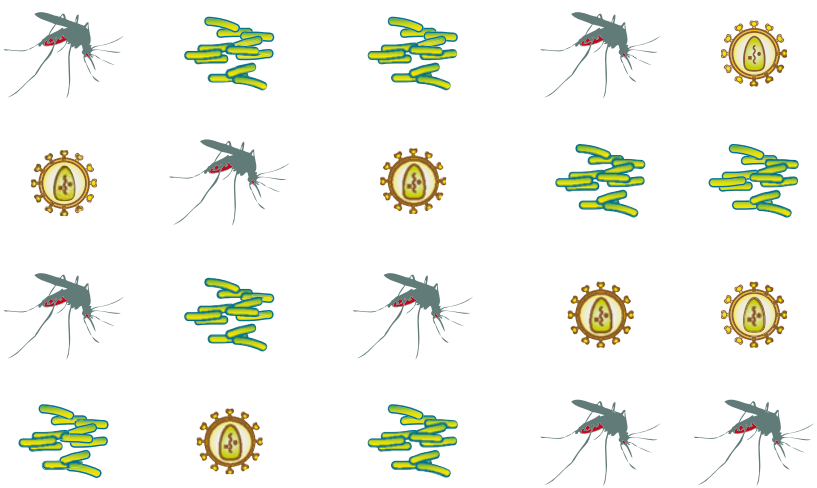
E D C T P

Sixth EDCTP Forum

Strengthening Research Partnerships for Better Health and Sustainable Development

9–12 October 2011 Addis Ababa, Ethiopia



European Union
Supported by the EU

Sixth EDCTP Forum

Strengthening Research Partnerships for Better Health and Sustainable Development

9–12 October 2011 Addis Ababa, Ethiopia

www.edctpforum.org
www.edctpforum.org/sixthforumblog

For more information about the Forum and to order Forum publications please contact: forum@edctp.org

Design: Sam Gobin, www.samgobin.nl

Content

Strengthening Research Partnerships for Better Health and Sustainable Development

Welcome

Dear Colleagues and Friends,

It is my pleasure to welcome all of you to the Sixth EDCTP Forum on behalf of the Organising and Programme Committee. The theme for this forum is **Strengthening Research Partnerships for Better Health and Sustainable Development**. This theme takes into account the past, present and future of EDCTP. It highlights the need for effective and sustainable partnerships for health research and development in the fight against diseases of poverty. This forum comes at a very exciting and opportune time, the bridging period between the end of the first EDCTP programme and the preparatory stage of the imminent second phase of the Partnership.

This forum will provide information on the outcomes of the projects that have been supported by the Partnership in collaboration with all our partners, share experiences and practical lessons learnt, and garner ideas that will contribute to the planning of future of research and development. In addition to EDCTP grantees, the forum brings together an extraordinary array of speakers and delegates from research institutions, universities, public–private partnerships, product development partnerships, like-minded organisations working on poverty-related diseases (PRDs), governments, regional bodies and industry around the globe, especially from Africa and Europe. It therefore presents a unique networking and discussion platform for the exchange of information and stimulation of new ideas to shape the future research agenda on PRDs.

An invigorating programme is presented featuring a wide range of research topics on HIV/AIDS, tuberculosis and malaria, as well as cross-cutting areas on health capacity development and networking, ethics and regulatory affairs. The discussions will be based on real-life situations, experiences and practical examples. The presentations will be in various formats including keynote addresses by invited speakers from North and South, oral presentations in plenary and parallel sessions, panel discussions, posters sessions, satellite meetings and a marketplace for research exhibitions. Moreover, the winners of the EDCTP Awards to Outstanding Junior and Senior African Scientists will be awarded during the closing session of the forum.

We trust you will find this forum stimulating, informative and enjoyable. We wish you a pleasant stay in the historical and beautiful city of Addis Ababa, Ethiopia in the Horn of Africa.

Dr Michael Makanga
Director South-South Cooperation and Head of Africa Office

Introducing the hosts

We extend our deepest thanks and appreciation to our local hosts for providing invaluable support to the organisation and making the stay in Ethiopia a truly memorable one.

Armauer Hansen Research Institute (AHRI)

Armauer Hansen Research Institute (AHRI) was founded in 1970 through the initiative of the Norwegian and Swedish Save the Children organizations seconded by the Ministry of Health of Ethiopia. AHRI was established as a biomedical research institute located next to the All Africa Leprosy Rehabilitation and Training Hospital (ALERT). The institute joined the Ethiopian Ministry of Health in 2004. AHRI research activities cover basic (immunology and molecular biology), epidemiological and translational research.
www.ahri-alert.org

Ethiopian Health and Nutrition Research Institute (EHNRI)

The mission of the Ethiopian Health and Nutrition Research Institute (EHNRI) is to protect and promote the health of the Ethiopian people by addressing priority public health and nutrition problems through problem-solving research, public health emergency management, establishing and maintaining quality laboratory system. Currently the institute is focusing on priority disease research and strengthening the national public health laboratory services in the country. It is also the technical hand of the Federal Ministry of Health.
www.ehnri.gov.et

Federal Ministry of Health of Ethiopia

The Federal Democratic Republic of Ethiopia Ministry of Health aims to reduce morbidity, mortality and disability and improve the health status of the Ethiopian people through providing a comprehensive package of promotive, preventive, curative, rehabilitative and regulating health services via a decentralized and democratized health system in collaboration with stakeholders.
www.moh.gov.et

Belgium
Institute of Tropical Medicine
www.itg.be

Germany
Federal Ministry of Education and Research
www.bmbf.de

Ireland
Irish Aid
www.irishaid.gov.ie

Luxembourg
Fonds National de la Recherche Luxembourg (FNR)
www.fnr.lu

Netherlands
NACCAP
www.nwo.nl/naccap

South Africa
Medical Research Council
www.mrc.ac.za

Spain
Institute of Health Carlos III (ISCIII)
http://aes.isciii.es

Sweden
Sida
www.sida.se

Switzerland
Swiss Agency for Development and Cooperation
www.sdc.admin.ch

UK
Medical Research Council
www.mrc.ac.uk

Aeras
www.aeras.org

Emergent BioSolutions
www.emergentbiosolutions.com

Novartis
www.novartis.com

ShinPoong Pharm
www.shinpoong.co.kr/eng

Our sponsors

We gratefully acknowledge our sponsors for their generous support

The organisers

Chair
Michael Makanga (EDCTP)

Executive organising committee
Hager Bassyouni (Abstracts, EDCTP awards)
Chris Bruinings (Finance)
Suzanne Hoogervorst (Travel, venue and registrations)
Gert Onne van Klashorst (Communications, abstracts)
Sophie Mathewson (Sponsors)
Thomas Nyirenda (Abstracts)
Daniela Pereira (Communications, abstracts, EDCTP awards, sponsors)
Gail Smith (Administration)

Scientific committee
Alioune Dieye (EDCTP-DCCC member, malaria expert, Senegal)
Christiane Druml (EDCTP-GA member, Austria)
Martin Grobusch (EDCTP-PB member, TB expert, Netherlands)
Nkandu Luo (EDCTP-DCCC member, HIV expert, Zambia
Modest Mulenga (EDCTP-DCCC member, malaria expert, Zambia)
Rosemary Musonda (EDCTP-PB member, HIV expert, Botswana)
Veronique Penlap (EDCTP-DCCC member, TB expert, Cameroon)
Hulda Swai (EDCTP-DCCC member, TB expert, South Africa)

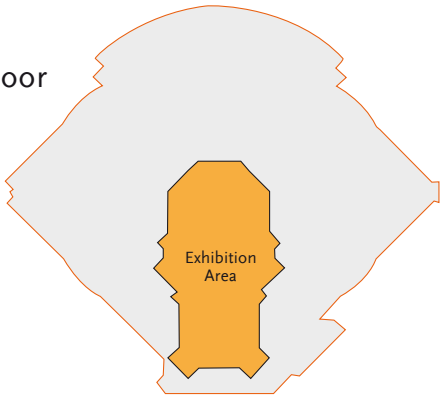
Forum objectives

The Sixth EDCTP Forum will be held from 9 to 12 October 2011 in Addis Ababa, Ethiopia. The theme of the Forum is **Strengthening Research Partnerships for Better Health and Sustainable Development**, taking into account the past, present and the future of EDCTP. This Forum provides an international platform for the presentation and discussion of frontier research for everyone involved in combating the three main poverty-related diseases (HIV/AIDS, malaria and tuberculosis) and the appropriate capacity development and networking activities. It presents a unique opportunity to establish and reinforce cooperation and synergy among EDCTP stakeholders at various levels including scientific, policy, funding and political interactions. Scientists involved in EDCTP-funded projects are particularly encouraged to use this opportunity to share new developments and results from their projects.

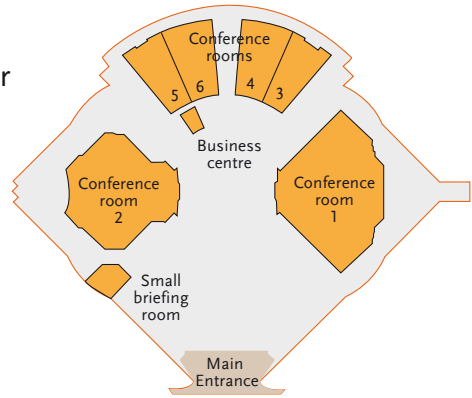
The main purpose of the Sixth EDCTP Forum is to bring together the various EDCTP stakeholders and to share the achievements of the eight years of the Partnership's existence, to showcase project outcomes of EDCTP research, capacity strengthening and networking activities in sub-Saharan Africa. Additionally, the forum aims to:

- Promote African and European leaders' support for research in HIV/AIDS, tuberculosis and malaria and increase awareness of the need for clinical trial activities in Africa
- Provide a platform for bridging partnerships by bringing together Member States and third-party partners
- Support engagement between African and European scientific communities, as well as partners from other regions in order to shape an effective and appropriate research agenda.

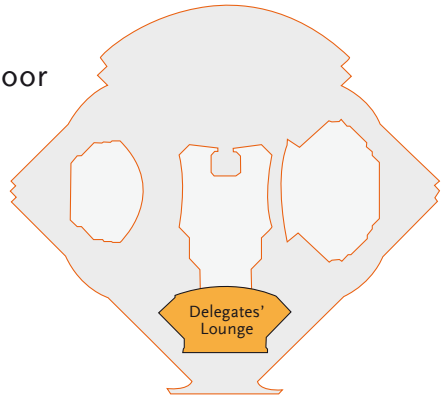
Ground Floor



First Floor



Second Floor



The venue

This year's Forum venue is the United Nations Conference Centre (UNCC) in Addis Ababa, which has hosted many high-profile conferences and offers versatile facilities to the Forum.

The UNCC is composed of 4 floors:

- The **basement** consists of the reproduction unit and the technical teams
- The **ground floor** consists of the communication team, clinic, media centre, translation team and Training centre
- The **first floor** is composed of all the conference rooms, caucus rooms and offices of the Conference Coordination Unit (CCU)
- The **second floor** is mainly composed of the cafeteria, dining rooms and coffee shop.

Facilities within the UNCC

A fully equipped Business Centre on the first floor provides access to international telephone and fax service, simple straight photocopying, computer workstations and Internet use at set charges to users. In addition, Internet connectivity to WiFi enabled laptops and personal computers will be provided. Participants are welcome to take advantage of these services.

Social events

All Sixth EDCTP Forum delegates are cordially invited to attend the social events on the evening of **Sunday 9 October** and **Monday 10 October**. During these events, food and drinks will be provided, and our guests will have the opportunity to meet, catch up and enjoy the entertainment programmes. Please refer to the information below for the times and locations of this Forum's social events.

Sunday 9 October

Welcome reception
18:20–20:30
Banquet Room
United Nations Conference Centre

Monday 10 October

Official forum dinner
19:00–20:00
Yod Abyssinia Restaurant
(Ethiopian cuisine)
Addis Ababa

Sixth EDCTP Forum blog

The Sixth EDCTP Forum blog is the communications hub on Forum activities before, during and after the Forum. The blog complements the Forum website and will update both delegates that are at the Forum and others that wish to know what is happening. During all days of the Forum, the blog will offer a mix of daily summaries of sessions, interviews and audio/visual material such as photographs and podcasts.

In addition, presentations of the plenary and parallel sessions will be available for download and in audio/slideshow format. Forum delegates are also welcome to post their comments and share their views on the Forum activities and discussions.

The Sixth EDCTP Forum blog is available at
www.edctpforum.org/sixthforumblog

Sunday 9 October 2011	Monday 10 October 2011
	08:00–09:00 **Registration** [LOBBY]
	09:00–10:30 **Plenary session I** Forum prologue [CONFERENCE ROOM 1]
	10:30–11:00 Coffee / Tea break
	11:00–12:00 **Parallel sessions** Clinical research achievements and findings in sub-Saharan Africa HIV/AIDS [CONFERENCE ROOM 1] Tuberculosis [CONFERENCE ROOM 3] Malaria [CONFERENCE ROOM 5]
	12:00–13:00 **Poster presentations / Marketplace** [EXHIBITION AREA]
15:00–17:00 **Registration** [LOBBY]	12:30–14:00 **Satellite meeting** Medicines for Malaria Venture meeting on drug access [DELEGATES LOUNGE]
	13:00–14:00 Lunch
14:00–16:00 **Satellite meeting** Professional recognition, career development and training for clinical trial investigators and staff [CONFERENCE ROOM 3]	14:00–16:10 **Parallel session** Clinical research achievements and findings in sub-Saharan Africa (cont.) HIV/AIDS [CONFERENCE ROOM 1] Tuberculosis [CONFERENCE ROOM 3] Malaria [CONFERENCE ROOM 5]
	16:10–16:40 Coffee / Tea break
17:00–18:20 **Official opening addresses** [CONFERENCE ROOM 1]	16:15–17:30 **Satellite meeting** Keeping the malaria medicine chest full: therapeutic options to treat malaria across the disease spectrum [CONFERENCE ROOM 3] 16:40–17:40 **Poster presentations / Marketplace** [EXHIBITION AREA]
18:20–20:30 Welcome reception [BANQUET ROOM]	19:00–20:30 Conference dinner

Tuesday 11 October 2011	Wednesday 12 October 2011
08:00–09:00 **Special sessions** Grant writing for scientists [CONFERENCE ROOM 3] Scientific publication writing for scientists [CONFERENCE ROOM 5]	08:00–09:00 **Special sessions** Grant writing for scientists [CONFERENCE ROOM 3] Scientific publication writing for scientists [CONFERENCE ROOM 5]
09:00–10:30 **Plenary session II** Recent advances in HIV/AIDS, tuberculosis and malaria [CONFERENCE ROOM 1]	08:00–10:30 **Plenary session III** Presentations from EDCTP partners [CONFERENCE ROOM 1]
10:30–11:00 Coffee / Tea break	10:30–11:00 Coffee / Tea break
11:00–12:00 **Parallel sessions** Developing scientific research capacity in sub-Saharan Africa HIV/AIDS [CONFERENCE ROOM 1] Tuberculosis [CONFERENCE ROOM 3] Malaria [CONFERENCE ROOM 5] 11:00–13:00 Cross-cutting: EDCTP-NACCAP [CONFERENCE ROOM 6]	11:00–12:00 **Parallel sessions** North-South and South-South partnerships for quality improvement research in sub-Saharan Africa HIV/AIDS [CONFERENCE ROOM 1] Tuberculosis [CONFERENCE ROOM 3] Malaria [CONFERENCE ROOM 5] Cross-cutting [CONFERENCE ROOM 6]
12:00–13:00 **Poster presentations / Marketplace** [EXHIBITION AREA]	12:00–13:00 **Poster presentations / Marketplace** [EXHIBITION AREA]
12:30–14:00 **Satellite meeting** Clinical trials in practice: how to achieve the best protection of the study subjects? [DELEGATES LOUNGE]	
13:00–14:00 Lunch	13:00–14:00 Lunch
14:00–16:10 **Parallel sessions** Developing scientific research capacity in sub-Saharan Africa (cont.) HIV/AIDS [CONFERENCE ROOM 1] Tuberculosis [CONFERENCE ROOM 3] Malaria [CONFERENCE ROOM 5] Cross-cutting: EDCTP-NACCAP [CONFERENCE ROOM 6]	14:00–15:30 **Parallel sessions** North-South and South-South partnerships for quality improvement research in sub-Saharan Africa (cont.) HIV/AIDS [CONFERENCE ROOM 1] Tuberculosis [CONFERENCE ROOM 3] Malaria [CONFERENCE ROOM 5] Cross-cutting [CONFERENCE ROOM 6]
16:10–16:40 Coffee / Tea break	15:30–16:00 Coffee / Tea break
16:40–17:40 **Poster presentations / Marketplace** [exhibition area]	16:00–17.20 **Plenary session IV** Recommendations, award giving ceremony and closing remarks [CONFERENCE ROOM 1]

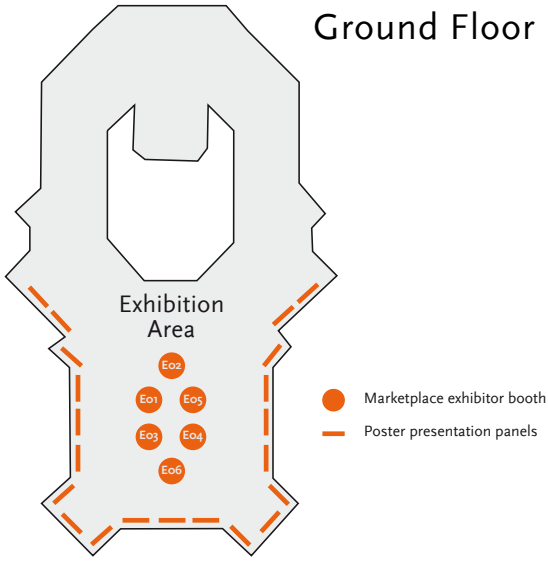
Marketplace
for research exhibitions

During the Forum, there will be marketplace exhibitions where organisations will highlight their activities to the Forum delegates. The marketplace will be located at the exhibition area in the ground floor.

E01 European Commission
The Framework Programmes for Research aims to strengthen the scientific and technological base of European industry, and to encourage its international competitiveness while promoting research that supports EU policies. The EU policies of developing research for the global knowledge based economy focus increasingly on collaborative research, both within the EU and with external research partners. Coordinating national or European teams, setting up research networks, and increasing the mobility of individual researchers are at the heart of such policies.
http://ec.europa.eu/research/fp7

E02 European and Developing Countries Clinical Trials Partnership
EDCTP aims to accelerate the development of new or improved drugs, vaccines, diagnostics and microbicides against HIV/AIDS, tuberculosis and malaria, with a focus on phase II and III clinical trials in sub-Saharan Africa. At the marketplace exhibition, Forum delegates will find out more information about EDCTP activities. In addition, members of the EDCTP Calls & Grants team will be available to answer queries from grantees regarding their projects.
www.edctp.org

E03 Aeras
Aeras is a non-profit product development organization dedicated to the development of effective tuberculosis (TB) vaccines and biologics to prevent TB across all age groups in an affordable and sustainable manner. Aeras utilizes its broad capabilities and technologies in collaboration with numerous partners and stakeholders to support the development of vaccines and other biopharmaceuticals to address TB and other significant public health needs of underserved populations.
www.aeras.org



E04 Novartis
Novartis' mission is to discover, develop and market innovative products to prevent and cure diseases, ease suffering and enhance quality of life. For over a decade, the Novartis Malaria Initiative has been a pioneer in the fight against malaria. Focused on access, treatment, R&D and capacity-building, the initiative is the largest access-to-medicine program of Novartis measured by the number of patients reached annually.
www.novartis.com

E05 Shin Poong
ShinPoong Pharm.Co.,Ltd makes a commitment to guard human life with sincerity and effort and to become one of the worldwide pharmaceutical companies with continual researches. In 2008, ShinPoong has completed the new plants in compliance with EMA to produce PYRAMAX®, which is a new fixed-dose combination of Pyronaridine-Artesunate for malaria treatment.
www.shinpoong.co.kr/eng

E06 African Union
The vision of the African Union is that of: "An integrated, prosperous and peaceful Africa, driven by its own citizens and representing a dynamic force in global arena." This vision of a new, forward looking, dynamic and integrated Africa will be fully realized through relentless struggle on several fronts and as a long-term endeavour. The African Union has shifted focus from supporting liberation movements in the erstwhile African territories under colonialism and apartheid, as envisaged by the OAU since 1963 and the Constitutive Act, to an organization spear-heading Africa's development and integration.

Special sessions

Special session on scientific grant writing

During the Sixth EDCTP Forum a mini-workshop will be held on grant writing for early career investigators. The aim of the workshop is to assist investigators to prepare better grant proposals in order to improve funding success. During the workshop, the group will identify key principles, demystify key processes, draw on experiences and common sense, and identify good practice tips.

The grant writing sessions will include aspects such as:

- How to identify funders and their priorities and schemes
- The criteria and principles of how peer review works
- Proposal writing – common reasons for failure; key contributors to success
- Proposal checklist

This will be an informal and dynamic workshop involving both presentations and interactive discussions. The special sessions on scientific grant writing will take place on Tuesday 11 October (08:00–09:00) and Wednesday 12 October (08:00–09:00), and will be facilitated by Dr Morven Roberts, Programme Manager Global Infections and Global Health Trials, MRC UK; Dr Assan Jaye, Senior scientist, MRC West Africa Collaboration MRC Laboratories, Banjul, The Gambia; and Dr Ousmane Sarr, Senegal Harvard Malaria Initiative, Le Dantec Teaching Hospital in Dakar, Universite Cheikh Anta Diop de Dakar.

Special sessions on scientific publication writing

The two sessions on scientific publication writing will provide an editor's perspective and tips to help researchers publish their studies. The presentations will also be of interest to those who fund research and other stakeholders who are keen to facilitate publication. Both sessions will use regional examples and include time for questions. The first session provides a solid grounding for the second session, but is not a pre-requisite for attending the second session, as each presentation is independent of the other.

Writing for publication I

Tuesday, 11 October, 08:00–09:00
Conference room 5

How research is planned influences the way it is written, and ultimately, the manuscript's acceptance for publication. This presentation describes how reporting guidelines can inform the structure of scientific writing. Study registration and publication ethics will also be discussed. By the end of the session, delegates will be able to select an appropriate reporting guideline and use it to strengthen the presentation of their manuscript.

Writing for publication II

Wednesday, 12 October, 08:00–09:00
Conference room 5

Understanding what editors look for in manuscript submissions may increase your chance of publication in a preferred journal. This presentation describes the process of manuscript selection at *The Lancet* and the importance of the cover letter and abstract. Revisions, rejections, and appeals will also be discussed. By the end of the session, delegates will be able to write a more effective cover letter and know how to structure an abstract in a way that best communicates their study.
The sessions will be facilitated by Dr William (Bill) Summerskill, a senior executive editor at *The Lancet* where he oversees the journal's clinical trials strategy, protocol submissions, and research content. His clinical background is in primary care. Bill is a senior fellow of the Centre for Evidence-based Medicine at Oxford University and collaborates with several academic centres and international organisations. Among these are groups to improve the quality of design and reporting for meta-analyses and randomised controlled trials – and to enhance their relevance to users in developing countries.

Poster presentations

Some abstracts have been selected for presentations in large poster format. The poster presentations will cover a wide range of research topics on HIV/AIDS, tuberculosis and malaria, as well as cross-cutting issues such as health research networking and capacity building including ethics and regulatory affairs. Posters will be displayed all days of the Forum in the exhibition area in the ground floor from 8:00–17:40. The authors will stand by their posters on each day to answer questions and provide further information on their study results. See the Programme at a glance to find out more about the times for poster presentation.

EDCTP awards
to outstanding Junior and Senior African scientists

These awards funded by EDCTP will recognise outstanding Africans scientists working on HIV/AIDS, tuberculosis and malaria. The awards consist of certificates of recognition together with a cash prize of for one junior scientist (less than 30 years old) and one senior scientist. These awards are aimed at fostering the research activities of the winners.

The prizes will be awarded on **Wednesday 12 October** after plenary session IV.

Sunday 9 October 2011

15:00–17:00 **Registration**
[LOBBY]

14:00–16:00 **Satellite meeting**
Professional recognition, career development and training for clinical trial investigators and staff
[CONFERENCE ROOM 3]

17:00–18:20 **Official opening addresses**
[CONFERENCE ROOM 1]

18:20–20:30 Welcome reception
[BANQUET ROOM]

OFFICIAL OPENING ADDRESS

Brief statements

17.00–18.20

Conference room 1

17:00–17:10

Welcome address

Prof. Charles Mgone • EDCTP Executive Director

17:10–17:20

Dr Pascoal Mocumbi • EDCTP High Representative

17:20–17:35

Hon. Koen Vervaeke • Head of Delegation, EU delegation to the Africa Union

17:35–17:50

Hon. Dr Tewodros Adhanom • Minister for Health, Republic of Ethiopia

17:50–18:05

Mr. Robert-Jan Smits • Director General, DG Research and Innovation, European Commission

18:05–18:20

Hon. Jean Ping • African Union Commission Chairperson

Monday 10 October 2011

08:00–09:00 **Registration**
[LOBBY]

09:00–10:30 **Plenary session I**
Forum prologue
[CONFERENCE ROOM 1]

10:30–11:00 Coffee / Tea break

11:00–12:00 **Parallel sessions**
Clinical research achievements and findings in sub-Saharan Africa
HIV/AIDS [CONFERENCE ROOM 1]
Tuberculosis [CONFERENCE ROOM 3]
Malaria [CONFERENCE ROOM 5]

12:00–13:00
Poster presentations / Marketplace
[EXHIBITION AREA]

12:30–14:00 **Satellite meeting**
Medicines for Malaria Venture meeting on drug access
[DELEGATES LOUNGE]

13:00–14:00 Lunch

14:00–16:10 **Parallel session**
Clinical research achievements and findings in sub-Saharan Africa (cont.)
HIV/AIDS [CONFERENCE ROOM 1]
Tuberculosis [CONFERENCE ROOM 3]
Malaria [CONFERENCE ROOM 5]

16:10–16:40 Coffee / Tea break

16:15–17:30 **Satellite meeting**
Keeping the malaria medicine chest full: therapeutic options to treat malaria across the disease spectrum [CONFERENCE ROOM 3]
16:40–17:40
Poster presentations / Marketplace
[EXHIBITION AREA]

19:00–20:30 Conference dinner

PLENARY SESSION I
Forum prologue session
09.00–10.30
Conference room 1

CHAIRS
Ms Marja Esveld
Prof. John Gyapong

RAPPORTEUR
Mr Paul Chinnock

09:00–09:15

Prof. Hannah Akuffo • EDCTP General Assembly Chairperson

09:15–09:35

Mr Robert-Jan Smits • Director General, DG Research and Innovation, European Commission

09:35–09:55

H E Commissioner Jean-Pierre Ezin • African Union Commissioner of Human Resources, Science and Technology

09:55–10:10

Dr Luis Sambo • The World Health Organisation Regional Director for Africa

10:10–10:30
Introduction of the theme

Prof. Charles Mgone • EDCTP Executive Director

HO 01

11:00–11:15

HIV inhibitory antibodies elicited by heterogeneous HIV-DNA prime boosted with HIV-MVA vaccine in healthy Tanzanian volunteers

Agricola Joachim • Muhimbili University of Health and Allied Sciences (MUHAS), Dar es Salaam, Tanzania

Introduction | A phase I/II placebo-controlled HIV vaccine trial using multiclade, multigene HIV-1-DNA prime boosted with HIV-MVA vaccine was conducted among healthy volunteers in Dar es Salaam, Tanzania. Functional antibody responses were assessed in two assays.
Methods | The trial included 60 HIV-uninfected volunteers, randomised into groups of 20 volunteers who received placebo or 1 mg HIV-DNA intradermally or 3.8 mg intramuscularly. DNA plasmids containing HIV-1 gp160 subtypes A, B, C; rev B; p17/p24 gag A, B and Rtmut B were given at months 0, 1 and 3 using a needle-free Biojector device. Placebo or MVA expressing CRF01-AE HIV-1 env, gag, pol was administered intramuscularly by needle injection at months 9 and 21. Sera were tested four weeks post-second HIV-MVA boost using both TZM-bl pseudovirus and PBMC assays.
Results | While there was no neutralizing activity demonstrated in the TZM-bl assay using pseudoviruses from clades B, C and CRF01-AE, HIV inhibition was detected using a PBMC assay. The antibodies and a luciferase-expressing infectious molecular clone (IMC) remained in the assay for four days of culture. The response was highest against the clade CRF01-AE CM235-IMC (24/29, 83%), followed by SF162-IMC (72%) and BaL-IMC (31%) against clade B viruses. The responses were not significantly different between vaccinees that were primed with HIV-DNA intradermally versus intramuscularly.
Conclusion | HIV-DNA priming followed by two HIV-MVA boosts elicited strong HIV inhibitory antibodies in Tanzanian volunteers. The mechanism for the inhibitory activity in this PBMC assay remains to be defined and is currently under investigation.

CHAIRS
Prof. Nkandu Luo
Prof. Shabbar Jaffar

RAPPORTEURS
Dr Wendy Burger
Dr Pauline Mwinzi

HO 02

11:15–11:30

PedVACC 001 and 002: building foundations for infant HIV-1 vaccine trials against breast milk transmission of HIV-1

Tomáš Hanke • The Jenner Institute, University of Oxford, UK

Introduction | Over 60% of the global HIV-1-infected population lives in Africa and about half of the infected adults are women of childbearing age. Approximately half of mother-to-child transmission is due to breast-feeding, but formula feeding is not an option for many HIV-1 infected mothers. Antiretrovirals substantially decrease breast milk HIV-1 transmission. However, the development of a safe, effective, accessible vaccine is the ideal approach for protecting infants against HIV-1 from breastfeeding, infected mothers.
Methods | Two PedVacc infant HIV-1 vaccine trials examine the safety and immunogenicity of a novel HIV-1 vaccine, MVA.HIVA, in infants. The trials are taking place in The Gambia and Kenya and will randomise 120 healthy, HIV-negative infants born to healthy, either HIV-positive or HIV-negative mothers. Both trials entail a single injection of MVA.HIVA into the deltoid muscle of infants aged 20 weeks. HIV-1-positive women in this study are provided with antiretrovirals and feeding counselling during pregnancy and breastfeeding to reduce risk of HIV transmission to their infants. Half of the infants in the study are randomised to receive MVA.HIVA study vaccine in addition to their regular childhood immunizations. The other half receives their regular immunizations, but not the study vaccine, and serves as a control group.
Results | Initial MVA.HIVA vaccine safety and immunogenicity data will be presented.
Conclusion | The two PedVacc trials contribute to capacity building for infant vaccine trials in Africa and will provide insights on infant immunogenicity and vaccine interference. These trials represent the first stage towards a more complex heterologous prime-boost vaccine regimen.

HO 03

11:30–11:45

Therapeutic HIV-1 vaccination of untreated healthy HIV-1 positive individuals in the Republic of Guinea Bissau using HLA-supertype CTL epitope peptides in new CAF01 adjuvant: a phase 1 study

Anders Fomsgaard • Department of Virology, Statens Serum Institut, Copenhagen, Denmark

Introduction | Therapeutic vaccination is a novel prevention and treatment possibility for HIV/AIDS. Cellular immunity is important for control of viral load and disease progression. We tested a CTL based candidate HIV-1 vaccine in the Republic of Guinea Bissau (RGB) after its safety had been carefully assessed in Danish HIV-1 infected individuals and was approved by the ethical and health authorities of Denmark and RGB. The vaccine aims at directing immunity to conserved areas on HIV-1 infrequently targeted during the infection (subdominant epitopes).
Methods | The GMP produced and toxicology tested vaccine contains 3 CD4 Th epitopes and 15 CD8 CTL epitopes in CAF01 adjuvant. The CTL epitopes are conserved among different HIV-1 clades and their restriction match HLA tissue types in RGB and Denmark, based on HLA-supertypes. Following testing in Denmark, 20 healthy HIV-1 infected ART-naive individuals in Bissau (>18 years, CD4 >400, VL >1000) received the vaccine (15) or saline (5) intra-muscular week 0, 2, 4, 8 in a single-blinded placebo-controlled study. VL, CD4, and immune responses (IFN-γ ELISPOT) were measured before vaccination and at 2 weeks, 3 months and 6 months after.
Results | The vaccine was safe without vaccine related serious adverse events. The vaccine induced new immunity in 5 of 14 individuals. CD4 remained stable but with no sustained lowering of VL.
Conclusion | The first HIV-1 vaccine trial was successfully conducted in RGB. New immunity could be induced in 36% of patients albeit with little effect on VL. The capacity generated during this clinical trial will be sustained as we continue to produce additional HIV vaccine candidates.

CHAIRS
Prof. Nkandu Luo
Prof. Shabbar Jaffar

RAPPORTEURS
Dr Wendy Burger
Dr Pauline Mwinzi

HO 04

11:45–12:00

AFREVACC 001: feasibility and acceptability of an HIV vaccine trial among men in Johannesburg, South Africa

Sinead Delany-Moretlwe • Wits Reproductive Health & HIV Institute, University of the Witwatersrand, South Africa

Introduction | The African-European HIV Vaccine Development Network (AfrEVacc) 001 study is aims to assess the acceptability and feasibility of recruiting men into a future HIV vaccine trial in Johannesburg.
Methods | 284 consenting men aged 18 years or older were screened prior to enrolment into a prospective, randomised pilot study comparing immediate vaccination to deferred vaccination using the Hepatitis B vaccine as a surrogate HIV vaccine. Socio-demographic and medical history data were collected. Blood and urine samples were tested for HIV, HSV-2 and Hepatitis B (HB) serology, and bacterial STIs respectively. Risk factors for HB were assessed using logistic regression.
Results | Mean age was 30 years. The majority of men were South African-born (67%), single (81%), employed (54%) and perceived themselves to be in good health (87%). 40% reported >10 lifetime sexual partners, 32% had never used a condom in the last 3 months, and 36% were circumcised. 8% reported genital symptoms at screening, and 12% were found to have chlamydia while <3% had gonorrhoea or trichomoniasis respectively. HIV, HSV-2 and HB prevalences were 9%, 33% and 34%. HB was found to be associated with number of lifetime sexual partner and a history of STIs.
Conclusion | Enrolling high risk men into future HIV vaccine trials is feasible. Interventions to prevent HIV, HB and other STI are needed in this population.

TO 01

11:00–11:15

PanACEA: using brokering to develop a research agenda

Martin Boeree • Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands

Introduction | An EDCTP expert meeting for TB drug development (Dublin 2007) concluded that since funding for clinical trials was scarce and options limited, a brokered call would be most efficient a) to form a consortium with a portfolio free of political/commercial constraints; b) to develop a network of African trial centres large enough to host pivotal phase II and III trials; and c) to establish a drug development platform that would attract future product development projects.
Methods | A selection of research groups agreed upon the urgency of further trial studies of three drugs each aiming at the development of a shorter treatment regimen for tuberculosis: moxifloxacin (REMox study), high dose rifampicin (HIGHRIF study), and the new compound SQ 109.
Results | The PanACEA network encompasses 11 African institutions in 6 countries with capacity ranging from basic patient care to ICH-GCP compliant research. Upgrades and epidemiological studies are planned for several sites. By June 2011 REMox had randomised 1000 patients (out of required total of 1900). HIGHRIF started a dose-escalating study to explore the maximum dose and a second trial to study 10, 15 and 20 mg/kg. 50 patients were randomised. The 'right' dose of rifampicin will be established in the final trial. For SQ109 the first study completed enrolment of 90 patients in June 2011, a second trial will start in 2012.
Conclusion | PanACEA can fulfil a complementary role in the existing network of institutions to conduct TB clinical trials. It can respond to the need to try multiple drug regimens simultaneously.

CHAIRS
Dr Veronique Penlap
Prof. Martin Grobusch

RAPPORTEURS
Prof. Mark Hatherill
Dr Getnet Yimer

TO 02

11:15–11:30

An international multicentre controlled clinical trial to evaluate high dose rifapentine and a quinolone in the treatment of pulmonary tuberculosis (rifaquin)

Amina Jindani • Centre for Infection & Immunity, St. George's, University of London, UK

Introduction | Optimal cure rates of the standard 6 month regimen are not achieved under routine conditions due in part to duration. Adherence could also be improved if treatment in the continuation phase is administered once, or twice weekly. The long half-life of rifapentine (13 hours) suggests it could be given once weekly. Moxifloxacin is a candidate as companion drug with a half-life of about 14 h. This trial is of non-inferiority design; it assesses whether rifapentine and moxifloxacin in the continuation phase can reduce duration to 4 months and whether a 6 month regimen with a once weekly continuation phase is as effective as standard treatment. A second objective is to assess whether high dose rifapentine will eliminate acquired rifamycin monoresistance in relapsing HIV-positive patients.
Methods | New smear-positive patients randomised to either: Control Regimen: 2 months of daily ethambutol, isoniazid, rifampicin, and pyrazinamide followed by 4 months of daily isoniazid and rifampicin (2EHRZ/4HR). Study Regimen 1: 2 months of daily ethambutol, moxifloxacin, rifampicin, and pyrazinamide followed by 2 months of twice weekly moxifloxacin and rifapentine (2EMRZ/2P2M2). Study Regimen 2: 2 months of daily ethambutol, moxifloxacin, rifampicin, and pyrazinamide followed by 4 months of once weekly moxifloxacin and rifapentine (2EMRZ/4P1M1). The target is 1100 patients. Participating countries are Botswana, South Africa, Zambia and Zimbabwe.
Results | Recruitment began August 2008. At the end of May 2009, with 810 patients enrolled, 52 serious adverse events are reported, 9 due to drugs including 3 hepatic events. The Data Monitoring Committee has reviewed the results at regular intervals and has expressed no safety concerns.

TO 03

11:30–11:45

Plasma levels of tuberculosis drugs in TB patients in northern Tanzania

Charles Mtabho • Kilimanjaro Clinical Research Institute, Tanzania

Introduction | Although first line standard tuberculosis treatment with isoniazid, rifampicin, pyrazinamide and ethambutol can cure more than 95% of the patients infected with sensitive *M. tuberculosis*, cure rates are often lower. Pharmacokinetic variability may contribute to suboptimal response to tuberculosis drugs. As data on the pharmacokinetics of tuberculosis drugs in sub-Saharan Africa is limited, we conducted an observational pharmacokinetic study in Tanzania.
Methods | Twenty tuberculosis patients in the intensive phase of treatment were recruited. A full 24–hour pharmacokinetic curve was obtained at week three by measuring tuberculosis drug plasma levels before and at 1, 2, 3, 4, 6, 8, 10, and 24 hours after observed drug intake. Patients had breakfast half an hour after observed drug intake.
Results | The geometric mean C_{max} was 2.8 mg/L (range 1.0–4.6) for isoniazid (n=19; all other drugs n=20), 8.9 mg/L (range 5.9–14.8) for rifampicin, 38.2 mg/L (range 29.0–50.8) for pyrazinamide and 3.3 mg/L (range 2.2–5.8) for ethambutol. Ten patients (53%) had isoniazid peak plasma levels below the reference range (3–5 mg/L) and seven patients (35%) had rifampicin peak plasma level below the reference range (8–24 mg/L). Sex, age, body weight, body mass index, HIV status and malnutrition were not associated with low plasma levels of isoniazid or rifampicin.
Conclusion | Half of the patients had isoniazid peak plasma levels below reference levels and one third of patients had rifampicin peak plasma levels below reference levels. Individual variability, spaced food and drug intake, and question of compound stability before analysis need to be explored as possible culprits.

CHAIRS
Dr Veronique Penlap
Prof. Martin Grobusch

RAPPORTEURS
Prof. Mark Hatherill
Dr Getnet Yimer

TO 04

11:45–12:00

Optimization of TB and HIV co-treatment: pharmacokinetic and pharmacogenetic aspects of interaction between rifampicin and efavirenz (EFV)

Eleni Aklillu • Karolinska Institute, Stockholm, Sweden

Introduction | Rifampicin, potent inducer of CYP enzymes reduces plasma level of EFV by 22–26% and the appropriate daily dosage of EFV (600 *vs* 800mg/day) remains uncertain for use with rifampicin. We investigated the pharmacogenetic and pharmacokinetic interaction between efavirenz and rifampicin to identify whether there is a need for efavirenz dosage adjustment or not when administered with rifampicin.
Methods | A total of >800 treatment naive HIV patients without tuberculosis (arm-1) and TB-HIV co-infected patients (arm-2) were enrolled and followed for up to one year in Addis Ababa (Ethiopia) and Dar es Salaam (Tanzania). Efavirenz kinetics, pharmacogenetic analysis and safety/efficacy (VL and CD4 count) were recorded at different points in time and data were compared between the two arms and the two countries.
Results | Significant difference in genotype and efavirenz kinetics was found between patients from Ethiopia and Tanzania and its relevance for clinical outcome will be presented. Both CYP2B6 genotype and duration of therapy influence long-term efavirenz auto-induction in the absence of rifampicin. However in the presence of rifampicin, CYP2B6 genotype but not duration of efavirenz therapy is important. Effect of rifampicin on efavirenz kinetics is apparent during early therapy but has no significant effect in the long-term. Enzyme induction is pronounced mainly in patients with CYP2B6*1/*1 genotypes to cause sub therapeutic efavirenz plasma concentration.
Conclusion | We report for the first time CYP2B6 genotype dependent effect of rifampicin on long-term efavirenz auto-induction and disposition. The preliminary result indicates no need for efavirenz dosage adjustment during concomitant rifampicin based TB therapy.

MO 01

11:00–11:15

A head-to-head comparison of four artemisinin-based combinations for treating uncomplicated malaria in African children: a randomised trial

Umberto D'Alessandro • Institute of Tropical Medicine, Antwerp, Belgium

Introduction | Artemisinin combination therapies (ACTs) are the mainstay for the management of uncomplicated malaria cases. However, up-to-date data relevant for sub-Saharan countries in formulating appropriate antimalarial drug policies are scarce.
Methods | Between July 2007 and July 2009, a randomised, non-inferiority clinical trial was carried out in twelve sites in seven sub-Saharan countries. Each site compared three of four ACTs, namely amodiaquine-artesunate (ASAQ), dihydroartemisinin-piperaquine (DHAPQ), artemether-lumefantrine (AL) or chlorproguanil/dapsone and artesunate (CD+A).
Results | Overall, 4,116 children 6–59 months old with uncomplicated *P. falciparum* malaria were treated, actively followed up until day 28 and then passively for the next 6 months. At day 28, for the PCR adjusted efficacy, non-inferiority was established for three pair-wise comparisons: DHAPQ (97.3%) *vs* AL (95.5%); DHAPQ (97.6%) *vs* ASAQ (96.8%) and ASAQ (97.1%) *vs* AL (94.4%). For the PCR unadjusted efficacy, AL was significantly less efficacious than DHAPQ (72.7% *vs* 89.5%) and ASAQ (66.2% *vs* 80.4%), while DHAPQ (92.2%) had higher efficacy than ASAQ (80.8%) but non-inferiority could not be excluded. CD+A was significantly less efficacious than the other three treatments. Day 63 results were similar to those observed at day 28.
Conclusion | This large head-to-head comparison of most currently available ACTs in sub-Saharan Africa showed that AL, ASAQ and DHAPQ had excellent efficacy, up to day 63 post-treatment. The risk of recurrent infections was significantly lower for DHAPQ, followed by ASAQ and then AL. DHAPQ should be deployed on a large scale while ASAQ could be used in Eastern-Southern Africa.

CHAIRS
Prof. Alioune Dieye
Dr Sodiomon Sirima

RAPPORTEURS
Dr Pauline Byakika-Kibwika
Prof. Takafira Mduluza

MO 02

11:15–11:30

Clinical research capacity development: the experience of the West African Network for Clinical studies of Antimalarial drugs (WANECAM)

Abdoulaye Djimde, WANECAM Network • University of Bamako, Bamako, Mali

Introduction | Malaria is a major threat to public health and economic development in Africa. The goals of malaria control and elimination may never be achieved without strong involvement of those scientists who are directly affected by this terrible disease in their daily life.
Methods | With EDCTP's support, the West African Network for Clinical trials of Anti-malarial drugs was established with the participation of four West African countries (Burkina Faso, The Gambia, Guinea and Mali) and four European countries (France, Germany, Sweden and UK). The overall objective of this Network is the development of a West African sub-region equipped with state of the art clinical trial sites, laboratories, research teams and well characterized populations ready to undertake phases I–IV clinical trials for the development of new drugs.
Results | Infrastructure and capacity development, training, networking, a baseline epidemiological study and major steps towards the launch of longitudinal trials in the context of repetitive treatment with artesunate-pyronaridine and dihydroartemisinin-piperaquine are current achievements of the project.
Conclusion | Updates on these various activities will be presented.

MO 03

11:30–11:45

Co-administration of artemisinin-based combination therapies (ACTs) and antiretroviral (ARV) drugs: any evidence of adverse events or poor ACT pharmacokinetic profile?

Victor Mwapasa • College of Medicine, Community Health, Blantyre, Malawi

Introduction | The WHO recommends ACTs such as artemether-lumefantrine (AL), artesunate-amodiaquine (AS-AQ) and dihydroartemisinin-piperaquine (DHA-PPQ) for treating malaria. Because of geographic overlap between malaria and HIV infections, some HIV-infected patients on ARV drugs will require treatment with ACTs when infected with malaria. Yet, little is known about drug-drug interactions between ACTs and ARVs, which are partly metabolized by similar liver enzymes.
Methods | In an open label pharmacokinetic (PK) and safety clinical trial, half the adult doses AL, AS-AQ or DHA-PPQ were administered to otherwise healthy HIV-infected individuals receiving ARVs containing nevirapine (NVP, n=6), efavirenz (EFV, n=6) or protease-inhibitors (PIs, n=6) and those not on ARVs (controls, n=18). Participants were followed up for 28 days. Blood samples were collected at pre-determined intervals for PK assays using High Performance Liquid Chromatography (HPLC). We compared PK parameters (AUC, C_{max} and T_{max}) and occurrence of clinical and sub-clinical adverse events in participants taking ARVs plus ACTs and those taking ACTs only.
Results | By June 30th 2011, 66 participants were enrolled; 48 in the ACT plus ARV arms and 18 in the control (ACT only) arms. A total of 64 participants completed follow-up. Two serious adverse events (SAEs) occurred: one minor stroke in the DHA-PPQ plus NVP arm and one road traffic accident in the AS-AQ plus NVP arm. These participants have recovered fully. Full assessment of the relationship between the SAEs and the study drugs and comparisons of PK profiles are awaiting PK assays which are ongoing.
Conclusion | Preliminary assessment of safety of co-administration of ARVs and ACTs will be presented.

CHAIRS
Prof. Alioune Dieye
Dr Sodiomon Sirima

RAPPORTEURS
Dr Pauline Byakika-Kibwika
Prof. Takafira Mduluza

MO 04

11:45–12:00

Efavirenz significantly affects pharmacokinetic exposure of artemether-lumefantrine in HIV-infected Ugandan adults

Pauline Byakika-Kibwika • Infectious Diseases Institute, Makerere University, Kampala, Uganda

Introduction | Malaria and HIV are two major infectious diseases causing significant morbidity and mortality in sub-Saharan Africa. Treatment of malaria with artemether-lumefantrine (AL) in HIV-malaria co-infected individuals receiving antiretroviral therapy poses significant challenges. The non-nucleoside reverse transcriptase inhibitors efavirenz and nevirapine are substrates and potent inducers of cytochrome (CYP) enzymes 3A4 and 2B6. Induction of CYP3A4 and 2B6 enhances metabolism and may reduce plasma concentrations of co-administered substrates. We investigated drug-drug interactions between artemether-lumefantrine and efavirenz in HIV-infected Ugandan adults.
Methods | A cross-over study in which HIV-infected adults received standard 6-dose fixed combination AL 80/480mg before and at efavirenz steady-state. Artemether, dihydroartemisinin, lumefantrine and efavirenz plasma concentrations were measured.
Results | Pharmacokinetic exposure of artemether, dihydroartemisinin and lumefantrine was significantly reduced during co-administration of AL with efavirenz. Median (range) artemether maximum concentration (C_{max}) and area under the concentration-time curve (AUC) were 29 *vs* 12 ng/mL p<0.01 and 112 *vs* 25 h × ng/mL, p<0.01, dihydroartemisinin C_{max} and AUC were 123 *vs* 27 ng/mL, p<0.01 and 345 *vs* 86 h × ng/mL, p<0.01 and lumefantrine C_{max} and AUC were 8,737 *vs* 6,331 ng/mL, p=0.03 and 280,370 *vs* 124,381 h × ng/mL, p<0.01. Co-administration did not affect efavirenz exposure.
Conclusion | Co-administration of AL with efavirenz significantly reduces artemether, dihydroartemisinin, and lumefantrine pharmacokinetic exposure. Dosage modification of AL when co-administered with efavirenz is advised.

HO 05

14:00–14:15

Measuring adherence to antiretroviral therapy in northern Tanzania: feasibility and acceptability of the medication event monitoring system

Ramsey A. Lyimo • Kilimanjaro Clinical Research Institute, Kilimanjaro Christian Medical Center, Moshi, Tanzania

Introduction | An often used tool to measure adherence to antiretroviral therapy is the Medication Event Monitoring System, an electronic pill-cap that registers date and time of pill-bottle openings. Despite its strengths, data can be compromised by inaccurate use and acceptability problems due to its design. These barriers remain, however, to be investigated in resource-limited settings. We evaluated feasibility and acceptability of using the caps to monitor adherence among infected patients attending a rural clinic in Tanzania's Kilimanjaro Region.
Methods | Eligible patients were approached and asked to use the cap for three consecutive months. Thereafter, qualitative, in-depth interviews about its use of were conducted with the patients. Data were used to corroborate the interview results.
Results | 23 out of 24 patients approached agreed to participate. Apart from use on travel occasions, patients reported no barriers regarding use. Unexpectedly, the bottle design reduced the patients' fear for HIV-status disclosure. Patients indicated that having their behaviour monitored motivated them to adhere better. Data showed most patients had high levels of adherence and there were no bottle-openings not accounted for by medication intake. Non-adherence in the days prior to clinic visits was common due to the clinic dispensing too few pills.
Conclusion | Use of the cap was readily accepted by patients. Although the bottle was used accurately by most patients, patients need to be more explicitly instructed to continue use when travelling. Even HIV-clinics with sufficient staff and free medication may impose structural adherence barriers by supplying insufficient pills.

CHAIRS
Prof. Omu Anzala
Dr Rosemary Musonda

RAPPORTEURS
Dr Cissy Kityo Mutuluuza
Dr Wendy Burger

HO 06

14:15–14:30

Evaluation of HIV-1 viral load among mothers in a PTMCT programme with CD4 count above 350 cells/µL

Wendyam Marie Christelle Nadembèga • Promise-Pep ANRS 12174 study group, Ouagadougou, Burkina Faso

Introduction | Programs to prevent mother-to-child transmission of HIV (PMTCT) recommend a prophylactic antiretroviral regimen for women not eligible for highly active antiretroviral therapy (HAART), during pregnancy and one week post-partum. We determined the virological efficacy of this prophylaxis regimen in a non-research setting, by quantifying the HIV-1 viral load of mothers around delivery.
Methods | HIV-1 infected pregnant women at the 28th week of amenorrhoea and with CD4 count >350 cell/µL were screened for their upcoming baby to participate in a peri-infant prophylaxis trial (ANRS 12174), in Ouagadougou, Burkina Faso. Women received AZT alone during pregnancy, AZT+3TC+NVP at labour, AZT+3TC during one week after birth. Quantification of viral load was done 5–9 days after delivery using a real time PCR technique (Biocentric®/MiniOpticon).
Results | Among 114 women enrolled from August 2009 to February 2011, (mean age: 27.9 ± 5.3 years), the HIV-1 viral load was undetectable for 35 (30.7%) women, low (<5,000 copies/mL) for 66 (83.5%) women and moderate (5,000–30,000 copies/mL) for 13 (16.4%) women. No infant was HIV-1 infected at birth.
Conclusion | For pregnant women not eligible for HAART and managed by the national PMTCT programme, a simple regimen based mainly on AZT alone during pregnancy achieved a low or undetectable viral load soon after labour, which certainly explains the very low (or null) transmission rate in our sample. Although to be confirmed in a larger sample, the efficacy of this simple regimen, now well implemented in Burkina Faso, challenges the use of HAART as a prophylactic regimen for these women.

HO 07

14:30–14:45

Intrapartum single-dose carbamazepine shortens nevirapine elimination half-life and may reduce resistance

Eva Muro • Kilimanjaro Christian Medical College, Moshi, Tanzania

Introduction | WHO guidelines recommend zidovudine+lamivudine for seven days from labour onset in HIV-infected women receiving single-dose nevirapine to cover prolonged subtherapeutic nevirapine concentrations. Although effective, this is complicated and does not eliminate resistance; alternative strategies could add benefits.
Methods | Antiretroviral-naive, HIV-infected, pregnant women aged 18–40 years, with CD4 >200 cells/μL, able to regularly attend the antenatal clinics in Moshi, Tanzania were enrolled 1:1 by alternate allocation to receive 200mg single-dose nevirapine alone (sdNVP), or in combination with open-label 400mg single-dose carbamazepine (sdNVP/CBZ) at delivery. The co-primary outcomes were nevirapine plasma concentrations one week and nevirapine resistance mutations six weeks post-partum. Analyses were based on those still eligible at delivery.
Results | 97 women were assigned to sdNVP and 95 to sdNVP/CBZ during pregnancy, of which 75 sdNVP and 83sdNVP/CBZ were still eligible at delivery at study sites. The median (interquartile range) nevirapine plasma concentration was 1.55 (0.88–1.84) mg/L in sdNVP (n=61) and 1.40 (0.93–1.97) mg/L in sdNVP/CBZ (n=72) at delivery (p=0.91), but 1 week later was significantly lower in sdNVP/CBZ (n=63; 0.09 (0.05–0.20) mg/L) than in sdNVP (n=52; 0.20 (0.09–0.31) mg/L; ranksum: p=0.004) (GMR: 0.64, 95% CI: 0.43–0.96; p=0.03). Six weeks postpartum, nevirapine mutations were observed in 11/52 (21%) in sdNVP and 6/55 (11%) insdNVP/CBZ (odds ratio=0.46, 95% CI: 0.16–1.34; p=0.15).
Conclusion | Addition of sdNVP/CBZ at labor in HIV-infected, pregnant women did not affect nevirapine plasma concentration at delivery, but significantly reduced it one week postpartum, with a trend towards fewer nevirapine resistance mutations.

CHAIRS
Prof. Omu Anzala
Dr Rosemary Musonda

RAPPORTEURS
Dr Cissy Kityo Mutuluuza
Dr Wendy Burger

HO 08

14:45–15:00

Nevirapine-associated hepatotoxicity and rash among HIV-infected pregnant women in Kenya

Frank Angira • Kenya Medical Research Institute, Kisumu, Kenya

Introduction | Nevirapine use reportedly increases the risk of hepatotoxicity in women with a CD4 cell count >250 cells/μL.
Methods | From 2003–2006, we enrolled HIV-infected pregnant women who initiated either nevirapine-based or nelfinavir-based triple antiretroviral prophylaxis regimens at 34 weeks of gestation. Participants were evaluated for rash and serum alanine transferase (ALT) elevations at enrolment, then every 2 weeks until delivery, and at 2, 6, and 14 weeks, and 6 and 9 months postpartum. Using Fisher's exact test we evaluated for risk factors for incident severe hepatotoxicity and rash-associated hepatotoxicity.
Results | HIV-infected pregnant women (n=522) with a median CD4 cell count of 398 cells/μL initiated either nevirapine- or nelfinavir-based antiretroviral therapy. Overall, 14 (3%) women developed severe hepatotoxicity and 9 (2%) developed rash-associated hepatotoxicity. Among women who initiated nevirapine at any CD4 cell count (n=254), a baseline CD4 cell count ≥250 cells/μL was not associated with severe hepatotoxicity (5% *vs* 3%; p=0.52) or rash-associated hepatotoxicity (4% *vs* 3%; p=0.69) but the number of outcomes compared was limited. Among women with a CD4 cell count >250 cells/μL (n=402), women who initiated nevirapine had higher rates of severe hepatotoxicity (5% *vs* 1%; p=0.03) and rash-associated hepatotoxicity (4% *vs* 0%; p=0.003) compared with women who initiated nelfinavir.
Conclusion | Although nevirapine use was associated with hepatotoxicity, these events were infrequent and successfully managed. Our data support the continued use of nevirapine-based ART in pregnant women with a CD4 cell count >250 cells/μL.

HO 09

15:10–15:25

Efficacy and safety of immediate *vs* deferred initiation of HAART in TB/HIV co-infected patients with CD4 counts <200 cells/µL

Wondwossen Amogne Degu • Addis Ababa University, School of Medicine, Ethiopia

Introduction | The optimal timing for antiretrovirals in TB/HIV co-infected patients has not yet been clearly defined. This study aims to find out the optimal time to initiate efavirenz (EFV) based HAART in TB/HIV co-infected patients with baseline CD4 count less than 200 cells/µL.
Methods | This was an open-label, randomised clinical trial comparing efficacy and safety of EFV based ART initiated 1 week, 4 weeks and 8 weeks after initial anti-TB. The primary hypothesis was that initiation of HAART one week after anti-TB will reduce overall mortality at 24 weeks.
Results | A total of 512 patients were randomised, 170 at week 1 (arm 1), 196 at week 4 (arm 2) and 146 at week 8 (arm 3). They were followed for 9,468 person weeks. At initiation of ART the median CD4 count was 78 cells/µL (IQR 44–128) and median HIV RNA was 5.1 log 10 copies/mL (IQR 4.5–5.5). The overall incidence rate of mortality in arm 1 patients was 6 per 1000 person weeks (95% CI 3.7–9–7), in arm 2 was 3.4 per 1000 person weeks (95% CI 1.9–5.9) and in arm 3 was 3.8 cases per 1000 person weeks (95% CI 2.1–7). These differences are not significant with Kaplan-Meier's method for estimating survival considering all cause mortality as an end point (X2 Log rank=2.2, df=2, p=0.33). Incidence of TB-IRIS was significantly higher with arm 1 patients (X2 Log rank=11.9, df=2, p=0.002). There were no significant differences in the rate of AIDS defining illnesses, discontinuation of therapy because of drug induced liver injury or CD4 increase at 12 and 24 weeks.
Conclusion | In patients with TB/HIV co-infection and CD4 counts <200 cells/µL, initiation of ART one week after anti-TB therapy as compared to 4 and 8 weeks did not reduce overall mortality and the rate of ADI, albeit increased risk of TB-IRIS.

CHAIRS
Prof. Omu Anzala
Dr Rosemary Musonda

RAPPORTEURS
Dr Cissy Kityo Mutuluuza
Dr Wendy Burger

HO 10

15:25–15:40

High plasma efavirenz, slow NAT2 acetylators and ABCB1 genotype are associated with anti-tubercular and efavirenz-based ARV drugs induced liver injury in TB-HIV patients

Getnet Yimer • Department of Pharmacology, Medical Faculty, Addis Ababa University, Addis Ababa, Ethiopia

Introduction | Implication of pharmacogenetic variations and efavirenz pharmacokinetics with concomitant efavirenz based antiviral therapy and anti-tubercular drug induced liver injury (DILI) has not been yet studied. We performed a prospective case-control association study to identify the incidence, pharmacogenetic, pharmacokinetic and biochemical predictors for DILI in HIV/TB co-infected patients.
Methods | Newly diagnosed TB-HIV co-infected patients (n=297) were enrolled to receive efavirenz based ART and rifampicin based anti-TB therapy, and assessed clinically and biochemically for DILI up to 56 weeks. Quantification of plasma efavirenz and 8-hydroxyefaviernz levels and genotyping for NAT2, CYP2B6, CYP3A5, ABCB1, UGT2B7 and SLCO1B1 genes were done. The incidence of DILI and identification of predictors was evaluated using survival analysis and Cox Proportional Hazards Model.
Results | The incidence of DILI was 32.3% or 46.1 per 100 person-years. A statistically significant association was found between DILI and higher plasma efavirenz level (p=0.009), efavirenz/8-hydroxyefavirenz ratio (p=0.036), sex (p=0.001), baseline AST (p=0.022), ALT (p=0.014), haemoglobin (p=0.008), and serum albumin (p=0.007), NAT2 slow-acetylator genotype (p=0.039) and ABCB1 3435TT genotype (p=0.001) and CYP3A5*1 allele (p=0.041).
Conclusion | We report high incidence of anti-tubercular and antiretroviral DILI in Ethiopian patients. Between patient variability in systemic efavirenz exposure determines susceptibility to efavirenz induced liver injury in HIV patients. Close monitoring of plasma efavirenz level and liver enzymes during early therapy and/or genotyping practice in HIV clinics is recommended to optimize safety.

HO 11

15:40–15:55

Case definition for immune reconstitution inflammatory syndrome in HIV-schistosomiasis co-infected patients undergoing HAART

Pauline Mwinzi • Kenya Medical Research Institute, Kisumu, Kenya

Introduction | Immune reconstitution inflammatory syndrome (IRIS) is due to recovery of pathogen-specific immune responses to pre-existing or latent infections, associated with (HAART). IRIS is one of the most important early complications of HAART, specifically where other concomitant infections like helminths and schistosomiasis exist. To date there is no case definition for schistosoma-associated IRIS.
Methods | A study was conducted among fishermen occupationally exposed to *S. mansoni* in western Kenya to develop a case definition. Ultrasound examination, CD4+ count and viral load were evaluated at enrolment, 2 weeks, 1 month and 3 months post start of HAART and every time IRIS-related clinical developments were suspected. Medical records were reviewed for receipt, type of HAART, and response to therapy.
Results | Preliminary data show that schistosoma-associated IRIS in patients with HIV-*Schistosoma mansoni* co-infection develops generally within 3 months upon successful HAART characterized by overall steady increase in CD4+ T cells from 178.83 ± 106.07 cells/mL to 312.85 ± 127.48 cells/mL coupled with significant decrease in viral load log copies/L from 5.21 log copies/mL to undetectable levels (p=0.0001). Case definition specific to schistosoma-associated IRIS involves radiological examination showing worsening or emergence of hepato-splenomegaly and vein enlargement, with adequate adherence to successful HAART.
Conclusion | Upon successful HAART treatment, a proportion of patients with HIV/*Schistosoma mansoni* co-infection develops schistosoma-associated IRIS.

CHAIRS
Prof. Omu Anzala
Dr Rosemary Musonda

RAPPORTEURS
Dr Cissy Kityo Mutuluuza
Dr Wendy Burger

HO 12

15:55–16:10

Immune reconstitution inflammatory syndrome among HIV/AIDS patients during highly active antiretroviral therapy in Addis Ababa, Ethiopia

Kahsay Huruy Ghezehegn • College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia

Introduction | Suppression of viral replication is followed by increases in CD4+ lymphocytes, and this has been shown to result in decreased susceptibility to opportunistic infections after initiation of highly active antiretroviral therapy (HAART). However, clinical aggravations after the initiation of HAART have been thought a consequence of the restored ability to mount an inflammatory response: the immune reconstitution inflammatory syndrome (IRIS). The degree of IRIS observed in HIV-infected patients following initiation of HAART is variable.

Methods | A prospective study was conducted to determine the proportion of IRIS and the pattern of opportunistic infections among 186 HIV/AIDS patients receiving HAART at Zewditu Memorial Hospital, Addis Ababa, Ethiopia, between December 2006 and July 2007.

Results | The proportion of IRIS was 17.2% (32/186). The mean number of days of IRIS occurrence for each disease ranged from 26 to 122 days with a mean of 80. Opportunistic diseases associated with IRIS were tuberculosis (68.8%, 22/32), herpes zoster rash (12.5%, 4/32), cryptococcosis (9.4%, 3/32), toxoplasmosis (6.3%, 2/32) and bacterial pneumonia (3.1%, 1/32). Compared to baseline readings there were significant increases in CD4 count, aspartate aminotransferase and alanine aminotransferase levels while haemoglobin values decreased during the development of IRIS.

Conclusion | The proportion of IRIS and the pattern of opportunistic infections in HAART-treated patients in Ethiopia mirrored those reported in other countries. Further prospective surveys on epidemiological, immunological, microbial and clinical studies are needed to assess the proportion and pattern of IRIS and the effect of HAART in Ethiopia.

TO 05

14:00–14:15

Comparison of yield in sputum smear microscopy from specimens collected at different times in the diagnosis of pulmonary tuberculosis

Samuel Kudzawu • Korle-Bu Teaching Hospital, Accra, Ghana

Introduction | Cardinal symptoms of pulmonary tuberculosis present at night, coupled with less efficient mucosal ciliary's clearance of mucus in the bronchial tree makes a midnight sputum specimen yield more than a spot sputum specimen and equals an early morning one if not more. Inclusion of midnight specimen in the diagnosis of pulmonary tuberculosis can increase the chances of early diagnosis in some spot specimen negative cases.
Methods | Data from the sputum smear microscopy results of 257 smear-positives cases diagnosed with three specimens collected at midnight, early morning and spot was analysed.
Results | Of the spot specimens, 17% were negative, 12% scanty, 28% plus one, 16% plus two and 17% plus three. 10% did not produce spot specimens. The early morning and the midnight specimens yielded 5% each for negative, 14% and 12% for scanty, 29% and 43% for plus one, 26% and 20% for plus two and 26% and 28% for plus three respectively. All were able to produce early morning specimen and 0.5% did not produce midnight specimen.
Conclusion | Data available suggests that midnight sputum specimens yield more than early morning with the spot having the least yield. There is enough evidence to prove that the early morning specimen yields more than the spot but no such study on midnight specimen was available. There is a need for a standardized study in this direction to increase case detection rates.

CHAIRS
Dr Hulda Swai
Prof. Tumani Corrah

RAPPORTEURS
Prof. Mark Hatherill
Dr Getnet Yimer

TO 06

14:15–14:30

Optimal number of samples required to diagnose tuberculosis by sputum culture among HIV-infected smear-negative TB suspects in Kampala, Uganda

Willy Ssengooba • Makerere University, Infectious Disease Institutes, Kampala, Uganda

Introduction | The World Health Organization recommended sputum culture among smear-negative HIV-infected TB suspects. However, the number of samples to be examined is still unspecified. We set to determine the optimal number of sputum samples required to diagnose TB among HIV-infected smear-negative suspects by culture.
Methods | In this cross sectional study, we examined sputum samples (spot-Morning-spot) provided by participants in two days each providing not more than three samples. We determined the prevalence and the incremental yield (IY) of TB cases from serial sputum cultures and the reciprocal of the product of the fractions gave the number of sputum samples needed to find one additional TB case.
Results | Out of 170 participants, 52 (30.6%) by the first, 35 (20.6%) by the second and 19 (11.2%) by the third sputum sample culture were TB cases. The IY of the second and third sputum culture was 12.7% and 6.8% by Lowenstein Jensen (LJ), 23.6% and 7.5% by Liquid (MGIT), 12.6% and 7.3% by MGIT plus LJ culture methods respectively. The number of samples needed to find one additional TB case and their 95% CI by the second and third sputum culture were 29.9 (16.6–156.5) and 55.6 (26.4–500.4) by LJ, 11.3 (7.6–21.9) and 35.7 (19.0–313.8) by MGIT and 20.8 (12.5–62.7) and 36.1 (19.1–330.9) by MGIT plus LJ culture methods respectively.
Conclusion | Among HIV-infected smear-negative TB suspects in Kampala Uganda, two sputum samples are optimal for TB diagnosis by culture.

TO 07

14:30–14:45

Comparison of performance between Ziehl Neelsen (ZN) microscopy and the Xpert MTB/RIF assay in detection of *M. tuberculosis* in sputum at KEMRI/CDC TB lab

Albert Okumu • KEMRI/CDC Research and Public Health Collaboration, Kenya

Introduction | Tuberculosis (TB) is a major public health threat in Kenya, with 100,000 new cases reported annually, and approximately 50–60% HIV-infected. Due to limited access to mycobacterial culture, TB diagnosis is usually based on sputum microscopy. However, this method is insensitive, especially in persons with HIV. Xpert MTB/RIF, an automated PCR-based assay, with high sensitivity and a turn-around time <2 hours, has the potential to revolutionize *Mtb* detection. We studied the added value of this test compared to ZN microscopy in people with HIV enrolled in a TB screening and diagnosis study in Nyanza province, Kenya.
Methods | Sputum specimens from Kisumu District Hospital patients with HIV were tested to compare diagnostic yield with ZN microscopy and Xpert MTB/RIF at KEMRI/CDC TB laboratory.
Results | From October 2010 to April 2011, 262 specimens were tested using both ZN microscopy and Xpert MTB/RIF. Of these, 34 (13%) were positive by Xpert MTB/RIF and 8 (3%) were positive by ZN microscopy. ZN microscopy identified only 8 of 34 (24%) positive specimens identified by Xpert MTB/RIF.
Conclusion | Xpert MTB/RIF more than quadrupled the yield of TB diagnostic testing in specimens from HIV-infected persons. Given the high mortality rate of undiagnosed TB in people with HIV, this could save many lives.

CHAIRS
Dr Hulda Swai
Prof. Tumani Corrah

RAPPORTEURS
Prof. Mark Hatherill
Dr Getnet Yimer

TO 08

14:45–15:00

Cycle-threshold (CT) values of an automated TB-specific PCR platform (Xpert Mtb/RIF) as a predictor of smear status and grade

Grant Theron • University of Cape Town, South Africa

Introduction | Infection control guidelines suggest precautionary measures be taken in smear-positive patients so as to minimise transmission. Xpert MTB/RIF is a new TB-specific molecular test endorsed by the World Health Organisation as a frontline test for individuals suspected of HIV-TB co-infection. Xpert MTB/RIF will be used to diagnose patients who have not undergone a test by smear microscopy. It is unclear how these patients should be handled within the context of existing infection control and contact tracing guidelines.
Methods | Here we present the performance of average CT values in 496 patients with suspected TB, alone or in combination with other demographic and clinical factors, for the detection of smear-positivity and, of those who are smear-positive individuals, the ones with the highest smear grade. This was evaluated using receiver operator characteristic (ROC) curve analysis. In an attempt to improve predictive outcomes, we also performed a multivariable regression analysis using clinical and chest radiographic data.
Results | (i) CT values have poor clinical utility as a rule-in test for smear positivity (sensitivity of 32.3% and specificity of 97.1% at a cut-point of ≤20.2) (ii) Xpert MTB/RIF had a moderately high rule-out value for smear positivity (NPV of 80.0% at a cut-point of >31.8) (iii) clinical and radiological determinants known to be associated with mycobacterial burden failed to improve the predictive ability (iv) average CT values correlated well with TTP, a validated surrogate of patient outcomes.
Conclusion | Our preliminary findings, which require confirmation in larger studies, indicate that Xpert MTB/RIF-generated average CT values of >31.8 provides moderately good rule-out value for smear positivity.

TO 09

15:10–15:25

High mortality risk among individuals assumed to be TB-negative can be predicted using a simple test

Paulo Rabna • Bandim Health Project, Indepth Network, Bissau, Guinea-Bissau

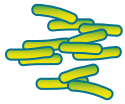
Introduction | Little is known about post-consultation mortality among individuals consulting hospitals with symptoms of TB, but with normal X-Ray and a negative TB sputum smear result. This prospective cohort study aimed to assess subsequent post-consultation mortality among these assumed TB-negative (aTBneg) individuals. Furthter, we wanted to investigate whether the level of plasma soluble urokinase plasminogen activator receptor (suPAR) can be used to identify presumed TB negative (pTBneg) individuals with a high mortality risk.
Methods | 1682 individuals with symptoms of TB were examined and 1007 of these were pTBneg individuals. To compare their mortality with the mortality in the general population, 4983 age-matched controls were followed. Plasma suPAR levels were measured using the suPARnostic ELISA (ViroGates, Denmark).
Results | The mortality was 12 per 100 person-year-observation (PYO) among pTBneg individuals compared to 4 per 100 PYO in the general population (mortality rate ratio=3.21 (95% CI 2.51–4.09)). SuPAR values ranged between 0.9 and 45 ng/mL. A log-linear relationship was found between suPAR and mortality in pTBneg individuals. A 1 ng/mL increase was associated with a 27% increase in the mortality rate, mortality rate ratio=1.27 (95% CI 1.21–1.33).
Conclusion | Our results showed an increased mortality among pTBneg individuals and demonstrate that suPAR carries very relevant prognostic information on mortality among these individuals. Measuring suPAR is a technically simple method for identifying individuals with a high post-consultation mortality risk among presumed TB negative individuals.

Reference: Trop Med Int Health, 2009 Sep; 14(9): 986–94

CHAIRS
Dr Hulda Swai
Prof. Tumani Corrah

RAPPORTEURS
Prof. Mark Hatherill
Dr Getnet Yimer

TO 10



15:25–15:40

Population structure of *M. africanum* and differences in ESAT-6 immunogenicity between different lineages

Florian Gehre • Medical Research Council, Fajara, The Gambia

Introduction | In contrast to *M. tuberculosis*, *M. africanum* was previously shown to induce an attenuated host immune response, with only 63% of infected patients producing a positive ELISPOT result when stimulated with early secreted antigen target-6, ESAT-6 (De Jong *et al.*, 2006). We hypothesize that an underlying genetic component introduces variations in the ESAT-6 secretion machinery of the tested *M. africanum* isolates and renders certain sub-lineages less immunogenic for the host and therefore difficult to detect by ELISPOT assay.
Methods | In order to identify these sub-lineages we aim to establish the population structure of these *M. africanum* isolates using spoligo- and MIRU-VNTR-typing. Subsequently we will correlate this phylogeny with existing ESAT-6 ELISPOT data and classify distinct lineages according to their ESAT-6 immunogenicity.
Results | When analysing the spoligotype data of 137 *M. africanum* strains from patients who had an ELISPOT assay done at baseline, we identified several spoligotype patterns associated with an absent IFN-γ response to ESAT-6. As spoligotyping alone does not have the power to reliably identify respective *M. africanum* sub-lineages, we are completing MIRU-VNTR typing, a method with lower homoplasy, of these isolates, in order to build a proper population structure and identify lineages that may not secrete ESAT-6.
Conclusion | Identifying *M. africanum* lineages defective in the secretion of ESAT-6 and subsequently performing comparative genomics with isolates from lineages that are able to secrete ESAT-6, will not only shed light on composition and function of the secretion machinery of the major virulence factor ESAT-6 but also on the immunogenicity of mycobacteria in general.

TO 11

15:40–15:55

Development of a rapid serological screening test for tuberculosis

Carol Holm-Hansen • Norwegian Institute of Public Health, Oslo, Norway

Introduction | The diagnosis of tuberculosis (TB) is based on sputum smear microscopy and culture of *M. tuberculosis* (*Mtb*), methods that require laboratory facilities. A simple and rapid serological screening test for active TB that is suitable for use at the health post level in the developing world is urgently needed.
Methods | Blood and saliva samples were collected from patients with active TB and controls in Ethiopia, Tanzania, Sudan, South Africa, China and Vietnam. Relevant *Mtb* antigens were identified and different antigen mixes investigated by Bio-Plex using minute serum volumes. Antigen mixes were evaluated for sensitivity and specificity. The most suitable antigen mix will be transferred to a rapid lateral flow platform and evaluated in the field.
Results | A promising combination of 5 antigens has been identified and an ELISA prototype developed. Correlation between Bio-Plex and ELISA is good. The prototype test has a sensitivity of 70% among persons with active TB and a specificity of 95% among community controls. Technology transfer to a serum-based rapid platform is ongoing. Antigen reactivity in saliva is currently under investigation.
Conclusion | A sensitive and specific screening test for active TB will reduce diagnostic delay and expedite referral and treatment. This will reduce the *Mtb* infectious pool, limit transmission and help curb the TB pandemic. Assay modification for use with non-invasive saliva samples will increase the suitability of the test for screening patients at the health post level.

CHAIRS
Dr Hulda Swai
Prof. Tumani Corrah

RAPPORTEURS
Prof. Mark Hatherill
Dr Getnet Yimer

TO 12

15:55–16:10

Distinct phases of changes in host gene expression reflect successful tuberculosis drug treatment

Hazel Dockrell • London School of Hygiene & Tropical Medicine, UK

Introduction | Accurate assessment of TB drug efficacy would facilitate clinical trials of new drugs, as currently the rate of relapse is measured in a 2-year follow-up period, leading to long and expensive trials. Infection with *M. tuberculosis* has a complex effect on the host immune system, and such changes can be detected in blood.
Methods | We assayed blood samples collected longitudinally from 27 pulmonary TB patients, recruited in Cape Town, through conventional tuberculosis treatment. All patients were successfully cured and remained disease-free in the 2 years that followed. We measured the expression of approximately 47,000 transcripts using Affymetrix U133 Plus 2.0 microarrays.
Results | Significant changes in expression of approximately 4,000 host genes occurred during the 6 months of treatment, with a dramatic down-regulation of around 1,000 genes occurring within the first week, likely reflecting the rapid action of isoniazid on actively-dividing bacilli. These early changes included a dampening of the inflammatory response, especially in C1q of the complement pathway. Later in treatment, changes in expression of different subsets of genes occurred, with a notable increase in B cell markers during the sterilising and disease-resolution phase of treatment. We are validating these findings in further samples, while investigating the roles of some of the other differentially expressed genes.
Conclusion | A test could be developed to determine novel TB drug efficacy, incorporating measurement of host gene expression, protein biomarkers and microbiological changes, to assist in decision-making and eventually clinical management.

MO 05

14:00–14:15

Assessment of the fixed-dose combination of artesunate mefloquine (ASMQ) as an alternative antimalarial treatment for children in Africa

Nathalie Strub-Wourgaft • Drugs for Neglected Diseases Initiative (DNDi), Geneva, Switzerland

Introduction | The combination of artesunate (AS) and mefloquine (MQ) has been a highly efficacious and safe treatment for uncomplicated *P. falciparum* malaria since 1992 in Latin America and Asia. The FACT Consortium led by the Drugs for Neglected Diseases initiative developed artesunate mefloquine fixed-dose combination (ASMQ FDC), a simple age-based treatment, easy to use, with one single daily dose of one or two tablets of ASMQ FDC for three days. This new treatment, registered in Brazil in 2008, could play a significant role in delaying the emergence of resistance to artemisinin.
Methods | With the support of EDCTP, a phase IV multicentre clinical study is being conducted in Africa to compare the efficacy and safety of ASMQ FDC with artemether-lumefantrine (Coartem®) in children under five with uncomplicated *P. falciparum* malaria. The project takes place in Burkina Faso, Kenya and Tanzania in collaboration with CNRFP (Burkina Faso), KEMRI (Kenya), NIMR (Tanzania), CRP-Santé (Luxembourg), CHUV (Switzerland) and Cardinal Systems (France). 940 children are expected to be enrolled in the study and will be followed up over 63 days.
Results | The inclusions started in December 2010 for Burkina Faso and in July 2011 for Tanzania and Kenya. As of August 2011, 186 children were enrolled. No major safety problems have been encountered.
Conclusion | The results of this study will provide information to consider ASMQ as a safe and efficacious alternative treatment for children in Africa.

CHAIRS
Dr Modest Mulenga
Prof. Robert Sauerwein

RAPPORTEURS
Dr Pauline Byakika-Kibwika
Prof. Takafira Mduluza

MO 06

14:15–14:30

Safety and efficacy of dihydroartemisinin-piperaquine *vs* artemether-lumefantrine in the treatment of uncomplicated *P. falciparum* malaria in Zambian children

Michael Nambozi • Department of Clinical Sciences, Tropical Disease Research Centre, Ndola, Zambia

Introduction | Malaria in Zambia remains a public health and developmental challenge, affecting mostly children under five and pregnant women. In 2002, the first-line treatment for uncomplicated malaria was changed to artemether-lumefantrine (AL) which has proved to be highly efficacious against multidrug resistant *P. falciparum*.
Methods | In order to determine whether dihydroartemisinin-piperaquine (DHA/PQP) had similar efficacy, safety and tolerability as AL for the treatment of children with uncomplicated *P. falciparum* malaria, 304 children (6–59 months old) with uncomplicated *P. falciparum* malaria were enrolled, randomised to AL (101) or DHA/PQP (203) and followed up for 42 days in Ndola, Zambia, between 2005 and 2006.
Results | No early treatment failure was observed. At day 28, PCR-uncorrected ACPR was 92% in the DHA/PQP and 74% in the AL arm (OR: 4.05; 95% CI: 1.89–8.74; p<0.001). Similar results were observed for day 42, i.e. higher PCR-uncorrected ACPR for DHA/PQP, mainly due to the difference observed up to day 28, while the PCR-corrected ACPR was similar: DHA/PQP: 93% (179/192), AL: 93% (84/90), (OR: 0.92; 95% CI: 0.30–2.64; p=0.85). Except for cough, more frequent in the DHA/PQP arm (p=0.04), there were no differences between treatment arms in the occurrence of adverse events.
Conclusion | DHA/PQP was as efficacious, safe and well tolerated in treatment of uncomplicated malaria as AL, though in the latter group more new infections during the follow-up were observed.

Reference: Malaria J 2011, 10:50.

MO 07

14:30–14:45

Burden of malaria in HIV-positive pregnant women in Ibadan, Southwest Nigeria

Catherine Falade • Department of Pharmacology & Therapeutics, University of Ibadan, Ibadan, Nigeria

Introduction | Pregnancy and HIV infection each increase susceptibility to malaria and HIV-positive pregnant women suffer a double burden.
Methods | The prevalence of malaria parasitaemia was evaluated at booking by microscopy of Geimsa stained thick blood smear among HIV-positive and HIV-negative women at the PEPFAR and antenatal clinics of a tertiary Hospital in Ibadan (Nigeria) between July 2009 and June 2010.
Results | Malaria parasitaemia was significantly more prevalent ($p<0.0001$) among HIV-positive women (13.7% (56/408)) than HIV-negative women (5.9% (24/406)). The geometric parasite density was also significantly higher among HIV-positive women (962 *vs* 340). Mean haematocrit was significantly lower ($p<0.0001$) among HIV-positive women compared with HIV-negative women whether parasitaemic (28.89 ± 4.15 *vs* 32.45 ± 4.18) or free of malaria parasite ($31.19\% \pm 4.35$ *vs* $34.40\% \pm 3.75$). Opportunistic infection chemoprophylaxis or antiretroviral therapy did not significantly influence the prevalence of malaria parasitaemia. HIV-negative women booked significantly earlier than the HIV-positive women (20.16 ± 7.45 week *vs* 22.52 ± 8.78 weeks; $p<0.0001$). All socio-economic indicators for the women and their spouses (level of education, occupation, type of wall in accommodation, type of toilet facility, type of portable water and ownership of various gadgets) were significantly ($p<0.0001$) lower among HIV-positive women.
Conclusion | Malaria imposes a significant burden on HIV-positive women in southwest Nigeria. These findings underscore the need for adequate malaria control measures (IPTp, ITN, IRS and prompt case management) specifically targeted at HIV-positive women.

CHAIRS
Dr Modest Mulenga
Prof. Robert Sauerwein

RAPPORTEURS
Dr Pauline Byakika-Kibwika
Prof. Takafira Mduluza

MO 08

14:45–15:00

Different approaches for delivery of intermittent preventive treatment with sulfadoxine pyrimethamine (IPTp/Sp) to pregnant women in Burkina Faso

Alphonse Ouédraogo • Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso.

Introduction | In many sub-Saharan countries, IPTp/SP is being adopted to replace chloroquine chemoprophylaxis shown to be inefficacious. The new strategy is being implemented but no delivery approach was defined. IPTp/SP is only delivered to pregnant women presenting at clinics. Weak health services may limit the effectiveness of this strategy. In this study, we compare three approaches of IPTp/SP delivery in terms of improving coverage and compliance. These approaches are: passive health centre services, extended delivery outreach services and community based distribution.
Methods | It is an open randomised, controlled clustered trial, conducted in the district of Saponé. Each community clinic and its catchment areas were considered as a cluster. Clusters were also randomly assigned to intervention and control arms. Two cross sectional surveys were planned to measure key outcome indicators at the beginning and at the end of the trial. Clinical & biological data were collected.
Results | The mean coverage of any dose of IPT is higher in the community based arm than in the control group (33% *vs* 24%; p<0.001). The compliance was better in the control group than in intervention groups (p=0.001). After the intervention, there was a decrease of peripheral parasitaemia from 32.2% for health units to 25.9% for the community based approach (p=0.03). There was also a slight decrease of anaemia: 68.1% for the outreach distribution approach compared to 81.5% (p=0.01) for health units.
Conclusion | A combination of health facility-based and community-based approaches might be needed to maximise the impact of IPTp.

MO 09

15:10–15:25

Intermittent preventive therapy post-discharge (IPTpd) to prevent rebound severe malaria anaemia in young children

Kamija Phiri • College of Medicine, Blantyre, Malawi

Introduction | Severe malarial anaemia requiring blood transfusion is a major cause of in-hospital childhood morbidity and mortality in sub-Saharan Africa. Previous follow-up studies from high malaria transmission areas in southern Malawi and western Kenya have shown that children with severe malarial anaemia that had blood transfusion are also at high risk of dying after discharge from the hospital. We hypothesized that failure to clear the initial malaria infection due to ineffective antimalarial treatment and the acquisition of new infections after discharge, negate the initial improvements in haemoglobin concentrations that result from the blood transfusion. The study aimed to compare the efficacy of a single treatment course with lumefantrine-artemether (Coartem®) at discharge to three treatment courses with Coartem® given at discharge, 1 and 2 months (IPTpd) in the post-discharge management of children who have recovered from severe malarial anaemia.
Methods | This was a randomised double-blind placebo controlled trial in which children aged between 4–59 months were randomised to receive IPTpd with Coartem® or with placebo. Children were followed up for a period of 6 months with the primary efficacy endpoint being the incidence of recurrent severe anaemia or death.
Results | A total of 1402 children were recruited and randomised from 4 sites in Malawi. There was effect modification by HIV status and age. Among children who were HIV negative and <3 years of age, death/severe anaemia/severe malaria was reduced by 32% (CI 5–51%) and uncomplicated malaria by 25% (CI 11–37%).
Conclusion | This study shows that IPTpd can drastically reduce post-discharge morbidity and mortality. It is important to start considering the challenges of the implementation of this intervention in our present health delivery systems.

CHAIRS
Dr Modest Mulenga
Prof. Robert Sauerwein

RAPPORTEURS
Dr Pauline Byakika-Kibwika
Prof. Takafira Mduluza

MO 10

15:25–15:40

A simplified artesunate regimen for severe malaria in children

Peter G. Kremsner • Universitätsklinikum Tübingen, Institut für Tropenmedizin, Tübingen, Germany

Introduction | Despite decades of experience with artesunate in the treatment of severe malaria, the currently recommended parenteral dosing regimen is empirically derived. We conducted a randomised trial comparing the conventional with a newer simplified regimen for parenteral artesunate in severe malaria.
Methods | In a randomised, double-blind and placebo controlled trial, the conventional 5–dose regimen of intravenous artesunate was compared with a simplified 3-dose regimen in African children. The patients aged 6 m–12 years were hospitalised with *P. falciparum* malaria and received a total dose of 12 mg/kg cGMP artesunate. As primary endpoint, the proportion of children who had cleared at least 99% of their admission parasitaemia at 24 h has been assessed. Safety data, secondary efficacy endpoints and pharmacokinetics were also analysed.
Results | In the 'per protocol' population of 171 children, 78% of the recipients (95% CI:69–87%) in the 3–dose group achieved at least 99% parasite clearance 24 hours after the start of treatment compared with 85% of the recipients (95% CI:77–93%) receiving the 5–dose regimen. The number of (serious) adverse effects was comparable in both groups and not considered drug-related. Pharmacokinetics of artesunate was dose independent, whereas a slightly slower clearance of dihydroartemisinin was observed in children receiving the higher dose of 4 mg/kg of the 3–dose regimen.
Conclusion | Our phase II study addresses the use of a 3–day, once daily dosing regimen for intravenous artesunate in African children hospitalized for severe malaria. This 3–dose regimen is now studied further in a dose-optimization trial, including the intramuscular administration route, with the aim to establish a simplified treatment of severe malaria.

MO 11

15:40–15:55

FEAST (Fluid Expansion as Supportive Therapy) trial: mortality after fluid bolus in African children

Peter Olupot-Olupot • Mbale Regional Referral Hospital, Mbale, Uganda

Introduction | The role of fluid resuscitation for children with shock and life-threatening infections is not established and was investigated in FEAST in Uganda, Kenya, and Tanzania.
Methods | Children aged >60 days with severe febrile illness and impaired perfusion were randomised to 20–40 mL/kg boluses of 5% albumin (albumin-bolus) or 0.9% saline (saline-bolus) or no bolus (control) at hospital admission (Stratum A). Severely hypotensive children were randomised to bolus arms only (Stratum B). Primary endpoint was 48-hour mortality.
Results | The Data Monitoring Committee recommended halting recruitment in Stratum A after 3141/3600 children enrolled. Arms were well-matched for clinical severity or malaria-status (57%) at baseline. 48-hour mortality was 111/1050 (10.6%), 110/1047(10.5%) and 76/1044 (7.3%) in albumin-bolus, saline-bolus and control arms respectively. Relative risk (CI 95%) saline-bolus versus control 1.44 (1.09–1.90, p=0.01); albumin-bolus versus saline-bolus 1.01 (0.78–1.29, p=0.96); any bolus versus control 1.45 (1.13–1.86, p=0.003). Most (87%) fatalities occurred before 24 hours. However, few developed the predicted severe adverse effects of fluid overload. In Stratum B, 9/13 (69%) albumin-bolus and 9/16 (56%) saline-bolus died, (RR 1.23(0.70–2.16), p=0.45)). Mortality patterns were consistent across centres and subgroups: malaria, coma, sepsis, acidosis, severe anaemia, shock severity.
Conclusion | Albumin or saline boluses increased 48-hour mortality by 3.3% (absolute risk) in critically ill African children and cannot be recommended in resource-limited settings. The FEAST trial results challenge the primacy of bolus resuscitation as a life-saving intervention in non-hypotensive paediatric shock in resource-limited settings, and raise questions on fluid resuscitation elsewhere.

Reference: N Engl J Med. 2011; 364(26):2483–95.

CHAIRS
Dr Modest Mulenga
Prof. Robert Sauerwein

RAPPORTEURS
Dr Pauline Byakika-Kibwika
Prof. Takafira Mduluza

MO 12

15:55–16:10

Rare clinical features on malaria in children in eastern Uganda

Judith Atiang • Mbale Regional Referral Hospital, Mbale, Uganda

Introduction | Malaria remains the number one killer of children in Uganda. There has been some description of the clinical spectrum of malaria elsewhere in sub-Saharan Africa, but the features of malaria in Mbale subregion in Uganda remain rare, even in the current literature on childhood severe malaria. Many of the children that we see with severe malaria present with blackwater fever. We conducted a descriptive pilot study to understand the burden and the clinical features of malaria in children in this region.
Methods | Prospective survey of severe malaria with blackwater fever as done among children presenting to the acute care unit of the hospital. All with a positive blood smear for malaria parasites and with no known toxic effects to drugs, underwent treatment with *i.v.* quinine.
Results | All the 5 patients showed improvement after 2 days of treatment . Their vital and clinical signs gradually stabilized ending in a good survival outcome.
Conclusion | This unique presentation, notably of macroscopic haemoglobinuria and jaundice are features that are uncommon in the current literature of severe malaria in children. This also became an eye-opener for a long-standing prospective study on aetiopathogenesis of dark urine in children led by Dr Peter Olupot-Olupot.

Tuesday 11 October 2011

08:00–09:00 **Special sessions**
Grant writing for scientists
[CONFERENCE ROOM 3]
Scientific publication writing for scientists
[CONFERENCE ROOM 5]

09:00–10:30 **Plenary session II**
Recent advances in HIV/AIDS, tuberculosis and malaria [CONFERENCE ROOM 1]

10:30–11:00 Coffee / Tea break

11:00–12:00 **Parallel sessions**
Developing scientific research capacity in sub-Saharan Africa
HIV/AIDS [CONFERENCE ROOM 1]
Tuberculosis [CONFERENCE ROOM 3]
Malaria [CONFERENCE ROOM 5]
11:00–13:00
Cross-cutting: EDCTP-NACCAP
[CONFERENCE ROOM 6]

12:00–13:00
Poster presentations / Marketplace
[EXHIBITION AREA]

12:30–14:00 **Satellite meeting**
Clinical trials in practice: how to achieve the best protection of the study subjects?
[DELEGATES LOUNGE]

13:00–14:00 Lunch

14:00–16:10 **Parallel sessions**
Developing scientific research capacity in sub-Saharan Africa (cont.)
HIV/AIDS [CONFERENCE ROOM 1]
Tuberculosis [CONFERENCE ROOM 3]
Malaria [CONFERENCE ROOM 5]
Cross-cutting: EDCTP-NACCAP
[CONFERENCE ROOM 6]

16:10–16:40 Coffee / Tea break

16:40–17:40
Poster presentations / Marketplace
[EXHIBITION AREA]

PLENARY SESSION II

Recent advances on HIV/AIDS, tuberculosis and malaria (keynote addresses)

09:00–10:30

Conference room 1

CHAIRS

Prof. Alioune Dieye

Prof. Eric Sandström

RAPPORTEUR

Mr Paul Chinnock

09:00–09:30

HIV/AIDS

Prof. Elly Katabira, Makerere University, Uganda

09:30–10:00

Tuberculosis

Dr Abraham Aseffa, Armauer Hansen Research Institute, Ethiopia

10:00–10:30

Malaria

Prof. Robert Sauerwein, University Medical Center St Radboud, Nijmegen, The Netherlands

HO 13

11:00–11:15

Behavioural determinants for HIV incident infections in a fishing population being prepared for future HIV prevention research

Gershim Asiki • MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

Introduction | Fisher folk are among the most-at-risk populations but also hard to reach for HIV prevention. In preparation for future prevention research a cohort of HIV-uninfected adults was established in 5 fishing communities along shores of Lake Victoria, Uganda. We report behavioural determinants for HIV incident infections identified during the follow-up of this cohort.
Methods | Between February-August 2009, we screened 2,074 and enrolled 1,000 HIV at-risk uninfected adults (46% women) aged 13–49 years. At-risk for HIV infection was defined as a self-report of: unprotected sex with ≥1 sex partner, STIs, knowledge of HIV-positive partner, and being away from home for ≥2 nights per month. HIV risk assessment and testing were repeated 6 monthly, and syphilis testing 12 monthly for 18 months. Risk reduction counselling and condoms were provided at every visit, and STI treatment when indicated. Cox regression was used to explore risk factors for HIV infection.
Results | A total of 59 HIV incident cases were identified during 1207 person years of observation (pyo). Overall incidence rate was 4.9 per 100 person year at risk (men 5.2, women 4.5; p=0.09). Using multivariate analysis, having sex under influence of alcohol RR (95% CI); 4.0 (1.8– 8.6), weekly alcohol consumption 5.4 (1.9–14.8), mobility 2.5 (1.1–5.5) and living <5 years in a fishing village 7.3 (1.6–33.8) were significantly associated with sero-conversion.
Conclusion | Our study shows that fisher folk may be a suitable population for conducting efficacy trials as supported by their high risk behaviour and high HIV incidence.

CHAIRS
Prof. Nkandu Luo
Prof. Shabbar Jaffar

RAPPORTEURS
Dr Pauline Mwinzi
Dr Jonathan Kayondo

HO 14

11:15–11:30

Transmission clusters and evidence of HIV-1 transmitted drug resistance among recently infected ART-naive individuals from Ugandan fishing communities of Lake Victoria

Jamirah Nazziwa • MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

Introduction | HIV-1 prevalence and incidence in the fishing communities on the Lake Victoria shores in Uganda are high (28.8% and 4.9% respectively). This population may play a major role in driving the HIV epidemic in Uganda including the spread of transmitted drug resistance (TDR). We report data on TDR in this population among ART-naïve recently infected individuals.
Methods | Using blood specimens from a cohort of 1000 originally HIV-negative individuals, population sequencing of the pol gene (protease/reverse transcriptase) was performed on plasma derived virus from all 51 volunteers who sero-converted over a period of 2 years. Drug resistance mutations (DRMs) were scored using the 2009 WHO list for surveillance of TDR. TDR prevalence categories were estimated using the WHO -recommended truncated sampling technique, and categorized as low (<5%), moderate (5–15%), or high (>15%) for each of the three drug classes.
Results | 92.2% (47/51) of the samples were successfully genotyped. HIV-1 subtype frequency was: 15/47 (32%) A, 20/47 (43%) D, 1/47 (2%) C, 1/47 (2%) G, and 10/47 (21%) unique recombinant forms. Mutation K103N was identified in 2 samples and V106A in 1 sample, equivalent to 6.4% prevalence of NNRTI-resistance. No NRTI or PI DRMs were detected. We also identified 5 transmission clusters supported by high bootstrap values (>90%), 1 cluster included the 2 individuals with K103N.
Conclusion | The level of TDR to NNRTIs in these ART-naïve individuals was still moderate and hence repeated surveys are warranted. The transmission clusters suggest a high degree of sexual mixing in these communities.

HO 15

11:30–11:45

Is the fishing community a hotbed for HIV and STI transmission? Evidence from Mangochi, Malawi

Victor Mwapasa • University of Malawi College of Medicine, Blantyre, Malawi

Introduction | Previous studies suggest that fishing communities are at high risk of HIV and sexually transmitted infections (STIs) and could potentially serve as target populations for assessing the efficacy of novel HIV and STI interventions. We assessed the prevalence and incidence of HIV and STIs and risky sexual behaviour in a fishing community in Mangochi, southern Malawi.
Methods | We report baseline and 9-month follow-up data from an ongoing prospective cohort study which started in June 2009. We screened study participants for HIV, syphilis and herpes simplex virus-2 (HSV-2), using serological tests and assessed risky sexual behaviour using a questionnaire. We repeated these assessments at 3-monthly intervals in HIV-negative participants.
Results | We screened 740 participants with a median age of 26 years (IQ range: 22–32). Of these, 61.2% were female and 69.7% were married. The prevalence of HIV, syphilis and HSV-2 were 13.1%, 3.0% and 45.7%, respectively. Only HSV-2 infection was significantly more common in females than males (51.6% versus 36.4%, $p<0.05$). In the preceding 3 months, a history of genital sores and genital discharge were reported in 4.9% and 5.4% of all participants, respectively. Also, new sexual partnerships were reported in 18.8% of males and 5.5% of females. Overall, at 9 months, the cohort retention rate of HIV-negative participants was 80%. HIV, HSV-2 and syphilis incidence rates were 1, 11 and 4 per 1000 person-months, respectively. Five of the six new HIV cases originated from one village.
Conclusion | Compared with the national averages, fishing communities had a higher prevalence of risky sexual behaviour and STIs but similar HIV prevalence. New HIV cases appeared to be clustered.

CHAIRS
Prof. Nkandu Luo
Prof. Shabbar Jaffar

RAPPORTEURS
Dr Pauline Mwinzi
Dr Jonathan Kayondo

HO 16

11:45–12:00

An assessment of the quality of life of HIV/AIDS patients and their families during the scaling-up of antiretroviral treatment in Ghana

Sybill Sory • Ghana Health Service, Accra, Ghana

Introduction | Existing research that documents the negative impact of HIV/AIDS on patient physical and mental health and suggests spillover effects to family caregivers, is mainly qualitative. While patient health is expected to improve with antiretroviral intake, the largely qualitative research on family caregivers rarely explores physical and mental health in a dynamic perspective. This study aims to address these gaps by quantitatively assessing the quality of life of people living with HIV and AIDS (PLWHAs) and their family.
Methods | We used survey data collected from 9 out of 10 regions. The Medical Outcomes Survey Instrument was administered twice. Responses from 507 patients, 415 family members and 387 neighbours, used as reference population, were used to generate physical and mental health indices which were regressed on characteristics including respondent medical status, controlling for survey round, gender, age and individual fixed effects.
Results | On average, mean physical and mental health indices increased for patients from baseline to follow-up, although they remained significantly lower than those of their families and neighbours. Family members appear mentally worse off than neighbours at baseline with at least 5 out of 8 mental health indices significantly lower at the 5% significance level. In addition to a general improvement at follow-up, notable and significant increases occur in family member's mental health indices.
Conclusion | Evidence suggests that family members of HIV-positive people suffer a psychological burden that may erode over time as patients improve physically and mentally. Patients improve mentally and physically over time but remain worse off when compared to their families and neighbours.

TO 13

11:00–11:15

M. tuberculosis-specific lung innate immunity in close contacts of TB index cases

Keertan Dheda • University of Cape Town, South Africa

Introduction | Tuberculosis (TB) is a global health problem causing the death of almost 10 million people annually. There is a gap in knowledge concerning the mechanisms of innate immunity in the lung. Only a few studies have investigated innate immune processes in alveolar cells.
Methods | Both the latently infected (LTBI) and non-infected (NI) close contacts of smear-positive patients underwent bronchoscopy (n=11 patients) to obtain alveolar lavage cells, and phlebotomy to obtain PBMCs. The immune phenotype of both groups was characterized using flow cytometry and the frequency and profile of innate immune responses was compared in PPD-stimulated and unstimulated cells. The pattern recognition receptors (TLRs, MR), innate immune mechanisms (autophagy, cathelicidin, perforin, granulysin, granzyme) and adaptive immunity biomarkers (Th1, Th2, Th17, Treg, TNF, apoptosis) were characterized in both groups using both PBMCs and alveolar lavage cells.
Results | Nine of the 11 patients were used for the analysis (4 LTBI and 5 NI contacts). In the peripheral blood compartment the microbial peptide cathelicidin, the autophagy marker LC3BII, and the cytotoxic molecule granulysin, and in the alveolar compartment the pattern recognition receptor TLR9 and the mannose receptor (MR), were found to differ between the two groups.
Conclusion | Both groups, in the peripheral and lung compartments, have distinct cellular, pattern recognition receptor, and innate immune signatures.

CHAIRS
Dr Antonio Martin
Dr Christian Burri

RAPPORTEURS
Prof. Jean Nachega
Ms Thuli Mthiyane

TO 14

11:15–11:30

Variation in IFN-γ responses to different infecting strains of *M. tuberculosis* in acid-fast Bacillus smear-positive patients and household contacts

Niaina Rakotosamimanana • Unité des Mycobactéries, Institut Pasteur, Madagascar

Introduction | Most healthy individuals exposed to *M tuberculosis* will not develop tuberculosis (TB), though many may become latently infected. More precise measurement of the human immune response to *M. tuberculosis* infection is needed to potentially identify those subjects most at risk of developing active disease. IFN-γ production has been widely used as a proxy marker to study infection and to examine the human immune response to specific *M. tuberculosis* antigens. Genetically distinct *M. tuberculosis* strains may invoke different immune responses. How these differences influence the immune responses and clinical outcome in human tuberculosis is still poorly understood.
Methods | We evaluated the antigen-specific IFN-γ production responses in peripheral blood mononuclear cells from two cohorts of subjects recruited in Antananarivo, Madagascar, from 2004 to 2006 and examined the influence of the *M. tuberculosis* strains on this response. The cohorts were sputum positive index cases and their household contacts. Clinical strains isolated from the TB patients were typed by spoligotyping.
Results | Comparison of the IFN-γ responses with the spoligotype of the infecting clinical strains showed that 'modern' *M. tuberculosis* strains, like Beijing and Central Asian (CAS) strains, tended to induce lower IFN-γ responses than 'ancient' strains, like East African-Indian (EAI) strains, in index cases and their household contacts.
Conclusion | These results suggest that new strains may have evolved to induce a host response different from that of ancient strains. These findings could have important implications for therapeutic and diagnostic strategies.

Reference: Clin Vaccine Immunol. 2010; 17(7):10

TO 15

11:30–11:45

Decreased IFN-γ and increased Cd4+Cd25+Foxp3+ regulatory T-cells in patients with extensively drug resistant tuberculosis (XDR-TB)

Keertan Dheda • University of Cape Town, South Africa

Introduction | XDR-TB is an emerging problem in South Africa and globally. Drug treatment options are very limited and patient prognosis is poor. Consequently, alternative treatment approaches such as immunotherapeutic options are being considered. However, such approaches depend upon understanding the immunology of XDR-TB.
Methods | Peripheral blood mononuclear cells from subjects with XDR-TB (n=15), drug-sensitive TB (DS-TB; n=15) and latent TB infection (LTBI; n=7) were cultured with purified protein derivative (12µg/mL) for 7 h. IFN-γ, IL-13, IL-17, IL-22, CCR6, FOXP3, CD25, IL-10, TNF-α, CD3, CD4 and CD8 were assessed by flow cytometry. Immune profiles in XDR-TB patients were correlated with host and mycobacterial-associated factors. A ^{3}H-thymidine incorporation assay was used to assess the suppressive capacity of CD4+CD25+FOXP3+ cells. A mycobacterial stasis assay was used to assess the effect of CD4+CD25+FOXP3+ cells on mycobacterial survival.
Results | CD4+IFN-γ cells were decreased in XDR-TB (median: 0.1%) compared to DS-TB (0.4%; p=0.04) and LTBI (0.7%; p=0.02). CD8+IL-17 cells were also decreased in XDR-TB (median: 0.5%) compared to DS-TB (1.4%; p=0.01) and LTBI (1.1%; p=0.01). CD4+CD25+FOXP3+ cells were increased in XDR-TB (median: 14.9%) compared to DS-TB (1.8%; p=0.04), even after correcting for disease duration. CD4+CD25+FOXP3+ cells (T_{reg}) inhibit T cell proliferation by up to 90% and enhances mycobacterial survival.
Conclusion | XDR-TB patients have an altered immuno-phenotype compared to DS-TB and LTBI, exemplified by increased proportions of T_{reg} and decreased IFN-γ, even when taking into account disease chronicity. These findings inform the selection of approaches in managing XDR-TB.

CHAIRS
Dr Antonio Martin
Dr Christian Burri

RAPPORTEURS
Prof. Jean Nachega
Ms Thuli Mthiyane

TO 16

11:45–12:00

Cellular and soluble biomarkers in the pleural fluid, absent from the peripheral blood, accurately diagnose pleural TB in a TB-endemic setting

Jayne Sutherland • Medical Research Council, Banjul, The Gambia

Introduction | TB still remains one of the leading infectious disease killers world-wide. Pleural TB is notoriously difficult to diagnose due to its paucibacillary nature yet it is the main cause of pleural effusions in TB endemic countries such as The Gambia.
Methods | We analysed cellular and soluble components of the pleural fluid form patients presenting with pleural effusion who were subsequently classified as having TB (n=30) or not TB (n=11).
Results | We identified both cellular and soluble biomarkers in the pleural fluid that were not present in the peripheral blood and allowed highly accurate diagnosis of pleural TB. Multi-plex cytokine analysis on unstimulated pleural fluid showed that IP-10 resulted in a positive likelihood ratio (LR) of 9.6 versus 2.8 for IFN-γ; a combination of IP-10, IL-6 and IL-10 resulted in an AUC of 0.96 and positive LR of 10. A striking finding was the presence of a distinct PPD-specific IFN-γ+TNF-α+ cell population (PPD-IGTA) in the pleural fluid of TB subjects.
Conclusion | Presence of this PPD-IGTA population resulted in 95% correct classification of pleural TB disease with a sensitivity of 95% and specificity of 100% making it an exquisite biomarker for accurate and early diagnosis of pleural TB disease. Importantly, this cell population was neither present in the pleural fluid of non-TB subjects (negative predictive value=100%), nor in the peripheral blood of TB or non-TB subjects, suggesting that diagnostic tests for TB reliant on the peripheral blood at this acute stage of disease are inaccurate.

MO 13

11:00–11:15

Safety and immunogenicity of prime-boost immunization of Kenyan adults with candidate malaria vaccines based on a chimpanzee Adenovirus and MVA

Caroline Ogwang • KEMRI Wellcome Trust Research Programme, Kilifi, Kenya

Introduction | Malaria causes nearly a million deaths and hundreds of millions of cases annually. There is a need for additional intervention tools such as an efficacious malaria vaccine. We report a phase Ib trial in Kilifi, Kenya of the viral vectored candidate malaria vaccines Adch63 ME-TRAP and MVA ME-TRAP.
Methods | Thirty consenting healthy male volunteers were recruited and randomised to receive a single low or high dose of ChAd63 ME-TRAP intramuscularly as a prime and a single MVA ME-TRAP boost, the latter administered either intradermally or intramuscularly with an eight week interval between the vaccines.
Results | The local solicited symptoms reported were swelling, itch, warmth, pain, redness, scaling and blistering while the general symptoms were fever, headache, arthralgia, myalgia, nausea/vomiting and malaise. All the symptoms reported post-vaccination were mild to moderate in nature, all soon resolved, and overall the safety profile was excellent. There was no significant difference between the immunogenicity observed with the intramuscular and intradermal routes of MVA vaccine administration at any time point. The highest peak response, measured by an *ex vivo* IFN-γ ELISpot assay was at day sixty three: an arithmetic mean, for the high dose group, of 1,792 spots per million PBMCs; with a 95% confidence interval of 1,229 to 2,355.
Conclusion | This immunisation approach is safe and highly immunogenic for induction of IFN-γ T cell responses in Kenyans using either intradermal or intramuscular MVA administration.

CHAIRS
Prof. Jasper Ogwal-Okeng
Prof. Robert Sauerwein

RAPPORTEURS
Dr Kamija Phiri
Dr Badara Cisse

MO 14

11:15–11:30

Safety and immunogenicity of heterologous prime-boost vaccine strategy with Adch63 ME-TRAP and MVA ME-TRAP in healthy adults and children in The Gambia

Muhammed Afolabi • Medical Research Council Unit, The Gambia

Introduction | A safe and effective malaria vaccine remains a global priority especially for prevention in vulnerable age groups. We report a phase I trial of viral vectored candidate malaria vaccines consisting of AdCh63 ME-TRAP prime and MVA ME-TRAP boost.
Methods | Sixteen consenting healthy adults aged 18–50 years were allocated into high or low dose groups; followed by 36 children aged 2–6 years randomised into vaccine and control groups based on age stratifications. Safety of the vaccines was determined by comparing adverse events, reactogenicity, biochemical and haematological data of high and low dose groups in the adult study and between vaccine and control arms in the paediatric study. Immunogenicity was measured by IFN-γ ELISpot and flow cytometry.
Results | The mean haemoglobin, white blood cell count, alanine transaminase and creatinine at pre- and post-vaccination visits in adult and paediatric studies were within acceptable ranges. Adverse events included pain, swelling and itching at injection site, headache, malaise, nausea and arthralgia. In the paediatric study, low grade fever, reduced oral intake and reduced activities were reported. In the adult study, the vaccines were safe and immunogenic at high doses with mean ELISpot responses of 1,233 SFU/10^6 PBMC (SD 1,081) 1 week after MVA boost vaccination. Similar levels were maintained at 1 month post-MVA boost. Among children vaccinated with high dose AdCh63 and low dose MVA ME-TRAP, mean ELISpot responses were 1,426 SFU/10^6 PBMC (SD 1,245).
Conclusion | The heterologous prime-boost malaria vaccine regimens AdCh63 ME-TRAP and MVA ME-TRAP are safe and immunogenic in semi-immune Gambian adults and children aged 2–6 years.

MO 15

11:30–11:45

Antibody levels to Msp1-Block 2 Hybrid, GLURP R2 and As202.11 and the risk of malaria in under five year old children of Burkina Faso and Ghana: an Afro-Immuno Assay project

Daniel Dodoo • Noguchi Memorial Institute, University of Ghana, Legon, Ghana

Introduction | Antibodies have been demonstrated to play an important role in natural protection against clinical malaria, but antigens that induce this immunity have not been conclusively identified. The Afro-Immuno Assay (AIA) network project was initiated, with the aim to develop and introduce standardized immuno-epidemiological study designs, immunological assays and statistical methods. These could form part of a set of tools for validating promising malaria vaccine candidate antigens, provide essential baseline information for clinical trials and enhance quality assured laboratory capacity and capability.
Methods | In a phase II study, 7 African and 2 European institutions focused on using similarly designed studies, standardized ELISA and statistical methods to assess isotypes and IgG subclass levels against GLURP R2, MSP1-block 2 hybrid and AS202.11 in cohort samples in relation to protection from clinical malaria.
Results | Data from two of the study sites, Burkina Faso and Ghana showed IgG3 levels to GLURP R2 independently correlating with protection from malaria in both Ghanaian (0.48 (0.25–0.91); p=0.02) and Burkinabe (0.82 (0.74–0.91); p<0.0001) children. IgM levels to MSP1-block 2 hybrid (0.85 (0.73–0.98); p=0.02) were associated with reduced risk to malaria in Burkinabe but not Ghanaian children whereas antibody levels to the malaria peptide AS202.11 were not associated with the risk of malaria in the study sites.
Conclusion | The data has shown the potential of GLURP R2 and MSP1-block 2 antigens as potential malaria vaccine candidates. The disagreeing conclusions in the two studies may be due to differences in malaria transmission and genetic background of the populations studied.

CHAIRS
Prof. Jasper Ogwal-Okeng
Prof. Robert Sauerwein

RAPPORTEURS
Dr Kamija Phiri
Dr Badara Cisse

MO 16

11:45–12:00

Studies of new adjuvants and formulations of GMZ2 with the aim to enhance immunogenicity

Michael Theisen • Statens Serum Institut, Copenhagen, Denmark

Introduction | The GMZ2 malaria vaccine candidate is a fusion protein of P.f.GLURP-R0 and the c-terminal part of P.f. MSP3 expressed in the Lactococcus system. These two antigens have been chosen because we repeatedly found that high titer cytophilic antibodies against GLURP and MSP3 are statistically significantly associated with protection against clinical malaria. Additionally, human IgG antibodies against these antigens kill *P. falciparum* in the *in vitro* ADCI assay.
Methods | 1) Sera from three European and African phase 1 clinical trials on GMZ2 in $Al(OH)_3$ were tested by xMAP technology; 2) New adjuvant formulations were screened in mice.
Results | Comparative analysis of serum samples from the three phase I trials have shown that: immunizations elicit anti-GMZ2 IgG antibody levels in malaria exposed children which are comparable to those elicited in non-exposed and exposed adults. Thus, a pre-existing IgG response against GLURP and MSP3 does not prevent or reduce the vaccine response. Detailed epitope mapping studies demonstrate that peptides containing the P3 epitope are strongly recognized by all groups. However, the current adjuvant formulation cannot elicit IgG responses which exceed those found in exposed individuals. New adjuvant formulations have therefore been screened in mice. We found that oil in water formulation supplemented with the Toll receptor agonist GLA (MPL analogue) elicits a strong antibody response predominantly consisting of cytophilic IgG2a and IgG2b mouse antibodies. Importantly, this formulation also induces strong B-cell memory.
Conclusion | We have now established a novel formulation of GMZ2 which in preclinical studies is superior to the previous formulation with $Al(OH)_3$.

PARALLEL SESSION | CROSS-CUTTING

EDCTP-NACCAP capacity building and networking session

11:00–13:00

Conference room 6

11:00–11:05

Welcome note and session introduction

Dr Garry Aslanyan

11:05–11:15

Introduction NACCAP

Prof. Willy Spaan

11:15–11:45

Overview of the NACCAP programme

INTERACT partnership programme

Prof. Elly Katabira • College of Health Sciences, Makerere University, Kampala, Uganda

Dr Joseph Ntaganira • National University of Rwanda, School of Public Health, Kigali, Rwanda

CoMMAL partnership programme

Dr Victor Mwapasa • College of Medicine, University of Malawi, Blantyre, Malawi

Dr Exnevia Gomo • College of Health sciences, University of Zimbabwe, Harare, Zimbabwe

ART-A partnership programme

Dr Michelle Bronze • University of the Witwatersrand, Johannesburg, South Africa

Dr Susan Aitken • ARTA-UMCU, Utrecht, The Netherlands

CHAIRS
Prof. Willy Spaan
Dr Andrew Kitua

RAPPORTEURS
Ms Amber Abrahams
Dr Stephen Rulisa

NO 01

Building clinical research capacity through an adaptable modular approach: The applied research and evidence based medicine course

Dr Stella van Beers • Royal Tropical Institute, Biomedical Research, Amsterdam, The Netherlands

Introduction | The Applied Research and Evidence-Based Medicine (ACREM) course was established to address the need for training in Clinical Research and Evidence-Based Medicine in Africa.
Methods | Following a training needs assessment in 2006 in Uganda and Rwanda,10 research training modules were developed and piloted in 2007-2008. The course was then adjusted and is now conducted annually.
Results | Ten intensive classroom 1-week modules were developed using a variety of educational methods, including: interactive lectures and group-work; self-learning and review (competency test); learning-by-doing (assignments); and output-oriented (developing a research proposal). Modules are followed by 3 to 4 weeks of self-directed assignments and regular tutorials. The modules include: introduction to clinical research, designing and interpreting research, evidence-based medicine, research proposal writing; clinical trial management; understanding clinical trials; diagnostic studies; data management; multivariate analysis; and manuscript writing. Special attention is given to professional skills development, e.g. theory of knowledge, management and communication skills. A selection of ACREM modules has been conducted for 67 Uganda and 95 Rwanda participants (MMED and other clinical specialities and faculty members).
Conclusion | The modular ACREM course increases the accessibility of skills and knowledge in research and evidence-based practice for clinicians with a full-time job and study. The modular, interactive approach has shown high acceptability with both participants and lecturers. Participants following 4 modules receive a certificate. Eight modules fulfil the requirements for a diploma and after completing 10 modules with a thesis, candidates receive a master's degree. The course is adaptable to incorporate local curriculums and structures.

INTERACT

NO 02

Barriers to evidence-based practice in doctors and nurses in Rwanda and Uganda

Dr Kimberly Boer • Royal Tropical Institute, Amsterdam, The Netherlands

Introduction | The Collaboration for Evidence-based Healthcare in Africa (CEBHA) aims to determine barriers to practicing evidence-based medicine (EBM) for healthcare workers in Rwanda and Uganda to better implement EBM in Africa.
Methods | Doctors and nurses were interviewed using a structured questionnaire in Kigali, Rwanda and Kampala, Uganda at the Kigali University Hospital (CHUK) and Mulago Teaching Hospital respectively.. The McColl questionnaire and Barriers to Research Utilization Scale were compiled and adjusted for Africa.
Results | 66 general and specialist doctors and 67 nurses and midwives responded, (49% Uganda; 60% women). 43%, 33% and 24% had <5 years, 6 to 10 years and >10 years of experience respectively. Doctors and nurses (>80%) recognized the benefits of EBM. 88% of Rwandans and 42% of Ugandans felt EBM should be included in education ($p<0.001$). Most important barriers reported: research results not readily available (60%), facilities inadequate for implementation (66%), insufficient time to read research (63%) or to implement new ideas (53%). Barriers to accessing literature included: no access to internet (RW:31% UG:49%); slow internet (RW:51% UG:38%); no access to computers (RW:21% UG:41%), no access to articles of interest (RW:43% UG:42%); not knowing where to find articles (RW:33% UG:29%); no time to search for articles (RW:58% UG:39%). 30% felt research is not relevant to Africa or their country, and 20% felt EBM conclusions contradict WHO guidelines.
Conclusion | Attitudes about EBM were positive, but barriers were numerous and varied between nurses and doctors and Ugandans and Rwandans. Interventions to improve EBHC must be specific to each group.

CHAIRS
Prof. Willy Spaan
Dr Andrew Kitua

RAPPORTEURS
Ms Amber Abrahams
Dr Stephen Rulisa

NO 03

Knowledge, attitudes and practice of evidence-based medicine in doctors and nurses in Rwanda and Uganda

Dr Joseph Ntaganira • National University of Rwanda School of Public Health, Kigali, Rwanda

Introduction | The Collaboration for Evidence-Based Healthcare in Africa (CEBHA) measured knowledge, attitude and practice (KAP) regarding EBM in health-care workers in Rwanda and Uganda.
Methods | Doctors and nurses were interviewed using a structured questionnaire in Kigali, Rwanda (RW) and Kampala, Uganda (UG) at the Kigali University Hospital (CHUK) and the Mulago Teaching Hospital respectively. The McColl questionnaire and Barriers to Research Utilization Scale were adjusted for Africa.
Results | 66 general and specialist doctors and 67 nurses and midwives responded (49% from Uganda and 60% women). Doctors in Uganda/Rwanda report similar knowledge levels on different study designs (30–40%), absolute risk-difference (>45%) and measures of association (45%) and for EBM-specific terminology: critical-appraisal (36%), systematic-review (52%), evidence-based healthcare (RW: 42% versus UG: 23%, p=0.044) and EBM summaries/guidelines (>40%). Nurses (3%) and doctors (41%) are co-authors on publications, with Rwandan doctors publishing more (53% vs. 29% p=0.05). Rwandan and Ugandan doctors recognized the benefits of EBM (>93%), however Ugandan nurses differed in perceived benefits (RW: 88% UG: 59%, p=0.007). Benefits included improved patient care (doctors: 98%, nurses: 67%) and improved relationship between patients and doctors (>70%). Upon discovering evidence that contradicts clinical practice, 43% (RW) to 12% (UG) would follow the evidence (p<0.001), and 55% would further evaluate the evidence. 19% of healthcare workers feel that they are seeking and applying evidence and follow evidenced-based guidelines (RW: 32% UG: 60%, p<0.001).
Conclusion | Most participants perceived benefits of EBM, however <50% knew basic epidemiological and EBM terminology and <30% of participants felt that they were presently practicing EBM.

CoMMAL

NO 04

Opportunities and challenges in establishing a conducive research environment in academic institutions in resource-limited countries

Dr Michael Boele van Hensbroek • Global Child Health Group, AIGHD, University of Amsterdam, The Netherlands

Introduction | Despite the large investment in capacity building, African research institutions continue to demonstrate inadequate critical mass for sustainable high quality research and training. While the weak capacity is often attributed to brain-drain, there is growing recognition that the approach, focused primarily on building individual research skills, may be a major factor. We describe an innovative capacity building approach that integrates individual skills development with creation of a supportive research environment in the College-of-Medicine (CoM), University of Malawi.
Methods | The CoM was awarded a NACCAP grant to establish a Research Support Centre (RSC) with a platform of clinical studies for training of clinical scientists and introduction of GCP. The RSC planned activities included developing capacity for grants management, strengthening institutional research governance, developing research information systems, individualized research support, and research skills building through short courses.
Results | A robust research support unit was established which currently manages over 36 projects (valued over $17 milj.) trained over 200 staff and supported under/post-graduate research training. The RSC has developed clinical trial monitoring capacity and monitors regulatory trials. These activities have generated significant income (30% of the expenses). The improved research environment contributed to retention of scientists and reversing brain drain. The success of the RSC model has received attention in the region with University of Zimbabwe and Zambia adopting these models.
Conclusion | The RSC model is an effective approach to building sustainable research capacity in an African setting. Rolling out the model may sustainably enhance research capacity.

CHAIRS
Prof. Willy Spaan
Dr Andrew Kitua

RAPPORTEURS
Ms Amber Abrahams
Dr Stephen Rulisa

NO 05

Development and field evaluation of a set of more affordable HIV treatment monitoring technologies for Africa: the ART-A project

Prof. Tobias Rinke de Wit • Academic Medical Center, Amsterdam, Netherlands

Introduction | With >5 million HIV patients on antiretroviral treatment, it is a challenge that crucial tests for monitoring viral load and drugs resistance are lacking in resource-limited settings, due to cost, lack of laboratory infrastructure, technical assay demands and cold chain requirements.
Methods | Molecular biological techniques were used to develop a dried-blood spot based semi-quantitative viral load test for HIV-1 (SQ-VL) and a novel HIV drugs resistance test for Africa. The SQ-VL is an internally controlled, subtype-independent, real-time PCR targeting conserved parts of HIV-1. The drugs resistance test is a simplified assay for detection of major RTI mutations associated with first-line HAART. Operational evaluation of these assays was performed in a 3-level laboratory network structure in Uganda and South Africa. Technology transfer and capacity building was achieved through exchange visits between Africa and Europe.
Results | The ART-A assays for SQ-VL and HIV resistance have been developed and tested in laboratories in Europe, subsequently adjusted, implemented and evaluated in Uganda and South Africa. A three-tiered approach of field sites, regional sites and central reference sites was adopted. Data from Uganda indicate high success rates for SQ-VL in dry blood spot samples above 5,000 cp/mL.
Conclusion | We have demonstrated a network design linking remote sample collection sites to regional and central laboratories to screen for virological failure of patients on antiretroviral treatment and subsequent resistance testing on samples identified as failing therapy. This concept demonstrates that improved patient monitoring can be achieved in Africa at more affordable rates and for more patients than previously possible.

PARALLEL SESSION | CROSS-CUTTING

EDCTP-NACCAP capacity building and networking session

11:00–13:00

Conference room 6

APRIORI partnership programme

Prof. Gibson Kibiki and Dr Reginald Kavishe • Kilimanjaro Clinical research Institute (KCRI), Kilimanjaro Christian Medical Centre (KCMC), Moshi, Tanzania

11:45–12:00

Dr Garry Aslanyan and representatives of research programmes: Interview

CHAIRS
Prof. Willy Spaan
Dr Andrew Kitua

RAPPORTEURS
Ms Amber Abrahams
Dr Stephen Rulisa

12:20–12:35
Panel discussion

Prof. Irene Agyepong, Dr Val Snewin and Dr Opokua Ofori-Anyinam

12:35–12:55
ESSENCE on health research, monitoring and evaluation

Prof. Hannah Akuffo

12:55–13:00
Conclusion of the morning programme

Dr Garry Aslanyan

HO 17

14:00–14:15

Bacterial vaginosis as a risk factor for acquiring sexually transmitted diseases

Innocent Afeke, • Noguchi Memorial Institute for Medical Research, University of Ghana, Accra, Ghana

Introduction | A few studies have demonstrated that bacterial vaginosis (BV) is associated with sexual behaviour risk factors similar to those for other sexually transmitted diseases (STDs). Here, the prevalence of STDs was observed in a multivariate analysis of data from women infected with BV and either *chlamydia trachomatis* (CT), *Treponema pallidum* (TP); syphilis, *Neisseria gonorrhoeae* (NG) or HIV. Non-BV infected women were used as control subjects.
Methods | Data from 788 women screened in the SAVVY HIV gel phase III clinical trial in Accra (West Legon Study Site; 2004–2006) were analysed. Presence of BV, CT, TP, NG, *Trichomonas vaginalis* (TV) and HIV was evaluated and participants were interviewed on sexual behaviour. Statistical comparisons were made using t-test, chi-squared test (Pearson) and logistic regression multivariate analysis.
Results | A high association exists between BV and HIV ($p<0.01$) with risk factor (0.4), which does not occur in other sexually transmitted diseases like NG, syphilis and chlamydia with non-significant association ($p<1$) and risk factors 0.6, 0.7, and 0.9 respectively. HIV was the most prevalent STD with 11.2%, chlamydia 9.2%, TV 2.3%, syphilis 1.7% and NG the least with 1.5%. Also, BV and candidiasis were the commonest cause of vaginitis. We also observed mixed-infection with the organisms that cause vaginitis.
Conclusion | Bacteria associated with bacterial vaginosis increase female genital tract infection with HIV but the mechanism is not clear. Bacterial vaginosis (not an STD) predisposes to HIV infection. All symptomatic and asymptomatic cases of BV presented in sexual health clinics should be treated to reduce the risk of PID, pre-term delivery, and/or HIV transmission. Moreover, sexually active and pregnant women should be encouraged to regularly visit sexual health clinics for BV screening and treatment.

CHAIRS
Dr Abraham Alabi
Prof. Eric Sandström

RAPPORTEURS
Dr Cissy Kityo Mutuluuza
Dr Louis Marie Yindom

HO 18

14:15–14:30

Prevalence of anogenital human papilloma virus among PLWHA in Ibadan, Nigeria

Samuel A. Fayemiwo • College of Medicine, University of Ibadan, Ibadan, Nigeria

Introduction | Genital Human Papilloma Virus (HPV) infection is usually asymptomatic and is most frequently recognised as genital warts when symptoms are present. This study aimed at providing information on prevalence among PLWHA attending ART clinic at the University College Hospital, Ibadan, Nigeria.
Methods | This is a descriptive cross-sectional survey of PLWHA attending ART clinic between January 2009 and December 2010. Diagnosis of genital warts was based on the clinical findings of typical lesions on the external genitalia, vaginal, cervix or perianal region. Data was analysed using SPSS 15:0.
Results | There were 9,504 patients with a mean age of 34.67 years (SD=9.16; range 19–77 years). 8.95% (851) had at least one STI based on history and examination at baseline. The male to female ratio was 1: 4. 388 (45.6%) of those with STIs were treatment naive to HAART. Of the 851 PLWHA with STIs, 3.8% had undetectable viral load (<200 copies/mL) while 470 (55.3%) had low CD4 count (<200 cells/µL) The prevalence of genital HPV was 33.3%. Other viral STIs diagnosed were Hepatitis B Virus infection (45.7%), *Herpes genitalis* (21.3%) and *Molluscum contagiosum* infection (0.03%). Treatment experienced patients were found to be associated with increased use of condom (OR=3.23 (95% CI: 2.15–5.00).
Conclusion | Screening for genital warts and follow-up of HIV-infected patients should be performed routinely. HBV and HPV vaccine should be offered to HIV-infected women between the ages of 9 and 26 years to reduce the risk of acquisition of HIV.

HO 19

14:30–14:45

Prevalence of human papilloma virus infection in HIV-infected women during the third trimester of pregnancy

Kishor Mandaliya • International Centre for Reproductive Health, Mombasa, Kenya

Introduction | Research findings on the effects of antiretroviral drugs (ARVs) on the natural history of genital human papilloma virus (HPV) infection are not conclusive. This study aims to determine the influence of different HAART regimens on the incidence and clearance of HPV infection post delivery in women infected with HIV.
Methods | Adult HIV-1 infected women at 27–34 weeks gestation were enrolled into the Kesho Bora Study, a randomised controlled trial assessing the effects of HAART on HIV-1 mother-to-child transmission (MTCT) during pregnancy, delivery and postpartum. For the purpose of HPV typing all women were selected for whom a cervico-vaginal lavage sample during pregnancy and 3 months postpartum was available.
Results | The 309 women enrolled at the Mombasa site had a mean age of 27.7 years (SD 4.88). Of these, 62% (191) were in WHO HIV stage I, and 30% (94), 5.2% (16) and 2.6% (8) were in stages II, III and IV respectively. 12% (37/305) received HAART and the rest were given either triple ARVs or a short course treatment for PMTCT, based on the CD4 count. The presence of 28 different HPV genotypes is currently being assessed using the INNO-LIPA HPV Genotyping Extra assay.
Conclusion | HPV prevalence and distribution of the different genotypes during the third trimester of pregnancy will be presented. Overall, with this study we aim to address whether the use of HAART in HIV-positive pregnant women leads to improved clearance of the virus through partially restoring immune competence.

CHAIRS
Dr Abraham Alabi
Prof. Eric Sandström

RAPPORTEURS
Dr Cissy Kityo Mutuluuza
Dr Louis Marie Yindom

HO 20

14:45–15:00

Attitudes and intentions of mothers and adolescent daughters regarding the adoption of human papilloma virus vaccination in Akinyele local area, Rachuonyo

Omondi Ochieng • ILO/IPEC, Nairobi, Kenya

Introduction | The Human Papilloma Virus (HPV) vaccine has been shown to be effective in reducing its incidence. The study sought to determine the attitudes and intentions related to the HPV vaccine among adolescent girls and their mothers in Kendu Bay.
Methods | This was a descriptive cross-sectional survey that used a four stages random sampling technique with 160 mothers and their daughters. Six focus group discussion sessions were conducted and semi-structured questionnaires were used for demographic data collection relating to HPV and its vaccine. 25 point attitudinal scales were used where <12 points is a negative and >12 points is a positive attitude.
Results | The mean age of the adolescents and their mothers were 13.2 ± 1.6 and 35 ± 5 respectively. The majority (77.0%) of the adolescents had secondary education. Most (97.0%) mothers were married and (71.0%) petty traders. 85% of the adolescents and 71.0% of the mothers were unaware of cervical cancer and the HPV vaccine. Women affected by cancer showed an association with the willingness to be vaccinated (OR: 1.42; 95% CI: 1.21–1.66) and willingness to be vaccinated without any previous awareness of those affected (OR: 1.96; 95% CI: 1.75–2.20). Most mothers (69.0%) agreed that every woman needs the HPV vaccination. Vaccine safety beliefs were strong correlates of willingness to give permission for vaccination by the mothers. Few mothers (21.0%) thought that administration of HPV vaccine to adolescent girls will promote promiscuity among girls.
Conclusion | Making information available to mothers and adolescent girls using the health promotion strategy and approaches to promote and enhance informed decisions to fully accept the HPV vaccine.

HO 21

15:10–15:25

HIV-positive women in Enugu, Nigeria: an assessment of current use of cervical cancer screening and willingness to pay in the absence of donor support

Cyril Dim • Department of Obstetrics & Gynaecology, University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria

Introduction | HIV-positive women require frequent cervical cancer screening. In Nigeria, routine screening for this group where it exists is included within the donor supported HIV care. Sustainability of this free programme remains a concern. Therefore we need to determine the willingness of HIV-positive women pay for cervical cancer screening, if necessary.
Methods | Questionnaires were administered to 400 consenting HIV-positive women randomly selected at the Adult HIV clinic, University of Nigeria Teaching Hospital, Enugu, Nigeria from May to July 2007.
Results | The mean age of respondents was 35.6 ± 9.7 years. A majority (81.0%) of respondents were diagnosed HIV-positive within 4 years prior to the study. Sixty nine (17.3%) women had knowledge of cervical cancer while only 6 (8.7%) of them were aware of their increased risk. Eleven (2.8%) respondents were aware of Pap smear, but only 1 (9.1%) of them had used it. After counselling, 378 (94.5%) respondents were willing to pay for Pap smear irrespective of cost. This willingness showed no trend across educational or parity groups. Respondents who were 40 years or younger, were more likely to express willingness to pay for Pap smear (OR=2.2 (CI 95% 0.88–5.34)).
Conclusion | Uptake of Pap smear among HIV-positive women in Enugu is low. Withdrawal of donor support for HIV care in Nigeria and possible introduction of out-of-pocket payment for cervical cancer screening, may not affect the uptake of the screening by informed women. Advocacy for provider initiated counselling on cervical cancer screening should be maintained.

CHAIRS
Dr Abraham Alabi
Prof. Eric Sandström

RAPPORTEURS
Dr Cissy Kityo Mutuluuza
Dr Louis Marie Yindom

HO 22

15:25–15:40

Prevalence and risk factors of major depressive disorders in HIV/AIDS as seen in semi-urban Entebbe District, Uganda

Eugene Kinyanda • MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

Introduction | Increased access to highly effective antiretroviral therapy for people living with HIV even in low income countries including in sub-Saharan Africa, has delayed HIV disease progression and prolonged survival. This brings into sharp focus issues of quality of life including mental wellbeing. A major cause of psychiatric morbidity in HIV/AIDS is major depressive disorder. Not much is known about the risk factors of major depressive disorder in HIV/AIDS in the African socio-cultural context. The aim of this study was to examine the prevalence and risk factors of major depressive disorder in HIV/AIDS in semi-urban Uganda.
Methods | A cross-sectional study was undertaken among 618 respondents attending two HIV clinics in Uganda.
Results | Prevalence of major depressive disorder in this study was 8.1% (95% CI, 5.9%- 10.2%). Factors associated with major depressive disorder at univariate analysis only were female gender, family history of mental illness, negative coping style, alcohol dependency disorder, food insecurity and stress. Factors independently associated with major depressive disorder were psychosocial impairment, adverse life events, post traumatic stress disorder, generalised anxiety disorder and life-time attempted suicide. Not associated with major depressive disorder were social support, neurocognitive impairment, CD4 counts and body mass index.
Conclusion | Psychological and social factors were the main risk factors of major depressive disorder among ambulatory HIV-positive persons with no evidence for the role of the neurotoxic effects of HIV. Treatment approaches for major depressive disorder among these patients should be modelled on those used among non-HIV patient groups.

TO 17

14:00–14:15

Clinical trials with MVA85A, a candidate TB vaccine

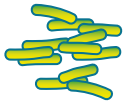
Martin Ota • Medical Research Council Unit, Banjul, The Gambia

Introduction | There are 8.8 million new cases of tuberculosis (TB) every year, leading to 1.7 million deaths annually. A new and more effective vaccine is urgently required. MVA85A is an attenuated poxvirus that cannot replicate in human tissues and is a safe vector for the *M. tuberculosis* antigen 85A.
Methods | Since 2002, a series of phase I/IIa clinical trials with MVA85A have taken place in the UK, South Africa, The Gambia and Senegal. 1967 people have received MVA85A in 15 completed trials and three ongoing trials. Trials have included adults, adolescents, children, infants, latently-infected adults, and HIV-infected adults.
Results | MVA85A is well tolerated and immunogenic in all clinical trials to date. Mild local reactions and mild systemic side effects are common, but there are no signs of immunopathology and no effect on CD4 count or HIV-RNA load in HIV-positive individuals. BCG prime-MVA85A boost induces high and sustained antigen 85A-specific immune responses. The key question is efficacy: does MVA85A protect against development of TB disease?
Conclusion | MVA85A is safe, immunogenic and the most clinically advanced candidate TB vaccine. Efficacy trials in two important target populations are now underway with MVA85A. An infant efficacy trial is fully enrolled, and an efficacy trial in HIV-positive adults is ongoing.

CHAIRS
Prof. Mecky Isaac Matee
Dr Christian Burri

RAPPORTEURS
Prof. Jean Nachega
Ms Thuli Mthiyane

TO 18



14:15–14:30

A phase I study evaluating the safety and immunogenicity of a new TB vaccine, MVA85A, in healthy volunteers who are infected with HIV in Senegal

Allé Baba Dieng • Université Cheikh Anta Diop de Dakar, Senegal

Introduction | TB disease is increasing in recent years because of a combination of factors and the lack of an effective vaccine. New strategies are developed to fight tuberculosis such as heterologous prime-boost immunisation regimens which include BCG. We have assessed the safety and immunogenicity of TB vaccine MVA85A in HIV-infected subjects.
Methods | Phase I safety study of two intradermal injections of 1×10^8 pfu MVA85A at day 0 and week 24–52. 24 adults have been enrolled: 12 HIV1, ART naive, CD4 >300 and viral load <100,000 copies/mL; 12 HIV1, stable on ART for at least 12 months. Follow-up period was 24 weeks after vaccination. Safety was evaluated clinically by occurrence of adverse events (AE), and by monitoring CD4 count, HIV-1 viral load and haemato-biochemical tests. Cellular immunogenicity has been evaluated by *ex vivo* IFN-γ Elispot assay.
Results | According to severity of AE, 87.7% were mild, 11.6% were moderate and 0.7% was severe. 29.2% were systemic and solicited and 70.8% were local and solicited. A significant immune response to antigen 85A was detected on Day 7 post immunization using a single or summed pool 85A peptide. This had reduced by day 28. Using a second dose of MVA85A 12 months later, we showed a strong Elispot response on Day 7 which was significantly higher on Day 28, 84 and 168 than after the primary immunization.
Conclusion | MVA85A had an excellent safety profile. MVA85A was immunogenic. A second dose of MVA85A enhances the magnitude and durability of the immune response.

TO 19

14:30–14:45

VPM1002 in a phase II clinical trial: all steps to neonate immunization

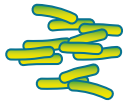
Leander Grode • Vakzine Projekt Management GmbH, Hannover, Germany

Introduction | VPM1002 is a live vaccine against tuberculosis. It is based on the well known *Mycobacterium bovis* Bacille Calmette-Guérin (BCG) strain which has been applied approximately 4 billion times worldwide. As BCG is not sufficiently effective to stop the spread of tuberculosis, two modifications have been implemented in VPM1002 to improve its immunogenicity. Our phase I study in humans used multiparameter flow cytometry to characterize the quality of the T cell response following immunization with VPM1002 or BCG.
Methods | In two phase I open label, randomised, controlled, dose-escalation studies in Germany and South Africa safety and immunogenicity of VPM1002 was evaluated compared to BCG. We enrolled 104 healthy subjects stratified for history of BCG vaccination.
Results | Safety and tolerability revealed no serious adverse events after VPM1002 vaccination and only mild to moderate adverse events were reported. VPM1002 was well tolerated in cohorts, the naïve and BCG pre-immunized volunteers. Higher total IFN-γ production was measured in the VPM1002 group *vs* the BCG group. VPM1002 induced an improved multifunctional CD4+ and CD8+ T cell response compared to BCG.
Conclusion | VPM1002 induces multifunctional T cell subsets which are thought to play a crucial role in protection against tuberculosis. At the same time VPM1002 reveals a superior safety profile in immunocompromised species (SCID mice) compared to BCG. VPM1002 shows all characteristics of a safe, well tolerated and efficacious tuberculosis vaccine, which could replace BCG immunization in the future. Based on the phase I results a phase II trial in newborns has been initiated.

CHAIRS
Prof. Mecky Isaac Matee
Dr Christian Burri

RAPPORTEURS
Prof. Jean Nachega
Ms Thuli Mthiyane

TO 20



14:45–15:00

Updates from a randomised, double blind placebo controlled phase IIb tuberculosis vaccine trial in HIV-negative infants in Western Kenya

Grace Kiringa • Kenya Medical Research Institute, Kisumu, Kenya

Introduction | BCG protects against severe forms of tuberculosis (TB) in childhood but protection wanes thereafter. New, safe and effective TB vaccines are an important strategy in disease elimination. We sought to identify the safest, most immunogenic dose of AERAS 402, a heterologous prime boost to BCG.
Methods | This is a multicentre study taking place in Kenya, South Africa, Mozambique and Uganda. Four to six month old healthy, HIV-negative infants were screened and randomised 3:1 to receive two doses of intra-muscular AERAS 402 or placebo. Three escalating doses of vaccine were given to each group of 32. An independent pharmacist prepared identical formulations of AERAS 402 and placebo. Infants were followed for 6 months for safety and immunogenicity by intracellular cytokine staining from peripheral blood mononuclear cells. A Data Monitoring Committee reviewed data before recruitment for the next dose commenced.
Results | We approached 270 infants, 260 consented, 10 (3%) declined. We screened 260 infants, 96 were randomised. 82 (32%) were ineligible due to abnormal chemistries, indeterminate/positive QFTs despite general good health. There have been 44 serious adverse events deemed unrelated to vaccine. There was a single hospitalization due to respiratory distress related to the highest dose of the vaccine.
Conclusion | There was high acceptability of the vaccine trial. A significant proportion of infants were screened out due to stringent eligibility criteria. The large number of adverse events is attributed to the high childhood morbidity in study area due to malaria, and pneumonia. Further safety evaluation is ongoing.

TO 21

15:10–15:25

Reduced frequency of specific IFN-γ producing T-cells in Ugandan infants when Bacillus Calmette-Guerin vaccination is delayed from birth to 6 weeks of age

Frederick Lutwama • South African Tuberculosis Vaccine Initiative (SATVI), Cape Town, South Africa

Introduction | In Uganda, home births are prevalent therefore not all newborns receive the Bacillus Calmette-Guerin (BCG) at birth as recommended by the country's vaccination policy. We aimed to compare BCG-induced T cell responses in infants who received BCG soon after birth with those that received the vaccine at 6 weeks of age. Our hypothesis was that infants who were vaccinated at birth would show lower BCG-specific T cell response compared with infants vaccinated at 6 weeks of age.
Methods | In a cross-sectional study, we enrolled 9 months-old infants who had received BCG at birth (n=44) or at 6 weeks of age (n=40). Peripheral blood was drawn from each infant and was left unstimulated or stimulated with BCG in a short-term whole blood assay. The cells were stained for intracellular cytokines and acquired on a multicolour flow cytometer to measure the BCG-specific T cell responses.
Results | Males and females were equally represented in both vaccination groups. All infants showed a robust BCG-specific Th1 (IL-2, IFN-γ and TNF-α), Th17 (IL-17) and Tc (Perforin) CD4 and CD8 T cells response. Birth vaccinated infants showed a higher frequency of CD4 and CD8 T cells producing IFN-γ. Also the frequency of BCG-specific CD8 T cells producing TNF-α was higher in birth than 6–week-old vaccinated infants.
Conclusion | Our findings do not support the hypothesis. We speculate that in infants vaccinated at 6 weeks, co-administration of alum-containing Diphtheria Pertussis and Tetanus (DPT) vaccine may have attenuated BCG-induced IFN-γ producing T cells by priming for Th2 responses.

CHAIRS
Prof. Mecky Isaac Matee
Dr Christian Burri

RAPPORTEURS
Prof. Jean Nachega
Ms Thuli Mthiyane

TO 22

15:25–15:40

In silico mapping of *M. tuberculosis* proteins for Cd4+ T-cell epitopes

Simani Gaseitsiwe • Botswana-Harvard AIDS Institute, Gaborone, Botswana

Introduction | CD4+ T-cells which recognize peptides as presented by MHC class II, have been shown to play an important role in the immune response to *M. tuberculosis* (*Mtb*) infection. We here use a recently described bioinformatics tool, NetMHCIIPan which predicts peptide binding to different MHC class II alleles. The results were compared to published CD4+ T-cell epitopes determined using functional assays.
Methods | 22 *Mtb* proteins were selected for bioinformatics analysis and nine HLA-DR alleles were chosen for the prediction server. The epitope densities for each protein were calculated and ranked. The epitope density is defined as the total number of peptides characterized as high or low binders over the total number of possible binding peptides.
Results | The prediction server predicts the HLA-DRB1-0101 allele as the most active allele with HLA-DRB1-0701 and HLA-DRB1-0401 as second and third. Allele HLA-DRB1-0101 binds 60.24% of the peptides, with 24.68% of those being defined as high affinity binding. Conversely, allele HLA-DRB1-0301 is the least active allele, binding 10.36% of all peptides and contributing to only 4.85% of all peptide binding. Rv0916c was predicted as the protein with the highest epitope density. Comparison with published epitopes show the prediction server has greater than 85% accuracy.
Conclusion | *Mtb* has not been well explored for immune epitopes. We here identify proteins with high epitope densities and show that different HLA-DR alleles have different binding affinities for peptides from the proteins. These data is useful in determining universal epitopes which can be useful in vaccine design and in immune-monitoring.

MO 17

14:00–14:15

Challenges in carrying out multicentre clinical trials in a consortium: the GMZ2 experience

Dawit Ejigu • African Malaria Network Trust, Dar es Salaam, Tanzania

Introduction | Funded by EDCTP, the GMZ2 consortium with 6 African and 2 European partners was set up to foster capacity in African sites through the conduct of GMZ2 malaria vaccine trials and networking. The consortium has 4 clinical trial sites. This paper is based on experiences gained in the GMZ2 consortium.
Results | GMZ2 consortium sites varied in the level of experience and capacity to conduct vaccine clinical trials. Opinions differed whether to carry out clinical trials only in experienced sites or to build capacity in the younger sites. As implementing trials is the best way to acquire experience, a win-win strategy was agreed upon where the experienced sites mentor upcoming sites to ensure quality and share experience. Joint review of trial applications is the current trend for multicentre trials in Africa. This is efficient and allows for further development of African regulatory authorities. The GMZ2 consortium, however, incurred delays because of the logistics of the review. Due to tight malaria transmission season, a joint review was not possible. Expenditure on capital equipment took place early in the project. After baseline studies, in one of the sites the trial could not be initiated due to a decline in malaria. This resulted in various pressures within the consortium. However, the site that could not recruit remained a partner in the consortium where it contributes data management and in other ways.
Conclusion | To ensure successful clinical trials in a consortium, issues such as planning for trial approval, timely expenditure and mentorship for younger sites need to be addressed.

CHAIRS
Dr Modest Mulenga
Prof. Peter Kremsner

RAPPORTEURS
Dr Kamija Phiri
Dr Badara Cisse

MO 18

14:15–14:30

Successful experiences in setting up a new site for phase II malaria vaccine testing in Uganda

Fred Kironde • College of Health Sciences, Makerere University, Kampala, Uganda

Introduction | In fighting malaria, an effective vaccine will be an asset. Makerere University is a member of the GMZ2 malaria vaccine consortium. To prepare for a phase IIb trial of the GMZ2 malaria vaccine candidate, we conducted capacity building activities including a baseline study designed to characterize our trial site in Iganga district, to enhance community awareness about malaria and assess the incidence of malaria in local children.
Methods | This paper describes activities and achievements in establishing a well functioning clinical trial site at Iganga in Eastern Uganda.
Results | A team consisting of young professionals has been set up and trained. In the process, the site underwent several site assessment and audit visits. We undertook training in standard operating procedures for clinical, community, data management and laboratory procedures. In this regard, we carried out intensive workshops and mentorship by local and visiting experts from other collaborating sites. Some of our staff members travelled abroad to attend workshops or gain hands-on skills. Several staff members registered for long term training. We now have a strong team consisting of senior scientists, a senior paediatrician, an internist, several other physicians, pharmacists, nurses, and well trained laboratory and data personnel. The site also boasts more than 20 GCP trained field workers. Using the capacity developed, the site is running the GMZ2 clinical trial smoothly.
Conclusion | The Makerere University Iganga site has been developed and is running its first vaccine clinical trial.

MO 19

14:30–14:45

Prospective study of the incidence of clinical malaria in the malaria vaccine candidate GMZ2 future trial site

Tiga David Kangoye • Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso

Introduction | An effective malaria vaccine will be a great asset in the global effort to reduce the malaria burden. To prepare for a phase IIb trial of the GMZ2 malaria vaccine candidate, a study was conducted as part of the site characterization activity, to assess the incidence of malaria in children aged 6–60 months.
Methods | Two cohorts of children were followed up during the high malaria transmission season of 2009. In the active cohort (AC), field workers visited the children twice a week to document occurrence of malaria episodes. In the passive cohort (PC), caregivers of children were encouraged to attend to the nearest health facility, should the child feel sick. In both cohorts, a malaria smear was obtained when there was fever (tympanic temperature ≥38.0°C).
Results | A total of 1110 children (513 in PC and 597 in AC) were enrolled. Using the most stringent case definition for malaria episode (temperature ≥38.0°C + *P. falciparum* density ≥5000 trophozoites/µL), 122 episodes were recorded in the PC and 147 in the AC. The cumulative incidence of episodes was 24.7 in the PC *vs* 26.5 in the AC. The incidence rate of clinical malaria was 0.09 episodes/child/month (95%IC (0.07–0.11)) in the PC *vs* 0.09 (95% CI (0.07–0.11)) in the AC.
Conclusion | Malaria burden is high in the study area. For the future GMZ2 malaria vaccine trial, either methods (active and passive) could be used with the confidence to capture the maximum data required for endpoints efficacy analysis.

CHAIRS
Dr Modest Mulenga
Prof. Peter Kremsner

RAPPORTEURS
Dr Kamija Phiri
Dr Badara Cisse

MO 20

14:45–15:00

Baseline epidemiological study in preparation for a phase IIb efficacy trial of GMZ2 candidate malaria vaccine

Kalifa Bojang • Medical Research Council Unit, The Gambia

Introduction | In preparation for a phase IIb proof of concept efficacy trial of GMZ2 candidate malaria vaccine, we carried out a baseline epidemiological study in children aged 3–84 months living in the Upper River Region of The Gambia. The objective was to determine incidence rates of clinical malaria in the malaria transmission season.
Methods | Passive and active case detection (PCD and ACD) cohorts were followed throughout the malaria season. Mothers/guardians of children in the PCD cohort were encouraged to take their child to the health centre closest to their home at any time after enrolment if the child became unwell. Children participating in the ACD cohort were visited by trained field workers twice a week. In both cohorts, a malaria smear was obtained whenever fever (tympanic temperature 38.0°C or higher) or history of recent fever was present. A clinical episode of malaria was defined as an illness associated with a tympanic temperature of 38.0°C or more and with a *P. falciparum* parasite density of 5000/µL or more.
Results | 1681 children (1328 in PCD cohort and 353 in ACD cohort) were enrolled and followed during the malaria transmission season. 18 first or only clinical episodes of malaria were recorded in the PCD cohort (incidence 0.1 per 1,000 child days at risk) and 10 in the ACD cohort (incidence 0.3 per 1,000 child days at risk).
Conclusion | In recent years, there has been a dramatic reduction in the incidence of malaria in The Gambia. Thus, a malaria vaccine trial in the study area would require large sample sizes.

MO 21

15:10–15:25

A randomised controlled phase Ib trial of the malaria vaccine candidate GMZ2 in African children

Larissa Aurore B. Hounkpatin • Medical Research Unit, Albert Schweitzer Hospital, Lambaréné, Gabon

Introduction | GMZ2 is a fusion protein of *P. falciparum* merozoite surface protein 3 (MSP3) and glutamate rich protein (GLURP) that mediates an immune response against the blood stage of the parasite. Two previous phase I clinical trials, one in naïve European adults and one in malaria-exposed Gabonese adults, showed that GMZ2 was well tolerated and immunogenic. We present data on safety and immunogenicity of GMZ2 in 1–5 year old Gabonese children, a target population for future malaria vaccine efficacy trials.
Methods | 30 children 1–5 years of age were randomised to receive 3 doses of either 30 µg, 100 µg of GMZ2, or rabies vaccine. GMZ2, adjuvanted in aluminum hydroxide, was administered on days 0, 28 and 56.
Results | All participants received a full course of their respective vaccination and were followed up for one year. Both 30 µg and 100 µg GMZ2 vaccine doses were well tolerated and induced antibodies and memory B-cells against GMZ2 as well as its antigenic constituents MSP3 and GLURP. After three doses of vaccine, the geometric mean concentration of antibodies to GMZ2 was 19-fold (95% CI: 11–34) higher in the 30 µg GMZ2 group than in the rabies vaccine controls, and 16-fold (7–36) higher in the 100 µg GMZ2 group than the rabies group. Geometric mean concentration of antibodies to MSP3 was 2.7-fold (1.6–4.6) higher in the 30 µg group than in the rabies group and 3.8-fold (1.5–9.6) higher in the 100 µg group. Memory B-cells against GMZ2 developed in both GMZ2 vaccinated groups.
Conclusion | Both 30 µg as well as 100 µg intramuscular GMZ2 are immunogenic, well tolerated, and safe in young, malaria-exposed Gabonese children. This result confirms previous findings in naïve and malaria-exposed adults and supports further clinical development of GMZ2.

CHAIRS
Dr Modest Mulenga
Prof. Peter Kremsner

RAPPORTEURS
Dr Kamija Phiri
Dr Badara Cisse

MO 22

15:25–15:40

Novel methods to diagnose malaria by detecting hemozoin in intra-erythrocytic parasites -possible limitations

Thomas Hänscheid • Instituto de Microbiologia & Instituto de Medicina Molecular, Faculdade de Medicina de Lisboa, Lisbon, Portugal

Introduction | Laboratory diagnosis of malaria is important in the light of artemisinin based treatments. Novel diagnostic methods are currently being developed; several are based on the detection of hemozoin. First reports are promising, but sensitivity is still low. In fact, young parasite forms may have insufficient hemozoin, which may be an important limitation for these novel methods. This problem was assessed in the study.
Methods | A bench top flow cytometer was used to detect depolarized side scatter as a measurement for hemozoin. Blood from *P. berghei* infected rodents and synchronized and non-synchronized *P. falciparum* cultures were investigated. *P. berghei* parasites were detected by Green-Fluorescent-Protein and *P. falciparum* after DNA staining (SYBR Green). This was compared with the detection of hemozoin in intraerythrocytic parasites.
Results | Using rodent blood (*P. berghei*) only 65% of all GFP+ parasites showed the presence of hemozoin, while in non-synchronized *P. falciparum* cultures only 16%-23.5% were positive by depolarization. In a synchronized *P. falciparum* culture (1.5% parasitaemia, ringworms) only 2% of all parasites showed depolarization. In this culture only 0.09% of all erythrocytes showed depolarization, with a 'background noise' of 0,03% depolarizing events in an uninfected control.
Conclusion | These results confirm that the detection of hemozoin may be a promising diagnostic method. However, at best, 60–70% of parasites could be detected. Insufficient amounts of hemozoin may lead to false negatives and 98% of a population of immature parasites were not detected. This may constitute a significant limitation for these methods in *P. falciparum* infections with predominantly young forms.

PARALLEL SESSION | CROSS-CUTTING

EDCTP-NACCAP capacity building and networking session

14:00–16:10
Conference room 6

14:00–14:05
Introductory remarks

Dr Garry Aslanyan

14:00–14:20
Networks of Excellence East and West Africa

14:20–14:40
Networks of Excellence Central and Southern Africa

CHAIRS
Prof. Willy Spaan
Dr Andrew Kitua

RAPPORTEURS
Ms Amber Abrahams
Dr Stephen Rulisa

NO 06

Building a sustainable Eastern Africa network for capacity strengthening and mentoring in research and health

Prof. Pontiano Kaleebu and Dr George Miiro • MRC/ UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

Introduction | Health research in Eastern Africa is insufficiently funded and this problem is compounded by: fragmented or uncoordinated efforts; inadequate infrastructure; diminishing indigenous experts and deficient networking. Since May 2009, EDCTP supported the establishment of the East African Consortium for Clinical Research (EACCR). To date it consists of 34 regional institutions and 6 northern partners and aims to promote research capacity development, networking and collaborative research.
Methods | EACCR work packages are categorized into: governance, infrastructure, training/mentoring, research, and networking. Governance is structured regionally into 4 nodes: malaria (Kenya), TB (Tanzania), HIV (Uganda) and training (Tanzania). The Uganda Virus Research Institute hosts the secretariat. EACCR integrates scientists, health practitioners, academicians and policy makers from the region (including Ethiopia and Sudan) and Europe. It networks with other capacity-building consortia and development partners.
Results | Upgrades of health, training, data management, and office facilities are on-going at 17 institutions and the nodes. 95 participants engaged in 5 short courses and 3 mentoring visits. 21 masters' fellowships are on-going and 4 EDCTP senior fellowships were secured. A reciprocal monitoring scheme of > 20 regional monitors, overseeing research quality, is operational. Three collaborative research proposals were submitted; a regional social science survey is underway and a communication plan and an interactive website are in use. EACCR secured additional funds from NACCAP and MRC-UK.
Conclusion | EACCR potentially can sustain coordinated collaborative research, improvement of infrastructure, training of human resource and resource mobilization in Eastern Africa in partnership with policy makers and development partners.

Networks of Excellence
East and West Africa

NO 07

The West African Node of Excellence for TB, AIDS and Malaria (WANETAM)

Prof. Souleymane Mboup • Laboratoire Bacterio-virologie, Hôpital Aristide Dantec, Dakar, Senegal

Introduction | TB, HIV-AIDS, and malaria, considered as poverty-related diseases, constitute a burden in terms of morbidity and mortality for West Africa. The management of this dramatic situation is hampered by the limited critical mass of qualified health staff, lack of adequate research infrastructure, and rare funding opportunities for the local research institutions. EDCTP has then considered that bringing together West African scientists from 14 institutions located in 7 countries and making south-south collaboration effective through a network of excellence may be the way to manage the problem.
Methods | The objectives of the consortium are capacity building and technology transfer to prepare the successful conduct of clinical trials and the creation of a network for sub-regional scientific collaborations, including multi-site clinical trials. A work package approach is adopted to run the consortium ranging from project management, training, networking, HIV-related lab training and survey, TB-related lab training and survey, and malaria-related lab training and survey respectively.
Results | In total, 4 cross-cutting training sessions and 2 disease-specific (hands-on) training sessions have been conducted so far by WANETAM. This training has targeted 180 junior and senior West-African scientists. The training has covered the following topics: GCP, GCLP, ethics, grant writing, data analysis, data management, HIV drug resistance, and TB diagnostics.
Conclusion | The training sessions conducted by WANETAM have significantly increased the critical amount of qualified personnel within our institutions. The south-south collaboration has become a reality within our network.

CHAIRS
Prof. Willy Spaan
Dr Andrew Kitua

RAPPORTEURS
Ms Amber Abrahams
Dr Stephen Rulisa

Networks of Excellence
Central and Southern
Africa

NO 08

Central Africa at front stage through CANTAM for conduct of clinical trials

Prof. Francine Ntoumi and Dr Odile Ouwe-Missi-Oukem-Boyer • Fondation Congolaise pour la Recherche Medicale, Brazzaville, Congo

The aim of the Central Africa Network for Tuberculosis, HIV/AIDS and Malaria (CANTAM) is to establish clinical trials sites in one of the less developed regions of Africa regarding clinical research. Therefore, CANTAM has chosen to make important investments in capacity building, networking activities and advocacy at the local, regional and international levels. Since 2009, CANTAM has organised specific workshops in developing SOPs for malaria and tuberculosis, and crosscutting workshops on GCP, writing skills, ethics, and search of scientific literature. Exchanges between CANTAM institutions have allowed staff to experience different laboratory and field settings, data management, and collaborative protocol writing. CANTAM has supported staff development and academic training and at least 10 PhD students have been registered so far. In each country, CANTAM has invested in research advocacy and has facilitated interactions between scientists and national authorities. In order to avoid duplication of efforts and strengthen synergies, CANTAM has developed relationships with other regional Networks of Excellence, including WANETAM, EACCR, and TESA and organisations like ARCEAU, WWARN, AMANET, CAMBIN, TRREE for Africa, CLEAR, and ISHReCA. Capacity building, networking and advocacy activities carried out by the management team of CANTAM have helped to put Central Africa front stage Now the challenge is to move the network forward with additional regional partners and additional funding including from local sources. Lessons have been learnt and CANTAM will definitely continue to play a leading role in the region.

Networks of Excellence Central and Southern Africa

NO 09

TESA: A model of clinical research capacity building in Southern Africa

Dr Alexander Pym and Mrs Maerangis Rahmani • Medical Research Council, Cape Town, South Africa

Introduction | To strengthen clinical research capacity on TB, HIV/AIDS and malaria in Southern Africa, in 2007 EDCTP called for the establishment of four African consortiums. Trials of Excellence in Southern Africa (TESA) presents a model for a Southern network.
Methods | In absence of a standard evidence- based tool, we simulated a framework used for institutionalising quality assurance and adopted three approaches: we identified current research institutes, benchmarked the research capacity of these institutes based on 10 identified indicators, and devised a capacity building strategy following a ranking exercise.
Results | Eleven research institutes and academia working on the three major infectious diseases HIV, TB and malaria were identified in 6 Southern African countries: Botswana, Malawi, Mozambique, South Africa, Zambia, and Zimbabwe. The UCT-Lung Institute (mean rank 3.9), Stellenbosch University (3.7) TB Unit of Medical Research Council (3.1) plus the Manhiça Research Centre in Mozambique (3.1) scored the highest ranks. The mean score of all eleven institutes on the ten capacity building indicators reached 2.93 (out of 4).
Conclusion | 11 heterogeneous research institutions in 6 countries were identified. Four institutes (UCT-Lung Institute, SUN-Immunological Department, SAMRC-TB Research Unit and Manhiça Research Centre in Mozambique) ranked as the strongest institutions. No significant variation in the indicators of research capacity was observed when benchmarking the institutions. Therefore the ten research capacity indicators are equally important as regards strengthening the institutions. TESA represents a collaborative, evidence-based model, replicable in other settings. The combination of long-term academic training, short courses, infrastructure upgrades plus practical research opportunities is recommended.

CHAIRS
Prof. Willy Spaan
Dr Andrew Kitua

RAPPORTEURS
Ms Amber Abrahams
Dr Stephen Rulisa

14:40–15:00
Panel discussion

Prof. Irene Agyepong, Dr Val Snewin and Dr Opokua Ofori-Anyinam

15:10–15:25
Reflection on the NACCAP programme and integration of activities with future EDCTP programme

Dr Andrew Kitua

15:25–15:55
General discussion on new ideas for input into future research strategy

Dr Garry Aslanyan

15:55–16:05
Presentation NACCAP final booklet

Dr Eva Rijkers

16:05–16:10
Closing remarks

Prof. Willy Spaan and Dr Garry Aslanyan

Wednesday 12 October 2011

08:00–09:00 **Special sessions**
Grant writing for scientists
[CONFERENCE ROOM 3]
Scientific publication writing for scientists
[CONFERENCE ROOM 5]

08:00–10:30 **Plenary session III**
Presentations from EDCTP partners
[CONFERENCE ROOM 1]

10:30–11:00 Coffee / Tea break

11:00–12:00 **Parallel sessions**
North-South and South-South partnerships for quality improvement research in sub-Saharan Africa
HIV/AIDS [CONFERENCE ROOM 1]
Tuberculosis [CONFERENCE ROOM 3]
Malaria [CONFERENCE ROOM 5]
Cross-cutting [CONFERENCE ROOM 6]

12:00–13:00
Poster presentations / Marketplace
[EXHIBITION AREA]

13:00–14:00 Lunch

14:00–15:30 **Parallel sessions**
North-South and South-South partnerships for quality improvement research in sub-Saharan Africa (cont.)
HIV/AIDS [CONFERENCE ROOM 1]
Tuberculosis [CONFERENCE ROOM 3]
Malaria [CONFERENCE ROOM 5]
Cross-cutting [CONFERENCE ROOM 6]

15:30–16:00 Coffee / Tea break

16:00–17.10 **Plenary session IV**
Recommendations, award giving ceremony and closing remarks [CONFERENCE ROOM 1]

PO 01

08:00–08:12

International AIDS Vaccine Initiative (IAVI) collaborative network in Africa

Mr Jean-Louis Excler • International AIDS Vaccine Initiative, USA

The HIV pandemic takes its greatest toll in Africa where intense research activities carried out by African research teams and their international collaborators have led to a better understanding of the epidemic. IAVI supports a network of clinical and laboratory teams in Kenya, Rwanda, South Africa, Uganda and Zambia, and lab activities in Malawi along with multiple co-funders including EDCTP. All teams conduct their work according to the highest standards of ethics, Good Clinical Practices and Good Clinical Laboratory Practices.

A framework of sustainable funding on which African teams can build is critically needed in order to maintain long-term research capacity and expertise in Africa and to provide a basis for multiple intervention trials. Lake Victoria's fishing industry involves more than a million men, women and children, who are severely medically underserved. IAVI was a key partner in the EDCTP-funded Fisherfolk Project, which has established that this population is amenable to research, with acceptable follow-up. As part of the project, service providers were engaged in basic medical services, family planning and HIV services, previously inaccessible to this population. Both HIV prevalence and incidence in this group are about 5 times that of the general population, the group is suitable for prevention and intervention studies, including vaccines. This project, initiated at a pilot level by the institutions at Uganda Virus Research Institute (UVRI) and carried forward with EDCTP support, provides a model of collaboration and achievements. UVRI-IAVI and MRC-Uganda plan to continue the research, as resources allow, developing a cohort for future studies.

CHAIRS
Prof. David Ofori-Adjei
Dr Christian Burri
Dr Opokua Ofori-Anyinam

RAPPORTEUR
Mr Paul Chinnock

PO 02

08:12–08:24
UNITAID: innovative financing for health

Dr Philippe Duneton • UNITAID, Switzerland

Established in 2006, UNITAID has raised over US$ 2 billion through an innovative financing mechanism aimed at impacting markets for public health benefits in HIV/AIDS, tuberculosis and malaria. 80% of UNITAID funds come from a small levy placed on air tickets.

UNITAID's unique business model uses interventions in carefully chosen niche markets for the treatments, diagnostics and prevention of the three diseases. These interventions are selected in order to create or improve markets of these products by providing incentives for manufactures to enter or develop a market, by negotiating better prices, ensuring the use of quality products that are made available in a timely manner.

To date over 94 countries benefit from UNITAID funded commodities in the fight against HIV/AIDS, tuberculosis and malaria. UNITAID success relies on partners such as EDCTP to ensure that better quality and adapted treatments that suit patient's needs are developed. Through its business model and careful investment, UNITAID can assist in work towards the uptake of such products and promote positive market impact and sustainability.

PO 03

08:24–08:36
Wellcome Trust research capacity building initiatives

Dr Val Snewin • Wellcome Trust, UK

Here we will present examples of research capacity building initiatives. This includes the £30 million African Institutions Initiative, which aims to develop institutional capacity to support and conduct health-related research by strengthening Africa's universities and research institutions, and develop research networks. More than 50 institutions from 18 African countries are partnered in seven international and pan-African consortia. Each is led by an African institution and includes partners from Europe, the US and Australia.

The Health Research Capacity strengthening initiative is a £20 million partnership with the UK Department for International Development, which aims to strengthen the capacity for generating new health research knowledge within Kenya and Malawi and to improve its use in evidence-based decision making, policy formulation, and implementation.

Another example is the H3 Africa (Human Heredity and Health in Africa Project), established by the Wellcome Trust and the US National Institutes of Health. H3 Africa will see African researchers leading studies of population-wide diseases on continent including non-communicable diseases and disorders such as diabetes and mental health, as well as infectious diseases. Over the next five years, H3 Africa will receive £8 million from the Wellcome Trust

The MRC-DFID-WT Joint Global Health Trials scheme provides funding for the best proposals to generate new knowledge about interventions that will contribute to the improvement of health in low and middle income countries. This scheme is primarily focused on late stage (equivalent to phase III/IV) clinical and health intervention trials evaluating efficacy and effectiveness.

CHAIRS
Prof. David Ofori-Adjei
Dr Christian Burri
Dr Opokua Ofori-Anyinam

RAPPORTEUR
Mr Paul Chinnock

PO 04

08:36–08:48

Strengthening research partnerships: the Bill & Melinda Gates Foundation perspective

Ms Siobhan Malone • Bill & Melinda Gates Foundation, USA

The Bill & Melinda Gates Foundation's efforts in global health aim to harness advances in science and technology to save lives in developing countries. We work with partners to deliver proven tools such as vaccines, drugs, and diagnostics, and to invent new solutions where they don't exist. We invest heavily in vaccines across our portfolio in the hope that one day they can be used to prevent HIV, tuberculosis and malaria; wipe out polio; and prevent deaths due to diarrhoea and pneumonia.

Achieving lasting change in health requires bringing together diverse groups, each with critical roles to play. A large portion of our grant making involves building and strengthening partnerships with organisations around the world, including governments, private companies, research institutes, and international and community organizations. Research partnerships are critical to successful implementation of our HIV, tuberculosis and malaria strategies to improve or develop new drugs, vaccines, and diagnostics.

The foundation supports a number of projects involving research partnerships that either directly or indirectly link with EDCTP-funded activities in sub-Saharan Africa. This presentation will provide examples of those projects and what they have achieved to date to meet the foundation and EDCTP's common goal of ensuring the development and delivery of new and affordable drugs and vaccines for HIV, tuberculosis and malaria for those most affected in developing countries.

PO 05

08:48–09:00

ESSENCE on health research

Dr Garry Aslanyan • World Health Organization, Switzerland

ESSENCE (Enhancing Support for Strengthening the Effectiveness of National Capacity Efforts) on health research is an initiative to increase effectiveness of research for health in Africa and is a collaborative framework between funding agencies to scale up coordination and harmonisation of the research capacity investments. It aims to improve the impact of investments in institutions and people, and provides enabling mechanisms that address needs and priorities within national strategies on research for health.

Based at the TDR Special Programme for Research and Training in Tropical Diseases executed by the World Health Organization in Geneva, ESSENCE's current Executive Steering Committee consists of Sida, the Wellcome Trust and the Dutch Organization for Scientific Research (NWO/WOTRO, Netherlands). ESSENCE on Health Initiative is open to a broad range of funders interested in collaboration, harmonisation and better alignment with country needs. Some of the current members include the UK Department for International Development (DFID), Canada's International Development Research Centre (IDRC), Norwegian Agency for Development Cooperation (Norad), Ministry of Foreign Affairs of Denmark (Danida), the Bill & Melinda Gates Foundation, FIOCRUZ Brazil, Howard Hughes Medical Institute, NEPAD (New Partnership for Africa's Development), EDCTP and NIH/FIC (US National Institutes of Health/Fogarty International Center), Rockefeller Foundation and Canada's Global Health Research Initiative (GHRI).

ESSENCE members embrace the strong agreement within the international development and research communities that funding should be aligned with national priorities. The initiative recognises that successful research capacity also requires competencies in issues such as governance and management, strategic planning, evidence assessment, ethics and translation of evidence into policy.

CHAIRS
Prof. David Ofori-Adjei
Dr Christian Burri
Dr Opokua Ofori-Anyinam

RAPPORTEUR
Mr Paul Chinnock

PO 06

09:00–09:12

Partnering to develop the next generation of medicines to combat malaria

Dr Stephan Duparc • Medicines for Malaria Venture, Switzerland

After the development of fixed dose artemisinin combination therapies (ACT), the challenge now is to develop non-ACT drug combinations. Medicines for Malaria Venture (MMV) has pioneered three new ACTs: Coartem-Dispersible (artemether-lumefantrine), with Novartis, which was approved in 2008 by the stringent authority Swissmedic, then by WHO prequalification; Eurartesim (DHA-piperaquine), with sigma-tau, which has obtained the first positive opinion for an antimalarial drug from the European Medicines Agency (EMA) in June 2011 and Pyramax (pyronaridine-artesunate), with Shin Poong, submitted to the EMA in March 2010 and still under review. We will briefly discuss the advantages and challenges of each medicine. In addition, MMV has supported Guilin pharmaceutical for the development of Artesun (artesunate injectable) which is the first parenteral artesunate to have obtained WHO pre-qualification in November 2010.

We are profiling the next generation of synthetic peroxides with a view to identifying suitable next generation medicines that could be effective against the emerging *P. falciparum* strains resistant to the artemisinins. Our hope is to simplify the treatment regimens eventually to a single dose. The major medium term objective is the development of OZ439, a new endoperoxide, currently in phase IIa. The next step will be to develop suitable combinations with this promising compound. Other compounds currently in phase I should move to phase IIa in the next few months. Finally, with our partners we are pioneering the next generation of therapies for the eradication agenda, including transmission blocking medicines, and medicines targeting the hypnozoite of *P. vivax* – the cause of relapsing malaria.

PO 07

09:12–09:24

Aeras and EDCTP: partnering to support TB vaccine clinical trials

Dr Vicky Cárdenas • Aeras, USA

Aeras and EDCTP share a common objective of accelerating the development of efficacious TB vaccines through the formation of partnerships with research institutions in high burden countries to ensure there is sufficient capacity, resources and support for clinical trials.

Large-scale clinical trials for new TB vaccines require multiple field sites with the infrastructure and capacity to screen, enrol, monitor, diagnose and follow up several thousand participants. Clinical staff must be current in good clinical practice (GCP) training, have experience in the diagnosis of TB and have established a trusting relationship with the populations they serve. Further, sites must have access to accredited microbiological and immunological laboratories and have strong quality control mechanisms in place. An important part of the Aeras-EDCTP partnership is to collaborate with local research institutions to strengthen these capacities and to provide technical support and financial resources for site development and the conduct of clinical trials.

Aeras and EDCTP have partnered with institutions in Kenya, Uganda, Mozambique, South Africa and Senegal to ensure capacity for large-scale trials. Aeras and EDCTP are also working with institutions in these countries to implement two significant TB vaccine clinical trials: a multicentre phase IIb study of vaccine candidate AERAS 402/Crucell Ad35 in healthy infants, and a phase IIb trial of vaccine candidate MVA85A/AERAS-485 in HIV-positive adults.

Efficacy trials for TB vaccines are large, complex and costly. Collaboration amongst multiple partners, such as that between Aeras, EDCTP and local research institutions, is critical to their success.

CHAIRS
Prof. David Ofori-Adjei
Dr Christian Burri
Dr Opokua Ofori-Anyinam

RAPPORTEUR
Mr Paul Chinnock

PO 08

09:24–09:36

African Society for Laboratory Medicine (ASLM): advancing the laboratory profession and networks in Africa

Dr Giorgio Roscigno • FIND, Switzerland

The mission of the ASLM is to advance professional laboratory medicine practice, science, systems, and networks in Africa needed to support preventive medicine, quality care of patients and disease control through partnership with governments and relevant organisations. ASLM is a Pan-African professional body, endorsed by the African Union, working with countries to advocate for the critical role and needs of laboratory medicine and networks.

ASLM has eight strategic areas: advocacy; laboratory accreditation and quality management systems; laboratory workforce development; laboratory-clinical interface; research capacity and publication; laboratory strategy and networks; technical assistance; and policy.

Laboratory services are indispensable to health systems. The medical laboratory plays a pivotal role in diagnosis, surveillance, outbreak investigation, initiation and monitoring of therapy, as well as in research and development. In sub-Saharan Africa, health systems are undervalued and seldom adequately provided with resources. This compromise the quality of patient care due to misdiagnosis and consequent under/over treatment of disease. This presents significant economic and public health challenges. An historical movement toward accreditation and enhanced laboratory systems has gained momentum in the past few years throughout Africa and amongst the international aid community.

The successful implementation of ASLM strategy depends on consistent dedication and involvement of the Ministries of Health and other development partners. The health and future of Africa will be revolutionized as African laboratories will unify their partners and strengthening country ownership and involvement, with the goal of strengthening health systems.

PO 09

09:36–09:48
AAVP: building partnerships for the common good

Dr Chidi Nwneka • African AIDS Vaccine Partnership (AAVP), Uganda

The African AIDS Vaccine Programme (AAVP) was established in 2000 by the WHO and UNAIDS, in partnership with African scientists and other major HIV vaccine R&D partners across the world, to address the gap in Africa's involvement in HIV vaccine R&D. As the African voice with respect to HIV vaccine issues, AAVP's primary goal is to ensure significant African ownership of and contribution to all phases of development of an effective HIV vaccine suitable for use in Africa.

The primary focus of AAVP's activities is the promotion of the African HIV vaccine agenda with four main interrelated programme areas: resource mobilisation for HIV vaccine R&D; capacity building; HIV vaccine advocacy; and partnership support programme.

AAVP focuses on building partnerships which will enhance the common good. Being a non-funding body, and non-research implementer, AAVP's activities are geared towards enhancing the work of its partners who are either funding institutions or research implementers.

For example, AAVP plans to work with African business communities and governments to set up an HIV vaccine research and development trust fund. When established, this fund will be used to promote HIV vaccine research and development in Africa led by Africans in collaboration with groups from other parts of the world.

In doing this AAVP will utilise the mechanisms of established funding organisations such as EDCTP which will act as administrators of the research and development grants. Thus AAVP, in addition to being Africa's voice on HIV vaccine issues, works towards building effective partnerships for the common good.

CHAIRS
Prof. David Ofori-Adjei
Dr Christian Burri
Dr Opokua Ofori-Anyinam

RAPPORTEUR
Mr Paul Chinnock

PO 10

09:48–10:00

Global health trials: supporting clinical research by sharing practice, methods and knowledge

Dr Trudie Lang • Kemri-Wellcome Programme, Kenya and University of Oxford, UK

Communities in developing countries are under-represented in research and there is also a need for more clinical trials to bring new treatments and vaccines, as well as trials that answer disease management questions.

Global Health Trials is an open partnership project that is working closely with EDCTP. It is a free website for all those who work in and around clinical trials, to access each other and build professional networks and to seek guidance, support, resources and tools. It already has over 11,000 users from 56 developing countries.

At this meeting we are launching the Global Health Trials professional membership scheme. This offers all levels and roles of staff the opportunity to build a valid and recognised training record and have personalised career support, whilst developing and enhancing professional recognition. This scheme is linked to the free e-learning centre and is developed in partnership with WHO/TDR, EDCTP and WWARN with funding from the Bill and Melinda Gates Foundation.

PO 11

10:00–10:12

Microbicides Development Programme (MDP): future plans

Dr Sheena McCormack • Medical Research Council, UK

With emerging evidence that early treatment is beneficial to the HIV-positive individual, as well as highly effective at preventing transmission, there is a risk that new prevention technologies will be side-stepped in favour of scaling up treatment.

In order to capitalise on the momentum created by the clinical trial results, it is important to focus on what is feasible to implement. A single dose of tenofovir 1% vaginal gel applied prior to sex would be easy to roll out, in contrast to a daily tablet regimen that would require more intensive safety and resistance monitoring, and be challenging to promote in regions where no more than 50% of those in need are on anti-retroviral therapy. Efficacy will be undermined by missed doses to a greater extent than daily or 'before and after' regimens.

The Microbicides Development Programme has completed a trial of coital gel (MDP301) and daily gel (Top-Up), and collected extensive qualitative data in five countries in sub-Saharan Africa. We propose two alternative designs to assess the effectiveness of a single dose of gel applied prior to sex: one using placebo, and one open-label.

Each of the trials is designed to assess the effectiveness of a single dose of tenofovir 1% vaginal gel, applied prior to sex, in the prevention of HIV and HSV-2 acquisition. MDP302 would compare this to a single dose of placebo gel applied prior to sex, and MDP401 would compare the HIV incidence in women on gel to those that are not given any gel for the first 12 months.

CHAIRS
Prof. David Ofori-Adjei
Dr Christian Burri
Dr Opokua Ofori-Anyinam

RAPPORTEUR
Mr Paul Chinnock

PO 12

10:12–10:24

African Network for Drugs and Diagnostics Innovation (ANDI)

Dr Solomon Nwaka • World Health Organization, Switzerland

ANDI is an African-led innovation network that provides a time-efficient and cost-effective approach to achieving the overarching goal of linking innovation to development in the field of pharmaceuticals and health. The vision is to create a sustainable platform for R&D innovation in Africa to address Africa's health needs.

Specific Goals:

- Increase R&D collaboration among African institutions and countries, including through the management of Centres of Excellence in health innovation
- Fund and manage a portfolio of health R&D projects
- Support the establishment of public-private partnerships and new firms for the development and manufacture of new drugs, diagnostics and other health products in Africa
- Manage and explore innovative mechanisms to encourage and reward local innovation while promoting access, including research drawing on traditional medicine and intellectual property management
- Leverage existing capacity to support south-south and north-south collaboration
- Promote long-term economic sustainability through supporting R&D and access to health products in Africa.

Highlight of progress to date include the development and endorsement of the strategic business plan based on local priorities; identification of UNECA as the host agency in Africa; establishment of a ministerial level governance board; implementation of the first pan-African Centres of Excellence; and the successful launch of first call for product R&D projects, with over 200 proposals received.

The establishment of ANDI is supported by several African institutions, WHO through TDR, AFRO and EMRO regional offices, UNECA, African Development Bank and others. We acknowledge financial support from the European Commission.

HO 23

11:00–11:15

Cohort study among female bar and hotel workers in Tanzania in preparation for phase III microbicide and other HIV intervention clinical trials

Joseph Elieza Chilongani • National Institute for Medical Research, Mwanza Centre, Tanzania

Introduction | This study was designed to evaluate the feasibility of establishing a cohort of women at high risk of sexually transmitted infection (STIs), including HIV, for future phase III microbicide and other HIV intervention trials; and to obtain information on key indicators required to design future trials.
Methods | Women aged 18–44 years, working in recreational facilities were screened and if eligible recruited. Eligible women were enrolled and followed up quarterly for 1 year. At each visit, participants were interviewed to obtain information about potential HIV risk factors, sexual behaviours and factors associated with lost to follow-up. Samples were collected and tested to measure the burden of STIs and other genital infections and pregnancy rates. We analysed data collected at enrolment and during the follow-up period to determine independent risk factors for STIs, pregnancy and trend of changes in risky sexual behaviours.
Results | Majority of participants were aged 20–19 years (57%), with primary education (87%), widowed, separated or divorced (49%). HIV prevalence at screening was 22% and was associated with age, education, marital status and type of job. HIV incidence was 4.1/100 person years. Overall prevalence of other STIs was also very high. Overall pregnancy incidence was high 30.3/100 person years and was associated with age, use of contraceptives and number of previous pregnancies. Many women reported multiple sexual partners (32%) and very low condom use, apart from high level knowledge on condom (99%).
Conclusion | We observed very high prevalence and incidence of HIV and other STIs in the study population. Likewise, high pregnancy incidence and reported risky sexual behaviours were common. Effective interventions to reduce the burden of HIV and other STIs and to promote safer sexual practices are urgently needed in this population.

CHAIRS
Dr Modest Mulenga
Dr Rosemary Musonda

RAPPORTEURS
Dr Jonathan Kayondo
Dr Louis Marie Yindom

HO 24

11:15–11:30

Prevalence of reproductive tract infections (RTI) in women targeted for microbicide trials: the microbicide safety biomarkers study in Kenya, Rwanda, and South Africa

Mary Mwaura • International Centre for Reproductive Health, Mombasa, Kenya

Introduction | The ideal microbicide should reduce the risk of HIV infection while preserving the integrity of the cervicovaginal epithelium. Reproductive tract infections (RTI) could hamper the effect of microbicides.
Methods | The Microbicide Safety Biomarkers study seeks to establish baseline RTI prevalence in a prospective cohort of adult pregnant and non-pregnant women and adolescents from three sites in East and South Africa. 430 women will be enrolled by August 2011 and followed up over 7 visits. Biomarkers of cervico-vaginal inflammation, target cells, the microbiome, and RTI will be studied. Preliminary screening data are presented here.
Results | In 202 women screened to date, mean age is 24.8 years. Mean age at sexual debut is 17.6 years (SD 2.8), half have never been married, and median parity is 1. RTI prevalence by site is presented in table 1. According to Nugent's criteria 28.7% of women had bacterial vaginosis, 11.2% intermediate flora, and 60.1% normal vaginal flora. Updated results will be presented at the meeting.

Table 1: RTI prevalence at screening for the three study sites

	Candida	TV	CT	NG	syphilis	HSV-2	Bacterial vaginosis
Kenya all (n=130)	14.1%	3.9%	2.4%	0.8%	0%	25.4%	25.2%
Adolescents (n=22)	4.8%	13.6%	0%	0%	0%	9.1%	13.6%
Rwanda (n=30)	10.3%	10.3%	10.7%	7.1%	10.3%	46.4%	37%
South-Africa (n=42)	7.1%	11.1%	28.6%	2.4%	0%	43.6%	35.3%

Conclusion | Among African women targeted for microbicide trials, RTI are common and may vary by region. Therefore, it is essential that the effects of RTI on the efficacy and safety of microbicides are evaluated.

HO 25

11:30–11:45

Community trial to prevent HIV/STDs among rural youths in post-conflict Liberia

Stephen B. Kennedy • University of Liberia, Monrovia, Liberia

Introduction | Due to a destroyed public health system and the loss of trained health personnel in post-conflict Liberia, HIV surveillance and prevention efforts are in a nascent stage. Rural youths often lack access to HIV/STD-related prevention knowledge, services and/or resources, especially in a post-conflict setting like Liberia where risky sexual behaviours have not been adequately studied.
Methods | Four rural communities were matched and randomised to either an evidence-based HIV/STD risk reduction program or a corresponding general health comparison program. 250 youths aged 14–17 years completed the baseline surveys and received 8 modules of the respective programs over 4 consecutive weeks by trained co-facilitators. After program administration, longitudinal follow-up surveys were administered to each participant in order to assess the impact of the programs on mitigating HIV/STDs among rural youths.
Results | Overall, the immediate post-test results revealed that youths in the intervention communities were relatively more likely to be knowledgeable about HIV/AIDS, have positive attitudes about condoms, have used condoms in the past three months, use condoms in the next 3 months, and carry condoms when compared to youths in the general health comparison communities.
Conclusion | Post-conflict countries in sub-Saharan Africa are in urgent need of evidence-based HIV/STD behavioural-driven intervention programs. With limited resources to address the nascent HIV/AIDS epidemic, changing the norms, attitudes and behaviours of youths may be the key to preventing the spread of HIV/STDs.

CHAIRS
Dr Modest Mulenga
Dr Rosemary Musonda

RAPPORTEURS
Dr Jonathan Kayondo
Dr Louis Marie Yindom

HO 26

11:45–12:00

Methicillin Resistant Staphylococcus aureus nasal carriage in HIV-infected patients in Lagos, Nigeria

Adesola Olalekan • Ladoke Akintola University of Technology, Ogbomosho, Nigeria

Introduction | Methicillin resistant *Staphylococcus aureus* (MRSA) nasal colonization is an important risk factor for *S. aureus* infection in HIV patients because of the morbidity and mortality associated with staphylococcal infections. Therefore, detection of MRSA is important for therapy and management of HIV-infected patients. The objectives of this study are to determine the rate of *S. aureus* nasal colonization, the prevalence of MRSA, and to study the *in vitro* antibiotic susceptibility pattern in association to MecA gene in this population.
Methods | This is a cross sectional study in which nasal swabs were collected from 187 ambulatory HIV adults attending the Mainland General Hospital outpatient clinic in Lagos. Antibiotic susceptibility disk diffusion was used to characterize the phenotypic expression while the identification of the MRSA was aided by the amplification of the MecA gene using PCR..
Results | The results showed that 35% 176/500 (at least one positive culture) were nasal carriers of *S. aureus*, 27% (51/187) are intermittent carriers, 25% (47/187) were persistent carrier, while 48% (89/187) are non-carriers. The MecA gene was detected in 16% (27/176) of *S. aureus* isolates from this study. Most of the MSSA (Methicillin Sensitive *S.aureus*) and MRSA were multiresistant to ampicillin (100%), cotrimixazole (92%), tetracycline (81%), and amoxyllin (75%).
Conclusion | This study shows that multidrug resistant *S. aureus* and MRSA are common among HIV patients in Nigeria. Continuous survellance of resistant data, as well as emphasizes on the need for MRSA monitoring in HIV-infected patients is necessary to reduce associated secondary infections.

TO 23

11:00–11:15

Detailed functional assessment of the immune response to *M. tuberculosis* in HIV-TB co-infected individuals

Wendy Burgers • University of Cape Town, South Africa

Introduction | HIV and TB interact in a deadly synergy. HIV causes increased infection *by M. tuberculosis* (*Mtb*), whilst TB accelerates progression to AIDS. A better understanding of the immune interactions of these two diseases is paramount. Susceptibility to TB is increased from the earliest stages of HIV infection. We examined the effect of HIV co-infection on adaptive immune responses to *Mtb*.
Methods | We studied co-infected persons early in HIV infection, with CD4 counts higher than 500 cells/μL, in order to study early defects in the immune response that are not the result of CD4+ T cell depletion. PBMC were stimulated with mycobacterial PPD and a range of cytokine and cytotoxic mediators were measured by intracellular cytokine staining and polychromatic flow cytometry. T cells from the lungs were obtained by bronchoalveolar lavage.
Results | We found significantly decreased frequencies of T cells specific for PPD in HIV-infected individuals compared to uninfected individuals. *Mtb*-specific CD4+ cells were impaired in their ability to produce IFN-γ, IL-2 and TNF-α, and defects in the production of newly-formed perforin and granzyme B were apparent for CD8+ T cells, indicating a reduced cytotoxic ability. Preliminary results from bronchoalveolar lavages indicate the presence of *Mtb*-specific cells in the lungs.
Conclusion | HIV causes defects in a range of functions mediated by *Mtb*-specific T cells. A better understanding of the immune response to *Mtb* in the context of HIV infection may highlight immune parameters important for control of *Mtb*, and may ultimately lead to new immune interventions, such as more effective vaccines.

CHAIRS
Dr Hulda Swai
Prof. Tumani Corrah

RAPPORTEURS
Prof. Jean Nachega
Dr Getnet Yimer

TO 24

11:15–11:30

M. tuberculosis complex within the tuberculosis case contact study in MRC Unit The Gambia

Tutty Isatou Faal • Medical Research Council Unit, Banjul, The Gambia

Introduction | Tuberculosis is one of the major disease burdens in sub-Saharan Africa. The Gambia has an intermediate incidence of TB, with around 80 smear positive TB cases/100.000/year. In the context of a TB household case contact study, we assessed the proportion of TB due to transmission within the household by genotyping isolates of patients and their diseased household contacts.
Methods | The Tuberculosis Case Contact (TBCC) study from the TB Clinic of the MRC enrols all smear-positive patients (index) and their immediate contacts. 130 index cases with relevant clinical features and a positive Mantoux test, and 46 secondary cases were enrolled between 2002–2009. Sputum was collected, microscopy was done and culture performed by both Bactec 9000MB or MGIT960. Positive cultures were confirmed by standard methods and whole genomic DNA extraction was done for spoligotyping. MIRU VNTR was done on those with similar pairs of spoligotype patterns.
Results | 41 index cases have individual secondary cases of which 34 pairs (index and secondary) have the same genotypes. 27 pairs of those are *Mycobacterium tuberculosis* (TB) and 7 pairs are *Mycobacterium africanum*. 17 pairs of TB and 3 pairs of *M. africanum* with similar spoligotyped patterns and had MIRU VNTR done. 9 pairs have the same allele numbers while the remaining 11 pairs are different.
Conclusion | Applying spoligotype analysis and MIRU-VNTR typing to paired isolates from TB patients and their household contacts that developed TB during two years of follow-up suggests that most TB transmission in The Gambia occurs outside of the household.

TO 25

11:30–11:45

Estimates of genetic variability of *M. tuberculosis* complex and its association with drug resistance in Cameroon

Larissa Kamgue Sidze • Laboratory for Tuberculosis Research, University of Yaounde, Cameroon

Introduction | This study investigates the genetic diversity and drug resistance spreading in *M. tuberculosis* isolates from Cameroon.
Methods | Molecular typing (spoligotyping and MIRU-VNTR) and DNA sequencing (katG, inhA, ahpC and rpoB) were performed on a set of 120 isolates including isoniazid and/or rifampicin resistant and susceptible strains obtained from smear-positive pulmonary TB patients.
Results | Of the 19 isoniazid resistant isolates, 9 (47, 36%) harboured a katG315 mutation. Alterations were found in the inhA (42, 10%) and ahpC (5, 26%) promoters. rpoB531 point mutation was observed in 3 of the 4 rifampicin resistant isolates. Spoligotyping revealed that the majority of strains (65%) belonged to the 'Cameroon family' followed by the 'Haarlem family' (10%). MIRU-VNTR and spoligotyping showed 21 clusters of 2–11 strains.
Conclusion | Genotyping confirmed the predominance of the 'Cameroon family'. The findings suggest that transmission and emergence of drug resistance during chemotherapy might occur simultaneously in our setting, emphasizing the importance of early diagnosis and adequate treatment.

CHAIRS
Dr Hulda Swai
Prof. Tumani Corrah

RAPPORTEURS
Prof. Jean Nachega
Dr Getnet Yimer

TO 26

11:45–12:00

Nanomedicine for improved efficacy of tuberculosis drugs

Rose Hayeshi • Council for Scientific and Industrial Research (CSIR), South Africa

Introduction | Current tuberculosis treatment experiences low success rates due to poor pharmacokinetics and thus reduced efficacy. Nanomedicine offers a possible solution by presenting the ability to alter the pharmacokinetics of the conventional drugs to enhance bioavailability, increase the half-life of the drugs and reduce the toxicity. The aim of this work is to reduce the dose of TB drugs, as well as the dose frequency using nanomedicine.
Methods | Isoniazid and rifampicin were nano-encapsulated in poly(lactide-co-glycolide) using a novel multiple emulsion spray-drying technique. The nano-encapsulated drugs were administered to TB infected mice once a week for 4 weeks compared to the conventional drugs administered everyday for 4 weeks. The bacterial burden in the spleen and lung was determined as well as the pulmonary pathology.
Results | Nanoparticles of 250 nm to 400 nm were obtained with an encapsulation efficiency varying from 50% to 65%. The once weekly treatment with nanoparticulate drug resulted in a similar reduction in bacterial burden as the daily treatment with conventional drug. This was supported by the lung pathology.
Conclusion | The results suggest that there is a slow release of drug from the nanoparticles due to an increase in half-life. There is therefore the potential to develop a low dose, low frequency TB nanomedicine with the aim to improve efficacy and patient compliance. The technology is generic and may be applied for malaria, HIV/AIDS as well as other diseases, which suffer from patient non-compliance and are major burdens in Africa.

MO 23

11:00–11:15

Validation of new biomarkers for monitoring *P. falciparum* reduced susceptibility/tolerance or resistance to artemisinin derivatives and partner drugs in Nigeria

Christian Happi • Malaria Research Laboratories, IMRAT, College of Medicine, University of Ibadan, Ibadan, Nigeria

Introduction | Research leading to the definition of new and reliable biomarkers/molecular determinants of parasite responses to artemisinin derivatives and partner drugs are crucially needed. These biomarkers/molecular determinants may serve as early warning signs that could guide appropriate countermeasures in preventing the spread of drug resistant parasites. Ultimately this will extend the therapeutic shelf life of artemisinin-based combination therapies, especially in Africa.
Methods | We used a unique, innovative and integrated approach that combines clinical studies with essential molecular parasitology and epidemiology and cutting edge genomics analysis of fresh *P. falciparum* samples directly from patients, in order to identify and validate *in vitro* and *in vivo* new biomarkers/molecular determinants of parasite response to artemisinin derivatives and partner drugs.
Results | We identified new biomarkers/molecular determinants (single nucleotide polymorphisms and copy number variation of genes) of parasite reduced susceptibility/tolerance or resistance to ARTs and partner drugs.
Conclusion | New markers identified in this project could be potentially used as molecular markers for monitoring reduced susceptibility/resistance to artemisinin derivatives or partner drugs in Africa.

CHAIRS
Dr Saadou Issifou
Dr Sodiomon Sirima

RAPPORTEURS
Dr Alfred Tiono
Dr Leah Mwai

MO 24

11:15–11:30

Documented fever and malaria in pregnancy in Africa

Anna Maria van Eijk • Child and Reproductive Health Group, Liverpool School of Tropical Medicine, Liverpool, UK

Introduction | Malaria infection in pregnancy in Africa is predominantly asymptomatic. The presence of symptoms depends on the degree of acquired immunity and malaria transmission intensity. We reviewed the literature to assess the relationship between probabilities of documented fever and malaria transmission intensity in pregnant women with malaria.
Methods | Using the Malaria-in-Pregnancy Library (www.update-software.com/publications/malaria), we identified studies from malaria endemic Africa with information on malaria prevalence and documented fever. Data was extracted and evaluated using random effects model. Malaria transmission intensity indicators were obtained from the malaria map project (Wellcome Trust/KEMRI, Nairobi, Kenya).
Results | 53 studies were identified. The summary-prevalence of documented fever was 3.6% during pregnancy (95% CI 2.5–5.3%, 40 studies) and 6.0% at delivery (3.3–10.8%, 13 studies). Prevalence of documented fever at delivery was higher (23.3%, 95% CI 15.7–33.1) in 3 studies in low malaria transmission areas compared to 10 studies in areas with medium-to-high transmission (3.9%, 95% CI 2.9–5.3, p<0.001), but not during pregnancy. Summary-prevalence of peripheral parasitaemia was 19.8% (95% CI 16.8–23.1) during pregnancy and 13.6% (95% CI 8.9–20.3%) at delivery. There was no correlation between documented fever, peripheral parasitaemia and malaria transmission intensity.
Conclusion | Only a small proportion of malaria infections in pregnancy were associated with documented fever; the risk of malaria associated fever was not associated with transmission intensity.

MO 25

11:30–11:45

High prevalence of *P. falciparum* dhfr mutations correlates with sulfadoxine pyrimethamine usage among pregnant women in Nigeria

Daniel Olusola Ojuronghe • Department of Medical Microbiology & Parasitology, Ladoke Akintola University of Technology, Osogo, Nigeria

Introduction | Intermittent preventive treatment with sulfadoxine-pyrimethamine (IPT-SP) is currently recommended by WHO for prevention of malaria in pregnancy. This study determines the rate of SP usage and correlates it with the prevalence of dihydrofolate reductase (dhfr) gene resistant alleles among pregnant women in Nigeria.
Methods | Thick and thin blood films confirmed by PCR were used for malaria parasite detection. Mutations in dhfr gene were analysed by sequencing. A questionnaire was used for the collection of information on antimalarial usage among the 200 women enrolled in this study.
Results | Prevalence of falciparum malaria in the study population was 30% (60/200). The prevalence of the dhfr triple mutant alleles (Ile-51, Arg-59 and Asn-108) was 63.3% (38/60) and no Leu-164 mutant isolate was observed. Of the women studied, 18%, 13.5%, 8.5%, 20.5% and 34% used alaxin, chloroquine, daraprim, SP and no drug respectively. Highest prevalence of malaria (36.7%) was observed among those that used no drugs, while the least (10%) was among the group that took daraprim but the difference was not statistically significant (p=0.7735). Highest triple mutant alleles were observed among the group that took SP (90%), no drug (81.8%) and daraprim (66.7%) while the least was observed among those that took CQ (11.1%) and the difference was statistically significant (p=0.007).
Conclusion | Increasing prevalence of the dhfr triple mutant genotypes are consistent with the loss of efficacy of SP for treatment of clinical malaria in most parts of Nigeria and sub-Saharan Africa. Timely review of IPT-SP policy is therefore recommended.

CHAIRS
Dr Saadou Issifou
Dr Sodiomon Sirima

RAPPORTEURS
Dr Alfred Tiono
Dr Leah Mwai

MO 26

11:45–12:00

Benchmarking two multisite intermittent preventive treatment of malaria in pregnancy (IPTp) clinical trials in five sub-Saharan countries

Golbahar Pahlavan • Barcelona Centre for International Health Research, Barcelona, Spain

Introduction | Currently two multisite clinical trials are being conducted in 5 sub-Saharan countries within the framework of the Malaria in Pregnancy Preventive Alternative Drugs trials, funded by the Malaria in Pregnancy Consortium and EDCTP. Multisite clinical trials provide the joint advantage of facilitating the achievement of large target sample sizes and collecting information from different populations enriching thus the interpretation of the intervention's results. Important issues are the logistics and the standardisation challenges of simultaneously implementing trials in varied locations. Other important factors to be considered are the existing local health systems, the associated regulatory structures and how the trials are embedded in these settings. Given the limited resources available, interventions in developing countries, particularly those directed at vulnerable populations including pregnant women and children, should take into account both short-term clinical trial objectives as well as longer-term ones. These include integral health service delivery, empowerment of local health service providers and acceptance by the community at large.
Methods | In view of benchmarking the two multisite trials, an on-site evaluation is currently being carried out by the trial management team. The first objective of this evaluation is to identify best practices and to implement these across sites in order to optimise recruitment and data collection. The secondary objective is to assess the impact of the trials on health service delivery, training of health professionals, community involvement and acceptance, as well as impact on infrastructure upgrades or improvements in the relevant cases.
Results | Preliminary results of this benchmarking shall be presented.

CO 01

11:00–11:15

PACTR: An update on prospective clinical trial registration in Africa

Amber Abrams • The Pan African Clinical Trials Registry, cape Town, South Africa

Introduction | The Pan African Clinical Trials Registry is a prospective clinical trials registry based at the South African Cochrane Centre at the Medical Research Council. The European and Developing Countries Clinical Trial Partnership provided the start-up grant for this registry: the first African open-access resource collecting the 20–item-minimum-data-set advocated by the World Health Organisation (WHO) and the International Committee of Medical Journal Editors. In July 2011 PACTR will celebrate two years as a member of the WHO Network of Primary Registers.
Methods | We searched www.pactr.org and present a descriptive and spatial analysis of registered applications.
Results | Between May 2007 and February 2011 there have been 86 applications: 43 are registered trials; 33 applications were ineligible and ten are incomplete. The 43 registered trials mainly concern HIV/AIDS (12), malaria (9), TB (7), co-morbid TB and HIV/AIDS (3), and co-morbid malaria and HIV/AIDS (3). Nine trials evaluate diseases other than TB, HIV/AIDS or malaria. There are 24 single-centred trials and 19 multi-centre trials have sites in 18 African countries. 54 principal investigators (PI) are listed, and 42 (78%) PIs are from African countries.
Conclusion | PACTR's membership in the WHO Network of Primary Registers has increased its visibility and firmly established it as the registry of choice for the region. Since the formal launch of www.pactr.org, applications to the registry have more than tripled. Continued promotion will likely ensure that the registry succeeds in its goal of providing users with a complete database of on-going clinical trials in Africa.

CHAIRS
Dr Aïssatou Toure
Dr Christiane Druml

RAPPORTEURS
Dr Christine Wasunna
Dr Stephen Rulisa

CO 02

11:15–11:30

Emerging ethical and practical challenges for health researchers in Africa

Wen Kilama • African Malaria Network Trust (AMANET), Dar es Salaam, Tanzania

Introduction | Researchers and other research stakeholders in Africa have to address increasingly complex health research issues (e.g. genomics, informatics, cloning, GMOs, first in human trials). Yet current ethics capacity strengthening efforts in Africa are only focusing on Ethics Review Committees (ERCs).
Methods | Investigators need good grounding in health research ethics since they interact closely with research participants, prepare study and trial protocols, and informed consent statements. They directly deal with funders, research collaborators, ERCs, national regulatory authorities, policy and decision makers, health workers, and study communities. Researchers may have to address issues in biosafety, litigation, and transboundary movement of GMOs. Given the new wave of democratization, and weak markets in Africa, researcher involvement has to extend beyond phase III trials to implementation research and product deployment. Human research ethics is needed for each of these.
Conclusion | The presentation will highlight attempts by AMANET to develop real life African ethics case studies and to address challenging topics in trials, such as public health settings, genetically modified mosquitoes, transmission blocking malaria vaccines, traditional medicines, and legal issues. We also cover the role of researchers in sharing, ownership and/or storage of samples and data as well as issues of intellectual property rights, patents, publications, packaging of research findings for various targeted stakeholders, and responsibilities when the research or trial is completed. The presentation will propose ways of addressing the emerging challenges.

CO 03

11:30–11:45

Mapping African research ethics review and medicines regulatory capacity

Boitumelo Mokgatla-Moipolai • University of KwaZulu Natal, South Africa

Introduction | The capacity to ethically review study protocols and provide ethical oversight of drug trials is a core component of responsible research systems. Each country and major institution involved in the conduct of clinical trials should have adequate capacity to conduct such ethics review. The MARC project aims to document this capacity in Africa, to promote the strengthening of capacity that exists, and to contribute to the development of African accreditation criteria.
Methods | The MARC project aims to map Health Research Ethics committees and Regulatory Activities in Africa. The MARC project links the 'ethics review capacity' and 'ethics review capacity building initiatives' with the Health Research Web platform of the Council for Health Research and Development. The platform allows ethics capacity analysis in relation to general research system development, encourages comparisons between countries inside and outside Africa, and facilitates the sustainability and knowledge sharing throughout the project.
Results | To date, MARC has mapped 125 Research Ethics Committees in over 25 African countries, and 896 Research Ethics Committees in Latin America. It has just launched mapping of Medicines Regulatory Authorities and online research ethics social networking (discussion groups).
Conclusion | We contribute to better communication between African Research Ethics Committees, and better links between Research Ethics Committees and Medicines Regulatory Authorities.

CHAIRS
Dr Aïssatou Toure
Dr Christiane Druml

RAPPORTEURS
Dr Christine Wasunna
Dr Stephen Rulisa

CO 04

11:45–12:00

TRREE online training project: mapping its first two years

Jérôme Ateudjieu • Division of Health Operations Research, Ministry of Public Health, Yaoundé, Cameroom

Introduction | Training of ethics committee members and researchers on the ethics and regulation of research involving humans significantly improves the protection of research participants. Until 2007, access to such training was very limited in Africa, and especially in languages other than English. Training and Resources in Research Ethics Evaluation (TRREE, www.trree.org) is a web-based training and capacity building initiative that aims at making freely available e-learning and e-resources.
Methods | Training needs and priorities in research ethics evaluation were identified through a questionnaire that targeted research ethics committees in three African countries. To date, four training modules have been developed to respond to these training needs and are available on-line in four languages.
Results | TRREE was launched in June 2009 with two modules (module 1 Introduction and M2 Ethics evaluation) in two languages (English and French). Available modules have considerably increased since then with two more modules (M3 National supplements from eight countries and M4.1 on the theme of informed consent). Much of the material is also available in two more languages, German and Portuguese. With these developments, the on-line courses have been taken in over 98 countries from the five continents and registered 33,059 visits, 1690 subscriptions (with 714 from Africa), 1607 trained participants (with 54% in English, 31% in French and 14% in German).
Conclusion | The initiative, the methodology and resources allocated for the TRREE project have contributed to significantly improving the accessibility and use of training in research ethics evaluation for those involved in research participants' protection in Africa.

HO 27

14:00–14:15

HIV-1 subtype distribution, multiple infections, sexual networks and partnership histories in female sex workers in Kampala, Uganda

Deogratius Ssemwanga • MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

Introduction | We investigated for the first time the subtype distribution, prevalence of multiple HIV-1 infections, sexual networks and partnership histories in a cohort of women engaged in high risk sexual behaviour such as female sex workers and women employed in entertainment facilities.
Methods | Viral RNA was extracted from blood samples collected from 324 HIV-1-positive women. The gp-41 and pol-in genes were directly sequenced. Women found to have closely related viruses and those with recombinant viruses were further analysed in pol-in gene by clonal sequencing to determine HIV-1 multiple infections. The individual partnership histories were used to provide information on when sex work was undertaken and where.
Results | Subtyping in both gp-41 and pol-in was successfully done in 210/324 (64.8%) women. Subtype distribution in these two genes was 54.3% (n=114) A/A; 2.9% (n=6) C/C; 24.3% (n=51) D/D; 11.9% (n=25) A/D; 4.8% (n=10) D/A; 0.5% (n=1) C/A; 1.0% (n=2) B/A; and 0.5% (n=1) B/D. Sexual networks were identified in six pairs and one triplet of women with closely related subtype A viruses. Partnership histories showed that women having phylogenetically closely related viruses had worked in the same localities. Five cases of multiple infections were confirmed; four dual infections and one triple infection.
Conclusion | In this first molecular epidemiology study among female sex workers in Kampala, subtype A was the predominant subtype. About 9% of a subgroup had multiple infections. Partnership histories and multiple infections observed in this population suggest sexual mixing of the sex workers and their clients confirming their high risk characteristics.

CHAIRS
Prof. Peter Ndumbe
Dr Simon Agwale

RAPPORTEURS
Dr Wendy Burger
Dr Pauline Mwinzi

HO 28

14:15–14:30

Influence of HLA class I and HLA-KIR compound genotypes on HIV-2 infection and markers of disease progression in a community in West Africa

Louis-Marie Yindom • Medical Research Council (MRC) Laboratories, Fajara, The Gambia

Introduction | Overall, the time to AIDS after HIV-2 infection is longer than with HIV-1 and many individuals infected with HIV-2 virus remain healthy throughout their lives. Multiple HLA and KIR gene products have been implicated in the control of HIV-1 but the effect of variation at these loci on HIV-2 disease is unknown.
Methods | DNA was extracted from 513 blood samples collected from HIV-2-infected and uninfected individuals belonging to a well characterized community cohort at the north western coast of Guinea Bissau. KIR genotyping was performed by PCR-SSP (sequence specific priming) using a panel of 58 KIR-specific primers to detect 15 known KIR genes.
Results | Here we show for the first time that HLA-B*1503 associates significantly with poor prognosis after HIV-2 infection and that HLA-B*0801 associates with susceptibility to infection. Interestingly, previous data indicate that HLA-B*1503 associates with low viral loads in HIV-1 clade B infection, but has no significant effect on viral load in clade C infection. In general, alleles strongly associated with HIV-1 disease showed no effect in HIV-2 disease.
Conclusion | These data emphasize the unique nature of the effects of HLA and HLA/KIR combinations on HIV-2 immune responses relative to HIV-1, which could be related to their distinct clinical course.

HO 29

14:30–14:45

Evolution of neutralizing antibodies against HIV-1C molecular envelope clones from acute heterosexually acquired infections in Botswana

Keabetswe Bedi • Botswana Harvard AIDS Institute Partnership, Gaborone, Botswana

Introduction | Since the discovery of HIV-1 infection over twenty-five years ago, the search for a potent and effective vaccine has proved to be a big challenge. As with other pathogens, neutralizing antibodies against HIV-1 could play critical role in the prevention of the infection. Whilst the role of neutralizing antibodies has not been clearly defined in preventing the infection, recent discovery of broad and potent HIV-1 neutralizing antibodies such as PG9 and PG16 has shown the potential role of neutralizing antibodies in prevention efforts.
Methods | A cohort of 8 HIV-1C acutely infected individuals were enrolled and followed for a period of up to twenty-four months. Plasma samples were collected at different time points during the follow-up and stored at -80°C. HIV-1C envelope glycoprotein 160 from these individuals was cloned into pcDNA3.1D/V5-TOPO expression vector. HEK293 cells were then co-transfected with envelope and backbone vectors to produce pseudoviruses. The pseudoviruses were used to infect the TZM-bl cells expressing CD4, CXCR4 and CCR5 receptors. Plasma samples showing neutralizing capacity on autologous virus were tested for cross neutralization at different time points.
Results | Plasmas from the follow-up time points were observed to have neutralizing capacity on the autologous generated pseudoviruses. The fluctuation of the antibody profiles revealed the late development of the transmission blocking antibodies toward viral strains at early time points.
Conclusion | Infective pseudoviruses were produced and used to assess autologous and heterologous neutralizing capacity of plasmas from the acutely infected HIV-1C individuals.

CHAIRS
Prof. Peter Ndumbe
Dr Simon Agwale

RAPPORTEURS
Dr Wendy Burger
Dr Pauline Mwinzi

HO 30

14:45–15:00

Assessment of TB-HIV treatment responses in co-infected patients receiving combined treatment

Thuli Mthiyane • Medical Research Council, Cape Town, South Africa

Introduction | Our objective was to compare the response to TB treatment in patients co-infected with tuberculosis and HIV receiving tuberculosis treatment only or tuberculosis treatment and antiretrovirals using IFN-γ release assay.
Methods | Blood for IFN-γ release assay was taken in co-infected patients on day 0, months 3, 6 and 12. Quantiferon-TB Gold in-tube (QFT-G) has been chosen for the test. After incubation, the concentration of IFN-γ in the plasma was determined by ELISA. The amount of IFN-γ released was determined by subtracting the amount in the nil from the amount in the ESAT-6, CFP-10, or mitogen-stimulated plasma.
Results | 62 patients were evaluated, 45% were men, average age 32.4%. Of the 62 patients, 21 had tuberculosis treatment only, while 41 had tuberculosis treatment and antiretroviral therapy. Median quantiferon levels at baseline were 2.1 for the tuberculosis treatment only group and 0.8 for the tuberculosis plus antiretroviral group, 1.25 and 3.76 for month 3, 0.24 and 0.7 for month 6 and 0.24 and 0.297 for month 12. Median quantiferon levels according to CD4 count levels: CD4 count above 220 for tuberculosis treatment only group versus tuberculosis treatment plus antiretrovirals: baseline 2.1 and 0.7; month 3: 1.25 and 3.725; month 6: 0.24 and 0.24; and month 12: 0.24 and 0.35. CD4 count below 220 on antiretroviral therapy: baseline 0.975; month 3: 3.76; month 6: 0.875; and month 12: 0.24.
Conclusion | There was a general decline in quantiferon results from six months onwards consistent with smear and culture results.

HO 31

15:00–15:15

High prevalence of Hepatitis B and syphilis co-infection among newly diagnosed HIV patients in the northwest region of Cameroon

Elias Onyoh • Mbingo Baptist Hospital, Bamenda, Cameroon

Introduction | Co-infections with syphilis and Hepatitis B virus contribute to significant morbidity in HIV patients. We aim to delineate the burden of syphilis and Hepatitis B co-infection in HIV patients starting antiretroviral therapy in the North West Region of Cameroon.
Methods | Since 2006 all consecutive HIV patients commencing primary antiretroviral therapy at the Mbingo Baptist Hospital were screened for Hepatitis B and syphilis co-infections using commercially available tests. Baseline data for age, sex, CD4 count, WHO stage, and liver function tests were analysed using demographic statistics. Risk factors for a positive Hepatitis BsAg and syphilis status were analysed using a multivariable logistic regression.
Results | A total of 695 patients completed their pre-therapeutic work-up. Mean age at commencing antiretroviral therapy was 35.1 years (SD 9.5) and 35% of patients were male. Median CD4 count was 155.5 (IQR79–245) and the majority of patients (59%) had WHO stage III or IV diseases. Overall prevalence for Hepatitis BsAg was 12.6% and male patients were more likely to have a positive result than female patients (16.5% *vs* 10.3%, p=0.02). Antibodies against syphilis were also more common in male patients (15.6% male patients *vs* 8.9% in females, p<0.01) and overall prevalence for syphilis antibodies was 11.3%.
Conclusion | Hepatitis B and syphilis co-infections are common among HIV patients starting ARV in North West Cameroon. The prevalence of both, HBV and syphilis antibodies were significantly higher in male patients. Older patients seem to be particularly vulnerable to syphilis co-infection.

Reference: Eur J Clin Microbiol Infect Dis 2000, 19:237–239

CHAIRS
Prof. Peter Ndumbe
Dr Simon Agwale

RAPPORTEURS
Dr Wendy Burger
Dr Pauline Mwinzi

HO 32

15:15–15:30

The ANRS initiative on clinical trials good clinical practices in resource-limited countries: development of quality indicators

Mina Hanna • INSERM U897, Bordeaux, France

Introduction | Since 1994, the French Agency of Research on AIDS and Viral Hepatitis (ANRS) funds sites in resource-limited countries. These sites are able to implement research with a high potential impact on HIV infection and Hepatitis C. A major evolution and proliferation of international regulations and recommendations for clinical trials have taken place. However, little guidance exists on how they should be interpreted and applied in non-investigational trials in resource limited countries.
Methods | Our program aimed to establish by consensus a range of indicators to assess the capacity to implement GCP and ethical principles in clinical trials. A selected group was brought together with a researcher representing each ANRS site (Cote d'Ivoire, Senegal, Cameroun, Burkina Faso, Egypt and Cambodia). Our structured interaction method aimed to combine evidence and experts' opinion to identify: (i) clinical trial processes involved; (ii) aspects specific for resource limited countries regarding the application of GCP and ethical recommendations; (iii) quality goals and relevant indicators.
Results | A typical trial process was identified. Cultural and organisational particularities were described. Indicators covering the main trial steps were chosen by consensus based on responses of the nine people who took part in the nominal group meetings. Eight steps were covered detailing the need for 28 quality achievements. For each, one or more indicators were proposed (n=58).
Conclusion | Our preliminary list requires further analysis for indicators of SMART (Specific, Measurable, Achievable, Relevant and Time-bound) behaviour. This pioneer study represents the first phase in our process to develop an assessment tool for GCP compliance.

TO 27

14:00–14:15

Predominance of the Ghanaian strain of *M. tuberculosis* in the coastal region of Cameroon

Jean Paul Assam Assam • University of Yaoundé I, Cameroon

Introduction | Little epidemiological and molecular data is available on human tuberculosis in Cameroon, as in most other African countries. The available data suggested that predominant families of closely related strains are common in these areas. Apparently such families could be endemic in particular geographic areas.
Methods | In order to determine the nature and extent of genetic diversity in the *M. tuberculosis* populations circulating in the coastal region (Littoral and South-West regions) of Cameroon, we conducted a study involving 69 patients with symptomatic disease and sputum culture positive for the *M. tuberculosis* complex over an 18 months period. Genetic characterization, using mycobacterial interspersed repetitive-unit–variable-number tandem-repeat (MIRU-VNTR) typing and spoligotyping, was applied following culture.
Results | The comparison of spoligotypes from these regions with an international spoligotype database (SpolDB4) showed that the majority of isolates belong to major clades of *M. tuberculosis* (Haarlem, 10.42%; Latin American-Mediterranean, 20.12%; and ST 47%). The predominant group of isolates (33.33%) corresponds to spoligotype 53, described as the 'Ghanaian strains'. Comparison of our data showed that MIRU-VNTR had greater resolving power than spoligotyping and defined additional genotypes in the same cluster.
Conclusion | Our investigation revealed the presence of a group of *M. tuberculosis* of the Ghanaian strains (ST 53) which was responsible for most smear-positive pulmonary cases of tuberculosis. Further studies are needed to understand the expansion in Cameroon of this group of predominant strains.

CHAIRS
Prof. Richard Adegbola
Dr Abraham Aseffa

RAPPORTEURS
Prof. Mark Hatherill
Ms Thuli Mthiyane

TO 28

14:15–14:30

Non tuberculous mycobacteria among children with suspected TB in a rural setting in Uganda

Anne Wajja • Infectious Diseases Institute, Makerere University, Uganda

Introduction | The incidence and clinical significance of non tuberculous mycobacteria (NTM) is largely unknown in resource limited settings where culture and species identification is not routine. We assessed frequency and clinical significance of NTM among children suspected to have TB in rural Eastern Uganda.
Methods | 2 cohorts of 2500 infants and 5000 adolescents (12–18 y) under active TB surveillance for 1–1.5 years were investigated for TB using gastric aspiration and sputum induction from infants and early morning and spot sputum samples from adolescents. ZN staining, culture on LJ and MGIT and species identification for positive cultures were done. We reviewed frequency and characteristics of children with NTM.
Results | NTM were isolated from 37 (33 infants) of 2859 samples (crude yield 1%). Most NTM (n=24) were isolated from the gastric aspirates. 2 infants grew NTM from both gastric and induced samples. Over 70% of the infants with NTM were symptomatic, 30% reported household TB contact and 21% were TST positive. Among 127 adolescents, NTM were isolated from 137 of 2,988 samples (crude yield 5%). Only 5 of the NTM isolates were smear-positive. 9 adolescents grew NTM from both early morning and spot samples. None of the participants with NTM were HIV-positive or being treated for TB based on clinical grounds. Speciation of the NTM is on-going.
Conclusion | NTM were isolated in 1% of infants and 5% of adolescents. Whereas no clear clinical significance was demonstrated, NTM may complicate diagnosis of PTB and is therefore of concern for clinical trial end points based on positive culture.

TO 29

14:30–14:45

Risk factors for tuberculosis infection among adolescents in rural Uganda

Ronald Mutunzi • Infectious Disease Institute, Makerere University, Uganda

Introduction | There is limited data on TB disease and infection among adolescents. For this reason, the Uganda TB vaccine trial site preparation project is being conducted in the Iganga/Mayuge demographic surveillance site (DSS), which is located in a rural setting of eastern Uganda.
Methods | Adolescents aged 12–18 years were enrolled from schools and the community and followed for 2 years. Each enrollee received a baseline TST which was read within 48–72 hours.
Results | A total of 5000 adolescent were enrolled into the study and received a TST of which 4,982 (99.6%) were available for reading. Of these, 801 (16%) had a positive TST (>10mm). Among the group 12–14 years of age, 13% were positive, 15–16 years, 16% were positive and 17–18 years, 21% were positive. The proportion TST positive was higher in males than among females (OR 1.5, 95%, CI 1.3–1.7), higher in those with a history of TB diagnosis contact (OR 2.5, 95% CI 1.8–3.7). Those with a BCG scar were 1.3 times more likely to have a positive TST than those without BCG scar (95% CI 1.1–1.6).
Conclusion | Proportion with positive TST was high. Risk factors for positive TST were sex, TB-diagnosis contact and presence of BCG scar. These may be used for TB control, e.g. a low proportion of TB contact and higher risk on positive TST among those with contact, indicates possible usefulness of contact tracing.

CHAIRS
Prof. Richard Adegbola
Dr Abraham Aseffa

RAPPORTEURS
Prof. Mark Hatherill
Ms Thuli Mthiyane

TO 30

14:45–15:00

Community sensitisation in preparation of enrolment of infants and adolescents into a study to assess TB incidence

Elizabeth Nangobi Mwanja • Infectious Disease Institute, Makerere University, Uganda

Introduction | As part of site preparation for TB vaccine studies in Eastern Uganda, we conducted a sensitisation exercise to provide the study population with background information on the studies and to respond to concerns identified in an earlier community entry study, community acceptance of studies being the desired outcome. The objective was to describe community sensitisation processes, strategies and limitations.
Methods | The sensitisation campaign targeted 180 villages, 138 schools, 14 health facilities and community leaders in the study area of a population of 110,000. Sensitisation campaigns were delivered through direct talks, formal meetings and mass media.
Results | Sensitisation talks were done at 70 points for 180 villages and 138 schools. We organized meetings: 4 with local leaders, 2 for school head teachers and 1 with in-charges of 14 local health facilities. In addition, 3 radio talk shows were done. Immediate outcomes for the study included expressions of willingness by parents and head teachers to facilitate access to school-going adolescents, and health facilities agreed to collaborate with the study. Challenges included inability to deliver messages close enough to the communities, misconceptions, competing studies targeting same community and limited resources available for local leaders to mobilize the community. However, staff acquired a good understanding of the community and the geography of the area which was useful during study implementation. Contact through sensitisation talks facilitated the identification of village volunteers/scouts who later supported study implementation.
Conclusion | Sensitisation is useful for community-based studies to ensure acceptance and buy-in.

TO 31

15:00–15:15

Retention patterns of an adolescent cohort in western Kenya in preparation for future TB vaccine trials

Patience Oduor • KEMRI/CDC Research and Public Health Collaboration, Kisumu, Kenya

Introduction | The risk of TB disease following infection increases in adolescence making this age group a prime target for new TB vaccines. Ability to track and retain an adolescent cohort are therefore essential prerequisites to conducting TB vaccine trials in this group as a high participant retention rate is required in order to measure end points.
Methods | Adolescents aged 12–18 years were enrolled for one year and followed up every four months for up to two years. We compared the retention rate over the course of study follow-up between various age groups using the youngest cohort of 12–14 years as the reference group. Lost to follow-up is defined as participants who did not complete the minimum follow-up time of 12 months, excluding those who died.
Results | 5004 adolescents were enrolled; 2425 (48.5%) were female; mean age was 14.4 (SD=1.9); 275 (5.5%) were urban residents and 4686 (93.6%) were enrolled in school. Average retention for this cohort was 79%. There was a significant difference in retention between 12–14 years (85.21%), 15–17 years (72.15%) and 18 (59.71%) year olds (p=0.002). We identified out of school (p<0.0001) and being female (p=0.0002) as independent risk factors for loss to follow-up.
Conclusion | Younger adolescents might comprise a more successful TB vaccine trial target group than the older ones due to higher retention rates and lower loss to follow-up. Being female and out of school were independent risk factors for loss to follow-up. TB vaccine trials will need targeted retention strategies for these groups.

CHAIRS
Prof. Richard Adegbola
Dr Abraham Aseffa

RAPPORTEURS
Prof. Mark Hatherill
Ms Thuli Mthiyane

TO 32

15:15–15:30

Comparison between active and passive case finding of tuberculosis among adolescents in eastern Uganda

Amos Ndaabe • Infectious Diseases Institute, Makerere University, Uganda

Introduction | An epidemiological study to estimate the incidence of tuberculosis among adolescents (12–18 y) in the Iganga/Mayuge Demographic Surveillance Site, Eastern Uganda is being conducted in preparation for future TB vaccine trials. The prevalence and incidence of TB in this age group will be estimated. The objective was to assess the yield of passive *vs* active case finding of TB among adolescents.
Methods | In active case finding, 5000 adolescents enrolled in the study were screened for TB disease based on signs and symptoms at baseline and every 6 months for 1–1.5 years. Two sputum samples were collected from TB suspects for AFB smear and mycobacterial culture. In the passive approach, the surveillance team reviewed patient records in all health units and laboratories within the study area for adolescents diagnosed with TB during a comparative time period.
Results | In the study sample, 11 TB cases (8 prevalent at baseline and 3 incident during follow-up) were identified, a case notification rate of 220/100,000 population. The passive approach yielded 32 cases diagnosed out of 56,841 adolescents in the study area, a case notification rate of 56/100,000 population.
Conclusion | TB case notification rate was lower in the passive than the active one. The active approach led to early identification of TB cases that may have otherwise been missed. Early case detection is vital in TB control programs since it is an entry point to early treatment and prevention of transmission. The active approach may supplement the passive one for increased early case detection among adolescents.

MO 27

14:00–14:15

Impact of artemisinin-based combination therapy on malaria transmission in Mali

Bakary Fofana • Malaria Research and Training Centre, Bamako, Mali

Introduction | Most African countries have now changed their first line treatments from monotherapies to artemisinin-based combination therapies (ACTs). ACTs are known to decrease the rate of gametocyte carriage and gametocyte density in a treated population. However, the impact of ACT treatment on gametocyte infectivity and malaria transmission is still debatable. **Methods** | During a randomised controlled phase IV trial in Bougoula-Hameau, Mali, we compared the infectivity of post-AS/AQ, AR-L and AS/SP gametocytes to *Anopheles gambiae*. Patient with uncomplicated malaria were randomised to one of the three treatment arms and followed for 28 days. Gametocyte carriage was assessed by microscopy before and after treatment. Whenever gametocytes were found, starved mosquitoes were direct-fed and kept in laboratory for 8 days. The presence of oocysts was determined and the number estimated by dissection on day 8 post feeding. **Results** | Before any treatment 5.8% (n=172) of direct-fed mosquitoes were oocyst positive at day 8 *vs* 30.2% (n=252), 40.2% (n=174) and 8.0% (n=601) of oocyst-positive mosquitoes direct-fed after AR-L; AS/AQ and AS/SP treatments, respectively. AR-L and AS/AQ significantly increased gametocyte infectivity to anopheline mosquitoes ($p<0.0001$) while AS/SP had no impact on infectivity in this setting ($p=0.2$). **Conclusion** | These data show that the impact of ACT treatment on malaria transmission and spread of resistance may vary from one ACT to the other. The implications of these observations for large-scale ACT deployment in Africa remain still to be debated.

CHAIRS
Dr Andrew Kitua
Dr Christine Manyando

RAPPORTEURS
Dr Alfred Tiono
Dr Leah Mwai

MO 28

14:15–14:30

Systematic screening and targeted treatment of *P. falciparum* asymptomatic carriers with artemether-lumefantrine in a community setting in Burkina Faso

Bernhards Ogutu • Kenya Medical Research Institute, Nairobi, Kenya

Introduction | Despite wide adoption of artemisinin-based combination therapy and decline in malaria-related deaths, additional interventions are still required to further reduce the disease burden.
Methods | This 18–cluster (9 intervention clusters in villages; 9 control), randomised, single-centre, controlled, parallel study will evaluate the impact of targeted treatment of asymptomatic carriers (ACs) of asexual forms of *P. falciparum* with artemether 20 mg-lumefantrine 120 mg (AL, Coartem/Coartem Dispersible, twice daily for 3 consecutive days) in approximately 9,000–14,000 subjects (male/female adults, children, and infants) from a community setting in Burkina Faso. The primary objectives are to evaluate whether treatment of *P. falciparum* ACs is associated with a lower number of symptomatic malaria episodes, RDT confirmed per person-year over a 12-month follow-up period and an improvement in haemoglobin levels after 28 days. Criteria for exclusion from receiving AL include severe malaria, history of congenital QTc prolongation or sudden death, body weight <5 kg, hypersensitivity to AL, or first trimester of pregnancy. Excluded patients will be treated with alternative drugs according to current national guidelines. Responsibilities of the investigator's central site include microscopy, data entry, source data archiving, and supervision of the Demographic Surveillance System (DSS). DSS will monitor each cluster population every 2 months during the study for births, deaths, and migrations; and provide an up-to-date demographic status of the study population.
Conclusion | If the reduction of ACs and disease burden is confirmed, then this approach may be considered by public health policy makers as part of the multifaceted malaria control strategies being implemented across Africa.

MO 29

14:30–14:45

The influence of mefloquine malaria prophylaxis on HIV disease progression: a randomised placebo-controlled trial

Victor Chalwe • Department of Clinical Sciences, Tropical Diseases Research Centre, Ndola, Zambia

Introduction | Malaria infection leads to transient increase of HIV-1 viral load and decrease of absolute CD4 count. Therefore, malaria might accelerate progression of HIV disease in co-infected patients. Our objective was to evaluate the impact of mefloquine (MQ) prophylaxis on the progression towards AIDS in HIV-infected individuals.
Methods | A randomised double-blind placebo-controlled trial of weekly MQ prophylaxis in asymptomatic HIV-positive individuals was carried out in Luanshya, Zambia. Inclusion criteria were HIV infection with a CD4 cell count ≥350/µL. CD4 count and clinical examination were carried out every 6 months. Cox regression model was used to estimate the time to AIDS or low CD4 count and repeated measurements modelling to asses CD4 count decline.
Results | Median CD4 count at enrolment was 471/µL. The median duration of follow-up was 16 months (range: 24 months). In the placebo group, 14.8% (22/149) reached a CD4 cell count of <200/µL or developed AIDS stage III/IV, compared to 19.5% (29/149) in the MQ group (p=0.27). The placebo group had a CD4 count decline 49 cells/µL/y compared with 53 cells/µL/y in the MQ group (p=0.21). Haemoglobin increased from 12 g/L to 14.5 g/L in the placebo compared to 12.5 g/L to 13.5 g/L in the MQ group over the period of follow-up (p=0.14).
Conclusion | MQ chemoprophylaxis did not have any effect on the evolution towards AIDS. The result could be underpowered as malaria transmission decreased strongly during the short study period due to scale up of malaria control. Furthermore, only participants still immune competent and semi-immune for malaria with high CD4 count were selected.

CHAIRS
Dr Andrew Kitua
Dr Christine Manyando

RAPPORTEURS
Dr Alfred Tiono
Dr Leah Mwai

MO 30

14:45–15:00

An opportunity to establish quality indicators and benchmarks for clinical laboratories supporting clinical trials in sub-Saharan Africa

Kennedy Awoundo • Kenya Medical Research Institute (KEMRI), Kilifi, Kenya

Introduction | Clinical laboratory services in sub-Saharan Africa are typically set in environments which lack comprehensive national policies to regulate their practices. Further, lack of strategy and prioritisation is a major drawback invariably resulting in weak infrastructures, poor staffing, malfunctioning equipment, shortage of reagents, and failure of quality systems. Against this background, there is a need for rational and pragmatic quality indicators and benchmarks for laboratories supporting drug and vaccine trials in the region, particularly for malaria, HIV and TB.
Methods | We developed an eighty-question survey form and employed a web-based system for assessment of laboratories with established quality systems across Africa. Forty qualifying laboratories were targeted.
Results | Thirty seven responses were received. The range of quality indicators and benchmarks prominently practised in the laboratories include: staff training, internal quality control, proficiency testing, reporting critical value results, and samples turnaround time. The least available quality indicator was the assessment of clients' satisfaction with laboratory service.
Conclusion | Our results show a positive trend on quality indicators and benchmarks taking root in Africa. Well documented and objective surveys are critical to support capacity building efforts and to monitor progress. There is a need to cascade the model practices to other laboratories supporting clinical trials in Africa.

MO 31

15:00–15:15

Characteristics of some quality essentials in clinical laboratories in Nigeria

Rosemary Audu • Human Virology Laboratory, Nigerian Institute of Medical Research, Lagos, Nigeria

Introduction | The importance of implementing a quality management system in clinical laboratories cannot be overemphasized. This study focused on identifying the strengths and gaps that exist in some clinical laboratories in order to bridge these gaps.
Methods | This was a cross sectional study. A well structured questionnaire was administered to 106 out of 111 laboratories that consented. The laboratories were randomly drawn from the six geographical-administrative zones in the country. Data entry and analysis used SPSS v14.
Results | Out of the 106 laboratories, 73 (69%) were public while 33 (31%) were private. Distribution of qualifications of staff working in these laboratories showed that 35% were medical laboratory scientists. Overall, good results were reported from a checklist of good laboratory practices. However, less than 30% of the surveyed laboratories had a preventive maintenance agreement and access to internet services. Investigations of quality assurance for HIV diagnosis showed that 67% of these laboratories were not registered for any proficiency testing. For TB diagnosis, only 31% reported to be registered for any proficiency testing. For the diagnosis of malaria, 82% of the laboratories were not registered for any proficiency testing. Most of the laboratories not registered for any external quality assurance indicated interest to enrol if made available.
Conclusion | A concerted effort is required in training on laboratory management, particularly as regards the culture of preventive maintenance and the provision of external quality assurance, in order to provide reliable results for clinical management of patients.

CHAIRS
Dr Andrew Kitua
Dr Christine Manyando

RAPPORTEURS
Dr Alfred Tiono
Dr Leah Mwai

MO 32

15:15–15:30

Using digital technology to support and enhance clinical trials in resource-limited settings

Trudie Lang • Global Health Trials, Oxford, UK

Introduction | Clinical trials in developing countries lag far behind wealthier regions through a lack of knowledge and skills. Existing capacity development activities are linked to specific trials and are disease focused. This limits diversification. Other factors such as the cost of travel and the remote location of potential research sites also restrict clinical trial capacity development in these regions.
Methods | Global Health Clinical Trials (www.globalhealthtrials.org) is a new collaborative web-based platform. It is a free, open access and entirely collaborative platform where anyone working on trials not only can access guidance, tool resources but also share their knowledge, views and experiences.
Results | The platform was released as a pilot in May 2010 and attracted over 1000 members from 56 developing countries within a year.
Conclusion | Researchers and their staff use the platform to seek expert and peer advice on diverse issues, such as data management, intention-to-treat-analysis and setting up community advisory boards. There are free e-learning short courses and in partnership with WHO/TDR there is a continuous professional development scheme. This novel and free opportunity to build personal learning and training portfolios whilst being guided in one's professional development will be highly impactful in creating a cadre of clinical trialists in developing countries.

References: PLoS Negl Trop Dis. 2010; 4(6):e619; Science. 2011; 331(6018):714–7.

CO 05

14:00–14:15

Understanding participants' consent in an entero-toxigenic vaccines trial in the Misisi Township in Lusaka, Zambia

Bornwell Sikateyo • University of Zambia, Department of Public Health, Lusaka, Zambia

Introduction | Informed consent is considered a prerequisite for ethically sound research on humans. The aim of this study was to interrogate the consent undertaken by research participants. Rather than considering the principles upon which informed consent is based, this study aimed to understand how ethical and moral behaviours emerge in the context of a complex and challenging trial in a poor- resource setting.
Methods | This study employed an ethnographic approach to explore the evolving relationships between researchers and participants' expectations over the course of the trial, and the responsibilities these inspired.
Results | This study found that abstract ethical principles alone do not seem to adequately reflect the nature of ethical practice in the field. Although informed consent processes were rigorously followed, a number of important stages of the trial were not well understood. Participants viewed trials as an opportunity to enhance their well-being and that of their families although it required work.
Conclusion | Ethical issues raised by trial participation are not about African values versus those in the West. Rather, the particular problems that arise when conducting research in Africa are the same wherever research is conducted on poor, vulnerable and disadvantaged people. We must therefore look for new analytical resources that take into account the inseparability of medical research from the unequal and exploitative political economy in which it takes place and extend our appreciation of the everyday realities of participation in clinical trials. Because research settings are highly context-specific, supplementing ethical review with ethnographic approaches in medical research practice should be encouraged.

CHAIRS
Dr Christiane Druml
Prof. Juhani Eskola

RAPPORTEURS
Dr Christine Wasunna
Ms Amber Abrams

CO 06

14:15–14:30

Training of lay members of ethics committees on how to review protocols

Morenike Ukpong • New HIV Vaccine and Microbicide Advocacy Society, Lagos, Nigeria

Introduction | Ethics committee members are important stakeholders in the conduct of research studies. With increasing interest and promotion of community engagement in research, the role of laypersons – specialised group of community representatives on the ethics board – becomes critical. In recognition of this, NHVMAS designed and implemented three training curriculums that address the capacity needs of laypersons to constructively review protocols as well as the ability to monitor research.
Methods | Between June 2008 and April 2010, NHVMAS developed three training curriculums for laypersons and ethics committee members on: (i) how to review protocols and provide constructive feedback; (ii) monitoring of research in the field; and (iii) community engagement in research. Training curriculums were reviewed and approved by the National Health Research Ethics Committee. Four training courses were conducted for laypersons and one for chairpersons on ethics committees over the period. The impact of the training was assessed.
Results | Post training, statistically significant differences were observed in the pre and post knowledge and skills of participants in all the five training courses. Six to 12 months post training, the post test was re-administered and there was significant knowledge and skills retention. The IDIs and FGDs showed that training did impact on Ethics committee functions with laypersons playing critical, unbiased roles in the ethics committees.
Conclusion | Addressing the capacity needs of laypersons on ethics committees is an important way of promoting community engagement in research.

CO 07

14:30–14:45

Improving efficiency of ethics review in Zimbabwe through decentralization

Rosemary Musesengwa • Medical Research Council, Harare, Zimbabwe

Introduction | Since its inception as an Ethics Committee in 1974, the Medical Research Council of Zimbabwe (MRZ) evolved due to the changes in the field of research and the emergence of research ethics as a discipline. Since the 70's the MRCZ has operated as an Ethics Committee and conducted reviews of all health related studies in Zimbabwe. In 1995 the MRCZ and WHO sponsored the training of Institutional Review Boards (IRBs) in academic institutions. These IRBs were not supervised, accredited or given recognition for their work and as a consequence studies had to be submitted to the MRCZ for review and approval. This created a duplication of activities and a multilayer, 8 week approach to the approval of research, while in most cases the outcomes were the same.
Methods | The MRCZ will conduct a nationwide survey to ascertain the burden of review. New legislation and a regional IRB system will be put in place. Accreditation and training will take place over a period of one year. Auditing will be done once a year for each regional IRB.
Conclusion | In Zimbabwe expert reviewers are few and resources are limited. A decentralized system would create a more favourable environment for research. However the practicality of such a system introduces new challenges such as funding, training, development of an accreditation system, development of appropriate legislation to empower the IRBs and to decongest the MRCZ. The paper will focus on the challenges Zimbabwe is facing in an effort to decentralize ethics review and to improve its efficiency.

CHAIRS
Dr Christiane Druml
Prof. Juhani Eskola

RAPPORTEURS
Dr Christine Wasunna
Ms Amber Abrams

CO 08

14:45–15:00

Building effective and sustainable partnerships for global health research: the useful role of a partnership assessment tool

Liya Dubale Wassie • Armauer Hansen Research Institute, Addis Ababa, Ethiopia

Introduction | A large proportion of health research in Africa is carried out through international partnership. With increasing interdependence, the need and demand for enhanced collaboration is likely to increase. Successful collaboration is mutually beneficial and enhances health research quality and sustainability. Nevertheless, global health research partnership is often afflicted with inequity and a short life span.
Methods | A series of consultations were carried out by the Canadian Coalition for Global Health Research (CCGHR) and partners in Latin America, Africa and Asia to explore the Southern perspective on global health partnership. The African consultation, hosted by the Armauer Hansen Research Institute (AHRI) in Addis Ababa in March 2009, brought together participants from research institutions, universities, and non-governmental organisations of eight African countries and Canada.
Results | Participants felt strongly about the need for actionable items and tools to improve the quality of health research partnerships. A Partnership Assessment Tool (PAT) was thus developed at working sessions. The PAT will allow for monitoring of partnerships and will provide those involved with the means to negotiate mutually beneficial collaborations. The tool will evaluate partnerships across: inception, implementation, dissemination and 'Good endings and new Beginnings'. The tool will be disseminated to Northern institutions, with a focus on donors and development organisations, in the hope that they will adopt it when entering into future global health research partnerships.
Conclusion | The PAT components will be discussed. The development and dissemination of this tool is a significant step towards mainstreaming the practice of Research Partnership Ethics.

CO 09

15:00–15:15

Data management in non-commercial north-south collaborative clinical research: lessons learned from some EDCTP trials

Mary Thiongo • International Centre for Reproductive Health, Mombasa, Kenya

Introduction | Clinical Data Management (DM) faces many difficulties and challenges. This is especially true in academic environments, where limited budgets generally allow for no more than small DM teams. Nevertheless, these teams have to comply with the same GCP and regulatory standards as the private sector and have to adapt to progress in medical research and rapid IT developments. Resource-limited settings can present additional difficulties (e.g. intermittent internet connections).
Methods | A group of Northern and Southern clinical data managers met at the Antwerp Institute of Tropical Medicine in December 2010, to share their knowledge and experience with DM of non-commercial clinical research. In particular, lessons learned from the EDCTP 4–ABC and PREGACT malaria trials, the EDCTP Microbicide Safety Biomarkers trial, as well as other Southern-based studies were shared.
Results | Some challenges were found to be common at the start of projects: late involvement of data managers; workload underestimation and inadequate budget for some activities, e.g. database validation; lack (or handover) of human resources and of solid expertise in validation and programming; heterogeneous use in software and documentation at different sites, and sometimes low internet connectivity and power instability. In addition, finding open access software suitable for multicentre trials remains a challenge.
Conclusion | There is a clear case for promoting a North-South collaborative platform of clinical data managers (as is the case for clinical researchers) aiming for good clinical DM practices. Training, the design of common operating procedures and document templates, and the development of a collaborative network are seen as the obvious next steps in meeting this goal.

CHAIRS
Dr Christiane Druml
Prof. Juhani Eskola

RAPPORTEURS
Dr Christine Wasunna
Ms Amber Abrams

CO 10

15:15–15:30

ISHReCA: Consolidating gains and setting new directions for longer term impact and sustainability in health research capacity building in Africa

Palmer Netongo • The Initiative to Strengthen Health Research Capacity in Africa-ISHReCA, Yaoundé, Cameroom

Introduction | There have been several efforts to improve health research capacity in Africa and currently such capacity is visible although unevenly distributed throughout the African regions. Likewise, perceptions exist that progress in its development has been slow. **Methods** | At the ISHReCA (Initiative to Strengthen Health Research Capacity in Africa) Forum 2010 in Ouagadougou, Burkina Faso these questions were addressed. This paper builds upon discussions held by African health researchers, policy makers and international funders. Moreover, it also discusses challenges identified through social networking platforms (e-forum and linked-In) run by ISHReCA. We examined the methodological issues and the relevance of novel schemes for capacity building with the goal of longer term impact and improved sustainability. **Results** | We highlight enabling factors for and potential barriers to the progress and sustainability of the efforts to strengthen health research capacity. We begin by presenting these barriers as well as the expectations of African health researchers vis-à-vis funders and governments to consolidate gains and to promote sustainability. Across all regions, the lack of funding information is a common challenge. While lack of funding and non-supportive country policies appear to be peculiar to Central Africa, unfair partnership features highest in Western and Southern Africa. **Conclusion** | We conclude with recommendations for sustainable models of partnership for building capacity for health research in Africa.

PLENARY SESSION IV

Recommendations, award giving ceremony and closing remarks

16:00–17:20

Conference room 1

16:00–16:30

Report back from parallel sessions focusing on recommendations and ideas for future strategy consideration

16:30–16:50

Award giving ceremony for outstanding African scientists

CHAIRS
Prof. Shabbar Jaffar
Dr Michael Makanga

RAPPORTEUR
Mr Paul Chinnock

16:50–17:20
Concluding remarks and closing ceremony

16:50–17:00

Prof. Charles Mgone • EDCTP Executive Director

17:00–17:10

Dr Ruxandra Draghia-Akli • Director, Directorate Health, DG Research and Innovation, European Commission

17:10-17:20

Dr Kassama Yankuba • Director of African Union Medical Centre (former Minister of Health of The Gambia)

Satellite meetings

Professional recognition, career development and training for clinical trial investigators and staff

Sunday 9 October 2011, 14:00–16:00
Conference room 3

Global Health Trials and WorldWide Antimalarial Resistance Network

This meeting is co-hosted by Global Health Trials and the WorldWide Antimalarial Resistance Network (WWARN) will mark the launch of the Global Health Trials Professional Membership Scheme, formed to boost the recognition of clinical research as a profession, and to provide career development and training opportunities for all levels of clinical research staff working in resource-limited locations.

Developed in partnership with the World Health Organization Special Programme for Research and Training in Tropical Diseases, and supported by funding from the Bill and Melinda Gates Foundation, this free service provides a personal training and career development record to help individuals document their research skills and experience as they develop. Members progress through the scheme as they learn new skills, gain qualifications and/or change roles. As well as guiding an individual's professional development, the scheme offers a secure mechanism for research sites to maintain staff review and training records.

Keeping the malaria medicine chest full: therapeutic options to treat malaria across the disease spectrum

Monday 10 October 2011, 12:30–14:00
Delegates lounge

Medicines for Malaria Venture (MMV)

MMV is recognized as the leading product development partnership (PDP) in the field of anti-malaria drug research and development. It was established as a foundation in 1999, and registered in Switzerland.
MMV's mission is to reduce the burden of malaria in disease-endemic countries by discovering, developing and facilitating delivery of new, effective and affordable anti-malaria drugs.
MMV's vision is a world in which these innovative medicines will cure and protect the vulnerable and under-served populations at risk of malaria, and help to ultimately eradicate this terrible disease.

Topics for discussion during the symposium:
- Why new drugs matter: Implementing new drugs into malaria case management
- Keeping pregnant mothers safe: Can IPTp make a difference?
- Saving lives, saving futures: Options to treat severe malaria

Satellite meetings

The Seventh EU Research Programme (FP7) – supporting international health and bio-medical research cooperation

Monday 10 October 2011, 16:15–17:30
Conference room 3

European Commission

The European Union (EU)'s Research Programme is the biggest international research programme worldwide fostering international partnerships and collaborations. In the current Seventh Framework Programme (FP7) health research cooperation is supported with 6.1 billion Euros to improve the health of citizens, to boost competitiveness of health-related industries, and tackle global health challenges. By the end of 2010, 564 projects with almost 6500 participations were receiving 2.5 billion Euro of EU funding. In average, 1 in 3 EU-funded projects have an international partnership and involve - in average - 11 partners. So far, 173 African institutions from 27 sub-Saharan African countries are cooperating in these projects and supported with 52 million Euro EU-funding. The session will provide an overview on funding opportunities for African researchers and international cooperation (with focus on infectious diseases and public health), outline the funding principles and application process, and present information and support services that are available for further guidance.

Clinical trials in practice: how to achieve the best protection of the study subjects?

The challenge of achieving appropriate protection of patients participating in clinical trials carried out in resource-constrained settings

Tuesday 11 October 2011, 12:30–14:00
Delegate lounge

'Switching the Poles' Clinical Research Network

This Clinical Research Network brings together researchers from Belgium, Benin, Burkina Faso, Cambodia, Cuba, DRC, Ethiopia, Indonesia, Nepal, Peru, Uganda, Vietnam and Zambia. It has the aim of jointly developing capacity, tools and procedures to apply universal standards for clinical research in resource-poor settings. The Network was officially launched in 2008, as part of a programme for institutional capacity strengthening funded by the Belgian Development Cooperation and coordinated by the Antwerp Institute of Tropical Medicine. Its motto is 'Switching the Poles', and its explicit aim to transfer not only expertise but also resources and decision-making to the South. Several network partners participate in EDCTP-funded projects.

Satellite meetings

ESSENCE, an initiative to increase effectiveness of research for health in Africa

Thursday 13 October 2011, 09:00–17:00
Caucus room 11

(by invitation only)

ESSENCE on Health Research (Enhancing Support for Strengthening the Effectiveness of National Capacity Efforts) is a collaborative framework between funding agencies to scale up research capacity. It aims to improve the impact of investments in institutions and people, and provides enabling mechanisms that address needs and priorities within national strategies on research for health.

HP 01

The missing link in capacity building and training of basic science researchers in HIV/AIDS: lessons learnt in Botswana

Rosemary M Musonda • Botswana Harvard AIDS Institute Partnership, Gaborone, Botswana

Introduction | In response to the enormous challenges to fight HIV/AIDS, the Botswana Harvard AIDS Partnership (BHP) was established in 1996 by the Government of Botswana and the Harvard School of Public Health (HSPH) to collaborate in HIV research and training. In 2002 a state of the art HIV reference laboratory was opened in 2002, now SANAS accredited. However, Botswana still lacks a critical mass of local scientists at PHD or Master's level.
Methods | This is an analysis of the missing link in capacity building of Botswana scientists in HIV/AIDS despite the excellent laboratory infrastructure with facilities for advanced molecular virology and immunology. The BHP Chairman and Harvard professor, Max Essex, invested his Fogarty AIDS Training grants to provide opportunities to more than 20 Batswana to train at BHP and Harvard laboratories in advanced HIV molecular techniques.
Results | There is a dire need for the University of Botswana to have strong post graduate programs in Biomedical Sciences to facilitate training of basic scientists. Botswana had no medical school until recently. The school does not yet have post graduate programs in biomedical sciences. The school of Biological sciences lacks a strong research portfolio in biomedical sciences but for food sciences.
Conclusion | Recent BHP capacity building grants from EDCTP, Wellcome Trust and Canadian Global Health Research Initiatives aimed at post graduate training of local staff up to doctoral degree level in HIV/AIDS related fields to stimulate interest in a career in basic science research. Hence an urgent need to strengthen post graduate programs locally.

HP 02

Implementation, technology transfer and quality assessment in four African sites of a real-time PCR test to diagnose HIV-1 in exposed infants: the Promise PEP ANRS 12174 trial

Valérie Maréchal • INSERM U1058, Université Monptellier 1, Montpellier, France

Introduction | The Promise PEP study has been designed to compare the efficacy and safety of infant peri-exposure prophylaxis (PEP) with lopinavir-ritonavir (LPV/r) *vs* lamivudine, to prevent HIV-1 transmission through breast milk. 1,500 babies born from HIV-infected mothers participate in the study.
Methods | In order to assess the efficacy of PEP, dry blood spots (DBS) are collected at birth, at day 7 (day of enrolment) and then each two months until week 50. Infant HIV-1 diagnosis is obtained by a commercial real time DNA PCR technique (Biocentric, France) using LTR primers.
Results | HIV DNA RT-PCR test using DBS, Qiagen for nucleic extraction, Biocentric HIV DNA cell kit and real time PCR equipment (MiniOpticon, BioRad) has been implemented and quality assessed at the central laboratory in MonTP ellier. Using standardised protocols, this technology has been then transferred to the four African laboratories participating in the study. In-site training sessions have been organised on sample collection, good laboratory practice and quality assessment procedures. The reliability of PCR results is routinely evaluated by the laboratory coordinator by analysing raw PCR data and by participating in the CDC external quality control. To date, the four laboratories have participated in six (representing 60 DBS samples) proficiency programs. Results delivered by the four Promise PEP laboratories are 100% in agreement with expected values.
Conclusion | Combined use of DBS and commercially available real time PCR reagents is a reliable and affordable tool to expand the capacity for early diagnosis and therapeutic management of HIV-1 infected infants in African sites.

HP 03

Using an open source electronic data-capturing system for clinical trials in low-income countries

Roselyne Vallo • INSERM U1058, Montpellier, France

Introduction | We report our experience in implementing OpenClinica® (OC), free-of-charge electronic data-capturing (EDC) software.
Methods | The ANRS 12174 trial (EDCTP -funded) is a randomised controlled trial conducted in Burkina Faso, South Africa, Uganda, and Zambia. It is enrolling 1,500 mother-infant pairs. We are using OC for direct data entry in electronic Case Record Forms (eCRFs). We outsourced building and hosting of our database to Akaza Research (owner of OC).
Results | It is simple to enter data in OC, but any type of EDC requires a decent internet connection, which is not the case for all our sites. When the connection was inadequate, we used paper CRFs with secondary electronic data entry. The full potential of the health staff entering data directly is then not realised. The current version of OC 3.1 cannot manage participants' appointments, so we have built an MS Access® database for this. OC can provide brief overviews of the study follow-up, but is insufficient to monitor the quality of follow-up. Managing the study in OC, like writing, implementing and running checks, is too time-consuming. For these tasks we use SAS® software.
Conclusion | EDC in clinical trials in Africa is increasingly feasible with improving internet connectivity. OC is still a bit immature compared to high-cost clinical trials software. This may create extra workload for the central data manager, depending on trial complexity. This should be considered when selecting software for clinical trials.

HP 04

Bacterial vaginosis in women of reproductive age in Osun State, south western Nigeria

Mariam Adebukola Adetunji • Nigerian Institute of Medical Research, Yaba, Lagos, Nigeria

Introduction | Bacterial vaginosis (BV) is a common cause of abnormal discharge in women of reproductive age. It is considered to be a major cause of significant reproductive morbidity and is increasingly associated with enhancing the transmission of HIV. It is therefore imperative to determine the occurrence of bacterial vaginosis among women of reproductive age.
Methods | High vaginal swabs were collected from 200 patients aged 18–45 years after consenting, and tested samples for bacterial vaginosis. The swabs were mixed with 10% potassium hydroxide (KOH) on a slide. Smell of fishy or none fishy odour was noted. A wet preparation was prepared and viewed to look for clue cells and motile trichomonals and yeast. The presence of clue cells on wet microscopy, a positive amine test, abnormal vaginal discharge and pH above 4.5 indicated bacterial vaginosis. Diagnosis of trichomoniasis was based on the presence of motile trichomonals in wet mount microscopy of the discharge.
Results | An overall prevalence rate of 78% for BV was recorded; other infections observed among women include candidiasis 15%, trichomoniasis 2% and mixed infections BV and yeast 5%.
Conclusion | Bacterial vaginosis remains an important reproductive health problem. There is need for health education among women of the reproductive age group. Treatment of BV should be considered in women presenting with abnormal vaginal discharge. BV could be a predisposing factor for HIV disease.

HP 05
Prevalence of sexually transmitted infections among women attending antenatal clinics in northeastern Tanzania

Mercy Chiduo • National Institute for Medical Research, Tanga, Tanzania

Introduction | Diagnosis and treatment of sexually transmitted infections and reproductive tract infections (STI/RTIs) among pregnant women is important to minimize peripartum and perinatal morbidity. In Tanzania all the pregnant women attending antenatal clinics (ANC) are screened with serological tests for HIV and syphilis. However, screening for other STIs is not routinely done. This study determined the prevalences of syphilis, *Trichomonas vaginalis*, gonorrhea, chlamydia and candida infection among pregnant women in Tanga, Tanzania.
Methods | Pregnant women enrolled in a randomised, prevention of-mother-to-child transmission trial (n=105) and HIV-uninfected pregnant women (n=100) attending antenatal clinics from three health facilities were enrolled between April 2009 and August 2010. The women were interviewed, examined and genital and blood samples were collected for *Neisseria gonorrhea*, *Candida albicans*, *Trichomonas vaginalis*, *Treponema pallidum* and chlamydia.
Results | Genital infections were more prevalent in HIV-infected women than HIV-uninfected women, statistically significant for trichomoniasis (18.8% *vs* 5.0%; p<0.003) and candidiasis (16.5% *vs* 2.0%; p<0.001) no significant differences were found for the prevalence of chlamydia infection (0% *vs* 3.0%; p=0.15), syphilis (2.4% *vs* 3.0%; p=0.57/), and gonorrhea (3.5% *vs* 0%; p=0.095). Though it was offered, none of the partners of the women with transmittable STIs reported for testing and treatment.
Conclusion | STIs/RTIs were common in both HIV-infected and uninfected pregnant women. Screening of every pregnant woman attending antenatal clinics should include microbiological investigations besides the rapid tests for syphilis and HIV. There is still a need to improve partner notification, investigation and treatment.

HP 06
The LEDGINs: first-in-class allosteric HIV-1 integrase inhibitors

Belete Desimmie • Katholieke Universiteit Leuven, Leuven, Belgium

Introduction | The development of resistance against raltegravir in patients demonstrated the necessity to develop second generation integrase inhibitors. In 2003 we identified lens epithelium-derived growth factor (LEDGF/p75) as a cellular co-factor of integration. Later studies pinpointed that LEDGF/p75 tethers and facilitates integration of the viral genome in the host chromatin validating this virus-host interaction as a potential antiviral drug target.
Methods | We identified and developed small molecules as potent inhibitors of the LEDGF/p75-in interaction (LEDGINs). Thorough evaluation has pinpointed their mode of action *in vitro* and in cell culture. Compounds with highest antiviral activity have been analyzed for their ADMETox and preliminary pharmacokinetic profile.
Results | LEDGINs inhibit the LEDGF/p75-in interaction *in vitro* and in cell culture. The lack of cross-resistance with raltegravir and elvitegravir as well as their binding mode on integrase, as demonstrated by co-crystallization and resistance selection, define the LEDGINs as genuine allosteric integrase inhibitors. We established a solid structure activity relationship with lead compounds demonstrating their antiviral activity in the low nanomolar range (EC50=114+64 nM) with high selectivity (SI=1152). Compatible ADMETox and pharmacokinetic properties have led to the further pre-clinical development of the LEDGINs.
Conclusion | We described the first selective small molecules allosteric integration inhibitors and HIV replication in the nanomolar range. Biological evaluation of LEDGINs gives proof-of-concept that virus-host interactions are genuine drug targets for antiviral therapy and demonstrates their potential for further pre-clinical development.

HP 07

Toxicity grading in clinical trials: implications for the use of western derived laboratory toxicity grading values

Sikhulile Moyo • Botswana-Harvard AIDS Institute Partnership, Gaborone, Botswana

Introduction | Clinical Trials on HIV, TB and malaria are increasingly being conducted in many parts of Africa with investments in research infrastructure, training and capacity building. In order to ensure appropriate inclusion of trial participants and safety evaluation, established reference intervals for clinical tests are required for the target population. Using locally defined reference ranges, we evaluated the laboratory based toxicity grading in clinical research studies in Botswana to determine concordance in classification with the US Division of AIDS (DAIDS) toxicity table.
Methods | Laboratory values were graded using the DAIDS toxicity table and classification was compared to local and regional reference ranges.
Results | Haemoglobin levels of the Botswana population are lower than those derived in western populations. 8% of healthy adults and 15% of females were graded as anaemic and would not qualify for phase I/II clinical trials. There was a 20–24% agreement (Kappa 0.026–0.036) in classification of toxicity grading for HIV-1 positive adults.
Conclusion | Using laboratory reference intervals derived from other populations excludes potential clinical trial volunteers in Africa and makes adverse event assessment challenging. Appropriate region specific grading tables are critical for clinical trials.

HP 08

Lipid profiles in two groups of HIV-1 infected patients in Cameroon on two treatment regimens with either efavirenz or nevirapine, in association with RTI

Ngoufo Nguemaïm • University of Yaoundé I, Yaoundé, Cameroon

Introduction | Abnormalities in lipid metabolism are described in HIV-1-infected patients on highly active antiretroviral therapies (HAART). The aim of this study was to determine the effect of two antiretroviral therapy regimens on lipid profiles. Patients were allocated to two treatment regimens: nevirapine (NVP) + stavudine (d4T) + lamivudine (3TC) (n=197) or efavirenz (EFV) + stavudine (d4T) + lamivudine (3TC) (n=181).
Methods | Serum was prepared from blood samples collected before the start of treatment (month 0) and at 24 months. Lipids and lipoproteins were measured using colorimetric enzyme assays or by calculation.
Results | Overall, there was an increase in all lipid parameters in patients on both treatment regimens at 24 months, although there were individual differences with respect to each lipid parameter that affected the atherogenicity indices for both regimens. Increase of high density lipoprotein cholesterol (HDLC) (42.82%) was significantly larger in patients on NVP than on EFV (24.03%) ($p<0.001$), as opposed to total cholesterol (TC), triglycerides and low density lipoprotein cholesterol (LDLC) that were significantly lower in patient on NVP than on EFV. Triglycerides, very low density lipoproteins and LDLC increased in both regimens. These changes were not much affected by changes in viral load and CD4 cell levels.
Conclusion | The changes in the atherogenicity indices showed that the regimen with NVP seems to have less risk of coronary heart disease compared to EFV.

HP 09
Training and strategy for HIV drug resistance testing in eastern Africa

Maurizio Zazzi • EuResist Network/University of Siena, Italy

Introduction | Genotypic HIV drug resistance testing (GRT) is seldom feasible in African laboratories. A possible strategy is to perform the first steps of GRT locally and sequence PCR products at distant laboratories. We have established an East African network for capacity building and training in HIV drug resistance.
Methods | The training was performed by two trainers at the Kenya Medical Research Institute, Nairobi. The ten trainees mainly had a background in serology and parasitology. The training consisted of RNA extraction from plasma by spin columns. This was followed by homebrew reverse transcription and nested PCR to obtain the HIV protease/reverse transcriptase which is normally sequenced for estimating susceptibility to protease and reverse transcriptase inhibitors. Amplification products were brought at room temperature to the University of Sienna for sequencing and quality control.
Results | Two complete runs of the procedure were done, the first conducted by the trainers and the second by the trainees. In the first and second run, 7/10 and 6/10 samples were successfully amplified. Although viral load data were not available, 7/7 amplification failures *vs* only 2/13 successful amplifications were derived from patients under treatment suggesting that most failures could be due to low or undetectable viral load. Sequencing of the PCR products carried to Italy worked as good as with fresh samples.
Conclusion | A one-week intensive hands-on training course was effective for learning plasma RNA extraction and generation of PCR products. The procedure to split GRT between a local and a remote site is perfectly feasible.

HP 10
Liver enzyme abnormalities and associated risk factors in HIV patients on efavirenz-based HAART with or without tuberculosis co-infection in Tanzania

Sabina Mugusi • Muhimbili National Hospital, Dar es Salaam, Tanzania

Introduction | The effect of pharmacogenetic variations, efavirenz pharmacokinetics and rifampicin co-administration on antiretroviral and anti-tubercular drug induced hepatotoxicity (DIH) has not been well investigated. We studied the incidence, timing and effect of efavirenz pharmacokinetics and pharmacogenetic variation in HIV patients with or without TB co-infection.
Methods | A total of 473 treatment naïve HIV patients (253 HIV only and 220 with HIV-TB co-infection) were followed. Quantification of plasma efavirenz and genotyping for CYP2B6, CYP3A5, ABCB1 and SLCO1B1 genes were done. Baseline demographic and clinical data, plus laboratory results of the 12 weeks were used for analysis. Case definition for DIH was an elevation of alanine aminotranferease (ALT) and/or aspartate aminotransferase (AST) above 3 times the upper limit of normal from a normal baseline AST or ALT. Incidence of DIH and identification of predictors was evaluated using survival analysis and Cox Proportional Hazards Model.
Results | The incidence of DIH was 7.8% (15 and 22 patients who were HIV only and HIV-TB respectively, p=N/S). A multivariate Cox regression model picked up HCV-positive and CYP2B6*6 genotype as predictors of DIH. Median time to DIH was 2 weeks after HAART initiation. No severe DIH was seen in any of our patients. Rise in CD4 was similar in patients with and without DIH.
Conclusion | DIH does occur in our setting, presenting early in treatment. The hepatotoxicity seen is not severe and does not require treatment interruption. There is good tolerance of HAART and anti-TB treatment with similar immunological outcomes. Genetic make-up influences the development of DIH.

HP 11

Nigerian surveillance program: assessing the status of HIV and reproductive health indicators

Bolakale Issa • Federal Ministry of Health/Nigeria, MEASURE Evaluation, Abuja, Nigeria

Introduction | Nigeria is committed to monitoring reproductive health interventions including HIV prevention. Since its discovery in Nigeria more than two decades ago, HIV has posed a risk to all and especially to women. The study assesses HIV and reproductive health indicators to enhance evidence-based decision making.
Methods | A cross-sectional population-based survey was conducted by the Federal Ministry of Health in 2007 with a total sample size of 11,521 (male 15–64 years; female 15–49 years). A further data analysis was carried out to obtain the needed indicators.
Results | The mean age was 29.8 ± 11.7 y; 53.5% were male and 46.5% female; 34.4% were urban and 65.6% rural. National HIV prevalence was 3.64% (male: 3.31%; female: 4.03%). Youths (15–24 y) that had sex before the age of 15 and 18 were 11.8% and 32.4% respectively. 18.4% had more than one sexual partner; 80.7% and 75.6% knew that a male condom protects against pregnancy and HIV respectively. 81.9% had sexual intercourse in the last 12 months of which 45.8% used a condom and 10.5% were engaged in intergenerational sex with partners 10 years older. Of all pregnant women, 62.7% accessed antenatal care and among HIV-positive women, 68.9% delivered with skilled birth attendants while 34.1% delivered with non-skilled birth attendants.
Conclusion | There is feminisation of HIV in Nigeria with more women infected than men. Similarly, 34% of HIV-positive pregnant women were not delivered by skilled birth attendants with the concomitant potential risk for mother to child transmission of HIV. Therefore, monitoring HIV and reproductive health status is vital in an expanded national response.

HP 12

Measuring outcomes in OVC/HIV programming using the Civil Society Fund (CSF) model

Simon Peter Mayanja • Chemonics International-Civil Society Fund, Kampala, Uganda

Introduction | For over 25 years, communities in Uganda have been struggling with the devastating effects of AIDS. Civil society organisations (CSOs) have significantly contributed to the national response but their efforts suffer from inadequate and/or inconsistent funding and limited capacity to implement. Since the inception of the CSF in 2008, funding from five international donors has been pooled and managed through the shared Civil Society Fund mechanism, and grants have been extended to 97 CSOs in the areas of HIV prevention, support for orphaned and vulnerable children (OVC), and paediatric AIDS.
Methods | A phased assessment took place from November to December 2010. The process involved desk reviews, analysis of program reports, and field interviews with CSO project and coordination teams and project beneficiaries. In total, 97 organisations were assessed from the four regions of Uganda.
Results | Evidence of increased behaviour change in terms of positive prevention practices and uptake of HIV testing and counselling (HTC) services was recorded. Accelerated condom use was reported by 44 of 49 HIV prevention CSOs assessed. The majority (43/49) achieved their set targets reaching approximately 250,000 people with HTC services. The proportion of CSOs providing life skills-based education to young people has increased to over 85%. CSOs supportted OVCs (43/45) reaching 71,500 children. Beneficiary satisfaction was recorded in 91 of 97 CSOs assessed.
Conclusion | Supporting CSOs in HIV/AIDS and OVC programs results in increased access, desired outcomes, and improved quality of the services. This model which emphasizes donor coordination and civil society support can be replicated elsewhere, in situations where public health systems are still weak.

HP 13
Trends in HIV related risky sexual behaviour among fishing communities participating in a cohort for future HIV prevention trials

Juliet Mpendo • UVRI-IAVI HIV Vaccine Program, Entebbe, Uganda

Introduction | Fishing communities are considered to be at high risk of HIV infection due to factors such as lifestyle and poor access to health services. They are also a potential population for HIV prevention trials. We assessed HIV risk behaviour among HIV-negative participants.
Methods | Trends in risk behaviour were assessed in a population-based cohort of 1000 participants aged 13–49 years in 5 fishing communities along Lake Victoria, Uganda. Data on sexual behaviours, STIs and blood for HIV serology were collected at baseline, 6, 12, and 18 months. Risk reduction counselling, condoms and STI treatment were provided. Chi-square for trend test was used to assess changes in risky sexual behaviour over time.
Results | Males constituted 55% of all participants. Men were more likely to report new sexual partners in the 3 months preceding interview (75% *vs* 38%), drinking alcohol (71% *vs* 55%), being away from home (86% *vs* 71%), drug abuse (23% *vs* 6%) and giving gifts in exchange for sex (59% *vs* 18%); all observations were significant at p<0.05. Women were more likely to report STIs (47% *vs* 34%, p<0.001) and condom use (27% *vs* 20%, p=0.058) and receiving gifts in exchange for sex (46% *vs* 25%, p<0.001). There were significant trends in the reduction of risky sexual behaviours over the follow-up period (trend test p<0.05).
Conclusion | Although risky behaviour is highly common in these communities, a significant trend in its reduction was observed, perhaps partly attributable to risk reduction counselling, provision of condoms and STI treatment.

HP 14
Pregnancy rates and associated factors in an HIV high risk community-based fishing population cohort along Lake Victoria Shores, Uganda

Ali Ssetaala • UVRI-IAVI HIV Vaccine Program, Entebbe, Uganda

Introduction | High pregnancy rates among high-at-risk fisher folk affect implementation of HIV prevention studies and programs. We explored pregnancy rates and associated factors in five fishing communities along Lake Victoria.
Methods | An 18 month prospective observational cohort study was conducted in five fishing communities of the Masaka, Mukono and Wakiso districts along the shores of Lake Victoria. Data on demographics, HIV risk behaviour and reproductive health were collected from 1000 participants aged 13–49 years. HIV serology and pregnancy testing were done at baseline and repeated every 6 months.
Results | Of the 449 women enrolled (median age 27 years, IQR 22–33), 442 were tested for pregnancy at enrolment and 106 pregnancies occurred during follow-up. Factors associated with pregnancy after multiple logistic regression were: age below 30 years (14% *vs* 8%, p=0.03); marriage (13% *vs* 10%, p=0.04); Muslim religion (15% *vs* 11%, p=0.03); staying away from home frequently (10% *vs* 15%, p=0.02); history of genital discharge (15% *vs* 10%, p=0.02); having new sexual partners (6% *vs* 14%, p=0.01); reporting forced sex (17% *vs* 12%, p=0.04%); and having a sexual partner at a previous visit (13% *vs* 5%, p=0.08). There was a decline in pregnancy rates from 18.6% at enrolment to 8.5% at last visit, possibly due to increased use of family planning, from 0.56% at enrolment to 3.6% at 18 months (trend, p-value=0.02).
Conclusion | Efforts to increase the use of modern family planning methods, treatment of STIs and reducing rates of forced sex would go a long way in reducing pregnancy rates in these communities.

HP 15
Evaluation of HIV incidence during pregnancy in Ouagadougou, Burkina Faso

Check Asken Hugues Traore • Centre de recherche Internationale pour la Santé, Ouagadougou, Burkina Faso

Introduction | The relevance of current PMTCT guidelines to test for HIV at each antenatal care (four tests in total) for West African countries with low HIV prevalence such as Burkina Faso is unclear.
Methods | To determine the HIV incidence during pregnancy among women consulting antenatal clinics (ANCs) in Ouagadougou, we carried out a prospective cohort study in 51 ANCs in Ouagadougou from June 2010 to June 2011.
Results | Of 8,776 consulting mothers, 8,632 were included and followed during the study period. The mean age of the women was 24.9 years, and they first consulted on average at 14 weeks of amenorrhoea. Most women were married (66.9%), homemakers (54.3%), with a poor level of education (37.4% went to school). The mean parity was 1.27 children. At the first visit, 144 mothers (1.64%, IC95% 1.77–1.50) were HIV-1 infected. No incident case was reported at the end of pregnancy among the 8,632 mothers. The mean time between the first and last HIV test was 22.8 weeks, which yielded 1,514 person-months of follow-up.
Conclusion | The absence of any seroconversion among more than 8,000 women consulting in routine ANCs in Burkina advocates for a marked reduction of HIV testing during pregnancy. A second test at the last ANC visit before delivery would be sufficient to detect any seroconversion and to implement an antiretroviral prophylaxis during the last month of pregnancy and labour. Such a strategy would save a considerable amount of resources in low-endemic countries such as Burkina Faso.

HP 16
Investigating monocyte and alveolar macrophage dysfunction in HIV-TB co-infection

Rubina Bunjun, Tracey • University of Cape Town, South Africa

Introduction | The HIV-TB co-epidemic has claimed millions of lives. HIV-infected individuals are more susceptible to tuberculosis even early in infection, due to a spectrum of immune defects induced by HIV. Innate cells such as monocytes and particularly alveolar macrophages in the lungs are the first line of defence against *M. tuberculosis* (*Mtb*). Innate cells sense pathogens via Toll-like receptors (TLRs), leading to their activation and triggering of adaptive immunity, functions critical for controlling or containing *Mtb*. We investigated whether these functions were compromised in HIV co-infection in response to *Mtb*-responsive TLRs.
Methods | Monocyte function was investigated in HIV-infected individuals with CD4 counts >500 cells/μL, as well as uninfected individuals, both groups infected with latent TB. Monocytes were stimulated with mycobacterial PPD or LPS, and IL-6 and TNF-α production was measured by intracellular cytokine staining and polychromatic flow cytometry. Lung alveolar macrophages were obtained by bronchoalveolar lavage.
Results | Monocytes from HIV-infected individuals produced less cytokine in response to *Mtb*-responsive TLR stimulation than those from HIV-uninfected individuals. Furthermore, these cells also produced significantly less cytokine per cell than monocytes from uninfected individuals. Interestingly, preliminary results from bronchoalveolar lavage samples indicate high spontaneous and TLR-induced cytokine production by alveolar macrophages.
Conclusion | HIV may cause a defect in the ability of monocytes to produce pro-inflammatory cytokines in response to TLR ligands, which may critically impair the immune response to *Mtb*. More studies are needed to gather insights into how HIV affects innate immunity at the site of mycobacterial infection, the lung.

HP 17

Pattern of HIV-specific IFN-γ responses, CD4 counts, viral load trajectory and CD8 mediated virus inhibition in recently HIV-1-infected Ugandans

Daniel Bugembe Lule • MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

Introduction | We evaluated the relationship between early T-cell responses, plasma viral load, CD4 count and CD8 mediated virus inhibition.
Methods | Fourteen early HIV-1 infections were identified in serodiscordant Ugandan couples. CD4 count, plasma viral load and HLA class I tissue types were determined. IFN-γ responses of cryopreserved PBMC to HIV-1 peptide pools covering subtypes a and D were screened using cultured ELISPOT assays. Epitope recognition was refined using single peptides in *ex vivo* ELISPOT assays and CD8 T cell mediated inhibition of HIV-1 was evaluated using viral inhibition assays. Regression models were fitted to show spot count associations to CD4 count and log-viral-load.
Results | At enrolment, median time post infection was 1 month (range: 1–4, Fiebig stage: IV-VI) and viral load 31810 copies/mL (738–750001). Seven individuals recognized Gag (range: 1–23 peptides), Pol (1–9) and Env (1–5). All showed changes in epitope recognition over time and 4/8 retained at least 1 initially recognized epitope. The magnitude of IFN-γ responses decreased with increased CD4 count (p=0.094) at baseline but no relationship at a later time point or to viral load. Longitudinally, magnitude was inversely associated to CD4 count (p=0.065). For 2 individuals tested there was cross clade inhibition of HIV-1 by CD8+ T-cells with retention and switches of inhibited clades over time.
Conclusion | No statistically significant associations between viral load, CD4 count and IFN-γ responses were seen in 8 individuals over the first 2 years of HIV-1 infection. Epitope recognition and viral inhibition specificity fluctuated over time. Cross-clade responses were observed.

HP 18

Fishing expedition in Botswana: search for plasma with broadly neutralizing antibodies against HIV-1

Takafira Mduluza • Botswana Harvard AIDS Institute Partnership (BHP), Gaborone, Botswana

Introduction | Neutralizing antibody assay techniques are now widely employed in different laboratories in search for correlates of immunity to discover the presence of protective immunity that is important in preventing transmission of HIV infection.
Methods | The samples were collected from participants recruited into a study conducted at the BHP in Botswana. 72 individuals aged 15–55 years, identified as being HIV-1C- infected formed the cohort that had samples already archived. Panels of well-characterized reference strains were used to assess plasma with a high ability of HIV-1 neutralization. The inhibitory dose ID50 or ID90 was defined as either the serum dilution or sample concentration that causes a 50% or 90% prevention respectively of the virus isolates infecting TZM-bl cells.
Results | Early results show that there are samples from individuals that depict broadly neutralizing of the HIV-1 virus strains but moderately on the HIV-1C strain that is prevalent and dominant in the southern African region. Of the 50 samples screened for broadly neutralizing antibodies, some observations were made at 90% infection inhibition of TZM-bl cells (ID90). We observed 1 patient who inhibited 4/5 strains but showing moderate inhibition of IN93 HIV-1 subtype C. Another participant inhibited 3/5 strains.
Conclusion | The plasma samples revealed no strong ID90 inhibition of the IN93 HIV-1C strain that is predominant in the region. The results show a potential of identifying some samples that show inhibition of virus strains. These samples would be studied further on their characteristics and the component that exhibits the neutralizing effect and the associated immune components assisting the responses.

HP 19

Molecular characterization and phylogeographic analysis of HIV-1 strains of chronically and recently infected individuals in Kigali, Rwanda

John Rusine • National Reference Laboratory, Kigali, Rwanda

Introduction | Molecular differences between different HIV strains have been shown to impact on viral fitness and pathogenicity, which might impact on prophylactic, immunogenic and therapeutic interventions. Little is known about HIV-1 subtypes circulating in Rwanda and in the region.
Methods | To assess the molecular epidemiologic of HIV-1 strains in naive, chronically and recently infected patients in Kigali, Rwanda with respect to HIV-1 subtypes circulating in the region. We conducted a descriptive study in recently and chronically HIV-1-infected patients. Pol gene sequencing was performed on plasma samples with HIV-1 RNA at least 1000 copies/mL. Aligned sequences were assembled and edited using the Viroseq v5.4 software and submitted to Los Alamos subtyping tool to determine HIV-1 subtype of each patient group.
Results | HIV-1 genotypic test results were obtained from 26 newly HIV-1 diagnosed. No HIV-1 drug resistance was identified. 69.2% of the patients (n=18) were infected by subtype A1; 15.3% (n=4) by subtype C; 7.6% (n=2) by subtype D; 3.8% (n=1) by A1-like subtype; 3.85% (n=1) by an unclassified type. In chronically HIV-1 infected patients (n=102) the frequencies of HIV-1 subtypes were: 75.4% (n=77) subtype A1; 11.7% (n=12) subtype C; 4.9% (n=5) C1-like subtype; 4.9% (n=5) A1-like subtype; 1.96% (n=2) subtype D; 0.97% (n=1) D-like subtype. The subtype distribution among the two groups was not different (p=0.409); 2 patients had transmitted HIV-1 drug resistance. No subtype's network transmission was identified among newly HIV-1 diagnosed or in chronically HIV-1 infected patients.
Conclusion | Subtype A1 followed by subtype C were predominant, with no subtypes network transmission identified among the two groups.

HP 20

Novel modular teaching of HIV patients and effect on adherence to HAART

Olusegun Busari • Federal Medical Centre, Ido-Ekiti, Nigeria

Introduction | Patient education plays a significant role in adherence to HAART, development of OIs, hospitalization and mortality. Unfortunately, in most resource-limited settings it is often not or casually done. The objective was to compare a modular teaching method (MTM) with traditional patient education (TTM), and evaluate its effectiveness on adherence to HAART, development of OIs, hospitalization and mortality.
Methods | 420 HIV-positive patients on HAART were recruited and divided into subject and control groups. A pre-test and post-test time-series design was used to collect data using a 30-item knowledge and skills assessment schedule with items rated on a 5-point Linkert-type scale. The schedule was pre-tested on 50 patients with Cronbach's score of 0.92 and a test-retest coefficient of 0.89 at a 4-week interval. MTM consist of 10 modules which address factors affecting adherence such as benefits of treatment, family and social support, adverse drug effects, etc. MTM was used to educate subject group while the controls received the traditional teaching. All the patients were followed for 8 months at 4-week intervals via outpatient clinic and home visits. Chi square and t-tests were used; $p<0.05$ was considered significant.
Results | Mean adherence rate for subjects was 98.9 ± 1.0% and for controls, 87.6 ± 2.4% ($p<0.001$). Frequency of OIs/patient/month in subjects and controls (0.51 *vs* 1.31, p=0.002). Mean number of re-admissions/patient/month in the 8-month follow-up was 0.18 ± 0.01 for subjects and 0.89 ± 0.02 for controls (p=0.0012). Subject group had shorter hospital stay (p=0.002) and lower mortality (p=0.008)
Conclusion | MTM has significant effect on adherence to HAART, development of OIs, readmission rate, hospital stay and mortality

Reference: JAIDS 2003; 34(Suppl 2):191–194.

HP 21
HIV-positive status disclosure to sexual partner among women attending Hawassa University Referral Hospital, south Ethiopia

Taye Gari • College of Medicine & Health Sciences, Hawassa University, Ethiopia

Introduction | Disclosure of HIV-positive status has a key role in the prevention and control of HIV/AIDS and therefore needs investigation.
Methods | A cross sectional survey was conducted to determine the magnitude and outcome of HIV-positive status disclosure to sexual partner. Using a structured and pre-tested questionnaire, data were collected through interview until the required sample (384) was obtained. Data was analysed using SPSS 12.1 for Windows.
Results | Overall, 85.7% of the women had disclosed their HIV-positive status to sexual partner. Barriers to non-disclosure were: fear of abandonment, break-up in relationship and stigma. 59% of the women faced negative partner reaction after disclosure. Women who were in a cohabiting relationship and who did not know the HIV status of their sexual partner were less likely to disclose their HIV-positive status than counterparts. Being on medical follow-up for more than one year was a predictor of HIV-positive status disclosure.
Conclusion | HIV-positive status disclosure was slightly lower than the report from Jimma and Addis Ababa, Ethiopia. Negative partner reaction following disclosure was higher. Effectively addressing issues of disclosure is recommended to encourage disclosure and coping with negative reactions after disclosure.

Reference: Ethiop J Health Dev. 2010; 24(1):9–14.s

HP 22
The role of community caregivers in the care of HIV/AIDS patients in Lambwe Division, rural Kenya

Zachary Kwena • Center for Microbiology Research, Kenya Medical Research Institute, Kisumu, Kenya

Introduction | Many people in rural areas of developing countries delay getting to health facilities, although it is desirable to enrol into HIV care early to benefit from timely initiation of antiretroviral therapy (ART). We assessed the role of community caregivers in identifying, encouraging enrolment into care and supporting patients to adhere to ART.
Methods | As part of a larger study to establish the role of witchcraft beliefs in healthcare seeking, we conducted 15 in-depth interviews with care providers (clinical officers, nurses and public health officials; n=8) and community caregivers (n=7). The participants were conveniently sampled based on their area of jurisdiction. In-depth interviews were conducted in quiet and private venues. Resultant transcripts were analysed thematically following the tenets of grounded theory.
Results | It emerged that the community caregivers were well-known, accepted and appreciated by their communities and the health facility management. The caregivers counselled the identified patients and discussed with relatives/guardians about their intentions to assist the sick person to get treatment. The caregivers' good working relationships with health facilities ensured that their patients were attended to in a friendly and humane manner. This encouraged patients to return on their own once they were enrolled into care and got better. The caregivers closely monitored patients' adherence to medication and return visits.
Conclusion | Community caregivers play a very critical role in ensuring that HIV/AIDS patients enrol into care and adhere to their medication in a community where stigma and lack of support keep away many people from accessing life-saving care.

HP 23

Fishing, HIV and sex: exploring transactional sex and gender based violence in fishing communities in southern Malawi

Eleanor MaCP herson • Malawi Liverpool Wellcome, Liverpool School of Tropical Medicine

Introduction | MAFESSTA is a combined social science and epidemiological study assessing transmission dynamics of HIV and other STIs in fishing communities in the Mangochi district, southern Malawi. Transactional sex and gender based violence were reported within both social science and epidemiological arms of the study and were followed up in-depth in a separate study.
Methods | Within the context of the MAFESSTA study, we are conducting a qualitative research project to explore drivers and facilitators of transactional sex and violence in two fishing communities. Methods employed include in-depth interviews and focus group discussions with male and female community members, including sex-workers, and participant observation in study villages.
Results | We found gendered power imbalances in relationships which means women are often unable to negotiate safe sex. In fishing communities transactional sex plays out across a spectrum, from gift giving within relationships, to sex for fish exchanges, to sex worker encounters, and this in turn shapes condom negotiation. The context and motive for transactional sex varies. For example sex work is shaped by poverty, with poor women dominating in local shebeens selling locally brewed beer, while better off women are using mobile phones to identify potential liaisons along the lake shore (for example high fish catch) and travelling accordingly. All sex workers interviewed reported experiences of violence from male clients.
Conclusion | Transactional sex is common in Malawian contexts but takes particular forms in fishing communities, where links with or to violence emerge. These require further investigation to better unpack resilience and vulnerability to STIs.

HP 24

Mitigating the impact of HIV/AIDS among pupils in Bolifamba and Muea Communities of the southwestern region of Cameroon

Dickson Nsagha • Faculty of Health Sciences, University of Buea, Cameroon

Introduction | There is paucity of data on HIV/AIDS determinants among pupils in Cameroon. Children are less bound by established behavioural patterns. HIV/AIDS programmes could have a greater impact on them than on adults.
Methods | A 30-item questionnaire was administered by trained interviewers to pupils after pre-testing during which ambiguous questions were fine-tuned. A participatory approach including pupils and teachers, guided a school-to-school survey. Data was checked for uncompleted questions and use of correct codes including range and consistency checks. Data was analysed using Epi-Info.
Results | 968 structured questionnaires were administered to grades 4–6 primary school pupils of 13 schools in Muea and Bolifamba communities. 913 (94.7%) (CI: 93.1–96) pupils had heard of HIV but only 784 (81.8%) (CI: 79.1– 84.1) had discussed it while 937 (97.3%) (CI: 96–98.2) had heard of AIDS. The HIV/AIDS information sources were from class lessons (906; 94.0%; CI: 92.2–95.4), friends (646; 67.0%; CI: 63.9–70), hospitals (796; 82.5%; CI: 79.9–84.8), churches (414; 42.9%; CI: 39.8–46.1), and radio (870(90.3%) (88.3–92.1). 21 pupils (2.2%) (CI: 1.4–3.4) had family members living with HIV/AIDS and 759 (80.9%) (CI: 78.2–83.3) acknowledged that anybody can contract HIV. 832 (86.7%) (CI: 84.3–88.7) pupils knew that HIV/AIDS treatment takes place in a health facility. HIV/AIDS social stigma was high with 155(16.1%) (CI: 13.9–18.6) pupils accepting that they could hug PLWHA; 315 (32.8%) (CI: 29.8–35.9) could eat with PLWHA and 367 (38.1%) (CI: 35.1–41.3) could use the toilet with PLWHA. 342 (35.6%) (CI: 32.6–38.7) pupils indicated HIV is transmitted through witchcraft.
Conclusion | Knowledge on HIV/AIDS is high but high social stigma could hinder the uptake of HIV/AIDS interventions.

HP 25
Perceptions of HIV/AIDS infection in a gerontological sexology study in Nigeria

Odor King • College of Medicine, University of Ibadan, Nigeria

Introduction | HIV/AIDS continues to pose a public health challenge in Africa and the pandemic affects all age groups including geriatrics. Despite their engaging in risky sexual activities, limited attention is paid to this group. This study therefore examined perceived HIV/AIDS infection among geriatrics in Nigeria.
Methods | A cross-sectional study with a multi-stage sampling procedure to select 400 geriatrics. A pre-tested questionnaire was developed, using information obtained from 10 Focus Group Discussions (FGDs), to collect information. FGD data were analysed thematically, while questionnaire data were analysed using descriptive and statistical methods.
Results | 25% of the participants had extra-marital sex since they attained geriatric age. However, among this subgroup that had extra-marital sex, few (6.8%) used a condom. More males (5.3%) than females (1.5%) used a condom during the last extramarital sex. Low level of condom-use was attributed to the opinions that condom use was not worthwhile (34.5%), and that condoms were not for geriatrics (50.0%). Moreover, FGD participants thought that sex could not lead to pregnancy. The majority (60.3%) posited patronizing traditional healers; few (10.3%) posited the use of herbs for concussion could prevent HIV/AIDS. Similarly, non-condom use was due to confidence in traditional herbs, perceived to protect against STIs including HIV/AIDS.
Conclusion | Engagement in risky activities among geriatrics is a growing HIV/AIDS challenge. Condom use is misconstrued probably due to a knowledge gap. Without urgent measures to enable them to protect themselves, development efforts will be in jeopardy. Investing in geriatric sex and health education is a cost-effective intervention in mitigating the HIV/AIDS pandemic.

HP 26
Disclosure of HIV/AIDS status to sexual partners as a preventive measure

Akua Dufie K. Wiafe • National Malaria Control Programme, Kumasi, Ghana

Introduction | Disclosure of HIV/AIDS status is guided by confidentiality policies limiting the disclosure to the client involved unless otherwise required by law. Disclosure is vital to ensure proper care. However, many people living with HIV/AIDS (PLWHA) are not disclosing their status to their sexual partners, thus hampering HIV/AIDS prevention. The question is: Should disclosure of HIV/AIDS to sexual partners be made compulsory?
Methods | A multi-stage sampling approach was employed for this study. First, a simple random sampling technique was used to select a range of people both reactive (n=72) and non-reactive (n=40). Secondly, a purposive sampling technique was used to select only PLWHA to be interviewed with a structured questionnaire. The questionnaire aimed to find out if PLWHA would disclose their status to their sexual partners; if they would like their partners to disclose their status to them if tested positive; what their reactions would be; their reasons for disclosure or non-disclosure; and possible means of contracting the disease.
Results | Many respondents desired that their partners would disclose their status but thought twice about disclosing their own status. 64% of the PLWHAs have not disclosed nor do they have any intention of disclosing their status to their sexual partners. 11% of reactive respondents acknowledged that they saw their partners take some medication some years back which they have come to know as antiretroviral. Even though women were more likely to suffer from break-up, stigma and discrimination, more women had disclosed their status.
Conclusion | PLWHAs should disclose their status to their sexual partners to aid HIV/AIDS prevention.

HP 27

Correlates of study dropout in a fisher folk HIV vaccine preparedness observational cohort, Uganda

Andrew Abaasa • MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

Introduction | Attrition of longitudinal cohorts can bias or decrease the statistical power of study results. We report dropout and associated factors for an observational cohort (HIV vaccine trial preparedness) among fisher folk in Uganda.
Methods | HIV-uninfected high-risk volunteers aged 13–49 years from fishing communities along Lake Victoria were enrolled and followed for 18 months. High-risk was defined as self-report of any of the following: unprotected sex with one or more sex partners; history of STIs; knowledge of HIV-positive partner; and being away from home for 2+ nights a month in the previous 3 months. Six monthly visits were carried out for HIV counselling and testing and sexual behaviour data collection. Socio-demographic and sexual behaviour characteristics of study dropouts (not returning for any follow-up visit) were compared with those of volunteers who returned for follow-up. Logistic regression was used to find factors independently associated with study dropout.
Results | Of 2,074 persons (51% women) screened from February-August 2009, 1,000 (54% men) were enrolled. A total of 753 (75%) completed all visits, 166 (17%) returned at least once and 81 (8%) dropped out. Dropout was independently associated with having spent <1 year in the study area; adjusted Odds Ratio (aOR) 3.37 (95% CI: 1.74–6.56), reporting new sexual partners in previous 3 months 1.74 (0.99–3.04), and drug use 2.64 (1.33–5.23).
Conclusion | Contrary to perceptions that fisher folk are highly mobile, our findings indicate a relatively low drop-out mainly fuelled by recent in-migrants and illicit drug users. Other correlates of dropout need to be identified to inform recruitment strategies.

HP 28

Adolescents perception of HIV vaccine trials in Nigeria

Ngozi Otuonye Onwuatuelo • Nigerian Institute of Medical Research Yaba, Lagos, Nigeria

Introduction | Routine vaccination of recommended vaccines in adolescents/children would prevent millions of disease cases and deaths over the lifetime of each birth cohort. The estimated national data of HIV seroprevalence for 15–24 years is 5.2%. Including adolescents in HIV vaccine trials makes them an important target for research in primary prevention of HIV infection. This study evaluated adolescent perception towards HIV vaccine trials in Nigeria.
Methods | 291 consenting adolescents were randomly selected, recruited from some secondary schools class rooms, university undergraduates' hostels and traders at shopping malls within Lagos State. Data were collected using a semi-structured questionnaire. Information was obtained on: knowledge of HIV status; willingness to participate in a vaccine trial; risky sexual behaviour; stigmatization; parental permission; and perceived risk associated with HIV vaccine. Data were collated and analysed using EPI INFO 2002 software (CDC, USA).
Results | Of the 291 respondents interviewed, 96% were single. 72.7% who were willing to participate in the HIV vaccine trial ($p<0.05$), were educated (97.5%) had knowledge of HIV vaccine (73.5%), and had no perception of risk of HIV infection from immunization (66.2%). Few respondents (31.3%) knew their HIV status. Unexpectedly, those seeking parental permission (66.2%) showed a significantly reduced willingness to participate ($p>0.05$).
Conclusion | Efforts should be made on sustained education campaigns for HIV vaccine trials which involve parents. Otherwise there could be potential obstacles to acceptance of experimental vaccines trials. Additionally, high risk sexual behaviour is an important factor in the retention of adolescents in future vaccine studies in Nigeria.

HP 29
Preparation of a young adult's cohort for HIV vaccine trials: experience from Dar es Salaam, Tanzania

Guerino E. Chalamilla • Dar es Salaam City Council, Tanzania

Introduction | An HIV vaccine is believed to be the best long-term solution for controlling the HIV/AIDS pandemic. Tanzania is currently conducting an HIV vaccine trial (TaMoVac-01) that includes young adults' volunteers. This presentation describes processes that were undertaken to facilitate the inclusion of this high-priority population in the trial.
Methods | Young adults of 18–25 years of age attending IDC were involved. Routinely filled clinical record forms were used to initially identify interested participants. Those identified were invited to attend sensitisation meetings followed by pre-screening workshops where discussions addressing contraceptives, STIs, HIV and vaccine trials. A cohort of young adults interested and willing to participate in the HIV vaccine trial was then identified.
Results | Of 1,299 young adults who attended IDC clinic during the study period, 318 were interested to attend the sensitisation workshops. Basic understanding about immunization in general and HIV vaccine trials was low. Youths were unclear of any benefit of participation, and raised concerns of safety of the HIV vaccine and if it would protect them from HIV infection. After the sensitisation workshops, 124 volunteers showed interest to be screened and 101 expressed further interest to participate in the HIV vaccine trial and took part in pre-screening workshops. Of those who attended the pre-screening workshops, 80/101 (79.2%) expressed willingness to participate in HIV vaccine trials. 69 were screened among which 26 were eligible and recruited.
Conclusion | It is essential to address concerns and identify incentives for young adults to participate in HIV vaccine trials in order to eliminate fears and maximize their participation.

HP 30
Bivalent paediatric vaccine against HIV-1 and *M. Tuberculosis*: pre-clinical development of BCG.HIVA222 strain

Joan Joseph • AIDS Research Unit, Hospital Clinic/IDIBAPS-HIVACAT, University of Barcelona, Spain

Introduction | Our starting platform was a heterologous BCG prime and MVA boost regimen delivering a common immunogen, HIVA. We have i) developed a BCG.HIVA222 strain containing an antibiotic free selection system (Cobra); ii) characterized such strain and prepared the Seed Lot System stocks; iii) evaluated the specific HIV-1 and BCG cellular immune responses induced after adult and newborn BALB/c mice immunisation with BCG.HIVA222 (kanamycin minus) prime and MVA.HIVA boost; iv) evaluated the biosafety profile by recording the body weight.
Methods | Adult mice were inoculated 2×10^6 cfu of BCG.HIVA222 intradermally, and newborn mice (7-days-old) subcutaneously. 10^6 pfu of MVA.HIVA was inoculated intramuscularly at 14 weeks post-BCG inoculation; 3 weeks later the animals were sacrificed. The specific HIV-1 cellular immune responses were analysed in spleen cells by intracellular cytokine staining and the BCG-specific immune responses by IFN-γ ELISPOT assay.
Results | The frequencies of HIV specific CD8+ T-cell producing IFN-γ were higher in adult mice (0.55%) than in newborn mice (0.3%). The BCG-specific immune responses were higher when newborn and adult mice were immunized with BCG.HIVA222 compared with parental BCG. In newborn mice the BCG-specific immune responses were higher when primed with BCG.HIVA222 kanamycin minus compared with BCG.HIVA222 kanamycin resistant (100 *vs* 55 sfu/10^6 splenocytes). No differences were observed in the body weight between the vaccinated and naïve mice groups.
Conclusion | The BCG.HIVA222 kanamycin minus strain was developed in GLPc and properly characterized. The strain was safe and immunogenic in newborn mice. It might be a good model for an infant HIV and tuberculosis bivalent vaccine.

HP 31

HIV pre-vaccine cohort with female commercial sex workers (CSW) in Ouagadougou, Burkina Faso: Is the youngest group suitable as most-at-risk population?

Nicolas Meda • Burkina Vaccine Development Project, CRIS/Université de Ouagadougou, Burkina Faso

Introduction | We questioned whether HIV infection among CSW (18–24 years) really presents a high dynamic profile for a suitable HIV pre-vaccine cohort in our setting.
Methods | We carried out a cross-sectional survey during the screening phase for inclusion in the pre-vaccine cohort of HIV-negative CSW. HIV status, socio-demographic and behavioural factors were collected. Then, we compared HIV status age-distribution in our population with the same results of the national HIV prevalence survey among CSW conducted in 2010. We finally searched for factors associated with HIV infection in our population.
Results | We screened 710 CSW in 2009–2010. Their median age at first sex was 16 years (interquartile range: 16–18). Mean casual sex partners at last week were 3 ± 6 clients. Desire for pregnancy was 15% (104/696) and 10% (72/633) were cohabiting with a male partner. The HIV prevalence was 7.63% (51/668) in our survey. This compared well with 5.51% (22/399) HIV prevalence in the age group of 15–24 years from the national survey. This survey also showed a prevalence of 22.16% (83/375) in the age group of 25–34 years and 29.46% (54/182) in the age group ≥35 years old. In our pre-vaccine survey, after multivariate analysis, only increasing age remained significantly associated with HIV infection (adjusted OR=1.18, IC 95% 1.07–1.30, p=0.0004).
Conclusion | Among female CSW, younger age seems a protective factor against HIV infection. Steady exposition to HIV infection while advancing in age, orients towards oldest CSW as the most-at-risk population in our setting.

TP 01

WANETAM TB capacity building in preparation of clinical trials in West Africa: case detection capacities training in MRC The Gambia Unit

Jacob Kweku Out • Medical Research Council Unit, Banjul, The Gambia

Introduction | Enhancing laboratory capacity is essential for generating reliable, reproducible, and accurate data from clinical trials research. The objective was to develop laboratory capacity to a level where tuberculosis (TB) clinical studies can be performed according to Good Clinical Laboratory Practise Standards.
Methods | Initial on-site visits to participating laboratories were conducted to observe these under routine working conditions. From 31 January till 25 February 2011, MRC The Gambia Unit organized its first training course in TB diagnosis for public and specialized institution laboratories from West Africa. This was funded by the West Africa Network of Excellence for TB, AIDS, and Malaria (WANETAM) under the auspices of EDCTP. Nine participants from Burkina Faso, Ghana, Guinea-Bissau, Nigeria, Senegal, and The Gambia attended. Training was conducted in an interactive manner with corresponding laboratory sessions. Hands-on training was provided to individual participants on acid-fast microscopy (light microscope and Primo Star iLED microscope), Culture (solid and liquid), identification, drug susceptibility testing (conventional and BACTEC MGIT 960 methods), quality control, biosafety, good clinical laboratory practise, and molecular-based methods for identification and drug resistance detection.
Conclusion | Opportunities were created to impart skills in appropriate and uniform laboratory methodology for culture and drug susceptibility testing of *M. tuberculosis* complex, molecular analysis and quality assurance. The next step will consist of on-site visits to participating laboratories to follow up on the application of some of the techniques, including preparation of surveillance of drug resistance TB clinical trials in West Africa.

TP 02

PanACEA collaboration and communications platform

James Sherwood • PanACEA, Sedgefield, South Africa

Introduction | Clinical trial networks exist to study various diseases across the globe. Focus, structure, funding and activities are quite variable. Networks in the developing world frequently are donor funded and have an additional responsibility for capacity development. One need common to all these networks is efficient and effective communication. Most networks have websites, some even full-fledged intranets, but many networks are still bound to a culture of collaboration through email. The volume of information shared has made email an inefficient medium for this purpose. Corporate intranets historically have required strict adherence to rigid and inflexible IT standards. The advent of hosted and flexible platforms is set to change our collaboration paradigm.
Methods | PanACEA has chosen Microsoft SharePoint as its collaboration and communication base. An 'out of the box'-hosted SharePoint site has been configured for three clinical development teams as well as capacity development and accommodates secure access for 102 users at 15 institutions, partners and the donor. Demonstrations at the annual meeting and online tutorials have been the only training provided to date.
Results | The platform was well received when launched at the annual network meeting and usage data shows a majority of users have accessed the system in the last six months.
Conclusion | As with any paradigm shift, especially those with a steep learning curve, user acceptance is challenging. Training, ease of access, speed and 'findability' all impact user uptake. PanACEA will assess and address impediments to use and offer additional training for the remainder of the PanACEA grant.

TP 03
Tuberculosis, malaria and HIV/AIDS at the Hospital Sanatório de Luanda, Angola

Emília Valadas • Hospital Sanatório de Luanda, Angola

Introduction | The three major public health problems, TB, malaria e HIV/AIDS, are frequent in Angola, often as co-infections in the same individual. In 2009, some 55,000 new cases of TB occurred in Angola. Interestingly, interventions like treatment/prevention of malaria appear to reduce mortality in HIV-infected and possibly TB co-infected patients. However, currently data on TB infection and co-infection rates is scarce.
Methods | Retrospective study during 2007 with the objective to characterize all TB cases seen at the Hospital Sanatório de Luanda, and to determine the co-infection rate with HIV and/or malaria. Demographic, diagnostic and clinical data were collected. TB diagnosis was based on clinical and radiological findings, Mantoux test and sputum microscopy. Malaria was diagnosed by standard microscopy and HIV-infection based on rapid tests (Determine®, Abbott).
Results | Of 4,666 patients seen, 87% were older than 14 years old and 57% were male. In 1,906 patients TB was diagnosed. The rate of HIV co-infection was 37% (n=712). Malaria was diagnosed during admission and hospital stay in 714 patients (37%), with *P. falciparum* the predominant species. Overall mortality was 15% (n=290).
Conclusion | Because no culture based diagnosis of TB exists in Luanda, the confirmation of TB is problematic. As expected from neighbouring countries, the HIV co-infection rate of 37% is high requiring integrated approaches to address this problem. Interestingly, more than one third of TB patients had also malaria, even during the hospital stay. This is important as prevention of malaria in TB patients appears to be a simple way to reduce overall mortality.

TP 04
Comparison of Ziel-Neelsen stain, ELISA and PCR techniques in diagnosis of pulmonary tuberculosis in Khartoum State

Elrayah Abbas • Military Hospital, Khartoum, Sudan

Introduction | To eradicate tuberculosis it is important to improve diagnostic techniques so that active tuberculosis can be treated at an early stage, before tubercle bacilli can be detected in sputum. This study aimed to develop and validate an Enzyme Linked Immuno-sorbent Assay (ELISA) technique based on antibodies to mycolic acid as surrogate markers for pulmonary tuberculosis infection.
Methods | A descriptive cross sectional laboratory based study of 100 patients suspected to have pulmonary tuberculosis conducted at some DOTS clinics in Khartoum state from February to May 2010. ZN technique and PCR amplification were performed on all sputum samples and ELISA technique was performed on serum samples.
Results | All sputum samples included, 18.9% were positive for acid fast bacilli while 81.9% were negative. Amplification of the IS6110 region reflected 87.8% positive and 12.2% negative. ELISA showed positive result in 68.7% and negative in 31.3% for anti-mycolic acid anti IgMs.
Conclusion | Diagnosis of pulmonary tuberculosis using tedious classical techniques like the ZN technique needs to be supported by new rapid techniques like PCR and detection of anti-mitochondrial antibodies by a serodiagnostic method (ELISA).

TP 05
Reliability of mycolic acid IgG antibodies in the diagnosis of pulmonary tuberculosis among Sudanese patients

Ahmed Dirar • Bashaier Teaching Hospital, Federal Ministry of Health, Khartoum, Sudan

Introduction | Early diagnosis of tuberculosis requires a rapid and reliable technique to create the possibility of rapid treatment and eventually eradication. TB serodiagnosis has the potential to fit the requirements while offering further benefit of easy sample collection. This study aimed to test the reliability of mycolic acid IgG antibody compared with polymerase chain reaction (PCR) in diagnosing pulmonary tuberculosis.
Methods | A cross sectional laboratory based study of 90 patients with symptoms of pulmonary tuberculosis attending Khartoum state DOTS clinics was conducted from January up to May 2010. 90 sputum samples were subjected to PCR to amplify the IS6110 segment and 80 serum samples were analysed by Enzyme Linked Immunosorbent Assay (ELISA) to detect anti-mycolic acid IgG antibodies.
Results | Of the 90 sputum samples included, 87,8% showed a band typical in size (123bp) for the target segment (IS6110), and 12,2% of the samples were negative. 20% of the serum samples were positive, while 82,2% were negative for anti-mycolic IgG antibodies when analysed with the ELISA technique.
Conclusion | Culture technique faces many problems which include lack of adequate equipement as well as trained staff. Detection of mycolic acid antibodies is a promising, rapid and reliable technique for the diagnosis of pulmonary tuberculosis.

TP 06
Detection of multidrug-resistant tuberculosis in Sudan using PCR method in comparison to the conventional proportional method

Neaam Aburas • Sudan University of Science and Technology, Khartoum, Sudan

Introduction | Multidrug-resistant tuberculosis (MDR-TB) is caused by bacteria that are resistant to at least isoniazid (INH) and rifampicin (RIF), the most effective anti-TB drugs. This type of resistance is the most problematic form of resistance because treatment options are limited and the second-line drugs used for therapy are more toxic, less effective, more expensive, and must be administered for a longer period of time than standard first-line drug therapy.
Methods | Sputum samples were cultured on Lowenstein-Jensen (LJ) medium. Resistant strains were tested for the presence of mutations conferring resistance using molecular techniques to amplify 315bp (RIF) and 146bp (INH), as markers for MDR among *M. tuberculosis*.
Results | 86% of isolated *M. tuberculosis* were confirmed as members of the *M. tuberculosis* complex using PCR amplified IS6110. The result of antibiotics susceptibility testing revealed that 57% of the strains were resistant to RIF, 64% to INH while 52% of the strains were found resistant to both drugs (MDR) using the conventional method, compared to 38% resistant to RIF, 57% to INH while 29% were resistant to both drugs (MDR) when using the PCR method.
Conclusion | Not all resistant strains detected by the conventional method were detected by the PCR method, 25% were missed for RIF, 18% for INH and 7% for both. This represents a significant lack of sensitivity of the PCR technique, which could be due to the presence of other types of mutations that needs other primers and PCR protocol.

TP 07

Use of rpoB gene in the diagnosis of multidrug-resistant tuberculosis in Sudan

Isam M Imam • Ariab Mining Company Clinic, Sudan

Introduction | Multidrug-resistant (MDR) strains of *M. tuberculosis* represent a major public health concern.
Methods | In order to identify *M. tuberculosis* and rifampicin-resistant *M. tuberculosis* among suspected tuberculosis patients in Sudan, conventional methods and polymerase chain reaction (PCR), and rpoB gene amplification were used respectively.
Results | 228 sputum samples were collected, Ziehl-Neelsen (ZN) stained smears showed positive rates of 21.7% (36/128) and 23% (23/100) in Khartoum and Gezira states respectively. Growth of *M. tuberculosis* patients in Lowenstein Jensen medium was shown in 36% (46/128) of samples collected in Khartoum. All isolates were sensitive to para-nitrobenzoic acid and resistant to thiophene-2-carboxylic acid hydrazide (TCH), positive for nitrate reduction and were catalase-negative. The 46 isolates showed 123bp bands for IS6110 gene. Of them 56.4%, (26/46) were MDR-TB, 34.8% (16/46) were sensitive to rifampicin, isoniazid, ethambutol and streptomycin, 4.4% (2/46) were resistant to streptomycin, and 4.4% (2/46) were resistant to isoniazid, ethambutol and streptomycin. The MDR-TB isolates (26) showed the existence of rpoB gene in 20.3%, of these 86.7% had resistance to rpoB gene. In Gezira state, out of 74 isolates the resistant strains were 25 (33%), only 19 (19%) gave a band typical in size for the target gene rpoB (193bp) as indicated by standard DNA ladder for the presence of rifampicin resistant gene, of these 76% had resistance to rpoB gene.
Conclusion | PCR is a valuable, rapid and sensitive technique which can replace conventional method and it is high time to introduce it as a diagnostic tool for tuberculosis in Sudan.

TP 08

Evaluation of new biomarkers for diagnosis of pulmonary TB

Maowia Mukhtar • Institute of Endemic Diseases, University of Khartoum, Sudan

Introduction | Diagnosis of pulmonary tuberculosis is based on demonstration of the Mycobacterium in sputum smear, with suboptimum sensitivity and/or culture of the bacterium that takes a long time, is cumbersome and requires a specialized laboratory and trained technicians.
Methods | Seven cloned MTB antigens were evaluated for diagnostic of pulmonary TB against serum samples collected from confirmed pulmonary TB patients, suspected patients and controls. IgM, IgG, IgA and IgE antibody classes were measured in the serum samples using indirect ELISA. The participants were recruited into the study following their consent to participate.
Results | Two MTB antigens were reactive and were able to differentiate between patients and controls. High background reaction was observed with the other antigens. Analysis of the urine samples of the participants using immune-blotting detected a low molecular weight antigen secreted in the urine of TB patients. Further characterization of the antigen is going on using 2D analysis.
Conclusion | Serological diagnosis of TB suffers from the low specificity of mycobacterium antigen. Detection of MTB antigen in the urine of patients is promising and requires further analysis. Tests based on antigen detection will be valuable for diagnosis and monitoring of response of patients to treatment.

TP 09
The kinetics of acid fast bacilli in smear-positive sputum samples

Cattherine Okoi • Medical Research Council Unit, Banjul, The Gambia

Introduction | The traditional diagnostic test for tuberculosis consists of an acid fast ZN stain followed by a culture from a sputum sample. However, little is known regarding sputum smear conversion (AFB smear-positive becoming negative) in untreated sputa after longer periods of storage especially in rural settings where it takes days for samples to be transported to testing facilities. This study aims at quantifying the time it takes to achieve conversion from positivity to negativity of AFB smear-positive samples.
Methods | From 100 positive samples received in the TB diagnostic lab, 2 smears (A and B) were prepared daily from each. The smears were stained using Auramine O and examined using Light Emitting Diode (LED) based fluorescent microscopy (FM), quantified using the IUATLD/WHO grading scale. The sputa samples were then refrigerated at 2–8°C and the process repeated for 21 consecutive days.
Results | Of the 4200 slides prepared from hundred samples over a period of 21 days, the positivity and quantification of the AFB in all of the smears remained the same.
Conclusion | There was no difference in status of positive smear microscopy conversion and quantification after three weeks of storage at 2–8°C. Thus the medium term storage of untreated smear-positive sputum samples does not affect their status. However, further studies can be carried out to ascertain the viability of the AFB in the sputa by culture methods.

TP 10
Nanomedicine for smart drug delivery in diseases of poverty: a case study of tuberculosis

Mirabel Akwa Nyamboli • Council for Scientific and Industrial Research (CSIR), Pretoria, South Africa

Introduction | Nanomedicine holds great potential to radically improve health, by reducing shortfalls such as poor drug bioavailability, safety, efficacy, stability, and resistance of new and existing therapeutic agents used against poverty related diseases.
Methods | We have encapsulated anti-retrovirals and are embarking on encapsulation of anti-malarials. Here we present some results for all four first line anti-TB drugs, which we successfully encapsulated in polymeric nanoparticles.
Results | *In vitro* release assays showed the drugs were released sustainably for up to 6 days. Intracellular drug delivery studies in two human cell lines demonstrated that the particles are taken up by the cells and delivered from the phagosomes into the cytoplasm. We also illustrated that the bacterial growth index in THP -1 cells treated with encapsulated rifampicin was reduced significantly, compared to cells treated with free rifampicin. Extracellular bacteria were also killed by the encapsulated drug over a period of time. Drug release was observed *in vivo* over a period of seven days. Further characterisation of the particles revealed that the particles did not elicit any inflammatory response when orally administered to both TB challenged and unchallenged mice. Preclinical studies on TB infected mice demonstrated that the encapsulated drugs, administered once weekly, over a period of 6 weeks, showed comparative efficacy against the TB bacterium, when compared to the free drugs that were administered once daily. Furthermore, we actively targeted TB infected macrophages with nanoparticles that are functionalised with aptamers against the target protein, and noted that intracellular delivery and slow release of the drugs is feasible.

TP 11

Local content rifampicin-loaded starch nanoparticles for the rapid treatment of tuberculosis

Emeje Martins • National Institute for Pharmaceutical and Research Development, Abuja, Nigeria

Introduction | Estimates reveal that 9 million cases of tuberculosis (TB) occur globally. Unless more effective and patient compliant anti-TB medications will be available at affordable prices, the annual number of TB deaths can be expected to increase. Rifampicin (RIF) is one of the most effective drugs against tuberculosis and considerable effort has been spent on improving its efficacy by new formulations with improved bioavailability or extended therapeutic value.
Methods | We used a cheap, non-toxic, renewable and generally compatible natural polymer source, *Manihot esculenta*, to synthesize succinyl-cassava starch. NMR, IR and Raman spectroscopy were used to confirm the synthesis, while DSC-TGA, SEM, XRD, viscosity profile, water absorption and solubility indices were used to characterize the new polymer. RIF nanoparticles were prepared by spray drying technology and characterized. *In vitro* release of the encapsulated RIF nanoparticles was also assessed.
Results | Results show that the modification resulted in an at least 200% increase of the swelling, hydration and solubility profile of the starch. XRD showed a decrease in crystallinity of the starch, while DSC-TGA showed improved stability. FTIR confirmed the presence of new bond formation; scanning electron microscopy showed presence of encapsulated drug particles in the starch matrix. RIF nanoparticles showed a mean particle size of 265 nm with polydispersity index of 0.135 and a negative zeta potential value -18.18 mV. *In vitro* release of encapsulated nanoparticles shows a significantly extended release profile.
Conclusion | This study shows that cassava starch may be a cheaper alternative source of polymer for a more affordable TB treatment.

TP 12

Prevalence of MDR-TB among HIV patients attending the DOTS clinic in a national tuberculosis reference laboratory in Nigeria

Lauretta Efere • Nigeria Institute of Medical Research, Lagos, Nigeria

Introduction | Multidrug-resistant tuberculosis (MDR-TB) is emerging worldwide and has been documented in nearly 90 countries including Nigeria. The close association of MDR-TB with HIV makes the disease a more serious concern in any country with a high TB incidence, such as Nigeria. This study assesses the rate of MDR-TB among HIV-positive patients using a molecular technique.
Methods | 244 smear-positive sputum samples from HIV-positive patients collected at the DOTS centre of the National Reference Laboratory of the Nigeria Institute of Medical Research Lagos were decontaminated with N-acetyl-cysteine sodium hydroxide and the deoxyribonucleic acid (DNA) extracted from the samples. These were subjected to MTBDRplus® assay, a line probe assay (Hain Life sciences, Germany). MDR is interpreted based on the absence of at least one of the wild type probes of rpoB, KatG, and InhA genes.
Results | Of the 244 samples, 109 (44.6%) were sensitive to both rifampicin and isoniazid. Forty (16.4%) were resistant to rifampicin only (RIF monoresistant) while 28 (11.5%) were resistant to isoniazid (INH monoresistant). However, 62 (25.4%) were resistant to both rifampicin and isoniazid (MDR). Five (2.1%) were non tuberculous mycobacteria.
Conclusion | HIV infection increases the risk of acquiring and developing active TB including MDR-TB. There is therefore a need for surveillance of MDR-TB in this subpopulation for targeted control strategies.

TP 13
Impact of chronic worm infection on host immunity to tuberculosis

Ebba Abate • University of Gondar, Ethiopia

Introduction | Helminth infections are common in most areas endemic for tuberculosis (TB). Evidence is accumulating that chronic worm infection exhibits impaired cell mediated immune responses. Such immune dysregulation may affect the host's ability to cope with subsequent infections including TB.
Methods | A double blind randomised clinical trial was initiated in Ethiopia (March 2009) to evaluate the impact of helminth infection on immune responses against TB and to assess whether deworming of helminth infected TB patients could improve the clinical outcome of the conventional treatment. TB patients (n=400) are being enrolled and randomised to albendazole 400 mg or placebo per os on three consecutive days. Clinical scoring, chest x-ray and smear conversion are used to assess the clinical outcome. T-cell responses, eosinophilia and IgE-levels are followed up to assess the immune profile of the patients.
Results | In the pilot study (n=112), 47% TB patients were positive for HIV. At baseline, worm infested TB patients had higher IgE and eosinophil levels compared to worm-negative TB patients. The worm infestation rate of HIV+/TB patients declined to a significantly lower rate compared to HIV-/TB patients and this trend was stable at 2 and 3 months. Enrolment in the clinical trial and laboratory work is in progress.
Conclusion | The study may shed new light on the importance of helminth infection in TB patients and whether treating concurrent helminth infections may enhance clinical outcome of TB treatment. These are questions of important public health concern in the developing world where both infections are common.

TP 14
Feasibility and acceptability of antimycolic acid antibodies in the diagnosis of pulmonary tuberculosis in TB/HIV co-infected patients

Ossama A Elhassan • Bashaier Teachimg Hospital, Federal Ministry of Health, Khartoum, Sudan

Introduction | There is a strong need for the development of reliable, rapid diagnostic methods for detection of pulmonary tuberculosis. TB emerged as an important co-infection of HIV which may affect the immune response to TB as well as the efficiency of TB treatment. This study aimed to determine the antibody levels of anti-mycolic acid surrogates (anti-IgG and anti-IgM) among TB/HIV co-infected patients.
Methods | Descriptive cross sectional laboratory based study in which 90 patients with symptoms of pulmonary tuberculosis attending TB centres in Khartoum state. Sputum samples were subjected to PCR to amplify the IS6110 segment; at the same time 80 serum samples were collected from the same patients and were subjected to ELISA to detect anti-mycolic acid IgG and IgM antibodies as well as HIV using ICT kit.
Results | The 90 serum samples were investigated for HIV using dot plot technique: 9 samples (10%) were found HIV positive and these were all TB positive with PCR. The 80 serum samples were analysed with ELISA: 16 (20%) gave a positive result for anti-mycolic acid IgG while 64 (80%) were negative and 55 (68.8%) were positive for anti-mycolic IgM, while 25 (31.3%) were negative.
Conclusion | Patients with a TB/HIV co-infection have less anti-mycolic acid antibodies. TB/HIV co-infection represents a significant ratio among Sudanese tuberculosis patients. ELISA for anti-mycolic acid IgG and IgM is a promising rapid diagnostic tool which may substitute the slow methods with low sensitivity.

TP 15
Mycobacterial infections in an urban hospital in The Gambia

Francis Mendy • Medical Research Unit, Banjul, The Gambia

Introduction | Tuberculosis is a public health challenge in The Gambia and the rest of the developing world. The incidence of TB in The Gambia is 263.4 per 100,000 (2008). To prepare for a possible TB clinical trial in The Gambia, we reviewed the mycobacterial infections in MRC hospital over the past nine years.
Methods | 34,998 clinical samples from 13,847 patients (7,843 males and 6,004 females) were received from January 2002 to December 2010. ZN and Fluorescence microscopy were performed on 32101(91.7%) samples and 11,834 (36.3%) samples were cultured using Bactec 9000MB or MGIT960 systems.
Results | 7456 (22.9%) samples were acid-fast bacilli seen by microscopy. Of the 11,834 cultured samples, 5,238 (16.1%) were confirmed to be *M. tuberculosis* complex (MTBC), 5435 (16.7%) had no bacterial growth and 1161(3.6%) were contaminants. Of the smear-positives, 4,691 (14.4%) were cultured of which 4,459 (13.7%) were confirmed MTBC, 178 (0.5%) no bacterial growth and 54 (0.2%) contaminated. Of the smear-negatives, 6,642 (20.4%) were cultured of which 719 (2.2%) were confirmed MTBC, 4,923 (15.1%) showed no bacterial growth and 1,000 (3.1%) were contaminated. Of those without smears 501 (1.5%) were cultured of which 60 (0.2%) were confirmed MTBC, 334 (1.0%) showed no bacterial growth and 107 (0.3%) were contaminated.
Conclusion | TB continues to be a major public health challenge in this setting. AFB smear alone may fail to reveal the presence of AFB in a sample. Culture greatly increases the chances of a definitive diagnosis of TB.

TP 16
HIV sero-prevalence among newly diagnosed adult pulmonary tuberculosis patients at Chest Clinic, Infectious Diseases Hospital, Kano, Nigeria

Yusuf Mohammed • Center for Integrated Health Programs, Kaduna State, Nigeria

Introduction | Tuberculosis (TB) is a global public health problem. Although curable it is the most common cause of HIV related illness and death. It was estimated that globally about 12 million people living with HIV/AIDS are co-infected with TB. The immune suppression resulting from HIV infection is a known risk for re-activation of latent or recent TB infection into active TB, and increases the rate of TB recurrence.
Methods | All patients meeting the TB case definition, diagnosis based on findings suggestive of pulmonary tuberculosis (PTB), on physical and radiological examination (chest X-ray), and on sputum testing for AFB (acid fast bacillus), were offered HIV counselling and testing using HIV 1/2 Unigold and Determine rapid test kits. A total of 2,456 of adult pulmonary tuberculosis patients who tested for HIV, were enrolled in a period of 2 years (2007–2009).
Results | A total of 462 (18.8%) out of 2,456 patients were HIV sero-positive. HIV prevalence was higher in female patients (15.9%) than in male patients (10.5%) with a statistically significant difference ($p<0.05$). HIV sero-prevalence also varied among the different age groups. The peak age prevalence was highest in the age group 25–34 years accounting for 48.2% and it was least, with 9.4%, in the group aged 60 and above.
Conclusion | Diagnosing HIV infection among patients with pulmonary tuberculosis should be an opportunity for referrals for measures of prevention and treatment of common HIV related illnesses, ongoing provision of social and psychological support and antiretroviral therapy (ART).

TP 17
Diversity of *M. tuberculosis* genotypes circulating in Ndola, Zambia

Chanda Mulenga • Department of Biomedical Sciences, Tropical Diseases Research Centre, Ndola, Zambia

Introduction | Tuberculosis is one of the major public health problems in Zambia. However, information about lineages of *M. tuberculosis* complex (MTBC) isolates useful for epidemiological investigations is lacking. We investigated the diversity of MTBC isolates from Ndola, an urbanized city with a high HIV prevalence.
Methods | Using sputum samples from smear-positive pulmonary TB patients, two genotyping methods, spoligotyping and 15-locus Mycobacterial Interspersed Repetitive Units–Variable Number Tandem Repeats (MIRU-VNTR), were used to establish the circulating lineages and recent transmission, respectively.
Results | Among 273 MTBC isolates, 98 different spoligotypes were identified. The majority (64.8%) belonged to 9 known families, while 96 (35.2%) were orphans. LAM was the largest spoligotype family (41.8%), most (87.7%) belonging to the SAF1 family, and others coming from the T (13.6%) and X (5.9%), the remaining 3.6% from the CAS, EAI, H, S, X1-LAM9 or U families. Among 156 isolates, MIRU-VNTR typing was highly discriminatory (h=0.988), and increased discrimination among 82 SAF1 isolates from 6–46 distinct patterns. Additionally, MIRU-VNTR showed 3.2% (5/156) cases harboured more than one MTBC strain (mixed infections).
Conclusion | Our findings show a limited diversity of MTBC in Ndola with a high clustering rate (37.7%), indicating that recent transmission plays an appreciable role in the dynamics of TB disease in this setting, emphasizing the importance of early diagnosis and timely treatment.

TP 18
Prevalence of tuberculosis (TB) infection and disease among adolescents in western Kenya, in preparation for future TB vaccine trials

Peter Nyamthimba Onyango • KEMRI/CDC Research and Public Health Collaboration, Kisumu, Kenya

Introduction | Adolescents are expected to be a critical target population for new TB vaccine candidates. We are conducting a TB incidence and prevalence cohort study targeting 5,000 adolescents aged 12–18 years in an area under continuous health demographic surveillance (HDSS). We report on the prevalence of tuberculosis infection and disease among the adolescents.
Methods | The study is a prospective cohort study of 5000 adolescents aged 12–18 years. Parental consent and adolescent assent sought and follow-up done every 4 months for 1–2 years TB suspects were identified through, history of household TB contact, clinical history and tuberculin skin tests (TST). Sputum microscopy, culture and speciation and chest x-rays were done. HIV testing was also done to suspects.
Results | Between August 2008 and August 2009 we enrolled 5,004 (90.3%) out of 5,541 adolescents approached to participate. Of 5,004 participants 2,498 (49.9%) were TB suspects of whom we had 22 prevalence TB cases ((F=822 M=14)) and 11 incident TB cases ((F=6 M=5). 2,068/2,498 (82.8%) received HIV test and 24/2,068 (1.2%) were HIV positive (F=21 M=3).
Conclusion | The preliminary results show that prevalence of TB is consistent with our expectations and we are waiting to obtain final TB incidence. The ability to rapidly enrol adolescents shows this will be a suitable site to conduct clinical trials in adolescents, especially TB vaccine trials.

TP 19
Tuberculosis: new cases still substantial

Sunny Oyakhirome • Université Marien Ngouabi, Brazzaville, République du Congo

Introduction | The HIV epidemic and TB drug resistance are sustaining tuberculosis in Africa. The implementation of TB control strategies is still suboptimal in many affected sub-Saharan countries. Presently, we are evaluating cases of pulmonary tuberculosis presenting at a major anti-TB centre in Brazzaville, a city of 1.3 million inhabitants.
Methods | From 16 February to 15 June 2011, a total of 530 new cases of suspected pulmonary TB were identified at the outpatient consultation by medical officers using patients' medical history and chest X-ray findings. Their sputum and blood samples were later screened by microscopy for acid fast bacillus and HIV test respectively.
Results | Median age (range) of this cohort is 34 years (8–83), with 52% male and 48% female. 35% (186 of 530) were smear-positive cases, 20% (83 of 422) were HIV positive with 3% of them having equivocal HIV results. The proportion of smear-positive cases that were HIV positive was 11% (19 of 170), while smear-negative cases showed a greater probability of being HIV positive than smear-positive cases (RR=2.4; p=0.001) with an odds ratio which is threefold higher than the latter (p=0.0001).
Conclusion | The proportion of new cases of pulmonary TB presenting at this care centre is quite high, which emphasizes the need to expand TB-control efforts in this region with particular attention to smear-negative case which may be infectious.

TP 20
The use of spoligotyping to determine the molecular epidemiology of *M. tuberculosis* complex circulating in The Gambia

Oumie Secka • Medical Research Council Unit, Banjul, The Gambia

Introduction | Tuberculosis remains a major public health problem in the Gambia: the incidence of tuberculosis is 263/100,000 (2008). The molecular epidemiology of the circulating genotype needs to be revisited. The aim of this study was to determine the genetic diversity of *M. tuberculosis* complex (MTBC) strains and identify the predominant spoligotypes circulating in our setting.
Methods | The current study included all consecutive smear-positives and smear-negative but culture positive cases received at the MRC hospital between February 2010 and February 2011. A total of 660 clinical samples from 394 suspected tuberculosis patients were culture positive. Whole genomic DNA extraction was carried out and spoligotyping method was used to genotype the MTBC isolates. We use the SpolIDB3 to analyse the results.
Results | Of the 394 clinical isolates confirmed to be MTBC, 126 isolates were spoligotyped. *M. tuberculosis* lineage was the most prevalent genotype (71%), followed by *M. africanum* type 1 lineage (27%). The Beijing lineage constitutes only 2% of the circulating genotypes. The *M. tuberculosis* lineage was further categorized into 15 spoligofamilies of which the T1 (19%), Haarlem3 (18%) and LAM9 (14%) families are the most frequent families within the *M. tuberculosis* lineage. The remaining 49% of the *M. tuberculosis* lineage belong to 12 different other families.
Conclusion | The current study demonstrated that tuberculosis cases in the Gambia are caused by a wide variety of circulating MTBC strains. *M. africanum* type 1, Haarlem3 and T1 families are the most predominant genotypes circulating in The Gambia.

TP 21

Field experience of sputum collection for TB diagnostic work-up in cohort of adolescents in a rural resource limited setting of Uganda

Richard Isabirye • Infectious Disease Institute, Makarere University, Kampala, Uganda

Introduction | A cohort study is being conducted in Iganga/Mayuge Demographic Surveillance Site in Uganda to determine the incidence of TB in a cohort of adolescents 12–18 years and to build capacity for future phase III clinical trials to evaluate new TB vaccines. The objective of this sub-study is to assess the usefulness and yield of the field sputum collection strategies used in the study.
Methods | Participants suspected of TB were identified at enrolment and during 1.5 years of follow-up. TST was done at baseline and at 12 months follow-up visit. Procedures for TB diagnostic work-up included a coached spot and an early morning sputum (EM) collection for smear and culture. Participants collected the EM which was picked up from their home by study staff.
Results | A total of 2,275 samples were collected at day 0, 183 at 6 months, 800 at 12 months and 16 at 18 months. The samples collected have so far yielded 14 *Mtb*-positive cases, 137 grew non tuberculous mycobacteria (NTM) and 21 samples were contaminated. 11 *Mtb* cases were grown from the EM samples while the yield for NTM from the EM and spot samples was similar. Over the study period, 290 adolescents who qualified for diagnostic work were unable to provide sputum samples largely due to logistical reasons such as failure to contact the participant.
Conclusion | Coaching and home visits were useful strategies for field sputum collection ensuring a low contamination rate of the samples.

TP 22

Practical considerations in recruitment and retention of adolescents for a rural community based study in Eastern Uganda

Zam Zinda • Infectious Disease Institute, Makarere University, Kampala, Uganda

Introduction | A cohort of 5,000 adolescents was recruited and followed for 1.5 years to estimate the incidence of TB. Recruitment and retention of adolescents in studies may present peculiar challenges. The objective was to share practical considerations for conducting studies in adolescents.
Methods | Adolescents aged 12–18 years were approached in school and informed about the study. Parents were then visited at home for written informed consent. Acquiring assent and enrolment of adolescents was mainly done at school or home. Assessment for TB included history of TB contact, clinical evaluation and a tuberculin skin test. TB suspects were asked to provide sputum samples for microbiology.
Results | A total of 7,142 (80%) of the adolescents approached expressed willingness to join the study. Parental consent was obtained for 5,422. Reasons for failure to obtain parental consent included ineligibility due to age and residence, parent refusals or parents away from home, failure to locate homes, move to school outside study area, but were unknown in most cases. Assent was obtained from 5,042 and 5000 were enrolled (sample size). Attendance for the 6, 12 and 18 month visits was 92%, 81% and 78% of expected visits respectively. Challenges included inability to verify potential participants' age, locating parents' homes and change of decision to participate. The main factors affecting follow-up included verification of participants' identity, school holidays or exams, change of participants' residence and/or school.
Conclusion | Recruitment and retention of adolescents for studies in the community maybe challenging but feasible if well planned with schools and parents.

TP 23
Molecular tools for tuberculosis surveillance in southwest Nigeria: a capacity building and networking experience

Olabisi Ojo • University of Pittsburgh School of Medicine, Pittsburgh, USA

Introduction | Nigeria had the fourth largest number of tuberculosis (TB) cases worldwide in 2009 (WHO Report 2010). The University College Hospital Ibadan, housing the only MDR-TB management ward in Nigeria, is a World Health Organization centre and hosts the regional reference laboratory for Southwest Nigeria. Unfortunately there is neither funding for basic research nor adequate understanding of mycobacteria genomics and molecular tools for rapid epidemiological surveillance of TB in this fledging centre.
Methods | With funding support from the UK-based Society for Applied Microbiology's Overseas Development Grant, and the Damien Foundation based in Ibadan Nigeria, we organized a 5-day mini course and practical workshop. The meeting had resource persons from outside and within Nigeria. Specific TB molecular typing tools exploiting the polymorphisms in the *M. tuberculosis* complex genome, phylogeny, diversity, epidemiology as well as biosafety issues were evaluated.
Results | Some research equipment and reagents were procured for transfer of knowledge and molecular tools for tuberculosis surveillance. 20 individuals were exposed to TB genomics for the first time. The meeting demonstrated networking between scientists in the USA and Nigeria bringing together 4 universities and 1 research institute. It promoted interaction between scientists in basic research and local TB stakeholders.
Conclusion | We are positive that the knowledge transfer through the workshop will stimulate sustainable interest in TB surveillance with molecular tools in Nigeria. We hope the procured research materials will be supplemented, for full use by students, local scientists and technicians that were trained, along with progressive collaboration between TB researchers in the region.

TP 24
Incentives to improve tuberculosis treatment adherence

Kimbugwe Yusuf • Youth Concern Foundation, Kaduna, Nigeria

Introduction | The hypothesis of this operations research (OR) study was that incentives/enablers to increase adherence is crucial for therapeutic success and reducing generation of multidrug-resistant TB (MDR-TB)
Methods | There were three study groups besides control: cash incentive, hot meal incentive and nurse enabler. In control corners, usual care was provided, in cash incentive corners, the equivalent was given at each visit, in hot meal corner, lunch was served at each visit; and in nurse enabler corner nurse, visited defaulters and gave psychosocial support. Sixteen DOTS corners were recruited and assigned to one of the study groups. Each of these groups have a patient mix that reflects the other groups and the oblast as a whole.
Results | Completion rates in the four groups did not differ significantly. However, completion rates in all groups were greater than 95%. This is much higher than rates in the oblast, probably a result of improved performance by virtue of being included in the number of missed doses. The hot meal group performed best and all three incentive groups better than control. The groups did not differ significantly in any of the potentially confounding factors examined. The average number of missed doses were control 3.03, money corner 0.98, hot meal corner 0.36, visiting nurse corner 0.92 ($p=0.016$).
Conclusion | In a low resource setting, feasible and low cost incentives can significantly increase patient adherence. This strategy could be replicated throughout the region, which is experiencing difficulty with treatment adherence and consequent increase of MDR-TB.

TP 25

Pattern of resistance to first line anti-tuberculosis drugs in Ibadan, Nigeria: preliminary observations

Olumide Sogaolu • Department of Medicine, College of Medicine, University of Ibadan, Nigeria

Introduction | Emergence of resistance to anti-tuberculosis drugs continues to plague our day. Patients with drug-resistant tuberculosis are classified as having primary or acquired drug-resistant disease on the basis of their history of previous tuberculosis treatment. We set out to determine anti-tuberculous resistance patterns among TB patients initiating therapy at some DOTs centres in Ibadan, the largest city in Nigeria.
Methods | The cross sectional study involved 87 adults, patients aged 15 years and above. These patients were classified as new or previously treated who were about to initiate anti-tuberculous therapy having been found to be smear-positive on sputum examination. Drug susceptibility tests (DST) for streptomycin, isoniazid, rifampicin and ethambutol were performed on 82 culture-positive samples on BACTEC-MGIT960.
Results | Of the 82 patients, 45 (54.9%) were males. Median age was 34.2 years. 43.5% of the 72 new patients had some form of resistance to first line anti-tuberculous drugs, while 21.4% of the 14 previously treated patients had a form of resistance. Multidrug resistance to rifampicin and isoniazid was observed in 5.5% of the new patients while none of the 14 previously treated patients has MDR-TB . Monoresistance to INH and EMB was the most common pattern seen in 14% and 7% respectively of previously treated and in 22% and 31% of new patients.
Conclusion | Multidrug resistance tuberculosis is present in our patients, but it does appear that drug resistant strains causing primary resistant TB may contribute significantly together with acquired resistance in previously treated patients. It will thus require further and wider studies to fully classify the type of anti-tuberculous drug resistance in our patients in Ibadan.

TP 26

Quality assessment of tuberculosis laboratory diagnosis in selected health facilities of public & private laboratories in Oromia Regional State, Ethiopia

Desalegn Ararso • College of Health Sciences, Addis Ababa University, Ethiopia

Introduction | Since 2000, the quality of TB laboratory diagnosis in both public and private health facilities was often a direct reflection of the success of TB control programmes and a key component of the DOTS strategy, yet it was one of the most neglected components of this programme.
Methods | A cross-sectional survey was conducted in 60 randomly selected public and private TB laboratories in the Oromia region (Ethiopia). Health care quality parameters of the Donabedian model were used to assess structural, process and output quality.
Results | The study showed that staff training is a neglected issue in most private TB laboratories resulting in a high false negative discordant rate of AFB (10%). A higher proportion of patients who visited the TB laboratories, were dissatisfied because of the lack of respect shown by providers. A statistically significant association was observed between structure and process quality (OR=2.9, 1.46–5.7; p=0.01) and between process and output quality parameters (OR=3.2, 3.13–10; p=0.02).
Conclusion | Poor training of laboratory technicians and a high false negative discordant rate of AFB results. Therefore, laboratory staff training and adherence to the National TB laboratory manuals are strongly recommended.

TP 27

Key considerations for dealing with high contamination rates in liquid culture (Mycobacterium growth indicator tube) in a TB laboratory

Susan Musau • KEMRI/CDC Research and Public Health Collaboration, Kisumu, Kenya

Introduction | MGIT (Mycobacteria Growth Indicator Tube) consists of liquid broth medium that yields better recovery and faster growth of mycobacteria. However, high contamination rates limit its utility. We evaluated interventions aimed at lowering contamination rates within a research lab in Kenya.
Methods | Natural and induced sputum, gastric aspirates, lymph node aspirates, and stool specimens were submitted to the laboratory for mycobacterial culture using the MGIT 960. Specimens were decontaminated using 4–6% NaOH-NALC; lymph node aspirates were directly inoculated without processing. MGIT tubes were first inoculated with 0.8 mL of PANTA (antibiotic), followed by 0.5 mL of specimen. The following interventions were implemented to reduce contamination: NaOH-NALC contact time was increased from 15 to 20 minutes (June–October 2010), PANTA concentration was increased from 1X to 1.5X (November–December, 2010; March 2011 to date), and the concentration of NaOH was increased from 4% to 6% (February 2011). Rates were compared for individual staff, and processing was limited to two experienced staff in the last two time-periods. Blood agar plates were used to determine contamination rates.
Results | At baseline, the contamination rate was 46%. With increased NaOH-NALC contact time, contamination rates ranged from 23–49%. In the second time period, with an increase in NaOH concentration contamination, rates were 17%. In the final period, with an increase in PANTA and two identified technologists processing, contamination rates were 16–20%.
Conclusion | Increased PANTA concentration in MGIT and optimizing aseptic technique (using fewer, more experienced technologists) was associated with reduced contamination rates in liquid culture in our laboratory.

TP 28

Ward admission and consenting challenges for sputum induction and gastric aspiration procedures in the infant TB cohort in Iganga, Uganda

Phionah Nabukalu • Infectious Diseases Institute, Makerere University, Kampala, Uganda

Introduction | An epidemiological study to estimate the incidence of TB among infants is being conducted in Uganda as part of capacity building for future evaluation of novel TB vaccines. Procedures for TB diagnosis include sputum collection by gastric aspiration and sputum induction which are unfamiliar in this population and relatively invasive. Possible refusal of admission or of procedures was anticipated. The objective was to assess willingness among parents/guardians to have their children participate in procedures.
Methods | Tuberculosis suspects were referred for admission to the TB case verification ward. Sputum sample collection by gastric aspiration and sputum induction are among the TB ward diagnostic procedures.
Results | Of the 877 referrals, 114 (13%) declined admission when first approached. Reasons given in 59 (52%) refusal cases involved family (parents not at home, father unavailable, lack of alternative caretaker for family or parents not ready). Three parents felt their children were well and in 59 (45.6%) cases reasons were not documented. However, through more explanation and planning, 35 (30.7%) of the 114 who initially refused, later accepted admission. Of the 798 that accepted admission, procedures were not performed in 113 (14.2%) cases. The reasons included logistical failures in 98 (86.7%) instances; informed consent failure in 6 (5.3%), fear of procedures in 6 (5.3%) and in 3 (2.5%) the parents felt that their babies were too young for these procedures.
Conclusion | There was good acceptance of admission and procedures. A well executed informed consent process and planning improved acceptance. Logistical failures were the most common reasons for not performing procedures.

TP 29
An electronic surveillance system for intensified TB case detection in an adolescent cohort study, in preparation for future tuberculosis vaccine trials, western Kenya

Joseph Opole • KEMRI/CDC Research and Public Health Collaboration, Kisumu, Kenya

Introduction | The age specific incidence of tuberculosis (TB) in developing countries gradually rises in adolescence, making adolescents a good target group for introduction of new TB vaccines. Phase III TB vaccine trials require solid measurable endpoints. We sought to do electronic surveillance in addition to scheduled active follow-up visits to maximize TB case finding.
Methods | The study area is under a continuous Health and Demographic Surveillance System. After enrolment, passively detected TB cases listed in TB registers were searched and matched with Health and Demographic Surveillance System registers to see if they resided in the same compounds as study participants. If so, these were contacted for investigation as TB suspects.TB cases aged 12–18 years were also searched in the study database to verify whether they were study participants. TB laboratory and chest x-ray records were searched to identify potential TB suspects.
Results | During follow-up 8 TB cases were identified, the person time accumulated by all 5,004 subjects was 6,002.4 years with a corresponding incidence density of 2.0 (95% CI: 1.14–3.52) per 1000 person years. In addition, 5 TB cases were identified through the surveillance system accumulating 5.36 years with a corresponding incidence density of 0.8 (95% CI: 0.3–2.0) per 1,000 person years.
Conclusion | The results of identification of TB cases through electronic surveillance indicate this is a useful approach that should be further explored. The additional cases yielded by electronic surveillance might help downward revision of required samples sizes or help in shortening follow-up time if TB cases are found more quickly.

TP 30
Capacity building for tuberculosis vaccine clinical trials in South Africa and Senegal

Samantha Vermaak • University of Oxford, UK

Introduction | There are 8.8 million new cases of tuberculosis (TB) every year, leading to 1.7 million deaths annually. A more effective vaccine is urgently required, but substantial infrastructure is required before a trial can be conducted to international Good Clinical Practice (GCP) standards.
Methods | Building on EU funding for capacity building, an EDCTP grant has enabled clinical and laboratory facilities to be built and/or updated and personnel to be appropriately trained to GCP requirements in key clinical trial sites in Senegal and South Africa.
Results | In South Africa clinical facilities have been updated, e.g. through the purchase of new digital X-ray machines for Brewelskloof Hospital and Khayelitsha, available for both routine and clinical trial screening. Clinical trial space has been renovated or built in Khayelitsha, Cape Town. Groote Schuur laboratory, the referral centre for mycobacterial culture, has been upgraded and is now accredited. Training in laboratory assays such as Elispot and Quantiferon has been conducted. In Senegal, clinical and laboratory staff have been trained in GCP and/or GLP, and techniques have been transferred to Senegal's staff through visits to Oxford and Cape Town. The vaccination unit is being upgraded.
Conclusion | EU funding has resulted in significant capacity building in South Africa and Senegal, allowing for future large-scale TB vaccine efficacy trials according to international GCP standards and improving TB diagnosis and treatment at these centres.

MP 01
Evaluation of alternative antimalarial drugs to sulfadoxine-pyrimethamine for IPTP in the context of insecticide-treated nets

Raquel González • Barcelona Centre for International Health Research, Barcelona, Spain

Introduction | Malaria in pregnancy is one of the most important preventable causes of low birth weight deliveries worldwide and a major cause of severe anaemia contributing to maternal mortality. Effective preventive interventions to reduce the incidence and consequences of malaria infection in pregnant women are a priority in endemic countries. The spread of parasite resistance to sulfadoxine pyrimethamine (SP) and the significant overlap in some regions of malaria transmission and high prevalence of HIV infection have raised concerns about the medium and long-term use of SP for intermittent preventive treatment in pregnancy (IPTP).
Methods | This project includes two clinical trials aiming to contribute to the development of new interventions by comparing the safety and efficacy of the available antimalarial drug alternative, mefloquine (MQ), with those of SP in the context of insecticide-treated nets. HIV-infected pregnant women on cotrimoxazole prophylaxis are included to assess the efficacy of IPTP-MQ. A randomised superiority trial conducted in Benin, Gabon, Tanzania and Mozambique compares the safety and efficacy of SP versus MQ recruiting 4,260 pregnant women followed until infants are one year old. In Kenya, Tanzania and Mozambique, where HIV prevalence in pregnant women is >10%, a superiority double-blinded trial compares MQ- to placebo-IPTP in 1,070 HIV-infected pregnant women receiving cotrimoxazole prophylaxis followed until infants are 2 months old.
Results | Over 60% of participants have been recruited in both trials to date and results shall be available by end of 2012. This presentation shall provide progress to date, challenges to implementation and community benefits of the study.

MP 02
Ten years of experience with Coartem: A patient-centric approach to fighting malaria

Paul Aliu • Novartis Pharma AG, Basel, Switzerland

Introduction | We review the experience with Coartem (artemether-lumefantrine), the current gold standard artemisinin-based combination therapy (ACT) for malaria that has been deployed in several endemic countries for the last 10 years, delivering over 400 million treatments.
Methods | Over the years, our focus shifted from providing a quality medicine in public/private partnership with WHO to a holistic, 'patient-centric' approach, involving multiple partnerships and focusing on educating caregivers and patients to ensure timely treatment and adherence to the full course of medication. To meet the specific needs of children, a dispersible formulation was developed jointly with Medicines for Malaria Venture (MMV).
Conclusion | Coartem dispersible tablets meet the specific needs of children as they can be given dispersed in a small amount of liquid and are sweetened to mask the bitter taste which is typical of most antimalarials. More recently, we have been evaluating novel approaches that may be of use in malaria elimination strategies. A study assessing the utility of Coartem in mass screening and targeted treatment for malaria in entire village populations, including carriers of the malaria parasite that are asymptomatic has been undertaken in an effort to reduce parasite transmission. New strategies to expand access to ACTs have been implemented: the Affordable Medicines Facility – malaria (AMFm) initiative, or the SMS for Life initiative, part of the Roll Back Malaria (RBM) program. These initiatives that maintain and further evolve a patient-centric approach and go beyond a mere deployment of drugs are essential for achieving a sustained health benefit in developing countries.

MP 03
Safety of artemisinins during early pregnancy, assessed in 62 Sudanese women

Elhassan Elhassan Eisihag • University of Gezira, Gezira, Sudan

Introduction | 90% of the burden of malaria occurs in sub-Saharan Africa, where 40% of the women are exposed to malaria during pregnancy. Malaria in pregnancy poses a substantial risk to the mother and to her foetus and the neonate. The objective was to assess the safety of artemisinins during early pregnancy, in 62 Sudanese women.
Methods | Between June 2006 and October 2008, the safety of artemisinins in early pregnancy was assessed in central–eastern Sudan. Pregnant women in the first or second trimester who were attending antenatal-care clinics at the Wad Medani eastern hospitals were interviewed. The women who had had malaria in the first trimester of the index pregnancy and had received artemisinins, were followed-up until delivery. Their babies were followed-up for one year. Data was appropriately analysed in SPSS.
Results | Overall, pregnant women reported receiving artemisinins-artemether injections, artesunate plus sulfadoxine-pyrimethamine or artemether plus lumefantrine during the first trimester. Medical records were available for all and, in each case, these records showed the reported treatment and that malaria had been confirmed. Only a few women were unaware of being pregnant when treated. Women who had received artemisinins delivered apparently healthy babies at term. No congenital malformations were detected. There was no preterm labour, or maternal death recorded during the follow-up, and none of the babies died during their first year of life.
Conclusion | Artemisinins may be safe to use during early pregnancy. Further study is clearly needed.

Reference: Ann Trop Med Parasitol 2009; 103(3),1–3.

MP 04
Pilot study on artesunate efficacy in non-severe malaria treatment in Mali

Aminatou Kone • University of Bamako, Mali

Introduction | Developing resistance of *Plasmodium* malaria to chloroquine and sulfadoxine-pyrimethamine has led to the use of artemisinine derivatives. Elevated efficacy has been observed with these derivatives in monotherapy or in combination with other molecules in several countries in Africa and Asia. Lately, some studies showed the selective action of the partner drugs leading to the development of resistance to these combinations. Increased parasite clearance time (PCT) has been observed in the Thai-Cambodia border region during artemisinine treatment and in other places in South-East Asia. In Mali, artemether-lumefantrine and artesunate-amodiaquine are in use since 2002. Therefore, it is important to evaluate resistance to the first component.
Methods | An *in vivo* prospective clinical assay has been conducted in Bougoula-Hameau (Mali) to evaluate the PCT during uncomplicated malaria treated with artesunate in 7 days monotherapy. 100 children between 1 and 10 years have been included and followed-up for 28 days with hospitalization until 3 consecutive smears showed up negative for *P. falciparum*. Proportion of negative subject has been assessed at H8, H16, H24, H32, H40, H48, H56, H64, H72, H80, H88, H96, H104, H112, H120, H128, H136, H144, H152, H160 and H168.
Results | The corrected cure rate was 98.9% (n=92) and compared with a previous artesunate study (2004), the respective median for the asexual parasite were 27,070 (15,390–57,050) and 16,575 (8,075–33,475) ($p<0.001$). 36.96% (92) of our study patients cleared their parasite within 24 h after treatment against 34.10% (217) in 2004 ($p=0.08$); 95% clearance by 24 h was observed for 98.9% (92) of our patients against 93.09% (217) in 2004 ($p=0.1$).

MP 05
In vitro antiplasmodial activity and cytotoxicity evaluation of extracts of *Acanthospermum Hispidum* DC and *Ficus thonningii* Blume

Felix Koukouikila-Koussounda • Fondation Congolaise pour la Recherche Médicale, Brazzaville, Democratic Republic of Congo

Introduction | This study aimed at evaluating extracts from two medicinal plants, *Acanthospermum hispidum* and *Ficus thonningii*, used in traditional medicine in Congo Brazzaville, for *in vitro* antiplasmodial activity against *P. falciparum* laboratory strains: chloroquine sensitive 3D7 and chloroquine resistant Dd2.
Methods | ELISA HRP2 assay was used to evaluate the *in vitro* inhibitory activity of the extracts alone or in combination with chloroquine. Cytotoxicity was assessed on human HeLa cell line and reflected by the selectivity index.
Results | Methanolic extract of *Acanthospermum hispidum* exhibited a strong and a moderate inhibitory activity on the growth of Dd2 and 3D7 (50% inhibitory concentrations of 2.82 and 9.2 µg/mL respectively) with selectivity index superior to 10. The combination of this extract with chloroquine showed a synergistic effect against both 3D7 and Dd2, and reversed the resistance of Dd2 to chloroquine. Extracts from *Ficus thonningii* showed no promising antiplasmodial activity, except for the fact that the methanolic extract exhibited a slight antiplasmodial activity against Dd2.
Conclusion | Methanolic extract of *Acanthospermum hispidum* exhibited moderate to high inhibitory activity on 3D7 and Dd2 and a strong synergistic antimalarial effect when combined with chloroquine. The good selectivity index of *Acanthospermum hispidum* on HeLa cells reflects the safety of this plant. *Ficus thonningii* seems to have no antimalarial activity. *In vivo* investigations using animal models and later clinical trials in collaboration with traditional practioners are necessary to clarify the potential antimalarial activity of both plants. This study was supported by CANTAM project for the purpose of PhD student training.

MP 06
A randomised clinical trial of artemisinin *vs* non-artemisinin-based combination therapy of uncomplicated malaria in Mali

Hamma Maiga • Malaria Research and Training Centre, University of Bamako, Mali

Introduction | *P. falciparum* resistance to artemisinin has been reported in South-East Asia. The potential spread of this resistance is real and makes a search for alternative non-artemisinin-based malaria therapy urgent. We tested the hypothesis that sulphadoxine-pyrimethamine plus artesunate (SP+AS) is as efficacious as sulphadoxine-pyrimethamine plus amodiaquine (SP+AQ) in the treatment of uncomplicated *P. falciparum* malaria.
Methods | From August to December 2004 and July to December 2005, we conducted a randomised single-blind trial of SP+AS and SP+AQ in two localities in Mali. Parasite genotyping by polymerase chain reaction (PCR) was used to distinguish new from recrudescent *P. falciparum* infections.
Results | We recruited a total of 610 children aged 6–59 months, with uncomplicated *P. falciparum* malaria and followed them for 28 days to assess treatment efficacy. Baseline characteristics were similar in both treatment groups. The analysis revealed no early therapeutic failures (ETF) in both arms; late clinical failures (LCF) were 1.7% for SP+AS (n=5) *vs* 0% SP+AQ (n=0) and late parasitological failures (LPF) were 3.4% SP+AS (n=10) *vs* 1.4% SP+AQ (n=4) (p >0.05). We observed a rate adequate clinical and parasitological response (ACP R) of 94.9% and 98.6% for SP+AS and SP+AQ respectively (p=0.98). Based on msp2 analysis, the rate of re-infection was respectively 4.1% and 1.4% for SP+AS and SP+AQ. After molecular correction, we obtained an ACP R of 99% for SP+AS, and 100% for SP+AQ (p=0.98).
Conclusion | Sulphadoxine-pyrimethamine plus amodiaquine therapy is as efficacious as sulphadoxine-pyrimethamine plus artesunate in the treatment of uncomplicated *P. falciparum* malaria in Mali.

MP 07
A high compliance referral rate is achievable in under five children with severe malaria given emergency treatment at community level: the Ugandan experience

Edison Mworozi • Makerere University College of Health Sciences, Kampala, Uganda

Introduction | Communities play a critical role in managing childhood illnesses. One of the strategies adopted in Uganda is home based management of fever using Community Drug Distributors (CDDs) for the treatment of uncomplicated malaria. However, management of severe malaria at community level remains a key challenge. WHO/TDR in 2004 supported a multi-centre study in five countries including Uganda. We conducted a descriptive study to document whether caretakers of under fives with *non per os* (severe) malaria given rectal artesunate as emergency pre-referral treatment by CDDs, would comply with instructions to take the treated children to health facilities for further management.
Methods | This study was conducted in four sub-counties of the Mubende and Mityana Districts in Uganda from June 2005–January 2007. Trained CDDs identified under fives with severe malaria and administered a single dose of rectal artesunate according to child`s age. After observing the child for 10 minutes they referred the child to a health facility for consolidation treatment. Health facility records were reviewed to find out whether those referred were taken there and what the outcome in their case was.
Results | A total of 1,502 children with *non per os* malaria were treated with rectal artesunate and referred to health facilities. 1,339 (89.1%) complied with referral instructions. Of those who went to health facilities, 923/1,339 (68.9%) went to government facilities.
Conclusion | A high referral compliance rate is achievable with appropriated counselling of caretakers of children with severe malaria given emergency treatment at community level by trained CDDs. In this study compliance to referral instructions was 89.1%.

MP 08
Clindamycin plus quinine: a forgotten antimalarial drug combination

Charles Obonyo • Kenya Medical Research Institute, Nairobi, Kenya

Introduction | Artemisinin-based combinations are the recommended treatment for uncomplicated falciparum malaria, but are costly and in limited supply. Clindamycin plus quinine is an alternative non-artemisinin-based combination, recommended by WHO as a second-line drug. The objective of this review was to compare the efficacy of clindamycin plus quinine versus other antimalarial drugs for the treatment of uncomplicated falciparum malaria.
Methods | We searched the Cochrane Infectious Diseases specialized register, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, and LILACS. Two authors independently assessed study eligibility, extracted data and assessed the risk of bias. The primary outcome measure was treatment failure by day 28. We compared dichotomous data using relative risk (RR) in a fixed effects model.
Results | Seven randomised controlled trials (929 participants) were included. The risk of day 28 parasitological failure was significantly reduced by clindamycin plus quinine compared with quinine (RR 0.14, 95% CI 0.07–0.29), quinine plus sulfadoxine-pyrimethamine (RR 0.17, 95% CI 0.06–0.44), amodiaquine (RR 0.11, 95% CI 0.04–0.27), or chloroquine (RR 0.11, 95% CI 0.04–0.29). There was no difference in failure risk when the combination was compared with quinine plus tetracycline (RR 0.78, 95% CI 0.20–3.02), artesunate plus clindamycin (RR 0.57, 95% CI 0.26–1.24), or chloroquine plus clindamycin (RR 0.38, 95% CI 0.13–1.10). The incidence of adverse events was similar across treatment groups but these were poorly reported.
Conclusion | Some promising evidence is available on the efficacy of clindamycin plus quinine as an alternative treatment for uncomplicated malaria, but more and larger trials are required.

MP 09

Efficacy of sulfadoxine-pyrimethamine + amodiaquine *vs* sulfadoxine-pyrimethamine + artesunate *vs* sulfadoxine-pyrimethamine alone on uncomplicated falciparum malaria in Mali

Zoumana I Traoré • Malaria Research and Training Centre, University of Bamako, Mali

Introduction | Artemisinin-based combination therapies are now first line drugs in malaria treatment in Africa. However, their deployment to remote areas remains a challenge. The purpose of this study was to investigate the efficacy of the combination of sulfadoxine-pyrimethamine (SP) + amodiaquine (AQ), two drugs readily available and affordable.
Methods | From 2004–2005, we carried out an open-label randomised trial of the efficacy of sulfadoxine-pyrimethamine + artesunate (SP+AS), sulfadoxine-pyrimethamine (SP) alone and sulfadoxine-pyrimethamine + amodiaquine (SP+AQ) for the treatment of uncomplicated malaria in two Malian savannah villages: Kollé and Bancoumana. 736 children under five years of age with uncomplicated malaria were included and followed for 28 days according to WHO 2003 protocols. MSP1, MSP2 and microsatellite CA1 were used to distinguish true recrudescent from new infections (molecular correction).
Results | These children were randomised between SP+AQ (n=244), SP alone (n=241) and SP+AS (n=251), and 6% of patients were lost to follow-up. After molecular correction total treatment failure of 0.4%, 1,6% and 0% were observed for SP+AS, SP, and SP+AQ, respectively. Peak gametocytes carriages were 16.5%, 32.3%, 18.3% for the same treatments in the same order.
Conclusion | This study demonstrated that SP+AQ was as efficacious as SP+AS in Mali and therefore could be used to treat uncomplicated malaria in areas where ACTs are not available.

MP 10

Identification of natural anti-malaria responses during repeated administration of three drug combinations based on artemisinin

Nouhoum Diallo • Faculty of Medicine Pharmacy and Dentistry (FMP OS), University of Bamako, Mali

Introduction | From July 2005 to June 2007 to Bougoula, Mali we conducted a prospective study comparing combinations AR-L, AS-AQ and AS-SP. We explored the impact of repeated administration of three artemisinin based drug combinations on natural antimalarial immune responses.
Methods | Cytokines IL-2, IL-4, IL-5, IL-10, TNF-α, INF-γ and immunoglobulins: IgG directed against AMA-1 Ag, GLURP, MSP-3 and IgM, IgG1, IgG2, IgG3 directed against AMA-1 Ag, GLURP, MSP-3, GBP-130, MSP-6, SERP and LSA-5, were analysed respectively by flow cytometry and ELISA in 212 symptomatic subjects aged 6 months or older, divided between arms by treatment and the number of malaria episodes.
Results | Specific titers of IgG anti-AMA-1 and anti-GLURP were significantly higher in the arms AR-L and AS-AQ than in the AS-SP arm ($p<0.05$ and $p<0.001$). The median levels of IL-2 and IL-4 were significantly higher in the arms AR-L and AS-AQ than in the AS-SP arm ($p<0.001$). Cons by the rate of INF-γ was significantly higher in arms AS-SP and AS-AQ than in arm AR-L ($p<0.05$).
Conclusion | Combinations AS-AQ and AR-L were associated with higher titers of IgG anti-plasmodial than the combination AS-SP. The artesunate-based combinations were associated with INF-γ response and the combination of artemether-based response to IL-4.

MP 11

Rapid clearance of peripheral *P. falciparum* schizonts by artesunate-amodiaquine and artemether-lumefantrine in Nigerian children with acute uncomplicated malaria

Michael Obaro • Department of Pharmacology and Therapeutics, University of Ibadan, Nigeria

Introduction | We evaluated the prevalence of schizonts and effects of artesunate-amodiaquine (AA) and artemether-lumefantrine (AL) on schizogony in peripheral blood of children with acute uncomplicated malaria.
Methods | Children aged 1–12 years with asexual parasite densities ≥1,000 parasites/µL were enrolled and randomly treated with standard doses of AA and AL. Peripheral blood smears were made hourly in the first 4 hours, 8 h, 16 h, 24 h, and daily up to day 42. Schizonts were classified as immature (Si <8 visible nuclear chromatins) and mature (Sm >8 nuclear chromatins).
Results | A total of 161 children (81AA, 80AL) were evaluated. Peripheral schizontaemia was present in 42 (26.1%) at presentation. Twenty (47.6%) of the schizonts were immature while 22 (52.4%) were mature. Geometric mean densities (range) of peripheral schizontaemia in the AA and AL groups were 24/µL (6–120) and 15/µL (6–300) respectively (p=0.1). Peripheral schizontaemia was significantly correlated with age ≤ 5 years, asexual parasite density ≥100,000/µL, and presence of hepatomegaly at presentation. Mean asexual parasite and schizont clearance times were 23.3 ± 14.1 and 5.0 ± 4.5 h (p=0.00000). Asexual parasite and schizont clearance times were similar in the two treatment arms (AA and AL).
Conclusion | Peripheral schizontaemia, though at low density, was not uncommon in the children with acute uncomplicated *P. falciparum* malaria. The rapid effects of the evaluated ACTs on peripheral schizonts may indirectly correlate with their effects in the deep tissues where most schizonts are normally sequestered, and supports their choice as first line therapies in uncomplicated and severe-complicated malaria.

MP 12

Efficacy of artesunate plus sulfadoxine-pyrimethamine and sulfadoxine-pyrimethamine alone in the treatment of uncomplicated *P. falciparum* malaria in Sinnar, central Sudan

Omer Waleed • Al-Neelain Medical Research Centre, Al-Neelain University, Khartoum, Sudan

Introduction | Treatment of *P. falciparum* malaria was changed in Sudan in 2004. This study aimed to determine the efficacy of artesunate plus sulfadoxine-pyrimethamine (AS+SP) and sulfadoxine-pyrimethamine (SP) alone in the treatment of uncomplicated *P. falciparum* malaria in Sinnar. Secondly, it aimed to determine the frequency of drug resistance mutations in *P. falciparum* DHPS gene.
Methods | A total of 117 patients were screened for malaria, 67 of them were positive for *P. falciparum* malaria, met the inclusion criteria and completed the 28 days of follow-up. Patients were treated either with AS+SP (n=38) or with SP (n=29). Classification of the treatment outcome was done using the WHO protocol; mutations in the *P. falciparum* DHPS gene were analysed by PCR/RFLP.
Results | Treatment outcomes in the AS+SP arm were: Adequate Clinical Response (ACR) (92.1%), Early Treatment Failure (ETF) (0%) and Late Treatment Failure (LTF) (7.9%). In the SP arm outcomes were: ACR (89.7%), ETF (0%) and LTF (10.3%). In the 57 samples analysed for PfDHPS mutations, 35% (20/57) of the isolates harboured the mutant allele in codon K540E; while in codon A437G 45% (26/57) of the isolates had the mutant allele. Development of post-treatment gametocyte was high in SP arm but not in AS+SP arm (p=0.001); this was associated with the Nuba tribe (p=0.001).
Conclusion | Although this study didn't show a high level of treatment failure, there was relatively high frequency of the drug resistance variants. Continuous monitoring of the efficacy of the drugs and prevalence of resistant alleles is recommended.

MP 13
Fighting malaria by making accessible anti-malaria mosquito repellent to Burundians

Bonne Ciza • Public Health Centre of Vugizo in Nyanza-Lac Health District, Burundi

Introduction | In Burundi, it is estimated that 80% of Burundi's population is at risk of contracting malaria whilst 50% of patients in health facilities suffer from malaria. Mosquito nets do help but people are being bitten by malaria mosquitoes when they wake up early morning and in evening before they go to sleep. They need protection during that time.
Methods | In that context, the Ethics Advisory Agency for International Cooperation (ACECI) in collaboration with Montreal's École Polytechnique (Canada) together with the Government of Burundi found a new solution in an herb called Catnip (*Nepeta cataria*). A steam distilled oil added to hydrogen becomes a malaria mosquito repellent applicable on the skin. It will be introduced soon in Burundi.
Results | A trial phase for the catnip oil product was started. Seeds have been distributed to vulnerable local people (Batwas) for planting and harvesting in Nyabiraba and Bubanza areas. Thereafter, more plantations were set up in Bujumbura. Catnip oil is relatively easy to produce and safer to use. It reduces the number of bites from mosquitoes by 9%. Findings prove that a 15% concentrate is non-toxic on touch. It is a cost-effective product that can be used even on children and pregnant women.
Conclusion | Making the catnip oil product available will increase the protection against malaria. The implication for stakeholders and decision makers is clear. This new anti-malaria strategy should be implemented in Burundi.

MP 14
Predation efficiency of *Anopheles gambiae* larvae by aquatic predators in western Kenya highlands

Eliningaya J. Kweka • Centre for Global Health Research, Kenya Medical Research Institute, Nairobi, Kenya

Introduction | The current status of insecticide resistance in mosquitoes and the effects of insecticides on non-target insect species have raised the need for alternative control methods for malaria vectors. Predation has been suggested as one of the important regulation mechanisms for malaria vectors in long-lasting aquatic habitats, but the predation efficiency of the potential predators is largely unknown in the highlands of western Kenya. In the current study, we examined the predation efficiency of five predators on *Anopheles gambiae* larvae in 24 h and semi field evaluations.
Methods | Predators were collected from natural habitats and starved for 12 hours prior to starting experiments. Preliminary experiments were conducted to ascertain the larval stage most predated by each predator species. When each larval instar was subjected to predation, third instar larvae were predated at the highest rate. The numbers of surviving larvae were counted after 24 hours in 24 hour evaluation experiments. In semi-field experiments, the larvae were counted daily until they were all either consumed or had developed to the pupal stage.
Results | Experiments found that habitat type ($p<0.0001$) and predator species ($p<0.0001$) had a significant impact on the predation rate in the 24 hour evaluations. In semi-field experiments, predator species ($p<0.0001$) and habitat type ($p<0.0001$) were significant factors in both the daily survival and the overall developmental time of larvae. Habitat type ($p<0.0001$) and predator species ($p<0.0001$) had a significant impact on the predation rate in the 24 hour evaluations.
Conclusion | Efficacy shown by these predators should be tested in small community trials.

MP 15

New exposure methods for measuring mosquito behaviour which influences malaria transmission intensity and the impact of vector control

Dennis Massue • National Institute for Medical Research, Dar es Salaam, Tanzania

Introduction | Mosquito feeding behaviour plays a major role in determining malaria transmission intensity and our ability to control it with specific prevention measures. Human Landing Catch (HLC) is the only method which can directly and consistently measure the biting rates of anthropophagic mosquitoes both indoors and outdoors. Its ethical problems and the lack of a realistic and feasible alternative method for measuring mosquito behaviour pose a need for this project to search for a new exposure-free method as an alternative to HLC.
Methods | Electrocuting grids (EG) were evaluated as alternative to HLC, for simultaneously measuring mosquito biting densities both indoors and outdoors so that we can assess where and when people are exposed to them, in a Latin square experimental design in Jangwani ward, Dar es Salaam, Tanzania.
Results | Results from the study showed that the estimated proportion of mosquitoes caught indoors, during sleeping hours and indoor during sleeping hours with EG were lower, by 38% (p=0.067), 65% (p<0.001) and 81% (p=0.001) respectively for *An. gambiae* s.l., than with HLC. Proportions of *An. coustani* caught indoors and indoors during sleeping hours were higher by 215% (p=0.002) and 140% (p=0.193), respectively.
Conclusion | Results suggests that EGs failed to accurately reproduce the results of HLC. Therefore new methods are still needed as alternative to HLC. In the absence of molecular data, this assay exactly reproduces the expectation for *An. arabiensis* and differs completely for the expectation for *An. gambiae* s.l.

MP 16

Community empowerment on the use of treated bed nets: Does it have an effect on the burden of malaria in children under five?

Amare Deribew Taddege • Jimma University, Jimma, Ethiopia

Introduction | Behavioural factors have been the core barrier to the utilization of Long Lasting Insecticide Treated Bed Nets (LLITN) in Ethiopia.
Methods | We conducted a cluster randomised trial to assess the effect of tailored training of the heads of the households in the use of LLITN and the community network system on the burden of malaria in vulnerable groups. A total of 11 intervention and 11 control GOTS (villages) were included in the Gilgel Gibe Field Research Centre, south-west Ethiopia. The intervention consisted of training of heads of the households in the use of LLITN and the community network system. The burden of malaria among vulnerable groups was monitored by mass blood investigation in the intervention and control villages.
Results | The utilization of LLITN has significantly improved from 72.9% to 97.1% in the intervention villages. However, in the control villages, the utilization of LLITN was not improved between the baseline (73.6%) and the end of the study (71.7%). The prevalence of malaria in children under-five in the intervention villages has declined from 11.4% at baseline to 6.2% at the end of the study. However, the prevalence of malaria in the control group has increased from 6% to 13% during the first six months and remained above 8% afterwards.
Conclusion | Community empowerment on the use of LLITN has an important impact on the burden of malaria among vulnerable groups.

MP 17
Cytokine and antibody levels and prevalence of congenital and neonatal malaria in Mali

Souleymane Dama • Malaria Research and Training Centre, University of Bamako, Mali

Introduction | At the paediatric ward of the National Teaching Hospital Gabriel Toure, which is the only tertiary paediatric reference hospital of the country, neonatal mortality was 30%, 36.7% and 61% in 1997, 1999 and 2000, respectively. Based on clinical signs, the great majority of these illnesses are categorized as of infectious origin. We proposed to test the hypothesis that the prevalence of congenital and/or acquired malaria is negligible in new born infants in Mali.
Methods | We used sensitive molecular biology and biochemical methods to measure the prevalence of malaria in preterm infants and in neonates admitted to the paediatric ward of Hospital Gabriel Toure.
Results | We found that all 300 infants were negative for malaria parasitaemia using both microscopy and PCR. The OptiMal IT was positive for *P. falciparum* in 3 infants (1%). Among the 146 mothers included in the study we found that 0 (0%), 1 (0.7%) and 10 (6.8%) were positive for malaria parasites using microscopy, OptiMal IT and PCR, respectively. Cytokine analyses showed that neonates had a strong anti-inflammatory response, significantly higher than their mothers ($p<0.05$). The response was significantly higher than that of PCR-positive mothers for IL2 and IFN-γ. Similarly, PCR-negative mothers had higher levels of MSP3 and GLURP antibodies.
Conclusion | Our data suggest that malaria is not a significant contributor to neonatal morbidity and mortality in this inpatient population of infants.

MP 18
Impact of maternal *P. falciparum* infection on immunological and haematological parameters on pregnancy and birth outcomes in Douala, Cameroon

Carole Eboumbou Moukoko • Faculty of Medicine and Pharmaceutical Sciences, University of Douala, Cameroon

Introduction | In malaria endemic areas, pregnant women and children constitute the most vulnerable groups. More than 50 million pregnant women are at risk of malaria infection yearly, and more than half of this number is in sub-Saharan Africa where the transmission of *P. falciparum* is most intense. The study sought to elucidate the haematological and immunological changes in women and their new born and their impact on improved diagnosis and therapy of childhood malaria.
Methods | In order to study the potential role of *P. falciparum* in immunological and haematological parameters, we enrolled pairs of newborns and mothers delivering at two government antenatal hospitals. Three types of samples (umbilical cord blood, placental blood and maternal peripheral blood) were collected at all patients included in the study. 113 women (40.65 per cent) out of 278 women followed through delivery were parasitaemic at least once.
Results | The following parameters were analysed: platelets, lymphocytes, eosinophils, red blood cell count and haemoglobin (Hb), absolute monocyte and neutrophil counts, and mean platelet volume (MPV). The association of *P. falciparum* infection with haematological and immunological parameters changes will be presented.
Conclusion | Children infected with *P. falciparum* exhibited important changes in some haematological and immunological parameters that could be associated with poor birth outcome. The determination of these parameters could also generate new hypotheses about the pathogenesis of malaria and suggest new therapeutic approaches.

MP 19
Malarial iron-deficiency anaemia among asymptomatic Nigerian children

Zaccheaus Jeremiah • Niger Delta University, Wilberforce Island, Nigeria

Introduction | The aim of this study was to investigate the prevalence of malarial iron-deficiency anaemia and the effect of asymptomatic malaria on iron status indicators.
Methods | Seven parameters, haemoglobin concentration, white blood cell (WBC) count, malaria parasite, serum iron, total iron binding capacity (TIBC), serum ferritin, and percentage transferrin saturation, were evaluated using standard haematological, colorimetric and enzyme-linked immunosorbent assay procedures.
Results | Of the 240 children surveyed, 66 (27.5%) were parasitized with *P. falciparum*. The overall prevalence of iron-deficiency anaemia (defined as haemoglobin <11 g/dl 1, serum ferritin <12 ng/mL 1 and transferrin saturation <16%) in this study population was 9/240 (3.75%). The prevalence of iron-deficiency anaemia among the parasitized children was 9/66 (13.6%). Their mean parasite density (3.35 × 10^3 parasites/µL) was higher than the mean parasite density of the entire study population (1.16 × 10^3 parasites/µL). No significant change in the haemoglobin concentration, WBC and serum ferritin values was observed between the parasitized and non-parasitized children ($p > 0.05$), whereas a marked decrease in the serum iron, TIBC and percentage transferrin saturation values in the parasitized children was observed when compared with the non-parasitized group ($p<0.02$, 0.02 and 0.01). The percentage transferrin saturation correlated directly and significantly with haemoglobin, serum iron and TIBC values ($r=0.317$, 0.617, 0.236; $p<0.01$, $p<0.01$ and $p<0.05$).
Conclusion | We conclude that: (1) asymptomatic malaria infection exerts significant effects on iron indicators; (2) an increase in transferrin saturation may be an indication of iron availability and vice versa.

MP 20
Malaria in children under ten years of age living in a suburban area of Makelekele (Brazzaville, Congo): preliminary data

Mathieu Ndounga • Centre d'Etudes sur les Ressources Végétales (CERVE), Brazzaville, Congo

Introduction | In order to prepare sites for malaria interventions including clinical trials, a cohort of 329 children under 10 years of living in a suburban area (South of Brazzaville) has been established and passively followed during 12 months.
Methods | From a census database of the overall population of the area, a random list of 420 children under 10 years of age was generated. After parent/guardian informed consent, 329 children were clinically examined and venous blood taken for thick blood smear, hematologic and biochemical analyses. All children were passively followed up from May 2010 to April 2011 to record clinical malaria episodes.
Results | From 329 followed children, 178 (54.1%) were under 5 years and 151 (45.9%) ≥5 years. 160 (48.6%) are female and 169 (51.4) male. At enrolment 52.7% children were anaemic (haemoglobin <12 g/dl) with 1.2% with severe anaemia. We found that 10% of children harboured *P. falciparum* infections with geometric mean parasite density=1,754/µL (range 62–588,679/µL). During the follow-up, 176 children (54%) presented at least 1 malaria episode. A total of 282 malaria episodes were recorded or 0.87 episodes per child per year. In November (beginning of the rainy season) and in June (dry season), 33% and 21.6% of febrile children had malaria respectively, while in august only 9% presented malaria.
Conclusion | The follow-up of children under 10 living in a suburban area of Brazzaville during one year gave basic data on malaria representation for further recruitment of a cohort for clinical trials.

MP 21
Spatial distribution and risk factors of malaria in infancy in Entebbe, Uganda

Juliet Ndibazza • MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

Introduction | Malaria is a major public health concern; in Uganda more than 9 million malaria cases were reported in 2009. The distribution of malaria is heterogeneous in space and time, and disease burden can vary greatly even within small geographical areas.
Methods | The study took place in Entebbe, a lakeshore community. 2,507 pregnant women were enrolled and their infants followed up to age one year. Participants' addresses were geo-coded and incident cases of symptomatic malaria recorded passively from May-2003 to March-2007. SaTScan software with the Discrete Poisson Model was used to identify malaria clusters. The distribution and statistical significance of the clusters were explored with the Monte Carlo method. Risk factors associated with spatial clustering of malaria were assessed using logistic regression methods.
Results | The rate of clinical malaria in infancy was 41/100 person years. SaTScan detected thirteen space clusters; four clusters were statistically significant ($p \leq 0.02$). In multivariate analysis, spatial clustering of malaria was associated with low altitude, greater distance from the lake, lack of net or insecticide use, household water source (lack of piped water) and fuel source (use of charcoal or wood). Maternal asymptomatic *P. falciparum* infection in pregnancy was associated with malaria in infancy and with malaria clustering.
Conclusion | This study suggests that there are 'malaria hot-spots' in this area. Description of the spatial distribution of malaria and the identification of local malaria clusters and geographical risk factors can provide valuable information for targeted interventions to optimize use of the limited resources for malaria prevention and control.

MP 22
Foetal and maternal haemodynamics during acute malaria: persistent maternal tachycardia after recovery from malaria

Stephen Rulisa • National University of Rwanda, University Teaching Hospital, Kigali, Rwanda

Introduction | The maternal and foetal haemodynamics during acute malaria in pregnancy were never studied properly.
Methods | Maternal and foetal heart rate (MHR & FHR) and maternal blood pressure (BP) were studied during acute malaria until 56 days after start of treatment with artemether-lumefantrine (38 pregnant women with acute malaria, 39 healthy pregnant control women). Malaria patients were hospitalized until recovery for a minimum of 3 days. FHR was measured every 4 hours (day 1), every 8 h (day 2–3) and then weekly. Maternal vitals were measured every 8 h for 3 days. Control women were examined once a week. Mean baseline characteristics of patients compared to healthy women were respectively: gestational age (wks) 28.8 and 24.6 ($p=0.006$); maximum FHR (bpm) 165 and 158 (p-value 0.054); minimum FHR (bpm) 137.6 and 128.7 ($p=0.016$); mean BP (mm Hg) 75 and 81 ($p=0.001$); pulse pressure (mm Hg) 40 and 42 ($p=0.3$); MHR 107 and 81 ($p<0.001$); geometric mean parasite count 13795/µL.
Results | Complete time series were collected from 29 malaria patients and 29 controls. Maternal body temperature normalized within 24 hours; BP was normal after 72 h. Whereas MHR in control women showed a physiological increase during the evolution of pregnancy of approximately 7 bpm between days 0–56, the initially increased MHR of malaria patients declined to 94 bpm on day 7 and stabilized at this level. There were no pathological CTG records. The mean FHR normalized after 72 h.
Conclusion | Acute malaria induces maternal and foetal hemodynamic changes that normalize at a different pace after initiation of treatment. FHR and BP normalized between days 3–7 after start of treatment. Surprisingly, maternal heart rate remained elevated.

MP 23

Assessing malaria morbidity during the first two years of life in two different malaria epidemiological settings in Senegal and Burkina Faso

Jean Baptiste Yaro • Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso

Introduction | Evidence for association between decreasing levels of maternally derived malaria-specific IgG and increasing risk of clinical malaria has been reported. To determine the interval between the loss of protection once maternal antibodies have disappeared and possible protection through vaccination, a study was designed to assess the malaria incidence in the first two years of life.
Methods | The study commenced in Banfora (Burkina Faso) and in Keur Socé (Senegal) in late 2010. Children from 28–42 days were enrolled and will be followed up to their second anniversary. For the assessment of malaria incidence, each child is visited at home bi-weekly for health status check. If a history of fever within the last 24 hours or a documented fever is observed, a blood smear is prepared for malaria diagnosis. In addition, each month a blood smear is prepared for each child.
Results | So far, 140 and 150 children have been enrolled in Banfora and Senegal respectively. 50 and 53 children from Banfora and Keur Socé respectively have completed their first six months of follow-up. For the same period, only one clinical episode of malaria (temperature ≥37.5°C and positive blood smear) is reported from the Senegalese site. One child was found infected in Banfora while no asymptomatic carriage of *P. falciparum* was detected in Keur Socé.
Conclusion | From our preliminary results, it appears that malaria incidence remains extremely low during the first six years of life. However, it should be noted that, in both sites, the period of has not yet coincided with the actual period of high malaria transmission.

MP 24

Slow parasite clearance and recrudescence in malaria patients treated with artemether-lumefantrine (AL): association with the NFD haplotype of PfMDR1

Khalid Beshir • London School of Hygiene and Tropical Medicine, London, UK

Introduction | In South-East Asia, reduced susceptibility to artemisinin, characterized by slow parasite clearance monitored by microscopy, has recently been reported. No genotype association was found but the phenotype has shown heritability. However, an alternative to frequent venous sampling is required, especially in Africa where the majority of participants are children. Our aim was to evaluate a new qPCR assay on filter-paper based blood spots taken daily; to measure parasite clearance and to examine phenotype-genotype associations, if any.
Methods | The *P. falciparum* samples were from a clinical trial comparing AL and DHA-PIP in children under 10 years conducted in 2009 in Western Kenya. 136 participants selected randomly were analysed by qPCR to measure parasite clearance time. Established genotyping methods were used to investigate polymorphisms in PfCRT at positions 72–76 and PfMDR1 codons 86, 184 & 1,246.
Results | A strong correlation between slow parasite clearance by qPCR and late microscopic recrudescence was found after AL treatment (p=0.013). This association has not been seen using microscopy. Genotypic analysis showed an association between the NFD haplotype of PfMDR1 on day 3 and slow parasite clearance using qPCR in the AL group (p=0.047). There was also a significant increase in CVMNK allele of PfCRT after AL and DHA-PIP treatments.
Conclusion | The new qPCR assay is a powerful tool for identification of novel phenotype which can be used as predictor of subsequent treatment failure. Our results support PfMDR1 and PfCRT as potential molecular markers for routine monitoring of drug resistance in trials of ACT.

MP 25
The evaluation of easy access groups as a tool for monitoring temporal changes in malaria transmissions and uptake of control interventions in Malawi: the EvalMal study

Sanie SS Sesay • Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Blantyre, Malawi

Introduction | Currently recommended tools for measuring transmission reduction involve large, logistically and financially demanding, population-based surveys done at intervals of 3–5 years. Since malaria transmission intensity and disease incidence can vary within a country, programmatic decisions are often made at district level. Therefore timely, valid, cost-effective estimates of short- and medium-term control progress at district level are urgently needed. Moreover, with the change of focus from control of burden to reduction of transmission and the recent progress made, malaria trends in older (and asymptomatic) age groups become more important.
Methods | We intend to assess a potentially cost-effective opportunistic sampling strategy using easy access groups (EAGs) of different age groups as a monitoring and evaluation tool at the district level. Over the next two years, children >4 months presenting at the EPI vaccination clinic at Chikwawa District Hospital and their accompanying older siblings aged <15 years will be surveyed monthly. A modified version of the WHO MERG MIS questionnaire will be presented to the parent/guardian. Impact assessment will be done on the parent, the child attending vaccination and any accompanying sibling. This will be compared to the same coverage and burden indicators derived from children in the same age range enrolled in the ACTia rolling MIS (gold standard) and expanded rMIS.
Results | Study enrolment started in March 2011. Preliminary results will be presented at the conference.

MP 26
Baseline malaria epidemiology and normal reference ranges for biological parameters in Maferinyah, Guinea

Abdoul Habib Beavogui • Centre de Formation et de Recherche en santé Rurale (CFRSR) de Mafèrinyah, Mafèrinyah, Guinea

Introduction | The emergence and spread of malaria strains resistant to widely available antimalarial drugs have greatly crippled malaria control in endemic countries. The identification of new therapeutic/prevention tools and the development of local skills remain a public health priority. This study aimed to determine the normal reference values for biological parameters. Furthermore, we aimed to measure the age specific disease incidence in children during two consecutive years to estimate the malaria burden and to monitor the efficacy of first line antimalarial treatment artesunate plus amodiaquine.
Methods | This is an observational study to determine the burden of malaria in children of 3 months to adults 45 years of age. A total of three cross sectional surveys will be carried out each year for two consecutive years: at the beginning and end of the transmission season and at the middle of the dry season.
Results | Overall 606 subjects were included and blood was collected in April 2011. The second blood collection is scheduled for July 2011 and the third for November 2011. 22 subjects were included in the *in vivo* study, 6 of whom have completed their follow-up without any therapeutic failure.
Conclusion | The results will ascertain baseline standards of biological and entomological values. The data will be used to calculate sample size for future clinical trial studies and also to define inclusion/non-inclusion criteria for clinical trial protocols and for intervention effectiveness in malaria control in the Republic of Guinea.

MP 27

The ABO blood group system and *P. falciparum* infection in three ethnic groups living in a stable and seasonal malaria transmission area of Burkina

Edith Bougouma • Centre National de Recherche et Formation sur le Paludisme, Ouagadougou, Burkina Faso

Introduction | Several genetic factors including red blood cell polymorphisms influence the severity of disease due to infection with *P. falciparum*. However, there is a paucity of information concerning the role of host genetic factors in asymptomatic malaria. This study aimed to investigate the prevalence of the ABO blood group and to explore the relationship between ABO blood type and the prevalence of asymptomatic *P. falciparum* infection.
Methods | The study was carried out in rural villages. We performed cross sectional surveys in children and adults. Blood groups were determined genetically.
Results | A total of 548 subjects (Mossi 163; Fulani 209; and Rimaibe 176) were included. The prevalence of blood groups was A 25.5%, B 26.6%, AB 7.3% and O 40.5%. Blood group O was not only the commonest blood type overall, but was higher in the Fulani (52.6%) than in the Mossi (29.4%) and the Rimaibe (36.4%). Subjects from the Fulani were associated with a reduced risk of infection from *P. falciparum* and with lower parasite densities than sympatric populations. The subjects with non-O blood were less susceptible to malaria infection. There was an association between ethnicity (CI=0.63–0.98, p=0.039) and malaria infection during the high transmission as well as an association between the non-O blood group and malaria infections according to all ethnicity (p=0.001). This was also true when ethnic groups were considered separately (p=0.03).
Conclusion | Individuals with non-O blood are at lower risk from infection than other groups. Correlation between ethnicity and blood group for the risk of malaria infection was shown.

MP 28

Malaria morbidity during the two first years of life in rural Senegal

Aly Gueye • Faculty of Medicine, Cheikh Anta Diop University, Dakar, Senegal

Introduction | Previous study has provided evidence for associations, at a population level, between decreasing levels of maternally derived malaria-specific IgG and increasing risk of clinical malaria. These maternal antibodies against pathogen-specific antigens disappear during the first months of life while the neonate's own immune system develops. The interval between the loss of protection once maternal antibodies have disappeared and possible protection by vaccination should be as narrow as possible for all vaccine-preventable diseases, because of the risk of early infection. Vaccination of children with maternally derived protection could potentially lower vaccine efficacy. The immune responsiveness to malaria vaccination in infants in areas where malaria is endemic therefore needs careful study.
Methods | We are following a dynamic cohort of 150 infants from birth to two years of age to characterize malaria maternal antibody waning, malaria infection and clinical malaria episodes in infants from 0–2 years in Keur Soce, central Senegal. It should be noted that all enrolled participants will be actively followed over 2 years.
Results | So far, 125 infants have been enrolled in study. We expect completing the enrolment by end of April 2011. Preliminary results with regard to incidence of malaria; prevalence of asymptomatic parasite carriage and anaemia etc. will be presented at the conference.
Conclusion | The data will be fundamental for understanding naturally acquired immunity to malaria, as well as for making an evidence-based choice of the appropriate immunization schedule for the malaria vaccine candidate.

MP 29
Defining malaria burden from morbidity and mortality records, self treatment practices and serological data in Magugu, Babati District, northern Tanzania

Charles Emilio Mwanziva • Kilimanjaro Christian Medical College KCRI, Moshi, Tanzania

Introduction | Malaria morbidity and mortality data from clinical records provide essential information towards defining disease burden in the area and for planning control strategies, but should be augmented with data on transmission intensity and serological data as measures for exposure to malaria. The malaria burden based on serological data and prevalence of malaria was estimated in Magugu, northern Tanzania.
Methods | Prospectively, 470 individuals were selected for the study. Both microscopy and Rapid Diagnostic Test (RDT) were used for malaria diagnosis. Seroprevalence of antibodies to merozoite surface proteins (MSP-119) and apical membrane antigen (AMA-1) was performed and the entomological inoculation rate (EIR) was estimated. Retrospective data on treatment history, prescriptions by physicians and use of bed nets were collected.
Results | Malaria prevalence in the area was 6.8% (32/470). Of 130 individuals treated with artemisinin combination therapy (ACT), 22.3% (29/130) were slide confirmed, while 75.3% (98/130) of them were blood smear negative. The majority of those who had fever received ACT. Immunoglobulin against MSP-119 was positive in 16.9% (74/437) while against AMA-1 it was positive in 29.8% (130/436). Transmission intensity was estimated at <0.2 infectious bites per person per year. The RDT was highly specific (96.3%) but with low sensitivity (15.6%).
Conclusion | Magugu is a low endemic area. There is substantial overdiagnosis, overtreatment and self-treatment in the community. The low sensitivity of RDT reflects the low number of immune individuals as well as the low parasite density. On the basis of medical records the burden of malaria was shown to have been overestimated.

MP 30
Comparison between molecular and conventional diagnostic tools for the diagnosis of malaria and sickle cell gene carriage

Orion Miantuasila • Congolese Foundation for Medical Research, Brazzaville, Republic of Congo

Introduction | Sickle cell-disease and malaria represent public health issues. Indeed, the determination of haemoglobin status and the presence of malaria parasites in blood are frequent analyses requested of medical laboratories in the Republic of Congo. This study aimed at comparing the conventional with the molecular diagnostic methods in Brazzaville.
Methods | Individuals were recruited at the medical centre COGEMO in Brazzaville. We considered 110 and 116 individuals who had a prescription for determination of haemoglobin status and diagnosis of malaria respectively. The acetate gel electrophoresis (standard method) compared with allele-specific PCR for the determination of normal or sickle cell β-globin allele. Microscopy, the standard method, was compared with the OPTIMAL rapid diagnostic test and malaria species- specific PCR. The sensitivity and specificity of these methods were assessed.
Results | Among 110 samples screened, 107 (97.27%) have a similar profile with both electrophoresis and PCR methods. The 3 remaining samples have AS phenotype by electrophoresis; two showed SS phenotype and one AA phenotype by PCR. Among 116 samples considered for malaria, parasites were detected in 30 samples by thick blood examination. The OPTIMAL test was *P. falciparum* positive in only 11 samples which were also positive by microscopy. Out of the 30 positive samples, 12 samples showed having *P. falciparum* by thin blood examination. The detection of malaria using molecular tools is in progress.
Conclusion | This is the first study to compare conventional with molecular methods in Congo. It will permit a better assessment of accuracy of standard methods. This study was supported by CANTAM.

MP 31

Marker value of microparticles in severe malaria associated with cerebral dysfunctions

Joel Pankoui Mfonkeu • Department of Biochemistry, University of Douala, Douala, Cameroon

Introduction | Cerebral malaria (CM) and severe anaemia (SA) are the most severe complications of *P. falciparum* infections. Enhanced endothelial microparticle (MP) release correlates with malaria severity, although the full extent of vascular cell vesiculation remains unknown. Here, we characterize for the first time the distribution of cell-specific MP in patients with severe versus uncomplicated malaria. We tested the hypothesis of a systemic vascular activation in CM by examining plasma MP origins and levels in relation to clinical syndromes, disease severity and outcome.
Methods | Patients recruited in Douala, Cameroon, were assigned to clinical groups following WHO 2000 criteria. MP quantitation and phenotyping were carried out using cell-specific markers in flow cytometry.
Results | Platelet, erythrocytic, endothelial and leucocytic MP levels were, irrespective of gender, found elevated in patients with cerebral dysfunctions, i.e., those with CM or CM+SA; at discharge they had returned to normal. In CM patients, platelet MP was the most abundant and their levels notably correlated with coma depth and thrombocytopenia. Despite limited mortality (n=5), endothelial MP levels in fatal cases were significantly higher than in CM survivors.
Conclusion | This study shows for the first time that platelet MP levels are most dramatically elevated in CM patients. Even though widespread enhancement of vesiculation in the vascular compartment is a feature of CM, remarkably it was not in SA without coma. Our data underpin the role of MP as a biomarker of severity in malaria and more specifically of neurological involvement.

Reference: PLoS ONE. 2010; 5(10):e13415.

MP 32

Molecular diagnosis of malaria in the field: Development of a novel 1-step nucleic acid lateral flow immunoassay for the detection of all four human *Plasmodium* species. and its evaluation in Mbita, Kenya

Patrick Sawa • ICIPE, Nairobi, Kenya

Introduction | Microscopy is frequently used for malaria diagnosis, but at low parasitaemia, it becomes less sensitive and time consuming. Molecular tools allow for specific/sensitive diagnosis, but current formats, such as polymerase chain reaction (PCR) combined with gel electrophoresis and real-time PCR assays, are difficult to implement in resource-poor settings.
Methods | Here the evaluation of a simple, fast, sensitive, and specific detection system is described: the nucleic acid lateral flow immunoassay (NALFIA) for amplified pan-Plasmodium PCR products. The NALFIA lower detection limit is 0.3–3 parasites/µL, tenfold more sensitive than gel electrophoresis analysis.
Results | Evaluating 650 clinically suspected malaria cases with the pan-Plasmodium assay under field conditions (rural Kenya) revealed that NALFIA detected more positives than microscopy (agreement, 95%; κ value=0.85), and there was an excellent agreement between gel electrophoresis and NALFIA (98.5%; κ value=0.96).
Conclusion | NALFIA is more sensitive than microscopy and a good alternative to detect PCR products. By circumventing the use of electricity or expensive equipment, NALFIA is the first step towards molecular field diagnosis.

MP 33
Evaluation of the relative performance of rapid diagnostic test products (Partec and Paracheck-Pf) in the diagnosis of malaria in febrile children

George Ademowo • Institute for Advanced Medical Research and Training, University of Ibadan, Nigeria

Introduction | Accurate and prompt diagnosis is important for proper management of malaria. Diagnosis of malaria requires availability of easy, rapid, sensitive, specific and affordable methods. We compared performance of the Paracheck rapid diagnostic test kit and the Partec rapid malaria test with microscopy.
Methods | 143 children aged 6 months to 12 years presenting with symptoms suggestive of malaria were enrolled at the University College Hospital, Ibadan, Nigeria. Patients were examined clinically. Blood was obtained through finger prick for thick and thin blood films stained with Giemsa stain for microscopy. Partec and Paracheck were also used independently to screen the patients.
Results | Light microscopy showed that 40 (28%) of the patients harboured malaria parasites. Partec detected all the positives (true positives) and 87 other false positives. There were 15 true negatives and no false negative. Paracheck results indicated 28 true positives and 17 false positives while 86 were true negatives and 10 false negatives. The results showed Partec and Paracheck had a sensitivity of 100% and 73.68% respectively. However, Partec had a low specificity of 14.71% against 83.5% of Paracheck. Thus diagnostic accuracy of 38.73% was obtained for Partec. Paracheck had an impressive diagnostic accuracy of 80.85%.
Conclusion | The high false positives obtained with Partec may be due to the presence of artefacts that fluoresce. Paracheck however gave false negative results mainly at low parasitaemia. Despite these limitations, the two rapid malaria test products will be suitable for diagnosis and clinical trials.

MP 34
Deficiency of CD36 predisposes children to clinical malaria

Debora Charles Kajeguka • Kilimanjaro Christian Medical College, Tumaini University, Moshi, Tanzania

Introduction | Susceptibility to malaria has been linked with human genetic variability. Polymorphisms in genes that encode crucial signalling molecules have been proposed as factors that determine the outcome of malaria. We studied the role of CD36 on immune IgG responses to MSP-119 antigen and malaria incidence.
Methods | Children were genotyped for the c.1264 T >G mutation at the beginning of the study using polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP). IgG levels and percent seropositivity to Merozoite surface protein 1 (MSP-119) were determined at the baseline by Enzyme linked immunosorbent assay. Children were followed for 12 months for malaria incidences across the genotypes and then IgG levels and percent seropositivity to MSP-119 determined at a final survey.
Results | Both mean IgG levels and percent seropositivity to MSP-119 increased significantly in normal (from 159/711 (22.4%) to 336/711 (66.7%)) and heterozygous (6/27 (22.2%) to 18/27 (66.7%)) children but not in homozygous mutants (CD36-deficient) children. We observed a similar trend with the IgG optical density readings which increased in normal and heterozygous children from 36.05 ± 0.452 to 47.05 ± 0.415 and from 33.41 ± 2.907 to 51.46 ± 0.946 respectively, but not in CD36-deficient children. Normal children had a significantly lower malaria incidence as compared to other genotypes (χ^2=115.59; p<0.05).
Conclusion | Deficiency of CD36 suppresses IgG responses to *P. falciparum* MSP-119 antigen. This results in a predisposition to acquire clinical malaria in children. The IgG antibodies are critical in protection against malaria in children.

MP 35
Determination of G6pd polymorphisms and their effects on antibody responses to malarial antigens in Rift Valley area of northern Tanzania

Modibo Daou • Malaria Research and Training Centre, Bamako, Mali

Introduction | Malaria is the leading cause of mortality worldwide. The disease causes clinical illness, often very severe in 300–500 million people globally (Chung et al., 2007). The G6PD deficiency has been found to be associated with protection against *P. falciparum* malaria (Weatherall, et al., 2002 and Santana, et al., 2009) and it is also considered as potential confounding factor in many malaria vaccine trials.
Methods | To define the effect of G6PD deficiency on IgG production against AMA-1 and MSP1–19, we did ELISA of 200 samples from a study done in Tanzania. The single specific nucleotide probe was used for the determination of the type of G6PD.
Results | The study shows that 29% and 26% of all G6PD normal are seropositive to AMA-1 and MSP1–19 respectively. None of the G6PD A-heterozygote was seropositive for AMA-1 or MSP1–19. 16% of the G6PD hemi/homozygote were seropositive to AMA-1 and MSP1–19. This difference in seropositivity among the G6PD genotypes was statistically not significant.
Conclusion | We have observed that while none of the G6PD heterozygous genotype was seropositive for anti-AMA-1 or anti-MSP1–19, G6PD A (normal) genotype had slightly higher but not significant prevalence of antibodies against AMA-1 and MSP1–19 compared to the homo/hemizygous genotypes. Our study needs to be repeated with a larger sample size before conclusions can be drawn.

MP 36
Geographic patterns of PfCRT and PfMDR1 polymorphisms in *P. falciparum* isolates from Nigeria and Brazil: evidence of different antimalarial drugs selection pressure

Onikepe Folarin • Malaria Research Laboratories, University of Ibadan, Nigeria

Introduction | Resistance to most aminoquinolines has been attributed to single nucleotide polymorphisms (SNPs) and copy number variations in PfCRT and PfMDR1, respectively, although these polymorphisms may vary from one endemic area to the other. This study was designed to determine the effect of antimalarial drug selection on SNPs on PfCRT and PfMDR1 genes in *P. falciparum* isolates from two distinct geographical locations in West Africa and South America.
Methods | Nested PCR followed by direct DNA sequencing approaches were used to determine haplotype in PfCRT (amino acids at codons 72–76) and PfMDR1 (codon 86).
Results | Pfcrt haplotype and N86Y PfMDR1 polymorphism were successfully determined in 70 and 18 *P. falciparum* isolates from Nigeria and Brazil respectively. All isolates from Brazil harboured the SVMNT PfCRT haplotype, while the most prevalent haplotypes in Nigerian isolates were the mutant CVIET (72%) and the wild-type CVMNK (21%). The emergence of the PfCRT CVMNT haplotype (7%) in Nigeria was also observed. The wild-type PfMDR1-Asn86 allele was present in 100% and 54% of *P. falciparum* isolates from Brazil and Nigeria respectively, while 46% (32/70) of isolates from Nigeria harboured the mutant PfMDR1-Tyr86 allele.
Conclusion | We provide first evidence of emergence of the CVMNT haplotype in West Africa. The high prevalence of the PfCRT CVIET and SVMNT haplotypes in Nigeria and Brazil respectively is indicative of different selective pressure by chloroquine and amodiaquine. Continuous monitoring of the PfCRT SVMNT haplotype is required in endemic areas of Africa, where the artesunate-amodiaquine combination is used for treatment of acute uncomplicated malaria.

MP 37
Pharmacogenetics determines treatment outcome of Lapdap in malaria

Ramatoulie Janha • Medical Research Council, Banjul, The Gambia

Introduction | CYP2C19 and CYP2C9 metabolise the antimalarials chlorproguanil and dapsone (co-formulated into Lapdap) respectively. Lapdap exhibited haematological adverse effects that led to its withdrawal.
Methods | Chlorcycloguanil pharmacokinetic parameters were associated with CYP2C19/CYP2C9 alleles and CYP2C19 metaboliser groups in 43 adult subjects. Additionally, 603 Gambian children were assessed for CYP2C19*17, *2 and CYP2C9*8 alleles. The effects of these on treatment outcome were analysed.
Results | CYP2C19*17 significantly increases pharmacokinetics of chlorcycloguanil; whilst CYP2C19*2 and rs12769205A >G allele have opposite effects on chlorcycloguanil pharmacokinetics. 1.0% CYP2C19*17 carriers had severe anaemia at day three compared to 3.5% non-carriers (OR 0.26, 95% CI 0.06–1.18. p=0.08). Among individuals who were glucose-6-phosphate dehydrogenase (G6PD) deficient, being a CYP2C19*2 carrier was associated with an increased risk of severe anaemia (25% *vs* 6%) whereas amongst G6PD normal individuals, the risk associated with CYP2C19*2 carrier status was decreased (0.7% *vs* 2.9%, interaction p=0.05). Haemoglobin at day three was on average increased by 0.48 (-0.02, 0.97; p=0.06) g/dL in CYP2C9*8 carriers compared to non-carriers. Among individuals with high initial parasite density, CYP2C19*17 carriers had a higher mean haemoglobin level than non-carriers, while for individuals with low parasite density at baseline this difference was reversed (interaction p=0.02). There was some evidence that CYP2C19*2-containing haplotypes, which confer slow metabolism, might be positively selected.
Conclusion | CYP2C19*2, CYP2C19*17, CYP2C9*8 and G6PD A- are a small panel of pharmacogenetic markers that could guide treatment for malaria using chlorproguanil/dapsone.

MP 38
Genetic polymorphism of merozoite surface protein-1 and 2 in *P. falciparum* isolates from Brazzaville, Congo

Pembe Issamou Mayengue • Fondation Congolaise pour la Recherche Médicale, Brazzaville, Republic of Congo

Introduction | The characterization of malaria parasite populations circulating in an area is part of site characterization. It is a basis for evaluating the impact of malaria interventions on genetic diversity, parasite species, and multiplicity of infection. The present study aimed to analyse genetic diversity of *P. falciparum* merozoite surface proteins 1 and 2 (MSP-1 and MSP-2) and to determine the multiplicity of infection (MOI) in clinical isolates collected from children living in Brazzaville, Republic of Congo. CANTAM financially supported the molecular work for this study.
Methods | A total of 125 isolates from patients with uncomplicated malaria attending Terinkyo and Madibou health centres were collected between January and June 2005 while evaluating the therapeutic efficacy of amodiaquine-artesunate combination. DNA was extracted and MSP-1 and MSP-2 genes were genotyped using allele-specific nested-PCR.
Results | Out of 468 distinct fragments detected, 16 MSP-1 and 20 MSP-2 genotypes were identified. For the MSP-1 gene, the K1 family was the predominant allelic type, whereas the 3D7 family was the most prevalent in the MSP-2 gene. Overall, the mean MOI was 2.2. Out of 125 samples, 104 (83%) harboured more than one parasite genotype. There was no statistically significant difference in the MOI for either sex or age of patients. However, a statistically significant correlation was found between parasite densities and the number of genotypes.
Conclusion | Polymorphism in falciparum clinical isolates from Brazzaville was high and mainly of multiple clones. The basis for the positive association between parasite densities and multiplicity of infection was discussed.

MP 39

Correlation between *P. falciparum in vitro* chloroquine resistance and level of PfCRT 76 T gene expression in Mali

Mamadou Wélé • Malaria Research and Training Center, University of Bamako, Mali

Introduction | PfCRT K76T point mutation has been associated with *in vitro* as well as *in vivo* chloroquine resistance of *P. falciparum*. However, the exact mechanism of the chloroquine resistance in parasites is still unclear. So in order to better understand this phenomenon of resistance, this study aimed to evaluate the correlation between the *in vitro* resistance with the rate of expressed PfCRT protein and level of PfCRT gene expression in field parasites from Mali.
Methods | Fields parasites were culture adapted; parasite proteins and mRNA were extracted for PfCRT protein rates and PfCRT gene expression evaluation. We found five chloroquine resistant strains identified as M1, M2, M3, M4 and M5 IC50 ranged from 193.52 ± 13.30 nM and 124.74 ± 10.29 nM.
Results | The strains M4 and M5 had the highest PfCRT protein rates, however M1 had shown the highest level compared to others. All our strains carried CVEIT haplotype which is present in resistant control Dd2. In some we didn't find a significant correlation between *in vitro* chloroquine resistance with the rate of PfCRT protein and PfCRT gene expression.
Conclusion | These results provide the evidence for the hypothesis that the phenomenon of chloroquine resistance may be under multigenic control including different transporters.

References: N Engl J Med. 2001; 344: 257–263; Mol Cell. 2000; 6: 861–871; Mol Biochem. 2004; 36, 2: 273–285.

MP 40

Genome wide adaptations of *P. falciparum* in response to lumefantrine selective drug pressure

Leah Mwai • KEMRI/Wellcome Trust Research Programme, Kilifi, Kenya

Introduction | The combination therapy of the Artemisinin-derivative artemether (ART) with lumefantrine (LM) (Coartem®) is an important malaria treatment regimen in many endemic countries. Resistance to artemisinin has already been reported, and it is feared that LM resistance (LMR) could also evolve quickly. Therefore molecular markers to track Coartem® efficacy are urgently needed.
Methods | We induced LMR by culturing the *P. falciparum* multidrug resistant reference strain V1S *in vitro* under continuous drug pressure for 16 months. We used the PFSANGER Affymetrix custom array to identify differentially expressed (DE) genes.
Results | The initial IC50 (inhibitory concentration that kills 50% of the parasite population) was 24 nM. The resulting resistant strain V1SLM, obtained after an estimated 166 cycles under LM pressure, grew steadily in 378 nM of LM; corresponding to 15 times the IC50 of the parental strain. However, after two weeks of culturing V1SLM in drug-free medium, the IC50 returned to that of the initial, parental strain V1S, demonstrating a transient phenotype. We identified 184 DE genes; amongst those 18 putative transporters including the multidrug resistance gene (PfMDR1), the multidrug resistance associated protein (PfMRP1) and the V-type H+ pumping pyrophosphatase 2 (pfvp2). We also observed a significant enrichment of genes associated with fatty acid metabolism and a clear selective advantage for two genomic loci in parasites grown under LM drug pressure.
Conclusion | We recommend further functional studies to identify the exact role of identified genes, and to ascertain if they can be useful molecular markers of LMR.

MP 41
GIA, ELISA and protection in a *P. knowlesi* model

Muzamil Mahdi Abdel Hamid • Institute of Endemic Diseases, University of Khartoum, Khartoum, Sudan

Introduction | *P. falciparum* apical membrane antigen 1 (PfAMA1) is a leading blood stage vaccine candidate in phase II clinical studies. We used *Plasmodium knowlesi* and rhesus macaque as a model to test efficacy of AMA1 and to identify correlates of protection.
Methods | PkAMA1 was produced and purified using similar methodology as for clinical grade PfAMA1. Two groups of six rhesus macaques were immunised on day 0, 28, and 56 with 50 µg Pk or Pf AMA1 in CoVaccine HT adjuvant. Monkeys were challenged on day 70 with *P. knowlesi* H strain iRBC intravenously re-boosted on day 202. Rhesuses were re-challenged on day 217 and 450. Parasitaemia were monitored daily after each challenge. ELISA and GIA were performed using standard protocols.
Results | Expression of PkAMA1 yielded a highly pure conformational intact protein. One of six rhesus monkeys was able to control parasitaemia, upon blood stage challenge with Pk H-strain. Four out of the remaining 5 showed a delay in parasite onset correlating with ELISA and GIA titres. Following the second challenge, four of the six monkeys were able to control parasitaemia; one had a delayed onset of parasitaemia, while all control animals became parasitaemic. Upon the third challenge 5 out of 6 PkAMA1 vaccinated animals were able to completely control parasitaemia. High GIA levels correlate with protection (Spearman's Rho=-0.93, p=0.008).
Conclusion | This study shows that: i) Heterologously expressed PkAMA1 can protect against blood stage challenge ii) Protection improves after challenge-boost and iii) Functional antibodies levels correlated inversely with the day of onset.

MP 42
Implementation and standardization of *in vitro P. falciparum* culture in Africa

Ayola Akim Adegnika • Albert Schweitzer Hospital Lambaréné, Gabon

Introduction | *In vitro* culture of *P. falciparum* is a key technique for pre-clinical compound screening, functional assays to test vaccine-induced immune responses, and basic research. However, it is technically demanding and infrastructure as well as capacity lack in most African research centres.
Methods | An existing North-South collaboration was used to set up continuous *in vitro* parasite culture (CPC) at expert level. A centre of excellence (CoE) was formed in Central Africa. Special emphasis was laid on developing personal networks between the partners.
Results | CPC was set up at the Medical Research Unit of the Albert Schweitzer Hospital in Lambaréné, Gabon. General and project-centred training was performed to achieve expert level performance, communication, and logistics. Procedures were adapted to site-specific conditions. Close collaboration between the African CoE and the Northern partners with training and common projects at either side are ongoing. A virtual repository for protocols and communications was established and it's usability is currently improved. The African CoE started to perform projects beyond collaborative work with Northern partners and is developing procedures to establish CPC in small and less experienced sites in Gabon. Other Central African centres and scientific networks were contacted to assess the demand for CPC implementation.
Conclusion | CPC is highly demanded at African research centres. Implementation is possible in experienced centres with a critical amount of scientific projects that require (or at least benefit from) CPC, such as basic research, malaria drug or vaccine trials. Facilitation of personal networks is essential for success and sustainability of technically demanding techniques.

MP 43

PfMDR1 codon 86 polymorphism: easy and effective solutions to practical challenges with DNA extraction, PRC amplification and gel documentation

Matthew Olatunde • Department of Pharmacology and Therapeutics, University of Ibadan, Nigeria

Introduction | The multidrug resistance gene of *P. falciparum* has been linked with resistance to the major classes of antimalarial therapies. Successful DNA extraction, PCR amplification, and Gel documentation of polymorphisms in specific codons of the gene is essential for the evaluation of its role in parasite responses to antimalarial therapies.
Methods | In a study carried out in 2009, 300 children with acute uncomplicated malaria had DNA extracted from filter paper blood samples obtained during the study. This was followed by DNA amplification by nested PCR, RLFP for codon 86, and Gel documentation.
Results | 110 filter paper samples were processed for PfMDR1 codon 86 polymorphism. 13% of the samples yielded poor or inconclusive results. Challenges encountered in this group of unsuccessful assays (and solutions) were: non amplification of isolated DNA fragment (DNA extraction method was changed and optimized); multiple band amplification (primer optimization); improper proximity of bands (annealing temperature was optimized); inconsistent amplification (ready to go PCR beads were used fresh); faint gel bands (DNA quantification and use of sufficient DNA concentration); unidentifiable base pairs (optimization of annealing temperature to eliminate primer dimmers); and power outages during PCR amplification cycles (use uninterrupted power supply source).
Conclusion | Appropriate optimization of the reactions eventually resulted in high quality products and near 100% consistency and repeatability of results. These challenges are not different from those encountered in similar work with polymorphisms on other gene sites.

MP 44

Hyperparasitaemia and delayed parasite clearance after ACTs treatment in Nigerian children with acute uncomplicated falciparum malaria

Sarah Yaria • College of Medicine, University of Ibadan, Ibadan, Nigeria

Introduction | Artemisinin based combination therapies (ACTs) have been recommended for the treatment of *P. falciparum* malaria. However, reduced susceptibility to ACTs have been reported. This study evaluated therapeutic efficacy of artemether-lumefantrine (AL) and artesunate-amodiaquine (AA) in the treatment of acute uncomplicated malaria in children from South-West, Nigeria.
Methods | Children aged 6 months-6 years with microscopically confirmed *P. falciparum* infection were enrolled and randomly treated with standard doses of AL or AA following informed consent. Pre- and post-treatment peripheral blood smears were obtained from each child. Clinical and parasitological response was determined after PCR correction.
Results | A total of 134 children were enrolled and treated with AL (57) or AA (77). Parasitaemia cleared in 84% and 79% of the patients who used AL and AA respectively by day 3 post-treatment. Mean parasite clearance time was 2.57 (95% CI 2.28–2.85) for AL and 2.61 (95% CI 2.40–2.83) for AA. Thirteen of the 134 children failed treatment with the two drugs, 7 of which were treated with AL. High parasite density (>100,000/µl) was significantly associated with delay in parasite clearance (Log rank statistics=6.92, p=0.009). PCR corrected cure rate at day 42 was 89% (AL) and 92% (AA) respectively.
Conclusion | Although AL and AA are still effective antimalarial drugs for the treatment of malaria, the delay in parasite clearance observed is an indication of reducing trend of sensitivity to these ACTs in South West Nigeria. There is a need for continuous monitoring of the efficacy of these ACTs in endemic areas of Africa.

MP 45
Assessment of laboratory reference values in the Kassena-Nankana districts of northern Ghana

Frank Atuguba • Navrongo Health Research Centre, Navrongo, Ghana

Introduction | A trial of potential malaria candidate vaccines requires making clinical observations of subjects and the performance of various laboratory tests including complete blood counts, serum creatinine and hepatic transaminases. Standard local values for use as reference values are however non-existent and these are known to vary with race and locality. In order to position the site to accurately assess vaccine safety and efficacy in the people of the Kassena-Nankana districts, we sought to establish laboratory reference ranges of biochemical and haematological parameters. We aimed to characterize the Kassena-Nankana population with respect to haematologic and biochemical parameters that may be used to establish inclusion/exclusion criteria for participation in malaria vaccine trials.
Methods | This was a cross sectional study using the DSS to generate potential participant's lists. All volunteers underwent a baseline medical history and physical examination. Venous blood was obtained from healthy eligable volunteers after informed consent was sought. The study was approved by the Ghana Health Service-ERC and the NHRC-IRB. The target sample size was 1,820 individuals selected to include 130 male and 130 female individuals from the following age ranges (<6 months, 6–23 months, 2–4 years, 5–9 years, 10–19 years, 20–39 years, ≥40 years).
Results | 1,874 individuals were enrolled and haematological and biochemical parameters analysed for seven age groups.
Conclusion | Local laboratory reference values for common haematological and biochemical parameters are now available in the Kassena-Nankana District that may be employed for screening purposes and in vaccine, clinical and epidemiological studies.

MP 46
Clinical laboratory reference ranges derived from population living in a malaria endemic area of Burkina Faso

Adama Gansane • Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Ouagadougou, Burkina Faso

Introduction | In most African countries, the biological reference ranges used are from Europe and the United States. For the planning of clinical trials in Saponé Health District, a malaria endemic area in Burkina Faso, we conducted a study to establish the biological reference ranges for biochemistry and haematology analysis among healthy members of the local population.
Methods | Two cross sectional surveys conducted during malaria high and low transmission season respectively in adults and children from 14 randomly selected villages out of 89 villages of Saponé Health District. They were stratified in 7 groups: 6 months–1 year, 1–3 years, 3–6 years, 6–10 years and 10–15 years, 15–45 years male, 15–45 years female. After informed consent and clinical examination, blood samples were obtained from participants fulfilling inclusion criteria. Laboratory analysis was done with validated automated analysers. Using methods described in the NCCLS-approved guideline, reference intervals for each measured parameter were calculated non-parametrically by taking the 2.5 and 97.5 percentiles of the observed values.
Results | From a total of 2,520 patients, 2,049 were enrolled with at least 270 volunteers per group. Estimated creatinine, haemoglobin and haematocrit references range were lower in our local population than the western ones while ALT, AST, urea, leucocytes and lymphocytes were higher. Similar reference ranges were found with electrolytes, RBC and glucose.
Conclusion | Laboratory reference ranges of our local population are not in agreement with estimated values of the population in developed countries. These findings supported implementation of clinical trials in this area using site-specific reference ranges for enrolment and monitoring of patients/volunteers.

MP 47
Networking to improve laboratory performance in a multicentre clinical trial in African centres

Issa Nebie Ouedraogo • Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso

Introduction | The GMZ2 consortium is a European-African partnership to undertake a multicentre phase IIb trial to assess the efficacy of the malaria candidate vaccine GMZ2 in different epidemiological settings for malaria in Africa. To comply with standard requirements for clinical trials, a laboratory working group has been set up and quality standards were set to produce reliable and auditable data.
Methods | Key elements in the conduct of GCLP compliant clinical studies supported by clinical laboratories have been implemented: training of personnel, assay validation and more specific elements of conducting assays, and laboratory oversight (SOP, audits and proficiency testing).
Results | To comply with standard requirements for clinical trial, GCLP training was organized for the 4 institutions involved in the GMZ2 consortium. In total 15 lab staff involved in various levels of lab activities was trained. In addition a training program has been provided to laboratory microscopists upon agreement for standardisation of slide reading. A laboratory management plan for the trial has been developed and validated and SOPs have been developed and shared within the network. A proficiency testing program is currently being set up. Regular teleconferences are held to update the sister laboratories on laboratory issues related to the vaccine trial.
Conclusion | Although some institutions started with limited experience in clinical trials, the network has greatly improved readiness for the phase IIb trial in different epidemiological settings of Africa.

MP 48
The East African Consortium for Clinical Research – malaria node external quality assurance programme for microscopy techniques

Peninah Menza • KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya

Introduction | The malaria node, one of the disease nodes of the East African Consortium for Clinical Research, introduced an external quality assurance programme to monitor proficiency by malaria microscopists within its network region.
Methods | Laboratory technologists across sites in the consortium network region had a two weeks training on microscopy techniques. This was followed up by the EQA process whereby each participating site was sent a set of twenty malaria blood film slides to work on in the first instance. At the site, slides were read by as many microscopists as possible and returned within two months upon receipt. Concordance in parasite presence or absence, species and density estimation was evaluated against the trainer's results.
Results | Slightly over 50% of microscopists were able to identify *P. falciparum*. The majority of microscopists were able to identify *P. malariae* and *P. ovale*. The sensitivity of microscopists varied from site to site with leading institutions performing better than sister institutions. Specificity for all malaria species was high across all sites. Generally, newly trained microscopists performed better than the earlier trained ones.
Conclusion | Training is essential to improve reading malaria microscopy slides. This underpins the need for periodic training on malaria slide reading. There is a need to build capacity and improve resources in sister institutions.

MP 49
Ethical challenges in the conduct of the study-evaluation of four artemisinin-based combinations for the treatment of uncomplicated malaria in African children at the Ndola site

Mike Chaponda • Tropical Diseases Research Centre, Ndola, Zambia

Introduction | A study to evaluate the 4 artemisinin-based combinations was conducted in 7 different African countries. Ndola was the only site in Zambia. The conduct of a multi-centre, multi-country clinical trial can pose ethical challenges. Some of the challenges will be common to all sites, others specific to a particular site. These specific ethical challenges should be highlighted and reviewed so that remedial measures can be taken.
Methods | We observed ethical aspects such as the oversight by the ethics committee during the conduct of the clinical trial in the Evaluation of 4 artemisinin-based combinations at the Ndola site in Zambia.
Results | Due to inadequate resources, the ethics committee was unable to visit recruitment sites. It had to depend on progress reports from the investigators. Most of the parents or guardians of the children in the study were of low literacy levels. As a result the informed consent process took longer and the process of recruitment was slower. Furthermore, low literacy levels contributed to the increased rate of participant dropout as many parents withdrew their consent because of poor understanding of the study.
Conclusion | Ethical challenges did have an effect on the quality of the clinical trial. In this case ethical challenges led to a reduced rate of recruitment. A longer recruitment period contributes to a higher cost of the trial. In this community programmes aimed at improving literacy levels should have been promoted. Generally, ethics committees need adequate funding to carry out their duties independently.

MP 50
Perception, knowledge and practices regarding malaria of the Congolese population and its willingness to participate in clinical trials

Thomas Serge Kivouele • Fondation Congolaise pour la Recherche Médicale, Brazzaville, Republic of Congo

Introduction | In the Republic of Congo, malaria remains a major public health problem and interventions were introduced in the country without exploring the social dimensions. This first pilot study which is part of the CANTAM project explores the perception, knowledge, practices and willingness of the Congolese population to participate in clinical trials.
Methods | A questionnaire was elaborated and submitted to the informants. One hundred informants aged 18–63 years living in Brazzaville were randomly selected on the sampling frame of the 2007 census.
Results | 60% of informants identified the mosquito as the causative agent of malaria and 47% indicated that cleaning the environment is a successful way for fighting malaria. More than 80% of respondents considered that malaria must be treated at the hospital. 21% thought that self-medication was important for children before referring to the hospital. 62% had knowledge on clinical trials. However, willingness to participate in clinical trials represented 37% and 62% for vaccine and drugs respectively. There was a relationship between level of education and knowledge about clinical trial.
Conclusion | This study showed that the population of Brazzaville has good knowledge of malaria. It was also shown that they had acceptable knowledge on clinical trials and two thirds of the study population felt ready to participate in a clinical trial.

MP 51
Characterization of the Iganga (Uganda) trial site for phase IIb study of GMZ2 malaria vaccine candidate

William Buwembo • College of Health Sciences, Makerere University, Kampala, Uganda

Introduction | Site characterization is a pre-requisite in conducting vaccines trials. This study was conducted in 6 villages to determine malaria incidence among children resident in the Iganga district.
Methods | A cross-sectional survey was conducted among resident children aged 12–60 months. We screened 1,000 children and subsequently enrolled a cohort of 900 children, 540 of whom were below 5 years of age. The 6 cohort villages from where the children were recruited into the study, were divided into two arms: (i) active follow-up, with 450 children in 3 villages and (ii) passive follow-up, with 450 children from the other three villages. While children (n=450) in the active arm were visited at home twice weekly by community health workers, village kids in the passive arm were not visited regularly. However, guardians of all children were asked to bring their child to the clinic whenever the child felt unwell. A malaria episode was defined as any parasitaemia with history of fever or body temperature more than 37.5°C. Malaria cases were treated with ACTs according to national drug policy.
Results | At screening, 58% of the children below 5 years had malaria parasites in their blood. The prevalence of splenomegaly and gametocyte was low. The malaria incidence rate was 1 to 2 malaria episodes per child per year. Loss to follow-up in the active arm was 7.6%.
Conclusion | Iganga trial site was successfully characterized for phase I-III malaria vaccine trials.

MP 52
Hematologic and blood chemistry reference ranges for Ugandan children in the Iganga-Mayuge demographic surveillance site for vaccine trial preparation

Mark Kaddumukasa • College of Health Sciences, Makerere University, Kampala, Uganda

Introduction | Site preparation is a pre-requisite in conducting malaria vaccines trials. This study was to determine population reference ranges within the study area.
Methods | In a cross sectional study conducted across census-listed households from six villages of Iganga district, we determined the reference ranges for commonly used haematology and clinical chemistry parameters in children aged one to five years.
Results | Median values (95% range) for major measured parameters were: haemoglobin 8.9–15.2 g/dL, erythrocytes 3.3–7.0 × 10^6/µL, leucocytes 4.1–17.0 × 10^3/µL, platelets 285 × 10^3/µL, alanine aminotransferase (ALT) 17.0 IU/L, Creatinine 23 µmol/L, serum protein: 5.0–9.2 g/dL.
Conclusion | Determining local reference ranges is important to avoid wrong decisions for patient care, inclusion in or exclusion from clinical trials and for assessment of post-intervention events.

MP 53
Association of antibody levels to multiple malaria vaccine candidate antigens with protection against clinical malaria episodes in children 1–5 years old in Mali

Bourema Kouriba • Malaria Research and Training Centre, University of Bamako, Mali

Introduction | The natural history of malaria exhibits continued susceptibility to infection and episodes of illness that decline in frequency and severity over time. Therefore, studies which attempt to relate immune response to protection must be longitudinal and have clearly specified definitions of immune status. Putative vaccines are expected to protect against infection, mild or severe disease or to reduce transmission. So far it has not been easy to clearly establish what constitutes protective immunity or how this develops naturally, especially among the affected target groups. Our research question was which malaria antigens induce antibodies that correlate with protection from *P. falciparum* malaria.
Methods | A cohort study was conducted in the malaria hyperendemic area of Bandiagara. The cohort was composed of 211 children aged 1–6 years. A standardized Afro-Immuno-Assay ELISA method was used to measure IgG antibody and subclasses levels specific to 5 malaria antigens (GLURP R2, MSP-1 Fvo, MSP-3 LSP and AMA=1Fvo).
Results | 35.3% of the children did not experience malaria and 64.7% of the children had at least one episode of malaria.
Conclusion | Analysis is ongoing to correlate antibody level with protection against a clinical malaria episode.

MP 54
Holistic capacity building through the EDCTP funded GMZ2 consortium

Brenda Okech • African Malaria Network Trust, Dar es Salaam, Tanzania

Introduction | Clinical trials are being conducted in Africa and efforts are underway to conduct them according to GCP standards. The trials require laboratory capacity and need to ensure an acceptable level of harmonisation if multiple laboratories are involved to ensure best practices and achieve accuracy. End point determination for trials requires efficient laboratories. To accomplish this, the guiding principles of GCLP need to be emphasized and implemented.
Methods | This paper summarizes endeavours in the GMZ2 consortium to ensure comparable data from the laboratories of all centres within the consortium for a quality trial.
Results | In some African centres the trend has been to carry out the basic assays in-house and have the more complex ones carried out in a developed country laboratory. As part of capacity building in the GMZ2 all assays will be carried out in African laboratories. In order to ensure that the data collected at the different laboratories are of high quality and comparable, the methods used for establishing primary end points were harmonized. All partner laboratories worked to ensure harmonized procedures for the baseline studies. At first different methods were used, but in the end a common method was agreed upon. GCLP capacity was strengthened and needs to be further strengthened. This experience can be used in other trials. There is a need for collaboration of laboratories working on clinical trials.
Conclusion | GCLP is steadily improving in Africa but wider training and collaboration should be encouraged and facilitated among African laboratories involved in clinical trials to ensure that GCLP principles are common.

MP 55

Baseline epidemiological study in preparation for a phase IIb proof of concept efficacy study of the GMZ2 candidate malaria vaccine: results from Lambaréné, Gabon

Ulysse Ateba • Medical Research Unit Albert Schweitzer Hospital, Lambaréné, Gabon

Introduction | In sub-Saharan Africa malaria remains one of the most important causes of morbidity and mortality in children under 5 years old. Due to intensive actions to control the disease a decrease of its burden is being reported in several countries. As this decrease is remodelling the epidemiological features of malaria there is a need to assess its amplitude mainly in areas where research activities are ongoing. This study was implemented in preparation for a phase IIb efficacy study of GMZ2 candidate malaria vaccine to assess the current epidemiological characteristics of malaria in Lambaréné, Gabon, one of the vaccine trial sites.
Methods | This study was designed as a prospective longitudinal study. Children from 1–5 years old were targeted. They were followed up either actively or passively. Thick smears were realised in case of fever for both groups and every two weeks for children followed actively. Prevalence of plasmodial infection was determined at the inclusion as well as the incidence.
Results | The study lasted 11 months. In total 611 children were included, among them 312 were followed actively. The sex ratio (male/female) was 0.95 with a mean age of 35 months at the time of the inclusion. The incidence of malaria and of the plasmodial carriage will be presented for both types of follow-up, as well as the prevalence at baseline.
Conclusion | This study will provide us with a current epidemiological characteristic of malaria in Lambaréné, a malaria vaccine trial site.

CP 01
Operationalising a multi-centre trial in critically ill African children in resource limited settings

Mukami Mbogo • KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya

Introduction | Trial management is key for the success of a clinical trial but few coordination centres have been established in Africa. The roles and challenges faced by an African based trial coordination centre in the management of a multi-centre trial in resource limited settings were established in a pragmatic trial. It was conducted in six hospitals in East Africa with the aim of addressing fluid resuscitation strategies in critically ill children. Four out of the six sites had never conducted trials previously.
Methods | An office was established within a clinical trials facility in a research organisation in East Africa to oversee the operations of the trial. It housed the Trial Management Team whose activities were conducted in consultation with research collaborators through emails, teleconferences and face–to-face meetings. Sub-offices were established in individual countries to provide administrative support. The overall conduct of the trial was governed by various independent committees. An organisation chart and memorandum of understanding were developed to inform proper communication channels. Standardised data collection tools and a website were utilised. Continuous training was provided to staff. Central data management and in-house monitoring were adopted.
Results | High international standards with good protocol adherence were observed despite the fact that the complex trial was conducted in challenging environments.
Conclusion | Multi-centre trials can be conducted and coordinated from resource-limited settings. This was simplified by sharing resources uploaded in the Global health trials website (www.globalhealthtrials.org).

Reference: N Engl J Med. 2011; 364(26):2543–4.

CP 02
Capacity building for research synthesis and conduct of Cochrane systematic reviews in Africa

Chukwuemeka Nwachukwu • Nigerian Branch of South African Cochrane Centre, Calabar, Nigeria

Introduction | Well conducted systematic reviews can provide reliable, up-to-date evidence to support health care decision-making. Relatively few Cochrane Systematic Reviews have been conducted by authors living in Africa. Reasons for this are many including a lack of relevant skills, poor access to electronic information/journals, limited internet access, excessive clinical responsibilities and the absence of a culture of evidence-based decision making. The mission of the South African Cochrane Centre (SACC) is to prepare, maintain and promote the use of the Cochrane Reviews that are relevant to Africa's health care needs.
Methods | The SACC used The Reviews for Africa Programme (RAP) as a model to build research synthesis capacity by actively recruiting, training and mentoring Cochrane review authors. First time authors of Cochrane Systematic Reviews were recruited from across Africa (Nigeria, Kenya, Cameroon, Uganda, and Malawi) between 2005 and 2010 and exposed to a 3-phased intensive workshop with the objective of completing their reviews for publication.
Results | RAP trained 30 authors who published 100% of protocols and 57% of completed reviews regarding infectious diseases, HIV/AIDS and maternal/child health in The Cochrane Library. Participants have become mentors and/or co-authors of systematic reviews and are also active in capacity development in systematic reviewing and evidence-based health care in their own or other countries.
Conclusion | The RAP has successfully built capacity in research synthesis in Africa. This is important for policy makers to be able to embrace the use of best evidence, and to commission new systematic reviews and randomised controlled trials (RCTs) to answer high priority questions.

CP 03
Using OpenClinica in data management in malaria studies at the clinical trials facility in Kilifi

Michael Otieno • KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya

Introduction | OpenClinica is open source Electronic Data Capture (EDC) and Clinical Data Management (CDM) software developed by Akaza Research Corporation. The KEMRI/Wellcome Trust Clinical Trial Facility adopted OpenClinica as the standard GCP compliant EDC for all its clinical trials in 2007. Since then, five large multisite trials have successfully used OpenClinica. It started with a training by the Akaza group and the implementation of Openclinica version 2.5. We have since upgraded to version 3.0 and are currently studying version 3.1.
Methods | Operating OpenClinica involves setting up the study by defining study parameters in the system. Followed by designing eCRFs using Excel spreadsheet templates. Study events are then designed to collect data per eCRF. Once this is done, the study is marked as available and data entry can begin. Lastly, the entered data can be extracted in one of the various output formats available in the system.
Results | Openclinica has reduced time to design and set-up a study database, and improved GCP compliance and flexibility in data entry through remote data entry. The current OpenClinica version 3.0 has enhanced electronic trial monitoring and made data extraction into different formats possible. As Open Source software, operating cost is minimal and there is freedom to customize the source code to meet unique requirements.
Conclusion | OpenClinca has reduced cost of data and trial management and it has improved trial monitoring. Multisite trials are on the rise in developing countries. OpenClinica will greatly cut cost, improve GCP compliance and improve data quality in running these trials.

CP 04
Gaining recognition as an 'African centre of excellence in applied nanomedicine research and training for poverty related diseases'

Hulda Swai • Council for Scientific and Industrial Research (CSIR), Pretoria, South Africa

Introduction | Sub-Saharan Africa bears the brunt of Poverty Related Diseases (PRDs) such as tuberculosis and malaria. Nanomedicine is a rapidly advancing area of biomedical research with great potential to revolutionize treatments for PRDs, as it has for other diseases such as cancer. We at the DST/CSIR nanomedicine platform find ourselves in a unique position in Africa.
Methods | We have built a substantial knowledge base in human capital, equipment/facilities and infrastructure in nanomedicine. Given our advantage, we see an urgent responsibility to stimulate sustained distinction in nanomedicine research, while simultaneously generating highly qualified human resource capacity. Towards this goal, we suggest that the platform be recognised as an 'African Centre of Excellence (CoE) in Applied Nanomedicine Research and Training'.
Results | The proposed CoE will seek to deliver alternative therapies for PRDs through sharing of resources, know-how and technologies, which will avoid wasteful duplication of effort and allow the most efficient use of pre-existing structures. Also geared at building and transforming human capital in Africa, the CoE will offer researchers a stimulating and dynamic research environment by providing guidance and support through mentoring, providing expertise, standards, methods, tools and knowledge repositories, shared learning (through training such as sensitisation seminars, workshops, summer schools, lab/researcher exchange programs, sabbaticals); measurement (through conferences, publications, patents, technology transfer); governance (through allocating resources across all possible areas, investment in valuable projects, creation of economies of scale for service offering).

CP 05
EDCTP capacity building achievements at the International Centre For Reproductive Health (ICRH) clinical research laboratory in Mombasa, Kenya

Sammy Wambua • International Centre for Reproductive Health, Mombasa, Kenya

Introduction | Guaranteeing the capacity of laboratories to generate reliable and accurate data is vital for successful clinical research. Capacity strengthening is not only acquisition of modern equipment and reagents but also sustained commitment to training, quality, and biosafety. Through an EDCTP capacity building grant, ICRH-Kenya undertook projects to improve clinical trial capacity. Key laboratory capacity building activities are summarised.
Methods | A holistic approach was taken to strengthen infrastructure, equipment, training, and testing capacity. Local and/or sustainable solutions were preferred and were executed with GCLP-compliance and a long-term goal of accreditation in mind.
Results | A spacious building was refurbished to house the laboratory, and then equipped with an access control system, reliable electricity and water backups, a state-of-the-art communication infrastructure serving staff and a temperature e-monitoring system. Equipment acquired includes: ultra low temperature freezers fitted with temperature e-monitoring auto-dial system, autoclave, real-time and conventional thermal cyclers. Training designed to establish capacity so that the laboratory is subsequently able to do/renew its own trainings, was done on biosafety, quality management systems, and GCLP. High-quality tests for chlamydia, gonorrhoea, HSV-2, HIV-1 viral load, and HPV genotyping, among others, were set up.
Conclusion | Overall, the laboratory experienced manifest capacity growth resulting in augmented staff competence and confidence and an expanded test repertoire. Improved appreciation of safety and quality led to the formation of a safety committee, and the preparation of safety and quality manuals. With good foresight and management, capacity building grants can have lasting impact in resource-poor settings.

CP 06
Capacity development by creating a laboratory science training module for Africa

Jacqueline Cliff • London School of Hygiene & Tropical Medicine, London, UK

Introduction | The London School of Hygiene & Tropical Medicine is a research-led postgraduate medical school, with a long history of teaching multi-disciplinary courses to contribute to improvement in global health. This training has recently expanded through the provision of distance-based learning courses, on which 2,700 students from over 130 countries are currently registered. We are committed to principles of open and universal access to education and will use creative commons licensing where possible, allowing wide dissemination.
Methods | The infectious diseases course covers a broad range of modules, including fundamentals of biology, statistics, epidemiology, public health, bacterial, parasite and viral infections, immunology, HIV/AIDS, malaria and TB. The course would be enhanced by the addition of practical laboratory and research skills training.
Results | We are developing a new module that will teach practical laboratory skills in a 'new media'-enhanced teaching environment. Through integration of written materials with high quality videos, interactive exercises, games and tests, we aim to engage our students in a process of quasi-experiential learning that will equip them to work in laboratories in the future. Components will include sample collection, nucleic acid extraction, PCR, ELISA, immunohistochemistry, microscopy, flow cytometry and cell culture. We will contextualise the procedural components within infectious diseases research. Narration will guide students from stages of experimental design, through the appropriate use of practical methods, to eventual analysis and interpretation of data sets.
Conclusion | This module is under development and we welcome input from Africa based scientists or stakeholders, particularly regarding what content would be useful.

CP 07

CANTAM-AMANET-CAMBIN: a winning trio for promoting health research ethics in central Africa

Odile Ouwe-Missi-Oukem-Boyer • Centre International de Référence Chantal Biya (CIRCB), Yaoundé, Cameroon

Introduction | Despite increasing international interest in Health Research Ethics (HRE), Cameroon and the Republic of Congo are known to be lagging behind in HRE.
Methods | In 2010, the Central Africa Network for tuberculosis HIV/AIDS and Malaria (CANTAM) organised a HRE workshop in Yaoundé for members of Ethics Review Committees (ERCs) and National Medicine Regulatory Authorities of Central Africa, in partnership with the African Malaria Network Trust (AMANET) and the Cameroon Bioethics Initiative (CAMBIN).
Results | After this successful workshop, members of the Comité d'Éthique de la Recherche en Sciences de la Santé (CERSSA), the first and only ERC in the Congo, organised a conference to promote ethics review and CERSSA. This event took place in Brazzaville in April 2011 and speakers from CANTAM, AMANET and CAMBIN gave presentations for an audience of government representatives, scientists, physicians, students, and the general public.
Conclusion | This year, CANTAM will organise a similar workshop in Yaoundé, for investigators and ERC members, again in partnership with AMANET and CAMBIN. CAMBIN will host and facilitate the workshop organised by AMANET. Equally, it hosts the AMANET sub-hub Translation Unit, which supports the organisation of workshops in francophone Africa. The objective of the workshop is to establish a network of Ethics Committee members to address specific issues raised by investigators. The CANTAM-AMANET-CAMBIN trio is working as a team to promote HRE in this region, demonstrating effective south-south collaboration.

CP 08

Keur Soce health and demographic surveillance site system in Senegal: site description, baseline findings and policy implication

Mansour Ndiath • University Cheikh Anta Diop, Dakar, Senegal

Introduction | The study area is Keur Soce, located in rural areas in the region of Kaolack, in the district of Ndiédieng. The area lies between longitudes 16°00'14.8" and 16°07'13" W and latitudes 13°51'53" and 14°00'00" N. It is located at 230 km from Dakar in the Sudano-Sahelian region of Senegal and covers an area of 478 km². There are an estimated 29,645 inhabitants. The population is composed mostly of Wolof (90%) and lives mainly on agriculture and livestock. It is distributed in 73 villages with an average density of 62.7 inhabitants/km². The climate is characterized by the alternation of a long dry season from November to June and a short rainy season from July to October. The area has 2 health posts and 9 functional health huts.
Methods | This multi-round prospective community based study (Initial Census 2010) produced a baseline description of each resident including age, sex, marital status, relationship with HH, education. A full demographic profile was created from the first phase Demographic and Health Surveillance in Keur Soce subdistrict, Senegal.
Results | The total population is 29,645 inhabitants, 42% of which were under 15 years of age. The sex ratio is more pronounced for male than female regarding all age categories, except for the reproductive age group. Over 50% of the population are not married. Thus, the married monogamous represent 20% of the population and married polygamous represent 18% of the population.
Conclusion | Results to be compared with national and international data and analysed for their relevance to health development.

CP 09 (TO BE CONFIRMED)
Developing capacity for carrying out clinical trials in the private sector at the grass root level in Ghana

Stephen Apanga • Yizura Hospital Company Limited, Kintampo, Ghana

Introduction | Few research centres or institutions exist in sub-Saharan Africa for carrying out medical research in general and clinical trials in particular. In Ghana the few (4) research institutions currently conducting clinical trials are all public ones. A locally based private health facility at Kintampo in the middle belt of Ghana is possibly fast paving the way for the first ever private site for conducting clinical trials at grassroots level.
Methods | Put up a team of young principal investigators and co-investigators to establish an efficient system for carrying out clinical trials at grassroots level; expand the infrastructural base of the facility; establish an additional facility in a virgin area for medical research and clinical care.
Results | Principal investigators (three young medical doctors) and co-investigators (a pharmacist, a laboratory technologist and a laboratory assistant, nurses, a data manager and a project coordinator). An efficient computer network system for collecting data on participants and patients. Three clinical trial feasibility questionnaires have been completed pending approval.
Conclusion | The private health sector remains an untapped resource for carrying out clinical trials. Sponsors of clinical trials need to support private initiatives such as this, in developing capacity for future clinical trials.

CP 10
Assessing participants' understanding and voluntariness of informed consent in a clinical trial in Nigeria

Babatunde Adewale • Public Health Division, Nigerian Institute of Medical Research, Lagos, Nigeria

Introduction | The tension between the need for research and the possibility of exploitation of participants' vulnerability mandates the development of reliable measures of ensuring that consent is voluntary and sufficiently informed. This study assessed the research participants' understanding and voluntariness of informed consent in a clinical trial in Ijede, Lagos.
Methods | This is a cross-sectional survey of 75 research participants in a malaria clinical trial using questionnaires and a forced-choice checklist to assess voluntariness and understanding of informed consent. Data was analysed using SPSS V 17.
Results | All the respondents involved in the clinical trial gave consent before they were recruited. Reasons given for consenting to participate included: opportunity to get treated (28%); opportunity for diagnosis of ailments (32%); to prevent illness (36%); and to receive news about medical care (4%). Payment was seen as a potential motivational factor for participation by 8% of the participants. Almost all the participants (98.7%) stated that they understood the information given to them during the consent procedure. However, in the formal assessment of understanding with a forced-choice checklist, only 37% understood issues concerning randomisation of participants.
Conclusion | This clinical trial in Nigeria demonstrated no serious threats to understanding and voluntariness. However, voluntariness was influenced by factors based on the benefits participants would receive through their participation. There is therefore the need to ensure effective communication between the investigator and research participants during the informed consent process to facilitate the participants' right to self-decision to participate in a trial except when incapable of consenting.

CP 11

Strengthening of an African Institutional Review Committee through North-South collaborations: the TASO Uganda experience

Josephine Birungi • The AIDS Support Organisation (TASO), Kampala, Uganda

Introduction | It is still a challenge for Institutional Review Committees (IRC) in Africa to ensure that all research conducted within their institutions is ethical and according to required scientific standards. This is partly due to inadequate knowledge and skills of the IRC members. The AIDS Support Organization (TASO) in Uganda is a national NGO providing care to HIV-positive patients but also involved in HIV research. It has an IRC comprised of 11 members. TASO established a partnership with more experienced members from the north to build the competencies of the TASO IRC members.
Methods | Members from institutions in the North (University of Ireland, London School of Hygiene and Tropical Medicine, University of Ottawa and Royal Tropical Institute of The Netherlands) supported the TASO IRC to win a grant for facilitating capacity building activities. They also joined with the members of the National Ethics Committee and Uganda National Council of Science and Technology to facilitate sessions at the capacity building workshops organised for TASO IRC. There has been continuous mentorship through exchange of materials and relevant literature between the partners.
Results | Updated and appropriate Standard Operating Procedures; standardized and objective tools for review of research protocols; improved record keeping by the TASO IRC; recognition and appreciation of the work of the committee by both the institution and investigators.
Conclusion | Through North-South collaboration, Institutional Review Committees in Africa will be strengthened and this will ensure protection of the human subjects involved in research.

CP 12

Structural and functional status of research ethics committees in Cameroon

Chi Che • Cameroon Bioethics Initiative (CAMBIN), Yaoundé, Cameroon

Introduction | In Cameroon, information on the regulation and the structural and functional status of research ethics committees (RECs) is largely unavailable. This study therefore seeks to identify such information, along with the perceived needs, strengths and challenges of RECs in Cameroon.
Methods | Self-administered questionnaire to chairs and administrators of RECs identified in the country.
Results | We identified 14 RECs; 9 functional and 4 non-functional. Of the 9 functional RECs, 8 representatives participated in the survey; 2 national and 6 research-institute based. The total membership of the 8 RECs was 106, with a range of 9–28. Members were predominantly medical doctors and scientists; women constituted about 38% of the total membership. 50% of the RECs met mainly on demand and on average RECs reviewed five protocols per meeting, with decisions arrived at mainly by 'consensus'. Over 80% of the participating RECs reported endorsing and utilizing the ICH-GCP guidelines, CIOMS guidelines, Declaration of Helsinki and Belmont Report for their ethics review processes. Key areas requiring training were related to determining the appropriateness of participant selection in vulnerable populations. The most highly rated constraints were the lack of ongoing training for members in health research ethics and insufficiency of resources.
Conclusion | Our study identified nine functional RECs in Cameroon, with scientists and medical doctors representing a significant proportion of the membership. We have equally identified some training needs and perceived strengths and challenges affecting their smooth functioning.

CP 13
Active monitoring of approved research protocols in Cameroon

Marceline Djuidje Ngounoue • Cameroon National Ethics Committee, Yaoundé, Cameroon

Introduction | The CNEC is currently strengthening its capacity to review research protocols and to actively monitor the approved studies.
Methods | 12 approved studies (3 clinical trials, 7 cohort studies, 2 cross-sectional studies; 2 involving transfer of biological samples out of Cameroon) were actively monitored in 6 different research centres, between May and June 2011. The assessment document developed by CNEC was complemented with discussions with local PIs and their team, a review of relevant documents, and inspection of laboratories and the specimen disposal facility.
Results | : 90% of PIs and key research staff were well informed; documents reviewed were identical to those submitted to CNEC; some investigators were trained on GCP and also received online-courses; laboratories were well equipped and specimen disposal well organised. Observed lapses were: data collection tools included names of participants in some sites; some consent forms not signed; participants interviewed unaware that administered product was investigational in nature; no Material Transfer Agreement (MTA) for studies with specimen-transfer. PIs reported difficulties to recruit participants, and slowness of the procedures for obtaining ethical and administrative authorizations prior to the protocol implementation.
Conclusion | Although there is progress in the conduct of research involving humans in Cameroon, the informed-consent process and the provisions for confidentiality should be more thorough. Projects with biological transfer should have an MTA.

CP 14
Role of National Institutional Review Boards (IRBs) in protection of research participants: experiences from the Medical Research Council of Zimbabwe

Resign Gunda • Medical Research Council of Zimbabwe (MRCZ), Harare, Zimbabwe

Introduction | The Medical Research Council of Zimbabwe MRCZ houses the National Ethics Committee (NEC) whose main mandate is to perform scientific review and ethical approval of all medical research. The role of research ethics in biomedical research cannot be over-emphasized. The research community as a whole suffers when even a few investigators ignore the basic principles of ethics. The consent process should go beyond the written consent form. Researchers need to understand that there should be a follow-up and continuous education of the participants throughout the research.
Methods | Researchers, IRB members, medical students and research teams were trained in research ethics and good clinical practice (GCP). After the training activities, MRCZ carried out routine inspection of all ongoing studies to ensure that researchers are adhering to their protocols and complying with ICH-GCP and other international guidelines.
Results | In 2010, 700 researchers were trained in Research Ethics and GCP. Those trained were made aware of the current versions of international guidelines on the ethical conduct of research. These guidelines include ICH-GCP, CIOMS and Helsinki Declaration. The training workshops that have been carried out in the last 3 years have greatly increased awareness of research ethics amongst researchers.
Conclusion | There has been significant improvement in the informed consent process as researchers in Zimbabwe are increasingly becoming aware of the importance of protecting the rights and welfare of research participants. The experiences of MRCZ in creating research ethics awareness will be shared.

CP 15
Striving for a comprehensible informed consent

Ernest M. Moseki • Botswana-Harvard AIDS Institute Parnership, Gaborone, Botswana

Introduction | Informed Consent is one of the eight elements necessary in any research to make it ethical. Therefore, it is required for all research involving human subjects. The research participant must adequately understand what is asked of her or him. It is thus important that Informed Consent is explained and phrased in simple everyday language familiar to the research participant. The Informed Consent materials should be translated into the research participant's mother tongue.
Methods | The Informed Consent text, translated into Setswana, was given to Community Advisory Board members with elements of the Informed Consent material put into a questionnaire form, for group discussions. This was done with Informed Consent texts from a number of studies and over a period of five months as part of the training and skills development of this group. Members come from various backgrounds including teachers, nurses, counsellors, priests and non-professionals.
Results | The translation was not fully comprehensible as many of the questions were left unanswered and members asked for clarification on certain words used in the documents. We noted that most technical words were difficult to translate and that the translator used words that were not part of everyday spoken language.
Conclusion | Since the Informed Consent text was not fully comprehensible, we proposed to be part of the translation process where we will assist in reviewing for comprehensibility. We requested that we do this before the Consent document is sent for ethical review. This will make the Informed Consent process more meaningful for our communities.

Reference: JID 2004; 189(5):930–7.

CP 16
Establishing and strengthening health research ethics committees in Ethiopia

Yimtubezinash Woldeamanuel Mulate • Ethiopian Bioethics Initiative (ETBIN), Addis Ababa, Ethiopia

Introduction | The health research environment in Ethiopia, like in most African countries, is characterized by low capacity for ethical review and clearance of projects. The Ethiopian Bioethics Initiative (ETBIN), which is a country chapter of the Pan African Bioethics Initiative (PABIN), has a mission to build capacity in ethical review of health research in the country.
Methods | Before implementation of the project, an assessment of needs was done first. A pre-tested well developed curriculum of the SIDCER recognition program (SIDCER-RP) – consisting of a human participants' protection course and Standard operating procedure (SOP) writing workshops – was conducted for members of newly established and existing ethics committees. The theoretical and practical training was provided to ethics committees, rather than to interested individuals. Subsequently, on site monitoring was done and office equipment was supplied for the EC's activities. The project was conducted with funds provided by EDCTP.
Results | At the end of the project, 76 IEC/IRB members from 10 health research and training institutions were trained. It also resulted in the successful establishment of ethics committees in the new regional universities. A booklet entitled Principles of Health Research Ethics, written in one of the local languages was printed and distributed. Capacity building needs and ongoing efforts on health research ethics were communicated to the public on national media.
Conclusion | Through implementation of the training program of the SIDCER-RP, 76 EC members were trained, existing institutional review boards strengthened, and new ones established in regional universities in Ethiopia. The project has contributed to the overall improvement of best practices in ethical review.

CP 17
A multi-step approach to informed consent: the experience from 2LADY, a second line ART randomised clinical trial

Laura Ciaffi • ANRS Hopital Central Yaoundé, Cameroon

Introduction | The informed consent (IC) signature is an essential step in ethical clinical research. Understanding the stakes is difficult for participants not used to their involvement in decision making concerning health care. We wanted to evaluate the understanding of participants enrolled in the ANRS 12169 2LADY clinical trial on second line ART treatment.
Methods | Participants to the ANRS 12169 2LADY who were in the study for at least 12 weeks, were invited to focus group discussions (FGD) to evaluate the understanding of informed consent content. A semi-structured interview guided the discussion.
Results | Four FGDs were organised between January and May 2011. 41 out of 99 patients participated. The objectives of the trial were not clear for the majority of them. General feeling of participating in an 'experimental new drug testing' was common. The perception of the signature of the IC was more that of a contractual relationship than an affirmation of understanding and voluntary participation. The main reasons for participation were their need for treatment and the offer of free care. Participants had the occasion to ask questions and the facilitator provided a renewed explanation of the main points in IC. After this experience, better dialogue between research team and participants was achieved.
Conclusion | The standard way of getting informed consent at the beginning of the study is not sufficient for a 'real' understanding of the stakes and for an 'efficient' participation. The IC should be conceived as an ongoing process with different steps during the research.

CP 18
Strengthening research ethics review capacity: the Botswana case

Mary Kasule • Council on Research for Development, Geneva, Switzerland

Introduction | The Botswana Ethics Committee was established in 1984. During the initial 10 years of its operation it focused on the review of minimal risk studies that did not require strong legal and ethical frameworks to protect research participants. The past two decades have seen an increase in volume and complexity of research conducted due to the HIV epidemic and the re-emergence of tuberculosis. This prompted the strengthening of the national research regulatory oversight system. This paper recounts the strategies the country has put in place to cope with this challenge.
Methods | The learning, behaviour and results of the members of the ethics committee and community advisory boards were measured post-training. Analysis of reports from workshops and meetings, financial reports, and guiding documents were also reviewed for the period of June 2008 to February 2011.
Results | Over 100 persons were trained. Feedback from the measurement indicated that most trainees felt the training was beneficial. It increased knowledge and skills which they applied at their work places.
Conclusion | Indications are that the efforts made so far had a significant impact on the ethics review capacity in Botswana.

CP 19
Egyptian Network of Research Ethics Committees (ENREC)

Azza Radwan • Egyptian Network of Research Ethics Committees (ENREC), Cairo, Egypt

Introduction | In response to the increase in health research and a recent accreditation requirement for universities, Egypt has established many research ethics committees (RECs) to enhance the protection of research subjects. Accordingly, there is a need to enhance coordination, efficiency and consistency between Egyptian RECs. The sharing of information, review strategies, policies, and intellectual resources should be augmented through networking.
Methods | In several steps a network has been established: a) a survey to obtain background information on the needs and existing resources of currently functioning RECs (data analysis was done); b) a conference for these RECs was held in Egypt in October 2008 (we obtained a seminar grant from the Wellcome Trust); c) the implementation of internet tools (www.enrec.com). To test and assess these internet tools, we used the Webex Online Conference Centre in February 2008 to broadcast a live session of an educational workshop for the REC members at Theodor Bilharz Research Institute to individuals in countries in the Eastern Mediterranean Region (Egypt, Jordan) and in Pakistan. The site contains resources of common interest (e.g., articles, Investigator Application form, REC checklist for review, elements of informed consent also in Arabic, Financial conflict of interest disclosure statement, Statement of confidentiality, and SOPs); d) six face to face meetings (October 2008, May 2009, December 2009, May 2010, January 2011 and 5 May 2011). After the Egyptian Revolution on 25 January 2011, a Facebook page was created for ENREC.

CP 20
A new paradigm in health research ethics in Liberia

Jemee K. Tegli • University of Liberia-Pacific Institute for Research and Evaluation Africa Center, Monrovia, Liberia

Introduction | As human research evolved, refinements to protocols and procedures for handling research subjects were highly prioritized. The advent of the post-conflict era in Liberia created a void in human subject research regulation; due diligence was non-existent. This led to the establishment of the first institutional review board as a collaborative effort between the University of Liberia and the Pacific Institute for Research and Evaluation Africa Centre in 2005.
Methods | Twenty-nine interviewees comprising supervisors, directors, deans, and students from the Graduate and Professional programs at the University of Liberia and Cuttington University were appraised through the administration of an ethical research survey. The objective was to gauge the level of knowledge and understanding of an Institutional Review Board.
Results | 6 (31%) had conducted social and education research; 4 (13.7%) had conducted scientific research; while 1 (6.8%) had conducted behaviour research. 19 (65.5%) had heard about human subject research while 10 (32%) had not. 19 (65.5%) have heard of an Institutional Review Board. 28 (96.6%) said they would like to see an IRB established at the University of Liberia. 24 (82.8%) said they would be prepared to submit their research proposal to an IRB.
Conclusion | The need to establish and capacitate the operation of ethical review committees in post-conflict settings is appropriate. It serves as regulator between investigators, human subjects and communities.

CP 21
Strengthening ethical and regulatory review capacity in Africa: unfinished business

Aceme Nyika • African Malaria Network Trust (AMANET), Dar es Salaam, Tanzania

Introduction | The increasing volume and complexity of health research conducted in Africa demands strengthening of both ethical and regulatory review processes. Published baseline studies identified some pressing needs of African Ethics Review Committees (ERCs). Consequently, various players were involved in capacity building of African ERCs. It is critical to assess progress made so far in order to avoid duplication of efforts and to focus on the critical needs. However, only limited effort has gone into empirically assessing and addressing the needs of National Regulatory Authorities (NRAs) in Africa, leading to unnecessarily long delays of clinical trials in some cases.
Methods | There is still need to train members of ERCs on such research fields as randomised clinical trials, public health research, and emerging technologies. In order to cope with the huge workload being experienced in most African countries, the ethical review process should be decentralised. In this manner the actual review is done by institutional ERCs while national ERCs restrict their roles to training, accrediting, registering and supervising the institutional ERCs. This could improve efficiency.
Results | It is therefore imperative to develop accreditation frameworks and to adequately train the institutional ERCs ahead of such decentralisation. With the volume of work increasing, data management systems of both ERCs and NRAs need to be upgraded from the current paper-based methods to more efficient electronic systems. This paper gives an overview of the progress made so far and the unfinished business in terms of building capacity for ethical and regulatory review processes in Africa.

CP 22
Navigating the terrain of human subjects protection in Malawi

Domoka Lucinda Manda-Taylor • College of Medicine, University of Malawi, Blantyre, Malawi

Introduction | The Human Subjects Protection course aims to reinforce the knowledge of the ethical obligations investigators have to protect the rights, safety and wellbeing of people taking part in research. The course complements GCP. Some of the topics covered include the history of research ethics, principles of research ethics, responsibilities in health research, community engagement, and benchmarks and models for community engagement.
Methods | The method of analysis employed here consisted of a quick survey of responses participants gave in the course evaluation forms, and of an interpretation of the results obtained in the exam that they sat at the end of the 3-day training course.
Results | The relevance of the course was revealed in the responses given in course evaluation forms. Participants stated that the presentations and topics were 'informative', 'interactive', 'useful for their professional development' and 'relevant to their goals'. The exam results corroborate the above assertions, because out of 26 participants, 9 obtained distinctions (26 out of 30 MCQ), 16 passed with credit (18–25 out of 30), and only 1 person did not pass the exam (17 out of 30). Although different arguments can be presented to explain the excellent pass rate, we would like to argue that this was a result of the relevance of the course content to their everyday experiences.
Conclusion | Such positive results show that we are enhancing human subjects protection in Malawi by providing relevant and essential training to people involved in clinical trial research.

CP 23
Successful management of an EDCTP collaborative grant by the Uganda Virus Research Institute-IAVI HIV Vaccine Programme

Robert Kajoro • UVRI-IAVI HIV Vaccine Program, Entebbe, Uganda

Introduction | The Uganda Virus Research Institute (UVRI) is a leading research institution in East Africa. Since 2001 it has collaborated with the International Aids Vaccine Initiative (IAVI) to develop the UVRI-IAVI HIV Vaccine Program. This programme has led the UVRI to manage a 4 year EDCTP -funded grant for building capacity to carry out future HIV prevention trials in fishing communities in Uganda and Malawi.
Methods | After signing the collaboration agreements in 2008, a kick-off meeting was held to form a core management team; review the four-year strategic, communication and yearly work plans; discuss the donor rules and regulations and the budget for each collaborator. Monitoring was carried out through annual face-to-face meetings and quarterly teleconferences.
Results | With all project activities being conducted in Africa, having the project led by the UVRI provided greater opportunities for sharing information on study progress, preliminary results and challenges. The strategic plans described how the partners were going to meet their objectives. The yearly work plans allowed close monitoring. Change requests were timely communicated and only implemented once approved. Capacity building included improvement in management and financial systems of partners, and training in project management. As a result, partners adhered to set guidelines, reports were submitted on time, and UVRI won other grants.
Conclusion | This project demonstrates that grants with multiple partners in the North and South can be efficiently implemented when using good project management practices such as adhering to agreed plans, observing reporting deadlines and respecting contractual terms, rules and regulations.

CP 24
Impact of strengthening research grants management capacity

Edith Tibahwa Bagambe • Infectious Diseases Institute (IDI), Makerere University, Kampala, Uganda

Introduction | The growth and sustainability of the Infectious Diseases Institute as an African centre of excellence for research depend on vigorous and systematic grant acquisition and a strong management function.
Methods | The Infectious Diseases Institute has developed over five years a grants acquisition and management function which supports the full range of the grants cycle from the identification of strategically suitable funding opportunities, right through to project closure. Key responsibilities include intensive support for proposal generation, contract negotiation, programmatic and financial compliance with funder requirements throughout implementation, and monitoring and evaluation and reporting. An automated System for Integrated Grants Management (SIGMA) has been created.
Results | IDI's quarterly reports of Key performance indicators show that post-award research grants at IDI grew from 18 to 41 over the five years to March 2011. Funding came from a wide range of sources and activities covered a broad spectrum related to HIV/AIDS and associated diseases. Ongoing signed research contract value during this period increased from $2,206,809 to $15,471,347.
Conclusion | The development of a dedicated, well trained and well-organised grants management team backed by efficient systems is essential for African research institutions. The Infectious Diseases Institute is already supporting other African institutions to enhance their grants management capacity and looks to extend this role. It seeks to be the hub of a supportive African grants management network.

Reference: IDI Grants Management Manual, 2007

CP 25
Experiences from an internal quality assurance programme

Godfrey Nyakaya • KEMRI/Wellcome Trust Research Programme, Kilifi, Kenya

Introduction | With the increase in clinical research evaluating future drugs and vaccines, quality assurance programmes remain a priority. At the KEMRI/Wellcome clinical trials facility an internal quality assurance programme has been set up to monitor conduct and adherence to the applicable regulations in trials.
Methods | To establish a working quality assurance programme, trial procedures were standardised. Internal monitoring and auditing schemes for clinical trials and the supporting trials laboratory were established. Consequently, the reports over a one year period were reviewed for consistency of findings and trends were evaluated. External audit reports over this period were reviewed and performance was evaluated.
Results | The number of major anomalies in the conduct of trials decreased over this period. Up to 60% of the recommendations from internal audits and monitoring were implemented directly or indirectly by the study team. The number of findings in external audits in the laboratory was also reduced. The laboratory maintained accreditation status without any conditions from the accrediting body. An external audit of the trials facility established that trials complied with the applicable standards. Adherence to Standard Operating Procedures and training of trial staff was also observed to have increased.
Conclusion | The contribution of the internal quality assurance programme was threefold. It facilitated adherence to regulations in trials; it enhanced the facility's image by upholding the accreditation of the trials laboratory; and improved the capacity of the trials facility to pass external audits and inspections. These observations will stimulate trialists to institute working internal quality assurance programmes in clinical research.

CP 26
Reciprocal monitoring: a pragmatic regional approach to quality assurance in health research

Daveline Nyakundi • Kenya Medical Research Institute (KEMRI)-CDC, Kisumu, Kenya

Introduction | In April 2010, the East African Consortium for Clinical Research (EACCR) initiated a reciprocal monitoring scheme as an affordable alternative to the use of contract research organisations (CROs) in monitoring the quality of health research conducted by its regional partners.
Methods | This scheme has built on best practices and experiences from a clinical trial facility at Kilifi to conduct cross-site monitoring of research in Eastern Africa, using nominated trained monitors. It promotes adherence to Good Clinical Practices, establishes protocols and other relevant regulations for conducting clinical trials and other health research. In targeted clinical trials, reciprocal monitoring shall be conducted concurrently with monitoring by CROs or sponsors to compare effectiveness and efficiency. It is jointly coordinated by 2 leading regional institutions. It conducts training, mentoring and networking.
Results | The monitoring scheme is now operating with 2 coordinators and 22 regional monitors. 10 teleconferences have been held; 28 participants trained in a 5-day workshop in February 2011; 13 clinical trials have been volunteered for monitoring and 1 oral scientific presentation was made. A new collaboration has been established with the Worldwide Antimalarial Resistance Network.
Conclusion | This alternative approach to monitoring the quality of health research in Eastern Africa creates a potential platform for training and mentoring new monitors; and for cross-site sharing of best practices and networking.

CP 27
Using internal monitoring to build capacity and support networks of excellence

Mary-Ann Richardson • African Clinical Research Organisation (Pty) Ltd, South Africa

Introduction | Once grant funded projects have ended, one of the many challenges facing clinical trial sites is maintaining sustainability. PanACEA selected the African Clinical Research Organisation (Pty) Ltd (ACRO) as their training partner to address this challenge within their network. The partnership aims to build capacity within the network for the internal monitoring of clinical trials, and establishing a reputation as having sites that provide credible, accurate and verifiable data whilst ensuring that the rights, safety, wellbeing and dignity of participants is maintained.
Methods | Each site in the PanACEA network is to select an employee to conduct internal monitoring of research projects. The employee attends part 1 of the ACRO Clinical Research Associate training in Johannesburg, South Africa. The course is accredited by the Institute of Clinical Research in the UK and combines international and local content. On completion, the monitors return to their sites and commence monitoring projects within a supported framework. At least one accompanied visit per site will be conducted over the next 6 months. Part 2 of the course will take place in October 2011 and will consist of 1 week of consolidation training.
Results | The delegates have completed Part 1 of the training and are currently selecting projects for monitoring.
Conclusion | It is planned that over time, internal monitors will be able to cross-monitor at PanACEA sites, and with experience be available to third party sponsors to monitor other grant and industry funded research projects. Sites in the network will achieve a reputation for working to international guidelines and delivering work of the highest standards This should lead to their inclusion in ongoing clinical research projects.

CP 28
System and tools for evaluation and survey of health research in Senegal

Samba Cor Sarr • National Ethical Committee of Health Research, Dakar, Senegal

Introduction | Since the creation of the Senegalese National Ethical Committee the challenges were in particular: funding of a functional institution (independent office and equipment); staff for day-to-day administration; adequate training for all members; finalisation and approbation of a specific bill on Research Ethics to have a legal framework; creation of a database for electronic archiving; creation of a website dedicated to the National Ethical Committee, and having specific tools and procedures for the committee. These different challenges were managed in order to achieve the objective. With the support of EDCTP, WHO and the Ministry of Health, we realise specific activities by using adapted strategies. In order to have an adapted standard operating procedure, we used the support of EDCTP to organise several activities: working groups and plenary sessions on drafting SOPS.
Methods | Bibliography review and elaboration of several drafts of procedures and tools; organizing a working group on procedures; organizing a working group on tools. After this phase, we will make a summary report and share it through the internet among the members of the Experts of bioethics and law. When we receive the contribution of the experts, we integrate all in the final draft to submit to the members of the National Ethical committee in order to validate it.
Results | Several checklists for registration of the different protocols; specific outline for analysing protocols; guidelines for elaborate protocols; operational procedures; outline of adverse event report; outline to follow the protocols on research fields.

CP 29
Clinical trials monitoring in Nigeria: the experience of Zeta-12, a clinical research organisation

Uzoma Chidimma Anosa • Zeta-12 CRO, Ibadan, Nigeria

Introduction | ZETA-12, a new contract research organisation (CRO) provides capacity building and consultancy services in bioethics, clinical trials, GxPs and QA of regulated research. Within the last two years, ZETA-12 has interacted with major industry stakeholders and engaged in GCP training, monitoring of sponsor-initiated phase III/IV clinical trials, survey of research ethics committees and community-based research projects.
Methods | Our experience and encounter with the clinical trial stakeholders are thought-provoking. For most sites, pre-qualification and site selection were done by sponsor companies before engaging ZETA-12. For these studies, not all staff, though qualified by education, did have the required experience and GCP training. Most did not have formal ethics training. These lapses manifested in issues like the invalid obtainment of informed consent, deviation from study protocol and wrong documentation. Instances of non-compliance with monitoring best practices on the part of the site teams also occurred. Regulatory inconsistencies, for instance in the requirement for insurance of clinical trial subjects, were noted.
Results | In a bid to address these challenges, ZETA-12 is promoting sustained capacity building efforts in which investigators use both onsite training and the online bioethics tools made available by West African Bioethics Initiative. This is in accordance with the requirements of NAFDAC and NHREC. ZETA-12 has also encouraged bioethicists to form the first central research ethics committee (ZIREC) in Nigeria.

CP 30
Current paradigms in regulatory quality assurance: a panacea for the challenges in the Nigerian regulated research industry.

John-Moses Maduabuchi • Society for Quality Assurance, Ibadan, Nigeria

Introduction | Much attention has been paid to capacity building for regulatory research in Africa. Nigeria typically has witnessed ample concerted international collaborative efforts to promote ethical conduct of human subject research and clinical trials. However, several instances raised concern about the extent to which the goodwill and resources from global funders translated into desirable goals for Nigeria.
Methods | Our experience as clinical trial industry stakeholders, bioethicists and quality assurance professionals reveals that the industry has yet to demonstrate the expected improvement considering the enormous amount of the committed resources. The status quo in Nigeria includes a disconcerted and sub-standard ethical review system and a relatively low institutional capacity for clinical trials, even in the area of endemic diseases like malaria, tuberculosis and HIV/AIDS. The level of collaboration between regulatory authorities in the promotion of regulatory research is low or absent in some respect.
Results | The emergence of the quality assurance industry in Nigeria has provided a great opportunity to galvanize the urgently needed human and institutional capacity for the promotion of regulatory research. Current paradigms in the Quality Assurance profession – one of which is the integration of a Quality Management System with Good Business Practice regulations – have shown to be very relevant to promoting the Nigerian ethical regulatory frameworks for clinical trials. The quality assurance industry also provides a platform for our regulatory authorities to collaborate in their oversight and quality assurance roles.
Conclusion | Regulatory authorities should be aware of these opportunities and of their potential to help developing countries in Africa.

CP 31

The regulatory pathway for a vaccine intended for developing countries: a case study of RTS,S As01

Deborah Mogaka • KEMRI- Wellcome Trust Research Programme, Kilifi, Kenya

Introduction | As more research and development takes place in Africa and in the light of the recent EU Article 58, there is need to document the state of the regulatory environment. Using the trial of the candidate malaria vaccine RTS,S as a case study, this project will review available literature on regulatory pathways. Data is being collected prospectively from African regulatory authorities involved in the process in order to document challenges and identify possible solutions. This work will also categorize post-licensure issues that must be considered when health interventions are developed exclusively aimed at diseases of poverty.
Methods | Literature review mainly by desk research as well as direct contact with key parties such as GSK Biologicals, AVAREF, and representative African regulatory authorities. Standard qualitative methods will be employed to collect data through interviews, and semi-structured questionnaires.
Results | This ongoing work will result in a clear documentation of the existing state of play for research and development. It will be publicly available; Specific regulatory bottlenecks will be highlighted and possible solutions proposed. Post licensure recommendations will also be proposed.
Conclusion | Capacity building efforts in Africa have not sufficiently addressed the regulatory environment in which research and development takes place. There is a need to highlight these issues and we will present results during the Forum.

CP 32

Promoting rational drug use among rural women in Egbeda local government of Oyo State, Nigeria

Hamidu Oluyedun • Oyo State Hospital Management Board Secretariat, Ibadan, Nigeria

Introduction | The WHO Action Programme on Essential Drugs has succeeded in promoting pharmaceutical policies in developing countries. However, much is still left undone regarding rural women who are deprived of access to standard health care and are left in the hands of charlatans and quacks for medical attention and medicinal needs. The study aimed at investigating the source of drugs been sold to the rural populace; the pattern of polypharmacy; and the effect of regulatory, educational and managerial interventions to use better drugs.
Methods | The study was conducted in four rural communities in Egbeda Local Government. A convenient sampling technique was used to select 200 women from the communities for a survey to assess their knowledge of rational drugs use. Ten in-depth interviews were held with key-informants among patent medicine sellers in the communities. We organized training for the medicine sellers to improve their knowledge of drugs and their skill to identify some simple diseases and when to refer.
Results | The results of the survey showed that polypharmacy (same-class, augmentation, multiclass, adjunctive and total) was practiced in the various communities. The women in the communities were not adequately informed and involved in medicinal decisions. After six consecutive training courses and monitoring by regulatory agencies, there was a relative improvement regarding indiscriminate selling and buying of drugs in the four communities.
Conclusion | Government and NGOs need to pay more attention to the rural community, where the vast majority of women abide, and to give them access to health care. Health care providers should be willing to accept rural posting.

Notes

www.edctpforum.org

For more information and daily reports, please check the Forum blog at **www.edctpforum.org/sixthforumblog**

European Union
Supported by the EU