroquine resistance mutation, Pfcrt 76T was detected in any of the 302 samples that were successfully amplified. This represents a 100% prevalence of *Pf* that are sensitive to chloroquine in the study population.

Conclusions This study demonstrates a total return of chloroquine-sensitive *Pf* in Nchelenge after over a decade of withdrawal of chloroquine. In combination with another drug, chloroquine could be a good substitute for the currently used artemether lumefantrine, and intermittent preventive treatment in pregnancy (IPTp) and children.

PA-004 EFFECT OF ARTESUNATE MONOTHERAPY ON *PLASMODIUM FALCIPARUM* IN VIVO GENOMIC EXPRESSION

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Background Artemisinin-based combination therapies (ACTs) are the main treatment for malaria in endemic countries. *Plasmodium falciparum* resistance to artemisinins is described as

delayed parasite clearance, which is associated with mutations on the parasite K13 propeller gene. Both the mechanisms of action and mechanisms of resistance to artemisinins are poorly understood. Transcriptomic studies can help in improving our understanding of these processes. Here we explore *P. falciparum in vivo* RNA expression profile after a curative dose of artesunate monotherapy.

Methods During a prospective study of the efficacy of artesunate in monotherapy in children aged 1–10 years and presenting uncomplicated *P. falciparum* malaria in Bougoula-Hameau, Mali, venous blood was collected on PAXgen blood RNA tubes before treatment (H0) and one (H1), two (H2) and three hours (H3) after treatment. RNA was extracted from these respective blood samples and used for microarray experiments with *Plasmodium*/*Anopheles* GeneChips and the Affymetrix® platform.

Results A total of 23 samples from 6 patients were included in the final analysis after quality control using Affimetrix® and Qlucore® softwares. With a 2-groups comparison of H0/H after treatment, 236 genes were identified as differentially expressed. Overall 42 genes were up-regulated including a knob-associated histidine-rich protein, rifins (pf.12.409.0, pf.13_399.0), stevors (pf.3.184.0), RESA-like proteins with DNAJ domain and thioredoxins. Heat shock protein (Pf.5.258.0), a number of AP2 domain-containing genes (Pf.6.27.0, Pf.11.99.0), an ABC transporter (Pf.12.250.0), genes involved in cell cycle regulation and many exported protein genes with unknown function and membrane proteins genes were among the 194 down-regulated genes.

Conclusions Our data support a role for these genes in the *in vivo* response of *P. falciparum* to artesunate administration.

PA-005 LIMITED IMPACT OF TREATMENT AND RE-TREATMENT WITH ARTEMETHER-LUMEFANTRINE AND ARTESUNATE-AMODIAQUINE ON THE SELECTION OF *PLASMODIUM FALCIPARUM* MULTIDRUG RESISTANCE-1 ALLELES

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Background The emergence of resistance against artemisinin combination treatment (ACTs) is a major concern for malaria control. ACTs are recommended as rescue treatment; however, there is limited evidence on the impact of treatment and re-treatment with ACTs on selection for drug-resistant parasites. We aimed to investigate the impact of treatment and re-treatment using artesunate-amodiaquine (ASAQ) and artemether-lumefantrine (AL) on the selection of *Plasmodium falciparum* multidrug resistance-1 (Pfmdr1) alleles.

Methods A total of 776 isolates were collected in 28-days follow-up involving children aged 0–59 months in a clinical trial in the Democratic Republic of Congo and Uganda. Nested PCR and RPFL was used to detect *Pfmdr1* single-nucleotide polymorphisms at codons N86Y, F184Y, and D1246Y. The analysis compared *Pfmdr*1 alleles in the pre-randomisation (pre-RCT), randomisation (RCT) and post-randomisation (post-RCT) phases of the trial.

Results The pre-treatment prevalence of *Pfmdr*1 (N86 and D1246Y) in the RCT phase varied significantly between the sites. *Pfmdr*1 *NYD* haplotype was significantly higher in Uganda while haplotype *YYD* was higher in the Democratic Republic of Congo, ($p<0.001$). Comparison between pre-treatment and post-treatment adequate clinical and parasitological response (ACPR) or PCR-adjusted treatment failure did not indicate increased selection of *Pfmdr*1 N86, D1246 and Y184 in either AL or ASAQ arm in the pre-RCT, RCT and post-RCT phases. The relative risk (RR) of treatment failure (TF) in patients harbouring *Pfmdr*1 N86 did not significantly increase in patients treated with AL (RR=0.2, 95% CI: 0.11–1.05, p=0.061) or ASAQ (RR=1.03, 95% CI: 0.47–2.26, p=0.94).

Conclusions Our findings suggest the limited impact of treatment and re-treatment with AL or ASAQ on selection for *Pfmdr1* variants and haplotypes associated with resistance to partner drugs. These findings support the recent WHO recommendation to use ACTs as alternative rescue therapy for *P. falciparum* malaria. However, enhanced resistance monitoring is warranted to maintain the drug's effectiveness in endemic settings.

PA-006 PF3D7_1343700 KELCH PROPELLER (K13-PROPELLER) POLYMORPHISMS AND ARTESUNATE MONOTHERAPY EFFICACY IN UNCOMPLICATED MALARIA TREATMENT IN MALI

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Background Several mutations in the PF3D7_1343700 kelch propeller (K13-propeller) were recently described as associated with artemisinin resistance *in vivo* and *in vitro* in Southeast Asia. In Mali, a preliminary study on artesunate efficacy in 2011 found no delay in parasite clearance. A larger study including two sites in Mali is conducted here in the context of regular monitoring of artemisinin resistance.

Methods From October 2015 to March 2016, we conducted a prospective study on artesunate monotherapy in Bougoula-Hameau and Faladje on uncomplicated malaria patients aged more than 6 months. Patients were treated for 7 days and followed up for 28 days. Blood smear was performed for parasite evaluation every 8 hours until three consecutive slides were negatives. MSP2, Ca1 and TA99 polymorphisms were used to distinguish new infections from recurrent parasites. The PfK13 mutations were genotyped using direct sequencing of PCR amplicons from dried blood spots of pre and post-treatment *falciparum* parasites. The results were compared with the studies conducted in a same area on 2011.

Results A total of 100 and 120 patients were enrolled in Bougoula-Hameau and Faladje, respectively. The uncorrected adequate clinical and parasitological responses (ACPR) were 92.0% in Bougoula-Hameau and 78.3% in Faladje. After molecular correction, we obtained 100% cACPR in both sites. The prevalence of the non-synonymous single nucleotide polymorphisms (SNPs) *K13* was 2% in Bougoula (found only at enrolment) but null in Faladje. However SNPs were 3% and 7% in Bougoula-Hameau and Faladje, respectively.

Conclusions Artesunate monotherapy remains effective on *P. falciparum* in Mali and there are only low levels of PfK13 mutations.

PA-007 VARIABILITY IN CLINICAL RESEARCH DATA MANAGEMENT PRACTICES: LESSONS FROM THE MALARIA COMMUNITY

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Background Appropriate data management (DM) is critical to produce valuable research data, especially with growing prospects for long-term archiving, sharing and individual patient data meta-analysis. The experience of the WorldWide Antimalarial Resistance Network (WWARN) in handling data from clinical studies is that DM practices vary greatly, which affects curation and optimal use of shared data. Our work explores how clinical trial data are usually managed and why this varies. We aim to understand the needs in DM systems (DMS) for resource-limited research settings within low- and middle-income countries (LMICs).

Methods Using published literature and discussions with key informants, we developed a semi-quantitative instrument to assess the robustness of the initial DMS and the resulting 're-usability' of clinical research data. We also defined study covariates which could account for the observed variability (e.g. type of sponsor/funding, partners involved, trial phase). The strength of correlations between indicators of good DM practices, resulting data quality and study context will be tested through statistical modelling.

Results The instrument covers the following dimensions of data robustness: meta-data availability, comprehensiveness and exhaustiveness; dataset completeness; and data accuracy. It is currently being piloted on a subset of 20 studies (about 5% of the total WWARN database), to test its applicability in highlighting DM practices' variations and in capturing other relevant study characteristics. After finalisation of the instrument, the analysis will be rolled out to 150 studies. We will present the patterns and correlations between specific indicators and study covariates we observe within this randomly selected sample, and discuss their implications in terms of DM capacity-strengthening.

Conclusions The significance of quantitative findings will be challenged using qualitative interviews and visits at institutions for in-depth case studies of DM practices. Results of the overall mixed-methods work could inform strategies for clinical research DM capacity-strengthening in LMICs, including initiatives relevant to the European & Developing Countries Clinical Trials Partnership (EDCTP).

PA-008 THE QUEST FOR BUILDING LABORATORY CAPACITY TO SUPPORT CONTROLLED HUMAN MALARIA INFECTION (CHMI) STUDIES IN SUB-SAHARAN AFRICA: EXPERIENCE WITH FIVE SITES

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Background Conducting Controlled Human Malaria Infection (CHMI) studies in sub-Saharan Africa presents unique challenges yet it provides enormous opportunities for fast-tracking malaria vaccine and drug development. Sanaria Inc. USA, has devised methods of producing, characterising and shipping aseptic, purified, cryopreserved *Plasmodium falciparum* sporozoites (PfSPZ). Unlike in the past, the sporozoites can be shipped to any field site including malaria-endemic countries in sub-Saharan Africa. CHMI studies need cutting-edge laboratory capacity to allow screening of potential study participants for their eligibility, perform safety tests, efficacy testing of the investigation product, and determine immune markers, responses and parasite kinetics.

Methods The sites were identified within sub-Saharan Africa, based on local population, malaria epidemiology status and clinical research capacity. The laboratory assays, equipment and consumables were identified. The methods and procedures were optimised, standardised and documented. The laboratory technical team were selected and trained. EDCTP provided financial support whilst Sanaria Inc. provided technical support.

Results The capacity strengthening successfully supported CHMI studies in five sites in Africa namely; IHI, Bagamoyo, Tanzania; KEMRI CRC, Nairobi, Kenya; EGMVI, Malabo Equatorial Guinea; CERMEL, Lambarane, Gabon; KEMRI-CDC, Siaya-Kenya and KEMRI-WT, Kilifi Kenya. Capacity strengthening was aimed at clinical and immunology laboratory systems required for CHMI studies.

Conclusions As more CHMI studies are anticipated, vigorous capacity strengthening will be required for laboratory facilities in Africa to accelerate the evaluation of malaria vaccines, antimalaria drugs, diagnostic assays and assessment of host immune response to malaria infection.

PA-009 EFFICACY AND TOLERABILITY OF REPEATED ADMINISTRATION OF ACTS OVER A PERIOD OF TWO YEARS IN CHILDREN AND ADULT PATIENTS WITH ACUTE UNCOMPLICATED MALARIA IN BURKINA FASO

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Background According to the guidelines of the Burkina Faso National Malaria Control Programme, artesunate-amodiaquine (ASAQ) and artemether-lumefantrine (AL) are the first-line drugs for uncomplicated malaria treatments. However, in some contexts where individuals will experience more than 1 episode of clinical malaria per year, it is unknown to what extent giving any of these ACTs repeatedly is safe. In the framework of the activities of the West African Network for Antimalarial Drugs (WANECAM) network, we have compared the efficacy and tolerability of repeated use of dihydroartemisinin-piperaquine (DHA-PQ) or artesunate-pyronaridine (PYR) with artesunate-amodiaquine (ASAQ).

Methods A randomised open-label parallel 3 arms trial was conducted to compare the efficacy of a three-day regimen of DHA-PQ and PYR with ASAQ. The trial involved children and adults with uncomplicated falciparum malaria. Participants were randomly assigned to one of the three treatment arms at the first clinical episode. During the subsequent clinical episodes, the same drug was administered. Follow-up duration was 42 days for each episode. Study duration was two years for each participant. Primary endpoints were the incidence rate of uncomplicated malaria over a period of 2 years and PCR corrected/uncorrected ACPR at day 28 and day 42. Safety parameters were also assessed.

Results Of the 763 patients enrolled, the incidence rate of clinical malaria was 1.4, 1.2, and 1.5 episodes / person-year at risk in the ASAQ, DHA-PQ and PYRAMAX arms, respectively. The PCR-uncorrected efficacy at day 28 versus day 42 was: ASAQ 93.4% *vs* 79.5%; PYR 98.1% *vs* 74.8%; and DHA-PQ 99.5% *vs* 95.2%. Bronchitis, rhinitis, abdominal pain, cough, QTc prolongation, headache, and vomiting were registered as the main adverse events in each of the three groups.

Conclusions The findings from our study support the current recommendations for using artemisinin-based combinations in the treatment of uncomplicated malaria in areas of high malaria transmission such as Burkina Faso.

PA-010 EFFICACY AND SAFETY OF ARTEMISININ-BASED COMBINATION THERAPIES IN PEOPLE WITH *PLASMODIUM FALCIPARUM* MALARIA RECEIVING ANTIRETROVIRAL THERAPY IN ZAMBIA

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Background The coverage of Artemisinin-based Combination Therapies (ACTs) for treatment of malaria and antiretroviral therapy (ART) is increasing rapidly in Sub-Saharan Africa. Because of the geographical overlap in areas of high malaria and HIV prevalence, HIV-infected people receiving ART may become malaria-infected and will need ACTs.

However, few studies have assessed the safety and efficacy of administering ACTs in people taking ART. The interactions might lead to high ACT drug levels which might cause toxicity or low drug levels which might adversely affect malaria parasite clearance, thereby fuelling resistance.

Methods We conducted a phase IIIb single arm (non-comparative), open label clinical trial. We enrolled and followed up 155 patients at St. Paul's Hospital in Nchelenge district of Zambia. The patients were enrolled in the study after they consented to participate and met strict inclusion and exclusion criteria.

Results Patient enrolment was completed in September 2015. The results of this study are currently being analysed.

Conclusions Data on the safety and efficacy of ACTs in people taking different types of ART are lacking since previous regulatory trials have systematically excluded HIV-positive people, including those receiving ART. Thus, the results of our study will assist in the following ways: determine whether HIV-infected individuals receiving specific types of ART require a specific type of ACTs, inform clinical practitioners about what sort of adverse events they should expect and monitor in people taking different combinations of ACTs and ARTs, and provide evidence-based recommendations to the WHO and National Malaria Control Programmes on safe and effective ACTs that can be used in patients' EFV-based regimen. This study was part of a multicentre trial including centres in Malawi and Mozambique.

PA-012 GAMETOCYTE CARRIAGE AFTER A TREATMENT WITH PRIMAQUINE COMBINED WITH DIHYDROARTEMISININ-PIPERAQUINE IN MALARIA-INFECTED, ASYMPTOMATIC INDIVIDUALS

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Background With the decrease of malaria burden, additional interventions capable of interrupting transmission from human to mosquitoes are required to achieve malaria elimination. Primaquine (PQ) is the only antimalarial drug recommended against mature gametocytes; however, its use has been limited because it causes a dose-dependent haemolytic anaemia. A clinical trial was conducted in The Gambia to evaluate the impact of dihydroartemisinin-piperaquine (DP) with and without PQ on gametocyte carriage and infectiousness to mosquitoes. As an ancillary study, we compared the efficacy of the four different treatments in asymptomatic *Plasmodium falciparum*-infected individuals.

Methods The main study was a four-arm, open label, randomised-controlled trial comparing the effect of three different single doses of PQ (0.75 mg/kg, 0.4 mg/kg, and 0.2 mg/ kg) on gametocyte carriage in malaria-infected, asymptomatic individuals with normal glucose-6-phosphate dehydrogenase status. All treatment arms received DP with the fourth arm acting as control. Our ancillary study aimed to determine the duration of gametocyte carriage in the PQ groups compared to the control group and to assess the adequate and clinical response of treatment (ACPR) at day 42 of follow-up.

Results A total of 694 individuals were enrolled; 175 were randomised to the control, 172 to the 0.75PQ, 175 to the 0.4PQ, and 172 to the 0.2PQ arms. The hazard ratio (HR) of gametocytes carriage was significantly longer in the control group compared to each of the PQ arms; 1.8 (1.2–2.6 p=0.002) in 0.75PQ, 1.5 (1.0–2.1 p=0.03) in 0.4PQ and 1.5 (1.0–2.1 p=0.04) in 0.2PQ. At day 42, ACPR was 97.04%; 95.48%; 92.45%; 99.37% in DP group; 0.75PQ; 0.4PQ and 0.2 PQ, respectively.

Conclusions Adding PQ to DP shortens the duration of gametocyte carriage and the adequate and clinical response of treatment (ACPR) is high.

PA-013 COMPARISON OF AUTOMATIC AND MANUAL MEASUREMENT OF QT AND QTC INTERVALS DURING A CLINICAL PHASE III-B/ IV IN KOLLE, MALI

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Background The detailed assessment of the QT and corrected QT (QTc) intervals prolongation is recommended when testing new drugs. The electrocardiograph automatically displays generally reliable values of the QT interval and corrected QT but morphological variations of the T wave may cause reading errors, hence the use of the manual measurement as an alternative method. Our objective was to evaluate the correlation between the automatic and manual measurement of QT values.

Methods In Kolle from March 2012 to December 2015, an open randomised, phase III-b/IV study comparing dihydroartemisinine-piperaquine, pyronaridine-artesunate and artemether-lumefantrine was conducted. An electrocardiograph cartridge 12 electrodes coupled to a computer with the Tele Touch software was used for the electrocardiogram on Day 0 before the study drugs administration and on Day 2, 2–4 hours after the administration of the last dose of the antimalarial. The manual measurement of QT and QTc was made using the Bazett method [QTcB_m=(Number leaded×0.04×QTcF) / QTcB]. For prolonged QTc cases on Day 2, another measurement was done during the next scheduled visit (Days 7, 14, 21, 28, 35 and 42) until the QTc normalisation.

Results A total of 764 ECG was recorded with 398 participants. Different automatic and manual values of QT and QTc are scattered around different medium. Comparisons of different values of QT ($p=0.1245$) and QTc ($p<0.001$) showed a statistically significant differences and the concordance between automatic and manual tests was QT: Rho_c=0.77 and QTc: Rho_c=0.46.
Conclusions Our results indicate no perfect match between automatic and manual methods for QT and QTc. Manual reading remains important to correct any machine errors during clinical studies.

PA-014 CXCL10 GENE PROMOTER POLYMORPHISM – 1447A>G IS ASSOCIATED WITH MALARIA IN GHANAIAN CHILDREN

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Background Recent studies indicate that interferon gamma inducible chemokine, CXCL10, is a strong predictor of both human and experimental cerebral malaria. We hypothesised malaria infection is associated with variation in CXCL10 expression. We determined whether polymorphisms in the CXCL10 gene promoter region played a role in the clinical status of malaria patients and addressed the genetic basis of CXCL10 expression during malaria infection.
Methods Basic demographics that may impact our assessments including age, gender, full blood count, sickle cell status and CXCL10 polymorphism were assessed. We assessed a single nucleotide polymorphism in the CXCL10 promoter (–1447A>G [rs4508917]) among 382 malaria and 117 non-malaria subjects using PCR-restriction fragment length polymorphism assay. Adjusted Odds Ratio (AOR) was used to find out if there was any association between CXC10 promoter polymorphism –1447 A>G and susceptibility to malaria.
Results The median age for malaria patients was 4 years and that for non-malaria was14 years. There was significant difference with regards to haemoglobin levels and White cell counts between malaria patients and non-malaria subjects ($p<0.0001$). Individuals with the 21447(A/G) genotype were susceptible to malaria (adjusted odds ratio [AOR]=2.60, 95% CI: 1.51–5.85, $p=0.021$). Additionally, individuals with the 21447(A/G) genotype had significantly higher plasma CXCL10 levels than individuals with the 21447(A/A) genotype. Stratifying patients according to gender, the observed association of malaria with over expression of CXCL10 were more pronounced in females than in male patients (AOR=5.47, 95% CI: 1.34–22.29, $p=0.018$).
Conclusions Polymorphisms in the CXCL10 gene promoter sequence were associated with increased CXCL10 production, which is linked to severity of malaria. These results suggest that the 21447A>G polymorphism in CXCL10 gene promoter could be partly responsible for the reported variation underlying severity of malaria outcomes particularly in females.

PA-015 GENE VARIATION AND SUSPECTED *PLASMODIUM FALCIPARUM* HISTIDINE-RICH PROTEIN 2 GENE DELETION AND ITS IMPACT ON SENSITIVITY OF MALARIA RAPID DIAGNOSTIC TESTS IN SUDAN

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Background Malaria rapid diagnostic tests (RDTs) play a significant role in malaria case management and case investigations. Variability or absence of antigens targeted by PfHRP2-based RDTs have been reported worldwide. However, little data is available concerning genetic variability within Sudanese *Plasmodium falciparum* isolates while variable sensitivity of PfHRP2 based RDTs has been observed. The objective was to find out the possible effect of PfHRP2 gene variation and suspected deletion on the performance of PfHRP2-based RDTs.
Methods Seventy-seven *P. falciparum* isolates were selected from three geographical regions of Sudan. Malaria HRP2-RDTs and Giemsa-stained blood films data were included for analysis. The *pfhrp2* exon 2 fragments were amplified to study genetic variation and suspected deletion. Chi-square test was used for testing significance of results.
Results Forty percent (31/77) of *P. falciparum* isolates showed amplification for PfHRP2 (which revealed five alleles of different sizes), whereas 60% of isolates were PfHRP2 PCR-negative. There is a concordance of positive and negative rates on PfHRP2 RDT and gene amplification results of (35%) and (33%) respectively. Eighty-seven percent (78%) of RDTs positive isolates were PfHRP2 negative (p-value=0.001), while 4 out of 31 *pfhrp2* positive isolates gave false negative results in RDT detection. Twenty out of 47 RDTs positive isolates were PfHRP2 negative (p-value=0.001). *Plasmodium falciparum* HRP2-RDTs showed higher sensitivity than microscopy in malaria detection (p-value=0.007).
Conclusions The study provided baseline data on genetic variation and suspected deletion in PfHRP2 and its potential effect on RDT performance.

PA-016 RE-EVALUATION OF MALARIA DIAGNOSIS BY MOLECULAR METHODS REVEALS MUTATIONS IN HRP-2 AND DRUG RESISTANCE MARKERS IN CAMEROON

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Background As the decline in malaria cases becomes obvious in most sub-Saharan African countries, a new major concern is accurate diagnosis of low parasitaemia which can cause subpatent infections and false-negative Rapid Diagnostic Test (RDT) results. We assessed the accuracy malaria diagnosis by RDT and microscopy are currently been conducted in Cameroon, by re-evaluating some samples from patients who sought medical care at three health centres in Yaounde. The study would provide information which can help the national malaria control program to reorient interventions strategies to enhance accurate diagnosis within the country.
Methods We undertook a research project within a period of six months to re-evaluate malaria confirmed cases by microscopy and RDT test (HRP2: SD BIOLINE Malaria Ag P.f/Pan: Optimal screening test for *P. falciparum* and other *Plasmodium species*). We used molecular methods such as nested PCR, in-house tailored loop amplified isothermal amplification (LAMP) and GenoType MalariaDR molecular assay to revalidate these samples. DNA was directly extracted from the RDT cassettes using qiagen spin columns.
Results Results showed discrepancies in malaria diagnosis by microscopy, RDT, PCR, LAMP and GenoType MalariaDR. Most false negatives results (RDT negative but positive by microscopy and molecular methods) are linked to low parasite density

usually<150 asexual parasites/µl. However, there were some cases where higher parasite density >5,00/µl could lead to false negative results (linked to a deletion of about 870 bp in the HRP-2 gene). GenoType MalariaDR revealed the presence of mutations on *Pfmdr1 and Pfcrt* associated with resistance to ART.

Conclusions The study provided factual information on the detected *P. falciparum* isolates, *HRP-2* mutations and the performance of RDTs and *Pfmdr1, Pfcrt* and *ART* resistance markers present in the population. The first-line of ACT in Cameroon is artesunate+amodiaquine, yet possible resistance isolates of amodiaquine and artesunate could be circulating in the country.

PA-018 SEASONAL MALARIA CHEMOPREVENTION WITH SULPHADOXINE-PYRIMETHAMINE AND AMODIAQUINE SELECTS DHFR-DHPS QUINTUPLE MUTANT GENOTYPE IN MALI

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Background Seasonal malaria chemoprevention (SMC) with sulfadoxine-pyrimethamine (SP)+amodiaquine (AQ) is being scaled up in countries of the Sahel in West Africa. However, the potential development of *Plasmodium falciparum* resistance to the respective component drugs is a major concern.

Methods Two cross-sectional surveys were conducted before (August 2012) and after (June 2014) a pilot implementation of SMC in Koutiala, Mali. Children aged 3–59 months received 7 rounds of curative doses of SP+AQ over two malaria seasons. Genotypes of *P. falciparum* dhfr codons 51, 59 and 108; dhps codons 437 and 540, pfcrt codon 76 and pfmdr1codon 86 were analysed by PCR on DNA from samples collected before and after SMC, and in non-SMC controls.

Results In the SMC population 191/662 (28.9%) and 85/670 (13.7%) of children were *P. falciparum*-positive by microscopy and were included in the molecular analysis before (2012) and after SMC implementation (2014), respectively. In the control population 220/310 (71%) were successfully PCR analysed. In the SMC children the prevalence of all molecular markers of SP resistance increased significantly after SMC including the dhfr-dhps quintuple mutant genotype, which was 1.6% before but 7.1% after SMC (p=0.02). The prevalence of Pfmdr1–86Y significantly decreased from 26.7% to 15.3% (p=0.04) while no significant change was seen for pfcrt K76T. In 2014, prevalence of all molecular markers of SP resistance were significantly higher among SMC children compared to the non-SMC control population (p<0.01). No dhfr – 164 mutation was found neither at baseline nor post SMC.

Conclusions SMC increased the prevalence of molecular markers of *P. falciparum* resistance to SP in the treated children. However, there was no significant flow of these resistance genes into the general parasite population after 2 years and 7 rounds of SMC.

PA-019 IMPACT OF TREATMENT OF UNCOMPLICATED MALARIA BY AMODIAQUINE–ARTESUNATE (AS-AQ) ON PFCRT 76T AND PFMDR1 86Y MUTATIONS SELECTION IN *PLASMODIUM FALCIPARUM* ISOLATES, REPUBLIC OF GUINEA

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Background The use of Amodiaquine monotherapy is associated with the selection of resistance markers (*Pfcrt* and *Pfmdr*1). The decrease in sensitivity and the emergence of *Plasmodium falciparum*-resistant strains have been reported.

It is therefore important to know the impact of treatment of uncomplicated malaria with amodiaquine–artesunate (AQ–AS) on *Pfcrt*76T and *Pfmdr*1 86Y mutations strains of *P. falciparum*.

Methods We applied the standard protocol of 28 days of WHO 2003, to determine the *in vivo* efficacy of the combination AQ–AS. In total 170 subjects were included in the study. Molecular analysis focused on 168 dried blood spots. The aims were to determine the frequency of *Pfcrt*76T and *Pfmdr*1 86Y mutations, to determine the rates of reinfection using polymorphism markers MSP1, MSP2, and microsatellite CA1, Ta87, TA99. Nested PCR followed in some cases by a restriction enzyme.

Results The level of *P. falciparum* clinical response was 92.85% (156/168) of ACPR before molecular correction and 7% (12/170) LPF. The ACPR after molecular was 97.01% (163/168). The frequency of mutation point *Pfcrt* 76T was 76.19% (128/168) before treatment and 100% (7/7) after treatment, p=0.14. For *Pfmdr*1 mutation the frequency was 27.97% (47/168) before treatment and 60% (6/10) after treatment, p=0.03. Rate of *Pfcrt*76T +*Pmdr*1 86Y was 22.02% (37/168) before and 50% (6/12) after treatment p=0.003.

Conclusions Despite the combination of AQ with AS, the treatment selected *Pfcrt*76T and *Pfmdr*1 86Y mutations in Guinea.

PA-020 FOSMIDOMYCIN-PIPERAQUINE AS NON-ARTEMISININ-BASED COMBINATION FOR ACUTE UNCOMPLICATED *PLASMODIUM FALCIPARUM* MALARIA

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Background As investment in research related to artemisinin resistance is a key objective of the Global Plan for Artemisinin Resistance Containment (GPARC), fosmidomycin and piperaquine are being developed to address the delay in parasite clearance following treatment with Artemisinin-based Combination Therapy (ACT). Though artemisinin resistance occurs principally in the Greater Mekong Region, there are concerns that it will emerge in sub-Saharan Africa.

Methods A proof-of-concept study has been conducted in Gabon to determine the efficacy, tolerance and safety of fosmidomycin and piperaquine when administered orally for three days. A total of 100 subjects, including 10 adults, 40 children aged 5–14 years and 50 children aged 1–5 years fulfilling the inclusion criteria of mono-infection with *Plasmodium falciparum* and initial parasite counts between 1,000 and 150,000/μL were enrolled and followed up for 63 days. The primary efficacy endpoint was per protocol, the PCR-corrected cure rate on Day 28. Safety endpoints included the incidence, severity, drug-relatedness and seriousness of adverse events and laboratory abnormalities. ClinicalTrials.gov Identifier: NCT02198807

Results The PCR-corrected 28-day cure rate in the older children was 100% (n=31). It was also 100% (n=38) in the younger children, a group deemed to be more therapeutically challenging on account of their lower immune status. Tolerance was excellent and there were no drug-related safety issues. Full results will be presented.

Conclusions Fulfilling the WHO criteria for combination therapy, fosmidomycin as a rapidly acting blood schizonticide and piperaquine with its prolonged post-treatment prophylactic effect have been shown to be highly efficacious for the treatment of acute uncomplicated falciparum malaria in an area of intense malaria transmission. Dose optimisation studies with the dual aim of achieving a reduction in the dose of fosmidomycin within a therapeutic regimen of once daily dosing are planned.

PA-021 SAFETY AND EFFICACY OF SAR97276A FOR TREATING MALARIA: TWO OPEN-LABEL MULTICENTER PHASE II CLINICAL STUDIES IN AFRICAN CHILDREN AND ADULTS

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Background SAR97276A, is a choline analogue inhibiting the phospholipid biosynthesis of *Plasmodium falciparum*. Treatment options for severe malaria are limited and SAR97276A represents a drug candidate for this indication.

Methods This is a report on two consecutive trials evaluating safety and efficacy of parenterally administered SAR97276A for the treatment of malaria.

The first study was a phase 2, multicenter, open-label study at six African hospitals (NCT00739206). At first adults with uncomplicated malaria were included receiving a single dose SAR97296A (IM: 0.18 mg/kg or IV: 0.14 mg/kg) followed by repeated dosing with daily administration of the IM dose for three days in case of lack of efficacy of the single-dose regimen before age de-escalation.

The second study was a phase 2, multicenter, randomized, controlled open label study at five African hospitals assessing safety and efficacy of a higher dose of SAR97276A IM once (0.5 mg/kg) or twice (0.25 mg/kg) daily for 3-days compared to artemether-lumefantrine in children 12–17 years before age de-escalation to younger children (NCT01445938).

Results In the first study 113 patients received SAR97276A: 30 adults single-dose IV, 34 adults single-dose IM, 30 adults 3-day dose IM and 19 children 3-day dose IM. SAR97276A given as a single-dose to adult patients showed insufficient efficacy by IM route (20 cured of 34; and IV route (23/30 cured). The 3-day treatment showed a sufficient level of efficacy when given IM to adults (27/30 cured) but not when given to children 7–17 years (13/19 cured).

In the second study 20 patients were recruited and randomly assigned (2:2:1 ratio) to receive once-daily SAR97276A, twice-daily SAR97276A or artemether-lumefantrine. All patients receiving SAR97276A once-daily and 5/8 patients receiving SAR97276A twice-daily required rescue therapy. All patients in the control group were cured.

Conclusion Both studies were stopped due to lack of efficacy. SAR97276A given as monotherapy up to three days is not efficaciously curing malaria.

The studies were funded by Sanofi.

PA-022 COMPARATIVE PROTECTIVE EFFECT OF REPEATED ADMINISTRATION OVER A TWO YEAR PERIOD OF 3 ACTS ON THE EMERGENCE OF HYPERPARASITEMIA IN MALARIA PATIENTS

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Background Hyperparasitaemia in malaria infection represents a worsening circumstance of the patient's condition; however, it still remains a concept with a controversial definition and seems likely to be understudied. The present study in the framework of the WANECAM activities aimed to assess the protective effect of 3ACTs on the emergence of the hyper-parasitaemia when repeatedly administrated over a period of two years to patients with uncomplicated malaria.

Methods A two-year prospective longitudinal study (763 adults and children) was conducted in a malaria endemic area of Burkina Faso. Passive detection of malaria cases with parasitaemia ≥200000 trophozoites/μl was done. Malaria smear was performed for hyperparasitaemia confirmation; a clinical examination and demographic data were recorded. Each patient was repeatedly treated with one of the three anti-malarials, pyronaridine-artesunate, dihydroartemisinin-piperaquine or artesunate-amodiaquine, at any uncomplicated malaria episode.

Results A total of 107 cases of malaria with hyperparasitaemia were diagnosed; 63.55% occurred in under-five years children. The geometric mean of parasite density was 283366 trophozoites/μl (CI 95%: 264644–302087). The 46 cases recorded in the pyronaridine-artesunate treatment arm (224 patients) was higher compared to the 39 cases in the artesunate-amodiaquine arm (315 patients), (p=0.0024) and to the 22 cases in the dihydroartemisinin-piperaquine arm (224 patients), (p=0.0022). The difference between dihydroartemisinin-piperaquine and artesunate-amodiaquine treatment arms was not statistically significant (p=0.40).

Conclusions From this study, children under five year of age were mostly at risk of hyperparasitaemia. Dihydroartemisinin-piperaquine and artesunate-amodiaquine seem the most protective antimalarial against the occurrence of hyperparasitaemia.

PA-023 ASSESSMENT OF SAFETY PARAMETERS FOLLOWING REPEATED ARTEMISIN-BASED TREATMENTS OF MALARIA-INFECTED PATIENT LIVING IN ENDEMIC AREA OF BURKINA FASO

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10.1136/bmjgh-2016-000260.60

Background Artemisinin-based combination therapies (ACTs) constitute the worldwide recommended antimalarial drug as first-line treatment of uncomplicated malaria. However, the safety of repeated administration of a given ACT is poorly documented. The aim of this study was to evaluate the safety of repeated administration of ACTs in malaria patients over a period of 2 years.
Methods A randomised, open-label phase IIIb/IV comparative three arms trial comparing pyronaridine tetraphosphate/artesunate (PA), dihydroartemisinine-pipéraquine (DHA-PQP) and artesunate-amodiaquine (ASAQ) was carried out in Burkina Faso site as part of the WANECAM (West African Network for Clinical Trials of Antimalarial Drugs) global study. The study involved patients from 6 months of age presenting with uncomplicated malaria (fever/history of fever and *Plasmodium* spp. density <200,000). The patients were treated repeatedly with the same ACT they were assigned to at enrolment. Safety assessments consisted with electrocardiographic and laboratory evaluations.
Results A total of 763 participants with uncomplicated microscopically confirmed *Plasmodium* spp. malaria were included. The proportion in ASAQ treated patients with creatinin abnormal value did not differ significantly between episode 1 and repeated malaria episodes (16.14% versus 13.98%, p=0.31). The proportion of patients with abnormal value of ALAT decreased significantly from baseline (25/234 versus 16/787, p< 0.01), but there is no difference in haemoglobin mean between the different episode (p>0.05) within each treatment arms. No evidence was found in the risk of QTc interval prolongation during repeated treatment in any arm.
Conclusions The findings showed that safety was similar on first malaria treatment versus retreatment of subsequent episodes. The safety parameters were also comparable between the 3 treatment arms. These results support the repeated use of the three ACTs in uncomplicated malaria patients in Burkina Faso.

PA-024 LUMEFANTRINE DISPOSITION AFTER REPETITIVE TREATMENT OF UNCOMPLICATED MALARIA PATIENTS WITH ARTEMETHER-LUMEFANTRINE IN MALI

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10.1136/bmjgh-2016-000260.61

Background Since 2006 the national malaria control program in Mali recommended artemether-lumefantrine (AL) as the first-line treatment of uncomplicated malaria. The role of lumefantrine in this combination is to eliminate remaining parasites after the action of artemether and to protect the patient against a new blood infection. Some studies showed a correlation between lumefantrine's day 7 concentration and the efficacy of AL after treatment of a single episode of malaria. The objective of this work is to validate this observation after repetitive treatment of uncomplicated malaria patients with AL.
Methods During a phase IIIb/IV comparative, randomised, multicentre, clinical study of artemisinin-based combination therapies, we collected plasma on Day 7 from patients treated with standard dose of AL in Sotuba, Bougoula Hameau, and Kolle (Mali). The age of the patients enrolled in this study was from 6 months old. The plasma samples were kept at – 80°C until lumefantrine analysis using high performance liquid chromatography was performed.
Results We included 1076 subjects, of which 595 were females and a mean age of 12 years old in this analysis.

The median concentration was 66% higher (p<0.0001) in patients without recurrent parasite on day 28 compared to patients with recurrent parasitaemia: 509.1 ng/ml (inter quartile range: 329.6–723.2; n=919) *vs* 372.5 (255.7–538.4; n=157). Day 7 concentrations increased with age; the difference between age group was statistically significant: 305.9 (207.3–491.5, n=140), 447 (290.7–622.9, n=399), 544.7 (383.9–738.5, n=254) and 571.1 (378.8–850.9), n=283) in patients under 5 years old, 5–9 years old, 10–14 years old and 15 years old and older, respectively. Girls under 5 years old had a lower lumefantrine concentration at day 7 compared to other age groups of 223.3 ng/ml (159.7–425.6, n=37).
Conclusions We found a lower concentration of lumefantrine in patients with recurrent parasitaemia at day 28.

PA-025 TO VALUE THE EFFICIENCY OF PYRONARIDINE-ARTESUNATE AND ARTEMETHER-LUMEFANTRINE IN THE TREATMENT OF UNCOMPLICATED MALARIA OF *PLASMODIUM* SPP. IN BURKINA FASO

Nouhoun Barry,[1] Naomie Kaboré,[1] Zachari Kabré,[1] Aminata Fofana,[1] Fréderic Nikèma,[1] Daniel Compaoré,[1] Fabrice Somé,[1] Issaka Zongo,[1] Abdoulaye Djimdé,[2] Jean Ouédraogo[1]. *[1]IRSS-DRO, Burkina Faso; [2]MRTC, University of Bamako, Mali*

10.1136/bmjgh-2016-000260.62

Background No safe and highly effective malaria vaccine is available today. The treatment drugs currently in use remain insufficient. Moreover, resistance to these drugs makes malaria control difficult. The development of new therapeutic drugs is required. This abstract is part of a survey from the WANECAM study entitled 'Randomised trial to assess the effect of repeated treatment of pyronaridine-artesunate (PA), dihydroartemisinin-piperaquine (DHA-PQ) and artemether-lumefantrine (AL) in patients presenting uncomplicated malaria in Bobo-Dioulasso, Burkina Faso'. We present here the analysis of the first episodes on the therapeutic efficiency of PA compared to AL, which is the first-line antimarial used in Burkina Faso.
Methods A total of 448 subjects were randomised to receive treatment (224 subjects in each arm). Malaria diagnosis was assessed by microscopy. Subjects were follow-up during 42 days. Treatment response was measured according to standard of care as per WHO guidelines of 2003. The correction of the cases of treatment failure by molecular biology techniques is under analysis.

Results On Day 28, the therapeutic failures were 3.35% in the PA group as against 18,10% for the AL group. On Day 42, a significant increase of the treatment failures in every group is observed with a higher rate in the AL group (31.43%), against 17.22% in the PA group.
Conclusions This survey shows that less cases of treatment failure occurred in the patients' group treated with PA compared to the group treated with AL. These findings contributed to evidence base for a change in malaria treatment policy guidelines for uncomplicated malaria in Burkina Faso.

PA-027 ADVERSE EVENT (AE) REPORTING FROM MALARIA MASS DRUG ADMINISTRATION (MDA) ROUNDS CONDUCTED IN SOUTHERN ZAMBIA

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10.1136/bmjgh-2016-000260.63

Background The National Malaria Control Centre (NMCC) of the Ministry of Health in Zambia is conducting a large-scale mass drug administration (MDA) community randomised-controlled trial to evaluate the effectiveness of different MDA distribution strategies on reducing malaria parasitaemia. The trial involved two MDA strategies: MDA, where all eligible individuals were treated with dihydroartemisinin and piperaquine (DHAp), and focal MDA (fMDA), where all eligible individuals residing in a household with at least one positive member (rapid diagnostic test) were treated with DHAp. This provides an opportunity to document the extent to which potential safety issues are reported or adverse events occur given the level of exposure to treatments.
Methods Field teams comprised of community health workers, enumerators and adherence monitors, and supervised by facility-based staff, received standardised training on the treatment campaign procedures, use of DHAp for eligible participants, adverse event monitoring, grading of events, and emergency and event handling procedures by grade. Adverse events were recorded on standard forms and in line with the national pharmacovigilance network recommendations. The principle aim of this data collection activity was to document and follow up on all adverse events (AEs) and serious adverse events (SAEs) occurring during the course of the MDA trial for individuals taking DHAp.
Results Four rounds of MDA were conducted over 2 years. During the first two intervention rounds, 280,638 participants were tested, 159,696 were treated with dihydroartemisinin-piperaquine (DHAp) in 40 health catchment areas. During the second two intervention rounds, 261,814 participants took part. A total of 687 AEs (0.13% of participants and 0.24% of treatments) were reported; four were recorded as serious adverse events (SAEs). The most common AE reported were gastrointestinal disturbances (diarrhoea, abdominal pain and nausea) 31.20%; dizziness 19.8%; vomiting 17.35%; headache 16.03%; and general body weakness at 11.37%.
Conclusions During this large MDA trial, the use of DHAp for malaria treatment was generally safe and well tolerated.

PA-028 TIME TO SECOND AND THIRD EPISODES OF MALARIA OF DIHYDROARTEMISININ–PIPERAQUINE *VS* ARTESUNATE–AMODIAQUINE AND ARTESUNATE –PYRONARIDINE *VS* ARTEMETER–LUMEFANTRINE IN BOUGOULA HAMEAU, MALI

Bakary Fofana, Abdoulaye Djimde, Hamadoun Diakité, Issaka Sagara, Ogobara Doumbo, Sekou Toure, Kassim Sanogo. *MRTC, University of Bamako, Mali*

10.1136/bmjgh-2016-000260.64

Background Currently, five artemisinin combination therapies (ACTs) are recommended by WHO for treatment of uncomplicated malaria in Africa. While artemisinin derivatives have a short half-life, the partner drugs give rise to differing durations of post-treatment prophylaxis. The pharmacokinetic and pharmacodynamic properties of drug regimens have implications for the public health benefit of the drugs. The development of new antimalarials is ongoing. The objective of this work is to evaluate the prophylactic effect of artesunate–pyronaridine (Pyramax) and dihydroartemisinin–piperaquine (Eurartesim) *vs* artemether–lumefantrine (AR_L) and artesunate-amodiaquine (ASAQ), respectively in Bougoula Hameau.
Methods Through the phase IIIb/IV clinical trial of the West African Network of clinical trial of antimalarial drugs (WANECAM) in Bougoula hameau (Mali) from January 2012 to December 2013, we evaluated the median time of occurrence for the second and third episodes of malaria on patients aged from 6 months to above. After the first randomisation, any other subsequent episodes of malaria as treated by the same ACT initially taken. Treatment failure before day 28 was treated by quinine.
Results Whilst 448 patients were randomised to receive DHA (224) *vs* ASAQ (224), 428 received PA (214) *vs* AR_L (214). The median time to second and third episodes of malaria were 116 days and 60.5 with PA versus 82.5 and 56.0 for AR_L, respectively. Otherwise, we found 118 and 98 *vs* 82.5 and 60 days as median time to second and third episode for DHA-PQP *vs* AS/AQ, respectively. DHA-PQP highly prolonged the median time to second and third episode as compared to ASAQ ($p=0.003$ and $p<0.001$, respectively).
Conclusions The ACTs artesunate–pyronaridine and dihydroartemisinine–piperaquine significantly prolonged the median time to second and third episode of malaria as compared to artemether-lumefantrine and artesunate–amodiaquine, respectively.

PA-029 ONE MERCK FOR MALARIA PROGRAM: AN INTEGRATED R&D APPROACH TO FIGHT AGAINST MALARIA

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Background Integrated health care approaches are the most effective ways to tackle infectious diseases such as malaria. Within its Global Health activities focusing on health issues of vulnerable populations within developing environments, Merck has launched a program named 'One Merck for Malaria' integrating development of new antimalarials with new sensitive diagnostic approaches together with improving access to personal protection.
Methods The first pillar of the program is based on drug discovery and development of new antimalarials. The second pillar focuses on development of diagnostics addressing the need for highly sensitive methods to identify low parasitaemia levels. The third pillar is to improve access to personal protection against malaria vectors.
Results Merck is carrying out screens and early drug discovery with its partners, Medicines for Malaria Venture (MMV, Switzerland) and H3D (University of Cape Town, South Africa),

to identify new compounds to address current gaps in existing antimalarials. Furthermore Merck is conducting regulatory pre-clinical activities to reach clinical phase 1 of a compound originated by Dundee University (UK). Based on its excellent efficacy and pharmaceutical profile shown in pre-clinical models, it is intended to be developed as a long-lasting single oral combination treatment for uncomplicated *P. falciparum* and *P. vivax*. Other research activities focusing on target identification are conducted. The portable MUSE® cytofluorometer system is launched in African countries to measure the number and % of CD4 cells. An additional set of *P. falciparum* and *P. vivax* detection kits are in development to detect type and parasitaemia levels in low blood quantities. Merck IR3535 is a widely used insect repellent being retested to assess the degree of its efficacy against various *Anopheles* carrying *P. falciparum* in Africa.

Conclusions Besides the drug and technology developments, the program covers also aspects of e-health, education, and local capacity building to complement the integrated approach being applied at Merck.

PA-030 THE IMPACT PROJECT: IMPROVING THE IMPACT OF EXISTING MALARIA PRODUCTS – ACTS

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Background The antimalarial dihydroartemisinin-piperaquine (DHA-PPQ) is one of the recommended drugs to treat uncomplicated *Plasmodium falciparum* malaria. However, DHA-PPQ has a relatively narrow, poorly defined therapeutic dose range and it is unclear whether PPQ concentration-dependent cardiotoxicity (QTc prolongation) poses a clinical risk for specific subgroups. Uncertainty about the exact safe upper PPQ concentration threshold and recognition of the vulnerability of children has led WHO to consider a complex weight-based dosing regimen. These complex dosing schemes may challenge DHA-PPQ introduction into national control programmes. It also highlights the urgent need to standardise the dose optimisation process.

Methods The IMPACT project aims to determine the frequency and severity of DHA-PPQ cardio-toxicity, and its correlation with dose and drug concentration through WWARN-pooled patient-level pharmacokinetic-pharmaco-dynamic safety analysis, and antiretroviral drug interactions using all available data. Using the established WWARN platform, an open study group has been established to allow data sharing and joint analyses by data contributors and other key stakeholders.

Results We will present a progress update of the IMPACT project and associated WWARN DHA-PPQ safety group. Findings will inform an up-to-date safety profile and upper PPQ dose thresholds across key risk groups and identify remaining research priorities. DHA-PPQ dosing challenges, lessons learnt, and opportunities to address these through a more standardised process for antimalarial dose optimisation will be reviewed, and awareness of dose optimisation research priorities will be raised among researchers, funders and control programmes.

Conclusions This work will help inform policy decisions on DHA-PPQ dosing regimens and help demonstrate the importance of identifying global research priorities for targeted antimalarial safety studies and of integrating pooled individual level safety analyses into WWARN's global efficacy data platform, as a powerful standardised process for dose optimisation.

PA-031 SPATIAL-TEMPORAL DYNAMICS IN HETEROGENEITY OF MALARIA INFECTION IN A SETTING WITH SEASONAL TRANSMISSION: A LONGITUDINAL STUDY IN THE GAMBIA

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Background The reduction in the malaria burden previously reported in The Gambia is largely due to the successful scaling up of control interventions. Understanding the current dynamics of malaria transmission in a context of high coverage of control interventions is critical to inform pre-elimination efforts.

Methods A cohort study was conducted in 12 villages across the country during the 2013 transmission season. Enrolled residents aged over 6 months old had a blood sample collected monthly for molecular analysis (PCR) and microscopy. Clinical malaria cases were captured by passive detection. Mosquito abundance and species distribution were determined by collections with CDC light traps, human landing catches.

Results A cohort of 4235 participants with a median age of 13 years (IQR 5, 28) was followed up. Long Lasting Insecticidal Nets coverage was 71.6% (2774/3876). The incidence rate of *Plasmodium falciparum* parasitaemia infection was 1.1 episodes per person-year (95% CI: 0.8–1.2). *P. falciparum* transmission was heterogeneous with low rates in the western region 0.47 episodes p-pyear (0.41–0.56) and highest in the eastern region 2.8 episodes per person-year (95% CI: 2.6–3.1). The peak mosquito densities were in September preceding peak *P. falciparum* incidence in December. *Anopheles (An.) Gambiae S* form and *An. arabiensis* were the predominant species in all the regions except the central and lower river regions where *An. gambiae* M form and *An. melas* were the predominant species. The risk of clinical malaria during the season was higher among individuals living with asymptomatic malaria at the start of the season; (Western region HR=3.9, 95% CI: 2.1–7.5) and eastern region (HR=1.5, 95% CI: 1.1–2.1).

Conclusions In The Gambia, malaria transmission is seasonal and heterogeneous across the country, with clustering of infection and disease at household level, suggesting the need for targeted interventions.

PA-032 GENETIC POLYMORPHISM OF MEROZOITE SURFACE PROTEIN-2 IN *PLASMODIUM FALCIPARUM* ISOLATES FROM DELIVERING WOMEN IN SOUTHERN BRAZZAVILLE, REPUBLIC OF CONGO

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Background In the Republic of Congo, the genetic diversity of *Plasmodium falciparum* has been extensively studied in isolates from children. However, limited data are available for isolates collected from delivering women. This study was conducted to

determine the genetic polymorphism of merozoite surface protein-2 (*msp-2*) gene in *Plasmodium falciparum* isolates from asymptomatic delivering women in Brazzaville.

Methods We used a total of 114 peripheral whole blood samples from delivering women collected from April 2014 to April 2015 at Madibou health centre in Southern Brazzaville and previously characterised as *P. falciparum*-positive by PCR technique targeting the *SSUrRNA* gene. After extraction of DNA using QIAamp DNA Blood Mini kit (Qiagen), the samples underwent nested PCR of the *msp-2* (block 3) and the allelic families, namely 3D7 and FC27, were determined.

Results All the isolates were successfully genotyped. A total of 33 *msp-2* alleles were detected, of which 17 belonged to the allelic family 3D7 and 16 to FC27 family. The 3D7 allelic family showed higher frequency (63.4%) compared to FC27 (36.6%) and 62 isolates (54.36%) harboured only 3D7 allele, while 22 (19%) harboured FC27 allele only and 30 (26%) showed both of these alleles. The mean multiplicity of infection (MOI) was 1.4 (95% CI: 1.33–4.01) and 35% of isolates had multiple genotypes. The MOI was lower in isolates from women who had not received any IPTp-SP (1.3) compared to those from women who had 3 doses of IPTp-SP (1.5) or in isolates from primiparous (1.3) compared to that of multiparous (1.5); however, the difference was not statistically significant ($p > 0.05$).

Conclusions This is the first report on genetic diversity of *falciparum* isolates from delivering women in the Republic of Congo. A noteworthy diversity was observed; the multiplicity of infection was neither influenced by IPTp-SP or parity.

PA-033 *PLASMODIUM FALCIPARUM* INFECTION IN FEBRILE CONGOLESE CHILDREN: PREVALENCE OF CLINICAL MALARIA TEN YEARS AFTER INTRODUCTION OF ARTEMISININ-COMBINATION THERAPIES

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Background The detailed assessment of the QT and corrected QT interval prolongation is recommended when testing new drugs. Generally the electrocardiograph automatically displays reliable values of the QT interval and corrected QT but morphological variations of the T wave may cause reading errors; hence the use of manual measurement as an alternative method. Our objective was to evaluate the correlation between the automatic and manual measurement of QT values.

Methods In Kolle from March 2012 to December 2015, an open randomised, phase III-b/IV study comparing dihydroartemisinine-piperaquine and pyronaridine-artesunate artemether-lumefantrine was conducted. An electrocardiograph cartridge with 12 electrodes coupled to a computer with the Tele Touch software was used for the electrocardiogram on Day 0 before the study drugs administration and on Day 2, two to four hours after the administration of the last dose of the antimalarial. The manual measurement of QT and QTc was made using the Bazett method [QTcB_m=(Number leaded×0.04×QTcF) / QTcB]. For prolonged QTc cases on Day 2, another measurement was done during the next scheduled visit (day 7, 14, 21, 28, 35 and 42) until the QTc normalised.

Results A total of 764 ECG were recorded with 398 participants. Different automatic and manual values of QT and QTc are scattered around different medium. Comparisons of different values of QT: $p=0.1245$ and QTc: $p< 0.001$ showed statistically significant differences and the concordance between automatic and manual tests was (QT: Rho_c=0.77 and QTc: Rho_c=0.46).

Conclusions Our results indicate no perfect match between automatic and manual methods for QT and QTc. Manual reading remains important to correct any machine errors during clinical studies.

PA-034 *PLASMODIUM FALCIPARUM* MEROZOITE SURFACE PROTEIN-1 GENETIC DIVERSITY AND MULTIPLICITY OF INFECTION IN ISOLATES FROM CONGOLESE CHILDREN CONSULTING IN A PAEDIATRIC HOSPITAL IN BRAZZAVILLE

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Background As in many countries in sub-Saharan Africa, the burden of malaria has been reduced in the Republic of Congo as a result of massive deployment of insecticide-treated nets and availability of artemisinin combination therapies.

However, limited data are available on the impact of these interventions on parasite populations. In this study, we investigated the *P. falciparum* genetic diversity and multiplicity of infection in isolates from Congolese young patients and we compared the results to previous studies conducted before the introduction of ACTs.

Methods A total of 229 children were enrolled at the paediatric hospital located in Northern part of Brazzaville. Inclusion criterion was fever (T°>=37.5°C); then thick and thin blood smears were done to detect malaria parasites and determine parasite density as well as plasmodial species. In order to identify submicroscopic infection, *P. falciparum msp1* gene was used as molecular marker. The genetic diversity and the multiplicity of infection (MOI) were determined.

Results We found 22 children with positive blood smear, therefore diagnosed with uncomplicated malaria (UM, 9.6%). Among the 216 microscopy-negative children, using msp1 marker, 57 were shown to harbour submicroscopic malaria infection (27,5%). In the age group 1–5 years, MOI was 1.4 and 2.4 in submicroscopic and UM children, respectively while in the age group >= 5 years, MOI was 1.7 and 3 in submicroscopic and UM children, respectively. The number of *msp1* alleles in isolates was 15 and 18 in SM and UM group, respectively. We observed that new alleles were detected only in isolates from UM children. Data are further analysed to investigate any association with age, living area, haemoglobin type carriage, and haemoglobin rate.

Conclusions This study shows no change either in *P. falciparum* genetic diversity or in MOI 10 years after the introduction of ACTs.

PA-035 FEASIBILITY OF IMPLEMENTING A CONTINUOUS HOUSEHOLD MALARIA INDICATOR SURVEY IN RARIEDA SUB-COUNTY, SIAYA COUNTY, WESTERN KENYA

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Background Malaria transmission in Siaya County is high and perennial with peak transmission in May-July and October-November. The Kenya Medical Research Institute (KEMRI) and Centers for Disease Control and Prevention (CDC) have historically conducted malaria surveillance in western Kenya during peak malaria transmission season through annual population-based cross-sectional surveys. However, it may be important to characterise the seasonal spatial variation in malaria transmission for surveillance purposes, to monitor malaria interventions, and to inform decisions for changing and targeting malaria control strategies. We describe the feasibility of implementing a continuous malaria indicator survey (cMIS) for malaria surveillance in Rarieda sub-County, Kenya.

Methods All households in the study area were GPS-mapped and household members enumerated. Community interviewers were trained and assessed in collecting blood for malaria rapid diagnostic tests (RDT), preparation of dried blood spots on Whatman 903 filter paper, preparing blood smears, and performing HemoCue® tests for haemoglobin determination. Community interviewers were also trained to provide appropriate treatment with antimalarials and haematinics based on test results. They visited a random subset of 5 houses in the study area each week and collected and transmitted data in real-time throughout the year.

Results Four trained community interviewers visited a total of 1041 compounds, and consented and tested a total of 4714 participants for malaria by RDT in year one. Approximately 27% were positive for malaria by RDT and were offered treatment.

Conclusions A large number of compounds were visited by few staff in year one. This suggests that cMIS may be a viable way to perform year-round surveillance, and to offer malaria testing and treatment in the community with minimal staff. Further analysis of results from cMIS and comparisons to existing surveillance platforms are warranted to determine if cMIS can provide accurate estimates of malaria case burdens throughout the year.

PA-036 ASSESSING THE COMMITMENT, MATURATION AND INFECTIVITY OF SEXUAL STAGES OF MALARIA PARASITES IN SCHOOLCHILDREN LIVING IN A HIGH MALARIA TRANSMISSION AREA OF BURKINA FASO

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10.1136/bmjgh-2016-000260.72

Background With the move towards malaria elimination, it becomes essential to understand the contribution of asymptomatic parasite carriers to disease transmission. However, the dynamics of infection and gametocyte development are poorly understood in asymptomatic versus symptomatic malaria infections. This was addressed in a longitudinal study of school children in Balonghin, district of Saponé, Burkina Faso.

Methods The study involved healthy schoolchildren (with no malaria parasite at microscopy) age 5–10 years. For the first year survey, children were cleared for subpatent infections using standard malaria therapy. No clearance will occur for the second year survey. Children are followed up for 6 months during which repeated finger prick blood samples for the detection and characterisation of infections are collected. Also at three occasions a venous blood sample is collected for direct membrane feeding assay (DMFA) to assess infectiousness to mosquitoes.

Results The first year survey was completed. Fifty (50) children were recruited and followed up. Almost all the children develop infection and symptomatic malaria during the follow-up period post clearance of initial infection. None of the children has infected mosquitoes during the DMFA assays. The second year survey is in process. The full results will be presented during the forum.

Conclusions These data will be pivotal in understanding human infectious reservoir. This will help designing interventions to tackle the spread of malaria from symptomatic and asymptomatic malaria individuals towards global in eliminating malaria.

PA-037 ANTIBODY RESPONSE TO SEVERAL MALARIA ANTIGENS IS ASSOCIATED WITH PROTECTION FROM SEVERE MALARIA IN UGANDAN CHILDREN

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Background Malaria is one of the leading causes of morbidity. Both natural infection and irradiated sporozoites have yielded partial and sterile immunity and contain multiple antigens so a malaria vaccine with multiple antigens may be protective. Our hypothesis is that responses to several malaria antigens may protect against severe malaria. Currently various candidate vaccines are being tested and are in various stages. This study is from a case control study conducted in Apac district in Northern Uganda.

Methods Children with severe and complicated malaria were compared with those having uncomplicated malaria in a matched case-control study. Antibody titers in serum samples of children were assessed by ELISA and parasitaemia was quantified by microscopy.

Results When all children who had antibodies to at least 4 of the antigens tested were compared to children who responded to less than 4 of the antigens, multiple responders were significantly more prevalent in the mild malaria group. For all the antibodies studied, there was a tendency for the children with mild malaria to have higher OD levels than the children with severe malaria. Children who were responders to AMA1, *P. falciparum* lysate, SE36, MSP1 42, GPI, MSP2–2FC or MSP2–3D7 were significantly more likely to be in the mild malaria group.

Conclusions There were significant differences between children with severe and mild malaria for antibodies. Higher levels of these antibodies were associated with protection from severe malaria disease and from high parasitaemia. Our data suggest a role for multiple blood stage antigen vaccines and denatured toxin vaccine supports the development of multiple component vaccines.

PA-038 COST-BENEFIT ANALYSIS OF MALARIA RAPID DIAGNOSTIC TEST IN ENUGU METROPOLIS, NIGERIA: THE PERSPECTIVE OF THE COMMUNITY PHARMACY PRACTITIONER

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10.1136/bmjgh-2016-000260.74

Background Malaria is a great health burden in Nigeria. Since 2010, the World Health Organization issued guidelines that call for a shift from presumptive to test-based treatment. However, test-based treatment is still unpopular in community pharmacies in Nigeria. This could be due to unwillingness of customers to spend more for a rapid diagnostic test (RDT). It could also result from lack of interest from community pharmacy practitioners since they may perceive that there is no financial gain attached to the service. This study assessed the costs and benefits of test-based malaria treatment for the community pharmacy practitioner.
Methods The study was a community pharmacy-based cross sectional survey. Potential benefit of RDT test to the practitioner was determined using customers' willingness-to-pay (WTP) for this service. Average WTP was estimated using contingent valuation. Binary logistic regression was used to assess correlates of WTP. Costs associated with provision of RDT test were estimated. Costing was based on the provider's perspective. Probabilistic sensitivity analysis through Monte Carlo simulation was used to capture parameter uncertainty. The Benefit-cost ratio was calculated to determine study objective.
Results Average WTP was $1.23 (95% CI: $1.03–$1.44). Educated customers were 1.8 more likely to prefer RDT test before taking malaria treatment. Customers that understood RDT as described in the fact sheet were 18.3 times more likely to prefer RDT test before malaria treatment. The predictive capacity of the model was 18.1%. Average cost [min – max] of the RDT test kit and the pharmacist's time spent for the test was 0.15 [0.13–0.17] and 0.41 [0.18–0.52], respectively. The benefit-cost ration of test-based malaria treatment was 6.7 (95% CI: 6.4–7.0).
Conclusions Test-based malaria treatment is cost-beneficial for pharmacy practitioners. Return on invested time was approximately 7 times. This finding should be capitalised upon to increase community pharmacy practitioners' interest and uptake of test-based malaria treatment.

PA-040 SEASONAL ABUNDANCE AND SPOROZOITE RATES IN MALARIA VECTORS IN NCHELENGE INCLUDING ISLANDS OF LAKE MWERU AN AREA WITH A HIGH BURDEN OF MALARIA IN NORTHERN ZAMBIA

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10.1136/bmjgh-2016-000260.75

Background Nchelenge district is a holoendemic malaria transmission zone in northern Zambia. The district occurs in a region characterised by a mix of water, marshes, islands and lagoons presenting a uniquely suitable ecology for mosquitoes. Annual indoor residual spraying (IRS) campaigns are carried out between September and December synchronised with other regions in the country with different environmental conditions. Targeted vector control interventions have been applied since 2008 without appreciable impact on disease burden. The timing and targeting of vector control measures are not guided by an informed entomological baseline. This study was aimed at providing entomological information on the seasonal abundance, spatial distribution and *Plasmodium falciparum* sporozoite infections in the local malaria vector species in order to guide implementation of vector control in the district.
Methods Entomological studies were conducted intermittently spanning the rainy, cold-dry, and hot-dry seasons from 2015–2016. Mosquitoes were collected by CDC light traps, identified to species both morphologically and by PCR techniques. Circumsporozoite ELISA assay was used to detect *P. falciparum* in mosquito salivary glands.
Results A total of 5437 female *Anopheles funestus* and *An. gambiae* and over 6000 culicines, mostly *Mansonia* mosquitoes were collected. The peak number of the *An. funestus* from all sites occurred in July. Overall *P. falciparum* infection rates in *An. funestus* were Kilwa island 2.7% (4/146), Mainland 2.5% (3/122), Chisenga island 0.4% (1/220), Isokwe 5.9% (2/34) and in *An. leesoni* from Kilwa 33% (1/3). The highest number of *An. gambiae* was collected from Kilwa and none was found infected with *P. falciparum* regardless of collection site.
Conclusions The annual IRS conducted between September and December may be ineffective in controlling malaria as this misses the vector peak abundance and peak transmission season. Two rounds of IRS covering more areas would be needed to control the two vector species with different population peak seasons and malaria transmission.

PA-042 EFFECT OF COMMUNITY-BASED SCHEDULED SCREENING AND TREATMENT (CSST) OF MALARIA IN PREGNANCY ON INFANT MALARIA INFECTION IN A SEASONAL MALARIA TRANSMISSION SETTING

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10.1136/bmjgh-2016-000260.76

Background Children born to mothers who had malaria in pregnancy have an increased risk of malaria infection in the first 24 months of life and they also experience earlier episodes of malaria compared to their counterparts. This study compared the pre- and post-seasonal prevalence of *P. falciparum* infection and anti-malarial antibodies among children whose mothers received either intermittent preventive treatment in pregnancy using sulphadoxine-pyrimethamine (IPTp-SP) plus community-based scheduled screening and treatment (CSST) of malaria in pregnancy or standard IPTp-SP.
Methods In 2015, two cross-sectional surveys were conducted before and after the malaria transmission season among children aged 0–24 months, born to women who participated in a 2-arm cluster-randomised trial to compare CSST plus IPTp-SP *vs* IPTp-SP alone in the Upper River Region of The Gambia. For each survey, finger prick samples were collected for slide microscopy and indirect ELISA to compare prevalence of malaria parasitaemia and IgG antibodies to 19-kDa merozoite surface protein 1.
Results Of 905 children recruited in the pre malaria transmission survey, the prevalence of malaria in the overall population, IPTp-SP alone and CSST plus IPTp-SP arms were 1.07%, 2.30% and 0%, respectively. Nearly 70% of children with parasitaemia were aged 1–5 months old. The seroprevalence in

children whose mothers received CSST plus IPTp-SP compared to IPTp-SP alone was 10.54% *vs* 11.85%. Seroprevalence analysis and reading of slide microscopy for 1172 children recruited in the second survey as well as final statistical analysis are currently on-going. Final results will be available by November 2016.
Conclusions Infants whose mothers received CSST plus 1PTp-SP appear to be less likely to have malaria infection compared to those whose mothers received IPTp-SP only. Community scheduled screening and treatment of malaria in pregnancy may also be protective against malaria in children.

PA-043 MALARIA PREVENTION PRACTICES AMONG PREGNANT MOTHERS IN OSOGBO, NIGERIA

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10.1136/bmjgh-2016-000260.77

Background Pregnant women are susceptible to symptomatic malaria due to invasion of the placenta by *Plasmodium*. The study aimed to find out the preventive measures put in place by pregnant mothers against malaria.
Methods It is a descriptive cross-sectional survey comprising 294 pregnant women selected randomly in three hospitals in Osogbo. The instrument used for data collection was a self-developed, structured questionnaire with reliability of 0.802 using Cronbach's alpha coefficient.
Results The results show that 87.8% of the respondents had adequate knowledge about malaria in pregnancy and 75.5% of them were knowledgeable about various available measures in malaria prevention. However, only 34.4% used the insecticide treated nets (ITNs) and 21.4% used intermittent preventive therapy (IPTp). Findings also revealed that the respondents practiced other preventive measures such as clearing of surrounding bushes (12.8%), maintenance of drainages and netting of windows and doors (15.4%). The results of the study revealed that various barriers to the use of ITNs were deficient knowhow (45.9%), spousal disapproval (36.7%), socio-cultural misconceptions about sleeping under ITNs (18.8%) and unaffordability of ITNs (45.5%). The hypotheses were tested using Pearson's chi-square method at 0.05 level of significance. There is no significant relationship between the pregnant mothers' knowledge and their practice of malaria prevention. However, there are respective significant relationships between the age, parity and educational status and practice of malaria prevention.
Conclusions It was concluded that the practice of malaria prevention was generally low among the respondents. It was therefore recommended that concerted effort be put in place by the nurses, more especially public health nurses to address the barriers to utilisation of the universally accepted effective methods of malaria prevention. This could be done through mass health education to market women at regular interval.

PA-044 WEIGHT STATUS ROLE ON ANTIMALARIAL DRUG EFFICACY AND SAFETY IN SUBURBAN CHILD POPULATION IN MALI

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Background Malnutrition and *Plasmodium falciparum* malaria are two major public health problems in sub-Saharan Africa. In this study, we described as our primary outcome the proportion of presence of *P. falciparum* during follow-up and explore the relationships between malaria drug safety and nutritional inadequacies.
Methods This was a secondary analysis of an *in vivo* prospective randomised control trial conducted in Bougoula-Hameau, Mali. Our analysis concerned 749 children followed during 28 days. We determined the BMI status of each child according to the cut-offs defined by WHO in 2007. R-software was used for statistical analysis.
Results The median of parasite density was higher in thin and severely thin children (17800). The median of haemoglobin levels at enrolment was lower in children who were thin and severely thin (9.85) compared to the children with normal weight, overweight and obesity. At 21 days, there was no parasite in thin and severely thin children. At the same point of follow-up, 7.5% of children with normal weight had parasites versus 8.4% of overweight and obese children. Between the three groups the difference was significant (p=0.03). On day 7 the highest ASAT level was observed in children with normal weight (p=0.03). We didn't observed differences between weight status groups regarding the level of creatinine. The p-value was respectively 0.99, 0.41 and 0.07 at enrolment, day 7 and day 14.
Conclusions This study showed that children with BMI deficiency had a higher parasite density and lowest haemoglobin level at enrolment. However, we did not observe a relationship between weight deficiency and the safety of antimalarial drugs used in our study.

PA-045 IMMUNOGENICITY OF MALARIA-VECTORED VACCINES IS NOT AFFECTED BY CO-ADMINISTRATION WITH ROUTINE EPI VACCINES IN A RANDOMISED CONTROLLED TRIAL IN GAMBIAN INFANTS AND NEONATES

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Background Recent global estimates show that *P. falciparum* malaria still constitutes an enormous public health concern. Chief amongst desirable interventions is an effective vaccine that could complement existing control measures. Heterologous prime-boost vaccinations involving chimpanzee adenovirus 63 (ChAd63) and modified vaccinia Ankara (MVA) encoding ME-TRAP have consistently shown acceptable safety, excellent immunogenicity and substantial efficacy in African adult and paediatric populations. When licensed, malaria vaccines would preferably be given to infants receiving routine childhood immunisations. Nevertheless, no studies have evaluated the interference of ChAd63/MVA ME-TRAP when co-administered with routine Expanded Programme Immunisation (EPI) vaccines.

Methods We enrolled 65 Gambian infants and neonates in an age de-escalating fashion, priming at 4 months, 8 weeks or 1 week of age, and randomised them to vaccine or control (EPI vaccines only) arm. Safety was assessed by the description of vaccine-related adverse events ascertained through clinical assessments, biochemical and haematological tests. Immunogenicity was evaluated by IgG ELISA, interferon-gamma ELISPOT, intra-cellular cytokine staining and flow cytometry. Antibody testing was performed to assess any interference of the EPI vaccines with responses to ChAd63/MVA ME-TRAP.
Results Overall, the vaccination regimes were well tolerated in all age groups with no vaccine-related serious adverse events. High level IgG and antigen-specific T cell responses were generated after boosting with MVA, with T cell responses highest in the infants 8 week old at priming dose. EPI vaccines retained unchanged antibody levels in all age groups.
Conclusions Potent humoral and cellular immunity induced by heterologous prime-boost immunisation with ChAd63 and MVA ME-TRAP did not interfere with the immunogenicity of co-administered routine EPI vaccines in infants and neonates. Potent T cell induction was again observed with the vectored malaria vaccines despite co-administration with EPI vaccines.

PA-046 A MALARIA VACCINE SITE CHARACTERISATION: PREVALENCE AND SPECIES DISTRIBUTION OF *PLASMODIUM* MALARIA IN A MALARIA ENDEMIC SETTING OF BURKINA FASO (WEST AFRICA)

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Background Any development of a vaccine strategy or its implementation is based on a good knowledge of the biology of the pathogen and its temporal and spatial distribution. In the case of malaria, the main four species responsible for the disease though having a similar biological structure are not equally represented spatially due to factors such as environment and susceptibility of human to species.
Methods In order to characterise a site for a future malaria vaccine implementation in terms of malaria prevalence and its species distribution, two cross sectional studies were conducted in October and March corresponding to the high and low malaria transmission season, respectively, in the Banfora Health District. A total of 1203 volunteers aged from 0.5 to 45 years consented to participate in the study. During each survey, after a brief physical examination, blood was taken from each volunteer by finger prick to perform thick and thin blood film examination. Blood smears collected were air dry and the thin film fixed with methanol. Dry smears were then stained with controlled PH Giemsa buffer solution and checked for malaria parasite using light microscope.
Results Malaria prevalence was markedly high during high malaria transmission: 54.26% compared to low malaria transmission season 39, 40%. *Plasmodium* index was 46.8% with a gametocyte index of 11%. Main species present in the study area were *P. falciparum*, *P. malariae and P. ovale*. Species distribution was almost the same across the two seasons with P. *falciparum* being more prevalent compared to other species with respectively 97.8% and 98.7%.
Conclusions *P. falciparum*, *P. malariae* and *P. ovale* are the three main species in the study area with almost the same distribution across the two seasons.

PA-048 *PLASMODIUM FALCIPARUM* PARASITE DYNAMICS DETERMINED BY QPCR AFTER CONTROLLED HUMAN MALARIA INFECTION IN SEMI-IMMUNES FROM GABON

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Background Characterising the effect of natural acquired immunity and sickle cell anaemia on the pattern of *Plasmodium falciparum* parasitaemia may be useful to understand the pathophysiological mechanisms of protection against malaria. Controlled human malaria infection (CHMI) by direct venous inoculation of aseptic, purified, cryopreserved sporozoites (Pf-SPZ challenge) is a new tool which can be used to investigate the pathophysiology of malaria.
Methods The study was performed in Lambarene, Gabon, one of seven African partners in the EDCTP-funded CHMI platform. Adults aged 18–35 from three groups NI: 5 non-immune (NI), 11 semi-immunes with haemoglobin AA (IA), and 9 semi-immunes with haemoglobin AS (IS) received 3,200 sporozoites after a curative treatment course with clindamycin. Capillary blood samples were taken daily up to Day 28 to determine parasitaemia by real-time quantitative polymerase chain reaction (RT-qPCR). Treatment was administered for a malaria episode or at Day 28, whichever came first.
Results Parasitaemia was detected in 5 (100%) subjects in the NI group, 9 (82%) in the IA group and 7 (78%) in the IS group. All volunteers in the NI group showed similar patterns with parasitaemia starting around Day 8 and rising quickly. Patterns for parasitaemia in the immune groups (IA and IS) were highly heterogeneous. Although time points of initial parasitaemia and duration of parasitaemia varied, all semi-immunes managed to control parasitaemia for at least several days. There were no discernible differences in patterns between the IS and IA group, including the area under curve of parasitaemia over time.
Conclusions No parasitaemia was detected in 20% of the semi-immunes, likely due to liver stage immunity. The highly variable patterns of parasitaemia did not allow us to discern immune mechanisms against blood stages. Haemoglobin AS had no visible effect on parasite dynamics at the low parasitaemia encountered.

PA-049 SOLUBLE HLA-G LEVEL EFFECT ON GMZ2 SPECIFIC IgG PRODUCTION AFTER IMMUNISATION

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10.1136/bmjgh-2016-000260.82

Background Malaria is a major public health problem particularly in Africa. Despite the relatively good immunogenicity profile of the vaccine candidates in naive population, most of them are poorly immunogenic in malaria endemic population.

This could be due to an induction of various immune regulatory mechanisms. It has recently been shown that high levels of an immune regulatory molecule sHLA-G in infants increased the risk of malaria, and question may arise as to whether it can equally impair vaccine induced immune response. In this study we have assessed the correlation between sHLA-G and the immune response induced by GMZ2 a blood stage malaria vaccine candidate.

Methods It was an observational study nested within a phase Ib trial aiming to assess the safety, immunogenicity and efficacy of GMZ2 adjuvanted with CAF01, on fifty Gabonese adults life-long exposed to *Plasmodium* spp. Three doses of either the vaccine candidate or Rabies vaccine were injected at Day 0, Day 28, Day 56. Peripheral blood sample was collected at Day 0 and Day 7 after the first vaccine administration as well as 28 days after the third vaccine administration (Day 84). sHLA-G level was measured by ELISA on Day 0 and Day 7, and the anti GMZ2, anti MSP3, Glurp IgG concentrations were determined by ELISA on Day 0, 7 and 84. Vaccine efficacy was assessed using *PfSPZ* Challenge.

Results sHLA-G level was significantly increased from Day 0 to Day 7 ($p=0.004$) and correlated with a significant decrease of anti-GMZ2 total IgG ($r=-0.35$, $p=0.04$). No correlation was found between sHLAG and anti MSP3, Glurp IgG production. Interestingly, individuals who did not develop malaria after the challenge had a lower level of sHLA-G at baseline ($p=0.03$).

Conclusions Vaccination with GMZ2 induces an increase of sHLA-G level resulting in a decrease of vaccine immunogenicity. This could have an implication for the design of malaria vaccine candidates in semi-immune individuals.

PA-050 ANTIBODY RESPONSES TO SURFACE ANTIGENS OF *PLASMODIUM FALCIPARUM* GAMETOCYTE-INFECTED ERYTHROCYTES AND THEIR RELATION TO GAMETOCYTAEMIA

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Background An essential element for continuing transmission of *Plasmodium falciparum* is the availability of mature gametocytes in human peripheral circulation for uptake by mosquitoes. Natural immune responses to circulating gametocytes may play a role in reducing transmission from humans to mosquitoes.

Methods Here, antibody recognition of the surface of mature intra-erythrocytic gametocytes produced either by a laboratory-adapted parasite, 3D7, or by a recent clinical isolate of Kenyan origin (HL1204), was evaluated longitudinally in a cohort of Ghanaian school children by flow cytometry.

Results This showed that a proportion of children exhibited antibody responses that recognised gametocyte surface antigens on one or both parasite lines. A subset of the children maintained detectable anti-gametocyte surface antigen (GSA) antibody levels during the five week study period. There was indicative evidence that children with anti-GSA antibodies present at enrolment were less likely to have patent gametocytaemia at subsequent visits (OR=0.29, 95% CI: 0.06–1.05; $p=0.034$).

Conclusions Our data support the existence of antigens on the surface of gametocyte – infected erythrocytes, but further studies are needed to confirm whether antibodies against them reduce gametocyte carriage. The identification of GSA would allow their evaluation as potential anti-gametocyte vaccine candidates and/or biomarkers for gametocyte carriage.

PA-051 *MYCOBACTERIUM TUBERCULOSIS* RESISTANCE TO ISONIAZID AND RIFAMPICIN IN A HIV-1 ENDEMIC POPULATION IN WESTERN KENYA IN 2014

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Background The spread of mono-resistant and multi-drug resistant tuberculosis (MDR-TB) has been enhanced by delays in the identification of resistant strains. However, resistance gene patterns and the extent and distribution of mono-resistant TB and MDR-TB is unknown, particularly for western Kenya where Human Immunodeficiency Virus (HIV) is common. As such, the overall objective of the current study was to identify cases of mono-resistant TB and MDR-TB among enrolled patients in health facilities in western Kenya.

Methods Patients with a suspected TB history were referred by clinicians to the health facilities for TB and HIV diagnosis. HIV testing was done using the Unigold and Abbott Determine kits. Early morning sputum samples were collected and cultured on *Mycobacteria* growth indicator tubes (MGIT) and incubated at 37°C. Drug susceptibility testing (DST) using the SIRE® kit was done on ZN smear positive MGIT tubes and line probe assay (LPA) performed to identify specific mutations on the *rpo* B, *kat* G and *inh* A genes. Mutations on discordant samples were confirmed by the BigDye® Terminator v3.1 Cycle Sequencing Kit.

Results The proportion of MDR-TB, RIF mono-resistant (RMR) TB and INH mono-resistant TB as estimated by LPA and DST, was as follows: MDR-TB: 1.38% / 1.26%; RMR-TB: 1.2% / 0.72%; INH mono-resistant TB: 2.1% / 2.4%, respectively. Our study showed that the H526Y *rpo* B and S315T1 *kat G* mutations were common in HIV-positive patients (8% and 18% respectively) and that the S3I5T1 and S531L was the most common mutation in MDR-TB strains in both HIV-positive and HIV-negative patients (5% and 8% respectively). Binary logistic regression, indicated that RMR-TB significantly predicted HIV status ($p=0.025$).

Conclusions Our findings show that RIF mono-resistant TB predicts HIV infection.

PA-052 MULTIDRUG-RESISTANT TUBERCULOSIS (MDR-TB): AN EMERGING PROBLEM IN WEST AFRICA

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Background Multidrug-resistant tuberculosis (MDR-TB) remains a clear threat to TB control. There is a paucity of data

on DR-TB for many countries especially in sub-Saharan Africa. The study was undertaken to measure the prevalence of DR-TB, including MDR-TB, from West Africa.

Methods Mycobacterial isolates were obtained from consecutive new and previously treated TB patients from Burkina Faso, Ghana, Guinea-Bissau, Mali, Nigeria, Senegal, The Gambia and Togo from December 2012 to December 2014. Phenotypic drug susceptibility testing to first- and second-line anti-TB drugs was performed using BACTEC MGIT 960 system.

Results Viable isolates from a total of 44% (416/950) new and 56% (534/950) previously treated TB patients were included. HIV results were available for 599 (63%) with estimated HIV-TB co-infection of 21% (95% CI: 18.2–24.9%). Pooled estimate of any DR-TB prevalence among new TB patients was 20% (95% CI: 16.4–24.4%) while for MDR-TB this was 6% (95% CI: 4.1–9.0%). Among previously treated TB patients, these were 53% (95% CI: 48.3–56.9%) and 34% (95% CI: 30.1–38.3%), respectively. Significant factor for the development of MDR-TB was the history of previous anti-TB treatment (Crude OR=0.13; 95% CI: 0.08–0.20; p=<0.001).

Mono-resistance was detected in 12% (95% CI: 10.2 –14.5%) with the highest resistance to streptomycin 6% (95% CI: 4.8–7.9%). Pooled estimate of pre-XDR-TB prevalence rate among MDR-TB patients was 21% (95% CI: 15.2–26.9%). Estimated resistance to ofloxacin, kanamycin, capreomycin and kanamycin and capreomycin were 7% (95% CI: 3.5–10.9%), 2% (95% CI: 0.6–5.1%), 9% (95% CI: 5.8–14.5%), and 3% (95% CI: 0.8–5.8%), respectively.

Conclusions The reported prevalence of MDR-TB and pre-XDR-TB are high compared to WHO estimates. Resistance to streptomycin may indicate a high risk of failure for the WHO standard regimen. MDR-TB patients with resistance to either the fluoroquinolone or injectables may have suboptimal response; thus the need for continuous surveillance of TB resistance.

PA-053 ROAD TO BUILDING AND SUSTAINING NOVEL CLINICAL RESEARCH CAPACITY IN RESOURCE-LIMITED SETTINGS: LESSONS LEARNT SO FAR FROM RWANDA

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Background Harnessing research for enhancing capacity for evidence-informed policies is key for sustainability in countries that are still facing poverty-related diseases. During current customised medicine and drug-resistance era, priority has shifted to clinical research making clinical trials a powerful tool in availing tailored and affordable drugs and medical interventions. There is need to address disparities in clinical research capabilities worldwide, particularly sub-Saharan Africa, where disease burden is rampant. We share our achievements and lessons learnt so far from establishing three new clinical research sites among the eleven targeted for in Rwanda.

Methods Referral, provincial and specialty hospitals have been selected by the Ministry of Health as potential clinical research sites. Based on the International Conference on Harmonization in Good Clinical Practice (ICH-GCP), a baseline assessment was conducted. Three best-scoring hospitals were developed to become clinical research sites by: alignment with the national priorities; acceleration of current laboratory accreditation processes, improvement of data management, clinical infrastructure, financial management systems; careful recruitment, continuous training and a retention plan of critical research staff; collaborations with private clinical research organisations; marketing of research sites to funders; strengthening institutional review boards; creation of local ownership; and diversification of the research portfolio.

Results Clinical research sites established are Centre Hospitalier Universitaire de Kigali (CHUK) in Kigali city, Centre Hospitalier Universitaire de Butare (CHUB) in Southern province, and Butaro Hospital in Northern province with 26, 26 and 11 dedicated staff, respectively. Sites have minimally a clinical research laboratory under accreditation process, 5 private medical/examination room, a counselling rooms, a data management unit, a waiting area, a pharmacy with restriction-area, administrative area, tele-conference/training room.

Conclusions Development of novel clinical research capacity in resource-limited settings is feasible, with considerable time and resources. Political initiative is a key element for sustainability. Staff retention is the main challenge. For minimising the risk, partnerships between experienced clinical organisations and sponsors are vital for financial stability and knowledge transfer.

PA-054 CORRELATION OF HIV-1 P24 ASSAY WITH CD4 T-CELL COUNT, HIV, HBV AND HCV CO-INFECTIONS AND ITS IMPLICATION FOR ART MONITORING IN VASTLY HIV-INFECTED POPULATION OF NIGERIA

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Background Reports indicate that extensive genetic diversity of HIV-1 impacts almost every aspect of HIV-1 epidemiology, including laboratory detection, ART/resistance, monitoring of ART and vaccine development. Therefore, in order to support the scale-up of access to HAART to mitigate the HIV-1 scourge, prompt, accurate and cost-effective diagnosis and monitoring of ART is crucial in Nigeria (a resource-limited country).

Methods Plasma of 200 confirmed HIV-1 patients on a specified and uniform ART regimen was monitored with P24 antigen assay and CD4 T-cell count as virologic and immunologic assessments of response to ART. The results of the assays (P24 and CD4 count) were compared to assess sensitivity, turn-around time and financial advantages of P24 over the CD4 count. Serological analysis of HBV and HCV were performed according to the manufacturer's instructions. Enumeration of CD4+ levels was done with a Partec flow cytometer.

Results Of these patients, 77.5% had HIV only, 14.5% had HIV–HBV and 11.5% had HIV-HCV. Evaluation of levels of P24 antigen revealed that lower limits for P24 antigen 0.577–2.308 were detected in the subjects with CD4 cell count >500. However, higher limits for P24 antigen 2.308–2.885 were detected in subjects with CD4 cell count within the range of 200–499. Correlation analysis showed an inverse relationship between CD4 count and level of P24 antigen (CD4 count of 200–499 cells/μl versus 2.308–2.885 of P24, r=–0.319, CD4 count≥500 cells/μl versus 0.577–2.307 of P24, r=–0.088).

Conclusions This study suggests that p24 could serve as one of such diagnostic and monitoring facilities that could be used in a

resource-limited area like Nigeria. This will in turn lead to selection of more specific ARV options that best suppress viraemia during initiation of ART, as well as for monitoring HIV-1 patients in Nigeria, knowing that the virus subtype impacts effectiveness of ART.

PA-055 LOW FALSE RECENT RATE OF LIMITING ANTIGEN AVIDITY ASSAY COMBINED WITH HIV-1 RNA DATA IN BOTSWANA

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Background Cross-sectional tests for recency of HIV infection are increasing in utility for estimating HIV incidence and evaluating impact of interventions. However, they have been shown to misclassify individuals with long standing infection as recent. Local performance characteristics are essential for their application. We estimated the false recency rate (FRR) among long term HIV-1 infected individuals from Botswana.

Methods A total of 1036 specimens from treatment naïve individuals known to be HIV-infected 1.5 to 2 years from baseline were tested using the limiting antigen-avidity assay (LAg) using a cut-off of 1.5 normalised optical density units (OD-n). Study participants were enrolled in HIV disease progression and did not qualify for treatment according to national guidelines at the time of enrolment. Baseline HIV status was determined using double ELISA. Viral and CD4 measures were done every 3 months.

Results Most participants were females (74.8%) and median age was 35 years (IQR 30–42). The median CD4 cell count and viral load were 394 cells/μL (IQR 303–524) and 4.25 copies/mL (IQR 3.51–4.87), respectively. Overall the FRR was 0.97% (10/1036; 95% CI: 0.46–1.77). Four samples had viral loads >1000 copies/mL, giving an adjusted FRR of 0.39% (4/1036; 95% CI 0.11–0.99).

Conclusions LAg had a very low FRR in this Botswana population using the algorithm involving viral load. We found viral load to be a complementary marker for improving the specificity of the LAg-avidity assay. To our knowledge, this is the first report of LAg-avidity FRR for the Botswana population, which is much lower than the 2% recommended by the WHO Incidence Assays Working Group.

PA-056 NEED FOR REANALYSIS OF CURRENT TESTING OF HIV-EXPOSED INFANTS

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Background In 2015, 12% of HIV-exposed infants in Malawi received an early infant diagnostic test (EID) in the first two months of life. Provider-initiated testing and counselling (PITC) is recommended as a standard component of comprehensive clinical management for inpatients and outpatients in entry points, including at mother-infant pair (MIP) clinics, nutrition rehabilitation units (NRU) and paediatric wards.

Methods An analysis of the 2015 databases of Community Management of Acute Malnutrition (CMAM), Laboratory Information Management System (LMIS) and EID at point-of-care (EID POC) was conducted to identify optimal entry points for identifying HIV-infected children. A chi-square test was used to determine differences between groups.

Results A total of 7629 children below 5 years of age were admitted in NRUs; 60% were tested for HIV and 17% were HIV-infected. The EID POC database showed that most (50%) of the children identified from the inpatient paediatric ward were HIV-infected as compared to 2.5% in MIP clinics and 11% in outpatient paediatric wards. A chi-square test of significance shows that the HIV positivity varies between entry points (chi-square value=182.34, with 2 degrees of freedom and p-value <0.001). The LMIS database showed that 45% of children identified in the paediatric ward were HIV-infected compared to 30% of children identified via NRUs and 4% in MIP clinics. A chi-square test of significance shows that HIV positivity varies between entry points (chi-square value=597.83, with 6 degrees of freedom and p-value <0.001).

Conclusions High yield of HIV positivity in children was found in the paediatric wards and NRUs as opposed to MIP and outpatient wards. Targeting EID POC testing to these settings can reduce infant mortality and morbidity as HIV-infected children will be identified and initiated on treatment more quickly.

PA-057 ENHANCING TUBERCULOSIS DETECTION BY TRAINED RATS AND TRACKING OF MISSED PATIENTS THROUGH COMMUNITY-BASED STRATEGY IN TB HIGH-BURDEN COUNTRIES

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10.1136/bmjgh-2016-000260.90

Background Tuberculosis (TB) diagnosis in most sub-Saharan African countries with high TB burden is by direct smear microscopy that has low sensitivity. More sensitive tests like GeneXpert are expensive and not yet available in most African settings. Therefore, a need for cheap and rapid tests is inevitable. Trained rats (*Cricetomys* spp.) detect TB by targeting the *Mycobacterium tuberculosis* specific volatile compounds. Accredited rats evaluated 150 sputa in 20 minutes. We report on intervention involving TB detection by rats and additional patient tracking by community healthcare workers from MUKIKUTE and PASADA for treatment.

Methods Sputum was collected in hospitals in Dar es Salaam, Coast and Morogoro, Tanzania after microscopy. Sputa were heat inactivated at 100oC×30 minutes to kill pathogens and thereafter presented to rats in random computer generated positions for evaluation. Samples indicated as TB-positive by rats were confirmed by concentrated smear microscopy whether they contained TB bacilli. Confirmed TB cases were reported to community healthcare workers and hospitals for tracking and treatment. Healthcare workers recorded contact details of presumptive TB patients for subsequent tracking when detected by rats.

Results From 2011 to 2015 detection rats evaluated 306,346 sputum samples from 152,118 presumptive TB patients, which

were also tested by microscopy in hospitals. DOTS smear-positive TB patients were 21,911 and rats detected an additional 7961 patients missed in hospitals. Community healthcare workers tracking the additional patients brought 2715 additional TB patients to treatment whereas treatment initiation increased from 56% (1020/1812) in 2013 to 73% (870/1,198) in 2015. This prevented TB transmission to 27,150 to 40,725 people since one untreated TB patient can spread the disease to 10–15 persons annually.

Conclusions TB detection using rats and involvement of community healthcare workers to track the additional TB patients for treatment can increase TB detection and treatment initiation rate of missed TB cases.

PA-058 A RAPID SEROLOGICAL TRIAGE TEST FOR DETECTING ACTIVE TUBERCULOSIS

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Background A rapid screening test for active tuberculosis (TB) will reduce diagnostic delay and expedite referral for confirmatory testing and treatment. Antigen detection tests, which may utilise a rapid lateral flow (LF) platform suited to point-of-care use, offer a promising alternative to conventional methods for TB diagnosis. To date, the lack of accurate biomarkers has precluded the development of a serological assay.

Methods Sera and saliva were obtained by our consortium partners from culture-positive TB cases and healthy asymptomatic controls in high-burden settings. *Mycobacterium tuberculosis* (Mtb) antigens with diagnostic potential were expressed in eukaryotic and prokaryotic systems, and antigen combinations evaluated for sensitivity/specificity on multiplex, ELISA and LF platforms.

Results Based on a comparison of proteins recognised by antibodies from patients and controls, we have identified a combination of secreted and membrane-associated antigens involved in cell wall/cell processes and lipid metabolism that differentiate between active disease and latent infection. Sensitivities of 84–94% among TB cases and specificities of 97–100% among healthy endemic controls were obtained by screening over 300 samples against combinations of eukaryotic-expressed antigens on different platforms. Results indicating active TB were also observed among samples from symptomatic smear/culture-negative TB suspects. Antibody reactivity was not Mtb strain-specific. Sera from Norwegian latent TB controls yielded negative results. Our LF assay detects TB in the context of HIV co-infection, and is currently being optimised using sera from well-characterised TB suspects in Cape Town.

Conclusions Screening our sample sets against a selected combination of Mtb antigens by multiplex and LF prototype assays yielded sensitivities and specificities superior to that obtained by sputum smear microscopy. Our LF prototype conforms to the WHO target product profile criteria for a community-based triage test. Modification of the lateral flow platform for finger-stick blood and/or saliva samples will further increase assay suitability for use at the health post level.

PA-059 MOLECULAR TYPING AND DRUG RESISTANCE IN *MYCOBACTERIUM TUBERCULOSIS* COMPLEX ISOLATES FROM JAMOT AND MBALMAYO DISTRICT HOSPITALS, CAMEROON

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Background Cameroon is a country where tuberculosis still remains a major public health problem. The aim of the present research was to evaluate the potential of molecular markers in predicting first-line drug resistance and to investigate the predominant genotypes representative of *Mycobacterium tuberculosis* strains in the Centre region of Cameroon.

Methods A total of 169 strains of *M. tuberculosis* isolate from the Centre Region of Cameroon were screened for mutations associated with first-line drug resistance by DNA sequence analysis. Spoligotyping and MIRU-VNTR (24 loci; mycobacterial interspersed repetitive units typing – variable number tandem repeat) were combined to identify clustered isolates.

Results Rifampicin-resistant strains had the *rpoB* mutations D516V, H526D or S531L; isoniazid-resistant strains had the mutations *katG* S315T or inhA promoter C15T; streptomycin-resistant strains had the mutations *rpsL* K43R, *gidB* V36G, H48N, P75S, L79W, or A138P; ethambutol-resistant strains had the mutation *embB* M306V. Among those *M. tuberculosis* isolates, 52.5% isolates were Cameroon genotypes followed by Haarlem genotype (22.1%). The frequencies of isoniazid, rifampin, streptomycin and multidrug-resistant isolates were equally distributed in Cameroon genotype strains and non-Cameroon strains. Furthermore, the analysis also shows the very low frequency of *M. africanum* since only 2.6% of isolates belong to this species.

Conclusions Mutations of common genes known to be involved in resistance had high specificities in detecting resistance. This study reveals the highly diverse *M. tuberculosis* population structure, It confirms a predominance of the Cameroon lineage in the Centre Region of Cameroon and the disappearance of *M. africanum* in Cameroon.

PA-060 EMERGENCE OF NONTUBERCULOUS MYCOBACTERIUM PULMONARY INFECTIONS, ANALYSIS OF ISOLATES FROM PREVIOUSLY TREATED TB CASES

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10.1136/bmjgh-2016-000260.93

Background The main objective of this study was to characterise supposed non-tuberculous mycobacteria (NTM) found in previously treated tuberculosis (TB) cases to inform policy on inclusion of NTM diagnosis and management as a differential in TB care. In addition, the objective was to test the sensitivity or otherwise of the identification algorithm used in Ghana to declare an isolate an NTM.

Methods Thirty-one supposed NTM isolates from previously treated TB patients were collected. The NTM identification was based on culture positivity by BD MGIT 960TM, smear positivity for acid fast bacilli and finally by BD MGIT TB-cIDTM test kit. DNA was extracted using the Hain Lifescience GMBH GenolyseTM kit. The specimens were further subjected to sequencing.
Results Five (16%) of the previously treated cases were *Mycobacterium tuberculosis complex (MTBC);* two (6.5%) were *M. abscesus/cholenae;* 1 case (3.2%) for *M. fortuitum* and *M. gordonae* each. One (3.2%) was an unknown mycobacterium and 4 (12.9%) were other bacteria. Streptomyces and Brevibacteria were 8 (25.8%) and 6 (19.4%), respectively. There were three incidences of mixture with other bacteria; 2 MTBCs (6.5%) and 1 NTM (3.2%).
Conclusions There is some evidence to suggest the prevalence of NTM colonisation and disease in previously treated TB patients. There is the possibility of some smear positive new cases being NTM lung diseases but may be put on TB treatment. Emphasis on differentiation of AFB positive smears before treatment especially for retreatment cases must be made. The rapid deployment of new molecular methods has the potential of bridging the gap. There is the need for a definite diagnostic algorithm that can detect both NTMs and MTBCs. Further studies are encouraged to determinate whether the other organisms identified are relevant possible pathogens or contaminants.

PA-061 COMBINED SPECIFIC IGG – AND IGA-BASED DIAGNOSIS OF TUBERCULOSIS IN AFRICAN PRIMARY HEALTHCARE CLINIC ATTENDEES WITH SIGNS AND SYMPTOMS SUGGESTIVE OF TUBERCULOSIS

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Background IgG-based tests for the diagnosis of active tuberculosis disease (TB) often show a lack of specificity in TB endemic regions, which is mainly due to a high background prevalence of latent TB infection (LTBI). Here, we investigate the combined performance of the responses of different Ig classes to selected mycobacterial antigens in primary healthcare clinic attendees with signs and symptoms suggestive of TB.
Methods We evaluated the sensitivity and specificity of serologic IgA, IgG and/or IgM to LAM, 7 mycobacterial protein antigens (ESAT-6, Tpx, PstS1, AlaDH, MPT64, 16 kDa and 19 kDa) and 2 antigen combinations (TUB, TB-LTBI) in the plasma of 42 individuals with other respiratory diseases (separated into 21 LTBI controls and 21 uninfected healthy controls), and 21 active TB patients at baseline, of whom 19 were followed up at month 6 at the end of TB treatment.
Results The leading single serodiagnostic markers were anti-16 kDa IgA, anti-MPT64 IgA, anti-LAM IgG and anti-TB-LTBI IgG. IgA responses to MPT64 and 16 kDa had the highest sensitivity/specificity of 95%/95% and 95%/90% in differentiating active TB from other respiratory diseases and active TB from LTBI controls, respectively. The combined use of 3 or 4 antibodies further improved this performance to accuracies above 95%. After successful completion of anti-TB treatment at month 6, only particularly anti-TUB IgG showed distinctively decreased levels.
Conclusions These results show the potential of combining IgG and IgA responses against selected protein and non-protein antigens in differentiating active TB from other respiratory diseases in TB endemic settings, and may provide a benchmark for vaccines.

PA-062 DISCORDANT RESULTS BETWEEN GENOTYPIC ASSAYS (XPERT MTB/RIF AND HAIN MTBDRPLUS) AND BACTEC MGIT 960 SYSTEM FOR DETECTION OF RIFAMPICIN-RESISTANT *MYCOBACTERIUM TUBERCULOSIS* ISOLATES IN ZAMBIA

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Background Combination of genotypic assays (Xpert MTB/RIF and MTBDRplus (LiPA) would be a powerful tool to shorten the time for diagnosis of MDR tuberculosis (TB). However, the algorithm used for these assays in Zambia has not yet been implemented and the most widely used drug susceptibility testing (DST) method remains MGIT DST. Missed rifampicin resistance on the MGIT 960 system has been reported by several studies due to silent rpoB gene mutations. We report comparative observations made on the performance of Xpert, LiPA and MGIT DST methods for detection of rifampicin resistance (RR) at the ZAMBART Central Laboratory (ZCL).
Methods Specimens were collected from consecutive patients with Xpert rifampicin resistance positive (RR+) or rifampicin resistance indeterminate (RRI) results at peripheral site laboratories for further testing at the ZCL. Each sample was tested using Xpert, LiPA and MGIT culture/DST.
Results 30 patient samples were received and 17 were RR+, 8 were rifampicin-sensitive (RR-) and 5 were TB-negative by Xpert. All 17 RR+ on Xpert were RR+ on LiPA and all 8 Xpert RR – were sensitive on LiPA giving a 100% concordance for diagnosis of RR. Three isolates that were rifampicin sensitive by the MGIT system (Gold standard) were RR+ by both genotypic tests. Genotypic tests showed evidence of mutation in the codon 526 region of the rpoB gene for all the three isolates with discordant RR MGIT DST results. Xpert positive predictive value for Multidrug Resistance (MDR) TB was 62.5% and 81.2% compared to MGIT DST and LiPA, respectively.
Conclusions There is need for Zambia to perform a full classification of rpoB mutations to determine the prevalence of silent mutations. This will optimise national guidelines for diagnosis of RR – and MDR-TB.

PA-063 ANALYSING THE TREND OF BIOMARKERS WITH TB TREATMENT IN TUBERCULOSIS DISEASE SUSPECTS

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Background The search for biomarkers of pulmonary tuberculosis (PTB) disease, infection, treatment progress among others is especially due to lack of suitable tests for diagnosis or differentiation of active PTB disease and mere latent TB infection. The existing methods have, among others, poor sensitivity, long

turnaround time, high cost and the need for skilled personnel and infrastructure. Therefore, this study analysed 27 analytes (previously identified as promising) in TB research for their trend during TB treatment among PTB disease suspects in Mulago Hospital in Kampala, Uganda.

Methods This study used plasma samples from 76 TB suspects enrolled as part of a bigger longitudinal African-European TB Consortium (AETBC) study funded by the EDCTP within Kampala, Uganda. 71% were males, average age was 32±10, 14% were HIV-infected. PTB was confirmed by MGIT (mycobacteria growth indicator tube) and speciated for MTB complex. Subjects were followed at month 2 and 6 of treatment. The 27 analytes: (IL-1b,1ra, 2, 4, 5, 6, 7, 8, 9, 10,12p70,13,15,17A, eotaxin, Basic FGF,G-CSF, GM-CSF, IFNg,IP10, MCP-1, MIP-1a,b, PDGF-BB, RANTES, TNF-a, VEGF) were analysed using Luminex. Of the TB suspects, 38 had confirmed MTB by MGIT. The 38 TB suspects, used as controls, had X-ray results ranging from normal to consistent with TB.

Results Levels of 14 of the analytes most notably MIP-1a, b, IP-10, RANTES, IL-8, IL-12p70, IL-17A and VEGF significantly reduced throughout treatment. Notably, levels of IFNg, IL-12p70, 4,6,IP10, and VEGF significantly reduced by month of treatment. Combinations of IP10, RANTES, MIP-1b and VEGF also showed promising abilities in identifying treatment success with an interesting trend appearing in suspects with non-TB chest infections and with HIV–TB co-infection.

Conclusions The above markers have promising abilities for PTB diagnosis and identification of possible relapse or treatment failures.

PA-064 IDENTIFICATION OF NOVEL PLASMA AND SALIVARY BIOSIGNATURES FOR THE DIAGNOSIS OF TB DISEASE AND MONITORING OF TREATMENT RESPONSE

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Background New tools are urgently needed for the rapid diagnosis of TB disease, especially in resource-constrained settings. We investigated the usefulness of host markers detected in plasma and saliva as biomarkers for the diagnosis of TB disease and monitoring of treatment response.

Methods We prospectively collected plasma and saliva samples from 55 individuals that presented with signs and symptoms suggestive of TB disease at a health centre in Cape Town, South Africa, prior to the establishment of a clinical diagnosis. Patients were later classified as having TB disease (n=22) or other respiratory diseases (ORD) (n=33), using a combination of clinical, radiological and laboratory findings. The concentrations of 74 host markers were evaluated in plasma and saliva samples from all study participants using a multiplex cytokine platform.

Results Out of the 74 host markers evaluated, 18 markers detected in plasma, and two detected in saliva, showed potential as TB diagnostic candidates, with area under the ROC curve ≥0.70. A six-marker plasma biosignature comprising of NCAM, SAP, IL-1ρ, sCD40L, IL-13 and Apo A-1 diagnosed TB disease with a sensitivity of 100% (95% CI: 86.3–100%) and specificity of 89.3%(95% CI, 67.6–97.3%), whereas a five-marker salivary biosignature comprising of IL-1ρ, IL-23, ECM-1, HCC1 and fibrinogen diagnosed TB disease with a sensitivity of 88.9% (95% CI: 76.7–99.9%) and specificity of 89.7% (95% CI: 60.4 –96.6%), both regardless of HIV status. The plasma concentrations of 11 of the host markers and 8 of the markers detected in saliva changed during treatment, indicating that they may be useful in monitoring of TB treatment response.

Conclusions We have identified novel plasma and salivary biosignatures which may be useful in the diagnosis of TB disease and monitoring of the response to TB treatment. Our findings have potential to be translated into point-of-care screening tests after further validation.

PA-065 FACTORS AFFECTING TB TRANSMISSION FROM ADULT TO CHILDREN WITHIN HOUSEHOLDS IN THE GAMBIA

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Background Childhood tuberculosis (TB) has significant impact on public health worldwide and it is believed that most children acquire TB from an adult smear-positive index case within their household. To further examine this hypothesis and to investigate transmissibility of strains within the household setting, we compared strain-types in adults and their child contacts. We also examined the influence of bacillary burden and strain-type on clinical outcome of contacts.

Methods Stored isolates from smear positive adult TB cases (n=136) were selected according to clinical outcomes of their household contacts (children<15 years old). Mycobacteria were isolated from both adult and – where available – children samples via culture, and typed using spoligotyping to enable strain classification.

Results The AFB grade of adult index cases correlated with clinical outcome of the children with microbiologically confirmed TB, clinically diagnosed probable TB, asymptomatic but TST positive, and asymptomatic, and TST negative children showed 60%, 35%, 34% and 33% highest AFB grade (3+) levels, respectively. Strain-type determination by spoligotyping showed that 93% of children had acquired Euro-American lineages, while 7% had *M. africanum* lineage. Combined results for adult index cases of children with confirmed and probable TB showed 76% Mtb-Euro-American, 17% *M. africanum* and 7% Mtb-Indo-Oceanic. Index cases of TST positive children showed 59% Mtb-Euro-American, 32% *M. africanum*, 8% Mtb-Indo-Oceanic and 2% Mtb-Beijing. Those of TST negative children showed 63% Mtb-Euro-American, 26% *M. africanum*, 9% Mtb-Indo-Oceanic and 2% Mtb-Beijing.

Conclusions The data so far support other published data, which show that a higher bacillary burden in the index case increases the likelihood of TB transmission to child contacts. Adult patients appear to be more likely to transmit TB if they were carrying Euro-American lineages rather than West African strains.

PA-066 VITAMIN D FOR TREATMENT AND PREVENTION OF TB-HIV

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Background Susceptibility to reactivate tuberculosis infection is influenced by immunosuppression. Amongst the greatest risk

factors for active TB are HIV-1 infection and vitamin D deficiency. These risks factors are not mutually exclusive and may exacerbate each other. However, the phenotype of immunodeficiency induced by each is different. Vitamin D deficiency not only associates with TB risks, but it is greater in HIV-co-infected patients. The effects of vitamin D on the immune system are pleiotropic, being both anti-inflammatory and antimicrobial. Evidence suggests that vitamin D may not only reduce risk of TB by increasing anti-mycobacterial immunity and reducing inflammation, but it may also reduce HIV replication and the associated effects on innate and adaptive immunity; thus concomitantly reducing the associated risk of HIV on TB.

Methods We investigated *in vitro* and *ex vivo* the effect of vitamin D supplementation on the response of monocyte-derived macrophages (MDM) and peripheral blood mononuclear cells (PBMC), respectively, to HIV-*M. tuberculosis* (*Mtb)* co-infection. The effects of pathogen growth and susceptibility to infection were correlated to cytokine, chemokine and antimicrobial peptide production, by expression, secretion and flow cytometry analysis.

Results MDM differentiated in the presence of vitamin D metabolites, significantly restricted HIV-1 replication, alone and during co-infection with *Mtb*. Type 2 MDM were considerably more susceptible to HIV-1 infection than type 1. This correlated with the level of CCL2 production, which was significantly inhibited by vitamin D metabolites. PBMC isolated from healthy individuals in summer and in winter after receiving vitamin D, significantly restricted HIV-1 infection, compared to PBMC collected in winter before supplementation. There was a significant difference in circulating cell populations and serum cytokines/chemokines in summer, compared to winter, and these were investigated for correlations with HIV replication.

Conclusions Vitamin D may prove a cheap, effective, tool for preventing TB-HIV disease progression and clinical trials are warranted in at-risk populations.

PA-067 PHARMACOKINETICS OF RIFABUTIN IN COMBINATION WITH LOPINAVIR-RITONAVIR IN ADULT PATIENTS WITH HIV AND TUBERCULOSIS CO-INFECTION IN BURKINA FASO

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Background This study aimed to assess the pharmacokinetic profile of rifabutin (RBT) given at 150 mg or 300 mg every other day (EOD) in tuberculosis (TB)-HIV co-infected adult patients.

Methods This is a pharmacokinetic prospective, pilot, open, randomised study of two doses of RBT in combination with lopinavir/ritonavir among HIV–TB patients in Burkina. Sixteen patients were randomised in two arms: TB treatment consisting HZE standard doses in association with RBT150 mg EOD (arm A, 8 patients) or RBT300 mg EOD (arm B, 8 patients) in combination with lopinavir/ritonavir. RBT plasma concentrations were evaluated after two weeks of combined HIV and TB treatment. Samples were collected at pre-dosing and at 1, 2, 3, 4, 6, 8 and12 hours after drug ingestion to measure plasma drug concentration using HPLC–MS/MS assay.

Results The mean Cmax and AUC in the RBT 150 mg arm (Cmax=0.35±0,18 μg/mL, AUC(0–24)=3.94±2,1 μg.h/mL) were significantly lower (p=0.01) than those of the RBT 300 mg arm (Cmax=0.75±0.54 μg/mL AUC(0–24)=7.1±2.7 μg.h/mL). There was no significant difference in Tmax (Tmax=3.44 ±2.01 hours *vs* Tmax=3.86±2.04 hours) p=0.687. RBT follows linear kinetics and no significant differences were apparent in the mean oral clearance (CL/F) estimates (p=0.683), which were dose independent and similar for the 2 assessment doses. Five of 8 patients in RBT150 mg arm had a Cmax below plasma therapeutic limit (<0.3 μg/ml). All patients in RBT 300 mg arm had a higher Cmax than this limit. Also, at 48 hours of drug ingestion, all patients in the RBT 300 mg arm (8/8) had a mycobacterial minimum inhibitory concentration (MIC) above the limit (>0.06 μg/mL) compared with 4 of 8 patients in the RBT150 mg arm. The means Cmax, AUC (0–24) and Tmax of 25-O-desacetyl rifabutin of the RBT 300 mg arm were increased by 100% and 50% respectively compared to the RBT150 mg arm.

Conclusions This study confirmed that the dose of rifabutin 150 mg three times a week in combination with lopinavir/ ritonavir is inadequate and could lead to the selection of rifamycin-resistant mycobacteria.

PA-068 CYTOLOGICAL PROFILE OF RED BLOOD CELLS IN HIV-INFECTED PATIENTS: CASE OF THE DOUALA GENERAL HOSPITAL (CAMEROON)

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Background Haematological abnormalities have been documented as strong independent predictors of morbidity and mortality in HIV-infected individuals. Those infected with HIV without antiretroviral treatment (ART) have a high prevalence of abnormal blood cells. HIV-1 induced dyserythropoiesis in conjunction with the effects of HIV-related inflammation and/or chronic immune activation. The objective of the study is to identify and characterise the different red cell morphological changes that occur during the evolution of HIV infection in patients according to clinical, biological and therapeutic variables.

Methods A total of 232 patients infected by HIV were included in this cross-sectional and descriptive study conducted at the Douala General Hospital (Cameroon) from June to December 2015. All the patients were screened for red blood cells abnormalities. Blood samples were taken in EDTA tubes for full blood counts (FBC) and blood films. chi-square test was used to compare the variables, and the statistical significance level adopted was p-value under 0.05.

Results Three quarters of patients in our study had abnormal quantitative or qualitative red blood cells, giving a prevalence of 77.5%. The mean value of haemoglobin was 11.9 g/dl with a prevalence of anemia at 61.2% for all participants. The main red blood cells abnormalities were the anisocytosis (43.1%), the anisochromia (34.5%), the macrocytosis (24.1%), the microcytosis (13.8%), the hypochromia (12.9%) and the poikilocytosis (12.5%). These abnormalities are statistically significant and are dependent on the severity of the anaemia the WHO clinical stage, the ART duration and the medication regime with all p< 0.05.

Conclusions The frequency of cytological abnormalities of red blood cells is high during HIV infection and proportional to the

severity of the anemia, the duration of antiretroviral therapy diet and its clinical evolution stage. We recommend that reading blood films is systematic of FBC prescription in the monitoring of HIV-infected patients.

PA-069 CYP2B6 GENOTYPE BASED EFAVIRENZ DOSE RECOMMENDATIONS DURING RIFAMPICIN-BASED ANTITUBERCULOSIS CO-TREATMENT FOR A SUB-SAHARAN AFRICA POPULATION

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Background Pharmacogenetics is a major determinant of the EFV–rifampicin interaction during HIV-TB co-treatment. We assessed genetic factors that influence EFV PK, treatment outcomes and provide genotype-based EFV dose recommendations for adult TB-HIV-1 co-infected Ugandans receiving rifampicin based anti-tuberculosis co-treatment.
Methods Steady state plasma EFV concentrations (n=1216) from 158 HIV-TB co-infected patients (76 females) treated with efavirenz/lamivudine/zidovidine and rifampicin-based TB treatment were analysed. Patient genotypes for *CYP2B6* (**6* & **11*), *CYP3A5* (**3*,**6* & **7*) and *ABCB1c.4046A>G*, baseline biochemistries and CD4 and viral load change from baseline were determined. A one-compartment population PK model with first-order absorption (NONMEMTM) was used to estimate genotype effects on EFV PK. Population genotype-frequency-based PK simulations predicted AUCs and trough concentrations were compared between the product label / known reference values and different dose simulations.
Results Compared to *CYP2B6**1/*1*, EFV post-induction CL/F was 2.5 and 1.7 times higher in *CYP2B6*6/*6* and *CYP2B6*1*/6*, respectively. A 23% increase in F1 was observed for the variant ABCB1 c.4046A>G. EFV mean AUC was significantly higher in *CYP2B6*6/*6* genotypes compared to *CYP2B6*1/*1* (p< 0.0001). Simulated AUCs for a 600 mg EFV dose were 1.2 and 2.4 times greater than the product label mean AUC for the Ugandan population in general and *CYP2B6*6/*6* genotypes, respectively. EFV daily doses of 450 mg and 250 mg for the general population and *CYP2B6*6/*6* genotypes respectively yielded simulated exposures that were comparable to the product label. Overall, only 8.9% patients had HIV RNA >40 copies/mL after 84 days of treatment.
Conclusions During rifampicin co-treatment, daily doses of 450 mg and 250 mg might meet the EFV dosing needs of HIV-TB infected Ugandans in general and CYP2B6*6 homozygous variants, respectively.

PA-070 PREVALENCE OF ADVERSE DRUG REACTIONS AMONG HIV/AIDS PATIENTS ON HAART IN UNIVERSITY OF MAIDUGURI TEACHING HOSPITAL (UMTH), NIGERIA: A FOUR-YEAR RETROSPECTIVE STUDY

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Background Current evidence on highly active antiretroviral therapy (HAART) indicates that each person will have to take the drugs for life [1]. Since 2000, the prevalence of HIV in Nigeria has shown a gradual consistent decline from 5.0% in 2003 to 4.1% in 2010 following the introduction of HAART. While HAART improves the quality of life among HIV patients, adverse drug reactions (ADRs) may compromise quality of life in some patients.
Methods We performed a retrospective study at HIV/AIDs clinic, UMTH Nigeria, among ART-naive adult patients recruited from January 2006 to December 2010 and followed up for 48 months from commencement of HAART. Database and clinical charts of eligible patients were extracted for clinical information, type of reported ADRs, and physician's decision on whether or not ADRs was serious according to ICH E2A guidelines. Data was analysed using SPSS Ver. 21. Logistic regression was used to calculate odds ratios and of ADR associated with patient and treatment characteristics.
Results Patients initiated on HAART (n=7260) were reviewed with a prevalence of serious ADRs (53.4%). Commonest ADRs were peripheral neuropathy (11.0%), itching (9.5%), anaemia (9.2%), dyspepsia (9.1%) skin rashes (9.1%), and various forms of dermatitis (5.5%). Almost all (96%) the reported ADRs occurred between 3–18 months of treatment. Patients initiating on a zidovudine and efavirenz-based regimen (p=0.015 and p=0.020 respectively), baseline CD4≤200/ mm3 (P=0.000), unemployed patients (P=0.000), students (p=0.000) and petty traders (p=0.000) were statistically significantly associated with increase occurrence of an ADR.
Conclusions The study has identified the prevalence, types and the determinants of ADRs among HIV/AIDs patients at UMTH, Nigeria. These findings might be helpful in developing clinical guidelines on ADRs profile as a major criterion for choosing HAART drugs, hence promoting pharmacovigilance of ARVs in Nigeria.

PA-072 GP41 DIVERSITY IN ANTIRETROVIRAL THERAPY NAïVE AND EXPERIENCED HIV-1 SUBTYPE C-INFECTED PATIENTS IN BOTSWANA: IMPLICATIONS FOR ENFUVIRTIDE (T-20) USE

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Background With the expansion of HIV treatment programs in sub-Saharan Africa, there are increased cases of HIV drug resistance. In Botswana where the national HIV treatment program has been in place since 2002, patients with HIV strains resistant to the core antiretroviral classes are a reality. There is need to investigate how some of the less frequently used antiretroviral classes such as enfuvirtide (T-20) and its derivatives would fair in this population.
Methods A total of 164 samples from 129 patients initiating combination antiretroviral therapy (cART) and 35 patients failing NRTI – and NNRTI-based cART in studies conducted in Botswana were available for analysis. Viral RNA was isolated from plasma and RT-PCR targeting HIV-1 gp41 was run and the product sequenced. Sequences were edited using Sequencher and alignments were made using Clustal-X. A

search on the Los Alamos HIV database yielded 106 gp41 sequences from unique Botswana patients and these were included in the analysis. The IAS-USA, 2015 Resistance Mutations update report was used to define the T-20 drug resistance mutations.

Results A total of 154 samples were successfully sequenced, 126 from treatment naïve patients and 28 from virologic failure patients. Additionally, 106 gp41 sequences from previous studies conducted in Botswana were included in the analysis. No major T-20 was detected in any of the 260 sequences. The N42S mutation which is associated with T-20 hypersensitivity was found in (87.3%) and this is consistent with published data from HIV-1C studies. The I69V mutation (95.6%) was the most common detected HR1 polymorphism. The most common HR2 polymorphism detected was I135L (98.4%) followed by E151A (92.3%).

Conclusions These results provide invaluable data on gp41 diversity in Botswana and show that there is no background resistance to T-20 or its derivatives. T-20 would be an alternative drug for patients failing cART in Botswana.

PA-073 BASELINE BACTERIAL LOAD AND RIFAMPICIN EXPOSURE ARE ASSOCIATED TO CULTURE CONVERSION IN A TWO-MONTH STUDY OF TUBERCULOSIS

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Background Early bactericidal activity (EBA) during the first two weeks of TB treatment is an important method for early efficacy evaluation of new anti-tuberculosis agents.

Methods We performed an observational; two-site clinical study in Tanzania in patients with newly diagnosed pulmonary TB during the first eight weeks of standard HRZE treatment. Baseline and treatment-related covariates including X-ray, baseline bacterial load and rifampicin pharmacokinetics were analysed for their correlation to treatment success.

Results From Nov 2011 to July 2013 we enrolled 74 pulmonary TB patients from Moshi (41) and Mbeya (33). Mbeya participants had a higher baseline bacterial load measured by log time to positivity (TTP) in the MGIT culture system (median 1.29; IQR 1.09–1.46 *vs* 1.58; IQR 1.44–1.87; p< 0.001) Overall, 56/68 (80%) of patients achieved a negative solid media culture, and 28/59 (47%) achieved a negative liquid culture at 8 weeks. Median time to negative on LJ culture was 45.5 days (IQR 21–56), in liquid culture 56 days. The strongest association with outcome for any covariate was found for baseline bacterial load: patients with a positive week 8 LJ culture had a median logTTP of 1.20 (IQR 0.94–1.35); patients with a negative week 8 culture had 1.48 (1.29–1.73; p=0.006). In exploratory analysis, rifampicin area under the concentration curve (AUC) was associated with shorter time to LJ culture conversion in patients who achieved negative culture, (hazard ratio 1.05, p=0.038), but not in the total population.

Conclusions This observation EBA study using standard HZRE was successfully implemented with methodologies thus far established for the first time at the two Tanzanian sites. Baseline bacterial load was confirmed as an important predictive parameter.

PA-074 HEPATITIS B VIRUS CO-INFECTION IS ASSOCIATED WITH INCREASED ALL-CAUSE MORTALITY AMONG HIV-INFECTED ADULTS ON TENOFOVIR-DISOPROXIL-FUMARATE CONTAINING ANTIRETROVIRAL THERAPY IN LUSAKA, ZAMBIA

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10.1136/bmjgh-2016-000260.106

Methods We prospectively enrolled HIV-infected treatment naïve adults in Lusaka, Zambia. At enrolment, we recorded patient's demographics, body mass index (BMI), WHO clinical stage, CD4+ count, and hepatitis B surface antigen (HBsAg) status. In HBsAg-positive patients we measured HBV viral loads (VL; Roche, COBAS® AmpliPrep/COBAS® Taqman® Assay, Pleasanton, California). We defined active HBV co-infection as having an HBV VL ^{3}20 IU/ml. TDF-based ART was the preferred first-line regimen. Follow-up visits occurred per national guidelines and we used phone and community tracing to optimise retention. Deaths were ascertained by clinic, family member, or community health worker report and losses to follow-up (LFTU) were defined as absences from clinic for 6+ months. Using multivariable Cox regression, we assessed the mortality risk among patients with HBV co-infection, adjusting for age, sex, WHO stage, BMI, and CD4+ count.

Results During 2013–2014, 822 patients were enrolled and analysed at 1 year after ART initiation. Among this group, 438 (53.1%) were women, median age was 34 years (interquartile range, 29–40), 367 (44.8%) had WHO stage 3 or 4, 229 (28.2%) had BMI <18.5, and median baseline CD4+ 224 cells/mm3. Of 126 HBsAg-positive individuals, 81 had active HBV infection. During the first year on ART, 48 patients died, 19 transferred out or withdrew, and 52 were LTFU. Those with HBV co-infection had twice the risk of death (adjusted hazard ratio, 2.23, 95% CI: 1.07–4.65) after adjustment for covariates.

Conclusions In Southern Africa, HBV co-infection is a mortality risk factor and these patients should be diagnosed and those with replicating virus may need closer monitoring. Further investigation of the causes of death in HIV-HBV patients is needed.

PA-075 RELATIONSHIP OF HIV-HBV CO-INFECTION WITH CD4 CELL COUNT AND ALANINE TRANSAMINASE LEVELS IN ANTI-RETROVIRAL THERAPY-NAïVE PATIENTS

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Background In sub-Saharan Africa, the prevalence of hepatitis B virus (HBV) is between 6–20%. In Zambia, prevalence of HIV and HBV co-infection has been reported to be between 7.1% and 31.1%. Patients infected with HBV are at increased risk of experiencing elevated alanine transaminase enzyme (ALT) and HIV-HBV co-infection may lead to further reduced CD4 cell count before initiating antiretroviral therapy (ART). We investigated the relation of HBV with CD4 cell count and ALT enzyme in HIV-positive antiretroviral therapy-naïve patients.

Methods This was a cross-sectional study conducted in 15 government clinics in Lusaka. There were 5436 adult patients who initiated antiretroviral therapy between 2011 and 2013. Cases were described as HIV-positive patients who tested HBsAg-positive and controls as HIV-positive patients who tested HBsAg-negative. HIV-HBV co-infection was defined as the number of patients who tested HBsAg-positive divided by the total tested (with 95% CI). Laboratory measures of CD4 and ALT were categorised in the analysis. Elevated ALT was defined as ALT≥66 IU/ml. CD4 cell count was dichotomised CD4 of >200 cells/μl.

Results The median age was 35 (29–41) years. The median CD4 cell count was 202 (102–305) cells/μl with the median ALT being 20 (14–30) IU/ml. HIV–HBV prevalence was 12.3% (95% CI: 11.4–13.1). Elevated ALT was reported in 11.1% cases and 4.7% in controls (p-value <0.001). The adjusted odds ratio (OR) of experiencing elevated ALT before ART initiation for HI-HBV patients was 2.4 (95% CI: 1.8–3.2) compared to their HIV-mono-infected counterparts. Of the cases, 53.5% had a CD4<200 while only 48.9% of controls had CD4 <200 before ART initiation (p-value 0.026).

Conclusions Prevalence of HBV is high among HIV-infected persons in Zambia. There is need to explore the interactions of these co-infections and their impact on CD4 cell count and ALT.

PA-076 CAN HIV TREATMENTS INFORM OTHER CONTEXTS? A TRIAL OF AN ADDITIONAL INDICATION FOR CO-TRIMOXAZOLE PROPHYLAXIS

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Background Co-trimoxazole prophylaxis is part of HIV management of opportunistic infections. However, it is not known if co-trimoxazole prophylaxis can prevent opportunistic infections among other vulnerable population such as people with complicated severe acute malnutrition (SAM). It is unclear if and how nutritional recovery may reduce susceptibility to infectious diseases like pneumonia with co-trimoxazole prophylaxis. We share secondary analysis results of multicentre, double-blinded, randomised clinical trial (ClinicalTrials. gov, number NCT00934492) of daily co-trimoxazole prophylaxis among HIV non-infected children with SAM in Kenya.

Methods We recruited 1781 hospitalised SAM children and randomised to either daily co-trimoxazole prophylaxis or matching placebo for six months and followed up for 12 months. Our outcome of interest was risk of subsequent pneumonia after index admission discharge, defined using the WHO guidelines. To determine changing susceptibility after discharge, cox regression model with monthly weight-for-height and height-for-age z-scores as time-varying covariates were used to identify risk factors of developing pneumonia.

Results Overall, 257 children died, 122 (14%) among the co-trimoxazole group and 135 (15%) of placebo group; Hazard ratio (HR) 0.90 (95% CI: 0.71–1.16, p=0.43). There were 1257 episodes of pneumonia, 603 (21%) among co-trimoxazole group and 654 (22%) among placebo; HR 0.93 (95% CI:0.79 –1.08, p=0.34) during 1556.6 child-years of observation (cyo). The monthly incidence rate for pneumonia and severe pneumonia declined over time (p=0.002 & p=0.001). Young age, urban residence, index admission with clinical signs of rickets and severe pneumonia, were associated with subsequent pneumonia. Index admission with diarrhoea and monthly weight-for-length z-score had protective effect. Protective effect of improving monthly anthropometric measures were evident from month two onwards. Proportion of pneumonia progressing to severe form declined with time (p=0.01) but there was no evidence case fatality ratios changed over time (p=0.41).

Conclusions Improving nutritional status during recovery correlates directly with reduced susceptibility, but not with case fatality of pneumonia.

PA-077 PREVALENCE AND PREDISPOSING FACTORS TO INTESTINAL PARASITIC INFECTIONS IN HIV/AIDS PATIENTS IN FAKO DIVISION OF CAMEROON

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Background Understanding the epidemiology of intestinal parasitic infections is essential for the effective management of HIV infection in areas where intestinal parasites are also endemic. Data on the prevalence of intestinal parasitic infections in people living with HIV/AIDS in Cameroon are scarce. This study was designed to determine the prevalence of intestinal parasitic infections, as well as assess the predisposing factors for the infections in HIV/AIDS patients in Fako division of Cameroon.

Methods Stool specimen was collected from consented participants and examined for ova, cysts, larvae or oocytes using the Kato-Katz, Formalin-Ether Concentration, Modified Ziehl-Neelsen and Modified field staining techniques. Statistical analyses performed included the Chi-square test and logistic regression.

Results At the end of the study, 300 participants were enrolled, the majority being females 236 (78.6%). The participants were between 21–70 years (mean±SD=40±10) of age. The overall prevalence of intestinal parasites was 82.6% (95% CI: 78.4–87.0). The prevalence of infection was associated with age, being more prevalent in the age group 51–60 years (p=0.032). Intestinal protozoa were more prevalent than intestinal helminthes (74.3% *vs* 11.3%). The parasites isolated included: *Cryptosporidium parvum* (44.0%), *Blastocystis hominis* (25.0%), *Microsporidium spp*. (21.0%), *Entamoeba histolytica* (7.3%), *Ascaris lumbricoïdes* (4.3%), *Isospora belli* (4.3%), *Trichuris trichiura* (2.3%), hookworm (2.7%), *Hymenolepis nana* (1.3%), *Strongyloïdes stercoralis* (0.7%), *Cyclospora cayetatensis* (3.7%) and *Giardia lamblia* (3.3%). The predisposing factors for infection with intestinal parasites included poor educational background (OR=0.33, p=0.02), unskilled worker (OR=0.27, p=0.04), a well as source of drinking water (OR=2.6, p=0.03), and living with cats as pets (OR=3.06, p=0.01).

Conclusions A very high prevalence of intestinal parasitic infections was observed in people living with HIV/AIDS. Routine screening for intestinal parasites should be instituted as part of HIV care in Fako division of Cameroon to improve the management of HIV/AIDS.

PA-078 IMPACT OF COMMUNITY TRACING ON HIV COHORT OUTCOMES IN URBAN ZAMBIA

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Background We investigated the impact of community tracing as recommended in national guidelines on outcomes within a prospective HIV cohort in Zambia.
Methods HIV-positive, antiretroviral therapy-naïve adults were enrolled at 2 Lusaka clinics. Per national guidelines we collected detailed baseline patient locator information including patient phone number, address, church, and a map from the clinic to their home. Study visits were aligned with routine ART program schedules and 3 telephonic attempts were made if visits were missed. Per guidelines, a lay health worker conducted a community home visit on lost to follow-up (LTFU) patients. Transfers to other clinics and deaths were ascertained when reported by the clinic staff, patients, or family members. At one year, we measured the percentage retained, transferred out, withdrawn (stopped ART), dead, and LTFU (>6 months absent). A lay health worker went into the community to make a home visit on LTFU patients. We recorded the change in mortality after tracing. We also estimated the time and costs per patient traced.
Results We enrolled 795 patients (median age 34 years; 53.7% were female; median CD4 228 cell/mm3). Prior to tracing, we recorded 45 deaths, 23 transfers, 1 withdrawal, and 83 LTFU who could not be reached by phone. At 63 attempted home visits, we learnt that 9 (14.3%) had died, 5 (7.9%) had transferred, and 2 had withdrawn. We could not locate 32 (50.8%) but neighbours/family reported that 12 of these had relocated (HIV care status unknown). After successful tracing, 15 (23.8%) returned to clinic and HIV care. Community tracing increased known mortality from 5.7% to 6.8% (95% CI: 5.1–8.8%) and increased retention at 1-year from 80.9% to 82.8%. Tracing required an average of 5 person-hours and K150.00 (~15 USD) in bus/taxi fares per patient.
Conclusions Community tracing was limited by patient mobility and had a modest impact on cohort mortality and retention.

PA-079 PREDICTORS OF RETENTION IN CARE OF HIV-INFECTED ADULTS IN TIGRAY, ETHIOPIA: A PROSPECTIVE COHORT STUDY

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Background HIV/AIDS represents one of the major health challenges of Ethiopia, despite a proven record of universal access to HIV care and treatment. Long-term antiretroviral therapy (ART) retention is a key factor for personal and public health benefits. Identification of determinants of attrition is needed to design appropriate interventions.
Methods We used data from the CASA project, a prospective, multisite study of a cohort of HIV-infected patients who started ART in seven urban and rural health facilities located in the Tigray. We analysed the retention in care and its associated determinants in over 1000 patients followed for two years. The main outcome measure was the retention in care rate, defined as the proportion of patients alive and receiving ART at the same health facility as at ART initiation. Kaplan-Meier method was used to estimate the probability of retention at different time points. Cox Proportional Hazards model with robust sandwich estimates to account for within health facility correlation was used to identify factors associated with retention.
Results Kaplan–Meier estimates of retention in care were 83.9%, 80.6% and 77.6% at 12, 18 and 24 months of follow-up, respectively. Attrition was mainly due to lost-to-follow-up and transferred-out patients. Multivariate Cox proportional hazard model showed that being male (HR 1.35, 95% CI: 1.04–1.75), CD4 count<200 (HR 1.49, 95% CI: 1.13–1.96), haemoglobin level <= 10 (HR 1.40, 95% CI: 1.11–1.76), the presence of active TB co-infection at ART initiation (HR 1.47, 95% CI: 1.04–2.08) and the type of health facility were significantly associated with attrition.
Conclusions According to our prospective data, combined interventions aimed to improve ART retention shall include expansion of HIV testing and earlier initiation of therapy, nutrition supplementation, early detection and treatment of TB. Observed retention differences among health facilities and according to gender suggest that innovative models of HIV care shall also be explored.

PA-080 CRYPTOCOCCAL MENINGOENCEPHALITIS IN HIV-INFECTED PATIENTS IN MADAGASCAR: HIGH PREVALENCE AND LETHALITY AND THERAPEUTIC CHALLENGES

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10.1136/bmjgh-2016-000260.112

Background In Madagascar the epidemiology of cryptococcosis is poorly documented. The main objective of this study was to estimate the prevalence of Cryptococcal meningoencephalitis (CM) in Madagascar and to describe the presentation of the cases.
Methods This is an observational transverse study conducted in the hospitals of Antananarivo and Toamasina cities. Between 3 November 2014 and 8 June 2016, HIV-infected adults presenting CD4 cell count ≤200/mm3 were selected. The crytococcocal antigen (CrAg) was screened in the blood using a lateral flow immunoassay (IMMYCrAg® LFA). If the result was positive and the patient symptomatic, CrAg was checked in the cerebrospinal fluid (CSF) and examined with India ink, and culture was performed. The isolated strains were subsequently analysed using MALDI-TOF and an antifungal susceptibility test was performed using the E-test method (BioMérieux).
Results Overall, 118 patients were included. The mean CD4 cell count was 86.4/mm3 (SD±60.6) and 35.6% of the patients were under ARV therapy at baseline. HIV-1 viral load of 88.5% of patients was positive. We compared the clinical characteristics of patients with cryptococcal infections to those of controls without CM. Eleven cases of CM were identified corresponding to a prevalence of 15.1% (95% CI: 7.8–25.4%). *Cryptococcus neoformans* var. *grubii* (serotype A) was isolated. Fever, headache, neck pain

and night sweats were the most common signs. In 7 cases, CrAg titres in the CSF were very high (≥2560) and did not decrease even 2 months post-treatment. The Case Fatality Rate was unacceptably high (69%).
Conclusions Overall, prevalence of cryptococcal meningoencephalitis (CM) in Madagascar was very high (15.1%) compared to that observed in some Sub-Saharan African countries. The point-of-care LFA CrAg test was confirmed to be reliable and cost-effective for the diagnosis. Challenges to facilitate access to more effective molecules to treat patients with CM include heavy administrative formalities linked to drug importation and low level of priority in implementing the national control programme.

PA-081 FACTORS AFFECTING ANTIRETROVIRAL DRUG ADHERENCE AMONG HIV ADULT PATIENTS ATTENDING HIV CLINIC AT THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA

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Background Effectiveness of anti-retroviral therapy (ART) requires strict adherence. Adherence ≥95% achieves optimum therapeutic levels and reduces drug resistance. We sought to determine factors associated with ART adherence within the context of patient demographics and factors, and explore care treatment and support strategies used by patients and health workers.
Methods A Mixed Method Sequential Explanatory Design (MMSED) was employed to study adult patients receiving ART from the University Teaching Hospital, Lusaka. Adherence was measured by missed clinic appointments and pharmacy collections over the last six months. The quantitative method assessed 715 complete pharmacy records extracted from the dispensing tool to ascertain demographic and patient factors. Bivariate and multivariate logistic regression analysis was employed. Qualitative research involved in-depth interviews with patients and key informants.
Results Results showed 79.4% of the patients were adherent to clinical appointments while 46.3% were adherent to pharmacy refills. Multivariate analysis showed lower adherence amongst the widowed on clinical appointments (OR=0.3; 95% CI: 0.1–0.9). The stepwise regression analysis revealed significant factors for adherence on clinical appointment and pharmacy refills for widowed, co-habiting and no education, (p=0.008, p=0.044, and p=0.018), respectively. About 80% of patients interviewed were adherent to ART.
Conclusions The results show moderate ART adherence (80%). However, in view of the identified factors affecting adherence, concerted and collaborative efforts through effective and efficient interventions are needed to improve the adherence levels to at least ≥95%.

PA-082 IMPROVING TUBERCULOSIS SCREENING AND DIAGNOSIS AMONG PEOPLE WITH HIV: UPDATES FROM THE INTENSIFIED CASE FINDING STUDY IN KISUMU COUNTY, KENYA

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Background Tuberculosis (TB) is the leading opportunistic infection and cause of death among people living with HIV (PLHIV). HIV predisposes latently TB-infected people to developing TB disease. Current TB screening algorithms lack sensitivity and specificity. We sought to determine the sensitivity and specificity of conducting a two-step clinical screening and testing for latent TB infection (LTBI).
Methods We enrolled 650 newly diagnosed HIV patients aged >7 years from HIV clinics in Kisumu County, Kenya. Study participants were screened for TB symptoms and sputum tested for smear microscopy, liquid culture and GeneXpert MTB/RIF (Xpert). Quantiferon (QFT) and tuberculin skin testing (TST) for LTBI. Positive results from liquid culture or Xpert defined a TB case. 'Negative for TB' was any participant with at least two negative Xpert or culture results from different specimens. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated and compared for one – and two – stage screening and stratified by QFT results.
Results Females were 62% of participants. TST-positive were 88 of 592 (15%); 274 of 648 (42%) were QFT-positive. TB prevalence was 15%. Screening results for one stage and second stage: 75% and 97% sensitivity, 31% and 12%, specificity, 89% and 96% NPV and 14% and 15% PPV, respectively. Screening performance stratified by QFT for sensitivity, specificity, NPV and PPV was 96%, 11%, 91% and 24% among QFT-positive.
Conclusions Two-step versus one-step screening increases sensitivity but reduces specificity. Positive QFT result increases the PPV of two-step screening.

PA-083 PREVALENCE AND FACTORS ASSOCIATED WITH HYPOCHOLESTEROLAEMIA AMONG ADULTS WITH PULMONARY TB AT DIAGNOSIS AND DURING TB TREATMENT IN KAMPALA

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10.1136/bmjgh-2016-000260.115

Background Hypocholesterolaemia is associated with altered immune function, possible delayed conversion at two months, and increased risk of mortality. However, lipid profiles are not done routinely for tuberculosis (TB) patients and there is paucity of data regarding the prevalence of hypocholesterolaemia and its associated factors among adult bacteriologically-confirmed pulmonary tuberculosis patients.
Methods This was a cross sectional study that consecutively enrolled 323 participants at diagnosis, 2, 5, 6 and 8 months of TB treatment, between February and April 2016. Physical examination and a structured questionnaire (administered by an interviewer) were used for data collection. Lipid profiles were determined from fasting blood samples from participants. Descriptive statistics were used to describe the patterns of dyslipidaemias and prevalence of hypocholesterolaemia. Log-binomial regression methods were used to determine the independent factors associated with hypocholesterolaemia.
Results Hypocholesterolaemia was identified in 140/323 (43.3%, 37.9–48.8) of adults with pulmonary TB with a high prevalence among those at diagnosis, 51/91 (56.0%, 45.8–66.3) but a lower prevalence among those who were at completion of treatment: 19/59 (32.2%, 20.9–44.3). On multivariate analysis, male gender (PR 1.57, 95% CI: 1.16–2.06), diabetes (PR 1.37, 95% CI: 1.05–1.78) and duration of anti TB treatment (1.12, 1.07–1.20) were associated with hypocholesterolaemia. There was no significant association between HIV infection status,

presence of cavities on chest x-ray and hypocholesterolaemia at diagnosis and during anti-TB treatment in this study.
Conclusions The overall prevalence of hypocholesterolaemia among participants was high. Males with pulmonary tuberculosis are 60% more likely to develop hypocholesterolaemia. There is a need for further research on dyslipidaemias in TB patients and policy improvements regarding assessment of these lipids and nutritional management.

PA-084 GENOTYPIC DIVERSITY AND DRUG SUSCEPTIBILITY PATTERNS AMONG *M. TUBERCULOSIS* COMPLEX ISOLATES RESPONSIBLE OF EXTRAPULMONARY TUBERCULOSIS IN CAMEROON FROM 2006–2015

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Background Extrapulmonary tuberculosis can cause major irreversible health complications if it is diagnosed late and not well treated. In Cameroon, it remains neglected with very few data concerning its different forms, causing species and their drug susceptibility, while these data may help to understand the global epidemiology of tuberculosis in Cameroon.
Methods We have made a retrospective study on 215 clinical isolates stored in Centre Pasteur of Cameroon. Isolates were genotyped using spoligotyping to identify lineages and families, and the drug susceptibility patterns were determined through proportion method.
Results The primary resistance rate of isolates was 12.5%, among which 3.12% were mono-resistant to isoniazid, 1.56% to rifampicin and 3.9% to streptomycin. No mono-resistance was recorded for ethambutol. Multidrug-resistance rate to at least isoniazid and rifampicin was 3.12%. Spoligotyping revealed that 97.67% (210/215) and 2.32% (5/215) of extrapulmonary tuberculosis was caused by *Mycobacterium tuberculosis* and of *M. africanum*, respectively. *M. bovis* was absent. Spoligotyping lineages identified among the *M. tuberculosis* complex (MTC) showed a dominance of Cameroon family (40.46%). The other families were the ubiquitous T (36.27%), Haarlem (13.95%), U (6.04%) and LAM (1.39%). Ten spoligotypes had no SIT numbers. Only *M. tuberculosis* strains were associated to resistance. But there was no significant difference for drug resistance between MTC lineages.
Conclusions To the best of our knowledge, this study is the first to give the population structure of MTC strains causing extrapulmonary tuberculosis (ETB) and their drug susceptibilities. That shows the predominance of *M. tuberculosis* species and the very low contribution of *M. africanum* and *M. bovis* as the causative agent of ETB. It also shows that the population structure of this MTC is similar to that observed in pulmonary tuberculosis suggesting the dissemination of the pulmonary tuberculosis.

PA-085 ETHICAL CONSIDERATIONS IN THE HANDLING OF A COMPLAINT REPORT AGAINST A STUDY TEAM: CASE OF A CLINICAL TRIAL (EARNEST) PARTICIPANT

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Background The major role of an ethics committee is to protect participants from harm through participating in a health research study. This includes investigating participant complaints to ensure that their wellbeing is being upheld and queries resolved satisfactorily. In this case, one clinical trial participant passed away and a report implying that her death was caused by trial medication received during participation was published by WEMOS foundation. This necessitated the National Ethics Committee (NEC) in Zimbabwe to investigate the case to understand and come up with resolutions.
Methods A case study design was used to investigate the case. Interviews with 5 conveniently selected study staff based on their involvement and roles in the study were conducted. Review of participant study records, the protocol, the WEMOS report, Serious Adverse Event reports and Data Safety and Monitoring Board reports were conducted. The investigation was used to determine which ethical principles applied and whether they were adhered to or not in the handling of the participant by the research staff.
Results Results indicated that the research team adhered to the necessary ethical principles enshrined in the major ethical codes and local Zimbabwean research ethics regulations for the conduct of clinical trials. Investigation showed that the report was mainly based on incomplete information and contradicted the actual events at the study site. There was also no record of the participant's complaint with NEC in the complaint register. Appropriate standard of care was given to the participant.
Conclusions The NEC continues to protect the rights of clinical trial participants by investigating complaints against study teams as their wellbeing is of primary importance. Researchers are being encouraged to adhere to best practises in conducting human participant researches. The media should also be engaged actively so that reporting is accurate to prevent incorrect information being relayed to the public.

PA-086 A REVIEW OF REGULATORY CAPACITY STRENGTHENING IN AFRICA IN HIV RESEARCH: THE NEED FOR A NEW PARADIGM

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Background Recent African initiatives suggest the need for new direction in capacity building and support for regulatory review of HIV prevention research. The African Vaccine Regulatory Forum recently harmonised practices to strengthen regulatory oversight and helped create the African Medicines Agency scheduled to be launched in 2018. The African Union, working through the New Partnership for Africa's Development, took a major step in 2016 adopting the African Union Model Law on Medical Product Regulation. These steps, as well as the work of the African Medicines Regulatory Harmonisation Programme, raise the question of how best to effect regulatory capacity building in this new environment.
Methods This paper assesses the evolving role of support for African regulatory systems using a desk review of various regulatory strengthening activities currently underway or planned, with focus on Africa. This review was supplemented by interviews with key informants related to activities intended to support regulatory capacity building in low- and middle-income countries focused upon efforts that were of potential assistance to HIV vaccine development. This analysis supplements findings

from a Regulatory Capacity Building Workshop held in Rwanda in 2015.

Results External capacity building efforts need to be responsive to new and/or recent priorities and mechanisms by African entities regarding the strengthening and coordination of regulatory systems. Current capacity building efforts will benefit from coordination and information sharing geared toward new initiatives, as well as focus around ethics review.

Conclusions Remarkable progress is being made towards the development of a safe and effective HIV prevention options, and several HIV vaccine efficacy trials are planned over the next few years. Recent ambitious African regulatory initiatives hold the potential to expedite review. It is time for capacity building efforts to consider how best to support the new coordinated and regional regulatory systems being developed and launched over the next few years.

PA-087 PREVALENCE OF HBV, HIV, AND HIV-HBV CO-INFECTIONS AMONG HEALTHCARE WORKERS IN IBADAN, NIGERIA

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Background HIV and HBV are endemic in Nigeria. HBV is globally the leading cause of death due to liver disease amongst HIV-infected persons. The study was done to ascertain the prevalence rate of HIV, HBV and HIV-HBV co-infections amongst health care workers in Ibadan, Nigeria.

Methods A total of 217 healthcare workers working in large hospitals in Ibadan, Nigeria were signed up for the study. The socio-demographical data of the health care workers were collected using a questionnaire. HIV antibodies were evaluated using Stat Pak HIV test strips and HBV was evaluated using the ABON HBsAg test strips.

Results There were 85 (39.2%) male and 132 (60.8%) female health care workers. Most were 21–35 years of age (109/217, 50.2%). Of the 217 health care workers 103(47.5%) and 21 (9.7%) were positive for HBsAg and HIV, respectively, while 3 (1.4%) had HIV-HBV co-infections. The prevalence of HBV infection was statistically significant ($p<0.005$) over HIV infection. Health care workers with 'other' level of education had the most predominant HBV prevalence (58/83, 69.9%, $p=0.0267$) while those with primary level of education had the highest HIV prevalence (2/12, 16.7%, $p=0.0267$. Females had the most predominant HBV (72/132, 54.5%) and HIV (17/132, 12.9%) ($p=0.03$). HIV was highest in age groups $\leq$20 years (2/16, 12.5%). Only widows/widowers (33.3%) had the highest HIV-HBV co-infection rates. Presence of tattoo in any part of the body, hepatitis B vaccination was significantly associated ($p< 0.05$) with HBV seropositivity among health care workers.

Conclusions This study reveals a high prevalence of HIV, HBV and HIV-HBV co-infections among female health care workers. From our finding, the high infection rates of HBV and HIV noted amongst health care workers indicate the need to regularly screen this group for these viruses to reduce the further transmission of these viral infections.

PA-088 DO XPERT MTB/RIF CYCLE THRESHOLD VALUES PROVIDE INFORMATION ABOUT PATIENT DELAYS FOR TUBERCULOSIS DIAGNOSIS?

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Background Early diagnosis and initiation to appropriate treatment is vital for tuberculosis (TB) control. The Xpert MTB/RIF (Xpert) assay offers rapid TB diagnosis and quantitative estimation of bacterial burden through Cycle threshold (Ct) values. We assessed whether the Xpert Ct value is associated with delayed TB diagnosis as a potential monitoring tool for TB control programme performance.

Methods This analysis was nested in a prospective study under the routine TB surveillance procedures of the National TB Control Program in Manhiça district, Maputo province, Mozambique. Presumptive TB patients were tested using smear microscopy and Xpert. We explored the association between Xpert Ct values and self-reported delay of Xpert-positive TB patients as recorded at the time of diagnosis enrolment. Patients with >60 days of TB symptoms were considered to have long delays.

Results Of 1483 TB presumptive cases, 580 were diagnosed as TB of whom 505 (87.0%) were due to pulmonary TB and 302 (94.1%) were Xpert positive. Ct values (range, 9.7–46.4) showed a multimodal distribution. The median (IQR) delay was 30 (30–45) days. Ct values showed no correlation with delay ($R2=0.001$, $p=0.621$), nor any association with long delays: adjusted odds ratios (AOR) (95% CI) comparing to >28 cycles 0.99 (0.50–1.96; $p=0.987$) for 23–28 cycles, 0.93 (0.50–1.74; $p=0.828$) for 16–22 cycles; and 1.05 (0.47–2.36; $p=0.897$) for <16 cycles. Being HIV-negative (AOR [95% CI]), 2.05 (1.19–3.51, $p=0.009$) and rural residence 1.74 (1.08–2.81, $p=0.023$), were independent predictors of long delays.

Conclusions Xpert Ct values were not associated with patient delay for TB diagnosis and cannot be used as an indicator of TB control program performance.

PA-089 CHILD PROTECTION AND DEVELOPMENT: ADDRESSING THE PROBLEMS OF HIV/AIDS ORPHANS – A CASE STUDY IN BAHIR DAR TOWN, ETHIOPIA

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Background HIV/AIDS has continued to be a world social, economic and political threat. Recent findings indicated that currently 34 million people are living with HIV/AIDS. Sub-Saharan countries are particularly vulnerable to this pandemic. Ethiopia's HIV/AIDS epidemic pattern marked regional variations across urban and rural areas. Ethiopia which is one of the largest populations in Africa has the highest number of orphans. The proportion of orphan children due to AIDS is also alarmingly increasing in this country. It increased from 26% to 43%

in Ethiopia in 2001 to 2010. The situation of AIDS orphans have become a serious problem in Ethiopia.

Methods A qualitative method of study, particularly a phenomenological approach, was used to guide the study. Data were collected through interviews, focus group discussions and case studies. In addition, a secondary review of documents such as reports, annual and strategic plans was done.

Results The study indicated that there are variations in the number of orphans across kebeles of the town. The Shinbit kebele has the highest number of orphans, both male and female. In Bahir Dar various forms of service are rendered to orphans living with HIV/AIDS such as psycho-social support, educational and medical support, economic strengthening through guardians, home to home support, legal support, vocational and skill development training.

Conclusions In Bahir Dar, various forms of service are rendered to HIV/AIDS orphans such as psycho-social support, educational and medical support, economic strengthening through the guardians, legal support, vocational and skill development training. These methods of addressing HIV/ AIDS orphans form a fragmented, only need-based approach, and are far from a right-based approach as they lack institutional networking, sustainability and community ownership. Therefore, in order to meet one of the objectives of the Cross–Cutting Sectors Development Plan of the Growth and Transformation Plan, it is recommended to address the multifaceted problems of AIDS orphans in an integrated and sustainable way.

PA-090 UNDERSTANDING PATIENT DECISIONS TO TRANSFER OR DISENGAGE FROM HIV CARE AND TREATMENT IN ZAMBIA

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Background Despite widespread roll-out of free HIV care and treatment (C&T), large numbers of HIV-positive Zambians are disengaged from care. Nested within a 4-province study of HIV C&T outcomes, we explored how interactions between system hardware (tangible components) and system software (normative & behavioural components) at the service-delivery level influenced patients' decision to transfer or disengage from care.

Methods In-depth interviews were conducted with a stratified random sample of 75 HIV-infected adults from 4 provinces and five patient categories: currently in-care, pregnant in-care, disengaged, transferred (to another facility), friend/ family of deceased patient. Sixteen focus group discussions were convened with lay and professional healthcare workers (HCW) providers serving the same catchment areas. Audio transcripts were translated, transcribed and subject to deductive and inductive analysis guided by a modified social-ecological framework.

Results Health system 'hardware' factors influencing patient decisions included distance and chronic understaffing that resulted in long wait-times and administrative mistakes (e.g. loss of patient records). Health system 'software' factors included various aspects of clinic organisational culture. Examples are limited consideration of HCWs of the way employment or family circumstances affected patients' ability to adhere to protocol-driven treatment schedules and a harmful power dynamic that compelled patients to 'humble' themselves and 'obey' HCWs to avoid being 'punished'. Described by many as a problem of HCWs 'lacking heart' or 'having a bad attitude', these phenomena were often linked to experiences of disrespect and/or abuse that influenced decisions to transfer or leave C&T.

Conclusions Findings demonstrate a dynamic and compounding effect of health system 'hardware' and 'software' factors on decisions to transfer/disengage. Data suggest a need for: i) improvements in physical resourcing and structuring of HIV services; ii) a move away from exclusively static clinic-based service models and iii) revisions to policy enabling a re-orientation of pre-service training, clinic leadership and workplace incentives to encourage health-promoting, person-centred care.

PA-091 MEETING FIELD-BASED CHALLENGES: INNOVATIVE APPROACHES TO COLLECTING DRY BLOOD SPOT SAMPLES IN THE COMMUNITY

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Background Community collection of dry blood spots (DBS) is ideal to capture viral load results from HIV-positive, patients lost to follow-up (LFTU) in order to monitor their health. We sought to optimise protocols for high-quality community-based DBS collection in resource-constrained settings such as Zambia.

Methods As part of a nested case-control study, we trained 23 non-medical interviewers who collected DBS from LTFU patients in rural and urban Lusaka. We visited another Zambian community-based DBS study improving upon their approach through team-based problem solving methods. We evaluated our innovation through field observations, bi-weekly meetings, interviewer reports, and two debriefing meetings. The laboratory assessed DBS quality for testing validity.

Results We transformed a first-aid box into a phlebotomy box to keep DBS contamination free and in ambient temperature. A styrofoam partition separated the DBS drying rack glued to one side of the box from phlebotomy supplies and kept DBS cards horizontal during transportation. Interviewers collected 229 DBS (60.6%) in participant homes or place of their choice with 149 refusals. DBS was air-dried in an area free of direct sunlight, water, insects and dust for a few minutes so blood was not flowing when placed on the rack. DBS was taken to the nearest health facility for further drying using public transport, or study motorbikes fitted with a custom made carrier to hold the box horizontal. The laboratory did not report any blotted or double spotted DBS cards. Barriers included privacy, visibility and awkward box size.

Conclusions We optimised community-based DBS collection in Zambia using non-medical staff and an innovative, low-cost light-weight phlebotomy box to transport DBS without contamination at ambient temperature. While we successfully collected DBS from 60.6% of found LTFU patients, concerted efforts are needed to re-engage LTFU patients who refuse HIV-related procedures even when made conveniently available.

PA-092 CHANGES IN VAGINAL PRACTICES AFTER CONTRACEPTIVE VAGINAL RING USE AMONG WOMEN IN KIGALI, RWANDA

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10.1136/bmjgh-2016-000260.124

Background Recent developments in HIV prevention, including the dapivirine vaginal ring, have shown promising results in protecting women from HIV. Additionally, a healthy vagina is protective against HIV/STIs but vaginal practices can disturb the vaginal environment. The objective of this study was to explore vaginal practices and assess the changes during contraceptive vaginal ring (CVR) use among Rwandan women.

Methods Rinda Ubuzima, a research site in Kigali, Rwanda, collected data on vaginal practices using mixed methods (in-depth interviews, observations, focus group discussions, surveys) during a safety and acceptability study of CVRs. Education about safe vaginal practices was provided at study visits after baseline. Descriptive and thematic analyses were conducted.

Results At baseline, 57% of the 289 participants reported washing inside and outside the vagina while 124 (43%) reported washing outside only. 65% of those washing inside and outside the vagina reported doing so once a day. Participants reported washing inside the vagina while bathing (93%), after sex (63%), and during menses (54%). A total of 157 (96%) participants reported inserting water and/or soap with fingers into the vagina. Qualitative data suggested that vaginal practices went beyond those listed in the survey and included herbs, stones, gels, and food in order to increase vaginal lubrication and tightness, treat vaginal symptoms, and clean the vagina. Only 14 of the 120 (12%) women reported a reduction/increase in their vaginal practices following ring insertion. However, after triangulation of data, over 25% of the participants reported changes in their vaginal practices resulting from study participation.

Conclusions Vaginal cleaning is frequent among the study population and increased education from the research site about vaginal practices encouraged some women to change their behaviour during the short duration of the study. Additionally, there are more vaginal practices that may need consideration for ring development and rollout in Rwanda.

PA-094 AGREEMENT OF QUANTIFERON TEST AND TUBERCULIN SKIN TEST IN DIAGNOSING LATENT TUBERCULOSIS INFECTION AMONG HIV-INFECTED PEOPLE IN KISUMU COUNTY, KENYA

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Background HIV-infected people are at greatest risk of progression from latent tuberculosis infection (LTBI) to development of active tuberculosis (TB) disease. Accurate diagnosis and treatment of LTBI in this group is an essential component of the WHO TB control strategy. Interferon-gamma assays have emerged as novel alternatives to the tuberculin skin test (TST) for the diagnosis of LTBI. Comparable performance for these two tests is not fully evaluated in regions with high incidence of HIV and TB. We compared the performance of QuantiFERON TB-Gold In-tube® assay (QFT) and TST tests for LTBI.

Methods Newly diagnosed HIV patients older than 7 years were enrolled from HIV clinics. Blood was drawn for QFT assay, thereafter TST was placed into the volar surface of the forearm. The TST was read at 48–72 hours and deemed positive at >or=5 mm. Statistical analyses were performed using SAS 9.2. Agreement evaluated using kappa (k) statistic.

Results Of the 650 HIV-infected participants, 62% were females; median age (IQR) was 32 (26–39). Among 592 (91%) who received TST, 88 (17%) were positive; QFT positives were 274 (42%). Indeterminate QFT results were 22 (3%). Overall agreement between QFT and TST was 37% (95% CI: 30–45%). Agreement was 56% (95% CI: 30–45%) and 15% (95% CI: 30–45%) for negative and positive QFT and TST results.

Conclusions Low prevalence of LTBI was found; however, agreement between the 2 tests was moderate. This lack of agreement calls for a search for a better diagnostic test for LTBI among HIV-infected persons in TB endemic regions since TST positivity is associated with better response to INH in LTBI patients.

PA-095 A CROSS-SECTIONAL STUDY OF HEPATITIS B VIRUS INFECTION IN HIV-INFECTED CHILDREN IN WINDHOEK, NAMIBIA

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10.1136/bmjgh-2016-000260.126

Background Hepatitis B virus (HBV) remains endemic in Africa and an important co-morbidity in the HIV epidemic. The HIV treatment guidelines of the World Health Organisation (WHO) recommend tenofovir–lamivudine (or emtricitabine) as first-line therapy for HIV–HBV co-infection management in children ≥10 years old. However, many children in sub-Saharan Africa are not screened for HBV and may remain on lamivudine monotherapy for many years. This study aimed to characterise HBV infection in HIV-infected children in Namibia.

Methods The study included HIV-infected/HBsAg-positive children, exposed to lamivudine monotherapy, attending the Katutura paediatric HIV clinic in Windhoek, Namibia. Dried blood spots and serum samples were collected from participants. Serological investigations were performed using Murex assays. HBV DNA viral load was determined using the automated AmpliPrep/COBAS TaqMan HBV test V2.0. Genotyping and mutation analysis were performed through the NCBI HBV Genotyping tool (www.ncbi.nlm.nih.gov/ projects/genotyping/ formpage.cgi) and Geno2Pheno (http:// hbv.geno2pheno.org/ index.php).

Results To date, 14 children have been enrolled; of whom 14 DBS and 11 serum samples were analysed. HBsAg was detected in 10 children (90%; 10/11); 7 were HBeAg-positive/HBeAb-negative and 3 HBeAg-negative. Among HBeAg-negatives, 1 was HBeAb-negative and 2 were HBeAb-positive. One child was non-reactive for all markers. Of the 14 children, 7(50%) tested HBV DNA-positive. Lamivudine drug-associated resistance variants, together with immune escape mutants in the overlapping surface gene, were identified in these children. Resistance mutation patterns included: *rt*V173L+*rt*L180M+*rt*-M204V (4/7; 57%), *rt*L80I+*rt*V173L+*rt*L180M+*rt*M204I (1/7; 14%) and *rt*L180M

+*rt*M204V (2/7; 29%); with the overlapping *s*E164D and/or *s*I195M variants. HBV strains belonged to genotype E (6/7, 86%) and genotype D3 (1/7, 14%).
Conclusions Half of the children included in this study had detectable HBV DNA and showed lamivudine resistance. Uncontrolled HBV infection is associated with an increased risk of severe liver damage and hepatocellular carcinoma. HBsAg screening of HIV-infected children, using cost-effective point-of-care methods, and treatment with tenofovir should be made more widely available in resource-limited settings.

PA-096 INSTITUTIONAL BARRIERS TO IMPROVE ACCESS TO DRY BLOOD SAMPLE COLLECTION IN NORTH-WESTERN NIGERIA: A 12-MONTH RETROSPECTIVE DATA REVIEW OF PARTNERSHIP WITH NIGERIA POSTAL SERVICE FOR SAMPLE TRANSPORTATION

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10.1136/bmjgh-2016-000260.127

Background Institutional challenges still limit access of exposed infants to dried blood spot (DBS) sampling at 6 weeks in Nigeria. There is a paucity of data to evaluate the impact of multiple interventions in addressing these challenges. The objective of the study was to review institutional barriers and issues regarding access of exposed infants to DBS sampling in 6 general hospitals. The study was supported by Management Science for Health and funded by USAID in Kebbi State, Nigeria.
Methods Review of the partnership with Nigeria Postal Service for DBS transportation (6 months after the take-off in October 2014) was conducted in April 2015. It revealed that 34% of exposed infants had access to DBS sampling at 6 weeks. This led to key informant interviews with 36 healthcare workers across 6 hospitals with identification of 5 major institutional challenges limiting access to DBS collection. Targeted interventions included: strengthening of Intra-facility referral; incorporation of adherence and tracking into PMTCT/Early Infant Diagnosis service, development of the capacity of hospital staff on the DBS collection process and documentation in PMTCT service tools. The outcome was then evaluated at 6 months.
Results By October 2015, the repeat evaluation showed that the number of DBS samples collected increased from 42 to 138 and results received increased from 31 to 112. The average turnaround time improved from 70 days to 43 days, and DBS sampling access increased from 32% to 86%, all within 6 months of the interventions.
Conclusions Multiple structured interventions have the potential to improve access of exposed infants to DBS sampling for early infant diagnosis. The study will inform implementers on how best to improve early infant diagnosis in poor-resource settings through interventions aimed at institutional barriers. Point-of-care testing for DBS needs to be scaled up.

PA-097 FEASIBILITY OF USING THE LYNX POINT-OF-CARE TEST FOR EARLY INFANT HIV DIAGNOSIS IN RURAL ZAMBIA

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Background Early infant diagnosis of HIV is challenging in sub-Saharan Africa, particularly in rural areas, leading to delays in diagnosis and treatment. A point-of-care test would overcome many challenges. This study was undertaken to evaluate the feasibility of implementing a point-of-care p24 antigen detection test (LYNX) in rural Zambia.
Methods A cross-sectional study of infants attending the Macha Hospital HIV or primary care clinics for early infant diagnosis was conducted in Choma district, Southern Province, Zambia during 2014 and 2015. Two blood samples were collected from each participant, one for immediate testing with the LYNX test and a second for standard HIV DNA testing at a central laboratory. Counsellors were trained to perform the LYNX test and observed for adherence to protocols.
Results A total of 210 LYNX tests were performed; 93% of tests were run according to protocol with a result available with a median time of 55 minutes (IQR:54, 57); 10% of tests were run on battery power. The median turnaround time for the availability of the HIV DNA test result was 2.5 months (IQR: 1.8, 5.0). The sensitivity and specificity of the LYNX test were 70% and 100%, respectively. Challenges to implementation included the long duration of the LYNX test and multiple steps, disruption of other daily activities, and managing variable patient volumes.
Conclusions Point-of-care tests for early infant diagnosis are urgently needed to increase access to testing. The LYNX test was successfully performed by counsellors and had several characteristics facilitating implementation in rural clinics. The LYNX test could address many challenges to testing in rural areas and allow for earlier diagnosis and treatment of HIV-infected infants, therefore improving outcome.

PA-098 UPTAKE OF ANTIRETROVIRAL THERAPY AMONG HIV-INFECTED PREGNANT WOMEN AND ITS IMPACT ON HIV MOTHER-TO-CHILD TRANSMISSION IN MBEYA, TANZANIA

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Background Maternal viral load (VL) and immunological status are important risk factors for mother-to-child transmission of HIV. In line with WHO recommendations (Option B+), Tanzania introduced the initiation of life long antiretroviral therapy (ART) in pregnant women in 2013. We present the uptake of ART and its impact on mother-to-child transmission.
Methods Between July 2015 and June 2016 data were obtained from HIV-infected pregnant women participating in the ongoing BABY Study (*ClinicalTrials.gov Identifier: NCT02545296*), which evaluates point-of-care testing in HIV Early Infant Diagnosis (HEID). Women were enrolled at the time of delivery, and neonates were followed-up until 6 weeks post-partum. Maternal HIV-RNA was assessed at delivery; neonatal HIV diagnosis was performed using the Cepheid Xpert point-of-care test and confirmed by qualitative dry blood spot HIV-DNA (Roche COBAS TaqMan).
Results In total 415 HIV-infected pregnant women were enrolled (median age 29 years). Nearly all women had attended antenatal care (96.4%); in 245 (59%) HIV was first diagnosed during pregnancy, and in 63.8% ART was initiated within 1 week following diagnosis. At the time of delivery 368 (88.7%) women were on ART, HIV-RNA >1000 copies/mL were detected in 78 (18.9%) and a CD4 count <200 cells/μL in 63

(15.2%). The overall mother-to-child HIV transmission rate was 2.4% (10/415) and 7/10 neonates were HIV diagnosed at the time of birth correctly identified by point-of-care testing. HIV-RNA >1000 copies/ml irrespectively of ART and low CD4 count <200 cells/μL were associated with higher risk of neonatal HIV transmission.

Conclusions Despite the implementation of life-long ART in all pregnant women, reduction of HIV transmission from mother to child is still sub-optimal. High HIV-RNA as the main risk factor for HIV transmission irrespective of maternal ART points to the need for maternal VL screening during the antenatal period.

PA-099 VARIATION IN NEONATAL MORTALITY AND ITS RELATION TO COUNTRY CHARACTERISTICS IN SUB-SAHARAN AFRICA

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10.1136/bmjgh-2016-000260.130

Background A substantial reduction in neonatal mortality is the main priority to reduce under-five mortality. A clear understanding of the variation in neonatal mortality and the underlying causes is important for targeted intervention. We aimed to explore variation in neonatal mortality and identify underlying causes of variation in neonatal mortality in sub-Saharan Africa.

Methods This ecological study used publicly available data from the World Health Organization, United States Agency for International Development and World Bank. Variation in neonatal mortality across 49 sub-Saharan Africa countries was examined using control chart and explanatory spatial data analysis. Associations between country-level characteristics and neonatal mortality were examined using linear regression analysis.

Results The control chart showed that 28 (57%) countries exhibited special-cause variation, fourteen countries were below and above the 99.8% control-limits. The remaining 21 (43%) countries showed common-cause variation. No spatial clustering was observed for neonatal mortality (Global Moran's I statistic – 0.10; p=0.74). Linear regression analysis showed HIV/AIDS prevalence among the population of reproductive age to be positively associated with neonatal mortality (β 0.463; 95% CI 0.135 to 0.790; p-value <0.01). Declining socioeconomic deprivation (β –0.234; 95% CI: –0.424— 0.044; p-value <0.05) and high quality of healthcare governance (β –1.327, 95% CI–2.073— 0.580; p-value <0.01) were inversely associated with neonatal mortality.

Conclusion This study shows a wide variation in neonatal mortality in sub-Saharan Africa. A substantial part of this variation can be explained by differences in the quality of healthcare governance, prevalence of HIV and socioeconomic deprivation.

PA-100 IMPACT OF A HOLISTIC INTERVENTION ON PMTCT UPTAKE WITHIN SUB-SAHARAN AFRICA: EVIDENCE FROM 'SAVE THE FAMILIES FOR AFRICA' IN MALAWI

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Background Prevention of mother-to-child transmission (PMTCT) option B+ makes effective the virtual elimination of HIV (<5%) among African children effective. Some major challenges remain, such as accessibility to PMTCT-services and male-partner involvement. To improve PMTCT-interventions/expansion, we evaluated PMTCT-service uptakes within a typical African context, using a holistic approach.

Methods As part of monitoring and evaluation of the '*Save the Families for Africa*', a comparative assessment of PMTCT-uptake was conducted within the Likuni Mission Hospital catchment area in Likuni, Malawi. Four performance indicators were measured before (July-November 2015) and during (December 2015-May 2016) project-interventions: i) HIV-infected pregnant women enrolled for antenatal care (ANC)/PMTCT-services; ii) HIV-related deliveries at the hospital; iii) male-partner involvement into PMTCT; iv) PMTCT community-outreach interventions. Comparison was performed using Mann-Whitney test (p< 0.05 considered significant).

Results During project-interventions, provision of free coupons for ANC/PMTCT-related services (including CD4/Haemoglobin point-of-care monitoring) and for nutritional supplements, invitation notes and counselling intensification for male-partners, as well as provision of a mobile unit (new ambulance) for PMTCT-services expansion to remote/rural communities, were implemented. Overall, target performances appeared to increase over time after interventions. Indeed, the total number of women enrolled before intervention was 58, and sharply increased thereafter (182). The median [interquartile] number of HIV-infected pregnant women enrolled per month for ANC/PMTCT-services was doubled (before *vs* during: 11 [10–13] *vs* 26[22–43], p=0.0043); HIV-related deliveries per month increased 12 times [11–13] *vs* 17[11–22], p=0.3160); male-partner involvement to PMTCT per month became effective [0% *vs* 23.1%[9.3–33.3%], p=0.0260); PMTCT community-outreach per month increased by 12 fold (1[0–2] *vs* 12[6–14], p=0.0286). Maternal mortality and HIV-vertical transmission were 0% throughout project-interventions.

Conclusions Our findings highlight that there is room for improvement of PMTCT, starting from option B+, by implementing a holistic interventional model. This can greatly contribute to eliminating MTCT and in ameliorating the well-being of the entire family (children, mother and father) living with HIV/AIDS in sub-Saharan Africa.

PA-101 FUNCTIONAL AND PHENOTYPIC CHARACTERISATION OF REGULATORY T (TREG) CELLS IN ANTIRETROVIRAL NAïVE HIV-1 INFECTED PEOPLE

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Background Regulatory T cells (Tregs) function in dampening excessive immune activation in steady state. However during HIV-1 infection there is sustained immune activation and it is not known how Tregs function in this context. To optimise immunotherapeutic strategies based on Tregs for HIV-1 infected people we assessed the phenotypic and functional properties of these cells from antiretroviral naïve HIV-1 infected adults in Cameroon.

Methods Tregs were purified by magnetic sorting from PBMCs obtained from adults aged 21 to 65 years using microbeads according to the manufacturer's protocol (Miltenyi Biotec). The phenotypic properties of the purified Tregs were then determined by multiparametric flow cytometry. Tregs functions were assessed by measuring inflammatory cytokine formation by monocytes following co-culture with autologous Tregs in the presence of either polyICLC or CLO97. Samples were acquired on BD Fortessa X5 cytometer using BDFACS Diva Software and data analysed with FlowJo version 9.8.5. Graph Pad Prism 5 was used for statistical analysis.
Results Tregs were defined as CD4+CD25+CD127LoFoxP3+ cells. However, the strong correlation between Foxp3 with the combination of CD25+CD127Lo (r=0,965; p< 0,001, Pearson's correlation) allowed us to use these surface markers as previously reported for tracking Tregs in subsequent experiments. With respect to surface expression there was a significant elevation of HLA-DR /CD38 in Tregs from HIV-1-infected people when compared to HIV-participants. When purified Tregs were co-cultured with autologous monocytes in the presence polyICLC (a TLR 3 agonist) and CLO97 (TLR7/8 agonist) they escalated the intracellular formation of both TNF-α and IL-6 by monocytes. The escalation was significantly higher in co-cultures of cells from antiretroviral naïve HIV-1-infected people relative to seronegative participants.
Conclusions Dysregulation in Tregs function can exacerbate inflammatory cytokine formation.

PA-103 DRUG RESISTANCE AND GENETIC PROFILE OF BACTERIAL SPECIES ASSOCIATED WITH BURULI ULCER WOUND INFECTIONS IN TWO DISTRICTS OF GHANA

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Background We identified secondary infection of Buruli ulcer (BU) wounds as a cause of healing delay. In order to contribute to the improvement of wound management and reduction of healing delay, we initiated a study to gain understanding of the possible routes of infection and also characterised the resistant profiles of Gram negative bacteria isolated from the wounds of patients attending two health facilities in Ghana.
Methods *Staphylococcus aureus* isolates were characterised by the *spa* gene, *mecA* and the Pantone Valentine Leukocidin (*PVL*) toxin followed by *spa* sequencing and whole genome sequencing of a subset of isolates. Phenotypic antibiotic susceptibility testing of Gram negative clinical isolates was performed and multidrug-resistant *Pseudomonas aeruginosa* identified. The *Enterobacteriaceae* were further investigated for ESBL and carbapenem production, and some resistance conferring genes were analysed by PCR.
Results Twenty-four isolates were identified as methicillin-resistant *S. aureus* (MRSA), and *lukFS* genes encoding PVL were identified in 67 isolates. Typing and sequencing of the *spa* gene from 91 isolates identified 29 different *spa* types with t355 (ST152), t186 (ST88), and t346 dominating. While many distinct strains were isolated from both health centres, genotype clustering was identified within centres pointing to possible health care-associated transmission. Phylogenomic analysis confirmed these clusters. Among the GNB, phenotype screening showed widespread resistance to ampicillin, chloramphenicol, ticarcillin-clavulanic acid, cefuroxime and sulphamethoxazole-trimethoprim. ESBL production was confirmed in 15 isolates phenotypically while 61.5% of screen-positive isolates harboured at least one ESBL-conferring gene. Carbapenem encoding genes were detected in 41% of the isolates.
Conclusions Our findings indicate that the health-care environment likely contributes to superinfection of BU wounds and calls for training in wound management and infection control techniques. The observed frequency of ESBL and carbapenem resistance indicates the need to set up surveillance networks and strictly enforce policies which guide the rational use of antibiotics.

PA-104 CURRENT PATTERNS AND PREDICTIVE TRENDS OF MULTIDRUG-RESISTANT *SALMONELLA TYPHI* IN SUDAN

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Background Enteric fever has a persistently great impact on public health. It is caused by *Salmonella enterica* associated with malaria during the rainy season; the bacterium is seldom detected in wastewater of stabilisation stations due to treatment processes. The aim of this study is to evaluate the recent state of antibiotics susceptibility of *Salmonella typhi* with special attention to multidrug-resistant strains and predict the emergence of new resistance patterns.
Methods *S. typhi* isolates were recovered from 128 wastewater samples collected from ponds at Soba Stabilization Station and Omdurman Hospital Stabilization Station. The isolates were identified using standard *Salmonella* identification guidelines and their susceptibility to seven antibiotics was determined. Minimum inhibitory concentration (MIC) of ciprofloxacin and minimum bactericidal concentrations (MBC) were also determined. Statistical predictions for the resistance emergence were done using logistic regression and forecasting linear equations.
Results A total of 12 *S. typhi* isolated strains were recovered from 128 samples of wastewater; they were resistant to antibiotics except Ciprofloxacin. Current patterns of ciprofloxacin breakpoints interpretations were in susceptible ranges by disc diffusion (S≥20 mm), minimum inhibitory concentration was recorded as (I=16 μg/ml) and minimum bactericidal concentration=(R≥32 μg/ml). The probability of an isolate to develop resistance was plotted for MBCs; the rate of resistance solved by ($y=0.0235\times-0.0411$). The predictive patterns of resistance were spontaneously solved using exponential trend ($y=n\ e^{x}$) for each isolate at 16 μg/ml and 32 μg/ml of ciprofloxacin in certain period and the high values of coefficient $R^2>0.5$ indicate the incidence rates of bacterial resistance.
Conclusions The current sensitivity patterns of *S. typhi* isolates against ciprofloxacin were acceptable, but the probability of emerging multidrug resistance to ciprofloxacin was observed in sensitivity which had begun to decline according to frequent consuming, drug policy and bacterial genetic mutations.

PA-105 AETIOLOGY, ANTIBIOTIC RESISTANCE AND RISK FACTORS FOR NEONATAL SEPSIS IN A LARGE REFERRAL CENTRE IN ZAMBIA

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Background In sub-Saharan Africa there is scanty data on the causes of neonatal sepsis and antimicrobial resistance among common invasive pathogens, which might guide policy and practice.

Methods This was a cross-sectional observational prevalence and aetiology study of neonates with suspected sepsis admitted to the neonatal intensive care unit, University Teaching Hospital, Lusaka, Zambia, between October 2013 and May 2014. Data from blood cultures and phenotypic antibiotic susceptibility testing were compared with multivariate analysis of risk factors for neonatal sepsis.

Results Of 313 neonates with suspected sepsis, 54% (170/313) were male; 20% (62/313) were born to HIV-positive mothers; 33% (103/313) had positive blood cultures, of which 85% (88/103) were early onset sepsis (EOS). *Klebsiella* species was the most prevalent isolate, accounting for 75% (77/103) of cases, followed by coagulase-negative staphylococci (6% (7/103)), *Staphylococcus aureus* (6% (6/103)), *Escherichia coli* (5% (5/103) and *Candida* species (5% (5/103). For *Klebsiella* species, antibiotic resistance ranged from 96–99% for WHO-recommended first-line therapy (gentamicin and ampicillin/penicillin) to 94–97% for third generation cephalosporins. The prevalence of culture-confirmed sepsis increased from 0–39% from December 2013 to March 2014, during which time mortality increased 29–47%. 93% (14/15) neonates with late onset sepsis and 82% (37/45) with early-onset sepsis aged 4–7 days were admitted >2 days prior to onset of symptoms. Culture results for only 25% (26/103) of cases were available before discharge or death. Maternal HIV infection was associated with a reduced risk of neonatal sepsis (OR 0.46 [0.23–0.93], p=0.029).

Conclusions Outbreaks of nosocomial multi-antibiotic-resistant infections are an important cause of neonatal sepsis and associated mortality. Reduced risk of neonatal sepsis associated with maternal HIV infection is counterintuitive and requires further investigation.

PA-106 RESISTANCE OF ENTEROPATHOGENS MAINLY ASSOCIATED WITH DIARRHOEA TO FREQUENTLY PRESCRIBED ANTIBIOTICS IN KOUSSERI (FAR NORTH, CAMEROON)

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Background The resistance of diarrhoea-causing enteropathogens to antibiotics is a global concern.

Methods A cross-sectional descriptive study that had as objective to test the sensitivity of these pathogens to antibiotics frequently prescribed in the Logone and Chari Division was carried out in Kousseri from 24 July to 23 October 2015. Stool samples were collected from patients (children and adults) presenting at the Kousseri Annex Regional Hospital, in sterile containers and analysed as required by SOPs in the cholera detection laboratory of the NGO 'Better Access to Health Care' (BAHCARE) in Kousseri. Microbial isolation and identification was done using Hektoen and EMB culture media and API 20E pack (Biomerieux). Antibiotic susceptibility testing was done using the Kirby Bauer method with Muller Hinton medium.

Results A total of 150 stool samples were analysed, out of which 45 enteropathogens were isolated (66% of isolated microbes were *Escherichia coli*), identified and tested with antibiotic discs. The rate of resistance of *Escherichia coli* was 83.33% to cotrimoxazole and 43.33% to both ceftriaxone and ciprofloxacin. Salmonella species had a resistance rate of 71.42%, 42.86%, and 28.57% to cotrimoxazole, ceftriaxone and ciprofloxacine, respectively. *Shigella spp* were 100% resistant to cotrimoxazole, ciprofloxacine and the combination of amoxicillin with clavulanic acid.

Conclusions These results underscore the need to systematically assess the sensitivity of enteropathogens to antibiotics so as to guide health workers on the prescription of antibiotics in the Lake Chad area, Cameroon.

PA-107 ANTIBIOTIC RESISTANCE PATTERNS OF POTENTIAL PATHOGENS ISOLATED FROM TWO MAJOR HOSPITALS IN LUSAKA AND NDOLA

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Background This study was conducted as part of an assessment of the effectiveness of existing hygiene and sanitation practices in two first-level hospitals in Lusaka and two central clinics in Ndola to determine the drug resistance patterns of potential pathogens in health care facilities in Zambia.

Methods In this cross-sectional study, the samples analysed were collected from health care workers' hands, touch surfaces, disinfectant buckets in delivery rooms, post-natal and paediatric wards, operation theatre, post-operation wards and outpatient departments. The swabs in Cary-Blair transport media were used for sample collection and inoculated to 3 (Blood-, Chocolate- and MacConkey agar) primary plates. For species identification and drug susceptibility testing BD Crystal ID System and disk diffusion method with panel of 20 antibiotics was used.

Results A total of 132 swabs were collected resulting in isolation of 275 Gram negative and positive bacteria. 65 bacterial isolates were successfully identified as the following species: *Acinetobacter, Enterobacter, Klebsiella, Pseudomonas, Staphylococcus, Streptococcus* spp. All identified bacteria were tested for drug resistance. Among the *Pseudomonas* spp, the highest level of resistance was detected to cephalosporins, amoxicillin and carbenicillin and was up to 70%, 90% and 60%, respectively. *Staphylococcus* spp had high resistance to penicillin, ampicillin, azithromycin and cephalosporins, up to 86%, 76%, 57% and 95%, respectively. Vancomycin resistance among *Staphylococcus* spp was 19%.

Conclusions High drug-resistance levels among potential pathogens isolated in health care facilities reflect the long-term empiric

use of antibiotics in Zambia. For better understanding of the scale of this problem a more comprehensive study including all central private and government health care facilities should be conducted. A large number of isolated bacteria (35%) remained unknown indicating that more than one identification method should be used in order to capture the full spectrum of potential pathogens colonising the health care facilities in Africa.

PA-108 LOCALLY DRIVEN RESEARCH IS BETTER FOR INFECTIOUS DISEASES OUTBREAK PREPAREDNESS: AN EDCTP CAPACITY-BUILDING PROJECT IN POST-EBOLA LIBERIA

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Background Liberia is recovering from an Ebola outbreak. Liberia suffers from brain drain and a low gross enrolment ratio in tertiary education alongside a dearth of institutions, skilled investigators and funds for research. Liberia needs to rebuild its capacity in epidemiological research. The Saint Joseph's Catholic Hospital (SJCH) in Monrovia –in collaboration with ISGlobal and the Juan Ciudad Foundation, received an EDCTP grant to strengthen its staff capacities to lead research in infectious diseases.
Methods In March 2016, a participatory planning process started. The hospital management team and medical department staff were engaged. The process was guided by scientists from ISGlobal. Thirty-two trainees were identified among staff of the Ministry of Health and SJCH; community leaders were sought to build a Community Advisory Board; and trainees' suggestions informed the design of a 6-months Moodle-based eLearning program.
Results Two workshops on Good Clinical and Laboratory Practices (GCLP) were conducted. In preparation for the SJCH to conduct biomedical research and clinical trials, another workshop to design Standard Operating Procedures was done. All trainees joined the eLearning program and received a certificate of completion. Furthermore, the SJCH defined its own institutional research program, submitted a research proposal to a local ethics board, and is pooling resources to undertake further research on infectious diseases in 2017.
Conclusions A collaborative multi-disciplinary framework that promoted participation of the community was an approach that fuelled the successful completion of all training activities of this EDCTP-awarded project. The trainees capitalised on their experiences during the Ebola epidemic to ensure all activities were planned as per best quality standards. All trainees were motivated to prevent that planning and implementation-related errors they witnessed during the Ebola outbreak, were repeated in new education and research initiatives. In addressing global health challenges today, these motivational driving forces need a responsible and prompt response from Northern countries.

PA-109 THE ROLE OF LOCAL CONTRACT RESEARCH ORGANISATIONS IN BUILDING GCP-COMPLIANT CLINICAL RESEARCH IN POVERTY-RELATED DISEASES IN AFRICA: A CASE OF CLINWIN RESEARCH SERVICES

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Background Africa carries the largest burden of the poverty-related diseases in the world. Most of her populations live in resource-limited settings. These act as catalysts for poverty-related diseases in those populations. There is urgent need for affordable, safe and effective health technologies to reduce the economic burden of those diseases. Clinical research provides an opportunity for access to new and improved health technologies, which have undergone evaluation in clinical trial settings, in compliance with Good Clinical Practice (GCP) and local regulatory requirements. The local Contract Research Organisations offer cost-effective solutions, human resource capacity and experience in poverty-related diseases research, regulatory affairs, culture and politics.
Methods ClinWin provides clinical development services for poverty-related diseases. It has partnered with industry, not-for-profits and academic sponsors to provide a suite of trial and site management, and sponsor oversight services to local clinical research programs. These services include: training, trial monitoring, quality assurance, ethical and regulatory expertise; contract negotiation and trial coordination among others. Leveraging its indigenous knowledge of the clinical trial landscape in the region, it has developed a database of potential and current local investigators capable of conducting registration trials. The lessons learnt in each project are documented and shared with investigator staff at new sites.
Results We conducted 23 monitoring visits at an academic site for a phase Ib HIV vaccine study and malaria phase IV drug trial monitoring visits in Kenya and Tanzania. Academic epidemiological tuberculosis studies were also conducted and we developed partnerships with professional development programs in industry and academia.
Conclusions Africa is the next frontier for clinical research enterprise, and the need for developing local human resource capacity is critical. This will make the region attractive for industry sponsored trials for poverty-related diseases and other indications.

PA-111 HARNESSING THE DIGITAL SHARING REVOLUTION TO DRIVE GLOBAL HEALTH RESEARCH: SHOWING SIGNIFICANT IMPACT THAT SHOULD SUPPORT EDCTP CAPACITY DEVELOPMENT

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Background The Global Health Network is a platform for research capacity development and improving evidence generation and quality, especially in low- and middle-income countries. This is achieved by delivering training and career development (through an on-line professional membership and training scheme as well as face-to-face workshops). The platform is also a mechanism for sharing research skills knowledge, experience and tools.
Methods The Network has been consistently monitored using web analytics data and targeted surveys which combine quantitative and qualitative data, including 600 user interviews to evaluate impact. The data have been compiled by four researchers working in collaboration; each researcher was responsible for analysing specific datasets, which were later combined for the overall evaluation to ensure a fully comprehensive and

in-depth assessment.
Results The Global Health Network is made up of over 30 interconnected research communities, with over 770,000 visits, over 73,000 individual site memberships and more than 30,000 tools or document downloads. It is clear that this is a much needed, trusted and well-used resource. In all, 89.5% of users indicated the quality of information provided on the Network is of high quality. Importantly, over 130,000 online eLearning modules have been taken. Ninety-six percent of users indicated they would recommend the training courses to others, and 82% had greater course-specific skills confidence after taking a course.
Conclusions The Network has a broad user base, from individual frontline research staff through to large collaborative groups who make use of the platform to disseminate their activities, and is viewed as a high-quality, cost-effective and trustworthy community. However, more needs to be done to ensure that the capacity development initiatives of key groups, like EDCTP, make greater and more effective use of this free and impactful resource.

PA-112 INTRODUCTION OF A NEW VACCINE INTO NATIONAL IMMUNISATION PROGRAMMES IN AFRICA: THE ROLE OF CAPACITY BUILDING

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Background Members of National Immunisation Technical Advisory Groups, policy-makers, EPI managers and vaccinators are tasked with making evidence-based recommendations and decisions on whether a new vaccine merits introduction into national immunisation programmes; implementation of new vaccine introduction; and efficient management of immunisation programmes. Therefore it is paramount that they are equipped with the latest state-of-the-art information on vaccines and immunisation.
Methods Capacity building activities – such as high-level in-service vaccinology courses, other interactive courses and workshops (mid-level management training and experience exchange workshops) – address all steps required for decision-making on new vaccine introduction into national immunisation programmes. These include establishing: 1) burden of disease to be prevented; 2) existence of a good intervention (i.e. is the vaccine efficacious, safe and acceptable for the target population); 3) the cost of the new vaccine, its implementation and the comparative effectiveness with other vaccines/interventions in terms of health gains; 4) whether finances to pay for the new vaccine are available; and 5) programmatic implications. Interested parties are trained on this rational decision-making process to be followed before embarking on new vaccine introduction, on key implementation steps, and efficient management of immunisation programmes.
Results Several inter-country vaccinology courses and interactive workshops, which were organised during the last years in the African region (e.g. Kenya and South Africa), will be presented in detail. These capacity building activities have contributed to successful introduction of new vaccines in the African region, key ones being rotavirus, pneumococcal and currently human papillomavirus vaccines. This concerted effort has contributed for example to the successful introduction of rotavirus vaccine in 29 African countries to date.
Conclusions Capacity building efforts, like high-level in-service courses and interactive workshops have enabled interested parties to make evidence-based recommendations and decisions on the introduction of any new vaccine, and to successfully implement new vaccine introduction.

PA-113 ACHIEVEMENTS AND PRIMED PROSPECTS OF INCREASING CAPABILITIES FOR MULTISITE CLINICAL TRIALS IN THE EASTERN AFRICA NETWORK OF EXCELLENCE

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Background In May 2009, EDCTP supported the establishment of the East African Consortium for Clinical Research (EACCR) involving 35 regional institutions and 6 northern partners to promote capacity development for collaborative multisite clinical trials and research. EACCR aims to contribute to overcoming a situation of: under-funded, fragmented and uncoordinated regional health research; too few African scientists; inadequate infrastructure; insufficient networking and knowledge-sharing. We present updates on achievements and lessons learnt on increased preparedness to conduct globally-competitive research and clinical trials on poverty-related, neglected and emerging infectious diseases.
Methods Retrospectively, we conducted a quasi-purposive summative evaluation through document review, participatory appraisal, direct observation and case studies of the EACCR work packages for governance, research, training and mentoring, infrastructure, and networking between November 2015 and February 2016.
Results In the past five years, the Eastern Africa-led consensus-driven consortium has contributed to the following results (at least): 15 new research and capacity-strengthening grants; 150 peer-reviewed publications; 15 trials monitored; 531 scientists and associates mentored; 12 electronic training modules on research and bio-ethics; 2 newly ISO-accredited laboratories; 24 research sites upgraded; 20 partnerships harnessed; 2 knowledge-sharing platforms of the East African Health Research Commission; an interactive website (www. eaccr.org); and an additional 2 million euros leveraged.
Conclusions EACCR has increased its capacity and partnerships for on-going and planned multisite clinical trials; we can sustain coordinated collaborative GCP-compliant multisite trials and health research. We can intensify high-level advocacy and resource mobilisation in Eastern Africa in partnership with policy makers, other consortia and development partners. We stand firm on the shoulders of current and promising giants of EACCR, other consortia, EDCTP and other like-minded partners and are thus prepared to conduct and disseminate more African-led health research and capacity-strengthening initiatives on poverty-related, neglected and emerging infectious diseases in Africa during the second programme of EDCTP.

PA-114 BLENDED-LEARNING USING THE GLOBAL HEALTH NETWORK ONLINE RESOURCES: A PILOT STUDY

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Background Enhancing The Global Health Network's online offerings (TGHN eLearning, www.theglobalhealthnetwork. org) through local facilitation of its outputs may enable its uptake by clinical research staff. To explore this issue, we aimed to design and pilot a blended-learning programme in collaboration with South African research team members.
Methods A participatory research design was used, with purposively-selected support staff and their line managers. Formative semi-structured interviews with the former and focus group discussions with the latter sought reflection on current learning opportunities and career development experiences and needs. Staff then helped design and pilot a practical, feasible blended-learning programme over an approximately 6-month period. The pilot was assessed on reflections of its value that were elicited in follow-up discussions with participants.
Results Forty-five clinical research field workers, nurses, co-ordinators, data managers and laboratory personnel (and their respective line managers) took part. Formative discussions suggested staff generally had the necessary skills for their jobs, however they often lacked time and finances to develop a career path. The blended-learning menu of options for staff that they then co-designed and piloted included: facilitated one-to-one or group TGHN eLearning sessions followed by a discussion forum hosted by a volunteer content-expert; job shadows; guidance in accessing training opportunities/ resources; twinning with other research groups or staff; and a skills-sharing workshop. Feedback on their experience of the programme was very positive from those who got 'hooked', particularly as regards the non-threatening learning environment, building of IT competence and networking opportunities. However, staff's personal time constraints, and our challenges in supporting remote teams, were evident for some despite the pragmatic design.
Conclusions This flexible, practical and feasible blended-learning program catalysed the self-development of many research staff in the pilot, and supported their busy line managers. As some challenges remain, the programme may require further modification when implemented in different contexts.

PA-115 FUNCTIONAL COMMUNICATION IN MULTISITE, MULTILINGUAL CONSORTIUMS: EVALUATION OF THE COMMUNICATION TOOLS USED IN THE WANETAM NETWORK

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Background Effective communication is a key challenge in managing multi-disciplinary teams (Bruce et al. 1995). This challenge is intensified when teams are dispersed in a multilingual consortium. Created in EDCTP's capacity building call, the "West African Network against TB, AIDS and Malaria" (WANETAM/WANETAM Plus) network partnered 19 research institutions from 10 West African countries. WANETAM's objectives are i) Capacity building and technology transfer to prepare West African sites for the successful conduct of clinical trials, ii) Creation of a network for subregional scientific collaborations. Whilst WANETAM successfully integrated capacity-building training, it is important to evaluate the effectiveness of the consortium's communication methods. This evaluation aims to i) Evaluate information sharing across a trilingual network; ii) Identify key successes, gaps in communications, iii) Identify tools that enable effective communication in multisite consortiums.
Methods Project documentation was reviewed to understand communication methods. An adapted Organizational Communication Audit questionnaire measured how communication systems aided desired project outputs/outcomes (Greenbaum et al 1988). Questions specifically evaluated the effectiveness of Basecamp, IP phones and email. This questionnaire was sent to WANETAM sites to gauge user perspectives.
Results Basecamp, the online collaboration project management software, enabled communications and document distribution in a single system. Despite efforts, usage was low. As predicted, technical difficulties with IP phones affected user acceptability. Email was the central communication method used to manage project milestones and deadlines. As the average person receives 121 emails daily over-reliance on email for primary communication poses challenges (Kane 2015).
Conclusions The role of e-collaboration is crucial in multi-site consortiums. Despite low usage, cloud computing networks remove the need for infrastructure (IP phones), lower costs and allow for accessibility regardless of location. When employed correctly, it achieves efficient, effective communication to achieve desired consortium objectives.

PA-116 DEVELOPING A GLOBAL CORE COMPETENCY FRAMEWORK FOR CLINICAL RESEARCH

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Background Lack of recognition for working in clinical research is widely cited as an impediment to its conduct. There is a lack of career structure for the many roles involved (investigators, trial managers, nurses, etc.), and a lack of understanding of who does what. Competency frameworks exist for some individual job roles, but these are infrequent; thus the need for a global framework describing roles and responsibilities in a research team. This would facilitate appraisal of staff, promote career development by highlighting acquired skills, and illuminate areas where training opportunities are lacking.
Methods In this project, we combine 28 frameworks created by external groups, with information from 116 job descriptions obtained from partners in clinical trial units worldwide, including input from the EDCTP Networks of Excellence, and from the web, to create a widely-encompassing framework derived from 11 different roles. Using qualitative analysis software, we systematically assess the activities performed by the clinical research team to categorise them and define underlying knowledge-, skill- or task-based competencies.
Results The resulting framework counts 50 competencies required throughout the research life cycle, from assessment of scientific literature to results dissemination via project

management, public engagement or grant application. It is applicable to studies that may differ in design, geographical location, disease, etc., and can be adapted to the particular needs of specific projects or roles. The framework was subject to an initial validation through consultations with over 30 global health research experts in collaboration with WHO-TDR in September 2015, resulting in enhancements and its subsequent beta release.

Conclusions The adaptable 'Global Core Competency Framework for Clinical Research' is now accessible via The Global Health Network, alongside a protocol for individuals who may wish to pilot test it in their work. The framework may be further refined before being finally approved and launched in collaboration with WHO-TDR.

PA-117 NEW E-LEARNING TOOL FOR FEMALE GENITAL SCHISTOSOMIASIS: A SUPPLEMENT TO THE WHO POCKET ATLAS OF FGS

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Background Schistosomiasis affects 261 million people worldwide, most of them in Africa. Female genital schistosomiasis (FGS) may cause abnormal vaginal discharge, contact bleeding, genital tumours, infertility, ectopic pregnancies and increased susceptibility to HIV. Visualisation of lesions is the key to diagnosis but there is little knowledge about FGS among health professionals. In order to facilitate the use of the WHO pocket atlas for FSG, we present an e-learning module for medical students in endemic areas. The e-learning material is usable on smartphones, and in areas with low internet speed.

Methods Two FGS atlases form the platform for the e-learning: The First Colposcopic Atlas of Schistosomiasis in the Lower Female Genital Tract (Norseth et al. 2014) and The WHO Pocket Atlas for FGS (WHO, 2015). Actors were recruited for demonstration of the examination techniques. Medical students were approached to explore their current e-learning platforms. Website creators of two existing e-learning modules were invited to collaborate. The project is part of a larger project that was granted permissions by the Biomedical Research Ethics Administration, University of KwaZulu-Natal (KZN), South Africa.

Results A new e-learning tool is presented: all lesions, history taking and the examination techniques for identification of FGS are shown. There is a post-learning quiz for self-evaluation. Medical students in an endemic area were asked to give a qualitative evaluation on the learning outcome.

Conclusions There is a need to raise the index of suspicion for FGS as a differential diagnosis among health care professionals. This e-learning may contribute to the dissemination of knowledge of FGS to all health care professionals who can access the internet when furthering knowledge in clinical practice. Furthermore, there is a need to disseminate knowledge to professionals who may not be using the internet.

PA-118 RESEARCH ETHICS CAPACITY BUILDING FOR THE NEXT DECADE – 'BEYOND TRAINING' – RHINNO ETHICS AS MODEL TO IMPROVE AND ACCELERATE ETHICS REVIEW OF HEALTH RESEARCH

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Background Wide social disparities and weak health care systems in Africa make timely development of essential medicines, vaccines, medical technologies in and for Africa a desperate need, given the burden of diseases facing the continent. We estimate that it takes, on average, 1.5 years to get research ethics clearance in many African institutions for complex research proposals needed to deal with disease and solutions. Such delay comes with potentially high human costs. The need for Research Ethics Committees (RECs) to promptly and competently review protocols is therefore critical. Competent and efficiently RECs can save human lives, reduce costs and ultimately contribute to scientific development.

Methods Research for Health and Innovation Organiser (RHInnO Ethics) is both an information management system and an expert-decision support system for individual RECs that is currently installed in 29 RECs in 8 African countries. It enables online, better quality, efficient and standardised reviews that can reduce review time in complex, multicentre trials by 12 months or more.

Results What progress has been achieved in the process of implementing RHInnO Ethics since its inception in 2013? While training courses (long and short) have been considered as the mainstay of research ethics capacity building for decades, the development of this software-as-a-service platform has led to a more substantial understanding of how we can both accelerate and enhance the quality of ethics review of health research. We present experiences of our end users on how RHInnO Ethics contributes in enhancing the quality and efficiency of ethics review process.

Conclusions Health research ethics review needs to go beyond training. We also present new functionalities in RHInnO *Ethics* version 2.0, including EthiCALL-(*RECs connecting with other RECs worldwide)*, Ethi*XPERT (RECs updates on research ethics developments)* as well as Invoicing, REC accreditation and pharmacovigilance functionalities that promise to revolutionise the research ethics review process in Africa and beyond.

PA-119 EBOLA AND CLINICAL TRIAL ACTIVITY ON THE AFRICAN CONTINENT

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Background Ebola virus disease (EVD) results in an often fatal acute, serious illness. There are no effective EVD treatments, however, there is ongoing research into potential interventions in affected African countries. Since 2005, in efforts to enhance transparency researchers must register trials on one of World Health Organization's clinical trials registries. WHO's International Clinical Trial Registry Platform (ICTRP) collates this data providing information about planned, ongoing or

completed trials for researchers, funders and the public. This study mapped African EVD trial activity as found on WHO's ICTRP and identified available evidence from trial publications.
Methods We conducted a cross-sectional analysis of EVD studies registered on ICTRP. Data extraction included trial location, intervention, participant age, and funders. We used registry identifiers to search PubMed for publications. Descriptive analysis was conducted in MS Excel™.
Results ICTRP was searched (20 June 2016) identifying 83 EVD studies. Of these 45 are Africa-based. Studies were registered from 2009–2016. Recruitment status indicates 6 completed, 2 withdrawn, 1 not started, 2 unknown status and 34 ongoing. Forty-one studies evaluate an intervention, 4 are observational. Interventions include vaccines (25), therapeutics (17), health services/care (1) and diagnostics (2). Children were included in 24 studies. Funding sources include local and international universities and governments, non-governmental organisations, and pharmaceutical industry. Of the 45 registered African studies, 11 records were found on PubMed, seven of which included results of EVD studies.
Conclusions Mapping EVD clinical trial activity on ICTRP and searching for completed studies on PubMed can provide data on planned, ongoing or completed trials. The current research focus is on identifying safe and efficacious vaccines to prevent EVD including in children. The low number of trial reports indicates that evidence is not yet publicly accessible which may impact on evidence-informed policy development for the region.

PA-120 THE UTILITY OF FINGERPRINT-BASED PARTICIPANT IDENTIFICATION AND CONSENTING IN CLINICAL TRIALS IN DEVELOPING COUNTRY SETTINGS

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Background Involvement in clinical research requires evidence of informed participant consent, and in many low-income countries with high illiteracy rates, this is done by a fingerprint impression on paper. Due to poor quality of the impression, the individual is often untraceable and this reduces the quality of the process. The study assesses the potential usefulness of fingerprints for consenting and automated participant identification.
Methods As part of a survey in villages in the North Bank West region of The Gambia, individuals of all ages were invited to provide a fingerprint scan to update the pre-trial census records. Using commercial software, scanned impressions were stored on encrypted templates and linked to a unique identifier. A scan is successful if any of the five fingers on the left hand is captured but documented as a failure if none of the five fingers on the left hand records an impression on the scanner. We determined the proportion of successful attempts, and the effect of age and gender on the successful scan using a logistic regression model.
Results A total of 5204 persons were scanned with 74.7% successes for any finger; 70.3% (1550/2206) in males and 78.0% (2339/2998) in females and gender was strongly associated with success rate (Chi2 <0.001). The success rate in children <5 years was 70.6% (726/1029) but lowest in adult males ≥ 40 years; 29.7% (96/323). The odds of a successful scan were lower in males (adjusted OR 0.53; 95% CI: 0.46–0.61; $p > 0.001$) and highest between ages 5–25 years (OR 8.32; 95% CI: 6.96–9.95; $p<0.001$) compared to adults ≥ 40 years.
Conclusions The use of fingerprint-based identification is promising. However, recognition rates are lowest in adult males, perhaps due to occupational practice. Potential for improving sensitivity and application in data retrieval and documenting consent is being explored.

PA-121 IMPROVING EFFICIENCY AND QUALITY IN CLINICAL TRIALS IN SUB-SAHARAN AFRICA

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Background Conduct of clinical trials is significantly regulated and requires substantial infrastructure and human resource investments and efforts. Clinical research centres in sub-Saharan Africa face particular challenges from the increasing trial-related workload and administration, paired with capacity limitations. We investigated the challenges in clinical trial conduct in sub-Saharan Africa to optimising efficiency of processes while maintaining quality. Our working hypothesis was that existing regulations, not adapted to these particular situations, and their possibly overly strict interpretation were the main challenge.
Methods We used an exploratory mixed methods design. Firstly, key informant interviews with questions about quality, guidelines, challenges, and inefficiencies in clinical trials were conducted with 60 clinical trial staff of different professional levels in two English- and two French-speaking African countries. Content analysis was performed to identify themes across settings and positions, respectively. Secondly, we developed an online survey to investigate trial protocol suitability based on the main interview themes and targeting trial staff working in sub-Saharan Africa.
Results According to the interviewees, constraints to trial efficiency arose from two themes: 'planning' (mainly poor planning and missing context-adaptation), and 'site organisation' (mainly staff turnover and workload). The two themes are of particular relevance since they relate only to sponsors and sites and are therefore independent of external conditions (e.g. lengthy approval processes and population issues). Unexpectedly, the administrative burden resulting from the guidelines was not perceived as a difficulty; rather, researchers were grateful for having guidance in their daily work. The online survey corroborated that trial protocols need to be adapted to local contexts by early involvement of the sites and careful consideration of local capacity, systems and conditions.
Conclusions Our data suggest that careful site assessment, appropriate and coherent planning, clear task allocation and management capacity strengthening may increase trial efficiency. Involvement of study sites in protocol development was perceived to be beneficial.

PA-123 FIELD PERFORMANCE OF POINT-OF-CARE TO DETERMINE HBSAG TEST FOR DIAGNOSIS OF ACTIVE HEPATITIS B VIRUS INFECTION IN ZAMBIA

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Background In Zambia, we evaluated the field performance of a rapid point-of-care test for hepatitis B surface antigen (HBsAg)

which could support decentralisation and scale-up of care and treatment of chronic hepatitis B virus (HBV) infection in sub-Saharan Africa.

Methods At two urban public health facilities in Zambia's capital Lusaka, we screened a cohort of HIV-infected adults for HBsAg per national guidelines. A subset was tested with both Determine HBsAg (Alere, USA), using finger prick in the clinic, and HBsAg serology (Access2Analyser, Beckman Coulter), using serum sent to a reference laboratory. If either test was reactive, we measured HBV viral load (VL) and determined HBV genotype with Sanger sequencing. We described patient demographic and clinical characteristics (including liver fibrosis biomarkers) and assessed the sensitivity, specificity, positive and negative predictive values (PPV and NPV) of the Determine test. In secondary analyses, we assessed sensitivity among patients with replicating HBV (VL >20 IU/mL) and with high HBV VL (>20,000 IU/mL).

Results Among 412 participants with both HBsAg tests, median age was 34 years, 51% were women, and median CD4 was 208 cells/mm3. By serology, 66 (16%) were HBsAg-positive. HBV genotypes were A1 (n=21; 52.5%) and E (n=19; 47.5%) among successfully sequenced samples. Overall, the Determine test had 87.9% sensitivity (95% CI: 84.7–91.0%), 99.7% specificity, 98.3% PPV, and 97.7% NPV. The majority of patients (6/8) with false negative results had undetectable HBV VL and no evidence of significant liver fibrosis. Test sensitivity increased to 95.9% among the 51 with replicating HBV and to 100% among the 28 with high HBV VL.

Conclusions The Determine HBsAg test accurately diagnosed HBsAg-emia in the majority of field-tested HIV patients, particularly those with higher HBV VL. False negatives tended to have inactive HBV infection further supporting the use of this low-cost test in public health settings in sub-Saharan Africa.

PA-125 EVALUATION OF CIRCULATING CATHODIC ANTIGEN (CCA) URINE-CASSETTE ASSAY AS A SURVEY TOOL FOR *SCHISTOSOMA MANSONI* IN DIFFERENT TRANSMISSION SETTINGS WITHIN BUGIRI DISTRICT, UGANDA

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10.1136/bmjgh-2016-000260.152

Background Diagnosis of schistosomiasis at the point-of-care is a growing topic in neglected tropical disease research. There is a need for diagnostic tests which are affordable, sensitive, specific, user-friendly, rapid, equipment-free and delivered to those who need it, and point-of-care is an important tool for disease mapping and guiding mass deworming.

Methods Our study was conducted among 500 school children randomly selected across 5 schools within Bugiri district, adjacent to Lake Victoria in Uganda. Duplicate Kato-Katz thick smears were prepared in the field upon receipt of the faecal samples and were read under a microscope within 60 minutes of slide preparation to determine hookworm status. The slides were again read 24 hours later for *Ascaris lumbricoides*, *Trichuris trichiura* and *S. mansoni* and this was repeated for all subsequent stool samples.

Results Of the 469 pupils who provided three stool samples for the six Kato-Katz smears, 293 (76%) children had no infection, 109 (23%) were in the light intensity category, while 42 (9%) and 25 (5%) were in the moderate and heavy intensity categories, respectively. Following performance analysis of CCA tests in terms of sensitivity, specificity, negative and positive predictive values, the overall performance of the commercially available CCA test was more informative than single Kato-Katz faecal smear microscopy, the current operational field standard for disease mapping.

Conclusions The current CCA assay is a satisfactory method for surveillance of *S. mansoni* in an area where disease endemicity is declining due to control interventions. The urine point-of-care CCA test is an attractive tool to augment and perhaps replace the Kato-Katz sampling within ongoing control programmes.

PA-126 COMMUNITY KNOWLEDGE, ATTITUDES AND PRACTICES (KAP) DURING MDA INTEGRATED MALARIA ELIMINATION AND SCHISTOSOMIASIS AND SOIL-TRANSMITTED HELMINTHS CONTROL STUDY IN NGODHE ISLAND, LAKE VICTORIA, KENYA

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Background Knowledge, attitudes and practices (KAP) of communities where mass drug administration based integrated malaria elimination and control of schistosomiasis and soil transmitted helminths (STH) is targeted will be critical in adhering to intervention strategies. KAP surveys have the potential to reveal lessons that will inform implementation in similar settings. This study sought to assess knowledge, attitudes and practices of Ngodhe islanders in Lake Victoria Kenya during mass drug administration (MDA) with artemisinin-piperaquine and low dose primaquine for malaria; albendazole for STH and praziquantel for schistosomiasis.

Methods The KAP study used a pre-tested interviewer questionnaire that was administered to 239 randomly selected adults. Additionally, 4 focus group discussions (each consisting of between 8–12 participants) was done with the elders, women, youth, and mixed group. Another 6 key informant interviews were also done.

Results All respondents (239) had heard about malaria and they acknowledged that it is preventable; 89.1% of respondents had heard about schistosomiasis; and another 87.4% had heard about STH. A high percentage of 96.2 had heard about the mass drug administration while 87% were aware of the integrated malaria, schistosomiasis, and STH strategy. 78.2% of participants favoured stopping MDA in case side effects were perceived to be common. Sanitation was a major challenge with only 41.3% of the respondents using latrines with the rest using bushes.

Conclusions This study revealed huge awareness of the integrated strategy for malaria elimination and schistosomiasis and STH control using mass drug administration. Nonetheless, concerns on MDA drugs side effects and poor sanitation practices will require greater engagement with the community.

PA-127 INTERRUPTED BANCROFTIAN FILARIASIS EXPOSURE RATES IN CHILDREN AFTER TWELVE ROUNDS OF MASS DRUG ADMINISTRATION AND USE OF LONG-LASTING INSECTICIDAL NETS IN RUFIJI DISTRICT, TANZANIA

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Background Tanzania started implementing the WHO strategy of mass drug administration (MDA) with ivermectin and albendazole to eliminate lymphatic filariasis (LF) in Rufiji District, which had a baseline prevalence of 49% in 2000. This study was conducted in April 2015, six months after the latest MDA to establish the impact of MDA and utilisation of long-lasting insecticidal nets on the exposure rates of LF among standard-one children born within the implementation period of the LF elimination programme after 12 rounds.
Methods A cross-sectional study for LF circulating filarial antigen (CFA) was performed in 5 primary schools from 5 different villages. A total of 659 standard-one pupils aged 6–9 years were recruited and screened for CFA using immunochromatographic test cards (ICT). Prior to blood sample collection, children were interviewed on their participation in the MDA. A finger prick whole blood sample (100 μl) drawn from each child was applied to ICT. Results were read after ten minutes for the presence of CFA. Also, the study involved 868 heads of household who were interviewed on their participation in MDA and utilisation of long-lasting insecticidal nets (LLINs).
Results The ICT results were negative for CFA and suggest that there has been an interruption of exposure of children to LF transmission in the study area. More than half of the screened children (54.3%) participated in 2014 MDA round. Household surveyed MDA coverage was 57.4% for the 2014 MDA, below the minimum effective coverage recommended by WHO. Majority (92.5%) of households possessed and utilised LLINs. Of those who did not take the drugs in the last round, 88.7% possessed and utilised LLINs suggesting its synergistic effect with ivermectin and albendazole on LF transmission.
Conclusions Additional MDA rounds and utilisation of LLINs in areas of high-baseline prevalence may result in considerable decreased lymphatic filariasis infection transmission.

PA-128 THE EFFICACY OF ALBENDAZOLE AGAINST SOIL-TRANSMITTED HELMINTHS AND THE IMPACT OF MASS DRUG ADMINISTRATION OF ALBENDAZOLE AND IVERMECTIN ON HEALTH STATUS

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Background The lymphatic filariasis (LF) control programme has been on-going in Ghana since 2000 with mass drug administration (MDA) of ivermectin (IVM) and albendazole (ALB). Soil-transmitted helminth (STH) infections control is augmented within this programme. Therefore this study aimed to determine the efficacy of ALB against STH infections and impact of MDA on study participants.
Methods This was a twelve months longitudinal study. A total of 412 subjects including school children (between the ages of 2–17 years) and pregnant women were randomly selected from four endemic communities in Kpandai district of the Northern region. Coprological assessment for parasites was based on the Kato–Katz technique in both dry and rainy seasons at baseline, 21 days and 3 months post treatment. Single dose albendazole treatment was administered to all patients at baseline.
Results Of all the parasites found (hookworm, *Trichuris trichiura*, *Hymenolepis nana*, and *Taenia sp.*), hookworm was the most prevalent. In the dry season, the overall STHs prevalence at pre-treatment was 29%, while 9% and 13% prevalence was recorded at 21 days, and three months after treatment, respectively. However, in the rainy season, the overall STHs prevalence was 8%, while 4% and 12% was recorded at 21 days and three months respectively after ALB treatment. In general, ALB treatment resulted in an overall hookworm egg count reduction rate of 89% in the dry season and 93% in the rainy season, while the *T. trichiura* egg count reduction rate was 100% in both seasons.
Conclusions STH infections still remain a significant public health burden in Ghana. Hookworm infection seems to respond poorly or suboptimally to ALB, raising concerns of possible emergence of resistance which may lead to a major setback for the control and elimination of STH infections, especially hookworm infections.

PA-129 CULTIVATION OF TWO IS2404 POSITIVE *MYCOBACTERIUM SPP.* FROM THE ENVIRONMENT OF ASANTE AKIM DISTRICT OF GHANA

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Background Buruli ulcer (BU) is one of the neglected tropical diseases. *Mycobacterium ulcerans* is the aetiologic agent of Buruli ulcer. Many extensive studies have failed to isolate *M. ulcerans* in pure culture from the environment, even in highly endemic areas of BU. We investigated the role of macro-invertebrates as possible hosts or vectors for *M. ulcerans* by attempting to cultivate *M. ulcerans* from these organisms.
Methods The study was conducted in 5 villages in the Asante Akim District of Ghana for 10 months. Primary detection of *M. ulcerans* was done by real-time PCR targeting insertion sequence IS*2404* coupled with the detection of IS*2606* and Ketone reductase genes for increased sensitivity and specificity. Primary cultures were done using routine bacteriological media for culturing mycobacteria, L-J and special enrichment liquid broth, BACTEC®.
Results The overall rate of detection of IS*2404* in the general macro-invertebrate population was 12.8%. Cluster of CT-values was observed around a mean value of 35.88 and range values of 28.35–38.61. Statistically, there were no significant differences between the various CT-values obtained, $p>0.05$. The difference in ΔCT values (IS*2606*-IS*2404*) for homogenate sample obtained from Naucoridae which was positive for the three targets on *M. ulcerans* genome was estimated to be 1.77. The present study reports the cultivation of two IS*2404* positive *Mycobacteria spp.* from two aquatic macro-invertebrates of the families Belostomidae and Notonectidae both of the order Hemiptera. The isolate from Belostomidae was identified as either *M. ulcerans* or *M. marinum* with 98% identities that from Notonectidae was 98% identical to *M. neoaurum*. The organisms are yet to be passaged through mice footpad and fully characterised.

Conclusions For the first time *M. neoaurum* species was reported to have harboured IS*2404* element. Aquatic Hemiptera are highly suspected to be vectors or hosts for *M. ulcerans* and they may transmit the pathogen to humans through biting.

PA-130 MODIFIABLE RISK FACTORS OF BURULI ULCER IN COMMUNITIES OF TWO ENDEMIC LOCAL GOVERNMENT AREAS OF OGUN STATE, NIGERIA

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Background Buruli ulcer (BU) remains a neglected tropical disease globally including in Nigeria despite its severe health and socio-economic consequences. This study was conducted as there is a paucity of data on community knowledge and risk factors of BU in Nigeria.
Methods The study was conducted in the BU-endemic Yewa North and Yewa South local government areas (LGAs) of Ogun State, Nigeria. Study population included community members selected using multi-stage sampling techniques. Household survey using a semi-structured questionnaire was used for data collection. Data were analysed using SPSS (version 20) software.
Results A total of 236 consented respondents were interviewed (Yewa North 76.7% *vs* Yewa South 23.3%; males 48.7% *vs* females 51.3%) with an average age of 33.1 years. Only 39.0% had a minimum of secondary education. A little over half (128; 54.2%) reported having knowledge of BU in their communities. However, only 35.6% adjudged BU a common disease in their communities while 56.0% perceived it as a serious health challenge. Few (14.0%) respondents had an average of one household member who had or have BU. Most (64.8%) did not know the cause of BU while 9.7% attributed it to witchcraft/*Olobutu*, bacteria (4.2%), water contact (3.0%) and poor hygiene (3.0%). 53.4% visit riverbanks for activities that were predominantly: washing (37.3%); swimming (35.7%); fetching water (19.8%); and agricultural activities (4.0%). Gender and age had no significant influence on respondents' knowledge of the cause of BU ($p>0.05$). Swimming and other activities on the riverbanks associated with BU had significant correlation with report of BU cases in the household ($p< 0.05$).
Conclusions Pervasive knowledge of BU cases and high-perceived seriousness of the disease in the study communities exist. Nonetheless, there is need for more public health education emphasising common modifiable risk factors and actual cause of BU. Overall, these results provide insights for BU programme planning and optimisation.

PA-132 EFFECT OF SCHISTOSOMA HAEMATOBIUM INFECTION ON *PLASMODIUM FALCIPARUM* MALARIA BURDEN IN LAMBARÉNÉ, GABON

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Background Malaria remains the first cause of death in Africa. In endemic area, it overlaps with other infections including helminths infections. It has been shown that there are interactions between the two parasites infection. Lambarene is the endemic area for urogenital schistosomiasis, which co-exist with *P. falciparum* malaria. Therefore, we decide to assess for the first time the effect of schistosomiasis infection on malaria infection burden.
Methods In order to assess the effect of *S. haematobium* on malaria infection burden, a cross-sectional study was conducted in school children aged 6–16 years old. One blood smear was performed and 3 urine samples were obtained to assess the presence of infections. Chi-square test and generalised linear model were used to compare the risk to be infected by *P. falciparum* parasite and Mann-Whitney-Wilcoxon test to compare the parasitaemia of *P. falciparum*. Demographic data was also collected.
Results A total of 741 children were included. The overall prevalence was 20% and 31% for *P. falciparum* microscopic carriage and *S. haematobium* infection, respectively. Co-infection of both was found in 65 (9%) participants. *S. haematobium* and *P. falciparum* are highly prevalent in PK compared to Bindo and Makouké areas. At univariable analysis, schistosomiasis-infected subjects have an odd of 2.11 [1.46–3.07] to be infected by *P. falciparum* parasite compared to non-infected subjects. Locality was found to confound the association which remains significant after adjustment for age, gender and locality (aOR=1.69, [1.13–2.59]). The effect of *S. haematobium* on the *P. falciparum* parasitaemia outcome was also assessed. There is no effect of Schistosoma infection on malaria parasite density (p-value=0.92).
Conclusions *S. haematobium* infection increases the risk of being infected with *P. falciparum* but doesn't affect the parasitaemia density of *P. falciparum* malaria in our study population.

PA-133 WATER SUPPLY AND SANITATION CONDITIONS IN RURAL SOUTHERN MOZAMBIQUE AND ITS ASSOCIATION WITH MORBIDITY AND MORTALITY INDICATORS, 2012–2015

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Background Water, sanitation and hygiene (WASH) are major health determinants, responsible for an estimated world-wide disease burden of 5.7%. However, the debate about the effect of water quality, hygiene and sanitation in preventing diarrhoea is still ongoing. The aim of this study is to describe access to improved water supply and sanitation infrastructure, as defined by the Joint Monitoring Programme, in the Manhiça Health Research Centre (CISM) study area and evaluate its association with morbidity and mortality indicators.
Methods We conducted a retrospective cohort study. All children under 15 living in the study area during the period 2012–2015 were included (N=61900). Children were followed up until they moved from the study area, turned 15 or until 2015. Water and sanitation household data were obtained from the CISM demographic surveillance system (DSS) in the Manhiça district, an area of around 2380 km2. Clinical data were obtained from CISM's round-the-clock morbidity surveillance system covering outpatient and hospital admissions at the Manhiça District Hospital (MDH) and rural health posts. A negative binomial regression model

using Wald test was performed to assess the minimum community-based incidence rates (MCBIR) for every morbidity-mortality indicator.
Results Preliminary data showed that 86% of the children lived at least once in a household with unimproved sanitation facilities, 27% with an unimproved water source. Spatial distribution of unimproved water and sanitation facilities showed to be clustered. Access to unimproved sanitation and water facilities was associated to higher rates of diarrhoea, a significant 30% of diarrhoea rate increase was observed for rivers, lakes and ponds as water sources. Other morbidity indicators (malnutrition, parasitaemia, anaemia) also showed a rate increase with the use of unimproved water and sanitation facilities.
Conclusions Obtained results are useful to inform sector-related decision-making processes and ultimately improve access to safe drinking water and sanitation in rural southern Mozambique.

PA-134 NONTYPHOIDAL *SALMONELLA* IN THE FOODSTUFFS AND THE HUMAN DIARRHOEAL STOOLS IN OUAGADOUGOU, BURKINA FASO

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Background The sanitary quality of food is a global concern. *Salmonella* infections are a major health problem in developing countries. Each year, food poisoning is affecting thousands of consumers. The objective of this study was to isolate strains of nontyphoidal *Salmonella* in food and in human diarrhoeal stools in Ouagadougou.
Methods Sixty-one samples of sandwiches bought in Ouagadougou and 177 diarrhoeic stools specimen collected at the University Hospital Yaldao Ouedraogo and the Medical Centre Schiphra from May to October 2015 to detect *Salmonella*. The antibiotic susceptibility testing of *Salmonella* strains was done by the disk diffusion method using 14 antibiotics. Statistical analysis of data was done with Epi Info 7.3.
Results From the overall samples analysed, 23 strains of *Salmonella* were identified including14/177 (7.9%) clinical strains, 9/61 (14.75%) food strains. After antigenic identification 15 isolates (6 from foods, 9 from stools) belonged to known serotypes including 9 typhoidal and 6 nontyphoidal stains. Eight strains (3 from foods, 5 from stools) could not be serotyped by the reagents available. All the serotypes identified were found in stools (2 *S. typhi*, 1 *S. paratyphi* B, 1 *S. paratyphi* C, 1 *S. enteritidis*, 3 *S. typhimurium* and 1 *S. dublin*) while *S. paratyphi* B (4), *S. paratyphi* C (1) and *S. enteritidis* (1) only were identified in foods. Eleven (47.83%) strains were resistant to cotrimoxazole (2/11), tetracycline (8/11), nalidixic acid (##) and ciprofloxacine (2/11).
Conclusions The overall frequency of *Salmonella* is higher in the foods than in the diarrhoeic stools. However, the serotype diversity of the clinical strains is more important than that of the food strains. The street sandwiches would not be the main sources of contamination by *Salmonella*. The high rate of the *Salmonella* resistance to antibiotics requires a more steady surveillance of the use of these antimicrobials.

PA-135 URGENT NEED TO EDUCATE NIGERIANS ABOUT THE EBOLA VACCINE TRIAL PROGRAM

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Background With the effort of the World Health Organization to start distributing an experimental Ebola vaccine in West Africa, there is need to assess knowledge and willingness to participate in Ebola virus vaccine trials (EBVT) and possible barriers to participation.
Methods From June to November 2015, a structured questionnaire was used to measure the participants' knowledge and attitudes about Ebola virus vaccine in Nigeria. Data were analysed with packages within SPSS software and $p < 0.05$ considered significant.
Results A total of 5000 participants aged 18–49 years were involved; mean age was 37 years; 3218 (64.4%) were female and 1782 (35.6%) male. Willingness to participate in Ebola virus vaccine trials was found in 803 (16.1%) in this population. It was higher in men than women ($p=0.001$), increased with education levels ($p=0.003$), higher among employed than unemployed ($p=0.005$) and higher among single than married ($p=0.01$). Those who wanted to participate were primarily youth and reasons for readiness to participate include: free health care, monetary gain, international connection and employment opportunity. Decreased willingness was associated with concerns about: fear of reverting back, side effect, refusal of spouses, physical harm, use of parenteral route for vaccine administration, multiple doses of vaccines and societal stigmatisation.
Conclusions This study showed reduced willingness to participate in EBVT. It also revealed limited knowledge about EBVT in Nigeria. Therefore, there is a need for proper education on the potential role of preventive Ebola virus vaccines in the control of epidemics and the importance of vaccination among the populace of Nigeria. Incentives for would-be subjects should also be part of the planning to encourage greater participation in these trials.

PA-136 EFFECT OF ONCHOCERCIASIS TREATMENT ON THE FREQUENCY OF SEIZURES IN PATIENTS WITH EPILEPSY AND ONCHOCERCIASIS

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Background A high prevalence of epilepsy is mainly observed in *Onchocerca volvulus* (OV) hyperendemic areas with no or low ivermectin coverage. There is anecdotal evidence that ivermectin may reduce seizure frequency in patients with onchocerciasis associated epilepsy (OAE).
Methods Between 2008 and 2012, Rethy in Ituri Province, Democratic Republic of Congo, was a study site for a phase III trial comparing moxidectin versus ivermectin as treatment for subjects infested with OV. Participants received a single oral dose of OV drug and were followed for 18 months. Parasitological efficacy was assessed by skin snip exams. In July 2016, the randomisation code has not been broken yet. In 2015 we traced 7 families of patients with epilepsy who had been enrolled in the trial. We interviewed them and reviewed the trial case report forms.

Results Of 472 trial participants, 13(2.7%) had a medical history of active convulsive epilepsy. After OV treatment, 6 (80%) of 7 male patients with epilepsy became seizure free during the following 18 months. Seizures continued in this period in only 1 person with a decrease in frequency; in the latter microfilariae remained detectable in the skin. In all subjects who became seizure free, the skin snips too became microfilaria free for at least 6 months. None of the patients received any anti-epileptic drug nor an additional dose of moxidectin or ivermectin during or after the trial. In all subjects the frequency of seizures increased again after the 18 months and 2 patients died in 2015, because of drowning in the river during seizures.
Conclusions This study suggests that moxidectin and/or ivermectin may be able to decrease the frequency of seizures in OV-infested people with epilepsy. A clinical trial will be needed to support this hypothesis.

PA-137 ASSESSMENT OF THE ENDEMICITY STATUS OF SCHISTOSOMIASIS AND SOIL-TRANSMITTED HELMINTHIASIS IN THE GAMBIA

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Background The Ministry of Health and Social Welfare, The Gambia with support from WHO and Task Force for Global Health (TFGH), conducted a national endemicity mapping survey for schistosomiasis (SCH) and soil-transmitted helminths (STH) to establish their endemicity status. The survey was meant to provide baseline information on endemicity in order to plan and implement strategic interventions. This is a critical step towards NTD elimination by 2020.
Methods A cross-section of fifty school-aged children (SAC, 25 boys and 25 girls) per school was sampled in 209 schools countrywide. Eligible SAC of 7 to 14 years old were randomly selected using formula (n/50) where n=total eligible pupils per school. Stool, urine and finger prick samples provided, were examined for SCH and STH using Kato-Katz, urine filtration, dip-stick and CCA techniques.
Results National prevalence of schistosomiasis and soil-transmitted helminthiasis were 4.3% and 2.5%, respectively. At district level, Niani had the highest prevalence of SCH, recording 22%. Whereas for STH, Banjul, the capital city, had the highest prevalence, recording 55%, followed by 22% prevalence in Kombo South. *Schistosoma haematobium* is the most dominant parasitic infection in The Gambia. Fourteen (38%) districts in the country are co-endemic for both STH and SCH. Generally, male pupils are more infected with urinary schistosomiasis than females.
Conclusions It was established that 19 (45%) of districts mapped are endemic for schistosomiasis; thus the need for treatment with praziquantel. Twenty (47%) of districts mapped are endemic for soil-transmitted helminthiasis at varying rates. However, only two STH endemic districts, Banjul (55%), and Kombo South (22%), within the high and very high prevalence rates of endemicity, are eligible for treatment with albendazole.

PA-138 PREVALENCE OF GASTROINTESTINAL PARASITES IN SOUTHERN MOZAMBIQUE USING A NOVEL MULTIPARALLEL QUANTITATIVE REAL-TIME PCR

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Background Intestinal parasitic infections are distributed worldwide presenting high prevalence in low-income countries. Gastrointestinal parasites in children are associated to inhibition of normal growth, low intellectual development, vitamin deficiency by malabsorption, chronic diarrhoea and dysentery. Available data point to global prevalence in Mozambique (2005–2007) of 65.8% for soil-transmitted helminthiasis. Diagnosis of gastrointestinal parasites relies on stool microscopy which has a lower sensitivity and specificity than molecular biology methods. Consequently, researchers have developed a novel multi-parallel quantitative real-time PCR to detect protozoa and helminths in stool. This technique was used in the current study to determine the prevalence of gastrointestinal parasites in the Manhiça district.
Methods Stool samples (10 g) for the detection of gastrointestinal parasites were collected from 175 children, aged 2 to 10 years, recruited at the Manhiça District Hospital. Clinical and laboratory data were obtained for all participants. Helminths and protozoa were detected through microscopy, the gold standard method, and through multi-parallel quantitative real-time PCR.
Results High prevalence was found for *Giardia lamblia* (61%). Other prevalent parasites were *Ascaris lumbricoides* (10.2%), *Strongyloides stercoralis* (8.6%), *Cryptosporidium* (4%) and *Necator americanus* (2.8%). *Ancylostoma duodenale* and *Entamoeba histolytica* were not detected in any samples studied. More than 60% of children with *A. lumbricoides* presented high egg burden that was correlated with increased *Giardia* burden co-infection (p=0.01).
Conclusions The preliminary results point to a high prevalence of *G. lamblia*. In our sample, a high *Giardia* burden was associated with higher *A. lumbricoides* egg count. Further analysis will allow us to correlate findings with clinical data and to evaluate the effect of the presence of gastrointestinal parasites on the immunological response to malaria.

PA-139 SOIL-TRANSMITTED HELMINTH INFECTIONS AND RISK FACTORS AMONG PRIMARY SCHOOL PUPILS IN LAGOS, NIGERIA

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Background A survey of prevalence of soil-transmitted helminth infections and associated risk factors among pupils of primary schools carried out between June and July 2015.
Methods Four primary schools were purposely selected for the survey (2 public and 2 private). All the pupils that consented to

participate were given sterile universal containers for the collection of stool samples which were processed for examination using Kato Katz technique. Structured questionnaires were administered to the pupils to obtain demographic and risk factors information.

Results A total of 243 pupils aged 5–15 years were recruited for the study while 207 (85.2%) complied and returned stool samples suitable for examination. The overall prevalence of infection was 34.8% (males 36.8%; females 33%). There was no significant difference between the male and female infection rate (p=0.6) and there was also no significant difference among the different age groups (p=0.7). About a quarter (24.2%) of the population studied had single infection of *Ascaris lumbricoides* and 1% had hookworm infection while 4.3% had multiple infections of *Ascaris lumbricoides* and *Trichuris trichiura*. Multiple infections of *Ascaris lumbricoides*, *Trichuris trichiura*, and *Taenia* spp. occurred in 0.5%. Large proportion of pupils engaged in risk factors such as cutting of finger nails with teeth (58.5%), unhygienic eating habits (41.4%), and irregular hand washing (28.5%). Majority (71.5%) of the pupils were not aware of school deworming programme among which 35.8% of them were positive for infection. Also 39.3% of the total number of pupils (56) who engage in open defaecation and use of pit latrines were positive for infection.

Conclusions This showed that unhygienic habits practiced by pupils predisposed them to infection and the need to combine the school deworming programme with health education to reduce the burden of infection among pupils.

PA-140 IS TRACHOMA ON TRACK FOR ELIMINATION BY 2020? MONITORING AND SURVEILLANCE AFTER MASS DRUG ADMINISTRATION WITH AZITHROMYCIN FOR ACTIVE TRACHOMA IN GUINEA BISSAU

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Background Guinea Bissau is a trachoma-endemic country that has pledged to eliminate blinding trachoma by 2020 by implementation of the SAFE strategy. Evidence for elimination is to be presented in a dossier to WHO. Mass drug administration (MDA) with azithromycin for active trachoma has been carried out in the Bijagos and Cacheu regions. Through collaboration with government and non-government agencies, we conducted coverage and impact surveys to evaluate success of MDA and build capacity in monitoring and surveillance activities within the Programa Nacional de Saude de Bissau. Our surveys demonstrate the feasibility of compiling the elimination dossier and show promising results.

Methods (1) Coverage survey (Bijagos): Seven households were randomly selected from 17 villages on five islands which had received MDA 1 month previously. Household members reported whether they had taken azithromycin and population coverage was calculated. (2) Impact survey (Cacheu): 15 households were randomly selected from 20 clusters. Trained ophthalmic nurses recorded cases of follicular trachoma (TF) amongst 1–9 year-olds and of trachomatous trichiasis (TT) amongst people aged 15 and above. Prevalence estimates of TF and TT were calculated.

Results (1) MDA Coverage (Bijagos): Estimated MDA coverage was 90.9% overall (n=518) and 94.4% amongst children aged 1–9. (2) Impact survey (Cacheu): 701 1–9 year-olds and 1557 >14 year-olds were examined. The estimated prevalence of TF1–9 was 0.3% and that of unoperated TT>14 was between 0.1 and 0.4%.

Conclusions These surveys provide evidence that MDA can achieve very high levels of coverage in remote and poorly accessible areas and can reduce TF to below the WHO elimination threshold. Successful TF elimination can allow focus to shift to operating TT, which remains a significant public health problem after MDA. These surveys demonstrate how sound epidemiological methods can be used in programmatic settings to evaluate elimination campaigns, guide future programme activities and contribute to global data collection.

PA-141 THE INTERNATIONAL GOOD CLINICAL PRACTICES GUIDELINES: TIME FOR A REVISION?

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Background The Good Clinical Practices (GCP) codes of the World Health Organization and the International Conference of Harmonization set international standards for clinical research. But critics argue that they were written without considering the challenges faced by clinical researchers in low- and middle-income countries (LMIC).

Methods We analysed the challenges met when conducting clinical trials in LMIC, including in several locations in sub-Saharan Africa and in EDCTP-funded trials. We compared these challenges to GCP guidance, in order to (a) verify if there are gaps between the international GCP codes and the field reality in LMIC, and (b) formulate recommendations for GCP improvement if needed.

Results We identified shortcomings in the GCP guidance concerning three broad domains: ethical, legal and operational. We identified also eleven specific issues: the double ethical review of 'externally sponsored' trials; the informed consent in children; the informed consent in illiterate people; the informed consent comprehension; the definition of vulnerability; the post-trial access to communities; the role of communities as key stakeholders in research; the definition of sponsor; the guidance for contractual agreements; the clinical monitoring; the laboratory quality management systems; and the quality assurance of investigational products. For each specific issue, we formulated a recommendation for the improvement of GCP.

Conclusions Clinical trials are increasingly conducted in LMICs, thus a comprehensive revision of GCP guidelines is needed, to ensure adequate guidance for researchers operating in these contexts, and to maximise protection of research participants. The revised GCP code should be strongly rooted in ethics, sensitive to different socio-cultural perspectives, and allow consideration of trial- and context-specific challenges. This can be only achieved if researchers, sponsors, regulators

and ethical reviewers from LMIC are transparently involved in the revision process, as well as non-commercial researchers and sponsors, and major agencies that fund international collaborative clinical research.

PA-142 ESTABLISHMENT OF A SUB-REGIONAL ETHICS COMMITTEE IN CENTRAL AFRICA TO ADDRESS THE NEEDS OF MULTICOUNTRY PROJECTS: AN OCEAC INITIATIVE

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Background The Universal Declaration on Bioethics and Human Rights, adopted by UNESCO, requires that governments establish National Ethics Committees (NECs) capable of reviewing ethical and scientific aspects on research involving human beings. These NECs are government gatekeepers tasked with ensuring that research conducted in their territories is in compliance with national and international ethics requirements. In Central Africa, NECs are lacking in some countries, barely functional in others either crippled by lack of expertise, scarce opportunities for training or by an environment not conducive to quality and ethical research. To remedy this shortcoming, OCEAC was awarded an EDCTP grant to put in place a common Ethics Committee for Central Africa.
Methods Six designated representatives of Ministries of Health, with appropriate background and skills, from Cameroon, Chad, Equatorial Guinea, Gabon, Republic of Congo, and the Central African Republic were selected to be members of the sub-regional Ethics Commitee. In order to ensure the proper composition of this committee, ethics experts originating from central Africa were selected through a call for candidates widely published in various ethics and research networks in the sub-region.
Results CERSAC (Comité d'Ethique de la Recherche et de la Santé en Afrique Centrale) is the designation of the resulting sub-regional Ethics Committee, assembling fifteen members from the six CEMAC countries and the Democratic Republic of Congo. Since 2014, CERSAC has provided streamlined reviews of health research projects conducted in more than one Central Africa country. A total of 37 local emerging-career researchers and ethics committee members were trained.
Conclusions CERSAC enhances the ethical conduct and social value of research and optimises the protection of human research participants for communities in dire need. The committee also provides a harmonised platform to address ethical challenges related to the conduct and output of health research in Central Africa.

PA-143 INVOLVEMENT OF STAKEHOLDERS IN THE REPORTING PROCESS OF SERIOUS ADVERSE EVENTS DURING CLINICAL TRIALS IN A SUB-SAHARAN RESEARCH CENTER, LAMBARÉNÉ, GABON

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Background The pharmacovigilance of medical products for human use should start during the clinical development and continues after licensure. In developed countries, regulatory agencies are actively involved in all steps of pharmacovigilance. In sub-Saharan African countries, the lack and weaknesses of national regulatory authorities are being addressed through regional regulatory authorities like AVAREF 2 which aims to oversee pharmacovigilance duties across countries. Informing such initiative about the current practices for the reporting of serious adverse events is needed.
Methods We reviewed the reporting of clinical trials performed in CERMEL from 2006–2016. The methods of serious adverse events (SAE) reporting and handling was the main objective of the review.
Results The most frequent methods used to reporting SAE for the clinical trials reviewed in Lambarene were: 31% (5/16) paper Case Report Forms (CRF) only, 25% (4/16) electronic case report form (eCRF) without alert, 13% (2/16) paper CRF +phone call and 13% (2/16) phone +email or fax+ paper CRF and 6% (1/16) electronic SAE reporting system with alert. Generally, all studies reported SAEs directly to the sponsors who reacted according to their guidelines. Only 2 of 16 studies could involve the Institutional Review Board (IRB), Ethics Committees, and the Data Safety Monitoring Committee (DSMC) and eventually reported to the Regulatory Authorities in the country. The Local Safety Monitoring was involved only in one study which used the eCRF with alert.
Conclusions It appears that in the current practices, the reporting and handling of SAEs are mainly done by investigators and sponsors. Although both are the key stakeholders to do so, more active involvement of regulatory authorities is an essential step towards establishment of a pharmacovigilance system and would improve the community engagement towards clinical trials. Electronic reporting with alert system could be one of the methods suitable to involve all partners.

PA-144 ACTIVE PHARMACOVIGILANCE IN CôTE D'IVOIRE

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Background In Africa, pharmacovigilance (PV) is a relatively new science. Yet the African context is favourable to the irrational use of medicines, the circulation of counterfeit drugs, and a high consumption of traditional medicine. This should make PV in African countries a critical and crucial issue to ensure the safe use of treatments available. The collection system used in pharmacovigilance in Africa is predominantly passive. This passive system suffers from significant underreporting because it detects only 1–10% of adverse events. The limit in the passive detection and the growing concerns about security in the long term of drugs widely used in health programs, have stimulated in many countries the implementation of active systems such as actively seeking to improve the development of PV in their countries. In Côte d'Ivoire, pharmacovigilance at the regulatory level started in 1988. What is actually the state of pharmacovigilance and the impact of active research in the development of pharmacovigilance?
Methods This is an observational descriptive study using a qualitative analysis of interviews in order to provide answers to these questions. The interview guides are constructed from a questionnaire already used in the monitoring of pharmacovigilance activities by the Uppsala Monitoring Center in countries with limited resources.
Results Active surveillance has several sources. A well-known source is the pharmaceutical industry in the conduct of clinical

trials and the risk management plans. The pharmaceutical industry accounts for over 80% of reports of adverse effects at national level. The second data source are research centres, but the reporting of adverse effects is not made at national level. The last source of data comes from active operational research studies which as a source are weak and this should be strengthened.

Conclusions Active pharmacovigilance is to be encouraged in Côte d'Ivoire because it will collect data to improve the safety of medicines consumed by the population.

PA-145 ETHICAL AND SCIENTIFIC CONSIDERATIONS FOR THE DESIGN AND IMPLEMENTATION OF THE PREP DEMONSTRATION PROJECT IN NIGERIA

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Background This abstract highlights the ethical and scientific considerations that informed the development and review of the Nigeria PrEP demonstration study protocol.

Methods A desk review was conducted on all the meeting reports that led to the choice of the study design and the decisions made to modify the protocol for the PrEP demonstration project in Nigeria. The study focused on the ethical and scientific rationales for modifying the Partners' PrEP Sero-discordant protocol for this study as well as for the first and second protocol amendments of this study.

Results The decision to conduct a PrEP study was based on the outcome of a modelling study that suggested that sero-discordant couples will benefit from access to condom, TasP, and PrEP. Next, the decisions on the target population for the PrEP demonstration study, the models for evaluation at specific project site, and the design of the community engagement programme were reached through a formative research which engaged 611 individuals using multiple media. The study did not exclude study participants based on Hepatitis status and HIV risk profile since Truvada was an effective hepatitis treatment and the prevalence of hepatitis infection is high in Nigeria. Participants' interest in PrEP use was considered enough reason to prescribe PrEP in a country where uptake of ARV is slow and stigma associated with ARV use is high. Also, HIV-negative partners could assess when the viral load of the HIV-positive partner was 400 copies/ml. Since adherence was a challenge for PrEP use, adherence was enhanced through the use of the MEMS Cap.

Conclusions A PrEP demonstration study that mimics real life scenarios for PrEP provision within public health care institutions and is designed on the basis of community consultations, ethical and scientific considerations, will enhance the success of PrEP roll-out in resource-limited settings like Nigeria.

PA-146 SCHISTOSOMIASIS, PRAZIQUANTEL AND FOOD: THE CONTROL OF A MALADY AMONG SCHOOL-AGE CHILDREN IN UGANDA

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Background Annual school-based mass treatment with praziquantel is the cornerstone for schistosomiasis control among school-age children in Uganda. However, uptake of treatment is low. We evaluated strategies for improved uptake of mass treatment and the effects on the prevalence and mean intensity of *S. mansoni* infection

Methods Through serial cross-sectional surveys conducted in 2011 and 2012 in 12 primary schools in Jinja district and a cluster randomised trial conducted in 2013, the levels of uptake of praziquantel and the prevalence and mean intensity of *S. mansoni* infection among school children were determined. Additionally, in 2012, the effect of increased teacher motivation to distribute treatment was assessed. In 2013, the effectiveness of provision of a pre-treatment snack in improving uptake was evaluated.

Results A total of 1010, 1020 and 1284 randomly selected children were enrolled in 2011, 2012 and 2013, respectively. Uptake of praziquantel was 28.2% (95% CI: 22.9%–33.6%) in 2011. Prevalence and intensity of *S. mansoni* infection was 35.0% (95% CI: 25.4%–37.9%) and 116.1 eggs per gram of stool (epg) (95% CI 98.3–137.1), respectively. With increased teacher motivation in 2012, uptake increased to 48.9% (95% CI: 45.8%–52.0%). The prevalence and intensity of *S. mansoni* infection was 32.6% (95% CI: 29.6%–35.5%) and 133.1 epg (95% CI: 99.0%–167.2%), respectively. Provision of a pre-treatment snack in 2013 increased uptake to 85.5% (95% CI: 82.5%–91.7%) and reduced the prevalence and intensity of *S. mansoni* infection to 8.2% (5.6%–12.2%) and 15.9 epg (95% CI: 12.3%–19.2%), respectively.

Conclusions Although teacher motivation increased uptake of mass treatment, the realised uptake was too low to affect the prevalence and intensity of schistosomiasis among school children. Conversely, provision of a pre-treatment snack achieved a high uptake. The increased uptake significantly reduced the prevalence and intensity of *S. mansoni* infection in this age group.

PA-147 PILOTING DHIS2 SYSTEM IN VISCERAL LEISHMANIASIS SURVEILLANCE

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10.1136/bmjgh-2016-000260.173

Background The District Health Information System 2 (DHIS2) is a tool for collection, validation, analysis and presentation of both individual (tracker) and aggregated data tailored to integrated health information management activities. DHIS2, developed by the Health Information Systems Programme (HISP) in collaboration with University of Oslo, is a modular web-based software package built with open source Java frameworks. Visceral leishmaniasis (VL) is not captured in the DHIS2 regional database, and therefore coming up with the modalities of aggregating available data from clinical trials and general patient records into the DHIS2 national database is crucial for surveillance.

Methods DHIS2 runs on Tomcat Server and PostgreSQL. We set up the VL surveillance program with different stages: enrolment and demographics, initial treatment outcome and follow-up visits. In this system, a patient is enrolled into the system and data is collected in individual data elements; data Indicators are built to help aggregate the data and thereafter used for report generation. It is programmed to visualise data

and display reports in the system dashboard which can then be used to present data.
Results Piloting DHIS2 has enabled us to set up a system that uses the set indicators programmed to aggregate data, thus able to produce reports on the data and the user is also able to select the type of report in the form of pivot tables, charts and graphs and also in GIS mapped data.
Conclusions DHIS2 system is an open source that can be customised and expanded to capture detailed individual surveillance data and shared in reports. This data is useful for tracking neglected tropical diseases such as VL. Data can be handled in the following modalities: i) use of off-line data synchronisation. ii) remote data collection using mobile devices iii) data aggregation and organisation iv) data visualisation and presentation through charts, graphs and pivot tables.

PA-148 STRENGTHENING PRISON HEALTH SYSTEMS: FEASIBILITY AND CHALLENGES OF INTRODUCING PRISON HEALTH COMMITTEES (PRHCS) IN ZAMBIAN CORRECTIONAL FACILITIES

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Background In Zambia, prison health and health services are in a state of 'chronic emergency'. Since 2013, the Zambian Corrections Service (ZCS) partnered with Centre for Infectious Disease Research in Zambia (CIDRZ) to understand and strengthen prisoner health and access to healthcare. A key component of this work was the establishment of 11 facility-level Prison Healthcare Committees (PrHCs) comprising officer and inmate members, with a specific remit to deliver health education and provide monitoring for facility level service access. Findings presented are from operations research evaluating the feasibility of these PrHCs.
Methods Mixed qualitative methods included, in-depth interviews (11 Ministry and ZCS officials; 6 facility managers) and focus group discussions (FGDs) with members of 6 PrHCs, and 6 groups of non-PrHC-inmates in the same facilities. Memos were generated from participant observation in workshops and meetings preceding and after implementation. All activities were subject to verbal informed consent and interviews and FGDs were audio-recorded with permission.
Results Key informants were strongly supportive of PrHCs, noting potential for improved health information dissemination, strengthened preventive service-coverage, routine service monitoring and facility-level accountability. PrHC members confirmed ZCS-led training had taken place and that they had been given authority to deliver information-based health interventions and facilitate quicker referrals to primary care. The early phase of implementation (3–6 months at data collection) produced mixed accounts regarding PrHCs' capacity to fulfil other preventive services or conduct data collection. Departure of PrHC members due to transfer and/or release was the most frequently listed challenge.
Conclusions These data suggest the feasibility of establishing a committee comprising both officers and inmates to address a fundamental gap in facility-level mechanisms for health information delivery and service accountability. Findings nonetheless suggest PrHCs will require iterative adjustments and ongoing problem-solving by local officials. Context-sensitive application of these principles to other settings may yield positive outcomes.

PA-149 DETERMINING THE ENVIRONMENTAL, SOCIAL AND CULTURAL CONTEXTS OF A PROPOSED SCHISTOSOMIASIS HEALTH EDUCATION INTERVENTION IN EGGUA, YEWA NORTH LOCAL GOVERNMENT AREA, OGUN STATE NIGERIA

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Background The role of health education in the control of schistosomiasis cannot be over-emphasised. Central to its utility is an understanding of the way a community perceives, understands and can explain how schistosomiasis occurs among them.
Methods In order to study the environmental, social and cultural determinants of continued schistosomiasis prevalence in Eggua, we administered a semi-structured questionnaire to 371 adults and 265 children between November 2012 and December 2015. We asked questions about their occupation, present and previous water contact pattern, knowledge of schistosomiasis, sanitation, smoking and alcohol behaviour and length of residence in the village.
Results The respondents ranged in age from 35 to above 60 years; 45% had no schooling and 30% had a least a primary education. Most were farmers (48%) and traders (30%) with a small number (2%) of fisher-folk and had been at this work for more than 15 years. The majority (93%) were Christian, of a denomination in which members spend long periods in the river praying. The rivers are the main source of water for a large number of respondents (63%). Water contact is frequent: 90% go at least daily to the rivers. All the respondents worked at non-itinerant jobs. Despite the research surveys were taking place in Yewa since 2009, 90% of respondents did not know the cause of blood in urine and self-reported haematuria was low (4.6%). Many homes did not have a latrine. Children respondents also didn't have knowledge of the cause of schistosomiasis (60%); those who had heard about it were not well educated on ways to avoid being infected; and 83% did not know they could be re-infected after treatment.
Conclusions Formal health education initiatives for the control of schistosomiasis in Eggua are imperative and these findings should be taken into account in designing them.

PA-150 MATERNAL UROGENITAL SCHISTOSOMIASIS, MONITORING DISEASE MORBIDITY BY SIMPLE REAGENT STRIPS

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Background Urine analysis is one of the recommended antenatal guidelines for early diagnosis of pregnancy-associated complications. While urine analysis by dipstick had been used in practice to provide useful information on other urinary tract infections, its application for early detection of urogenital schistosomiasis in pregnant women is often downplayed in most endemic areas. Our study therefore assessed the performance of some common urinalysis parameters in the diagnosis of maternal urogenital schistosomiasis in endemic rural communities of Nigeria.
Methods The cross-sectional epidemiological survey of urogenital schistosomiasis was conducted among pregnant women in

Yewa North Local Government, Ogun State, Nigeria. The women were examined for infection with *Schistosoma haematobium* microscopically and screened for macrohaematuria, microhaematuria and proteinuria using standard urine chemical reagent strips.

Results Of 261 volunteer participants, 19.9% tested positive for *S. haematobium* infection. The proportion of microhaematuria (23.8%) was significantly higher than that of macrohaematuria (3.8%) and proteinuria (16.8%) ($p<0.05$). Microhaematuria with sensitivity (82.7%) and specificity (89.0%) was the best diagnostic indicator of urogenital schistosomiasis.

Macrohaematuria with the least sensitivity (11.8%) was however the most specific (98.1%) for diagnosing urogenital schistosomiasis in pregnant women. Maximum microhaematuria sensitivity (100.0%) was observed in women between 15–19 years but sensitivity was consistently low in other older age groups. Maximum sensitivity, specificity and predictive values (100.0%) were recorded for microhaematuria in first trimester women. Diagnostic efficiency of proteinuria and macrohaematuria was also better in first trimester women except the 25.0% specificity recorded for proteinuria. The overall diagnostic performance of microhaematuria and proteinuria was best in secundigravidae.

Conclusions Microhaematuria can be used for early detection of urogenital schistosomiasis in endemic areas especially in younger and first trimester women. Treatment with praziquantel is recommended for the women in their late trimester in order to avert associated adverse pregnancy outcomes.

PA-151 FROM LABORATORY RESEARCH TO THE PUBLIC: SCIENCE COMMUNICATION FOR POLICY, RESEARCH COMMUNITY AND PUBLIC

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Background The Government of Uganda uses empirical evidence for policy formulation. The Uganda Virus Research Institute (UVRI) and the International Association of National Public Health Institutions (IANPHI) trained journalists and scientists to communicate research processes and findings to the public. This improved the capacity to communicate important information during outbreaks and to disseminate research findings as part of policy formulation.

Methods Through training workshops, 30 research scientists including study coordinators, research officers and principal investigators interacted with 12 health reporters from various media houses. Training covered writing policy briefs and press releases. Attendees were taken through the 'dos and don'ts' when being interviewed by television/radio journalist while journalists were trained in basic epidemiology terms and research processes. They analysed research papers to find different story angles. They conducted mock media talk shows for television and radio and these sessions were reviewed by all those in attendance, identifying areas for improvement.

Results Key findings revealed that journalists do not ably write about research findings because they do not understand the scientific research procedure. Training journalists on health research communication, ethical issues and research procedure enabled them to appreciate the scientific research process. Continued interaction was found to be of help to articulate research findings for health journalist before they are presented in print and audio media for the wider audience/public. This method built capacity of participating scientists to communicate to the lay audiences. It also helped the scientists plan for the media and policy makers during future dissemination of their research findings.

Conclusions Meaningful engagement of journalists and the public by scientists results in proper understanding of the ethical and scientific research procedure. This calls for systematic investment by research organisations and, during proposal development, budgeting for communication and knowledge translation of research findings to benefit policy makers and the wider research community.

PA-152 THE EFFECT OF HELMINTH CO-INFECTION ON MALARIA-SPECIFIC IMMUNOGLOBULIN G RESPONSES

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Background Malaria and helminthiases overlap extensively in their epidemiological distributions, and co-infections are common. Helminth infection has a profound effect on the immune system such as the induction of immuno-regulatory mechanisms such as potent regulatory T cell responses known to suppress cellular effector mechanisms.

Methods The prevalence of malaria parasitaemia, intestinal helminths, co-infection and anaemia was determined in a cross-sectional study (March 2011) of 372 children aged 6 months to 10 years resident in Mutengene in south-western Cameroon. Plasma total IgG and IgG1–4 subclass antibody levels to *P. falciparum* apical membrane antigen 1 (AMA1), the N-terminal non-repeat region (GLURP R0) and the C-terminal repeat region of glutamate rich protein (GLURP R2) and merozoite surface protein 3 (MSP3) were measured by standardised ELISA.

Results Prevalence was as follows: malaria parasitaemia (mp) 18%, pyrexia 25.4%, helminths 19.7%, and anaemia 71.5%. Amongst those who were mp-positive, 25.4% were symptomatic (4.5% overall). Almost all helminth infections were the soil-transmitted helminths *Ascaris*, *Trichuris* and hookworm (96.4%) with a few cases of *Hymenolepis* and *Enterobius*. Haemoglobin concentration (g/dl) correlated positively with age and negatively with mp density ($p\leq0.001$). The mean haemoglobin (g/dl) level of participants co-infected with both parasites (3.4%) was higher compared to participants infected with either *Plasmodium* (15.8%) or helminths (16.1%) alone ($p< 0.01$). IgG and IgG1–4 subclass antibody levels to all recombinant antigens correlated positively with age ($p< 0.01$). Total IgG, IgG1, 2 & 3 levels to all the antigens tested were significantly (except MSP3 IgG2, $p=0.08$) higher in participants infected with *Plasmodium* alone, compared to the co-infection, helminths only and no infection groups. Decreased levels of AMA1 IgG associated significantly with co-infection (OR=0.27, 95% CI:0.11–0.68). Increased MSP3 IgG and IgG1–4 levels were significantly associated with children infected with *Plasmodium* alone compared to children co-infected with both parasites.

Conclusions Infection with intestinal helminths stifles protective anti-plasmodial antibody responses.

PA-153 SAFETY OF RVSV EBOLA VACCINE, AFTER 6 MONTHS FOLLOW-UP, IN ADULTS: A PHASE 1 TRIAL CONDUCTED IN LAMBARÉNÉ, GABON

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Introduction The Centre de Recherches Médicales de Lambaréné (CERMEL) in Gabon, member of the 'VSV-EBola CONsortium' (VEBCON), evaluated safety and immunogenicity of the rVSVΔG-ZEBOV-GP vaccine in African volunteers from an area with previous Ebola outbreaks before its use during the last outbreak in West Africa.

Methods From November 2014 to April 2015 we performed an open-label, dose escalation phase 1 trial to assess safety, side-effect profile, and immunogenicity of rVSV-ZEBOV. A total of 115 healthy adults both male and non-pregnant or lactating female volunteers aged 18–50 years old living in Lambaréné (Gabon) were included. Participants were allocated to five vaccine dose groups: 3×10^3 PFU (n=20), 3×10^4 PFU (n=20), 3×10^5 PFU (n=20), 3×10^6 PFU (n=39) and 2×10^7 PFU (n=16). Here, we present data on adverse events (AE) and serious adverse events (SAE) between days 180 and 365 after vaccine injection (Day 0).

Results From Month six to Month 12, the proportion of volunteers with AE as well as number and grade of AEs per volunteer were similar in the five groups. A higher total number of events occurred in the cohort 3×10^6 PFU, the largest group. Most symptoms were mild to moderate. No clinically significant laboratory changes were observed. Three events - two episodes of *P. falciparum* malaria and one snake bite - were graded as serious, because they required hospitalizations. Both SAE were judged as non-related to the vaccine and resolved without sequelae. None of the adverse events was related to rVSV-ZEBOV vaccine.

Conclusions Our results confirmed an acceptable profile of safety and tolerability of rVSV-ZEBOV up to 12 months of follow-up. In order to investigate possible late-stage safety signals follow-up period of the study was extended to five years. Integrating data (assessment until 60 months) from all the VEBCON study sites is the next key step allowing a final conclusion about safety of rVSV-ZEBOV. The trial was registered on the Pan African Clinical Trials Network website with the number PACTR201411000919191

PA-154 RUBELLA SEROPREVALENCE AMONG HIV-INFECTED AND UNINFECTED ZAMBIAN CHILDREN AND ADOLESCENTS

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Background Congenital rubella syndrome remains a significant cause of morbidity and mortality among children in sub-Saharan Africa. A safe and effective vaccine is available and many countries, including Zambia, plan to introduce the measles-rubella vaccine by 2020. HIV-infected youths may be an important group to consider as they may remain susceptible to rubella virus due to waning immunity. More information is needed in this age group to guide policy on catch-up rubella vaccination campaigns after introduction.

Methods This cross-sectional study was nested within ongoing studies of HIV and malaria in Southern Province, Zambia. Dried blood spot cards from children and youths 5–15 years of age enrolled in these studies from 2009–2013 were selected and tested for IgG antibodies to rubella virus. Antibody levels among HIV-uninfected youth, HIV-infected treatment-naïve youth, and HIV-infected youth receiving antiretroviral therapy (ART) were compared.

Results 617 HIV-uninfected, 144 HIV-infected treatment-naïve, and 128 HIV-infected youth receiving ART were included in the study. The proportion seropositive for rubella virus was significantly higher among HIV-uninfected youth (54.7%) compared to HIV-infected treatment-naïve youth (41.7%) and HIV-infected youth receiving ART (49.6%). The proportion of youth with equivocal results was significantly higher for the two groups of HIV-infected youth (treatment-naïve=11.8%; receiving ART=7.9%) compared to HIV-uninfected youth (1.1%). Within groups, the proportion seropositive increased with age. Other than age, no demographic or clinical characteristics were associated with susceptibility among HIV-infected youth.

Conclusions Our results suggest that HIV-infected youth would benefit from vaccination against rubella virus. Half of all youth in rural Zambia were susceptible to Rubella virus. When rubella vaccine is introduced, failure to target older girls in immunisation campaigns could lead to an increase in congenital rubella cases.

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