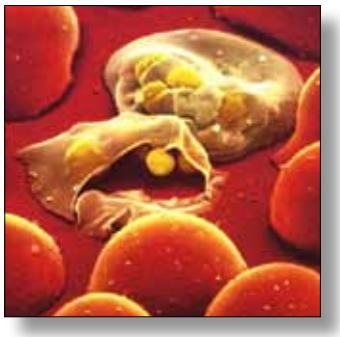
6th Pan-African Malaria Conference





ABSTRACT BOOK

MOVING TOWARDS MALARIA ELIMINATION: INVESTING IN RESEARCH AND CONTROL

The International Convention Centre
Durban, South Africa

6 -11 October 2013

Multilateral Initiative on Malaria

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Table of CONTENT

MESSAGE FROM MINISTER OF HEALTH

It gives me great pleasure to welcome each one of you to the 6th MIM Pan-African Malaria Conference. Both Durban and the ICC have previously played host to an extremely successful MIM conference. In the 14 years that have passed since that conference, the face of malaria and malaria research have altered considerably on the African continent. Today malaria elimination rather than malaria control is spoken of as a real possibility in regions of the developing world once ravaged by malaria.

South Africa is fortunate to be one of the countries where the burden of malaria has declined so significantly that elimination is now achievable. Regional collaboration in malaria control has been central to these successes, and underscores the importance of the coming together of the malaria community in our efforts to control and eventually eliminate the disease.

MIM Meetings are the largest global gathering of malaria experts and present the ideal opportunity for pioneers and leaders in the field to meet, engage, exchange ideas and inspire each other as well as the future generation of malaria specialists. The conference also provides a platform for networking and the establishment of collaborations aimed at increasing the body of malaria knowledge and building capacity.

During this conference you will have the privilege of hearing malaria experts from a variety of fields including vaccine development, drug development, parasite genomics, vector biology and malaria control deliver plenary lectures, scientific and symposium talks. I encourage you to use these occasions and the poster sessions to obtain as much information as possible to ensure a truly enriching conference experience. It is my hope that when you return to your countries and work-stations you use the knowledge gained at this conference to further malaria control and elimination efforts.

In closing I would like to thank each of you for attending this conference and bringing your expertise and in-depth knowledge to the meeting. I encourage you to stay engaged and proactive throughout this conference to help ensure malaria elimination becomes a reality in our life time.

Yours Sincerely,

Dr Pakishe Aaron Motsoaledi

Honourable Minister for Health South Africa

MESSAGE FROM MIM SECRETARIAT CHAIR

Moving towards malaria elimination is a concept that demands careful execution. To achieve this undoubtedly would require investing in research and control and these two must walk hand in glove. The MIM conference is the largest gathering of the malaria community that provides one of the best opportunities to show case novel and ground breaking research, and foster interaction between research scientists and the control community. The second MIM Pan African Conference was held in Duban in 1999. We return to Durban thirteen years later to examine how the global face of malaria has changed considerably, with malaria elimination now a viable option in many African countries.

The 6th MIM conference, returns to Durban to review successes, new problems and novel approaches. There has been some reduction in malaria burden. We have the artemisinins and now the possibility of the emergence of resistance, while the efficacy of IPTp with SP is being questioned. There is also the delineation of new dispersal routes of resistance of P. falciparum and anopheline vectors. We await the vaccine, and hope to hear more about its progress at this conference. Increasingly, we have detailed demographic surveillance that reports on habits and demographic changes. Close to 1500 young and eager minds will make it to the conference despite the economic downturn that affected sponsorship. Participants will be opportune to sample innovations from the Gates Foundation on the next new frontier in malaria programming, and on the Science of Eradication from the MalERA group, and the TDR with her new implementation research tool. A mix of control program managers will discuss new options from emerging data from academia and industry. Educational, networking and social events throughout the six days will bring participants to exchange ideas and addresses, make new contacts and forge new directions.

This forum provides and fosters learning with unique opportunities for meeting with professionals in both the research and control communities The junior scientists/researchers will have the opportunity to meet with world class experts in the varied fields of malaria research and control. We hope that this will be another setting for new initiatives. While we debate, learn and teach others, we must not forget that there are dying women and children as we hold our conference. With the changing patterns of disease epidemiology, new vulnerable middle class groups are emerging; those with co-morbid infections suffer unduly. And the emergence of non-communicable diseases is another factor that will confound the clinical management of the disease. We need to stay practical and not loose hope, we need to focus on the actionable reasons why research on malaria and other infections need to be pursued. Probably, no knew drugs will come to the market soon enough and therefore we need to rely on what we have and what we know to innovate and improve on intervention uptake. Social Sciences alone will directly contribute seven out of ten of the actionable reasons by suggesting ways to break the vicious cycle between poverty and infectious diseases; forging an escape route for the poor and vulnerable; providing solution for tackling multiple problems at the same time; finding ways to mitigate life-long chronic illnesses and stigma; reaching out to the hardest to reach population through health systems improvements; preventing loss in translation; acting on what we know now.
So let the band for the fight against malaria play on, with a better and improved tune, for a malaria free world.
Enjoy the meeting

Professor Rose Gana Fomban Leke

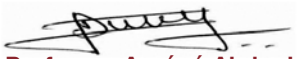
Chair, MIM Secretariat

MESSAGE FROM SCIENTIFIC COMMITTEE CO-CHAIRS

It is a pleasure to welcome you to South Africa for the 6th Multilateral Initiative for Malaria Conference. Our theme "*Moving towards malaria elimination: Investing in research and control*" reflects the substantial advances that have been made in the past decade, reducing the burden of malaria globally and making elimination in tens of countries a realistic goal, albeit highly ambitious, expensive and slow. Achieving malaria elimination will clearly require major changes to current thinking – broadening our focus to include targetting of asymptomatic carriers of sub-microscopic parasite densities, and malaria surveillance must be greatly strengthened. However, this shift will result in failure if it happens at the cost of sustaining malaria control. There will always be a limit to the resources available for reducing the burden of malaria, so we need to learn how to work together more efficently and effectively. This is already happening, as reflected in there being more consortia and networks participating in this MIM conference than ever before. We will see how to make better use of limited resources, by sharing available data and tools, and using epidemiological and mathematical models to help focus further research and public health strategies. By facilitating prompt sharing and critical debate of new evidence with the malaria control programmes and ministries of health, solutions can start being implemented, and scientists can be made aware of the research gaps identified by those who deal with burden of malaria on a daily basis. International health agencies, and foundations will share their strategies and visions, and hear feedback from the malaria community, fostering partnerships. We will learn from reflecting on past successes (and failures), ensure the optimal use of available tools in the present, and look to the future for the new drugs, vaccines, diagnostics, integrated vector control strategies, and health systems strengthening that are all essential for tackling the many challenges posed by ongoing malaria transmission. In this way, the 6th MIM conference provides a powerful platform to achieve the synergy needed for moving forward, bringing together many of the players on whose shoulders malaria control, elimination and eventual eradication depends.

Yours sincerely

Professor Karen Barnes
University of Cape Town, South Africa



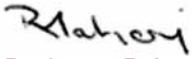
Professor Agrégé Abdoulaye Djimdé
University of Science, Techniques and Technology of Bamako

MESSAGE FROM THE LOCAL ORGANISING COMMITTEE

The Medical Research Council of South Africa (MRC) has the pleasure of hosting the 6th Pan African Multilateral Initiative on Malaria (MIM) together with the MIM secretariat. This is the second time that the MRC has the honour of hosting this prestigious malaria conference. The MRC has hosted the 2nd MIM conference in Durban in 1999 and this time round we strive to make this a more memorable conference than previously. The last time that the conference was held in Durban, the southern African sub-region was on the threshold of the worst malaria epidemic in the recent past. Thirteen year later, we see a different scenario where most of the countries in southern Africa are on the brink of eliminating malaria. At this opportune time in the history of the African continent, we are hosting the conference in the southern-most country to highlight this paradigm shift and have appropriately themed the conference "Moving towards malaria elimination: Investing in research and control".

In-keeping with the overarching theme, 18 sub-themes were selected which would help focus attention of the conference theme. It is hoped that these plenary sessions, parallel sessions and symposia will generate sufficient discussion to map the way forward. In the pre-elimination and elimination phases of malaria intervention implementation, research would play a vital role in getting to zero cases and staying there. The parasite, vector, host and the environment all influence malaria transmission and research cannot be divorced from malaria control.

It was the intention of the local organising committee to create a platform for African scientists to showcase the important research that is conducted on the African continent. Thereby we hope to encourage African scientists to share their research with their peers and to also afford all young scientists the opportunity to interact with seasoned malaria experts.



Professor Rajendra Maharaj

Malaria Research Unit, South African Medical Research Council

INTERNATIONAL SCIENTIFIC COMMITTEE MEMBERS

Dr John Waitumbi
Dr Patrick Duffy
Prof Kevin Marsh
Dr Margaret Gyapong
Prof Obinna Onwujekwe
Prof Dominic Kwiatkowski
Prof David Roos
Dr Immo Kleinschmidt
Dr Abdoulaye Djimdé
Dr Theonest Mutabingwa
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Prof Wilfred Mbacham
Prof Peter de Vries
Dr Palmer Netongo
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Mr Jasson Urbach
Mr Khumbulani Hlongwana
Ms Lindsey Verfaillie
Ms Mandy Salomo
Ms Natashia Morris
Mr Ndabezitha Shezi
Ms Sarah Bok

PLENARY SPEAKERS

Invited Speakers

Professor Kelly Chibale

University of Cape Town, South Africa

Kelly Chibale has been a full Professor of Organic Chemistry at the University of Cape Town (UCT) since 2007. He joined UCT in 1996 as a Lecturer. He is a Full Member of the UCT Institute of Infectious Disease & Molecular Medicine. In 2008 he was awarded a Tier 1 South Africa Research Chair in Drug Discovery under the South Africa Research Chairs Initiative (SARChI) of the Department of Science and Technology (DST) and administered through the National Research Foundation (NRF). In 2009 he became the founding Director of the Medical Research Council (MRC) Drug Discovery and Development Research Unit at UCT. In the same year (2009) he was elected a Life Fellow of UCT and a Fellow of the Royal Society of South Africa. In 2010 he became the founding Director of the UCT Drug Discovery and Development Centre (H3-D).

Kelly obtained his PhD in Synthetic Organic Chemistry from the University of Cambridge in the United Kingdom with Stuart Warren (1989-1992). This was followed by postdoctoral stints at the University of Liverpool in the United Kingdom as a British Ramsay Research Fellow with Nick Greeves (1992-94) and at the Scripps Research Institute in the United States of America as a Wellcome Trust International Prize Research Fellow with K.C. Nicolaou (1994-96). He was a Sandler Sabbatical Fellow at the University of California San Francisco in the United States of America (2002), a US Fulbright Senior Research Scholar at the University of Pennsylvania, School of Medicine in the United States of America (2008) and a Visiting Professor at Pfizer in the United Kingdom (2008).

His research has been in the field of drug discovery and has been underpinned by (Hit to Lead and Lead Optimization) medicinal chemistry.

Professor Alister Craig

Liverpool School of Tropical Medicine, United Kingdom

Background

Alister Craig graduated in Genetics from Edinburgh University in 1981 and obtained his PhD in Molecular Biology from Leicester University in 1984. He spent the next two years as an EMBO Fellow at EMBL in Heidelberg followed by two years as an ICRF Fellow in London working on developing techniques for genome analysis. He subsequently worked for ten years at the Institute of Molecular Medicine in Oxford on malaria before joining the Liverpool School of Tropical Medicine in 1999. In 2011 he became one of the first recipients of the Wellcome Trust Senior Investigator awards.

One aspect of malaria biology associated with severity of disease is the ability of erythrocytes infected with *Plasmodium falciparum* to adhere to the endothelial cells lining the small blood vessels. Several endothelial receptors are able to mediate this binding, but studies on patient isolates have identified a subset of these as important in the field. Proffesor Craig's research has focussed on one of the major receptors, intercellular adhesion molecule 1 (ICAM-1) and also uses live endothelium as a model of the interactions taking place *in vivo*, as recent studies have indicated that disease severity may be linked to the ability of parasites to adhere to multiple receptors. His group's work has recently extended into an analysis of post-adhesive effects on both the parasite and the host endothelium.

As well as wishing to understand the molecular processes underpinning sequestration in malaria, Professor Craig's group also carries out work on clinical correlation of specific types of adhesion with severe disease and the differential distribution of variant populations of parasites in the body due to receptor tropism. Their main goal is an understanding of the pathology of adhesion-based pathology in malaria and, thereby, the development of novel anti-disease therapeutics.

Professor Arjen Dondorp

Mahidol University, Thailand

Arjen Dondorp trained as an infectious diseases and intensive care physician in the Netherlands. He is a Professor of Tropical Medicine at the University of Oxford, United Kingdom, and a visiting Professor of Clinical Tropical Medicine at Mahidol University in Bangkok, Thailand. He is the Deputy Director and Head of Malaria Research at the Mahidol Oxford Tropical Medicine Research Unit in Bangkok, Thailand and chairs the Technical Expert Group on Antimalarial Drug Resistance and Containment for the World Health Organization. His main research interests include antimalarial drug resistance, the pathophysiology and treatment of severe malaria, and care for critically ill patients in resource poor settings.

Dr Stephen L Hoffman

Sanaria Inc., United States of America

Dr. Hoffman is the Founder (2003), Chief Executive and Scientific Officer of Sanaria Inc., a company dedicated to developing a whole sporozoite malaria vaccine. From 1987-2001 he was Director of the Malaria Program at the Naval Medical Research Center where he and his team were leaders in subunit malaria vaccine development and sequencing of the *Plasmodium falciparum* genome and conducted the first studies in the world that showed that DNA vaccines elicited killer T cells in humans. In 2001 he joined Celera Genomics as Senior Vice President of Biologics where he created a program to utilize genomics and proteomics to produce biopharmaceuticals, and organized sequencing of the genome of the mosquito, *Anopheles gambiae*.

He has held several professorships, and chairs or serves on multiple advisory boards, is a past president of the American Society of Tropical Medicine and Hygiene, authored more than 380 scientific publications, and has numerous patents. He is the most highly cited author in the world for scientific papers on malaria published between 1995 and 2005. He received his B.A. from the University of Pennsylvania, M.D. from Cornell, and Diploma in Tropical Medicine and Hygiene from the London School of Hygiene and Tropical Medicine, did residency training at University of California San Diego, and was elected to membership in the Institute of Medicine of the National Academies (United States of America) in 2004.

Professor Kiaran Kirk

Australian National University, Australia

Kiaran Kirk is Director of the Australian National University's Research School of Biology. He carried out his PhD in the Department of Biochemistry at the University of Sydney (1985-1988). From 1989 he worked at the Oxford University Laboratory of Physiology where he held an Oxford Nuffield Medical Fellowship, the Staines Medical Research Fellowship (Exeter College) and a Lister Institute Senior Research Fellowship. He returned to Australia in 1996 as Professor and Head of the Department of Biochemistry and Molecular Biology in the Faculty of Science at the Australian National University, holding this post until taking up his present position in June 2009.

The focus of Kiaran's research has, for twenty years, been the membrane transport physiology of the human malaria parasite, *Plasmodium falciparum*. Early work, focused on the increased membrane permeability of the malaria parasite-infected red blood cell, providing new insights into both the nature of the channels involved and the physiological role that these channels play in facilitating the uptake of a number of key nutrients into the infected cell, and in causing a profound perturbation of the ionic composition of the host cell cytosol.

More recently the work in his group has been on the transporters and channels of the intracellular parasite itself, and the role that these proteins play in the uptake of nutrients, the efflux of metabolites, ion homeostasis, and antimalarial drug resistance. The most recent work from the group has been on the mechanism by which a range of new-generation antimalarials, some of which are in clinical trials, kill the parasite.

Professor Dominic Kwiatkowski

Oxford University and Wellcome Trust Sanger Institute, United Kingdom

Dominic Kwiatkowski holds a joint appointment as Professor of Genomics and Global Health at Oxford University, and as head of the Malaria Programme at the Wellcome Trust Sanger Institute near Cambridge, United Kingdom. He is Director of the MRC Centre for Genomics and Global Health, which is a joint research programme of Oxford University and the Sanger Institute.

The overarching goal of his current research is to help solve practical problems in global health by using new approaches in genomics, epidemiology and statistical genetics. His team is developing methods for large-scale analysis of genome variation at the population level and using these to investigate, for example, how children living in malaria-endemic regions develop protective immunity against malaria, and how malaria parasites develop resistance against anti-malarial drugs. They work mainly on malaria, but many of the tools and methodologies that they are developing also have applications for other diseases.

One of Dominic's main interests is building data-sharing networks to tackle fundamental scientific problems that can be solved only by engaging many research groups around the world. As the coordinating centre for the Malaria Genomic Epidemiology Network, his group provides support and training in genetics, statistics, informatics and ethics for malaria researchers in over 20 countries.

Dr Alan Magill

Bill & Melinda Gates Foundation, United States of America

Dr. Alan Magill is the Director, Malaria, at the Bill & Melinda Gates Foundation in Seattle, Washington, United States of America. Dr. Magill is ABIM board-certified in internal medicine and infectious diseases. He has dual academic appointments as Associate Professor of Medicine and Associate Professor of Preventive Medicine and Biometrics at the Uniformed Services University of the Health Sciences (USUHS) in Bethesda, Maryland.

Dr. Alan Magill's research in malaria and leishmaniasis focus on new product development in vaccines, drugs, and diagnostics. Previous positions include Program Manager (2009-2012) at the Defense Advanced Research Projects Agency (DARPA) where he developed and enabled a plant based vaccine production capability. He retired in 2010 after 27 years active duty service in the US Army. He was formerly the Director of the Division of Experimental Therapeutics and the Science Director at the Walter Reed Army Institute of Research (WRAIR) in Washington DC, United States of America, the Head of Parasitology at the Naval Medical Research Center Detachment (NMRCD) in Lima and the Head of Clinical Research for the Malaria Vaccine Development Unit of the U.S. National Institutes of Health. He is a faculty member for the Gorgas Course in Clinical Tropical Medicine in Lima, Peru.

He participates in numerous national and international advisory committees and workshops. He is the current President Elect of the American Society of Tropical Medicine and Hygiene and a Past President of their Clinical Group. Dr. Magill is the immediate Past President of the International Society of Travel Medicine (ISTM). He is the Lead Editor of the 9th edition of Hunter's Tropical Medicine, and Medical Editor of the CDC Health Information for International Travel (the yellow book) for 2010, 2012 and 2014. He has authored more than 70 peer reviewed publications, 125 abstracts, and 13 book chapters. He is a Master of the American College of Physicians, a Fellow of the Infectious Disease Society of America, and a Fellow of the American Society of Tropical Medicine and Hygiene.

Dr Abdisalan Mohamed Noor

Kenya Medical Research Institute-Wellcome Trust Research Programme, Kenya

Dr Abdisalan Mohamed Noor is a Wellcome Trust Research Fellow at the Kenya Medical Research Institute/Wellcome Trust Research Programme (KEMRI-WTRP) in Nairobi. His areas of research include access to health care, mapping of malaria transmission, populations at risk and the coverage and impact of malaria control interventions in Africa. He is an Honorary Fellow of Nuffield Department of Clinical Medicine, University of Oxford and an Honorary Lecturer at the University of Nairobi, Department of Geospatial Engineering & Space Technology. In 2009, Dr. Noor was awarded the African Union National Scientific Award in Life and Earth Sciences in recognition of his research work in malaria. Dr Noor is currently the Head of the Spatial Epidemiology Unit of the Malaria Public Health Department. His other roles include: Chairman, National Council of Population and Development, Kenya; and Co-Chair, Roll Back Malaria - Monitoring and Evaluation Reference Group. He also provides support to National Malaria Programmes in several African countries including Kenya, Somalia, Sudan and Yemen.

Dr Vasee Moorthy

World Health Organisation, Switzerland

Vasee Moorthy, an infectious diseases physician, clinical trialist and immunologist, serves as Technical Officer at the World Health Organisation (WHO) Department of Immunization, Vaccines & Biologicals in Geneva, Switzerland. He is responsible for malaria vaccines at WHO working closely with the Global Malaria Programme. He acts as secretariat for two WHO malaria vaccine advisory committees. Dr. Moorthy facilitates the Malaria Vaccine Funders Group, which works to find synergies between funders to accelerate development of malaria vaccines suitable for low income countries. Dr. Moorthy has 18 years of experience working in clinical infectious diseases, vaccine development and immunization policy, 5 years of which he spent in sub-Saharan Africa conducting clinical trials of vaccines in The Gambia and clinical malaria research in South Africa.

He has a bachelor's degree (first class) in Natural Sciences from the University of Cambridge, a clinical medicine degree from the University of Oxford, and a PhD in malaria immunology from the Institute of Molecular Medicine, Oxford. He started his malaria research career working as a government medical officer in 1996-1997 at a rural district general hospital in Kwazulu-Natal, one of eight doctors serving a population of 200,000 South Africans.

Dr Fatoumata Nafo-Traoré

Roll Back Malaria Partnership, Switzerland

Dr. Fatoumata Nafo-Traoré brings to the RBM Partnership a wealth of expertise in maternal and child health, malaria control and health systems strengthening, as well as significant leadership experience in facilitating global, regional and country-level partnerships.

After distinguishing herself as the Director of an important sector investment program (SIP) and as Health Specialist at the World Bank in Bamako, she served as Minister of Health and also Minister of Social Affairs, Solidarity and the Elderly in Mali from 2000 to 2002. In 2003, Dr. Nafo-Traoré was appointed as the first RBM Executive Secretary and later on as Director of WHO/RBM Department. She subsequently served as a WHO representative to the Congo and Ethiopia.

Over the past fifteen years, Dr Nafo-Traoré has helped strengthen the health sector in a number of countries across Africa. She has served the African health community in different capacities, including as President of the Assembly of ECOWAS Ministers of Health and member of different working groups and regional mechanisms.

In her recent positions, she facilitated efforts to implement the Paris Declaration on AID effectiveness and the UN reform Delivery as One initiative (2006-2012). She also nurtured a policy dialogue among ministries and diverse sectors of the society to anchor health in key national agendas and increase domestic funding for health.

As Minister of Health in Mali, she oversaw a US$ 350 million partnership initiative to implement a national program for investment in the health sector and ensure that control interventions for major endemic diseases are rolled out in a coordinated and complementary fashion.

Dr Nafo-Traoré was twice awarded the national distinction of “Chevalier” and “Officer” de l’Ordre National du Mali, in 1996 and in 2007. She is a member of numerous professional associations and has authored a significant number of technical publications and studies.

Dr Robert D. Newman

World Health Organization, Switzerland

Dr Robert D. Newman is a pediatrician and Director of the Global Malaria Programme at the World Health Organisation (WHO) in Geneva, Switzerland. As Country Coordinator of Health Alliance International in Mozambique in the late 1990s, he was astounded at the human toll of malaria in Africa. He has dedicated the last 15 years to combating the disease, first at the Centers for Disease Control and Prevention in Atlanta, and since 2009, at WHO.

Dr. Newman received his BA in English Literature from Williams College (including a year of studies at Oxford University), his MD from Johns Hopkins University, and his MPH from the University of Washington. He completed his residency in Pediatrics at the University of Washington--Seattle Children’s Hospital in 1996, and stayed on to complete a National Research Service Award fellowship in General Pediatrics in 1998. Dr. Newman began his public health career studying Cryptosporidium in Fortaleza, Brasil in the early 1990s.

Dr Olumide AT Ogundahunsi

World Health Organisation, Switzerland.

Olumide AT Ogundahunsi (OAT) is a scientist with the Special Programme for Research and Training in Topical Diseases (TDR) at the WHO headquarters in Geneva, Switzerland. He was born in Lagos, Nigeria and educated in both Nigeria and America. Dr Ogundahunsi has degrees in Pharmacology, Therapeutics and Biochemical Pharmacology. He obtained a PhD from the University of Ibadan based on research on antimalarial drug resistance and immune responses to malaria. He was one of the first recipients and mentees of the MIM/TDR capacity strengthening grant programme.

Dr Ogundahunsi spent the first 15 years of his career (1985 to 2000) in academia and research in Nigeria. In 2000 he joined TDR to manage a $2,000,000 multidisciplinary Research Capability Strengthening Grants portfolio under the aegis of the of Multilateral Initiative on Malaria (MIM) as well as a multi-disciplinary portfolio of TDR Institution strengthening and re-entry grants. In this capacity he facilitated establishment and promotion of equitable partnerships between Academic, Research institutions and scientists in developing countries of the south and International research consortia, institutions and scientists in the north. In the past four years his work has increasingly focused on public health and development of resources and capacity for implementation research in Low and middle income countries.

Dr Ogundahunsi has served on several scientific or advisory boards such as South African Malaria Initiative, Malaria Capacity Development Consortium, the Malaria Research Reference Reagents Resource (MR4), the Poverty Related Diseases (PRD) College and the Multilateral Initiative on Malaria (MIM). He has co-author of several scientific publications, most of them on malaria. In 2009 the 5th MIM Pan African Malaria Conference recognized for his contribution to Malaria Research Capacity Strengthening in Africa with an award.

Professor Hilary Ranson

Liverpool School of Tropical Medicine, United Kingdom

Professor Hilary Ranson is Head of the Department of Vector Biology at the Liverpool School of Tropical Medicine, United Kingdom, one of the largest departments of its kind, with research strengths in malaria, neglected tropical diseases and monitoring and evaluation. Professor Ranson's own research focuses on the control of mosquito borne disease and, in particular, the use of insecticides in vector control. She is internationally renowned for her work on insecticide resistance and has contributed her technical expertise to a range of WHO scientific advisory boards and is a technical advisor to the Innovative Vector Control Consortium.

Professor Ranson is the scientific coordinator of AvecNet (www. AvecNet.eu), a European Union 'FP7-Call for Africa' project involving 15 European and African partners, working together to develop new and improved tools for malaria vector control.

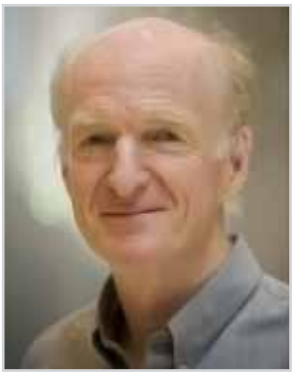
Professor Ranson obtained a BSc in Biology from the University of York an MSc in Medical Parasitology from the London School of Hygiene and Tropical Medicine and a PhD in Molecular Entomology from Cardiff University. She has held postdoctoral positions at the University of Notre Dame, United States of America and Imperial College London. She was awarded a personal chair in 2011 and is currently the holder of a Royal Society Wolfson Research Merit Award.

Dr Ken Vernick

Pasteur Institute, France

Dr Vernick's PhD research was conducted at the National Institutes of Health (USA) Laboratory of Parasitic Diseases (1988). He has held faculty positions in the Department of Parasitology of New York University School of Medicine (USA), Department of Microbiology of the University of Minnesota (USA), and is currently the Head of the research unit on Genetics and Genomics of Insect Vectors, and Director of the Department of Parasitology and Mycology of the Institut Pasteur (France).

The malaria transmission system is an ecological phenomenon resulting from the adaptation of human malaria parasites to anopheline mosquito vectors. Dr Vernick's laboratory studies the vector-parasite interaction using genetic mapping in mosquitoes, and functional dissection of mosquito genes. By working closely with research teams in Europe, Africa, and the United States, his research group merges concepts in statistical genetics with knowledge in malaria vector ecology. From work in Mali using natural populations of vectors and human malaria parasites, Dr Vernick's research group identified a natural genetic locus in mosquitoes for malaria resistance (2002). A genetic survey using a panel of wild pedigrees in Burkina Faso showed malaria resistance traits were frequent in wild vector populations (2006). The studies in field populations of vectors have involved extensive genotyping and population genetic analysis. From this work, a novel population subgroup of *Anopheles gambiae* has been discovered in West Africa (2011).

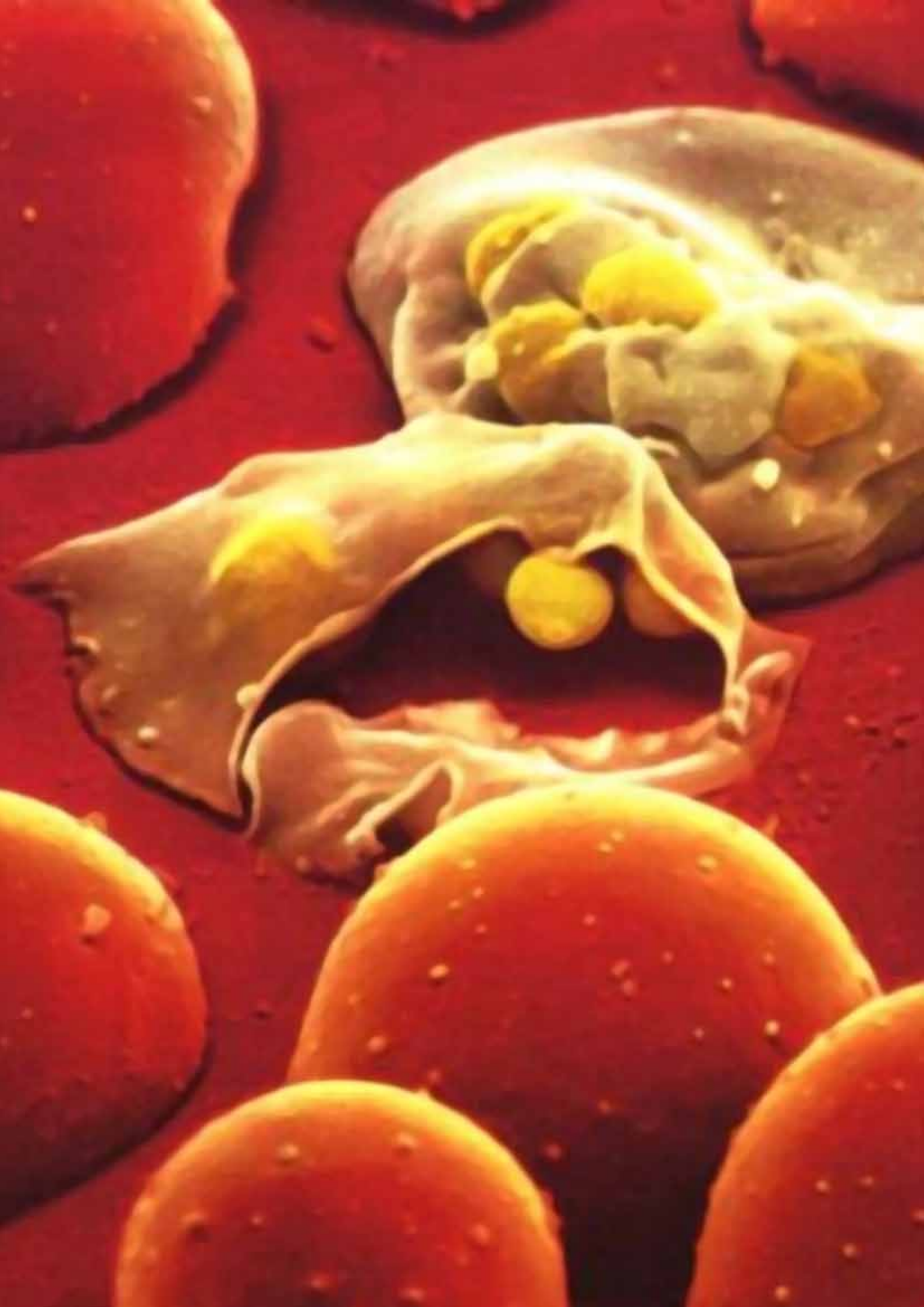


Professor Nick J White

Mahidol University, Thailand

Prof Nick White trained in medicine at Guy's Hospital, London. He is Professor of Tropical Medicine at the Faculty of Tropical Medicine, Mahidol University, Thailand and at Oxford University, United Kingdom, and is also Consultant Physician (Internal Medicine) at the John Radcliffe Hospital, Oxford. He is a Wellcome Trust Principal Research Fellow and chairs the Wellcome Trust Tropical Medicine Research Programmes in South East Asia. He has lived and worked in Thailand since 1980.

Prof White's research focus is the pathophysiology and treatment of malaria. He has concentrated on characterising antimalarial pharmacokinetic–pharmacodynamic relationships to improve the treatment of malaria and reduce the emergence of resistance. This contributed to developing artemisinin based combination treatment for *falciparum* malaria, and changing to artesunate for severe malaria. He currently chairs the WorldWide Antimalarial Resistance Network. Prof White also co-chairs the WHO GMP technical expert group on prevention and treatment of malaria and the WHO antimalarial treatment guidelines committee.



SCHEDULE FOR PLENARY SPEAKERS

Time	Monday 7th October 2013	Tuesday 8th October 2013	Wednesday 9th October 2013	Thursday 10th October 2013	Friday 11th October 2013
08:30-09:30	Plenary Lecture I **Prof Arjen Dondrop** Optimising severe malaria case management: what's new? CHAIR: Prof Lucille Blumberg	Plenary Lecture IV **Prof Kelly Chibale** African –led Innovation in Antimalarial Drug Discovery. CHAIR: Prof Oumar Gaye	Plenary Lecture VII **Prof Alan Magill** Accelerating to zero: Strategies for achieving malaria eradication CHAIR: Prof David Schellenberg	Plenary Lecture X **Prof Alister Craig** Endothelial Protein C Receptor (EPCR) and Plasmodium falicparum malaria - two side of a pathological coin CHAIR: Prof Kevin Marsh	Plenary Session XIII **Dr Olumide Ogundahunsi** Generation F3 and beyond – sustaining malaria RCS in Africa CHAIR: Prof Fred Binka
09:30-10:30	Plenary Lecture II **Dr Abdisalan Noor** The malaria epidemiological transition during the RBM partnership era. CHAIR: Prof Martin Akogbeto	PlenaryLecture V **Dr Robert Newman** From a one-size-fits-all to a tailored approach for malaria control and elimination. CHAIR Prof Graham Brown	Plenary Session VIII **Prof Nick White** Containing drug resistance while eliminating malaria - impossible or essential? CHAIR: Prof Karen Barnes	Plenary Session XI **Dr Ken Vernick** Mosquito genetic variation and malaria transmission. CHAIR: Prof Maureen Coetzee	Plenary Session XIV **Dr Stephen Hoffman** The road from concept to proof of principle to deployment of the PfSPZ vaccine for elimination of Plasmodium falciparum malaria. CHAIR: Prof Adegnika
10:30-11:30	TEA, POSTERS AND EXHIBITIONS				
11:30-12:30	Parallel Sessions	Parallel Sessions	Parallel Sessions	Parallel Sessions	Plenary Session XV **Dr Fatoumata Nafo-Traore** Malaria control and elimination in a resource constrained environment. CHAIR: Prof Rose Leke
12:30-13.30	LUNCH, POSTERS AND EXHIBITIONS				CLOSING CEREMONY
13:30-14:30	Plenary Lecture III **Prof Hilary Ranson** Insecticide resistance: a major hurdle on the path to malaria elimination CHAIR: Prof Rajendra Maharaj	Plenary Lecture VI **Prof Dominic Kwiatkowski** Translating genomics into practical tools for malaria control and elimination CHAIR: Prof Chris Plowe	PlenaryLecture IX **Prof Kiaran Kirk** Targeting ion transport in the malaria parasite with new-generation antimalarials CHAIR: Prof Dean Goldring	Plenary Session XII **Dr Vasee Moorthy** Formulation of WHO policy recommendation for malaria vaccines and the malarai vaccine roadmap CHAIR: Prof Wilfred Mbacham	

PLENARY SPEAKERS ABSTRACTS

African-led innovation in antimalarial drug discovery

Professor Kelly Chibale
Department of Chemistry and Institute of Infectious Disease and Molecular Medicine, University of Cape Town, South Africa

African-led innovation in antimalarial drug discovery has historically been hampered by a number of factors including, but not limited to, a limited skilled manpower base and poor access to technological platforms and/or enabling technologies. African scientists working in the area of drug discovery, to a large extent, must adopt pharmaceutical industry approaches to drug discovery. This requires harnessing modern pharmaceutical industry skills and expertise in the drug discovery value chain – integrating medicinal chemistry, biology, pharmacology as well as drug metabolism and pharmacokinetics studies.

One of the most effective ways of building capacity and expertise in drug discovery is to mount programmes with a specific focus on a tangible output and/or product. With funding from various sources, the University of Cape Town Drug Discovery and Development Centre (H3-D) has initiated a number of drug discovery projects that have access to enabling technologies that create a value chain.

This lecture will introduce H3-D, describe representative antimalarial drug discovery projects, and how these projects have been critical to build drug discovery infrastructure and expertise.

Endothelial Protein C Receptor (EPCR) and *Plasmodium falciparum* – two sides of a pathological coin

Professor Alister Craig
Molecular Parasitology, Liverpool School of Tropical Medicine, United Kingdom

Recent work from a number of groups identified groups of *P. falciparum* erythrocyte membrane protein-1 (PfEMP1) associated with adhesion in the brain and severe malaria that did not bind to any of the major receptors that had been identified, including ICAM-1. This talk will describe two different routes that implicate Endothelial Protein C Receptor (EPCR) as a key player in the pathology of cerebral malaria and a newly identified receptor for PfEMP1. Our work based in the Malawi-Liverpool-Wellcome Programme in Malawi analysed subcutaneous fat endothelial cells taken from patients with cerebral malaria and compared them with healthy controls, identifying specific changes in the expression levels of proteins involved in the regulation of coagulation/ inflammation, including EPCR. These changes mirrored histopathological observations from post-mortem samples from children dying of cerebral malaria in which EPCR levels were significantly reduced in brain vessels containing parasitized red blood cells (prbc), with the concomitant production of fibrin within the same vascular space.

In a separate study based in Copenhagen PfEMP1 proteins from variant sub-groups associated with severe malaria were screened for their ability to bind to a range of endothelial receptors, with the only protein showing binding being EPCR. Further analysis showed that the epitope for prbc adhesion overlaps the site for activation of Protein C in the coagulation control cascade, suggesting that parasite cytoadherence to EPCR would have functional consequences in dysregulating the coagulation/ inflammation pathway. This group also showed that adhesion of prbc from patients with severe malaria was significantly higher than those from uncomplicated malaria.

Taken together these two findings provide strong support for a novel mechanism of cytoadherence-associated pathology based on disruption of the Protein C pathway and localized inflammation of the endothelium in tissues such as the brain.

Optimising severe malaria case management: Whats new?

Professor Arjen Dondorp
Tropical Medicine, Malaria Research, Mahidol University, Thailand

Case fatality rates of severe falciparum malaria are around 10% in African children and 15% in Asian adult patients, but can increase to over 40% in cases with multi-organ involvement. To improve mortality, different components of the treatment can be targeted, including 1. antimalarial treatment, 2. treatment of concomitant diseases, 3. adjuvant treatments, 4. supportive treatments and nursing care. 1. In large trials, parenteral artesunate reduced severe malaria mortality by 22·5% in Africa and 34·7% in Asia compared with quinine and this large reduction in mortality was not at the expense of an increase in neurological sequelea. The cost per life saved when switching from quinine to artesunate is low, estimated as 120 US$ in African children and 150 US$ in Asian adult patients. Despite this, the deployment of artesunate for severe malaria in many of the malaria endemic countries is lagging behind. 2. Parenteral antimicrobials should be given to all children with suspected severe malaria in areas of moderate or high transmission, because of the high incidence of concomitant invasive bacterial disease in these settings. This is because severe malaria is an important risk factor for bacteraemia, but also because children with bacterial sepsis can present with co-incidental parasitaemia related to high background prevalence rates in these settings. Assessment of plasma PfHRP2 could be a tool to identify the latter group. 3. Adjuvant therapies have been uniformly unsuccessful to date. Therapies aiming at improving the microcirculation are currently being tested, including nitric oxide donors and compounds reversing cyto-adherence of the sequestered parasite biomass. 4. Fluid therapy in both adult and paediatric cases should be restricted. A large study of fluid bolus therapy in African children with compensated shock showed in the subgroup with *P. falciparum* malaria, that mortality in the bolus groups was 51% higher: 9.2% compared to 5.8% [(RR 1.51(1.17-1.95)]. Strategies proven beneficial for sepsis management in resource rich settings are not always applicable to the management of severe malaria in resource poor settings.

The Road from Concept to Proof of Principle to Deployment of the PfSPZ Vaccine for Elimination of *Plasmodium falciparum* Malaria

Stephen L. Hoffman
Sanaria Inc, United States of America

Eleven years ago at the Third MIM Pan-African Malaria Conference in Arusha, Tanzania, the plan was presented to form a biotechnology company, Sanaria, to develop, license, and deploy a highly protective (>80%), radiation attenuated, whole sporozoite malaria vaccine. At that time Sanaria was little more than an idea, as the company had no funds, facilities, or paid staff. The challenges to developing and manufacturing such a vaccine were formidable. *Plasmodium falciparum* (Pf) sporozoites (SPZ) that were aseptic (free of bacterial and fungal contamination), pure (associated with minimal mosquito salivary gland material), non-replicating/attenuated (could not cause malaria), and metabolically active/potent (highly immunogenic and protective) had to be manufactured in large quantities using *Anopheles stephensi* mosquitoes as "bioreactors." Furthermore, a method of administering the PfSPZ had to be devised, and the vaccine had to be shown to be safe and protective in humans. In August 2013 the U.S. National Institute of Allergy and Infectious Diseases, National Institutes of Health, Naval Medical Research Center, multiple other institutions and Sanaria reported that such a vaccine, the PfSPZ Vaccine, was safe, well tolerated, highly immunogenic, and protected all six individuals who received the highest dosage tested in a clinical trial. The first set of daunting challenges, including proof of principle that an injectable whole sporozoite vaccine could induce high-level protection, had been met. The current goal is to move the PfSPZ Vaccine through licensure for use to prevent *Pf* infection, disease, and transmission, and to deploy it in mass administration campaigns as a tool for elimination of *Pf* from geographically defined areas. Common misperceptions about the vaccine, remaining challenges and the strategies and timelines for meeting these challenges and achieving our goal will be presented.

Targeting ion transport in the malaria parasite with new-generation antimalarials

Professor Kiaran Kirk[1], Natalie J. Spillman[1], Adele M. Lehane[1], Adelaide Dennis[1], Markus Winterberg[1], David Floyd[2], R. Kip Guy[3], Akhil B. Vaidya[4]

[1]Research School of Biology, The Australian National University, Australia; [2]Rutgers University, USA; [3]St Jude Children's Research Hospital, USA; [4]Center for Molecular Parasitology, Drexel University College of Medicine, USA

As the malaria parasite grows within its host erythrocyte the concentration of Na^+ in the erythrocyte cytosol increases, ultimately approaching that in the external medium. By contrast, the intraerythrocytic parasite itself maintains a tight control over its internal Na^+ concentration which remains some ten-fold lower than that in the host cell compartment. The maintenance of a low intracellular [Na^+] by the parasite is reliant on the extrusion of Na^+ via a plasma membrane Na^+-ATPase. Bioinformatic analysis of the genome of the human malaria parasite *Plasmodium falciparum* reveals that the most likely candidate for the parasite's Na^+ ATPase is a protein known as PfATP4. Recent 'whole cell' screens of large compound libraries for the ability to inhibit the *in vitro* growth of *P. falciparum*, has led to the discovery of a number of highly active antimalarial compounds, one of which, a 'spiroindolone' (Rottmann *et al.* (2010) *Science* 329, 1175-1180), is now in advanced clinical trials. Prolonged exposure of *P. falciparum* parasites to sub-lethal concentrations of spiroindolones lead to the emergence of spiroindolone-resistant parasites, with the resistance attributable to mutations in PfATP4. For several other (structurally unrelated) candidate antimalarial drug classes, exposure of parasites to sub-lethal concentrations gives rise to resistant parasites that once again have mutations in PfATP4. In this talk I will introduce the cell physiology of the intracellular malaria parasite and present evidence for the hypothesis that a diverse range of compound classes, including the spiroindolones (Spillman et al. (2013) *Cell Host & Microbe* 13, 227-237) exert their antimalarial effect by inhibiting Na^+ extrusion via PfATP4, thereby disrupting parasite ion homeostasis.

Translating genomics into practical tools for malaria control and elimination

Professor Dominic Kwiatkowski

Genomics and Global Health, Oxford University and Malaria Programme, Wellcome Trust Sanger Institute, United Kingdom

One of the reasons for failure of previous malaria elimination campaigns has been lack of understanding about what is going on in the parasite population. With the emergence of artemisinin resistance, the situation is particularly dangerous and any attempt to eliminate malaria needs to be backed up by intensive surveillance of how the parasite population is changing and evolving. In this talk I will discuss new tools for surveillance of malaria transmission and drug resistance that are emerging from recent innovations in genome technology and parasite population genomics. Genome sequence data from over 2000 clinical samples of *P. falciparum* have been analysed in a MalariaGEN Community Project involving research groups in over 20 countries, yielding deep insights into the biology, demography and evolutionary adaptation of the global parasite population. The parasite population in Cambodia has an extremely unusual population structure due to multiple independent founder populations of artemisinin-resistant parasites that have undergone recent expansion. These discoveries are now being used to develop genetic tools to track the spread of existing artemisinin-resistant strains and to detect new strains of artemisinin-resistant parasites as they emerge. The next few years will see major developments in genetic mapping technologies to address practical questions such as where the main reservoirs of resistant parasites and hotspots of transmission are located, and how the parasite population is changing and evolving in response to malaria control interventions.

Accelerating to zero: Strategies for achieving malaria eradication

Dr Alan Magill

Malaria, Global Health Program, Bill & Melinda Gates Foundation, United States of America

Over the past decade, malaria control efforts have reduced global malaria mortality by 25 percent. While this progress is unprecedented, malaria still kills nearly 700,000 people and affects more than 200 million each year. Current control interventions are effective and save lives today, yet also entail high long-term costs and are threatened by drug and insecticide resistance. Accelerated pathways to elimination are the best way to sustain the progress gained by high level control and prevent resurgence. Innovations in science and delivery can help speed the trajectory to malaria eradication by targeting the human reservoir of infection in asymptomatic people combined with transmission prevention. While maintaining investments in current control efforts, a renewed emphasis on strategies to achieve eradication is vital today.

The malaria epidemiological transition during the RBM partnership era

Dr Abdisalan Mohamed Noor

Spatial Epidemiology Unit, KEMRI-University of Oxford - Welcome Trust Research Programme, Kenya

The decade of the Roll Back Malaria Partnership has witnessed substantial financial investments in malaria control. Data from different parts of the world suggest a declining burden of malaria. In Africa where the burden of the disease is greatest, however, very few countries have reliable data from health information systems to assess the magnitude of change in disease burden.

We assembled the largest geocoded and age-corrected community *Plasmodium falciparum* parasite rate ($Pf PR_{2-10}$) in 44 endemic countries in Africa from 1980 to 2012. The data were used within a Bayesian space-time geostatistical framework to predict $Pf PR_{2-10}$ in 2000 and 2010 at 1 x 1 km spatial resolutions across Africa. Population distribution maps at the same spatial resolution were used to compute population at risk across by endemicity class and estimate population adjusted $Pf PR_{2-10}$ ($PAPf PR_{2-10}$) per country for each prediction year.

Between 2000 and 2010, the percentage of population living in areas where transmission was hyper-to holo-endemic reduced from 226.2 million (34.2%) to 188.6 (22.2%). Most of the population transitioned to meso-endemic transmission which increased from 185.4 million (28.0%) to 291.8 million (34.4%). In 42 Africa malaria endemic countries where it was possible to predict change, 40 showed a reduction in $PAPf PR_{2-10}$ while a marginal increase occurred in South Sudan and Malawi. Only ten countries (Guinea, Togo, Mali, Mozambique, Burkina Faso, Ghana, Côte d'Ivoire, Uganda, Nigeria, DRC) contributed 85% of the population living in areas of hype- to holo-endemic transmission in Africa.

Significant reductions in malaria risk have been achieved in Africa over the period 2000-2010. However, over 60% of the population in malaria endemic countries in Africa remain exposed to moderate to intense transmission likely to be associated with a large clinical burden. Parasite surveys remain an effective source of data to track the changes in malaria risk in Africa and continued support should be provided especially in high burden countries.

This work was funded by the Wellcome Trust. The funder played no role in design of the study or interpretation of the results

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Formulation of WHO policy recommendation for malaria vaccines and the malaria vaccine roadmap

Dr Vasee Moorthy

Department of Immunization, Vaccines & Biologicals, World Health Organisation, Switzerland

One of WHO's core functions is the articulation of evidence-based policy options. In the case of malaria vaccines, the principal advisory committees in malaria (MPAC, Malaria Policy Advisory Committee) and immunization (SAGE, Strategic Advisory Group of Experts) will provide policy advice to WHO. In 2015, SAGE and MPAC will jointly make policy recommendations to WHO relating to RTS,S/AS01, the most advanced candidate malaria vaccine. The evidence-based recommendations will be based on a synthesis and appraisal of the full results from the ongoing pivotal Phase 3 trial, and the policy timings depend on the outcome of regulatory processes.

The Malaria Vaccine Technology Roadmap is the multilateral strategic R&D framework for malaria vaccines. Originally published in 2006, the first update has occurred during 2012-3 with a series of consultations leading to agreement on 2 new strategic goals for development of second generation malaria vaccines by 2030. Key progress since 2006 in the framework of the roadmap will be outlined in the talk, as will the ongoing development of Preferred Product Characteristics for malaria vaccines.

Malaria control and elimination in a resource-constrained environment

Dr Fatoumata Nafo-Traoré
Roll Back Malaria (RBM) Partnership, Geneva, Switzerland

This presentation focuses on the challenges facing the malaria community as it strives to meet the internationally agreed goals and targets including MDGs and Global Malaria Action Plan (GMAP) objectives, targets and milestones by 2015 in the context of general stagnation of development assistance.

Remarkable achievements have been made in the area of malaria control and elimination, with mortality rates estimated to have declined by a third since 2000 and malaria morbidity reduced by 75% in half of malaria-endemic countries, including nine in Africa. However, reaching the more aspirational targets and milestones that accompany the GMAP objectives will be very challenging, and any significant improvement between now and 2015 will require maximum support to high-burden countries, where scale-up has been more difficult and quality data lacking, impeding progress. On the other hand, the milestone set for elimination will be attained, with four more countries having eliminated malaria since 2008 and considerable momentum building in a number of countries.

This exciting new era will demand more results with fewer financial resources. It does not necessarily amount to an impossible task. It will imply improving business practices of some major funders to ensure alignment with the goals, and focusing on a simpler and permanent dialogue between donors, recipient countries and grant implementers. It will also mean better tailoring interventions to areas/populations most at risk, and strengthening partnerships at country level to support programme implementation. Capacity building needs to be effectively addressed with an integrated and long-term public health vision. Finally, our ability to collect and analyse data, long debated, will have to be prioritized so that reliable and timely information can guide the planning and delivery of our effective interventions.

If the malaria community can rise up to this challenge, we can then envision major steps towards malaria elimination in Africa and elsewhere, thereby achieving a major public health victory and contributing to remarkable child mortality reductions on the African continent.

From a one-size-fits-all to a tailored approach for malaria control and elimination

Dr Robert D. Newman
Global Malaria Programme, World Health Organisation, Switzerland

Over the past decade, malaria control has been reinstated as a global priority. International disbursements have risen from <$100 million (2003) to approximately $1.84 billion (2012), allowing for rapid scale-up of evidence-based interventions, including long-lasting insecticidal nets (LLINs), indoor residual spraying, universal diagnostic testing of suspected malaria, and treatment of confirmed cases with artemisinin-based combination therapies (ACTs).

As a result, 50 countries (including 9 in the WHO African Region) are on track to meet the target of a 75% reduction in malaria case incidence by 2015, however, these countries account for less than 3% of the global burden. Twenty countries are currently conducting pre-elimination or elimination programmes, and a further 5 are in the phase of preventing re-introduction of malaria. Since 2000, malaria mortality rates have declined by >25% globally, and by >33% in the WHO African Region.

Despite these successes, malaria remains an enormous global health problem, responsible for an estimated 219 million cases (uncertainty range 154-289 million) and 660,000 deaths (uncertainty range 490,000- 836,000) annually. Ten countries in Africa account for 430,000 malaria deaths, or approximately 70% of all malaria mortality in Africa. The WHO Global Malaria Programme (WHO-GMP), working with Roll Back Malaria (RBM), the African Leaders Malaria Alliance (ALMA), The International Federation of the Red Cross (IFRC), the office of the UN Secretary General's Special Envoy for Financing the Health MDGs and for Malaria and other partners has launched a "Malaria Situation Room" to support these 10 countries to proactively identify and resolve bottlenecks to universal access to life-saving malaria prevention and control interventions.

The greatest immediate threat to the continued success in the control and elimination of malaria is inadequate funding. Malaria resurgences have been documented where coverage with LLINs was not sustained. The Global Fund to Fight AIDS, Tuberculosis and Malaria has not categorized malaria prevention and control interventions as eligible for Continuity of Services funding, as is the case for anti-retroviral and anti-tuberculosis medicines, heightening the risk of reversing gains in malaria control. Full replenishment of the Global Fund in 2013 will be essential to sustaining and advancing gains made against malaria.

Plasmodium falciparum resistance to artemisinins and *Anopheles* resistance to insecticides represent major biological threats to continued success. WHO-GMP, working with countries and partners, launched the *Global Plan for Artemisinin Resistance Containment* (2011) and an *Emergency Response to Artemisinin Resistance in the Greater Mekong Subregion* (2013) which aim to protect ACTs as effective treatment for falciparum malaria. To ensure continued effectiveness of malaria vector control tools, WHO has released the *Global Plan for Insecticide Resistance Management* (2012).

Tremendous opportunities exist for enhancing malaria control efforts, notably universal diagnostic testing for suspected malaria, which when coupled with effective treatment and timely surveillance, will allow for acceleration of gains already achieved through vector control. To galvanize these efforts, WHO launched the *"T3: Test, Treat, Track"* initiative on World Malaria Day 2012. As malaria burden diminishes, the gathering and use of surveillance data at peripheral levels will be essential to guide efficient and effective control and elimination programmes. This epidemiological stratification will be a guiding principle for the Global Technical Strategy for Malaria Control and Elimination 2016-2025, which WHO-GMP is working with Member States and partners to develop for presentation to the World Health Assembly in 2015.

If political will and financial commitments can be sustained to fully fund global malaria efforts, including research and development for new tools (as well as for improving use of existing tools), then malaria control can be a leading wedge to strengthen primary health care services and achieve the health-related Millennium Development Goals by 2015, especially in Africa.

Generation F3 and beyond – sustaining malaria RCS in Africa

Dr Olumide AT Ogundahunsi
Research Capacity Strengthening, World Health Organisation, Switzerland

The establishment of the MIM in 1997 was a major boost for malaria research capacity strengthening(RCS)in Africa. Bringing together several donors and fostering North - South and South - South partnerships, MIM initiated programs to (a) strengthen malaria research capacity in Africa through improved access to malaria research information, reagents & materials, and (b) train and mentor a cadre of African scientists. In the subsequent decade and a half, access to information, connectivity and networking has increased and evolved to be sine qua non for research. The initial cohort of graduate students, post docs and young PIs (F2) supported by MIM have emerged as leaders contributing to malaria research and control, and public health in general in their own right. For example they are leaders /principal investigators in research consortia, heads of institutions and leaders of capacity building initiatives.

In spite of these achievements, agencies / organizations that consistently fund RCS for malaria in Africa are relatively few and RCS is not always a top priority. In order to consolidate the gains of the past 15 years, African governments must take on a bigger role in research and research capacity and donors must harmonize policy, strategies and procedures for efficiency of international cooperation.

This presentation will focus on the challenges and prospects of nurturing a new generation of African researchers (F3) capable of response to the renewed hope of effective malaria control and emergence of malaria elimination in many countries.

Insecticide resistance: a major hurdle on the path to malaria elimination

Professor Hilary Ranson
Vector Biology, Liverpool School of Tropical Medicine, United Kingdom

The 21st century has witnessed a dramatic scale up in malaria vector control activities across the globe, both via massive increases in the number of long lasting insecticide treated bednets (LLINs) distributed and a renewed investment in indoor residual spraying (IRS). These interventions are reliant on a very small number of classes of insecticide, with all LLINs and the majority of IRS, solely dependent on the pyrethroid insecticides. The impressive reductions in malaria cases that have resulted from the scale up of these interventions are in danger of being eroded by the rapid evolution and proliferation of insecticide resistant malaria vectors. Resistance to pyrethroids is now widespread across Africa and increasing in both prevalence and intensity every year. New insecticides for use in public health will not be available before the end of the decade and populations of mosquitoes that are resistant to all available insecticide classes are being increasingly reported.

Opinion differs on the current impact of this resistance, but there cannot be any doubt that, if left unchecked, the increase in resistance levels will lead to control failure. The effects could be devastating with up to half the lives currently saved by vector control lost. In recognition of the urgency of the situation the WHO launched the Global Plan for Insecticide Resistance Management (GPIRM), in 2012.

In this talk I will review the evidence for the impact of resistance on the efficacy of current malaria tools, describe some of the approaches being taken to manage resistance and highlight some of the key knowledge gaps that must be filled if we are to avoid widespread failure of existing tools.

Mosquito genetic variation and malaria transmission

Dr Kenneth D. Vernick

Unit of Insect Vector Genetics and Genomics, Department of Parasitology and Mycology, Institut Pasteur, 28 rue du Docteur Roux, Paris 75015, France.

Historically, all successful malaria control efforts have included measures targeted at the vector. *Falciparum* malaria is an infectious disease for the mosquito vector, as well as for the human host. Understanding differences in pathogen susceptibility between individuals or population subgroups is an important part of understanding the dynamics of any infectious disease. Genetic mapping in the natural population of malaria vectors shows that susceptibility to *P. falciparum* infection is controlled by relatively simple genetic factors with strong effect. Dissection of these genetic loci will add precision to our understanding of the malaria vectorial system, and may allow rational design of malaria control strategies tailored to local vector characteristics.

Containing drug resistance while eliminating malaria - impossible or essential?

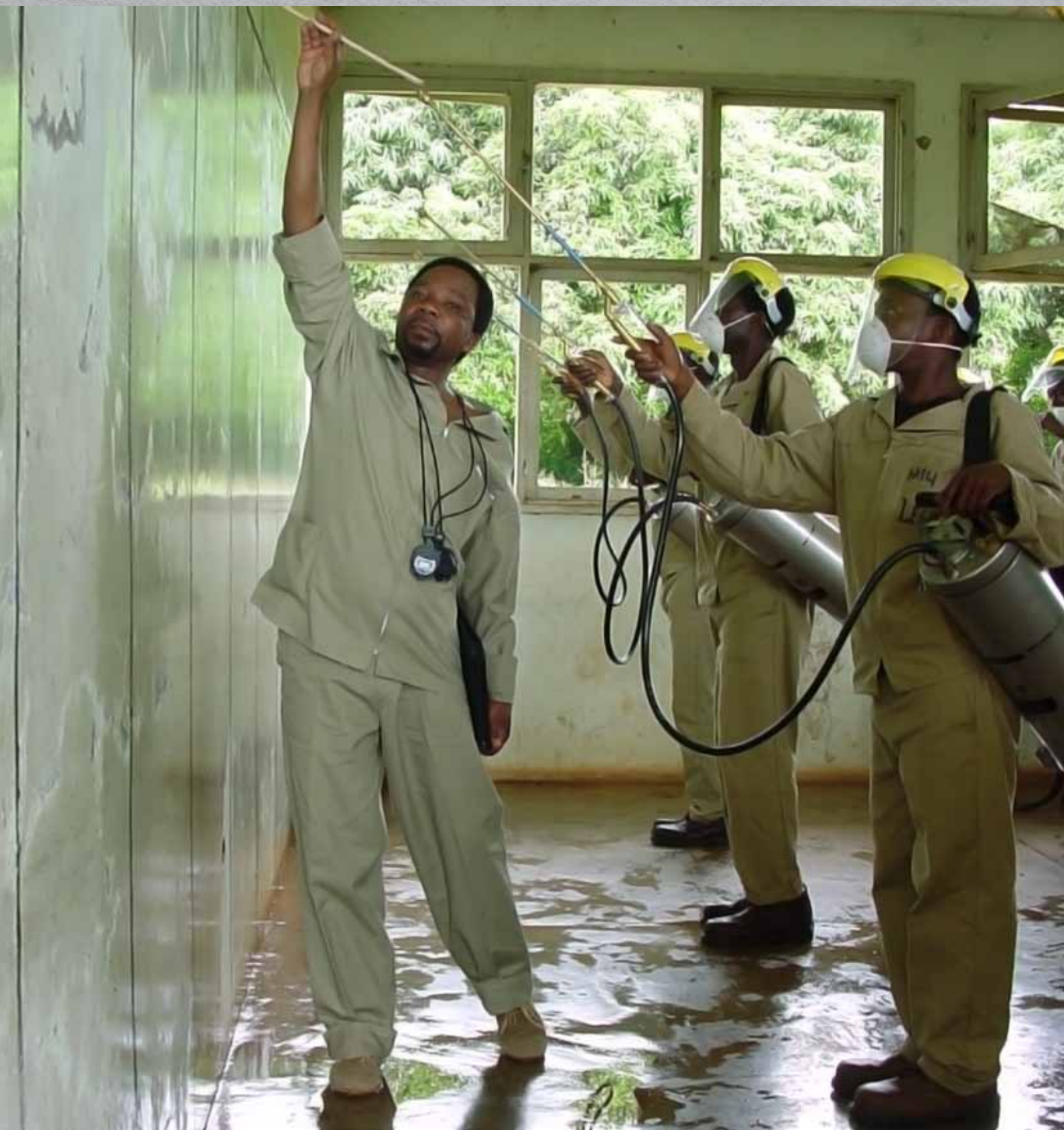
Professor Nicholas J White

Faculty of Tropical Medicine, Mahidol University,Bangkok, Thailand;

Considerable increases in the availability and use of artemisinin-based combination therapies (ACTs) together with increased deployment of insecticide treated bed-nets (ITN) have resulted in a substantial fall in global malaria morbidity and mortality. These gains and the prospects for malaria elimination are now threatened by the emergence of artemisinin resistance in *Plasmodium falciparum*. It is essential that all possible measures are taken to prevent spread of resistance genes to African malaria parasite populations.

Artemisinin resistance was reported first from Western Cambodia, where resistance to previous antimalarial drugs also first emerged, but has since either spread or emerged in other areas in mainland SouthEast Asia. There is now evidence for a decline in the efficacy of ACTs in foci of artemisinin resistance. This reflects the reduced contribution of the artemisinin to treatment efficacy, and inevitably places greater selection pressure on the partner drugs. In most of South-East Asia malaria transmission is low and seasonal, although the epidemiology there has certainly been underestimated. *Plasmodium vivax* comprises approximately half the malaria infections and is more difficult to eliminate than *P. falciparum*. ITN benefits are often small in settings with exophilic early evening biting vectors and a highly mobile adult population. Early diagnosis and effective treatment is the mainstay of malaria control. While the incidence of *falciparum* malaria continues to fall in this region there is still an opportunity to eliminate malaria, but if treatment efficacy falls further, and incidence begins to rise again, elimination of *P. falciparum* will not be possible without new medicines. Radical approaches may be necessary to achieve elimination of artemisinin resistance before it spreads to infect Africa. It is not clear whether there is an appetite for such radical action.

SYMPOSIA



MIM 2013

SYMPOSIA SCHEDULE

Time	Monday 7th October 2013	Tuesday 8th October 2013	Wednesday 9th October 2013	Thursday 10th October 2013
08:00-09:30	**Symposium 1:** Cost-effectiveness of intervention design to support the scaling up of RDTs. **Dr Kristian Hansen** Meeting Room 21	**Symposium 19:** Targeting malaria elimination in Zanziba. **Prof Anders Bjorkman** Meeting Room 21	**Symposium 37:** Insecticide Nets, IPTp for preventing malaria in pregnancy in sub-Saharan Africa. **Dr Jenny Hill Meeting** Room 21	**Symposium 54:** Beyond Corporate Social Responsibility: AngloGold Ashanti and the Global Fund teaming up for Ghana. **Dr Sylvester Segbaya** Meeting Room 21
	Symposium 2: Data-driven decision making in the context of IRS Scale up and increased insecticide resistance. **Dr Dereje Dengela** Meeting Room 22	**Symposium 20:** The role of vaccines in malaria elimination. Prof **Chris Plowe** Meeting Room 22	**Symposium 38:** Analytic challenges in measuring impact of malaria control programmes: Methodological approaches, confounders and lessons learned from the multi-agency malaria control impact evaluations. **Dr Yazoume Ye** Meeting Room 22	**Symposium 55:** Malaria surveillance, epidemic detection, epidemic preparedness and response: Zanzibar experience following increases in malaria cases during the 2013 transmission season. **Dr Jeremaih Ngondi** Meeting Room 22
09:30-11:00	**Symposium 3:** Introducing RDTs in different health sectors: interventions and impact on ACT consortium studies. **Dr Clare Chandler** Meeting Room 21	**Symposium21:** Improving malaria prevention, diagnosis and treatment through market-based interventions: challenges. **Dr Katherine Blumer** Meeting Room 21	**Symposium 39:** Mating Biology of Anopheles. **Dr Abdoulaye Diabate** Meeting Room 21	**Symposium 56:** What role can schools play in the control and elmination of malaria in Africa? **Dr Sueng Lee** Meeting Room 21
	Symposium 4: Field monitoring of malaria drug efficacy and safety. **Dr Andre Tchouatieu** Meeting Room 22	**Symposium 22:** Area-wide control of malaria vectors. **Prof Mark Benedict** Meeting Room 22	**Symposium 40:** How interventions effects depends on the setting: insights from mathemathical models. **Dr Tom Smith** Meeting Room 22	**Symposium 57:** Improving access to malaria treatment in rural Tanzania: multiple interventions for lasting improvements. **Prof Christian Lengeler** Meeting Room 22
11:30-13:00	**Symposium 5:** Multi-stage Multi-component malaria vaccines. **Prof Adrian Hill** Meeting Room 21	**Symposium 23:** Increasing access to malaria prevention among pregnant women: Results from systematic reviews and economic and anthropological studies by the MiP Consortium. **Dr Jenny Hill Meeting** Room 21	**Symposium 41:** The final decade of malaria in Africa: planning for the endgame. **Dr Jo Lines** Meeting Room 21	**Symposium 58:** Malaria eradication: identifying and targeting the residual parasite pool **Mr Simon Kunene** Meeting Room 21
	Symposium 6: Implementaion updates: Global Malaria Programme. **Dr Robert Newman** Meeting Room 22	**Symposium 24:** Ten years of Intensive malaria control on Bioko Island: Is elimination in sight? **Dr Immo Kleinschmidt** Meeting Room 22		**Symposium 59:** Evaluating the impact of malaria control interventions on under-five mortality in sub-Saharan Africa. **Dr Achuyt Bhattarai** Meeting Room 22
	Symposium 7: Drug quality and the fight against malaria. **Dr Patrick Kachur** Meeting Room 12	**Symposium 25:** Larval Source Management for malaria control. **Dr Steve Lindsay** Meeting Room 12	**Symposium 42:** MMV Collaborations in antimalarial drug development: from discovery to access and delivery. **Dr Pierre Hugo Meeting** Room 22	**Symposium 60:** EVIMalaR Symposium Research highlights in vectors and systems biology. **Prof Lars Hviid** Plenary Hall

13:30-15:00	**Symposium 8:** Delivering on the promise of better medicines for children. **Mr George Jagoe** Meeting Room 21	**Symposium 26:** Indoor residual spraying: Maximizing innovation, impact and sustainability. **Dr Bradford Lucas** Meeting Room 21	**Symposium 43:** Investing in Quality Surveillance for Malaria (pre-) Elimination Programs. **Dr Anna McCartney - Malstad** Meeting Room 21	**Symposium 61:** Multiple first line therapies and protecting the ACT class of Medicines. **Dr George Jagoe Meeting** Room 21
	Symposium 9: EVIMalaR Research Highlights in immunology, pathogensis and molecular biology **Prof Lars Hviid** Meeting Room 22	**Symposium 27:** Multilateral partnerships for malaria elimination. **Dr Andre Tchouatieu** Meeting Room 22	**Symposium 44:** Interactions between ACTs for malaria and ARVs for HIV, cause for concern? **Prof David Schellenberg** Meeting Room 22	**Symposium 62:** Adaptability and the state of monitoring and evaluation systems: measuring malaria now and in the changing contexts. **Dr Yazoume Ye** Meeting Room 22
15:00-16:30	**Symposium 10:** Does combined use of IRS and LLINs give better protection than one method alone? **Dr Immo Kleinschmidt** Meeting Room 21	**Symposium 28:** Insecticide resistance: prevention and management. **Dr Jo Lines** Meeting Room 21	**Symposium 45:** Roll Back Malaria Impact Series for South Africa. **Prof Lucille Blumberg** Meeting Room 21	**Symposium 63:** Towards strengthening the MIM into an organisation. **Malaria No More** Plenary Room
	Symposium 11: Answering key questions on ACT drug delivery in Africa: findings from the work of the ACT consortium. Prof **David Schellenberg** Meeting Room 22	**Symposium 29:** Malaria eradication in an age of artemisinin resistance. **Dr Phillippe Guerin** Meeting Room 22	**Symposium 46:** Implementing Seasonal Malaria Chemoprevention: putting research into practice. **Dr Paul Milligan** Meeting Room 22	
	Symposium 12: MESA Symposia Innovations in Malaria Eradication Research in Africa. **Dr Duncan Earle** Meeting Room 12	**Symposium 30:** Information to enhance program effectiveness. **Dr Thomas Teuscher** Meeting Room 12	**Symposium 47** MESA Symposia Science of Eradication: Global Lessons. **Prof Pedro Alonso** Plenary Hall	**Symposium 64:** Africa taking Leadership in Research Networks. **Prof Sewankambo Nelson** Meeting Room 22

17:00-18:30	**Symposium 13:** Building on 20 Years of experience with CoArtem: focussing on patient care. **Dr Kirstin Stricker** Meeting Room 21	**Symposium 31:** Nobody should die from malaria today: the significance of public-private partnerships. **Dr Kileken ole-Moi Yoi** Meeting Room 21	**Symposium 48:** Towards Sustainable Country-owned financing for malaria elimination. **Dr Robert Brinckman** Meeting Room 21	**Symposium 65:** Financing Community Driven Malaria Control. **Prof Peter De Vries** Plenary Room
	Symposium 14: Enhancing adherence to ACTs purchased from drug shops. **Dr Catherine Goodman** Meeting Room 22	**Symposium 32:** TDR Alumni Network building blocks. **Dr Olumide Ogundahunsi** Meeting Room 22	**Symposium 49:** Primaquinine, from P. vivax radical cure to P. falciparum malaria elimination? **Dr Andre Tchouatieu** Meeting Room 22	**Symposium 66:** Pharmacovigilance in Africa. **Dr Andre Tchouatieu** Meeting Room 22
	Symposium 15: Physical durability of LLNs. **Dr Stephen Smith** Meeting Room 11	**Symposium 33:** Indoor Residual House Spraying old and new tool for rapid malaria control and elimination. **Dr Shiva Murugasampillay** Meeting Room 11	**Symposium 50:** From sustainable malaria control to elimination: An African Approach. **Prof Tiaan de Jager** Meeting Room 11	**Symposium 67:** Scalable innovations for improved malaria control in the era of elimination. **Dr Karin Kallander** Meeting Room 11
	Symposium 16: Malaria Case Surveillance and Rapid Response: From Control to Elimination. **Ms Natashia Morris** Meeting Room 12	**Symposium 34:** Tracking artemisinin resistance. **Dr Elizabeth Ashley** Meeting Room 12	**Symposium 51:** Malaria RDTs: when it is and isn't Malaria. **Dr Hellen Gelband** Meeting Room 12	**Symposium 68:** New tools for management of insecticide resistance. **Prof Janet Hemingway** Meeting Room 12
	Symposium 17: Challenge of developing a pregnacy associated malaria vaccine. **Prof Alister Craig** Hall 4A	**Symposium 35:** Whole-organism pre-erthrocytic malaria vaccination strategies. **Dr Miguel Prudencio** Hall 4A	**Symposium 52:** Burden and control of Plasmodium falciparum and vixax malaria in pregnancy in Asia, the Pacific and Latin America. **Dr Jenny Hill** Hall 4A	**Symposium 69:** Pan African Mosquito Control Association (PAMCA) - Networking and paving the way forward for the future of mosquito control in Africa and beyond. **Prof Charles Mbogo** Hall 4A
	Symposium 18: Building interdisciplinary research capacity for the control of malaria in Francophone and Anglophone West Africa. **Prof Magaret Gyapong** Hall 4B	**Symposium 36:** Seasonal Malaria Chemoprevention. **Dr Graciela Diap** Hall 4B	**Symposium 53:** The updated Malaria Vaccine Technology Roadmap. **Dr Vasee Moorthy** Hall 4B	

S01: Cost-effectiveness of interventions designed to support the scaling up of rapid diagnostic tests for malaria

Chairs: Dr Virginia Wiseman and Dr Kristian Schultz Hansen

Speaker 1: Dr Virginia Wiseman, Economic evaluation of a cluster-randomized trial of interventions to improve health workers' practice in diagnosing and treating uncomplicated malaria in Cameroon, London School of Hygiene and Tropical Medicine

Speaker 2: Dr Kristian Schultz Hansen, Incremental cost-effectiveness analysis of introducing rapid diagnostic testing for malaria into registered drug shops in Uganda, ACT Consortium, London School of Hygiene and Tropical Medicine, London, United Kingdom

Speaker 3: Ms Theresa Tawaih, Cost–effectiveness analysis of test based versus presumptive treatment of malaria in under 5 children in rural Ghana, Kintampo Health Research Centre, Ghana

Speaker 4: Dr Sarah Staedke, Impact of RDTs and enhanced health facility-based care on costs and health outcomes in a high endemic area in Uganda, ACT Consortium, London School of Hygiene and Tropical Medicine, London, United Kingdom

OVERVIEW

OBJECTIVE: This symposium will present empirical data from ACT Consortium projects on the cost effectiveness of interventions designed to support the introduction and scale-up of Rapid Diagnostic tests across 3 countries: Cameroon, Uganda and Ghana. The range of factors influencing cost-effectiveness will also be highlighted.

RATIONALE: Presumptive diagnosis and treatment for uncomplicated malaria continues to be common in many parts of Africa both in the formal and the informal health care sectors. Current WHO guidelines on malaria case management recommend parasitological confirmation prior to treatment with an artemisinin-based combination therapy (ACT). Rapid diagnostic tests (RDTs) for malaria have been shown to perform generally well under a range of conditions and if used as intended, have the potential to improve the care of patients presenting with fever and reduce inappropriate use of antimalarials. Cost-effectiveness analyses to-date have suggested that their introduction may also be very cost-effective compared to presumptive diagnosis or microscopy. These analyses highlight that the relative cost-effectiveness of RDT diagnosis depends critically on a range of factors. Among the important factors identified are: the prescribers' degree of adherence to negative RDT results, the level of malaria prevalence (affecting the proportion of fever patients being parasite-positive), the accuracy of the RDT in general and compared to the alternatives, cost of the RDT as well as the cost of drug regimens for parasite-positive and parasite-negative patients.

CONTENT: The ACT Consortium was formed with the goal of developing and evaluating delivery mechanisms to improve ACT access, targeting, safety and quality. The purpose of this symposium is to present some of the findings of the Consortium's cost-effectiveness analyses which were conducted to assess the desirability of introducing malaria RDTs across a range of countries with different delivery systems. Special attention will be paid to the factors found to influence the relative cost-effectiveness of RDTs across these different settings. The symposium will begin with an overview of some of the key considerations in assessing cost-effectiveness of RDTs including the perspective, the alternative strategies, subsequent treatment seeking and outcomes of interest. Each of the four presentations will then show how different factors affect cost-effectiveness at these different loci. Each presentation shows results from cluster randomised trials in different malaria endemic countries.

Economic evaluation of a cluster-randomized trial of interventions to improve health workers' practice in diagnosing and treating uncomplicated malaria in Cameroon

Lindsay Mangham-Jefferies[1], Virginia Wiseman[1], Olivia Achonduh[2], Bonnie Cundill[1], Tom Drake[1], Akindeh Nji[2], and Wilfred Mbacham[2]

[1]London School of Hygiene and Tropical Medicine; [2]The University of Yaoundé I, Cameroon

WHO guidelines on malaria treatment recommend parasitological confirmation in all febrile patients before treatment is prescribed. This should ensure an efficient use of resources as patients receive appropriate treatment. Working with the Ministry of Health, basic and enhanced training programmes were designed to support the introduction of rapid diagnostic tests (RDTs). Both programmes sought to equip health workers with the knowledge and skills needed to diagnose and treat malaria, though the enhanced programme contained additional activities and used interactive methods to promote changes in prescribing practices.

A three-arm cluster-randomized trial was conducted to assess the cost-effectiveness of introducing RDTs with basic or enhanced training compared to current practice, and an enhanced 3-day training compared to a basic 1-day training package. RDTs with training were evaluated in Cameroon at public and mission facilities where microscopy was available. Individual patient data were collected from facility records and an exit survey. The primary outcome was the proportion of patients attending facilities that report a fever or suspected malaria and receive treatment according to guidelines. This required patients to be tested for malaria, ACT to be prescribed for confirmed cases, and no antimalarial to be prescribed for patients with a negative test result. Financial and economic costs of interventions

were estimated using project reports. Start-up costs were annualized using a 3% discount rate, assuming the training materials would remain relevant for a minimum of 4 years. The cost of malaria diagnosis and treatment was estimated for each individual from a societal perspective, in the local currency (CFA) and converted to US dollars at 2011 prices. The analysis applies the latest methods for estimating cost-effectiveness in cluster-randomized trials.

The enhanced 3-day participatory training was not only more effective, but also more cost-effective than the 1-day basic training: preliminary analysis indicates the cost per patient treated according to guidelines was $22.51 in the basic-arm and $9.74 in the enhanced-arm, when compared to control-arm. Upon scale up, it is estimated that introducing RDTs with enhanced training would cost-effective and save $1.28 per patient treated according to guidelines, compared to current practice.

Incremental cost-effectiveness analysis of introducing rapid diagnostic testing for malaria into registered drug shops in Uganda

Kristian Schultz Hansen[1], Anthony Mbonye[2], Sham Lal[1], Pascal Magnussen[3], Siân Clarke[1]

[1]ACT Consortium, London School of Hygiene and Tropical Medicine, London, United Kingdom; [2]Department of Community Health, Ministry of Health, Kampala, Uganda, [3]Faculty of Health and Medical Sciences, University of Copenhagen, Denmark

Universal access to diagnostic testing for malaria before use of artemisinin-based combination therapy (ACT) for positive cases is recommended by WHO. It is common in Uganda for people to seek treatment for malaria outside the formal health care sector often with private drug shops as their first choice. Parasitological diagnosis to guide malaria treatment is not usually offered in drug shops. A recent cluster-randomised trial in MUnited Kingdomono District, Uganda, demonstrated that testing with malaria rapid diagnosis tests (RDTs) in drug shops is feasible, can be associated with high provider compliance and resulted in significant increase in appropriate treatment compared to presumptive treatment. The incremental cost-effectiveness analysis of introducing RDTs in drug shops (intervention) as compared to current practice of presumptive diagnosis (control) was evaluated using a decision analytical approach. Provider costs incorporated the cost of community sensitisation, training of drug shop vendors, development of training material and the commodity costs of RDTs used and ACTs dispensed. Since treatment correctly targeted to malaria cases should result in more appropriate drug purchases and possibly improved ACT adherence, it is essential to estimate societal costs in order to assess the impact of potential savings arising from reduced expenditure and time lost on subsequent treatment seeking on the overall cost-effectiveness of the intervention. Household costs of health care seeking were captured in a sample of drug shop customers who were interviewed in their homes after their initial visit to a drug shop, to estimate all household costs incurred during a two-week period after the drug shop visit, including out-of-pocket expenditure for travelling, fees, diagnosis and drugs for the first and any subsequent treatment visits as well as the opportunity cost of lost time. The incremental cost and effects of introducing RDTs to increase appropriate ACT treatment in private, registered drug shops will be presented. Sensitivity analysis will be performed to identify factors influencing the incremental cost-effectiveness ratio of the intervention, such as provider adherence to test result, accuracy of the test, customers' willingness to purchase an RDT, and cost of different resource input.

Cost–effectiveness analysis of test based versus presumptive treatment of malaria in under 5 children in rural Ghana

Theresa Tawiah[1], Kristian Hansen[2], Frank Baiden[1], Seeba Amenga-Etego[1], Jayne Webster[2], Daniel Chandramohan[2], Seth Owusu-Agyei[1]

[1]Kintampo Health Research Centre, Ghana; [2]ACT Consortium, London School of Hygiene and Tropical Medicine, London, United Kingdom

Malaria still remains the number one cause of morbidity and mortality in the Brong Ahafo region in central Ghana. The availability of rapid diagnostic tests (RDTs) for malaria has made it possible for health facilities in the remote areas to parasitologically diagnose malaria where there are currently no microscopes to confirm malaria. Incremental cost effectiveness of RDTs (intervention) was compared to clinical judgement (control) for the diagnosis of uncomplicated malaria. A societal perspective was taken which included costs and benefits to all those affected by the interventions including children with fever and their carers. The provider perspective was also taken in assessing the cost implications for a District Health Management Team of introducing RDTs into their health centres. Effectiveness was measured in terms of health outcomes (presence of malaria or not as measured by research blood slides) and Disability Adjusted Life Years (DALYs). Cost data were collected at the household and facility level. At the household level, 100 children who were previously enrolled as participants in a recently completed trial (measuring the effects on malaria incidence of RDT-based diagnosis versus presumptive diagnosis), were randomly selected from 32 health facilities across 5 regions of Brong Ahafo. A structured questionnaire was used to collect data on direct costs (medical and non-medical) and indirect costs. Recurrent and capital costs were collected from purposely selected health facilities from each of the regions. Malaria treatment costs were estimated using both standard step-down costing and bottom-up costing methods. Sensitivity analysis was undertaken to examine the effects of varying uncertain variables on study findings as well as identifying the most important factors influencing the incremental cost-effectiveness ratio of the intervention.

Impact of RDTs and enhanced health facility-based care on costs and health outcomes in a high endemic area in Uganda

Eleanor Grieve[1], Catherine Maiteki-Sebuguzi[2], Deborah DiLiberto[1], Levi Mugenyi[2], Samuel Gonahasa[2], Florence Nankya[2], Kristian Hansen[1], Shunmay Yeung[1], Clare Chandler[1], Sarah Staedke[1 2].

[1]ACT Consortium, London School of Hygiene and Tropical Medicine, London, United Kingdom; [2]Infectious Disease Research Collaboration (IDRC), Kampala, Uganda

The ACT PRIME trial is designed to evaluate the impact of an intervention to enhance health facility care, including the introduction of malaria RDTs on malaria and febrile illnesses in children in Tororo, Uganda. Clusters were randomised to standard care or the health facility intervention, consisting of: (1) training in-charges in health centre management, (2) training of health workers in fever case management and use of RDTs, (3) training health workers in patient-centered services and (4) ensuring adequate supplies of artemether-lumefantrine and RDTs. While malaria RDTs should decrease overuse of antimalarial drugs, in an area of high malaria transmission, the cost-effectiveness of this strategy remains in doubt. This evaluation establishes the impact of RDTs and enhanced health facility-based care on costs and health outcomes in Tororo, an area of high malaria endemicity in Eastern Uganda.

Using outcome data collected from 1400 patient exit interviews and cost of resource use collected from household surveys, we adopt a decision analytic modelling approach to calculate the incremental cost-effectiveness ratio (ICER) of malaria cases appropriately treated in children under five, a primary outcome of the study. The appropriateness of treatment was assessed against an RDT performed by study personnel after the exit interview. Data on the costs of enhanced facility care and health facility were also collected.

As a method for summarising information on uncertainty in cost-effectiveness, cost-effectiveness acceptability curves (CEACs) will be generated using probabilistic sensitivity analysis. The CEAC indicates the probability that the health facility intervention is cost-effective compared with standard care, given the data observed and for a recommended cost-effectiveness threshold(s).

For policy makers to decide whether to scale-up such a programme, it is important to estimate the associated cost. Few studies report on costs of quality of care interventions. This presentation will estimate a full financial and economic costing to provide an estimate of the budgetary impact of a 'scale-up' to enhance public health facility-based care for malaria and febrile illnesses. We will examine a health service and societal perspective, the latter capturing both costs to the Ministry of Health and the (financial and opportunity) costs to patients and carers.

S02: Data-driven Decision-making in the Context of IRS Scale-up and Increased Insecticide Resistance

Chairs: Dr Derejee Dengela and Dr Christen Fornadel

Speaker 1: Dr Dereje Dengela, Maximizing Entomological Monitoring in Low resource Settings: Building Local Capacity, Abt Associates, Bethesda, MD, USA

Speaker 2: Dr Michael Coleman, The best bang for your buck: Using entomological monitoring and monitoring and evaluation to increase the impact of malaria interventions and save money, Abt Associates, Bethesda, MD, USA

Speaker 3: Dr Moussa Cisse, Mapping Insecticide Resistance for Malaria Control in Mali, West Africa, African Indoor Residual Spraying (AIRS), Bamako, Mali

Speaker 4: Prof. Akogbeto Martin, Dramatic Decline of Malaria Transmission after Implementation of bendiocarb using indoor residual spraying at a large scale in a context of high resistance of Anopheles gambiae to Pyrethroids, Benin, West Africa, Centre de Recherche Entomologique de Cotonou, Benin

Speaker 5: Dr William G. Brogdon, A new bioassay of insecticide resistance intensity and its use for analysis of the impact of IRS insecticide rotation on Insecticide Resistance Management (IRM), Division of Parasitic Diseases and Malaria, Center for Global Health, Centers for Disease Control and Prevention,Atlanta,Georgias,USA

Maximizing Entomological Monitoring in Low resource settings: Building Local Capacity

Dereje Dengela[1], Brad Lucas[1], Christen Fornadel[2], Allison Belemvire[2], Kristen George[2]

[1]Abt Associates, Bethesda, MD, USA; [2]PMI_U.S. Agency for International Development (USAID), Washington, DC, USA

BACKGROUND: Insecticide Treated Nets (ITNs) and Indoor Residual Spraying (IRS) have been scaled up significantly in the past ten years. The increase in the coverage of these interventions is associated with a decline in malaria burden in a number of malaria endemic countries. Although the spread of insecticide resistance presents a severe threat to control gains, many countries lack a strong entomological monitoring program to address the problem. The two most common factors that limit entomological monitoring activities are lack of skilled personnel and functional insectaries. In PMI supported IRS countries, efforts were made to address these constraints. As a result the use of entomological

data to inform selection of insecticides for IRS, monitor quality of spraying, and monitor residual life of the sprayed insecticides has become standard practice.
METHODS: In countries constrained by a lack of trained entomologists, junior health professionals or even high school graduates were recruited locally. Up to ten days extensive training was provided on basic entomological monitoring, with a focus on practical demonstrations and field exercises. In order to ensure the quality of their work, recruits were supplied with the necessary equipment and deployed to conduct field work under the direct supervision of experienced entomologists before being allowed to work independently. Continuous assessment, technical support, and on the job training were provided to improve their skills. In addition, a shipping container was converted to a functioning insectary where this infrastructure was lacking.
RESULTS: The newly trained professionals/technicians were able to collect good quality basic entomological data with minimum support from experienced entomologists, including insecticide resistance data. The insectary made from a shipping container adequately supported entomological monitoring.
CONCLUSION: In countries where there is lack of trained entomologists, training and deployment of junior professionals or technicians was sufficient, with mentorship from entomologists, to obtain the necessary entomological data. The container insectary is a cost effective innovation viable for replication in low resource settings.

The best bang for your buck: Using entomological monitoring and M&E to increase the impact of malaria interventions and save money

Mike Coleman
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The World Malaria Report estimates funding for malaria control at US$2600millions, and yet current funding falls short of the amount required for universal access to malaria interventions. Here we explore how improved monitoring and surveillance could improve the impact of current funds.

Vector control is primarily reliant on indoor residual spraying (IRS) and long lasting pyrethroid impregnated nets (LLINs). It has been over 30 years since the last active ingredient for insecticide was added to the arsenal. Insecticide resistance threatens these tools and new active ingredients, or, novel formulations are increasing the cost of vector control. Establishing if insecticide resistance is operationally important is challenging, but not impossible. Recently the Bioko Island Malaria Control Project reintroduced pyrethroids for IRS. These same tools have been applied in Zambia where insecticide resistance is a growing concern. Understanding the insecticide resistance in both instances has guided control efforts according to the WHO Global Plan for Insecticide Resistance Management, and potentially reduce costs.

A number of studies have focused on local targeting of vector control, targeting breeding sites or houses at higher risk of disease transmission. These can be of benefit and reduce the disease incidence at a lower cost. However, many countries have different ecological zones that support different malaria vectors that will have different behavior, transmission rates and insecticide resistance. By, tailoring the control programme in each zone it is feasible to reduce costs. In Zambia, large areas are dominated by *Anopheles funestus* susceptible to DDT and organophosphate; as well as areas dominated by *An. gambiae* susceptible to only OP's. By targeting the expensive OP's at *An. gambiae* the cheaper DDT could be targeted at *An. funestus.*

As countries move toward elimination then universal coverage becomes less cost effective and targeted vector control is important. Successful models of individual case surveillance that have been established in places like Saudi Arabia and South Africa, can and have been used to target hotspots and potential outbreaks of disease. They can also be used to target vector control activities in a more cost effective manner.

Mapping of Insecticide Resistance for Malaria Control in Mali, West Africa.

Moussa BM Cisse[1,2], Josepha Trore[1,2], Seydou Traore[1,2], Chitan Keita[1], Elie Benkineza[1,2], Dereje Dengela[2], Bradford Lucas[2], Jules Mihigo[3,4], Aboubacar Sadou[4], Kristen L George[5], Christen Fornadel[5], Suzanne Powell[3], and Raymond Beach[3]
[1]African Indoor Residual Spraying (AIRS), Bamako, Mali; [2]Abt Associates, Bethesda, MD, USA; [3] President's Malaria Initiative (PMI) _Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA; [4]PMI_Mali, Bamako, Mali; [5]PMI_U.S. Agency for International Development (USAID), Washington, DC, USA

BACKGROUND: There is growing concern that insecticide resistance (IR) may impede the effect of Indoor Residual Spraying (IRS) and Insecticide Treated Nets (ITNs) in Mali. Using PMI-supported IR data collected annually, the objective of this study was to investigate the susceptibility level and distribution of *An.gambaie s.l.*to four classes of insecticides recommended for malaria vector control in Mali to help mitigate resistance and plan future effective vector control interventions.
METHODS: The World Health Organisation tube bioassay test was used to determine susceptibility in geographic populations of *An.gambaie s.l.*to: dichloro diphenyl trichloroethane (DDT); fenitrothion; bendiocarb; deltamethrin and lamdacyhalothrin; and. One to five day old non-blood-fed female adults reared from field collected larvae and pupae were tested. Thirteen sites were chosen based on factors that affect levels of resistance such as scale of ITNs distribution, use of IRS and insecticides for agriculture and geographic diversity.

RESULTS: *Anopheles gambaie s.l.* test results from study areas depicted high levels of resistance to DDT. Full susceptibility to fenitrothion was recorded in all test sites. Reduced susceptibility to bendiocarb was noticed in 2 of 13 test districts that are known for growing cotton and intensive use of pesticides in cotton cultivation areas. Increased resistance to deltamethrin, and lambdacyhalothrin was detected in all areas where the tests have been conducted. This increase in resistance may be explained by cross resistance between DDT and pyrethroids and wide use of pyrethroids for agriculture and increased coverage of pyrethroid treated nets. The study revealed *An.gambaie s.l.* are resistant to DDT, deltamethrin, and lambdacyhalothrin, and increased resistance to bendiocarb in areas with intensive use of pesticides for agriculture and full susceptibility to fenitrothion.
CONCLUSION: These results highlight the importance of routine resistance monitoring, resistance mechanism identification, and the need to study the implication of reduced susceptibility to pyrethroids on the efficacy of ITNs.

Dramatic decline of malaria transmission after implementation of bendiocarb using Indoor Residual Spraying at a large scale in a context of high resistance of *Anopheles gambiae* to pyrethroids, Bénin, West Africa

Martin Akogbeto , Gil Padonou , Razaki Ossse , Rock Aïkpon
Centre de Recherche Entomologique de Cotonou, Benin.

In Benin, the National Malaria Control Program has been implementing Indoor Residual Spraying (IRS) using bendiocarb insecticide since 2008. The choice of IRS is a decision of Benin to reinforce the action of the Long Lasting Insecticidal Nets (LLINs) and in line with National Malaria Control strategy.

IRS is on-going in Benin since 2008. Bendiocarb is the insecticide of choice for IRS due to widespread vector resistance pyrethroids in IRS targeted areas. The application dose was 0,4g/m^2 of bendiocarb sprayed surface. Spraying was conducted by people recruited and trained from the community. For all the spray rounds, the coverage rate was more than 85%. During field operation, spray operators were provided with personal protective equipment to ensure their safety.

Entomological parameters recorded in the control areas were compared to those of intervention sites. Results obtained were encouraging. In southern Benin, the study has shown a drastic decrease of *An. gambiae* biting rate in areas under IRS intervention. ELISA analyses were negative for circumsporozoite (CS) antigen of *Plasmodium falciparum* during the whole period of intervention. Parous rate was low in areas under IRS with bendiocarb possibly due to the effect of IRS on mosquito survival. Similar results were registered in the North in Atacora department with more than 70% reduction of malaria transmission compared to the control area.
In Benin, bendiocarb insecticide was found a good alternative for IRS strategy in areas where *An. gambiae* has developed a high resistance to pyrethroids. However, after 2 years of IRS in the North, a decrease of *Anopheles gambiae* susceptibility to bendiocarb was noted. The emergence of bendiocarb resistance in the northern Benin might partially be explained the use of high quantity of various insecticides by farmers against cotton pests. The North of Benin is the region of the highest production of cotton and use of agricultural insecticides.

A new bioassay of insecticide resistance intensity and its use for analysis of the impact of IRS insecticide rotation on insecticide resistance management (IRM)

Willim G. Brogdon[1], Musapa Mulenga[2], Mulakwa Kamuliwo[2], Patricia M.Kasoma[2], Claudia Corredor_ Medina[1]
[1]Entomology Branch, Division of Parasitic Diseases and Malaria, Center for Global Health, Centers for Disease Control and Prevention ,Atlanta,Georgias,USA; [2]Zambia Integerated syetems strengthening Program, Lusaka,Zambia and National Malaria Control Centre, Lusaka, Zambia.

BACKGROUND: Practical field application of the WHO paper-based and CDC bottle-based bioassays have focused on measuring insecticide resistance frequency using diagnostic dosages of insecticides. With either method a range of dosages permits calculation of resistance ratios for assessing resistance intensity. Unfortunately, precise direct calculation of a resistance ratio in the field requires a prohibitive number of mosquitoes, especially where it is desired to assess resistance in wild caught mosquitoes that are more representative of the epidemiologically significant mosquito population.
METHODS: Our bottle bioassay-based intensity assay utilizes a series of bottles treated with multiples of the diagnostic dose. Here, we report measurement of resistance intensity in field-collected indoor resting *Anopheles gambiae* s.s. and Anopheles funestus.
RESULTS: *Anopheles gambiae* s.s. populations contained mosquitoes that survived five times the diagnostic dosage of deltamethrin and ten times the diagnostic dosage of DDT at the diagnostic time, while showing complete susceptibility to bendiocarb and lambda-cyhalothrin. Anopheles funestus populations contained mosquitoes that survived ten times the diagnostic dosage of deltamethrin while showing complete susceptibility to DDT, lambda-cyhalothrin and bendiocarb. Instances of higher intensity resistance were focal and associated with evidence of

control failure. Continued observation of high intensity resistance foci for both anopheline species revealed a rapid return to deltamethrin susceptibility following insecticide class rotations for one season.
CONCLUSION: The simple and inexpensive CDC bottle-based intensity assay shows promise as a rapid diagnostic tool for severe resistance foci associated with control failure whether based on IRS or bed nets. Moreover, the method has successfully documented a return to pyrethroid susceptibility following insecticide class rotations conducted as an exercise in resistance management techniques in Zambia.

S03: Introducing RDTs in different health sectors: interventions and impact in ACT Consortium studies

Chairs: Dr Clare Chandler and Dr Evelyn Ansah

Speaker 1: Dr Hugh Reyburn, Prescriber use of RDT results in primary and secondary care in Tanzania: findings from an observational study and a three-arm cluster randomised trial,
Speaker 2: Prof Obinna Onwujekwe, Effectiveness of provider and community interventions for the treatment of uncomplicated malaria in Enugu state, South-eastern Nigeria
Speaker 3: Dr Anthony Mbonye, Factors influencing RDT uptake, adherence, treatment and referral by community medicine distributors: findings from a community randomised trial in Uganda
Speaker 4: Dr Frank Baiden, Could treatment outcomes be a barrier to effective implementation of test-based management of malaria in under-five children in rural Ghana?
Speaker 5: Dr Clare Chandler, Chaired panel and audience discussion of RDT scale up: how, where and with what impact? Department of Global Health and Development, London School of Hygiene & Tropical Medicine

OBJECTIVE: This symposium will present findings from across ACT Consortium studies that have evaluated the impact of introducing RDTs using different implementation strategies in different health sectors.
Rationale: The challenges of ensuring valuable ACT antimalarials reach those who need them and are not taken in the absence of malaria parasitaemia are now well known. To address the overuse of antimalarials and improve patient care, WHO guidelines for malaria case management were updated in 2010 to recommend parasitaemic confirmation of all cases treated as malaria where possible. This has been made possible by the advent of Rapid Diagnostic Tests (RDTs) for malaria. RDTs have now been suggested to be introduced across different types of health care practitioner, from community health workers, to drug shops, to public health centres to hospitals. While the potential for RDTs to improve case management in these different arenas stands in theory, in practice researchers have reported mixed results of their uptake and of adherence to test results.
CONTENT: The ACT Consortium is a global research partnership of 16 projects working in 9 malaria endemic countries to tackle questions relating to access, targeting, safety and quality of ACTs. In this symposium, we will be presenting findings from four projects that have designed and evaluated novel interventions to support the introduction of RDTs in different health sectors. Each project invested significant time in formative research to understand existing behaviours in relation to diagnostics, and undertook careful design of supporting interventions to maximise RDT uptake and adherence. Each project utilised rigorous randomised controlled trial methods to evaluate the impact of RDTs under different conditions and supporting interventions. Panelists will present results from different health sector and country contexts to show what supporting interventions were effective, and to show the impact of introducing RDTs on uptake of tests, adherence to results and treatment of RDT negative cases and patient level outcomes. The symposium will finish with a chaired discussion with audience members to discuss how and where RDTs may be most appropriate to scale-up, and what impacts may be expected with such scale-up in different sectors.

Prescriber use of RDT results in primary and secondary care in Tanzania: findings from an observational study and a three-arm cluster randomised trial

Bonnie Cundill, Hilda Mbakilwa, George Mtove, Frank Mtei, Annie Willetts, Clare Chandler, Harry Mwerinde, Sia Msuya, Oscar Mafole, Florida Muro, Renata Mandike, Rahim Mwinyishehe, Raimos Olomi, Chris Whitty, Hugh Reyburn

A number of studies have demonstrated the preference for a diagnosis of malaria in Africa even in the face of negative parasitological test results and this threatens the success of the roll out of malaria rapid diagnostic tests (RDTs).
We conducted a 3-arm cluster randomised trial of interventions to improve prescriber practices with RDTs in 36 basic health facilities in NE Tanzania. All staff received the 2-day Ministry of Health (MOH) training in use of RDTs and intervention arms received 3 additional small group training sessions and a third arm received this in addition to the provision of patient leaflets. In the second half of the trial SMS feedback of prescribing and motivational messages were added.

Prior to the intervention, 37% of patients received an antimalarial drug and this fell to 753/8,975 (8%), 1250/10,147(3%) and 250/10,190(2%) in control, training and training plus leaflets arms respectively (p<0.001). A small additional effect was attributed to the use of SMS motivational messages (=0.02) but not feedback of prescribing results (p=0.08).

It appears that health staff are becoming more responsive to basic training messages on the use of RDTs, probably the result of increasing levels of trust in test results and a growing awareness of the likelihood of malaria.
In a separate study we compared the results of blood slides with RDT (Paracheck) results in children admitted to hospital for severe febrile illness. Of 3,639 children in the study 2,195 (60.3%) were slide-positive. The sensitivity and specificity of Paracheck were 97.5% (95% CI 96.9-98.0) and 65.3% (95% CI 63.8-66.9) respectively. There was an inverse relationship between age-specific prevalence of parasitaemia and the specificity of Paracheck and this was likely to be due to persistence of HRP2 following recent clearance of parasites.

The combination of a positive Paracheck and negative blood slide result identified a group of children at risk of bacterial infection. While Paracheck was highly sensitive, the tests failed to detect a small number of high-density infections. At high levels of malaria transmission caution should be used in restricting antimalarial treatment to children with a single negative parasitological test.

Effectiveness of provider and community interventions for the treatment of uncomplicated malaria in Enugu state, South-eastern Nigeria

Wiseman V, Ezeoke O, Nwala E, Mangham LJ, Cundill B, Enemuo J, Uchegbu E, UzochUnited Kingdomwu B, Onwujekwe O.

There is increasing interest in the use of parasitological testing for malaria case management in Nigeria. A formative survey for this study found that less than 1% of patients were tested for malaria. ACTs were received by only 22.4% of all patients and 37.9% of patients received SP. This study hence examined the effectiveness of interventions for improving the diagnosis and treatment of uncomplicated malaria amongst febrile patients attending public healthcare centres, patent medicine dealers (PMDs) and pharmacies (private).

The interventions were evaluated using a three-arm cluster randomized trial. The three arms were: the Control, with supply of rapid diagnostic tests (RDTs) with basic instruction; Intervention arm 1, with an interactive provider intervention and supply of RDTs; and Intervention arm 2, which was the provider intervention from arm 1 plus a school-based community intervention. There were some contextual differences in the interventions across different types of providers and clusters. The interventions were evaluated using a patient exit survey, log of malaria tests conducted, provider survey and a household survey. Data collection commenced approximately three months after the interventions were implemented. The primary outcome measure was the proportion of patients that reported a fever or suspected malaria and received treatment according to malaria guidelines. There were several secondary outcome measures.

This presentation will focus on the design and implementation of the provider and school based interventions. We will also discuss the logic model underpinning this study, which illustrates the expected effect of the interventions on the treatment received by patients. Primary and secondary outcomes will be presented. In summary, there was a relative general increase in testing compared to formative study, but the number of patients that were tested was still low across the three different arms despite the availability of RDTs in the facilities.

Factors influencing RDT uptake, adherence, treatment and referral by community medicine distributors: findings from a community randomised trial in Uganda

Anthony K. Mbonye, Richard Ndyomugyenyi, Pascal Magnussen, Clare I.R. Chandler , Sham Lal, Eleanor Hutchinson, Kristian S. Hansen, Sian E. Clarke[3]

Universal access to diagnostic testing for malaria is recommended by WHO, to encompass all treatment providers. Community-based strategies which aim to increase access to malaria treatment should also aim to promote the use of malaria rapid diagnostic tests (mRDTs) prior to treatment. Two key approaches where mRDTs could be introduced are (1) into community case management for children under 5 years and (2) at drug shops, where malaria treatment is often purchased, for all age groups. Yet limited evidence exists on the effectiveness or cost-effectiveness of mRDTs with different types of health care provider, or how this may vary in different transmission settings.

Three cluster randomised trials were undertaken to address this gap, comparing mRDT use with existing practice of presumptive treatment, including two large scale trials introducing mRDTs to community medicine distributors, in a high and a low malaria transmission setting in rural Western Uganda, and a third trial in 65 registered drug shops in Central Uganda. All providers in all arms received a package of training and job aids on communication skills, clinical algorithms to diagnose and treat malaria, identification of signs requiring referral to health facilities and record keeping. Providers randomised to mRDT clusters were also given training on how to perform, interpret an mRDT and

prescribe artemisinin-based combination therapy (ACTs) based on the test's result. Supporting interventions included activities to raise community awareness to emphasise that not all fevers are malaria, and that blood tests can confirm malaria before treatment.

High levels of provider adherence to RDT results were observed in all three trials, resulting in marked improvement in the targeting of malaria treatment in all settings. This talk will outline the design of the interventions with providers and other supporting interventions. Drawing on evidence from the trials, pre-intervention formative research, and post-intervention interviews with patients and providers, we shall discuss enabling factors that may have helped support mRDT introduction in Uganda, and compare and contrast findings across the different provider and transmission settings.

Could treatment outcomes be a barrier to effective implementation of test-based management of malaria in under-five children in rural Ghana?

Frank Baiden, Jayne Webster, Seth Owusu-Agyei, Daniel Chandramohan

World Health Organisation guidelines now require that all cases of malaria be confirmed through test before treatment is started. This presentation derives from lesson learnt in deploying test-based management of malaria in 32 health centres and 1 district hospital in the Brong Ahafo Region of Ghana. We used a mixed methods approach to evaluate treatment outcomes for malaria and non-malaria febrile illnesses managed using the revised approach, assessed adherence to current guidelines for the management of under-five childhood illnesses as proxy indicator of health worker adherence to the new policy and assessed the acceptability of the revised guideline to caregivers. Treatment outcomes for malaria and non-malaria febrile illnesses differ significantly in terms of recovery from fever, anemia and in caregiver perception of treatment outcomes, with relatively poorer outcomes for children with non-malaria fevers. Health worker adherence to current guidelines is poor. Respiratory rate is checked in only 4% of children. Out of the 11 required tasks, it is in only 35% of children that more than 6 tasks are performed. All 11 tasks were performed in only 1% of children. Caregiver acceptance of test-based treatment of malaria is however high (98% of caregivers). Factors that promote caregiver acceptability include the perception that blood test represents improvement in the quality of care and is likely to lead to improved treatment outcomes. Implementation of the revised guidelines in rural Ghana is likely to be bolstered by high caregiver acceptability, but undermined by poor health worker adherence to guidelines. Any perception that it leads to poorer treatment outcomes for children with non-malaria fevers could undermine acceptability. Improvement in the management of non-malaria fevers is important for effective implementation of the new policy.

S04: Field monitoring of malaria drug efficacy and safety

Chairs: Dr Godwin Ntadom and Dr Philippe Guérin.

Speakers 1: Dr. Philippe Guérin, An African platform for exchanging scientific and public health information on malaria drug resistance, World Wide Artemisinin Resistance Network, United Kingdom
Speakers 2: Dr Godwin Ntadom, Nigeria Drug Therapeutic Efficacy Tests, NMCP Nigeria
Speaker 3: Dr. Ambrose Talisuna, Antimalarial drugs' efficacy and safety in repeated administrations in a high-endemic area of Uganda, University of Oxford-KEMRI-Wellcome Trust Programme Nairobi – Kenya
Speaker 4: Prof. Wilfred Mbacham, Multiple First line Therapies: Farce or Solution to stifle the Emergence of anti-malaria drug resistance, University of Yaoundé, Cameroon

The risk of emergence of malaria drugs resistance and unexpected adverse events have always been a source of concern for the malaria community. Clinical studies performed for registration cannot mimic the conditions of real-life usage of medicines and must be complemented by additional studies. Signs of resistance to artemisinin derivatives have been shown in south East Asia requiring coordinated field monitoring and data sharing. This symposium will discuss available networks and processes to collect high-quality efficacy and safety data, as well as potential strategies to minimize the risk of emergence of resistances.

S05: Multi-Stage Multi-Component Malaria Vaccines

Chairs: Professor Adrian VS Hill and Dr Simon Draper

Speaker 1: Dr Caroline Ogwang, Efficacy of vectored prime-boost vaccines against malaria infection in Kenya, Kenya Medical Research Institute, Centre for Geographical Medical Research (Coast), Kilifi, Kenya
Speaker 2: Professor Adrian V. S. Hill, Multi-Stage Malaria Vaccines: Why and How. The Jenner Institute, University of Oxford
Speaker 3: Dr Simon Draper, Novel Blood Stage Vaccine Candidates, The Jenner Institute, University of Oxford

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S06: Implementation updates - Global Malaria Programme, WHO

Chairs: Dr Robert Newman and Prof Kevin Marsh

Speaker 1: Dr Andrea Bosman, Scaling up malarial diagnostic testing and effective treatment, World Health Organisation, Switzerland
Speaker 2: Dr Richard Cibulskis, Improving routine malaria surveillance,World Health Organisation, Switzerland
Speaker 3: Dr Franco Pagnoni, Expanding Access to integrated Community Case Management (iCCM): RAcE 2015, World Health Organisation, Switzerland
Speaker 4: Dr Abraham Mnzava, Global policy updates on malaria vector control, World Health Organisation, Switzerland

Scaling up malarial diagnostic testing and effective treatment

Andrea Bosman
Coordinator Diagnostics, Treatment and Vaccines, Global Malaria Programme, World Health Organisation

Since 2000, WHO recommends artemisinin-based combination therapies (ACTs) as 1st-line treatment of falciparum malaria. Between 2004 and 2007 most endemic countries adopted ACTs as national treatment policy. The delivery of quality-assured ACTs increased from low levels, 5 million treatment courses delivered in 2004, to 83 – 97 million in 2006-2007, increasing up to 278 and 332 million in 2011 and 2012. The significant increase in procurement of ACTs in 2011 (53% compared to 2010) is due to the implementation of the Affordable Medicines Facility for malaria (AMFm), an initiative hosted by the Global Fund to deliver co-paid ACTs mainly to the private sector. The numbers of ACTs delivered to malaria endemic countries in 2011 and 2012 exceeded the estimated total cases of malaria, ranging from 154 to 289 million according to WHO figures in 2010.

WHO issued guidance on malaria RDTs in 1998, but recommended universal access to malaria diagnostic testing to all malaria suspected cases, including children under five in areas of intense transmission, only in 2010. Already in 2011, the majority of countries with on-going transmission (87 out of 99) adopted the new WHO policy of universal diagnostic testing in all age-groups. The procurement of RDTs meeting international quality standards has rapidly increased from 45 million tests in 2008 to 155 million in 2011. Since 2008 WHO, in collaboration with TDR, FIND and CDC Atlanta, is implementing the product testing programme to assess the performance of RDTs on the market, and to evaluate RDT lots being procured. As a result, the quality of malaria RDTs has improved, with greater proportion of RDTs meeting WHO procurement criteria at each round of product testing (round 5 is currently ongoing).

WHO launched the T3: Test, Treat and Track initiative on World Malaria Day 2012. Through this initiative, the scaling-up of malaria diagnostic testing is being promoted to improve ACT targeting and detection of non-malaria febrile illness, and to improve the reliability of malaria surveillance data. In view of the changing malaria landscape, more international and national efforts are needed to correct the mismatch between ACT and RDT procurement data.

Improving Routine Malaria Surveillance

Richard Cibulskis
Coordinator Strategy, Economics and Elimination, Global Malaria Programme, World Health Organisation

Information on the number and distribution of malaria cases and deaths is critical for the design and implementation of malaria control programmes. It is needed to determine which populations are most affected by malaria so that resources can be targeted to those most in need. Information on the incidence of disease compared to past levels is needed to alert programmes about epidemics, so that control measures can be intensified. Data on changes in disease incidence and mortality are also needed to monitor the success of a programme and to determine whether it is performing as expected or whether adjustments are required.

The capacity of malaria surveillance systems to provide information on the distribution of and trends in malaria varies widely across the globe. WHO has provided guidance on designing and managing surveillance systems for malaria control and elimination so that malaria programmes can obtain more complete and accurate information on incidence and mortality, which can be used to help plan and monitor the programme.

Recent developments in diagnostic testing present new opportunities for malaria surveillance systems. The availability of inexpensive, quality-assured rapid diagnostic tests for malaria means that parasite-based diagnosis is now possible at the community level. Malaria surveillance can be based on confirmed rather than suspected cases at all levels of the health system. As malaria control measures expand and the proportion of fevers due to malaria falls rapidly, it becomes increasingly important to track confirmed malaria case, so that resources can be targeted and progress in malaria control is accelerated.

Despite this progress, malaria surveillance systems detect only 10% of cases estimated to occur globally. Case detection rates are lowest in countries with the highest number of malaria cases and in 41 countries around the world, accounting for 85% of estimated cases, it is not possible to make a reliable assessment of malaria trends due to incompleteness or inconsistency of reporting over time.

This presentation will (i) discuss bottlenecks in case detection that need to be overcome, (ii) describe the Disease Surveillance for Malaria Control and Disease Surveillance for Malaria Elimination manuals released by WHO.

Expanding Access to integrated Community Case Management (iCCM): RAcE 2015

Dr Franco Pagnoni

Team Lead for Rapid Access Expansion 2015, Global Malaria Programme, World Health Organisation

Despite progress since 1990 in reducing the under-five mortality in sub-Saharan Africa, it remains unacceptably high and most deaths are from infectious diseases, nearly all of which are preventable. Facility-based services alone often do not provide adequate access to treatment, particularly within the crucial window of 24 hours after onset of symptoms. Programmatic experience has demonstrated that integrated community case management (iCCM) for malaria, pneumonia and diarrhoea implemented at community level, increases equitable access to high impact treatments and leads to a reduction of child mortality. ICCM has been promoted by global agencies and adopted by national governments in many countries.

In 2012, the WHO Global Malaria Programme (GMP) was awarded a grant by the Canadian International Development Agency (CIDA) to support scaling up of iCCM in five countries of sub-Saharan Africa. The goal of the Rapid Access Expansion (RAcE) 2015 project is to assist countries with the highest mortality burden to achieve the Millennium Development Goals by increasing coverage of diagnosis, treatment, and referral services for these major causes of childhood mortality. In each country, RAcE 2015 will be implemented by civil society Organisations (CSO) selected by WHO to operate in full compliance with the disease control strategies of the Ministry of Health (MoH), as an integral part of the government's health services.

The sustainability of donor-funded programmes being a known, major challenge, measures have been taken to ensure the project's sustainability and complementarity to existing iCCM programmes. These include the full ownership by the national health authorities of the iCCM interventions to create the basis for a successful handover upon conclusion of the project. In each country, the Ministry of Heath was fully involved in providing guidance to CSOs during the conception of the programme, as well as in their selection and supervision.

This presentation will provide an introduction to the RAcE 2015 project and describe how it will lead to strengthened iCCM programmes in both target countries and more broadly in sub-Saharan Africa.

Global policy updates on malaria vector control

Abraham Mnzava

Coordinator Malaria Vector Control, Global Malaria Programme, World Health Organisation

During its meeting in September 2012, the Malaria Policy Advisory Committee (MPAC) recommended that the WHO Global Malaria Programme establish a Vector Control Technical Expert Group (VCTEG). The VCTEG was tasked with reviewing and providing guidance and making draft recommendations to the MPAC on the implementation of malaria vector control including programme management.

The responsibilities of the VCTEG are to review and recommend to MPAC the predicted effectiveness and appropriate mix of vector control interventions for particular situations, including: the adoption of new forms of vector control following recognition of "proof of principle" from the Vector Control Advisory Group (VCAG); the formulation of evidence-based norms, standards and guidelines for the implementation and management of malaria vector control; policy issues on building capacity for entomological monitoring and optimization of vector control investments; and identification of gaps in evidence and areas of research to improve the management of malaria vector control.

The VCTEG is distinct from the newly formed VCAG in that the latter is focused on tool development and validation across all vector control and is jointly managed by the WHO Departments of Neglected Tropical diseases (NTD) and the Global Malaria Programme (GMP), while the VCTEG is focused on strategies and implementation. The VCTEG comprises a mixture of skills, including public health entomology, insecticide resistance, epidemiology, impact assessment of vector control, program management and heath economics.

During its recent meeting in July 2013, the VCTEG reviewed evidence and made recommendations on key vector control strategic issues, including maintenance of universal coverage with Long Lasting Insecticidal Nets (LLINs); guidance on estimating the physical life span of LLINs in the field; and guidance on capacity building in vector control. The VCTEG also reviewed progress on guidance for prioritizing vector control interventions when resources are constrained; entomological surveillance; the rationale for combining LLINs and Indoor Residual Spraying; tools for personal protection; and vector control for early and outdoor transmission.

This presentation will introduce the newly established Vector Control Technical Expert Group and Vector Control Advisory Group at WHO and describe outcomes of the recent VCTEG evidence reviews.

S07: Drug quality and the fight against malaria

Standard and Novel Approaches to Assessing Antimalarial Drug Quality in the Reference Laboratory and the Field

Michael D. Green
US Centers for Disease Control and Prevention

The world-wide availability of poor-quality antimalarial medicines is a significant health issue and poses a threat to malaria disease management. Malaria is most prevalent in developing countries where drug regulatory agencies lack resources to adequately monitor and enforce good drug quality. Also, there are few quality-assured reference laboratories in the malaria endemic countries. As a consequence, suspicious samples destined for chemical analysis must be shipped to these reference laboratories thus increasing the sample burden for these labs thereby delaying results and subsequent action. The objectives of this presentation are to discuss the standard analytical techniques used by the reference labs and provide alternative and complimentary affordable field methods to quickly and accurately screen samples collected for drug quality evaluations. The pros and cons of standard non-destructive spectroscopic methods, colorimetric, and simple physico-chemical evaluations will be discussed along with suggested techniques adapted for use under various field conditions. Also, new ideas for detecting suspicious medicines will be presented.

S08: Delivering on the promise of better medicines for children

Chairs: Mr George Jagoe and Dr Georges Ki-Zerbo

Speaker 1: Dr Florence Camus-Bablon, Quality assured pediatric ACTs are available: why aren't they more widely adopted? The example of Western and Central Africa, A2Meds, MMV Consultancy, France

Speaker 2: Dr Hélène Degui, The importance of harmonization and other regulatory initiatives to reinforce medicine registration practice and support WHO-backed international guidance on the best treatment options for children. Executive Secretary of OCEAC, in charge of harmonization of national pharmaceutical policies in Central Africa

Speaker 3: Dr Kanza Nsimba Maurice, Addressing the demand barrier at community level - Integrated Community Case Management in DRC: lessons learned and challenges Directorate of Studies and Planning, Ministry of Health, DRC

Speaker 4: Dr Mamadou Lamine Diouf, An important breakthrough for protecting children: the opportunities and challenges of scaling up Seasonal Malaria Chemoprevention in Senegal, National Malaria Control Program, Senegal

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Quality assured pediatric ACTs are available: why aren't they more widely adopted? The example of Western and Central Africa.

Dr Florence Camus-Bablon
A2Meds, MMV Consultancy, France

Children are still paying a heavy toll from malaria: a child dies from malaria every minute. In 2010, between 610.000 and 971.000 lives were lost to malaria; 86% of those deaths occurred in children under 5 years old, and 90% occurred in Africa. Today, new WHO-approved options to treat children with uncomplicated malaria have emerged, yet their adoption is slow, especially in the private sector. Following WHO recommendations is critical, not only to ensure the

most appropriate treatment for sick children, but also to diminish drug pressure on ACTs, given the risk of the spread of artemisinin resistance that has now been documented in Asia. Dr Florence Camus-Bablon will present a study commissioned by MMV to identify barriers and levers of change to facilitate the adoption of WHO recommended options to treat non complicated malaria in children in 6 francophone Africa countries. Large numbers of prescribers and patients continue to use non-recommended antimalarials to treat children, including monotherapies, antimalarials of varying quality as well as syrups and suspensions. Apart from concerns about sub-standard drugs that slip into the informal unregulated private sector, there are multiple antimalarials legally approved for marketing in the formal private sector -over 150 in some countries-, and many don't follow WHO recommendations. The lack of demand for quality pediatric medicines can also be attributed to a paucity of information regarding essential medicines and to insufficient dissemination of international guidance on the correct use of recommended treatments, particularly with private sector Health Care Providers.

The importance of harmonization and other regulatory initiatives to reinforce medicine registration practice and support WHO-backed international guidance on the best treatment options for children.

Dr Hélène Degui

technical advisor of the Executive Secretary of OCEAC, in charge of harmonization of national pharmaceutical policies in Central Africa

Dr Hélène Degui, Organisation de Coordination de lutte contre les Endémies en Afrique Centrale (OCEAC), will present the OCEAC's regional perspective on regulatory barriers and initiatives aiming to address these barriers. Access to quality medicines remains a major problem, particularly in Africa. Effective drug regulation is one of the keys to ensure that patients get access to medicines of good quality. One of the barriers is an inappropriate system of medicine regulation with weaknesses of medicine registration system, quality control, market surveillance and rational use of medicine. At the regional level, OCEAC's strategy is to strengthen the regulatory framework with increased finance mobilization and human resources to ensure medicines quality. Dr. Hélène Degui, who supports the coordination of the Central Africa regulatory harmonization and pharmaceutical cooperation, will present the regional harmonized regulations approved on June 14th 2013 by the 6 heads of States of the Economic and Monetary Community of Central Africa. The next steps and the current OCEAC's strategy to create a network of country regulatory agencies will be highlighted.

Addressing the demand barrier at community level - Integrated Community Case Management in DRC: lessons learned and challenges

Dr Kanza Nsimba Maurice

Directorate of Studies and Planning, Ministry of Health, DRC

Dr. Kanza will present DRC experience with integrated Community Case Management (iCCM). Although no child should die today of malaria, pneumonia or diarrhea, combined, these diseases are responsible for over 60% of global infant mortality. Self-medication and the informal unregulated private drug market represent a critical barrier to access to WHO-recommended treatments. Access to basic healthcare is a major challenge in DRC, and iCCM has been implemented since 2004 with the aim to reduce children under 5 morbidity and mortality by providing access to quality services to hard-to-reach populations.

iCCM is the treatment of childhood diseases in the community by trained and supervised Community Health Workers (CHW)s. We also call it the «Community Sites», because we don't build a building, but only use CHWs' homes (unless the population contributes itself to a building). Diseases treated are malaria, diarrhea, and pneumonia (including malnutrition), through an integrated approach.

We will describe strategies developed, those implemented, those that succeeded and those for which there is still effort to provide.

Along with the goals assigned to the ICCM, we will present

- Some salient steps in implementation since 2004 to date,
- The geographical extension,
- The technical capacity built at the Provincial level and Nurses who manage the process,
- Data collected and results of the program to date,
- The performances of the CHWs in terms quality of care, including specifics related to malaria case management,
- Results on TDR use by CHWs: both in 2008 during the feasibility study on TDR use by CHWs, in collaboration with the School of Public Health, and since 2012 to date.
- Success factors, constraints and challenges.

In addition, Dr Kanza will present other initiatives aiming to address demand barriers, such as the Innovative approach of "family kits" lead by the Health Ministry with the aim to scale up ACTs use in 4000 new Community Sites in the Country.

An important breakthrough for protecting children: the opportunities and challenges of scaling up Seasonal Malaria Chemoprevention in Senegal

Dr Mamadou Lamine Diouf
National Malaria Control Program, Senegal

In Senegal, malaria is endemic in the entire country with a seasonal increase in the south and eastern, rainiest regions (Kolda, Kédougou, Sédhiou, Tambacounda). Malaria control interventions in health facilities led to a lower morbidity and mortality between 2006 and 2009 with a decrease in malaria cases from 1 555 310 to 174 890, malaria deaths from 1 678 to 574 and all causes child mortality by 40%. Yet malaria remains a major cause of death in infants and children and the NMCP adopted SMC as a new intervention in malaria control in the four above-mentioned areas in March 2012.

Dr Diouf will provide an update on opportunities and challenges for the scale-up of SMC in Senegal. While early-stage pilots have shown excellent results in reducing malaria prevalence in children in areas with seasonal transmission, SMC presents delivery and sustainability challenges that have yet to be routinely overcome. Delivery requires monthly distribution of three-day chemoprevention regimens for three-to-four months per year. It relies on a door to door campaign strategy with community volunteers. On Day 1, volunteers, trained by health agents, administer drugs under the surveillance of mothers or guardians who substitute to volunteers on the 2 remaining days. There are unanswered questions about ensuring that SMC medicines are not used inadvertently for the treatment of malaria, and about assessing the ease with which volunteers and guardians dispense and patients comply with the three-day regimen, especially as existing formulations, not flavored, may trigger acceptance, observance and dose confusion challenges. Insufficient availability of drugs, weaknesses in supply chain and risk of non-rationale use may compromise cycle's completion; difficulties in household conservation of remaining tablets may lead to waste. The high operational costs require a consistent support by state and partners, while considering the option to integrate SMC with other community interventions. Dr Diouf will focus on SMC major challenges, options and unanswered operational questions with regards to delivery and sustainability.

S09: EVIMalaR research highlights in immunology, pathogenesis, and molecular biology

Chairs: Professor Lars Hviid and Professor Alister Craig

Speaker 1: Professor Lars Hviid, Introduction – EVIMalaR research on immunology, pathogenesis, and molecular biology of malaria, University of Copenhagen, Denmark.
Speaker 2: Professor Alister Craig, Endothelial Protein C Receptor (EPCR) and *Plasmodium falciparum* malaria – two sides of a pathological coin. Liverpool School of Tropical Medicine, United Kingdom.
Speaker 3: Ms Wiebke Nahrendorf, Humoral responses against *Plasmodium falciparum* after chloroquine prophylaxis and sporozoite immunization correlate with parasite exposure rather than predict protection, UMC St Radboud, Nijmegen, The Netherlands and National Institute for Medical Research, London, United Kingdom
Speaker 4: Dr Abdi Abdirahman, Naturally acquired immunity modifies both the quantity and diversity of PfEMP1 expressed by *Plasmodium falciparum* field isolates, Kenya Medical Research Iinstitute, Kilifi, Kenya
Speaker 5: Dr Vanessa Zuzarte Luis, miRNA fingerprinting of individuals with an ongoing *Plasmodium falciparum* liver infection, Instituto Medicina Molecular, Lisbon, Portugal

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OVERVIEW

Lars Hviid
Centre for Medical Parasitology (University of Copenhagen and Rigshospitalet, Copenhagen, Denmark

EVIMalaR is a joint research FP7 Network of Excellence, funded by the European Commission and currently involving 62 partners from 51 institutes in Europe, Africa, India and Australia (coordinated at the University of Glasgow, Scotland, United Kingdom). It seeks to integrate malaria research that is directed towards a better understanding of the basic knowledge of the parasite, its vector and of the biology of the interactions between the parasite and both its mammalian host and vectors. In this introductory talk, I will briefly outline the mission, structure, and achievements of EVIMalaR, with emphasis on vector and systems biology.

S10: Title: Does combined use of IRS and LLINs give better protection than one method alone?

Chairs: Professor Christian Lengeler and Dr Abraham Mnzava

Speaker 1: Dr Armel Djenontin/ Georgia Damien , Combination of malaria vector control interventions in a pyrethroid resistance area in Benin: a cluster randomised controlled trial, Centre de Recherche entomologique de Cotonou/MiVEGEC

Speaker 2: Dr Hmooda Kafy Combination of IRS with LLINs versus LLINs alone in Sudan: results of a very large cluster randomised trial, Manager of National VC Programme. Federal Ministry of Health, Sudan

Speaker 3: Dr Maragaret Pinder/ Lamin Jarju, Can indoor residual spraying provide additional protection against clinical malaria over current best practice of long-lasting insecticidal mosquito nets in The Gambia: A two-armed cluster-randomized study, Gambia MRC Unit and National Malaria Control Programme, The Gambia

Speaker 4: Dr Natacha Protopopoff /Phillipa West, Indoor residual house spraying in combination with insecticide treated nets provides additional protection against malaria compared to insecticide treated nets alone: results of a cluster randomised trial, London School of Hygiene and Tropical Medicine, London, United Kingdom

Speaker 5: Professor Immo Kleinschmidt, One or both: What conclusions can we draw from trials and programmatic evaluations about combining vector control interventions?, London School of Hygiene and Tropical Medicine, Keppel Street, London, United Kingdom

Indoor residual house spraying in combination with insecticide treated nets provides additional protection against malaria compared to insecticide treated nets alone: results of a cluster randomised trial

Philippa A West[1] & Natacha Protopopoff[1], Alexandra Wright[1], Zuhura Kivaju[2], Robinson Tigererwa[3], Reginald Kavishe[4], Franklin W Mosha[4], William Kisinza[2], Mark Rowland[1] & Immo Kleinschmidt[1].

[1]London School of Hygiene and Tropical Medicine, Keppel Street, London, United Kingdom; [2]National Institute for Medical Research, Amani Medical Research Centre, Muheza, Tanzania; [3]Department of Health, District Medical Office, Muleba, Tanzania; [4]Kilimanjaro Christian Medical College, Tumaini University, Moshi, Tanzania

BACKGROUND: Indoor Residual Spraying (IRS) and Insecticidal Treated Net ITN) are the two most effective methods used to prevent malaria in Africa. They have been combined in some setting to increase the impact on malaria but with little evidence so far that the combination provides any additional benefit than one method alone.

METHODS: A two-armed cluster randomised controlled trial was conducted in 50 villages in North-West Tanzania to investigate a potential additional benefit from combining IRS and ITN compared to ITNs alone. In 2011, the National Malaria Control Program aimed to provide each household with enough nets to cover all the sleeping places. In 2012, half of the clusters were randomly allocated to receive two rounds of IRS with Bendiocarb (a carbamate). Cross-sectional household surveys at two, six and ten months after the first round of IRS were used to compare the *Plasmodium falciparum* prevalence rate (*Pf*PR) in children 0.5-14 years old between the two study arms. Monthly entomological cross sectional surveys have been carried out in 40 clusters using CDC light traps. Anopheles density and entomological inoculation rate were compared between the two arms.

RESULTS: IRS coverage was high (90%) and ITN use was moderate (36 to 53%). *Pf*PR was lower in the study arm with IRS plus ITNs than in the ITN only arm for all surveys combined (intervention = 13.3% versus control = 26.1%, odds ratio (OR) = 0.43, 95% CI = 0.19-0.97). There was weak evidence that the effect of the supplementary IRS was strongest (p-value for interaction = 0.08) in the survey at six months after the first IRS round and two months after the second round (12.7% versus 30.5%, OR = 0.33, 95% CI = 0.15-0.75). In the intervention arm (LLIN+IRS), anopheles density was lower compared to the control arm (Rate Ratio = 0.16, 95%CI = 0.06-0.44, p=0.001). The monthly entomological inoculation rate was also significantly lower (RR: 0.01, 95%CI: 0.00-0.08, p<0.001).

CONCLUSION: This is the first evidence from a randomised trial showing that combining IRS with LLINs provides greater protection against malaria than using LLINs alone when LLIN coverage is moderate.

One or both: What conclusions can we draw from trials and programmatic evaluations about combining vector control interventions?

Immo Kleinschmidt

London School of Hygiene and Tropical Medicine, Keppel Street, London, United Kingdom

Four cluster randomized trials have investigated whether combining IRS and LLINs provides additional protection against malaria compared to one method alone. Three trials show no added effect, whereas one trial clearly shows additional protective benefit for those sleeping under an LLIN in a sprayed house, compared to those sleeping under an LLIN in an

unsprayed house. Non randomized observational studies also give conflicting results, some showing no added benefit whilst others, for example in Bioko, consistently show that those sleeping under a net in a sprayed house have lower infection risk compared to those not sleeping under a net in a sprayed house. What conclusions, if any, can be drawn? Are there circumstances under which there is a benefit to combining vector control interventions, and when is this a wasted effort? Can the differences be explained by differences in coverage of the interventions, by differences in transmission intensity, vector species or insecticide used? This talk will summarise the available epidemiological evidence for combining the two interventions.

S11: Answering key questions on ACT drug delivery in Africa: findings from the work of the ACT Consortium

Chairs: Prof David Schellenberg and Dr Shunmay Yeung

Speaker 1: Prof. David Schellenberg, Overview of the ACT Consortium, London School of Hygiene and Tropical Medicine, United Kingdom
Speaker 2: Prof. David Lalloo, Monitoring safety of ACTs, Liverpool School of Tropical Medicine, United Kingdom
Speaker 3: Dr. Harparkash Kaur, Detecting fake ACTs, London School of Hygiene and Tropical Medicine, United Kingdom
Speaker 4: Dr Charles Festo, Improving access to ACTs, Ifakara Health Institute, Tanzania
Speaker 5: Dr Evelyn Ansah, Improved targeting of ACTs, Ghana Health Service, Ghana

The ACT Consortium is a global research partnership that aims to answer key questions on optimizing the delivery and use of ACTs in Africa and Asia. Although there is much evidence on the efficacy of ACTs, there is little evidence on *how* they can best be deployed. At the last MIM conference in Nairobi in 2009, we described how we hope to change this by developing, implementing and rigorously evaluating different interventions and delivery mechanisms. We are now concluding 25 studies in 10 countries and preparing to share our findings. Studies are organized broadly around the research themes of improving ACT access, targeting, safety and quality. Our multi-disciplinary approach looked at the effectiveness and cost effectiveness of different strategies to improve ACT access and targeting, exploring the acceptability and safety of different strategies, and how to improve the use of ACTs by prescribers and by patients.

Overview of the ACT Consortium

Prof David Schellenberg

London School of Hygiene and Tropical Medicine, United Kingdom

This talk will provide an overview of the ACT Consortium's use of formative research to inform the design of complex interventions, and their evaluation using randomized trials, cohort and descriptive studies, and an impact evaluation. Economic and anthropological assessments have also been used to help understand how best to optimize the delivery and use of ACTs by prescribers and patients.

Monitoring safety of ACTs

Prof David Lalloo

Liverpool School of Tropical Medicine, United Kingdom

This talk will describe how the ACT Consortium is collecting, collating and evaluating data on the safety of ACTs when routinely deployed, including repeated use and use in specific groups (eg HIV positive individuals) and evaluating the possibility of pharmacokinetic interactions between ACTs and other commonly used drugs.

Detecting fake ACTs

Dr Harparkash Kaur

London School of Hygiene and Tropical Medicine, United Kingdom

The project is assessing the prevalence of falsified and substandard ACT formulations sold in some African and SE Asian countries. This presentation will explore robust sampling approaches at the country level to ensure that reliable estimates on the quality of ACT brands are generated. These estimates will provide the information to enable the country specific malaria control efforts to take appropriate steps to ensure that the ACTs that the patients are taking are efficacious.

Improving access to ACTs

Charles Festo
Ifakara Health Institute, Tanzania

We are evaluating alternative models for the delivery of ACTs in a range of settings so as to maximize access to ACTs. This talk will describe activities to optimise access to ACTs in health facility settings, through community-based workers, and within the existing private sector. The talk will draw on results from the IMPACT2 study in Tanzania to demonstrate the importance of a multi-faceted approach to intervention evaluation.

Improved targeting of ACTs

Dr Evelyn Ansah
Ghana Health Service, Ghana

We are evaluating the potential of RDTs to reduce over-diagnosis and over-prescription of anti-malarial drugs in the public, private and informal sectors, and at the community level. Evaluations consider the effectiveness and cost effectiveness of alternative approaches, including a number of behavioral interventions to improve prescribing patterns and practices.

S12: Innovations in malaria eradication research in Africa.

Chairs: Dr Duncan Earle and Professor Pedro Alonso

Speaker 1: Dr Patrick Moonasar, The last 10,000 cases, challenges and opportunities, Malaria Program Director, South Africa
Speaker 2. Dr Abdullah Ali, Malaria surveillance for elimination – lessons from an island, NMCP Manager, Zanzibar
Speaker 3. Dr Mady Ba, Sub-national elimination: understanding "zero" and expanding malaria free zones, PNLS Director, Senegal
Speaker 4. Dr Busiku Hamainza, Three steps toward a malaria-free Province, Operations Research Technical Officer, National Malaria Control Centre, Ministry of Health, Zambia

This MESA – MACEPA organized symposium will highlight innovations in malaria eradication research in Africa. Our speakers will provide their different perspectives, from the big-picture view of strategic planning for elimination at the sub-national level, to an up-close look at the challenges and opportunities in approaching R0<1. Our presenters will also engage in a discussion of lessons learned from eliminating African regions to mapping out next steps toward the goal of malaria elimination in Africa.

S13: Building on 20 years of experience with Coartem®: Focusing on patient care

Chair: Dr Michael Makanga

Speaker 1: Dr Michael Makanga, Progress in the control and treatment of malaria in sub-Saharan Africa, EDCCTP, South Africa
Speaker 2: Dr. Bernhards Ogutu, Developing a patient-centric approach to malaria management: The Coartem® case study, KEMRI, Kenya
Speaker 3: Dr. Christine Manyando, Trust in experience: Optimal approaches to treating P. falciparum malaria in pregnancy, TDRC, Zambia.
Speaker 4: Dr. Jane Achan, Prevention and management of malaria in the HIV-positive patient. College of Health Sciences, Uganda.

Progress in the control and treatment of malaria in sub-Saharan Africa

Dr Michael Makanga
EDCTP, South Africa

In 2010, 81% of all cases of malaria worldwide were reported in the WHO African Region, which covers the majority of sub-Saharan Africa, with young children and pregnant women reported as being the most severely affected by this disease. Of the estimated 655,000 deaths due to malaria worldwide, 86% were children under 5 years of age, and 91% of malaria deaths occurred in the WHO African Region.[1]
Progress is being been made in the fight against malaria through the WHO initiative to eliminate the disease. Indeed, WHO re-evaluated their Global Malaria Action Plan in 2011 and proposed that by 2015, global malaria deaths should be near zero, global malaria cases should by reduced by 75% from 2000 levels and malaria should be eliminated in 10

new countries since 2008.[1] More recently, WHO launched a new initiative*: Test. Treat. Track,* urging malaria-endemic countries, donors and the global malaria community to scale up diagnostic testing, treatment and surveillance for malaria.[2] The initiative calls for every *suspected* malaria case be tested, every *confirmed* case to be treated with a quality-assured antimalarial medicine, and tracking of the disease through a timely and accurate surveillance system. In terms of effectively treating uncomplicated malaria, WHO guidelines recommend that artemisinin-based combinations therapies be used.[3] The choice of ACT in a country or region should be based on the level of resistance of the partner medicine in the combination; WHO also recommends a change in treatment policy for first-line antimalarials having a treatment failure rate of >10%. In terms of second-line treatment, patients can also receive an alternative ACT known to be effective in the region.

Evidence for the success of this approach has been confirmed by long-term clinical data showing that ACTs including artemether–lumefantrine (AL; Coartem®) used in the context of combined malaria control strategies, have significantly helped reduce malaria burden in many endemic countries. For example, the **A**rtemether–**L**umefantrine **I**n **V**ulnerable patients: **E**xploring health impact (ALIVE) trial surveillance study evaluated the impact of implementing AL as first-line malaria treatment in a rural, malaria-endemic region of Tanzania over a six year period.[4,5]

Developing a patient-centric approach to malaria management: The Coartem® case study

Dr. Bernhards Ogutu
KEMRI, Kenya

Recent increased political commitment as well as substantial international funding has enabled the implementation of effective malaria interventions in endemic areas and a resulting global reduction in malarial disease and mortality. This momentum has encouraged the World Health Organisation (WHO) to shift its goals from malaria control to eradication.[1]

The use antimalarial treatment is pivotal in elimination strategies, with the introduction of artemisinin-based combination therapies (ACTs) to replace previous single-agent therapies proving instrumental.[2] In particular, the adoption and continued deployment of artemether–lumefantrine (AL; Coartem®) has played a significant role in reducing rates of malaria in many endemic countries.

Coartem has demonstrated efficacy and safety in both adult and paediatric populations in a clinical development programme spanning over 16 years and enrolling approximately 20,000 patients.[3,4] Coartem *Dispersible* was developed in accordance with the WHO Prequalification of Medicines Programme and became the first paediatric ACT recommended in WHO guidelines. A multicentre study in 899 children aged ≤12 years showed that Coartem *Dispersible* was as efficacious as crushed tablets in infants and children, with a similar safety profile.[5] A study of Coartem in infants weighing <5 kg is ongoing.[6]

Eradication of malaria is an ambitious goal requiring the implementation of a number of complementary strategies, including mass drug administration, mass screening and targeted treatment and focal screening and targeted treatment. Use of prevention and surveillance programmes is also pivotal. In particular, it is essential to maintain adequate supplies of antimalarial medicines at health facilities in key sub-Saharan countries, through schemes such as the Novartis Access and SMS for Life programme, and AMFEM, Global Fund.[7] Community screening and treatment programmes for asymptomatic carriers are also essential.[8,9]

Future patient-centric approaches towards eradication of malaria are focused on reducing the pill burden for adult patients, leading to the development of Coartem 80/480 which reduces the number of tablets to be taken from 24 to 6.[10] This formulation has been welcomed by WHO, and has been submitted for approval to the Swiss health authority. This experience should inform the development of new antimalarials, so that appropriate target population-friendly formulations are available when new products are introduced.

Trust in experience: Optimal approaches to treating *P. falciparum* malaria in pregnancy

Dr. Christine Manyando
TDRC, Zambia

More than 25 million women in Africa become pregnant each year in malaria-endemic areas.[1] Pregnant women represent a particularly vulnerable risk group as malaria infection can lead to life-threatening disease for the mother and foetus, as well as an increased risk of miscarriage.[2]

The World Health Organisation (WHO) recommends preventive measures to limit the occurrence of malaria in pregnancy, including the use of insecticide-treated nets and intermittent preventive treatment. The WHO also advocates the use of artemisinin-based combination therapy (ACT) as a first-line treatment for uncomplicated malaria in the second and third trimesters of pregnancy, with use in the first trimester only if recommended treatments are unavailable or have failed, and the benefits outweigh the risks.[3] However, there are potential barriers to successful treatment of malaria during pregnancy, including pregnancy-induced changes in pharmacokinetics and issues relating to treatment compliance.[4]

Available data relating to the use of artemether–lumefantrine (AL; Coartem®) in pregnancy[1,4] show that this therapy is efficacious and generally well tolerated; it is not associated with increased adverse outcomes when compared with quinine, sulphadoxine-pyrimethamine or artesunate in the second and third trimesters. Furthermore, available data indicate no association between use of Coartem in the first trimester and increased risk for adverse pregnancy outcome.[5,6] However, the impact of pregnancy-induced pharmacokinetic changes on the efficacy and safety of Coartem requires further study.

A number of ongoing studies are currently seeking to provide further insights into the treatment of malaria in pregnancy. For example, a multicentre, non-inferiority trial on the safety and efficacy of four ACTs for the treatment of pregnant women in the second or third trimester is currently in progress.[7] Other pharmacovigilance initiatives have been established (e.g. WHO, ACT Consortium, INDEPTH Network, WARN) to investigate this area further.

Ongoing studies from sub-Saharan Africa and Asia will enable an informed risk–benefit assessment of disease versus treatment with ACT in pregnancy. However, there is noHoeed for standardisation of large studies that include pharmacokinetics and pharmacovigilance. Further studies comparing the efficacy and safety of ACTs and quinine with clindamycin during the first trimester are also required.

Prevention and management of malaria in the HIV-positive patient

Dr. Jane Achan

College of Health Sciences, Uganda

Malaria and HIV are two of the most important infectious diseases worldwide, and account for a combined 4 million deaths annually. Several interactions between malaria and HIV infection have been established .[1] In particular, HIV infection can increase the risk and severity of malaria infection in children, adults and pregnant women and may also facilitate higher rates of malaria transmission, leading to an increased risk of severe malaria and death in areas where malaria transmission is typically low or unstable.[1]

HIV also impacts on antimalarial immunity, with individuals in malaria-endemic areas that are considered semi-immune to malaria also being susceptible to clinical malaria if infected with HIV.[1]

Similarly, malarial infection may have an effect on HIV disease progression, facilitating CD4+ cell activation and upregulation of proinflammatory cytokines, encouraging the spread of the virus among CD4 + cells and providing an environment for rapid HIV-1 replication.[1] There is, however, less evidence currently available on the effects of malaria on HIV pathogenesis, transmission and immunity.

The treatment of malaria in HIV-infected populations presents another challenge with only few studies reporting on artemisinin-based combination therapy (ACT) treatment outcomes in HIV-infected individuals with uncomplicated malaria.[2] Regarding prevention of malaria in this population, one recent study showed that lopinavir–ritonavir-based antiretrovirals (ART) reduced the incidence of malaria in HIV infected children compared with nonnucleoside reverse-transcriptase inhibitor (NNRTI)-based ART.[3] Studies are ongoing to evaluate antimalarials for intermittent preventive therapy in HIV-infected pregnant women.[6,7]

There are also potential drug–drug interactions between antiretrovirals (ARV) and available antimalarial agents, including artemether–lumefantrine (AL; Coartem®).[4,5] Studies are ongoing to determine the pharmacokinetics of co-administered ARVs and antimalarials . This is important as therapies may impact upon the other, leading to unanticipated effects on drug efficacy or toxicity.

Given the geographical overlap between regions of high malaria and HIV prevalence, and the devastating effects of co-infection, dedicated studies looking at the impact of malaria on HIV progression and the effect of HIV infection on specific antimalarial immune responses are urgently needed. Full evidence-based recommendations and guidelines for the management of malaria in HIV-infected individuals are also required to help manage this growing patient population.

S14: Enhancing adherence to ACTs purchased from drug shops – results from four intervention studies

Chairs: Dr Catherine Goodman and Dr Kathleen Maloney

Speaker 1: Katia Bruxvoort, Cluster-randomized trial of text message reminders of appropriate practices for dispensing artemether-lumefantrine to retail staff in drug shops in Tanzania: effect on dispenser knowledge and patient adherence, Ifakara Health Institute, Dar es Salaam, Tanzania and London School of Hygiene and Tropical Medicine, United Kingdom

Speaker 2: Julia Goldberg, The impact of text message reminders on adherence to antimalarial treatment in a randomized controlled trial in Tamale, Ghana, Harvard School of Public Health, United States of America.

Speaker 3: Sham Lal, Patient adherence to ACT: Findings from a cluster randomised trial introducing rapid diagnostic tests into the private health sector in Uganda. London School of Hygiene and Tropical Medicine, United Kingdom

Speaker 4: Jessica Cohen, Can specialized packaging and malaria rapid diagnostic tests increase patient adherence to over-the-counter artemether-lumefantrine?: Evidence from a randomized controlled trial in Central Uganda, Harvard School of Public Health and Brookings Institution Boston, United States of America.

Patient adherence, the extent to which patients promptly and correctly take the full course of a drug, is a key component in ensuring drug effectiveness. Not only can incomplete dosage result in treatment failure, but it may arguably contribute to the spread of resistance. Artemisinin-based combination therapies (ACTs) are becoming more widely available in the private sector, especially in settings with ACT subsidy programmes. In many countries drug shops are a particularly important source of antimalarials. Monitoring and enhancing the use of privately purchased ACT is therefore essential, but until recently very little has been known about adherence in the private sector, its determinants and how it can be improved.

The objective of this symposium is to present and debate new results on patient adherence to ACT from four innovative studies that have implemented interventions to improve care in the retail sector in Africa.

Two studies report on the use of mobile phone text messages to improve adherence. Bruxvoort et al will present results from a cluster randomised controlled trial (RCT) in Tanzania using text messages to drug shop dispensers to improve advice provided to patients purchasing ACT. Goldberg et al report results from a study using text message adherence reminders to patients in Ghana. Two studies will present results from Uganda. Mbonye et al will report the findings of an RCT which introduced rapid diagnostic tests (RDT) to drug sellers. The second Ugandan study by Cohen et al explores the effects of both RDT introduction and enhanced packaging on patient adherence.

Discussions will focus on the implications of these studies for the appropriate role of the private sector in antimalarial distribution, and strategies that can enhance the quality of care provided to private sector customers.

Cluster-randomized trial of text message reminders of appropriate practices for dispensing artemether-lumefantrine to retail staff in drug shops in Tanzania: effect on dispenser knowledge and patient adherence

Katia Bruxvoort[1,2], Charles Festo[1], Admirabilis Kalolella[1], Matthew Cairns[2], Peter Lyaruu[1], Mitya Kenani[1], S. Patrick Kachur[3], Catherine Goodman[2], and David Schellenberg[2]

[1]Ifakara Health Institute, Dar es Salaam, Tanzania;[2]London School of Hygiene and Tropical Medicine, London, United Kingdom; [3]U.S. Centers for Disease Control and Prevention, Atlanta, USA

BACKGROUND: Patient adherence, the extent to which patients promptly and correctly take the full course of a drug, is a key component in ensuring drug effectiveness. As artemisinin-based combination therapies (ACTs) for malaria become more widely available in the private sector, there are concerns that patient adherence might be low due to insufficient or incorrect advice provided by dispensers with limited training. In this cluster-randomized trial in drug shops in southern Tanzania, we assess the effect of text message reminders to retail staff on advice to provide when dispensing artemether-lumefantrine (AL) on dispenser knowledge and patient adherence.

METHODS: Of 82 randomly selected drug shops in Mtwara region, 42 were randomized for dispensers to receive text message reminders for 14 weeks consisting of 7 content components based on government training materials about dispensing AL at drug shops. No intervention was delivered in the control arm. Eligible patients who purchased AL at drug stores in the intervention and control arms were followed up at home a minimum of 68 hours after drug purchase; consenting patients or their caregivers were administered a detailed questionnaire about when and how each dose of AL was taken, and patients were asked to present their blister packs for a pill count. Following patient data collection, dispensers were interviewed regarding their knowledge of AL dispensing practices, and mobile phone usage and receipt of malaria-related messages.

RESULTS: We interviewed 1476 patients and 112 dispensers from 76 drug stores. We report the effects of the intervention on dispensers' knowledge, the advice patients reported receiving from dispensers and the proportion of patients completing all doses within four days and those adhering to the correct timing of each dose.

The impact of text message reminders on adherence to antimalarial treatment in a randomized controlled trial in Tamale, Ghana

Julia Goldberg, SM and Guenther Fink, PhD
Harvard School of Public Health

BACKGROUND: Poor adherence to artemisinin based combination therapy (ACT) regimens for malaria could lead to drug resistance and pose a major threat to the sustainability of current anti-malarial efforts.
RESEARCH QUESTION: We aimed to determine whether text message reminders increased adherence to antimalarial treatment regimens.
METHODS: ACT vendors participating in the study distributed flyers advertising free mobile health information to patients receiving malaria medicine. Patients who enrolled themselves in the text messaging system based on the flyer were randomized with equal probability to the control group or the treatment group; those in the treatment group were further randomly assigned to receive either six short or six long reminder messages in 12-hour intervals. The main outcome was self-reported adherence based on follow-up interviews occurring three days after treatment initiation. The follow-up interview also included observed pill counts and household drug inventories as indicators of adherence.
RESULTS: Overall, text message reminders increased the odds of adherence by 21% from a baseline of 61.5% in the control group, but this increase was not statistically significant (adjusted OR 1.211, 95% CI [0.939 to 1.563], p-value 0.141). Larger effects were observed for the short reminder message (adjusted OR 1.385, 95% CI [1.006 to 1.906], p-value 0.046) while the long message did not have a statistically significant impact on adherence (adjusted OR 1.080, 95% CI [0.796 to 1.466], p-value 0.621). Self-reported adherence was associated with a decreased likelihood of still feeling sick (adjusted OR 0.676, 95% CI [0.514 to 0.889], p-value 0.005).
CONCLUSION: The results of this study suggest that short text message reminders can increase adherence to ACT regimens.

Patient adherence to ACT: Findings from a cluster randomised trial introducing rapid diagnostic tests into the private health sector in Uganda.

Sham Lal[1], Anthony Mbonye[2], Kristian Hansen[3], Pascal Magnussen[4], Sian Clarke[1]
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Private sector providers in developing countries are often the first and sole source of treatment for those living in malaria endemic countries. Global subsidy programmes such as the Affordable Medicines Facility - malaria aim to increase the availability of artemisinin combination therapies (ACTs) in the private sector and thus reach these underserved populations. There is limited evidence on patient adherence to a full treatment course of ACTs provided by private sector retailers. Poor adherence to treatment regimens could result in sub-therapeutic drug concentrations, delay recovery and encourage parasite resistance.

A cluster randomised trial was undertaken in Uganda to compare the effects of introducing malaria rapid diagnostic tests (mRDT) with a presumptive diagnosis on patient outcomes, including appropriate ACT prescription consistent with RDT results by the drug shop vendor, and patient adherence to ACTs. The trial was situated in a malaria endemic region where 65 shops in urban and rural localities were recruited. Drug shop vendors in each diagnostic arm received a comprehensive training package over the course of one week, including how to receive patients, record keeping, stock control, dosing of ACTs according to age and communication skills. The mRDT shops received additional training on how to conduct mRDTs and interpret them. A random sub-sample of 522 patients consulting all shops for a history of fever were identified from DSVs' registers and followed up at home four days after consultation. Semi-structured household interviews captured information on patient demographics, education, treatment seeking, knowledge of malaria, referral and adherence to ACT. The level of patient adherence to treatment was measured through a self reported description on how the tablets were taken and the presence or absence of pills in the blister pack. A blood sample was also taken to measure the concentration of lumefantrine at day 4 using high-performance liquid chromatography. This talk will highlight the successes and challenges of measuring adherence, the effect of diagnostic testing on patient adherence to ACTs compared with a presumptive diagnosis, and patient level factors affecting adherence.

Can specialized packaging and malaria rapid diagnostic tests increase patient adherence to over-the-counter artemether-lumefantrine?: Evidence from a randomized controlled trial in Central Uganda

Jessica Cohen[1,2], Elif Yavuz[3], Alexandra Morris[3], Jean Arkedis[4], Oliver Sabot[5]

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BACKGROUND: As the sale of artemisinin combination therapies (ACTs) for malaria in drug shops becomes increasingly common, strategies to ensure patient adherence (timely completion of the full, appropriate dose) are urgently needed. Drug shop attendants may not convey accurate or complete information to patients about how to take ACTs and the importance of finishing the full dose. Even if instructions are given patients may forget or misunderstand how to take the medication. In this randomized trial in drug shops in Central Uganda, we explore two strategies to increase patient adherence to over-the-counter artemether lumefantrine (AL): specialized packaging and malaria rapid diagnostic tests (RDTs).

METHODS: The study took place in the district of Luwero, Uganda between November 2010 and August 2011. A baseline survey was conducted with 2641 households in the catchment areas of nine drug shops. Households were given purchase ID cards, enabling the purchase heavily subsidized AL at the participating drug shops. Every day, study staff brought a stock of AL to each shop. The type of packaging for the AL in each shop on each day was randomly assigned ahead of time but study staff, shop attendants and patients were blinded to the assignment until the day of sale. A randomly selected subset of the households was also offered an RDT when they came to the shop to purchase AL. A subset (85%) of the enrolled sample were randomly assigned to be followed-up with at home (after purchasing ACTs) to measure adherence, assessed through observation of blister packs or self-report.

RESULTS: Nearly 42% of households purchased subsidized AL from study shops at least once, with a total of over 2500 redemptions. Among those followed up with at home, only 5% were lost to follow-up and 85% of cases included a blister pack observation. We report the impact of each package type on whether the patient completed the full dose and on the number of doses remaining, as well as patient awareness of proper dosing. We also report the impact of being given an RDT on adherence. Endline survey results explore potential reasons for non-adherence.

S15: Physical Durability of LLINs

Chair: Stephen C Smith

Speaker 1: Olivier J. T. Briët, Economic considerations of LLIN durability, Swiss Tropical and Public Health Institute, Basel, Switzerland

Speaker 2: Christen Fornadel, Physical durability of long-lasting insecticidal mosquito nets (LLINs) after use, Sub-Saharan African nations 2008-2012, US Agency for International Development, Washington, DC, USA; Centers for Disease Contrlol and Prevention, Atlanta, Georgia, USA.

Speaker 3: Stephen C. Smith, Progress toward laboratory test methods for predicting LLIN durability. Centers for Disease Control and Prevention, Atlanta, Georgia, USA; [2]College of Textiles, North Carolina State University, Raleigh, North Carolina, USA

Speaker 4: James F. Sutcliffe, Where do they go and what do they do when they get there? Studies of mosquito behavior around bed nets have implications for improved ITN damage assessment, Department of Biology, Trent University, Peterborough, Ontario, Canada

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Economic considerations of LLIN durability

Olivier J. T. Briët

Swiss Tropical and Public Health Institute, Basel, Switzerland

The words “long lasting” in the term long lasting insecticidal nets (LLINs) refer to the durability of the insecticide in these nets. Lack of physical durability is now the main factor limiting the serviceable life duration of LLINs. The main consumer reason for stopping to use nets for their intended purpose is their perceived inefficacy due to holes. However, holed LLINs that contain sufficient insecticide could still be effective against malaria transmission —that is, if used. The main causes of hole formation are tearing (snagging behind bedframes or mats), burning by hot lamps, and being damaged by rodents. Strategies that could cost-effectively improve the life duration include: improve tear resistance of netting material, use of electric light and rodent control. Also, stimulation of net repair or information communication that holes do not render LLINs useless against pyrethroid susceptible malaria mosquitoes (even if ineffective against nuisance mosquitoes) might be cost-effective ways to prolong the serviceable life duration of LLINs. The relative success of these strategies will vary geographically and depend on the prevalent causes for hole formation. The costs saved due to the lower LLIN distribution rate required to replenish the LLIN crop could outweigh the cost of prolonging the serviceable life.

Because the community effect of LLINs in reducing malaria is likely to be more important than the effect of personal protection, from a programme perspective, the duration of the serviceable life should be seen in terms of the epidemiological effect of the entire net crop on malaria. Also, since the effectiveness of LLINs decays continuously over time until the consumer stops using them, a threshold status beyond which an LLIN should be replaced is of little use at the programme level. However, such a 'net failure' threshold could be useful at the household level. In order to optimize LLIN distribution rates, instead of unit costs of LLINs, costs should be calculated in terms of cost per unit of malaria burden averted. Mathematical modelling has shown that in low transmission settings old LLINs might be sufficient whereas in high transmission settings new LLINs are regularly required.

Physical durability of long-lasting insecticidal mosquito nets (LLINs) after use, Sub-Saharan African nations 2008-2012

Christen Fornadel[1], John Gimnig[2], Ellen Dotson[2], Adeline Chan[2], Gabriel Ponce de León[2], Robert Wirtz[2]

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Understanding the physical durability (PD) of long-lasting insecticidal nets (LLINs) is critical to guide malaria programs on the frequency of LLIN replacement and on the selection of the most appropriate LLIN. With technical assistance and financial support from the U.S. President's Malaria Initiative (PMI), prospective evaluations were conducted in collaboration with Ministries of Health (MOHs) of several sub-Saharan African countries beginning in 2008. The PMI countries that have evaluated nets include: Angola, Benin, Kenya, Malawi, Mozambique, Rwanda, Senegal, and Zambia. We conducted prospective evaluations of LLIN PD after routine and mass distribution campaigns in 5 countries and conducted prospective studies with multiple net brands in 3 countries.

At the time of distributions, LLINs were coded using indelible ink and/or tags fixed to the nets. At intervals of 6 or 12 months, a random sample of households (HHs) was selected for sampling. Interviews on net ownership, use, and care were performed, and randomly chosen survey LLINs were collected. Nets were evaluated for presence (or attrition), hole number and sizes in the field and/or in a laboratory setting. In the lab, LLINs were stretched over a frame against a black background and all holes were quantified.

We will describe trends in rates of attrition and hole development, both in number and size, as well as compare brands and types of LLINs used and evaluated in countries and settings using various statistical analytic tests. Recommendations to manufacturers, MOHs, donors, and partners will also be presented during our presentation regarding LLIN production, procurement and distribution policies, as well as future evaluations.

Progress toward laboratory test methods for predicting LLIN durability

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Meaningful laboratory tests are needed in order to routinely evaluate LLIN quality and to guide the development of LNs with improved longevity. In most textile tests for strength and tear resistance, LLINs yield results with poor reproducibility. The only exception to this is the bursting strength test, which is currently cited by WHOPES to specify minimum strength requirements for LLINs. However, results from field testing have shown no correlation between bursting strength and hole development in LLINs.

Using the assumption that holes are initially formed by cutting (e.g., rodent bites) or melting (e.g., contact with hot surfaces), two approaches were taken to assess the ability of LLINs to retain strength after suffering initial damage. The first approach was to test the loss of bursting strength after a minimal cut or burn was inflicted on the test specimen. The second was to test the susceptibility of the fabric to unraveling, a process that does not require fiber breakage, after the sample suffers a small cut.

Polyethylene-based LLINs suffered much higher bursting strength loss after a minimal cut than polyester and polypropylene LLINs. It is unclear whether this is due to the polymer or due to the different knitting pattern of these nets. Although an exact correlation to field results is still not apparent, the worst performer in this test was also the worst performer in the field. These results could form the basis for new minimum requirements for net strength.

To date, attempts to quantify unraveling have been unsuccessful, but nets collected from the field do show strong evidence of unraveling as a mechanism of hole enlargement. For this reason, efforts to find tests to measure the tendency of netting to unravel after suffering initial damage should continue.

Where do they go and what do they do when they get there? Studies of mosquito behavior around bed nets have implications for improved ITN damage assessment.

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Insecticide-treated bed nets (ITNs) have proven to be an effective and sustainable method of reducing the global burden of malaria. As ITNs age, their timely replacement will be increasingly important for the continued success of this strategy. Unfortunately, there is currently no way to estimate how physical damage translates to bed net vulnerability because we know very little about how mosquitoes interact with human-occupied bed nets and damaged areas of them. To begin to address this deficiency, we are using large-scale laboratory "whole net" experiments to determine mosquito dispersion patterns on bed nets and video to determine how mosquitoes interact with holes in bed nets.

Whole net experiments, performed by recording on-net dispersion patterns ("pressure" patterns) of mosquitoes released into a tent housing a bed net, reveal that both *An. gambiae* and *An. albimanus* exert much greater pressure on parts of the roof of the occupied bed net irrespective of treatment, ambient conditions and net occupant. Pressure patterns are species-specific: *An. gambiae* exerts several times more pressure against the lower third of the bed net than *An. albimanus* while the latter species exerts more pressure than the former on mid- and high levels of the net sides.

Video studies performed by recording individual mosquitoes in behavioral arenas simulating areas of bed net with hole damage show that the probability of mosquito passage through a round hole is a function of hole area and orientation. On a per unit area basis, horizontally-oriented holes (roof holes) are much more penetrable than vertically-oriented holes (on the net sides or ends).

Results are discussed in terms of known mosquito host seeking behaviors and provide the basis for a prototype tool for estimating potential vulnerability of damaged bed nets. The prototype indicates that the Proportionate Hole Index (pHI) method, currently recommended by the WHO, is potentially misleading since it may assign identical pHI values to bed nets of very different vulnerabilities. Though refinement of the prototype is needed, it is already clear that improved ITN damage assessment will require more precise information about net damage location and extent than is routinely collected.

S16: Malaria Case Surveillance and Rapid Response: From Control to Elimination

Chairs: Dr Shiva Murugasampillay and Ms Natashia Morris

Speaker 1: Dr Shiva Murugasampillay, Case-Based Surveillance for Malaria Elimination and Prevention of Re-Introduction, World Health Organistaion, Switzerland.
Speaker 2: Ms Natashia Morris, Spatial Decision Support for Malaria Elimination, South African Medical Research Council, South Africa
Speaker 3: Dr Samson Katikiti, Malaria Score Card for Elimination, African Leaders Against Malaria, Malaria Programme, National Department of Health, Botswana.
Speaker 4: Dr Simon Chihanga, Malaria Notifications and Rapid Response for Malaria Elimination in Botswana, Malaria Programme, National Department of Health, Botswana.
Speaker 5: Ms Bridget ShandUnited Kingdomani, Case-Based Surveillance Towards Malaria Elimination in South Africa, Malaria Programme, National Department of Health, South Africa.
Speaker 6: Ms Zulu Zulu, Malaria Case Surveillance Using Mobile Phone Technology in Swaziland, Swaziland Malaria Program, Swaziland.
Speaker 7: Dr Bashir Adam, Entomological Surveillance of Malaria Vector Breeding Sites for Malaria Elimination in Khartoum State in the Sudan, Khartoum State Malaria Program, Sudan.

Case based surveillance for malaria elimination and prevention of re-introduction

Shiva Murugasampillay
Global Malaria Programme, World Health Organisation

Malaria surveillance is the intelligence system for effective directing and targeting of malaria control and elimination programs. The surveillance system changes in the continuum from high transmission in the control phase to low and zero transmission during elimination and the prevention of re-introduction.

The strategic change for elimination is where programs shift from using aggregate malaria data and epidemiological rates to detailed individual data on every confirmed malaria case followed by case investigation, active case finding with additional community and household screening, entomological surveillance, with rapid response for containment of secondary cases or outbreaks and elimination of malaria foci. This transition from aggregate data to line listing of each individual confirmed malaria case and mapping of malaria foci by lowest administrative level usually takes place in the low-transmission consolidation phase as case rates decline below 1 case per 1000 population at malaria risk.
Malaria case based surveillance is the rapid reporting supported by immediate legal notification of all parasite confirmed symptomatic cases and deaths from passive case detection in health facilities as well as asymptomatic infections from active case detection at household level through mass blood screening in response to confirmed cases passively reported at health facilities. The active surveillance around mapped malaria foci to include screening of all fever cases at health facilities as well as through two weekly household rounds for screening of all fever cases by field-based health extension workers such as malaria-specific surveillance agents or integrated community/village health workers.

The challenges in timely case based surveillance are: (a) timely change management in surveillance techniques from aggregate surveillance to individual case surveillance; (b) legal notification under the public health legislation; (c) enhancing timely reporting and feedback using Information Communication Technology (ICT) and Geographic Information Systems (GIS) and rapid follow-up using mobile malaria teams for elimination of malaria foci.

The outcomes of effective case-based surveillance is rapid reduction of indigenous malaria cases with increase in imported malaria cases, elimination or low density of adult Anopheles and limited larval breeding sites. The impacts are increased numbers of local administrative areas or malaria sectors certified free of local transmission resulting in an increase in districts and provinces free of malaria transmission and leading ultimately to countrywide certification of elimination.

Spatial decision support for malaria elimination

Natashia Morris
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The application of spatial decision support systems for successful malaria control has been extensively documented and ranges from mapping and modelling disease distribution to mapping the access and coverage of implementation of interventions and their impact upon both parasite and vectors.

During the malaria control phase, mapping of case aggregates, incidence and mortality rates at facility and district level enables the monitoring of trends and the impact of interventions and further facilitates informed programme management. Under an elimination campaign, the focus shifts to a finer resolution, with surveillance typically moving to the locality and the household level.

Malaria surveillance during elimination hinges most critically upon rapid notification, follow-up, investigation, classification and treatment of individual cases. Real time mapping of locally acquired cases at the higher resolution of village or locality level enables spatial cluster analysis to determine potential hotspots and to map malaria foci. Enhanced surveillance and intervention at known hotspots typically include outbreak response in the form of active case detection, treatment and awareness campaigns, entomological surveillance and vector control measures. Mapping of hotspots, adult vector collections at sentinel sites and larval collections at breeding sites can inform and expedite the effective targeting of these measures.

Confirmation of active transmission at hotpots through collection of parasitological followed by entomological information will further conclusively establish foci at which an appropriate combination of interventions including indoor residual spraying and larviciding of potential breeding sites might be targeted, thereby maximising impact and gradually interrupting transmission. Mapping of these foci of transmission will support eventual elimination of malaria foci in low transmission settings through targeting of appropriate combinations of interventions.

The gold standard in spatial decision support is, however, more easily postulated than implemented, particularly in resource-challenged settings. In practice, data collection is often of a less than ideal resolution, data quality is poor, skills are scarce and infrastructure is lacking. Nevertheless, spatial decision support is often attempted and its effectiveness varies depending on the levels and combination of the respective factors mentioned. In addition to exploring the set of spatial decision support tools and methods available for malaria elimination, we look at the ways in which typical challenges might be addressed, and at approaches which maximise the use of the available data to inform elimination while taking affordable and achievable measures to enhance existing efforts.

Malaria Notification and Rapid Response for Malaria Elimination in Botswana

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INTRODUCTION: Botswana has made significant strides in reducing the national malaria burden since 2000. Unconfirmed malaria declined by 99.8% between 2000 and 2012, confirmed malaria cases dropped 97.6% from 8,056 to 193 and deaths attributed to malaria declined 91.4% , from 35 in 2000 to 3 in 2012 respectively. Malaria incidence declined from 13.4% in 2006 to 0.15 per 1000 population in 2012, with all districts reporting less than 1 case per 1000 population by December 2012. The National Malaria Programme moved from malaria control to elimination in 2010.
METHODOLOGY: Rapid notification and response is being implemented as part of an integrated health system. Malaria cases are detected through routine passive surveillance at health facilities and by active surveillance during screening of contacts of patients (HiFSAT) and fever surveys. Diagnosis is done using RDT and microscopy. Patient diagnosed using RDTs have baseline slides and blood spots for PCR collected before treatment. Positive cases are reported immediately to DMHTs, who activate the District Rapid Response Team (DRRT) and alert at national level. The health facility, with support from the DRRT, investigates the cases at household level, maps the cases, screens household contacts within a 100 meter radius of the case and follows up the case for 28 days.
RESULTS: There are 214 cases in the database at national level. Cases were notified within 24 hours. The majority of cases were females and 40% of the cases were from Okavango District which experienced an outbreak in 2013. Of the 203 cases diagnosed by RDT, only 27.4% had baseline microscopy done. Case investigation was also poor with only 60 cases investigated. Local importation within Botswana accounted for 7 cases while 25 cases were imported from other countries. Screening of cases at households accounted for 23 cases. Malaria free districts accounted for the largest number of imported cases from outside Botswana. Malaria foci of transmission have been identified down to the ward level.
CONCLUSION: CBS has been implemented with some success in Botswana. Preliminary results indicate implementing CBS as an integrated program may not produce the desired results of malaria elimination in Botswana, however more data is required to make valid conclusions.

Case-Based Surveillance Towards Malaria Elimination in South Africa

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INTRODUCTION: South Africa is targeting malaria elimination by 2018 and has developed a strategic plan with key interventions to assist in achieving this goal, with surveillance one of the key strategies. Malaria became a notifiable disease in 1956, with all malaria cases required to be notified by law both in the public and private sectors. Malaria surveillance in South Africa follows the WHO recommended surveillance guidelines focusing on both passive and active case notification methodologies. Whilst all three malaria endemic provinces implement both these methodologies, Mpumalanga and KwaZulu-Natal have been robustly implementing active case detection programmes in the past several decades.
METHOD: The routine collection, analysis and interpretation of malaria case data underpins both control and elimination efforts in South Africa. Individual case data passively reported at health facilities are entered into provincial malaria information systems and then reconciled to a national database. Follow-up and investigation of all cases is conducted within 48 hours of reporting by locating the index patient at their place of residence by a trained malaria case investigator. In addition to patient details and test results, detailed travel history and date of onset of first signs and symptoms are collected in order to establish probable source of infection and to correctly classify the case. Active surveillance is subsequently effected in the vicinity of the index case by undertaking contact tracing using blood slide microscopy and rapid diagnostic tests. Appropriate action is taken when contacts are positive, including notification, treatment, further contact tracing, entomological surveillance and indoor residual spraying when required. Outbreak surveillance is also in place, with alert and action thresholds calculated digitally at all spatial levels and weekly exceedences triggering a series of appropriate interventions. An integrated web-based reporting tool provides the interface to near-live data from the national database in the form of case counts, incidence, deaths and other indicators at all spatial and temporal levels and includes the threshold-based outbreak alert system and automated mapping of case notifications down to the locality level.
RESULTS: Malaria cases in South Africa have shown marked reductions since the epidemic of the 1999/2000 season, from approximately 63100 cases to around 5100 in 2012/2013, a decrease in excess of 90%. Most notably, KwaZulu-Natal Province reported the highest burden of malaria cases amongst the malaria endemic provinces during 1999/2000, reporting 41437 cases, now reduced by some 98% to 476 during 2012/2013. Imported cases now account for 92%, 46% and 90% of all cases reported in the three malarious KwaZulu-Natal, Limpopo and Mpumalanga Provinces

respectively. During the 2013/2013 season, all nine malarious districts of South Africa entered elimination, reporting local case incidences of less than one case per one thousand population at risk.
CONCLUSION: Prompt follow-up and investigation of passive notifications, re-active and pro-active case surveillance albeit labour and cost intensive are important strategies for moving the malaria elimination agenda in South Africa, and similar low transmission countries in Southern Africa. Moreover, accurate and timely record keeping in the form of the national integrated malaria information systems are a critical management tool, ensuring that evidence-based decisions guide the malaria elimination campaign.

Malaria Case Surveillance Using Mobile Phone Technology in Swaziland

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BACKGROUND: Case-based passive surveillance and case tracking are necessary to achieve malaria elimination. Prior to embarking on an elimination campaign in 2009, the majority of cases in Swaziland were clinically diagnosed and reported monthly by health facilities through a paper-based system, delaying the entry and analysis of malaria case data up to 6 weeks after initial presentation of a case. To achieve elimination, Swaziland required an immediate case reporting system that could trigger a robust active surveillance response among malaria at-risk communities.
METHODS: In August 2010, Swaziland introduced an immediate disease notification system (IDNS), where data on 15 notifiable diseases, including confirmed malaria cases, are reported by healthcare workers to a central toll-free hotline and captured in real-time by a data entry clerk. Following data entry into the database, an automated short-message-service (SMS) text is immediately sent to the mobile phones of the entire National Malaria Control Programme (NMCP) surveillance team alerting them of the case and the reporting health facility. Information collected on each malaria case through the IDNS includes the name, gender, date of birth, contact information, directions to household, and condition details. Following case notification, the NMCP surveillance team attempts to visit the household of the case to confirm demographic details, collect travel history to determine source of infection, and identify potential risk factors associated with infection.
RESULTS: Between the 2008/2009 and 2011/2012 seasons, malaria cases reported to the health management information system (HMIS) decreased 91%, from 7507 to 643, while uptake in the use of the IDNS increased steadily over time. This decrease was both the result of the improved passive surveillance system as well as an increase in the confirmation rate of malaria cases through the introduction of diagnostic capacity at all health facilities. The proportion of cases investigated by the NMCP surveillance team, a system non-existent prior to 2010, is now 85%.
RECOMMENDATIONS: Countries aiming to achieve elimination must implement case-based reporting for passive surveillance at health facilities. Utilisation of mobile phone technology can expedite the reporting and follow-up of malaria cases. Health care worker sensitisation and training will facilitate the uptake of any new reporting system.

Entomological Surveillance of Malaria Vector Breeding Sites for Malaria Elimination in Khartoum State in the Sudan

Khartoum State Malaria Programme, Sudan

Bashir Adam, Toto H.K.

BACKGROUND: The Khartoum Malaria Free initiative (KMFI) project was initiated in 2002 as collaboration between WHO/EMRO, the Sudan National Malaria Control Programme and Khartoum State. The project adapted and implemented larval source management as the main weapon to fight malaria, and it succeeded in reducing malaria morbidity and mortality between 2002 and 2012 by 50% and 20 % respectively (KSMOH, 2006). Entomological surveys are an essential component of malaria vector control programmes, operational activities and researches. One of the key successful elements for KMFI is that the present of well organized and functional vector surveillance system.
METHODS: Vector Surveillance: Since 2000, the state malaria control programme has identified 24 sentinel sites to represent the whole area under control operations, at which to implement routine vector surveillance. In addition, 9/24 sentinel sites were chosen for monitoring of insecticide resistance in mosquito vectors. Three teams each comprising 4 people (1 entomologist and 3 entomology technicians) were employed with their complete survey tools and equipments. Each team visits 8 sentinel sites per week.

Adult Mosquito Sampling: Pyrethrum spray collection method was used to collect indoor-resting mosquitoes from 3-5 randomly selected houses in each sentinel site. In the field all mosquitoes collected were morphologically sorted to genera species and scored by their physiological status as unfed, blood fed, half gravid and full gravid, then preserved in petri dishes and processed further at the KMFI entomology laboratory. Using this collection method, measurements of proportions of mosquitoes resting indoors during the day, human-biting density (indirectly) and seasonal changes in indoor resting density were calculated.

Mosquito Larval Sampling: Larval collection was conducted in the same sentinel sites as adult samples using standard dipper or netting or anywhere appropriate depending on the type of breeding habitats. The main purpose of larval surveys are to determine vector species present in the area, the type of breeding habitats of each species/area and the geographical distribution of vectors, and to evaluate impact of anti-larval measures on larval density.

Monitoring of Insecticide Resistance: The insecticide resistance status of female An arabiensis against all four classes of insecticide was investigated annually in 9 sentinel sites. All tests were performed following standard WHO guidelines. Resistance status of mosquito larvae was also monitored using 4 WHO standard solutions of temephos, fenithion, chlorpyrifos and fenitrothion.

RESULTS: Between 2010 and 2012, a total of 1285 survey visits were carried out and 6378 houses sampled. Of a total of 12178 mosquito specimens collected inside rooms, 9958 (81.7%) were Culex and the remaining 2220 (18.3%) were Anopheles. Among Anopheles species, 51.0% (n=1133) were unfed, 28.2% (n=625) fresh fed, 17.3% (n=384) semi-gravid and 3.5% (n=78) were full gravid female Anopheles. Anopheles mosquitoes were the most predominant in Bahari and Khartoum localities. Regarding larvae, a total of 18945 aquatic habitats were sampled, 2481 (13.1%) contained Anopheles larvae and 6476 (34.2%) contained Culex larvae. Data from our routine survey indicated that breeding habitats could be classified into 13 categories, of which 6 are most important. Broken water pipes, brick-making pits and pools formed after river recedence dominated during winter (December to February), while minor irrigation canals, rain pools and drainage were found to be the most productive sources of mosquitoes during the peak rainy season (August to September). Results of resistance monitoring in adult malaria vectors from 2004 to 2012 indicated that An arabiensis is still highly resistant to malathion in all 9 sentinel sites, and varies spatially and temporally in resistance levels to DDT but is fully susceptible to deltamethrin, permethrin, lambdacyhalothrin, propoxur bendiocarb and fenitrothion insecticides. Larvae were also still susceptible to temephos, fenithion and fenitrothion with mortality rates varying between sites and areas.

CONCLUSION: Routine vector surveillance data, if carefully collected, analysed and interpreted, can be valuable for determining focus areas of active vector populations and, linked with malaria case surveillance data, could greatly benefit malaria elimination efforts.

S17: The challenge of developing a pregnancy associated malaria vaccine.

Chairs: Prof Alister Craig and Dr Odile Leroy

Speaker 1: Dr Michal Fried, General introduction on Pregnancy Associated Malaria (PAM) and the scientific basis for the decision making after the proof-of-concept phase to further develop the PAM vaccine candidate, National Institute of Allergy and Infectious Diseases, National Institute of Health, United States of America

Speaker 2: Prof Ogobara K. Doumbo, Pregnancy Associated Malaria (PAM) burden in sub-Saharan Africa and the need of new tools and PAM vaccines, Malaria Research and Training Bamako, Mali

Speaker 3: Dr Benoît Gamain, The challenges of selecting an antigen for a Pregnancy Associated Malaria (PAM) vaccine, Institut National de la Transfusion Sanguine; Paris Diderot University, France.

Speaker 4 : Dr Saadou Issifou, Overview of the clinical development plan of a var2CSA-based Pregnancy Associated Malaria (PAM) vaccine, Université d'Abomey-Calavi, Bénin.

Speaker 5 : Dr Freya J.I, Fowkes Relevant immunologic assays for evaluating vaccines for Pregnancy Associated Malaria (PAM), Burnet Institute, Australia.

General introduction on Pregnancy Associated Malaria (PAM) and the scientific basis for the decision making after the proof-of-concept phase to further develop the PAM vaccine candidate.

Michal Fried

National Institute of Allergy and Infectious Diseases, National Institute of Health, Rockville, USA

A vaccine to prevent PAM is justified by naturally acquired immunity that has been associated with improved pregnancy outcomes. PAM is initiated by the sequestration of a distinct subpopulation of parasites that adhere to chondroitin sulfate A (CSA) in the placenta. Naturally acquired immunity in the form of anti-adhesion antibodies is acquired over successive pregnancies and has been associated with reduced prevalence of infection, reduced parasite densities, and increased birthweight. The optimal vaccine to prevent malaria during pregnancy should mimic naturally acquired immunity to placental parasites, similar to that acquired by multigravid women. The pathway to develop a PAM vaccine may include the following phases: a) preclinical studies show immunogen induces antibodies with similar qualities as naturally acquired antibodies in animals; b) Phase I clinical trial demonstrates that the immunogen induces similar immune response in humans; c) Phase I clinical trial demonstrates that the immunogen induces similar immune response in the target population, non-pregnant African women. Defining primary and secondary end points can be

guided by our understanding of pregnancy malaria pathogenesis, and the benefits gained from naturally acquired immunity. One of the common outcomes of PAM is reduction in birthweight and increased rate of low birthweight deliveries, and acquired immunity has been associated with increased birthweight. To mimic acquired immunity, the primary outcome for consideration is birthweight, additional secondary outcomes may include infection rate, placental parasitemia, pre-term delivery and pregnancy loss. The target population for this vaccine is young adolescents prior to becoming pregnant, and the immune response elicited by the vaccine will be boosted by natural infection.

Pregnancy Associated Malaria (PAM) burden in sub-Saharan Africa and the need of new tools and PAM vaccines.

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PAM is a major public health concern in sub-Saharan Africa, associated with maternal morbidity and mortality, and poor pregnancy outcome including preterm babies and high infant mortality. More than 30 million pregnant women (PW) are exposed to *P. falciparum* malaria per year in sub-Saharan Africa. In Mali, the population at risk is estimated to be 800-900,000 PW exposed to falciparum malaria per year. No estimate exists until now of *P. vivax* PAM burden in Africa (*P.vivax* is endemic in the Sahel region across Africa). Little is known on the PAM burden of *P. malariae* and *P. ovale*, and on malaria species co-infection and co-infection of malaria and bacteria, helminths and viruses during pregnancy and their outcome. Co-infection of HIV with malaria has poor outcomes and is difficult to prevent.

The existing malaria control/elimination tools (Insecticide Treated bed Nets, Intermittent Preventive Treatment for pregnant women, and Case management/Rapid Diagnostic Tests) have not met the expected Abuja and Roll Back Malaria (RBM) goals in most of endemic countries in Africa. Most African countries will not meet MDGs 4, 5, and 6 by 2015, because of remaining malaria burden in pregnant women and under-fives. Diffusion of insecticide and sulphadoxine-pyrimethamine resistances are major concerns in Africa for the next five years. No cost-effective tools for PAM prevention are expected in the pipeline of MMV, RBM and WHO for the upcoming five years.

Field studies since the 1950's have demonstrated the differences of PAM burden between primigravida and multigravida in hyper endemic malaria transmission areas. This specific protection acquired over successive pregnancies against PAM is based on the development of antibodies against CSA-binding falciparum malaria parasite. Var2CSA is a well characterised surface antigen that binds CSA and is under study by different scientific groups. A PAM vaccine is in preclinical development, and plans should be developed for phase I testing in USA and Europe and soon thereafter in Africa. If vaccine efficacy is proven in teenage girls, this new tool could be elegantly integrated in existing programs to alleviate malaria burden during pregnancy in Africa.

The challenges of selecting an antigen for a Pregnancy Associated Malaria (PAM) vaccine.

Benoît Gamain
INSERM, U665; Institut National de la Transfusion Sanguine; Paris Diderot University, F-75739 Paris, France

Over 50 million women are exposed to the risk of malaria during pregnancy every year. Calculations indicate that as many as 363,000 neonates and at least 10,000 maternal deaths may be attributable to PAM every year. Adhesion of *Plasmodium falciparum*-infected erythrocytes (PEs) to placental chondroitin-4-sulfate (CSA) has been linked to the severe disease outcome of PAM. After multiple pregnancies, women acquire protective antibodies that block CSA-binding and cross-react with geographically diverse placental isolates suggesting that surface molecule(s) expressed by PAM-infected erythrocytes have conserved epitopes and that a PAM vaccine may be possible. Although the interaction between *P. falciparum* and its host is complex, accumulated evidence strongly supports var2CSA, a member of the *Plasmodium falciparum* Erythrocyte Membrane Protein 1 (PfEMP1) adhesins encoded by the *var* gene family, as the leading PAM vaccine candidate.

Conceptually, we are now in the process development phase of research and development of a vaccine that would protect pregnant women against PAM. However, before envisaging vaccine development, it is essential to identify a region of var2CSA that would induce neutralisation of the parasites in the placenta (either parasite de-sequestration and/or parasite phagocytosis). Indeed, although the full-length var2CSA is the leading PAM vaccine candidate, its size, polymorphism and the presence of cysteine-rich domains (more than a hundred cysteines within the full-length extracellular region) pose a challenge for vaccine development.

Furthermore, if var2CSA is crucial for PEs cytoadhesion to CSA and placental cells, it cannot be ruled out that other *P. falciparum* proteins could engage binding to co-receptors present in the placenta.

We will present the latest results on PAM vaccine antigens and the challenges of selecting the best one to design effective vaccine strategies aiming to provide protection of future pregnant women against PAM.

Overview of the clinical development plan of a var2CSA-based Pregnancy Associated Malaria (PAM) vaccine.

Saadou Issifou
Université d'Abomey-Calavi, Cotonou, Bénin

The most useful strategy to improve infectious diseases control remains vaccination. The ability of VAR2CSA specific IgG to inhibit the binding of maternal *P. falciparum* isolates constitutes a potential vaccine candidate for PAM.
The clinical development of this malaria vaccine candidate will be performed in three distinct steps.
Step1 will be performed in African countries to prepare the future phase II clinical trial (CT), including (i) the provision of data necessary for study design and (ii) the evaluation of the naturally acquired immunity against VAR2CSA in African nulligravid women during first pregnancy.
Step 2 and 3: A phase Ia/Ib CT will be conducted to assess the clinical and biological safety and immunogenicity of the vaccine candidate with the comparator vaccine. The phase Ia arm will be performed for dose-finding and adjuvant selection in malaria naïve adults in Europe, the phase Ib arm will be performed in African adults, exposed to malaria, fulfilling the established inclusion and exclusion criteria.
The phase Ia/b CT has the following objectives: (i) To evaluate the clinical safety of var2CSA in adjuvant in healthy adults receiving several doses of the trial vaccine based on solicited/unsolicited adverse events. Their severity will be evaluated as grade 1, grade 2 or grade 3, based on specific definitions with their duration, frequency, outcome and the relationship to the study vaccine. (ii) The biological safety will be determined in reference with the baseline before the first dose.
The immunogenicity evaluation objectives will be: (i) To assess the humoral response to the relevant vaccine antigens, (ii) To assess cellular immune response by evaluating the profile of Th1/Th2-type cytokines.
Additionally, any correlation between the results of the *in vitro* assays and the clinical trial will be assessed. The impact of the adjuvant on innate and acquired immune response will be determined. The study endpoints data will be analysed as a descriptive samples.
Decisions to proceed to the next step (go/no go criteria) will be based on safety as primary, and immunogenicity as secondary selection criteria. If the vaccine candidate has shown to be safe in the phase Ia/b CT, a phase IIb CT in healthy African female naturally exposed to malaria can be initiated.

Relevant immunologic assays for evaluating vaccines for Pregnancy Associated Malaria (PAM).

Freya JI Fowkes, James G. Beeson
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There is a strong rationale to support the development and evaluation of vaccines to prevent the burden of malaria in pregnancy. PAM vaccine development has primarily focused on var2CSA, a protein which allows *P. falciparum* infected erythrocytes to adhere to the placenta. Currently, var2CSA is the leading vaccine candidate for the prevention of malaria during pregnancy. Development of specific assays to measure immunity to var2CSA has enabled identification of targets of naturally acquired and vaccine-inducible immunity and the immunological mechanisms behind them. Assays to measure vaccine-induced immunity have included established ELISAs and flow cytometry to determine relative levels of antibodies to var2CSA domains and to the surface of the infected-erythrocytes infected with *P. falciparum* pregnancy-specific isolates respectively, with the cross-reactivity of immunity being investigated using agglutination assays. The ability of antibodies to inhibit adhesion of infected erythrocytes to CSA has been assessed using adhesion-inhibition assays and currently this assay is the best established functional assay to assess the adhesion inhibitory activity of vaccine-induced antibodies. There is now emerging evidence that antibodies can also facilitate clearance of erythrocytes infected with pregnancy-specific isolates through the development of high-throughput flow cytometry-based opsonic phagocytosis assay. Recent evidence from avidity assays has also shown the importance of high avidity antibodies in mediating protection against PAM. While the development and use of specific assays has identified pregnancy-specific antigens and functional mechanisms, key questions still remain around the longevity of pregnancy-specific responses and when best to measure them. Recent evidence suggests that naturally acquired antibody responses to var2CSA last decades which suggests that antibodies will be carried through to multiple pregnancies. These data on antibody longevity may be valuable for predicting the duration of responses induced by malaria var2CSA vaccine candidates. Furthermore var2CSA antibody responses are dynamic over time which suggests that measuring antibodies at a single time may not reliably reflect an individual's immune status. This has major translational implications for accurately assessing immune status and exposure in vaccine trials. Here we discuss the key questions of not only how do we measure pregnancy-specific immunity but when and how, with the aim of informing laboratory, epidemiological and vaccine trial design.

S18: Building Interdisciplinary Research capacity for the control of malaria in Francophone and Anglophone West Africa. Experiences from the Institute of Infectious Diseases of Poverty.

Chairs: Prof Magaret Gyapong and Prof Abdoulay Djimde

Speaker 1: Mr Souleymane Dama, Determinants of diminished response to artemether-lumefantrine in the field, Malaria Research and Training Center, University of Sciences, Techniques and Technologic of Bamako, Mali.
Speaker 2: Ms Akinola Olugbenga, Development of a new tool for validation of anti-malarial target genes using a riboswitch regulatory element in plasmodium berghei. University of Ibadan, Ibadan, Nigeria,
Speaker 3: Mr Hamma Maiga, Six years of intermittent preventive treatment using artemisinin-based combination therapy reduces malaria morbidity among school-aged children in Mali, Malaria Research Training Center, University of Bamako, Mali.
Speaker 4: Dr Elizabeth Awini, Patterns of mortality at three ecological zones in Ghana, Epidemiology and Disease Control, University of Ghana Institute of Infectious Diseases of Poverty, Ghana.

Determinants of diminished response to artemether-lumefantrine in the field

Souleymane Dama, Ogobara K. Doumbo, Issaka Sagara and Abdoulaye A. Djimde Malaria Research and Training Center, Department of Epidemiology of Parasitic Diseases, Faculty of Medicine and Dentistry, Faculty of Pharmacy, University of Sciences, Techniques and Technologic of Bamako, Bamako, Mali (West Africa)

BACKGROUND: Artemisinin based Combination therapy (ACT) is now used as first line treatment of uncomplicated malaria to face the resistance of *Plasmodium falciparum* to monotherapies. However, cases of in vitro resistance and delayed parasite clearance time in artemisinin treatment have been reported in Asia. In Mali, previous studies have shown 30-40% of recurrent parasites after treatment with artemether-lumefantrine. The aim of this study is to characterize the phenotype and genotype of recurrent parasites after treatment with artemether-lumefantrine.
Methods: The proposal was to conduct field studies and collect parasites before and after artemether-lumefantrine treatment in Mali. In vivo drug efficacy studies according to WHO protocols have been performed. Ex-vivo drug efficacy studies have been conducted using hypoxanthine based methods. QTL analyses performing are ongoing to assess the involvement of various loci in the decreased efficacy of artemether-lumefantrine on *Plasmodium falciparum*.
EXPECTED RESULTS: At the date, ninety three (93) samples have been collected, 43 samples have been treated in vitro and the rest were cryoconserved. Rates of in vivo drug resistance have been assessed with and without molecular correction. *Plasmodium falciparum* IC50s of artemether and lumefantrine were determined. Genetic variations associated with the above phenotypes are determined using a QTL approach.
KEY WORDS: Artemether-lumefantrine, *Plasmodium falciparum*, in vivo, in vitro.

Development of a new tool for validation of anti-malarial target genes using a riboswitch regulatory element in plasmodium berghei.

Akinola Olugbenga [1,2], Uthaipibull Chairat [3], kamchonwongpaisan Sumalee [3], Sowunmi Akintunde [1,2], Happi T Christian [2,4], Oduola MJ Ayoade [2], Gbotosho G Olusola [1,2], Shaw J Philip [3]

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BACKGROUND: Comparative genomics has revealed potentially many new drug targets that are yet to be explored, but it is not known how many are essential and thus are viable drug targets. In this study, a new method for validating potential drug targets in the malaria parasite was achieved through regulation of RNA stability, whereby a "riboswitch" regulatory element of bacterial origin is fused to the 3' end of the gene target RNA in Plasmodium berghei.
METHODS: Plasmids bearing the glucosamine-dependent glmS riboswitch element fused to the 3' end of a highly pyrimethamine resistant Toxoplasma gondii dihydrofolate reductase (Tgdhfr) gene sequence were linearized and transfected into Plasmodium berghei merozoites. Genetically modified parasites were selected with pyrimethamine after inoculation in naive mice. Clonal lines of transgenic parasites were obtained and their sensitivity to pyrimethamine and chloroquine was tested and compared with control parasites.

RESULTS: The transgenic parasites were ten-fold sensitized to pyrimethamine when cultured in media supplemented with 3.125 mM glucosamine. The IC50 of pyrimethamine on the riboswitch parasites is 5.612µM while in the absence of glucosamine the IC50 value was 58.43µM. However, the sensitivity of the transgenic parasites to chloroquine was not affected by the presence of glucosamine. The control parasite line's sensitivity to either drug was also not affected by the presence of glucosamine.
CONCLUSION: The results prove the hypothesis that glucosamine can activate the riboswitch to destabilize the Tgdhfr mRNA and thus reduce Tgdhfr expression in vivo. The reduction of Tgdhfr expression sensitizes the parasite to drugs specifically targeting dhfr, but not drugs with different modes of action.
Overall, this work provides proof of concept for an alternative tool for validating gene targets and determining mode of action for antimalarial drugs. This tool could thus be useful for triaging antimalarial compounds according to their modes of action and thus accelerate antimalarial drug development.

Six years of intermittent preventive treatment using artemisinin-based combination therapy reduces malaria morbidity among school-aged children in Mali

Hamma Maiga,[1]Breanna Barger,[2]Ousmane Toure,[1]Oumar Bila Traore,[1]Mamadou Tekete,[1]Intimbeye Tembine,[1]Antoine Dara,[1]Zoumana Isaac Traore,[1]Issaka Sagara,[1] Modibo Diarra,[1] Samba Coumare,[1]Aly Kodio,[1] Amadou Bamadio, [1] Bouran Sidibe,[1]Aboubacrine Haidara,[1]Ogobara K. Doumbo,[1] Abdoulaye A. Djimde[1]

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BACKGROUND: Previous studies showed that in areas of seasonal malaria transmission, intermittent preventive treatment of school children (IPTsc) targeting the transmission season, reduced the rates of clinical malaria. The efficacy of ACTs in the context of longitudinal IPTsc is poorly investigated.
METHODS: This was an open randomized controlled trial of seasonal IPT among school children aged 6–13 years in Kolle, Mali. The study began in September 2007 and completed follow-up in May 2013. Students were randomized to one of three study arms: Sulfadoxine–pyrimethamine plus artesunate (SP/AS), Amodiaquine plus artesunate (AQ/AS) or Control(C). All students received two full treatment doses, given 2 months apart during the season of high transmission from September to December. Groups were compared with respect to incidence of clinical malaria, asymptomatic parasitemia and anaemia.
RESULTS: A total of 296 students were randomized, and retention in the study was 99.3%. Clinical malaria incidence in the SP/AS and AQ/AS arms was reduced by 50.9% and 20.6%, respectively, vs. C (P< 0.001). There were fewer all-cause clinic visits among the children receiving SP/AS or AQ/AS (P< 0.001). The prevalence of asymptomatic parasitemia was higher in the Carm than SP/AS or AQ/AS (P< 0.001). At the end of the transmission period, children treated with IPT had lower rates of anaemia (SP/AS, 4.2%; AQ/AS, 7.8%; C, 12.7%; P = 0.012).
CONCLUSION: IPTsc reduced the rates of clinical malaria, all-cause acute clinic visits, asymptomatic parasitemia and anaemia among school-aged children.
KEYWORDS: malaria, artemisinin, intermittent preventive treatment, children, school.

Patterns of mortality at three ecological zones in Ghana

Elizabeth Awini[1,2], Philip Adongo[1,2], Patricia Akweongo[1], Margaret Gyapong [1,2]

[1]Epidemiology and Disease Control, SPH, University of Ghana); [2]Ghana Health Service/Institute of Infectious Diseases of Poverty (IIDP)

BACKGROUND: Whiles mortality remains a public health problem in developing countries, improvements over the years have been marginal. Timely, current and accurate information on the patterns deaths and the causes of these deaths which will allow for introduction of appropriate interventions to address the critical health challenges in our communities is also sparse in these populations. Where these have been reported, data is available mainly on children and show that there are seasonal and spatial patterns of mortality and these vary from one location to another. This study will seek to describe the patterns of mortality at three ecological zones in Ghana. It will estimate all-cause and malaria-specific mortality and determine seasonal and spatial patterns of all-cause and malaria-specific mortality at the three ecological zones in Ghana
METHODS: Secondary data from three Health and Demographic Surveillance System (HDSS) sites in Ghana are being used for the study. The operations of these sites are similar. Vital statistics are collected by field workers who visit each household periodically. The variables registered during updates include pregnancies, births, deaths, migration. Community Key Informants (CKIs) have also been trained to pick events in their communities to supplement those collected by the field workers. Field supervisors conduct verbal autopsies (VA) for all deaths registered in the districts. These VAs are normally coded independently by three clinicians to determine the cause of death.
RESULTS: This study will use six years (2006-2011) data from the three HDSS sites. All deaths registered during the period will be included in the study. The variables include deaths, cause of death, sex, age, coordinates, daily rainfall and temperature. Descriptive methods will be used to check data quality and outliers before the main analysis. Crude death rates and Cause-specific mortality rates will be estimated over the years. Seasonal and spatial patterns of mortality will be investigated using time series models and Spatial Scan statistic.
Results indicate that malaria was the first leading cause of under-five deaths for the period 2006-2010.

S19: Targeting malaria elimination in Zanzibar

Chairs: Prof Anders Bjorkman and Dr Abdullah Ali

Speaker 1: Dr Abdullah Ali, Malaria control in Zanzibar, Zanzibar Malaria Control Programme, Zanzibar.
Speaker 2: Professor Andreas Mårtensson, Malaria elimination in Zanzibar – is it possible?, Karolinska Institutet, Sweden.
Speaker 3: Dr Jackie Cook, Screen and treat using rapid diagnostic tests fails to identify the full extent of the asymptomatic reservoir of infection: Experience from Zanzibar, Karolinska Institutet, Sweden
Speaker 4: Dr Silas Majambere, Vector control and changing patterns of anopheline populations in Zanzibar, Ifakara , Tanzania.
Speaker 5: Dr Chris Drakeley, Trends of seropositivity and force of infection in Zanzibar, London School of Hygiene and Tropical Medicine, United Kingdom.

Malaria elimination in Zanzibar – is it possible

Prof. Andreas Mårtensson,
Malaria Research, Department of Medicine Solna and Global Health (IHCAR), Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden

Zanzibar has during the last decade undergone a rapid transition from high malaria transmission to a stage of pre-elimination following wide scale, high coverage combined malaria control interventions.
To pursue malaria elimination efforts new tools strategies are probably needed. This talk explores recent achievements as well as present challenges and opportunities in the new context of very low malaria transmission.

Screen and treat using rapid diagnostic tests fails to identify the full extent of the asymptomatic reservoir of infection: Experience from Zanzibar

Jackie Cook[1], Weiping Xu[1], Marlotte Vonk[1], Mwinyi Msellem[2], Abdullah Ali[2], Peter McElroy[3], Fabrizio Molteni[2], Roly Gosling[4], Anders Björkman[1], Andreas Mårtensson[1,5]
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INTRODUCTION: Malaria in Zanzibar has decreased substantially over the past decade due to multiple strategies, including vector control, improved diagnostics, effective treatment and weekly passive surveillance at all government health facilities. As the islands move closer to elimination, asymptomatic low-density parasitemia in the community becomes increasingly important. This study aimed to evaluate if screening all residents with a malaria rapid diagnostic test (mRDT) and treating all mRDT positive individuals would reduce transmission in specific, focal hotspots.
METHODS: Active case detection was undertaken in May and June 2012 in five communities where surveillance data indicated increased transmission at this time during the two previous years. The residents (approximately 6000 and 4000 people in the first and second rounds, respectively) were screened twice (4 weeks apart) using a *Plasmodium falciparum* specific RDT (Paracheck-Pf) and treated with ACT (artesunate-amodiaquine) if found positive. A filter paper blood spot was collected for polymerase chain reaction (PCR) analyses to retrospectively identify additional sub-patent infections, including species determination. Nearby control shehia's with comparable histories of hot spot identification were monitored through passive surveillance.
RESULTS: A total of 12 (0.01%) and 8 (0.02%) residents had positive mRDT results in the first and second round, respectively. By contrast, 80 (1.3%) and 180 (4.5%) PCR positive individuals (preliminary data) were detected in the first and second round. Many mixed infections were identified through PCR along with a high proportion of P. malariae infections. Surveillance data (malaria positivity rates in health care facilities) from the villages following the mRDT screening and treatment of positives detected no beneficial effect on subsequent transmission in the following weeks when compared with control areas.
CONCLUSION: Screening and treatment based on RDT and ACT did not reduce transmission due to the large proportion of missed infections. Field-friendly molecular based techniques with greater sensitivity are critical for improved malaria case detection in areas aiming for malaria elimination.

S20: The role of vaccines in malaria elimination

Chairs: Prof Christopher V Plowe and Prof Marcel Tanner

Speaker 1: Prof Christopher V Plowe,The potential role of vaccines in malaria elimination: Introduction and lessons from past eradication campaigns, University of Maryland School of Medicine, United States of America
Speaker 2: Dr Edward A Wenger, Towards elimination: Modeling vaccines that interrupt malaria transmission I, Intellectual Ventures Laboratory, United States of America
Speaker 3: Prof Marcel Tanner, Towards elimination: Modeling vaccines that interrupt malaria transmission II, Swiss Tropical and Public Health Institute and University of Basel, Switzerland
Speaker 4: Dr Stephen L Hoffman, Plans for development of the PfSPZ Vaccine for use in malaria elimination, Sanaria Inc., United States of America

The potential role of vaccines in malaria elimination: Introduction and lessons from past eradication campaigns

Christopher V Plowe
Howard Hughes Medical Institute/Center for Vaccine Development, University of Maryland School of Medicine, Baltimore, Maryland, USA

Vaccines have been essential to nearly all successful past communicable disease elimination/eradication campaigns, and were absent from all unsuccessful campaigns, including the past global malaria eradication campaign. Vaccines could play as important a role in the elimination of *Plasmodium falciparum* as they have played in the global eradication of smallpox and the elimination of polio from the Western Hemisphere and measles from the Americas. This presentation will consider the potential contributions of vaccines to the elimination and eventual eradication of malaria in light of the current status of malaria vaccine development and historical lessons from past campaigns to eradicate malaria and other diseases.

Towards elimination: Modeling vaccines that interrupt malaria transmission I

Edward A Wenger, Philip A Eckhoff
Institute for Disease Modeling, Intellectual Ventures Laboratory, Bellevue, Washington, USA

The impact of potential malaria vaccines is presented utilizing the EMOD model, a comprehensive model of the vector life cycle coupled to a detailed mechanistic representation of intra-host parasite and immune dynamics. Values of baseline transmission and vector feeding behavior parameters are identified, for which local elimination is enabled by layering pre-erythrocytic vaccines of various efficacies on top of high and sustained insecticide-treated net coverage.

Towards elimination: Modeling vaccines that interrupt malaria transmission II

Marcel Tanner[1,2], Thomas A. Smith[1,2],
[1]*Swiss Tropical and Public Health Institute, 4002 Basel, Switzerland*
[2]*University of Basel, 4002 Basel, Switzerland*

Current global health commitments to malaria elimination and eradication have increased interest in and need for the development of new tools for reducing malaria transmission, even ones with limited potential for the immediate control of disease or mortality. The presentation discusses the potential applications of transmission blocking vaccines (TBVs) against malaria (sexual stages vaccines as well as pre-erythrocytic vaccines) using a quantitative framework to explore their likely effects. Five key issues are considered: (i) the measurement of efficacy, (ii) how efficacy translates into effectiveness at the population level, (iii) the circumstances in which TBVs may make transmission interruption feasible, (iv) the rationales for combining TBVs with other interventions, and (v) the benefits TBVs could offer in the subsequent control of reintroductions. Further potential uses are protection of other vaccines from the evolution of parasite insensitivity to vaccine-induced responses. The combination of TBVs with biocides or other malaria vaccines will increase chances of interrupting transmission, whereas the value of TBVs for morbidity control will be limited. Vaccine combination will also protect against selection of insensitive para- sites. Simulations indicate that TBVs will reduce risks of re-establishment of transmission when vector control is withdrawn. Mathematical analyses show that efficacy and coverage are equally important, implying that a vaccine that requires a small number of doses (ideally one) is preferable to one that is difficult to deliver, even if this entails accepting a lower efficacy. Different scenarios to reach sustainable interruption of transmission in different epidemiological settings will be discussed.

Plans for development of the PfSPZ Vaccine for use in malaria elimination

Stephen L Hoffman
Sanaria Inc., Rockville, MD, USA

The term, Vaccine that Interrupts Malaria Transmission (VIMT) was introduced by the Malaria Eradication Research Agenda (malERA) initiative [malERA Consultative Group on Vaccines. A research agenda for malaria eradication: vaccines. *PLoS Med.* **8**, e1000398 (2011)]. VIMTs include not only vaccines that induce protective immune responses against the sexual and mosquito stages of malaria parasites, the so-called traditional, altruistic transmission blocking vaccines, but also any other vaccine approach that reduces transmission. An ideal VIMT would induce protective immune responses against all stages of the parasite life cycle. However, the ideal single stage VIMT would prevent infection at the pre-erythrocytic stage of the parasite life cycle, thereby preventing all parasite caused disease and transmission from humans to mosquitoes. The PfSPZ Vaccine is a pre-erythrocytic stage vaccine and the malaria vaccine closest to being able to be used as a VIMT. However, we are still at the early stages of development. We have set an ambitious 4-5 year timeline for moving from phase 1 through pivotal phase 3 clinical trials and then to licensure and demonstration of the capacity of the vaccine to eliminate *Plasmodium falciparum* from a population of greater than 200,000 individuals. The plans for doing so, including the challenges we face, our strategies for overcoming them, and the roles of the numerous international partners involved in the process will be discussed.

S21: Improving malaria prevention, diagnosis and treatment through market-based intervention: challenges, opportunities and approaches.

Chairs: Dr Prashant Yadav and Dr Bruno Moonen.

Speaker 1: Dr Alexandra Cameron, UNITAID's strategic approach to market approaches in public health, and examples from malaria, UNITAID, United States of America.
Speaker 2: Dr Tom Mclean, Fighting insecticide resistance: challenges and approaches to encourage the development of innovative vector control tools, IVCC, United Kingdom
Speaker 3: Dr Andrea Bosman, Improving malaria case management: integrated approaches to scaling-up malaria rapid diagnositic tests and ACTs and redressing the market imbalance between diagnostic testing and treatment, World Health Organisation, Switzerland
Speaker 4: Dr Wellington Oyibo, Creating a market for malaria diagnostic testing in Nigeria: experiences and perspectives, University of Lagos, Nigeria

Market-based approaches to improve public health are relatively new, and have emerged from increasing recognition that access to medicines, diagnostics, and preventive items is often limited by shortcomings in the marketplace. Through interventions aimed at redressing these shortcomings, market-based approaches can have substantial impact and are now widely recognized as powerful tools for increasing access to key commodities. Malaria stakeholders such as global health agencies, donors and governments, are increasingly adopting market-shaping strategies as an additional means of improving access to key commodities alongside traditional service delivery initiatives.

In the field of malaria, commodity markets are complex, dynamic and not well understood, particularly in the private sector where large proportions of people seek care for malaria. Market-based approaches to improve access to malaria products are therefore inherently challenging. This symposium will explore current issues and opportunities related to the use of market interventions to improve access to commodities used for the prevention, diagnosis and treatment of malaria through a series of presentations.

Presentations will be followed by a facilitated discussion on opportunities for improving malaria prevention and control through market-shaping interventions. Two discussants (*Dr Prashant Yadav, University of Michigan, Dr Bruno Moonen, Clinton Health Access Initiative)* will initiate the discussion with a short commentary, which will be followed by an open discussion.

S22: Area-wide control of malaria vectors

Chair: Dr Jeremie RL Gilles

Speaker 1: Dr Mark Q. Benedict, Area-wide control of vectors: Turning the control paradigm upside down, University of Perugia, Italy.
Speaker 2: Dr Richard MUnited Kingdomabana, Use of solar power in a mosquito mass trapping malaria control trial, International Centre for Insect Physiology and Ecology
Speaker 3: Dr Givemore Munhenga, Sterile insect technology: field feasibility study site selection, species abundance and monthly distribution of Anopheline mosquitoes in northern Kruger National Park and assessment of compatibility and competitiveness of laboratory reared irradiated males using con-specifics from Malahlapanga, NICD, South Africa.
Speaker 4: Dr Jeremie RL Gilles, Novel approaches to control mosquito vector population, progresses and challenges, International Atomic Energy Agency, Austria.

Sterile Insect Technique: field feasibility study site selection, species abundance and monthly distribution of Anopheline mosquitoes in northern Kruger National Park and assessment of compatibility and competitiveness of laboratory reared irradiated males using con-specifics from Malahlapanga.

Givemore Munhenga[1,2], Basil D Brooke[1,2], Belinda L Spillings[1,2], Leyya Essop[1,2], Richard H Hunt[1,2], Stephen Midzi[3], Danny Govender[4,5], Lizette L Koekemoer[1,2].

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[5]Department of Paraclinical Sciences, Faculty of Veterinary Science, University of Pretoria, Private Bag X04, Onderstepoort, 0110, South Africa.

BACKGROUND: The successful suppression of a target insect population using the sterile insect technique partly depends on the premise that laboratory insects used for mass rearing are genetically compatible with the target population, that mating competitiveness of these males are comparable to that of their wild counterparts, and that mass rearing and sterilization processes do not compromise male fitness to a degree that precludes them from successfully competing for mates in the wild. In addition before implementation of an Area Wide Integrated Vector Management Programme against malaria vectors which includes SIT requires comprehensive knowledge on the bionomics of mosquitoes in the targeted area. This study investigated these parameters with an aim of assessing the feasibility of using sterile insect technique as an additional vector control intervention under local setting and context.
METHODS: Wild caught An. arabiensisfemales were used to assess the mating compatibility and mating competitiveness between laboratory-reared, irradiated males and un-irradiated males in small laboratory cages. A survey of Anophelesspecies was made between July 2010 and December 2012. Mosquitoes were collected from five sites within the Nxanatseni region, Kruger National Park. Methods included carbon dioxide-baited traps, human landing catches and larval collections. Collected specimens were identified to species level using morphological characteristics and polymerase chain reaction assays.rEsuLts: A total of 3,311 specimens belonging to eight taxa were collected. The population densities fluctuated according to seasons. Tran-sectional distribution of anopheline showed that Anopheles arabiensiswas confined at Malahlapanga. Wild collected females successfully mated with laboratory reared males and irradiation of males resulted in near complete sterility. Competitive assays showed that irradiated males are as competitive as un-irradiated males for wild and laboratory reared females.
CONCLUSIONS: Anopheline species occur in northern regions of Kruger National Park and population densities fluctuate between seasons. There is a perennial presence of an isolated population of An. arabiensis at Malahlapanga site which declines in density during dry winter months. Irradiation of colonized Anopheles arabiensismales reduces their fertility to near zero. Mating competitiveness showed that irradiated males retain sufficient mating vigor to compete with un-irradiated males under laboratory conditions. This information provides a unique opportunity for assessing feasibility of SIT as an additional malaria vector control option.

S23: Increasing access to malaria prevention among pregnant women: results from systematic reviews and economic and anthropological studies by the MiP consortium.

Chairs: Dr Harry Tagbour and Dr Halidou Tinto

Speaker 1: Dr Anna Maria van EijK, Are coverage targets for intermittent preventive therapy and insecticide treated nets for the control of malaria in pregnancy in sub-Saharan Africa being reached?, Liverpool School Tropical Medicine, United Kingdom.
Speaker 2: Dr Jenny Hill, Factors affecting the delivery, access and use of interventions to prevent malaria in pregnancy in sub-Saharan Africa: A systematic review and meta-analysis, Liverpool School Tropical Medicine, United Kingdom.
Speaker 3: Dr Elisa Sicuri, Patient costs associatd with malaria in pregnancy: estimated from eight countries, University of Barcelona, Spain.
Speaker 4: Dr Sikle Lutzelschwab, Cost effectiveness analysis of 2 versus 3 or more doses of sulfadoxine-pyrimethamine as intermittent preventive treatment for malaria during pregnancy, London School of Hygiene and Tropical Medicine, United Kingdom.
Speaker 5: Dr Christopher Pell, The acceptability of intermittent preventive treatment (IPTp) and intermittent screening and testing (IST) in the context of clinical trials: findings from qualitative studies in Malawi and Ghana, University of Amsterdam, The Netherlands.

Description: Update on the coverage and cost effectiveness of MiP interventions and factors affecting their delivery, access and use, including results from multi-country economic and anthropological studies in Africa, Asia, the Pacific and Latin America.

Are coverage targets for Intermittent Preventive Therapy and Insecticide treated Nets for the control of malaria in pregnancy in sub-Saharan Africa being reached? A synthesis and meta-analysis of national survey data for 2009-2011

Anna Maria van Eijk[1], Jenny Hill[1], David A Larsen[2], Jayne Webster[3], Richard W. Steketee[4], Thomas P Eisele[5], Feiko O ter Kuile[1]

[1] Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, United Kingdom; [2] Department of Public Health, Food Studies and Nutrition, Syracuse University, Syracuse, New York, USA; [3] Disease Control Department, London School of Tropical Medicine and Hygiene, London, United Kingdom; [4] Malaria Control Program and MACEPA, PATH, Seattle, USA; [5] Department of Global Health Systems and Development, Tulane University School of Public Health and Tropical Medicine, New Orleans, USA

BACKGROUND: Pregnant women in malarious areas in sub-Saharan Africa are vulnerable to malaria. Recommended prevention strategies include intermittent preventive treatment (IPTp) with two doses of sulfadoxine-pyrimethamine and the use of insecticide treated nets (ITNs). However, progress with implementation has been slow. We reviewed the coverage of IPTp, ITN, and antenatal care (ANC) in Africa and explored associations with individual and country-level factors, including the role of funding availability.
METHODS: IPTp and ITN coverage among pregnant women were estimated using data from nationally representative household surveys from 2009-2011. Demographic data on births and published data on malaria exposure were used to estimate the number of malaria-exposed births (live- and stillbirths combined) for 2010 by country. Meta-regression was used to evaluate factors associated with coverage.
RESULTS: Of the 21·4 million projected malaria-exposed births in 27 countries in 2010, an estimated 4.6 million (21·5%, 95% CI 19·3-23·7%) were born to mothers who received IPTp. ITNs were used during pregnancy for 10·5 million out of 26·9 million births (38·8%, 95% CI 34·6-43·0%, 37 countries). Among countries with previous estimates projected for 2007, IPTp coverage increased from 13·1% (95% CI 11·9-14·3%) to 21·2% (95% CI 18·9-23·5%, 14 countries) in 2010, and ITN use from 17·9% (95% CI 15·1-20·7%) to 41·6% (95% CI 37·2-46·0%, 24 countries). Some countries experienced an absolute decrease in coverage of >10% for IPTp (2/24) or ITNs (3/30). Higher disbursement of funds for malaria control and a longer time interval since IPTp policy adoption were associated with a higher IPTp coverage. Higher disbursement of funds for malaria control and higher total fertility rate were associated with higher ITN use, whereas a high per capita Gross Domestic Product was associated with lower ITN use. IPTp coverage showed greater inequity overall than ITN use, with richer, educated, and urban women more likely to receive IPTp than their poorer, uneducated, rural counterparts.
CONCLUSIONS: Whilst IPTp coverage and ITN use among pregnant women has increased in most countries, coverage remains far below global targets. It will be important to evaluate whether WHO's recent policy update on IPTp leads to better gains in IPTp coverage.

Factors Affecting the Delivery, Access, and Use of Interventions to Prevent Malaria in Pregnancy in Sub-Saharan Africa: A Systematic Review and Meta-Analysis

Jenny Hill[1], Jenna Hoyt[1], Anna Maria van Eijk[1], Lauren D'Mello-Guyett[1], Feiko O. ter Kuile[1], Rick Steketee[2], Helen Smith[3], Jayne Webster[4]

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BACKGROUND: Malaria in pregnancy has important consequences for mother and baby. Coverage with the World Health Organisation–recommended prevention strategy for pregnant women in sub-Saharan Africa of intermittent preventive treatment in pregnancy (IPTp) and insecticide-treated nets (ITNs) is low. We conducted a systematic review to explore factors affecting delivery, access, and use of IPTp and ITNs among healthcare providers and women.

METHODS AND RESULTS: We searched the Malaria in Pregnancy Library and Global Health Database from their inception to 23 April 2013, without language restriction. Data extraction was performed by two investigators independently, and data was appraised for quality and content. Data on barriers and facilitators, and the effect of interventions, were explored using content analysis and narrative synthesis. We conducted a meta-analysis of determinants of IPTp and ITN uptake using random effects models, and performed subgroup analysis to evaluate consistency across interventions and study populations, countries, and enrolment sites. We did not perform a meta-ethnography of qualitative data.

Ninety-eight articles were included, of which 20 were intervention studies. Key barriers to the provision of IPTp and ITNs were unclear policy and guidance on IPTp; general healthcare system issues, such as stockouts and user fees; health facility issues stemming from poor organisation, leading to poor quality of care; poor healthcare provider performance, including confusion over the timing of each IPTp dose; and women's poor antenatal attendance, affecting IPTp uptake. Key determinants of IPTp coverage were education, knowledge about malaria/IPTp, socio-economic status, parity, and number and timing of antenatal clinic visits. Key determinants of ITN coverage were employment status, education, knowledge about malaria/ITNs, age, and marital status. Predictors showed regional variations.

CONCLUSIONS: Delivery of ITNs through antenatal clinics presents fewer problems than delivery of IPTp. Many obstacles to IPTp delivery are relatively simple barriers that could be resolved in the short term. Other barriers are more entrenched within the overall healthcare system or socio-economic/cultural contexts, and will require medium- to long-term strategies.

Patient costs associated with malaria in pregnancy: estimates from eight countries

Elisa Sicuri[1] Silke Lutzelschwab[2], Kara Hanson[2] *on behalf of all study collaborators*

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BACKGROUND: In 2007, 125.2 million pregnancies occurred in areas characterized by *Plasmodium falciparum* and/or *Plasmodium vivax* transmission. As well as causing clinical illness, malaria infection during pregnancy is associated with maternal anaemia, poor pregnancy outcomes and adverse health events for the newborn, including abortion, preterm birth, low birth weight, and neonatal and infant mortality. Despite this substantial disease burden, information on patient costs associated with malaria in pregnancy is extremely scarce. This is even more pronounced in low transmission areas where *Plasmodium vivax* predominates. This study aims to fill this gap by presenting malaria prevention and treatment costs incurred by pregnant women in a number of endemic countries with different epidemiological, socio-economic and health system characteristics: Brazil, Colombia, Ghana, Mali, Kenya, Tanzania, India, and Papua New Guinea.

METHODS: This study was conducted alongside several studies undertaken through the Malaria in Pregnancy consortium. Exit surveys were conducted in at least one site in each country at several health facilities representing different health system levels between 2010 and 2012. Using a standard questionnaire, pregnant women were asked about demographic and socio-economic characteristics and about costs incurred for the prevention and treatment of malaria during pregnancy.

RESULTS: A total of about 2000 pregnant women were interviewed. Costs associated with prevention and treatment of malaria in pregnancy will be presented, broken down by direct (out-of-pocket expenditures on medical and non-medical expenses) and indirect (value of time lost because of the disease) costs. Variation by malaria transmission level, health system level and characteristics, and women's socioeconomic status will be explored. Depending on health system features and on women's socio-economic status, out-of-pocket expenditures will range from low to catastrophic.

CONCLUSIONS: The information generated by this analysis will help health policy decision-makers to set priorities and improve the current control of malaria in pregnancy, as well as understanding the consequences of the disease for household well-being.

Cost Effectiveness analysis of 2 versus 3 or more doses of Sulfadoxine-Pyrimethamine as intermittent preventive treatment for malaria during pregnancy

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BACKGROUND: The emergence and spread of *Plasmodium falciparum* resistance against Sulfadoxine-Pyrimethamine (SP) has led to rising concerns about the effectiveness of SP as intermittent preventive treatment in pregnancy (IPTp). Following an expert meeting in June 2012, WHO released an updated recommendation for IPTp with SP, in which the originally recommended 2 treatment doses of IPTp-SP were increased to monthly IPTp-SP during the second and third trimesters. Part of the evidence supporting this decision was a meta-analysis by Kayentao *et al.* (2013) which compared 2 versus 3 or more doses of IPTp-SP based on results from 7 trials in 6 sub-Saharan African countries. This synthesis concluded that 3 or more doses of IPTp-SP were associated with a reduced risk of low birth weight (LBW) (RR=0.80, 95% CI, 0.69-0.94). In addition to understanding the epidemiological evidence it is crucial for policy makers to know the incremental cost-effectiveness of 2 versus 3 or more doses of IPTp-SP and therewith be able to predict the economic implications for their setting.

This analysis estimates the incremental cost-effectiveness of 3 or more doses of IPTp-SP versus 2 doses of IPTp-SP.
METHODS: The analysis is performed from a health provider and societal perspective. Outcome measures are estimated using the results published in the meta-analysis by Kayentao et al. and data retrieved from published literature. Cost estimates in the model use data from observational studies, exit surveys (Tanzania, Mali and Kenya) and health facility costing collected by the Economics Working Group of the Malaria in Pregnancy Consortium, as well as estimates found in the literature.
RESULTS: The cost per DALY averted will be presented, together with one-way sensitivity analysis over structural factors, such as what happens if average dose of IPTp increases to 5 per pregnancy, and parameters such as efficacy outcome measures, costs and their determinants, for example time taken to administer IPTp-SP during an antenatal care visit. Probabilistic sensitivity analysis will be presented over a range of parameters and plotted on the cost-effectiveness plane.
CONCLUSIONS: Results will help policy makers and programme managers in making decisions about the optimal regimen and policy of IPTp-SP in their setting.

The acceptability of intermittent preventive treatment (IPTp) and intermittent screening and testing (IST) in the context of clinical trials: findings from qualitative studies in Malawi and Ghana.

Christopher Pell[1,2], Arantza Meñaca[2,3], Lucinda Manda[4], Samuel Chatio[5], Abraham Hodgson[6], Linda Kalilani[4], Robert Pool[1,2]

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BACKGROUND: Malaria during pregnancy (MiP) is a major global health concern, resulting in adverse birth outcomes and poor maternal health. Intermittent preventive treatment of malaria during pregnancy (IPTp) is a WHO-recommended intervention to reduce morbidity and mortality in endemic areas of sub-Saharan Africa. Although sulphadoxine pyrimethamine (SP) is currently administered as IPTp in many countries, concerns about its sustained efficacy have prompted interest in alternative strategies to protect women from MiP. This presentation explores the acceptability – within the context of clinical trials – of IPTp and intermittent screening and testing (IST) in northern Ghana and southern Malawi.
METHODS: Data were collected as part of a larger multi-site qualitative study exploring the social and cultural context of MiP, which involved a range of data collection methods with various types of respondent. In this presentation, we focus on the section of fieldwork that addressed IST: focus group discussions with trial participants (Ghana: 8; Malawi: 6), interviews with clinical trial staff (Ghana: 10; Malawi: 2), and observations at the health facilities where the trials were conducted.
RESULTS: Although there were reports of a dislike of needles (and rumours of blood stealing in Malawi), at both sites, trial participants were keen to know about their health and malaria status and therefore positive about the availability of diagnostic tests as part of the trials. Indeed, this – combined with the perceived high-quality care – was often their main motivation for participating in the trials. At both sites, side effects (including dizziness and vomiting) were mentioned in relation to SP. Also, at both sites, respondents were positive about IST-arm antimalarials (artemether/lumefantrine in Ghana and dihydroartemesinin-piperaquine in Malawi), which were viewed largely without side effects and as effective against malaria, particularly in Malawi. Interviewed health staff also tended to be more enthusiastic about IST and viewed the testing as an important element.
CONCLUSIONS: Respondents' positive attitudes towards diagnostic tests offered in the trial and particularly the malaria testing provided in the IST trial arms suggest that, at these sites, IST would be acceptable (and possibly attractive) to pregnant women.

S24: Ten years of intensive malaria control on Bioko Island: Is elimination in sight?

Chairs: Prof Fred Binka and Dr Immo Kleinschmidt.

Speaker 1: Dr Matilde Riloha, Introduction to the Bioko Island Malaria Control Project, National Malaria Control Program, Equatorial Guinea
Speaker 2: Dr Immo Kleinschmidt, A decade of intensive malaria control: Determinants of Impact on malaria burden in Bioko, London School of Hygiene and Tropical Medicine, United Kingdom
Speaker 3: Dr Salim Abdulla, Plans for elimination with a Sporozoite malaria vaccine Ifakara Health Institute, Tanzania
Speaker 4: Mr. Praxedes Rabat Macambo, Practical challenges and opportunities for achieving elimination a proposed roadmap, Ministry of Health, Equatorial Guniea.

A decade of intensive malaria control: Determinants of Impact on malaria burden in Bioko

Immo Kleinschmidt
London School of Hygiene and Tropical Medicine, United Kingdom

Comprehensive malaria control measures were introduced in Bioko, Equatorial Guinea, nearly ten years ago. Significant reductions in EIR, malaria related disease burden, child mortality and sero-positivity to malarial antigens have been observed over this period, but these reductions have been uneven, and significant transmission persists in parts of the island. Interventions were initially applied more or less evenly across the island, but recently additional measures were undertaken in places where prevalence of infection has remained high. Do we know what factors have influenced transmission reduction in Bioko? This talk will examine factors that are associated with the impact of interventions in Bioko.

S25: Larval source management for malaria control.

Chairs: Dr Steve Lindsay and Dr Lucy Tusting

Speaker 1: Dr Steve Lindsey, Larval source management for malaria control, Durham University, United Kingdom
Speaker 2: Dr Lucy Tusting, A systematic review and meta-analysis of mosquito larval source management for controlling malaria, London School of Hygiene and Tropical Medicine, United Kingdom
Speaker 3: Dr Silia Majamabee, Larval source management: an African perspective, Liverpool School of Tropical Medicine, United Kingdom
Speaker 4: Dr Hmooda Toto Kafy, Larval source management in Khartoum, Sudan: a case study, Ministry of Health, Sudan.

Larval source management for malaria control in Africa

Steve Lindsay
Durham University, United Kingdom

The unprecedented decline in malaria experienced in sub-Saharan Africa over the past decade has been achieved largely by the massive roll-out of long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS). However, in many places malaria remains entrenched despite the introduction of either LLINs or IRS. There is a continual cry for new tools that not only attack vectors entering houses, but also those biting outdoors, and for technologies that can be used to contain the threat of insecticide resistance. Larval source management (LSM) can provide solutions to these problems and is now endorsed by the World Health Organisation as a supplementary tool for malaria vector control in certain situations. Steve Lindsay explains what is meant by LSM, discusses the advantages and disadvantages of this approach and presents the WHO guidelines for implementation of LSM in sub-Saharan Africa.

A systematic review and meta-analysis of mosquito larval source management for controlling malaria

Lucy Tusting
London School of Hygiene and Tropical Medicine, United Kingdom

Mosquito larval source management (LSM), which targets mosquito larvae as they mature in aquatic habitats, may be an effective supplementary method of malaria vector control. A Cochrane Review was conducted to evaluate the effectiveness of mosquito LSM for preventing malaria. 13 studies were included; four cluster-RCTs, eight controlled before-and-after trials, and one randomized cross-over trial. LSM significantly reduced malaria incidence and prevalence at sites across Africa and Asia. While further research is needed to evaluate whether LSM is appropriate in parts of rural Africa where larval habitats are extensive, the results of the Cochrane Review support LSM as another policy option in Africa and Asia for reducing malaria morbidity alongside LLINs and IRS in both urban and rural areas where a sufficient proportion of larval habitats can be targeted.

Larval source management: an African perspective

Silas Majamabere
Liverpool School of Tropical Medicine, United Kingdom

Renewed interest in the role of larval source management for malaria control has gained momentum and evidence is growing for the benefit of this intervention to complement long-lasting insecticide treated nets (LLINs) and indoor residual spraying (IRS). Although the World Health Organisation has now published an operational manual on LSM in Africa, implementation of its recommendations in different countries will require a systematic investment in capacity building for LSM within National Malaria Control Programs (NMCPs). This is hugely important because this type of intervention is not optimal in all settings, therefore informed decisions need to be made for the best use of resources. The lack of expertise within NMCPs can be exploited by private companies whose primary objective is business rather than malaria control. Although LSM is viewed as an expensive intervention, it is likely to be cost-effective if it is owned by communities in malaria endemic countries and if it is designed within an integrated vector management program. Most malaria-endemic sub-Saharan countries have a young and often unemployed population that can be organized to implement LSM. Some of these countries already have “cleaning days” where communities meet to clean roads, drains, and remove standing water. This system can be improved on to involve all sectors involved in water management (agriculture, infrastructure, and environment) and to comprehensively reduce mosquito abundance including vectors of malaria, lymphatic filariasis and dengue.

Larval source management in Khartoum, Sudan: a case study

Hmooda Toto Kafy
National Malaria Programme, Ministry of Health, Khartoum, Sudan

Malaria was the major cause of outpatient attendances, admissions and deaths in Khartoum in the 1980s and 1990s. This led to the launch of the Khartoum Malaria Free Initiative (KMFI) in 2002 by the State and Federal Ministry of Health, in collaboration with the World Health Organisation (WHO), with the aim of reducing malaria incidence in Khartoum State by 80% between 2002 and 2008 to less than 0.5 cases per 1000 people per annum. Larval source management (LSM) is the mainstay of the KMFI, including larviciding, repair of damaged water pipes, removal of water basins by law, intermittent irrigation, environmental management (draining and flushing breeding sites) and biological control using Gambusia fish in irrigated schemes. Case management has also been improved, while indoor residual spraying (IRS) and long-lasting insecticidal net (LLIN) distribution are not conducted in Khartoum. Significant reductions in malaria morbidity and mortality have been observed; parasite prevalence has declined from 0.3% in 2003 to 0.03 in 2008 and total confirmed and unconfirmed malaria cases, as a proportion of total outpatient attendances, declined from 26.3% in 1999 to 1.7% in 2010. Hmooda Toty Kafy discusses the impact of the program, the role of LSM, and ongoing challenges to malaria control in Khartoum.

S26: Indoor Residual Spraying: Maximizing Innovation, Impact and Sustainability

Chairs: Dr Bradford Lucas, Dr Allison Belemvire and Dr Kristen George

Speaker 1: Dr Peter Chandonait, Building a better toxic waste site: how mobile phones imporve environmental compliance management for a malaria prevention program in Africa, Abt Associates, United States and America

Speaker 2: Dr Christopher Helm, Using Insecticide Quantification Kits (IQKTM) to maximize the efficiency and impact of IRS through innovative and effective quality control , IVCC, United Kingdom

Speaker 3: Dr. Lassana Konate, The Impact of IRS on Malaria Prevalence and Entomological Indicators in Senegal, Universite Cheikh Anta Diop of Dakar, Senegal.

Speaker 4: Dr. Yemane Ye-ebiyo Yihdego, The Ethiopia Health Extension Program as a platform to make indoor residual of houses (IRS) more cost effective and sustainable, Abt Associates, Ethiopia.

Building a Better Toxic Waste Site: How Mobile Phones Improve Environmental Compliance Management for a Malaria Prevention Program in Africa

Peter Chandonait
Environmental Compliance Manager, Abt Associates

USAID's Africa Indoor Residual Spraying (IRS) project involves the application of pesticides with residual toxicity to the inside surfaces of millions of homes in order to kill the mosquitos that spread malaria. A strong environmental management system (EMS) is required to minimize or eliminate the negative consequences of this widespread use of toxic chemicals. Pesticides are stored, dispensed, and disposed of at hundreds of operational sites in remote and difficult to access locations, and the facilities at each of these sites must meet stringent criteria to avoid environmental, health, or safety problems.

Before each spray season, inspections are performed to assess the condition of the facilities, work lists are generated, and responsibilities assigned. A second inspection is performed just before spraying starts, to ensure that all concerns have been addressed and environmental compliance has been achieved. In Abt Associate's project country office and the US home office, senior staff members are ultimately responsible for granting approval to start activities at each site. They need timely access to the inspection information to get a true understanding of environmental compliance status.

Abt Associates has developed a mobile smart phone application that provides GPS and photo evidence of site visits and site conditions. Using the built-in capabilities of the smart phone, the inspector obtains the GPS coordinates of the site, and photographs standard key features, as well as any special or non-compliant aspects. The completion of a rigorous checklist on the phone creates a data record, including photographs and GIS location, that is uploaded to a server as soon as the phone connects via mobile or fixed wireless service. There, integrated, web-based applications are exploited for report development, geographic visualization of field locations, and other uses by management.

With this system, management in the US home office and in the thirteen country offices can be confident in making well-informed decisions about the readiness for spraying operations. In addition to the timeliness of the reports, accuracy is improved by the use of mandatory responses. Considerable savings can be realized by reducing the need for site visits, and eliminating the need for scanning or transcription and emailing of reports.

Using Insecticide Quantification Kits (IQKTM) to maximize the efficiency and impact of IRS through innovative and effective quality control.

Christopher Helm
IVCC, United Kingdom

Indoor Residual Spraying (IRS) is a major control measure in the fight against malaria, and has been a significant factor in the reduction of deaths from vector-borne diseases over the past decade. However, the success of an IRS programme depends heavily upon spray quality and until now it has proved challenging to indentify a time and cost-effective means to assure quality.

To solve this problem IVCC has worked with leading research teams in Europe, to develop innovative new quality control technologies. Insecticide Quantification Kits (IQKTM) are chemical or enzyme-based, biochemical assays that cover the insecticide classes most commonly used in IRS campaigns and can be used at or near the spray site to assess the level of insecticide present on the sprayed surface.

The IQK tests involve a simple sampling step followed by a vial or strip test with a sensor unit and a 'traffic light' type indicator. This allows immediate visual assessment of the amount of insecticide in the sample.

Until the IQKs were developed, the only means available to spray programme managers for testing the effectiveness of spraying were tests using live mosquitoes or high performance liquid chromatography. Both of these methods have proved impractical or unsatisfactory. By contrast the IQKs are cost-effective, easy to use and have a unique ability to provide a rapid assessment of spray team performance so that any problems can be rectified promptly, whether by re-spraying, retraining or improved supervision.

The IQK technologies have passed the "proof of concept" stage, having been proved effective both in the laboratory and also in field trials.

Following these research successes, IVCC has been engaged with an industry partner, Avima Pty., to develop a fully commercial version of the IQK technologies. Prototype demonstrations have been carried out in conjunction with "early adopter" spray programs to confirm the effectiveness of the developed product prior to putting the IQK into full scale manufacture.

This presentation will describe the process of bringing the IQK into full scale manufacture from the laboratory bench and discuss the findings from the early adopter prototype demonstrations."

The Impact of IRS on Malaria Prevalence and Entomological Indicators in Senegal

Dr. Lassana Konate, Research Entomologist
Universite Cheikh Anta Diop of Dakar (UCAD)

BACKGROUND: Vector control using universal coverage with long-lasting insecticide treated nets (LLINs) is the primary strategy of malaria prevention in Senegal. Since 2007,with the support of the President's Malaria Initiative, indoor residual spraying (IRS) has been implemented in select districts, in combination with ITNs since 2009. To date, there has been no assessment of the impact in terms of gains of this intervention on malaria transmission and its morbidity.
METHODS: Entomological and parasitological data were compared in two districts sprayed with carbamate and two neighboring unsprayed districts, all of which had received LLIN universal coverage campaigns in the past two years. Cone bioassays for spray quality and insecticide duration and collection of resting mosquitoes to determine vector density, behavior, blood fed status and longevity were collected, as well as parasite prevalence in a convenience sample of children brought for blood testing in response to an invitation.
RESULTS: The duration of insecticide on walls did not exceed three months with both the laboratory (An. gambiae M) strain and the locally collected populations. A reduction of 30-50% for longevity of females and of 65% for resting density was observed in treated districtscompared to untreated districts, though the proportion of fed females as well as the endophagous rate remains relatively comparable between treated and untreated districts. Parasite prevalence among children in treated districts also showed a marked reduction compared to untreated districts.
CONCLUSION: While there is a lack of baseline data and of rigorous methodology for sampling of the parasite prevalence, this suggests that there may be a reduction in parasite prevalence in the two districts in which IRS and ITNs were combined, compared to ITNs alone. More rigorous methods of sampling parasite prevalence and collection of baseline data prior to initiating IRS are necessary to determine if the reduction in entomological indicators is due to IRS, and if so, if these then translate to decreases in parasite prevalence. Future plans for available data include calculation of entomological inoculation rate and comparison of health facility incidence data in treated and untreated districts.
KEYWORDS: Malaria, Indoor residual spraying, Effectiveness, transmission, P. falciparum, prevalence

The Ethiopia Health Extension Program as a platform to make indoor residual of houses (IRS) more cost effective and sustainable

Dr. Yemane Ye-ebiyo Yihdego
AIRS-Ethiopia Chief of Party, Abt Associates, Ethiopia

BACKGROUND: Traditionally, IRS in Ethiopia has been planned and implemented by the district health office (DHO) with technical and operational inputs from regional, zonal, and central health offices.

The health extension program (HEP) in Ethiopia is a new community based health care delivery system aimed at achieving a universal coverage of preventive and promotive services in rural villages where the burden of communicable diseases is high.

In 2012, with support from PMI and in collaboration with the Oromia regional health bureau, Abt/AIRS-Ethiopia piloted the feasibility of incorporating IRS operation to the HEP at the community level. Pilot was conducted in one district with 20 kebeles.
METHOD: With the help of the project, the DHO of Kersa trained 40 HEWs from 20 kebeles on key IRS implementation strategies. HEWs recruited five spray operators (SOPs) from each kebele and trained them for six days on key IRS components. HEWs in close collaboration with village leaders and supervision from districts experts carried out the spray operation in their respective kebeles.

RESULTS: SOPs sprayed 22,744 unit structures covering 98% of all eligible housing units found. There was about 10 percent savings in the HEP based IRS model and saving is estimated to be up to 40 percent in the second year. Wall bioassay tests conducted 1-3 days after spraying showed mosquito mortality at 100 percent. Positive feedback was received from SOPs, communities and district health workers. No incident was reported with environmental compliance (EC) and safety issues.
CONCLUSION: The pilot study showed that the operation was of adequate quality, more cost effective and well accepted when IRS is incorporated to the HEP in Ethiopia. The HEP based IRS and having one operation site in each village is the best way to make the EC components introduced PMI in the last five more sustainable.

S27: Multilateral partnerships for malaria elimination

Chairs: Dr Kaka Mudambo and Dr Milijaona Randrianarivelojosia

Speaker 1: Dr Kaka Mudambo, Armed forces, a forgotten group vulnerable to malaria: South African Regional Roll Back Malaria network initiatives, RBM-SARN, Botswana.
Speaker 2: Dr Milijaona Randrianarivelojosia, Atelier Paludisme de Madagascar, 10 years partnership in training next generation malaria expert, Institut Pasteur de Madagascar, Madagascar
Speaker 3: Dr Ponni Subbiah, Development of semi synthetic artemisinin, a path to stablising ACTs availability and accessibility, PATH, Switzerland.

OVERVIEW
Malaria continues to be a public health burden for African states that are also plagued by limited resources. Malaria control and elimination requires multiple types of activities from multiple stakeholders at different levels. Only through focused partnerships can the relevant sets of expertise and resources be effectively shared to have a durable impact. This symposium will discuss several types of partnerships. One was designed to address the specific needs of African armed forces.

Another one was designed to train the next generation of malaria scientists in order to make them capable of using modern tools for long-term self-education. This was made possible through a public private partnership, but its long term sustainability may require designing new models. The third partnership addressed the issue of the high dependence of artemisinin production to environmental factors leading to large cost variations. Semi synthetic artemisinin production is expected to become a more predictable alternative source, able to fill the gaps of natural production and stabilize costs.

S28: Insecticide resistance prevention and management

Chairs: Dr Jo Lines and Dr Abraham Mnzava

Speaker 1: Dr Abraham Mnzava, GPIRM implementaion – roll out globally with emphasis on the African region, World Health Organisation, Switzerland.
Speaker 2: Dr Basil Brooke, Updated WHO guidelines for monitoring of insecticide resistance, NICD, South Africa
Speaker 3: Prof Maureen Coetzee, The African Nework for Vector Resistance, University of Witwatersrand, South Africa
Speaker 4: Dr Jo Lines, Methods of resistance management, London School of Hygiene and Tropical Medicine, United Kingdom
Speaker 5: Dr Tessa Knox, Role of IRAC in supporting the prevention and management of insecticide resistance, Vestergaard Frandsen Ltd, Kenya.
Speaker 6: Prof Charles M Mbogo, Vector control and the Pan-African Mosquito control association (PAMCA), PAMCA, Kenya

GPIRM Implementation – Roll out globally with emphasis on the African Region

Dr. Abraham Mnzava
Global Malaria Programme, World Health Organisation, Geneva, Switzerland

The remarkable success of malaria control efforts over the past decade can be largely attributed to the scale up of vector control, especially Indoor Residual Spraying (IRS) and Insecticide Treated Mosquito Nets (ITNs). These gains are now threatened by the emergence and spread of insecticide resistance, particularly to pyrethroids, the most inexpensive and common class of insecticide used for IRS and the only class that can be used for ITNs. Loss of the pyrethroids could be catastrophic. Responding to this crisis, WHO and RBM launched the Global Plan for Insecticide Resistance Management in malaria vectors in May 2012. GPIRM lays out a comprehensive strategy to manage resistance and preserve pyrethroids through five main “pillars”. The first two pillars are actions at the country level,

to plan and implement insecticide resistance management strategies and to ensure proper, timely entomological and resistance monitoring as well as effective data management systems. The third pillar is a broad collaboration among industry, academia, WHO, national programs, regulatory authorities and partners to develop and bring to market new, innovative vector control tools. Fourth is improved monitoring and field research to fill knowledge gaps on mechanisms of insecticide resistance and the impact of current insecticide resistance management strategies. The fifth pillar is to ensure that enabling mechanisms (advocacy, human and financial resources) are in place. Now, 1 ½ years after the launch of GPIRM, there is still much to be done in many countries, especially to develop the human resources, the network and the systems, the technical support and continued communications to fully implement GPIRM, preserve the fragile gains and continue on the path towards elimination. The success of GPIRM cannot be realized through the efforts of a single agency or single ministry, but requires coordinated efforts across sectors. As will be discussed in the other presentations of this symposium, from the national programmes and institutes, from industry partners, and from nascent professional networks, we have commitment and common vision, but still face many challenges to address the looming threats of insecticide resistance.

Updated WHO guidelines for monitoring of insecticide resistance

Basil Brooke[1,2], Maureen Coetzee[1,2], Fabrice Chandre[3], Abraham Mnzava[4], Jo lines[5], Michael MacDonald[4]

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Insecticide resistance surveillance is a critical component of successful mosquito disease vector control. The WHO insecticide susceptibility bioassay is a controlled, direct response-to-exposure test in which mosquito samples are exposed to a diagnostic concentration of an insecticide for a fixed period of time, with final mortalities recorded 24 hours post exposure. This test is designed to distinguish between baseline susceptibility and resistance to insecticides in adult mosquitoes. As such, the test is intended to be used as a field and laboratory surveillance tool with the limitation that it gives little information on the underlying mode(s) or mechanism(s) conferring resistance where detected. It is recommended that the standard WHO susceptibility test should continue to be the primary method by which insecticide resistance is detected and identified in vector populations. However, it was considered necessary to update the existing guidelines in order to reflect new priorities and information needs as well as to highlight the need for accurate species identification of all test mosquitoes. Specific objectives for updating the insecticide resistance guidelines were: to provide an update to the WHO test procedures for monitoring insecticide resistance in malaria vectors to align with new developments in vector resistance management; to provide an updated list of discriminating dosages for adult mosquitoes for all insecticides used either in malaria vector control or for research purposes; to refine the definition of 'resistance' which triggers pre-emptive action to manage resistance; to identify mechanisms for the process of reporting, collating and interpreting resistance data so as to inform resistance management plans and strategies for vector control. The updated guidelines also recommend and provide links to the alternative CDC bottle bioassay method as well as to supplementary test methods for determining the underlying mechanisms of resistance. The updated guidelines are available at http://www.who.int/malaria/publications/atoz/9789241505154/en/index.html

The African Network for Vector Resistance

Maureen Coetzee

Wits Research Institute for Malaria, School of Pathology, Faculty of Health Sciences University of the Witwatersrand, Johannesburg, South Africa

The African Network for Vector Resistance (ANVR) was established in 1999 by WHO/AFRO to draw together all the malaria countries of the region to build capacity for monitoring resistance in malaria mosquitoes across the continent. Training courses were held between 2000 and 2003. An atlas of resistance in the different vector species is produced by WHO/AFRO on a regular basis and published on the AFRO web site and in VectorBase.

Methods of resistance management

Jo Lines
London School of Hygiene and Tropical Medicine, London, United Kingdom

Management of insecticide resistance is a critical issue for malaria control as a whole: it is an arms race between humans and mosquitoes. In the Global Plan for Insecticide Resistance Management (GPIRM), the malaria community has acknowledged that genes for insecticide susceptibility in malaria vector mosquito populations represent a precious and finite resource. Every time we do insecticidal vector control, we use up some of this resource in return for a hoped-for health benefit. Depending on how the insecticides are deployed, genes for susceptibility may be used up quickly or slowly, and the health benefits gained may be large or small. A core objective for malaria vector control is therefore to gain the maximum possible health benefit whilst not losing the arms race.

Unfortunately, in mosquitoes, our understanding of resistance as an evolutionary phenomenon remains superficial and largely theoretical. Part of the problem is that research projects are normally small-scale and short-term, whereas evolution happens over several years, and over the large scale. A specific problem within GPIRM is the need to assess the relative effectiveness of alternative resistance management methods, both at the strategic level (e.g. mixtures vs rotations, LLINs vs pyrethroid-IRS) and at the level of particular commercial products (e.g. two novel LLINs with different insecticide mixtures).

We would like to compare not only the ability of interventions to control malaria despite resistance, but also their ability to minimise further selection for resistance. The former can be done using standard epidemiological indicators and well-established village-scale trial designs, but the latter, with evolutionary outcomes, is more difficult. Normally, there is substantial mosquito movement between villages, and this means that village-level observations of gene frequency change over time cannot give a reliable measure of the degree of Darwinian selection exerted by the alternative products or interventions.

Nevertheless, there may be a simple and informative way to measure fitness differentials and the impact of resistance on transmission at the village scale: by measuring, in local mosquito populations, the association (if any) between resistance genes and either age or sporozooite infection. The assumptions, and the likely advantages, limitations and biases of this approach will be discussed.

Role of IRAC in supporting the prevention and management of insecticide resistance

Tessa B. Knox[1,2], Helen Pates Jamet[2] and Mark Hoppe[3]
[1]Vestergaard Frandsen (East Africa) Ltd., Nairobi, Kenya; [2]Vestergaard Frandsen SA, Lausanne, Switzerland; [3]Syngenta Crop Protection AG, Basel, Switzerland

Insecticides have been extensively used since the 1940s to control mosquito vectors of disease, and have been a vital component in the fight against malaria. However, resistance has developed in populations of the major mosquito vector species to the four classes of insecticide currently recommended for adult vector control. As insecticide resistance continues to develop and spread, there is a real danger that these valuable tools will be lost. Whilst much energy is being spent with the aim of bringing insecticides with new modes of action to public health insect control, we must maintain the effectiveness of tools currently available as well as have in place strategies to preserve the long term utility of novel insecticides as they are developed.

The Insecticide Resistance Action Committee (IRAC) is a specialist technical working group of the Agrochemical industry association CropLife International. The member companies of IRAC have come together with the aims of facilitating communication and education on insecticide resistance and promoting the development of resistance management strategies in order to maintain insecticide efficacy for sustainable agriculture and improved public health. Within IRAC, the Public Health team focuses exclusively on the technical aspects of insecticide resistance issues in public health, in particular the insect vectors of human disease. Through the production of educational material and an insecticide mode of action classification scheme, the IRAC Public Health team aims to promote best practice Integrated Resistance Management (IRM), within the context of Integrated Vector Management (IVM). IRAC believes that IRM should be an integral part of all vector control programmes. Using insecticides in such a way that their effectiveness is maintained is a stewardship responsibility of the commercial companies that produce and market them. It is also a stewardship duty of those who design and implement the vector control programmes that use them.

It is argued that only through IRM can the sustainable use of insecticidal vector control interventions be maintained. The commercial companies which form the IRAC Public Health team support this contention and work together to realise it.

Vector Control and the Pan-African Mosquito Control Association (PAMCA)

Charles M. Mbogo[1,2]
[1]Pan-African Mosquito Control Association (President), [2]Kenya Medical Research Institute, Kilifi, Kenya

A thorough knowledge of the vectors and diseases they cause is the foundation for the development and implementation of any vector management strategies. Much can be learned from a review of the historical context of vector-borne diseases. A perspective of the evolution of our knowledge on the role of arthropods in the transmission of diseases and the implication this has had on research and control will provide a view of what is known and what control has actually worked. Despite ongoing control efforts, diseases transmitted by mosquitoes, such as malaria, filariasis, dengue, and other arboviruses continue to pose an enormous global health burden.

Multinational public health Organisations have called for the eradication of malaria and major mosquito-vector diseases. There is broad recognition of the need for improved tools to combat these diseases. Currently available methods to control mosquito vectors of malaria and mosquito borne diseases are based on use of insecticides and elimination of breeding sites. In considering the potential of new technologies to address the unmet needs of mosquito control, it is necessary to evaluate the risks and benefits in the context of the current situation. Thus, the risk incurred by testing new and unproven strategies should be assessed against the risks to human health and the environment posed by maintaining the status quo, which includes both ongoing disease and exposure to broad spectrum insecticides.

The intensity of transmission and insecticide resistance are key components which provide information on the risk of epidemic development and also base line information for planning vector control interventions. Such information is not readily available for real time-decision making process. In order to address these ideals and challenges that professionals in mosquito research and control face today and what needs to be done in the future, a professional body, PAMCA was established. The main function is to coordinate the sharing of information and use of real time data in decision making processes whilst promoting control of and research on mosquitoes and other vectors. The mission of PAMCA is to provide leadership, information and training leading to the enhancement of health and quality of life through the suppression of mosquitoes and mosquito-transmitted diseases, and the reduction of annoyance levels caused by mosquitoes and other vectors. Further, PAMCA provides mentorship to young professionals in the field of mosquito control and research.

S29: Malaria eradication in an age of artimisinin resistance

Chair: Prof Carol Hopkins Sibley

Speaker 1: Dr Phillip Guerin, Setting the context: Artemisinin and ACT resistance in Southeast Asia, WWARN, United Kingdom
Speaker 2: Dr Ambrose Talisuna, Parasite clearance in Africa: an indicator of ACT efficacy, KEMRI-Wellcome Trust, Kenya
Speaker 3: Prof Abdoulaye Djimde, Molecular approached to tracking resistance: validating and using candidate markers, University of Bamako, Mali
Speaker 4: Dr Christian Nsanzabana, Drivers of resistance: getting the treatment dose right for all patients, WWARN, United Kingdom
Speaker 5: Prof Bernhards Ogutu, Drivers of resistance: Why do drug levels matter and why should we measure them? KEMRI-Wellcome Trust, Kenya
Speaker 6: Dr Edwin Kamau, Transmission, selection and the potential for resistance, Walter Reed Army Institute of Research, United States of America.

Setting the context: Artemisinin and ACT resistance in Southeast Asia

Phillip Guerin
WWARN, United Kingdom

The recognition of diminished efficacy of artemisinins in Southeast Asia has increased markedly the need to track the efficacy of ACTs in Africa. Although the overall clinical efficacy of ACTs has remained high in Africa, we must devise and adopt approaches that will allow detection of early signs of resistance to either artemisinins or their partner drugs, amodiaquine, lumefantrine and piperaquine. In this symposium, we will explore approaches that can give early warning of diminished efficacy of ACTs, and consider in the discussion, how these can be implemented in a variety of African settings.

Parasite clearance in Africa: an indicator of ACT efficacy

Ambrose Talisuna
KEMRI-Wellcome Trust, Kenya

Slow clinical and parasitological response after artemisinin therapy for uncomplicated *Plasmodium falciparum* malaria has been reported in the Mekong region. Further spread of these parasites poses a major global public health threat, especially in sub-Saharan Africa where the disease burden is greatest. Since the rate of parasite decline is a complex trait, dependent on both host and parasite factors, its measurement is not easy. It is critical to begin to define this parameter in different African settings, so that variations that result from different host factors- levels of transmission, immunity and others can be established. As a first step, assessement of the fraction of parasites who are still parasitemic in the first three days after ACT treatment can help to set the baseline. In a preliminary study of individual patient responses, baseline parasitaemia at enrolment was the most important risk factor affecting parasitological response at day one, day two and day three. Patients who remained parasitaemic on any of the first three days were at substantially greater risk of subsequent recrudescent infection. These results revealed no evidence in African clinical studies of declining artemisinin efficacy, but greater surveillance coverage is needed to fill current data gaps. Furthermore several potential "hot spots" for resistance will require urgent investigation using more sensitive diagnostic tools. Working within the WHO treatment guidelines, it will be important to devise appropriate and feasible methods for measuring parasite clearance rates more accurately. Efficient and feasible methods that can detect early signs of extended parasite clearance are needed for the African setting. Early detection of these signs is crucial to allow time for appropriate measures to be put in place to assure that artemisinin resistance does not spread and threaten these crucial antimalarials. parasiis the In this pooled analysis, we report the geographical and temporal trends of early parasitological response following artemisinin-based combination therapy (ACT) treatment in African clinical trials.

Molecular approached to tracking resistance: validating and using candidate markers

Abdoulaye Djimde
University of Bamako, Mali

Molecular markers carried by *Plasmodium falciparum* have allowed detailed studies of resistance to sulfadoxine-pyrimethamine, chloroquine and mefloquine, but these studies have mainly been conducted retrospectively, after resistance was well established. Delayed parasite-clearance time (PCT) following artesunate treatment defines P. falciparum artemisinin resistance in South-East Asia. Several Single Nucleotide polymorphisms (SNPs) have recently been described as associated to delayed PCT in Asian parasites. It is now crucial to work prospectively to define and actively use makers associated with artemisinin and its partner drugs in combined therapy (ACTs. we have investigated the presence of four SNPs in P. falciparum parasites during artesunate monotherapy in Mali (West Africa). Polymorphisms at the SNPs Mal10, Mal13 and AP2-199 were analyzed in 300 patients treated with aretesunate monotherapy after DNA amplification by pyrosequencing and direct sequencing. We did not observe polymorphisms for any of the three analyzed positions in this study. These candidate markers and new ones proposed should be rapidly analysed so that they can allow identification of any regions where even low levels are observed. This proactive approach will allow policy makers time to respond to these early signs, and slow the spread or even eliminate the parasites before they affect clinical efficacy of ACTs

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Drivers of resistance: getting the treatment dose right for all patients

Christian Nsanzabana
WWARN, United Kingdom

Artemisinin Combination Therapies (ACTs) have been recommended as first-line treatment for uncomplicated falciparum malaria by the WHO since 2001. The efficacy of ACTs is influenced by both the artemisinin derivative and the partner drug. The artemisinin component ensures a rapid reduction of the initial parasite biomass and the residual parasites are removed by the slowly eliminated partner drugs. The dosage of partner drugs with longer half-lives must be sufficient to ensure that blood concentrations exceed the minimum inhibitory concentration of the parasite until all parasites have been cleared to prevent recrudescence. Although target doses are usually given as a total mg/kg over three days; in practice manufacturers' recommendations are often pragmatic and based upon weight "banding". This approach inevitably results in some patients at the margins of having either lower or higher dosages. Young children are particularly vulnerable to suboptimal dosage and are at a greater risk of being exposed to doses

below or above the therapeutic dose range; as drug administration is often based on tablets (or fractions of tablets) rather paediatric formulations. The WorldWide Antimalarial Resistance Network (WWARN) is conducting a series of individual patient data meta-analyses in which the dosing strategies of the recommended ACTs are being reviewed, in order to define the spectrum of doses actually administered and the degree to which these dose variations might impact on the therapeutic efficacy. Dosing strategies of artemether-lumefantrine (AL), artesunate-amodiaquine (ASAQ), and dihydroartemisinin-piperaquine (DP) were assessed in the context of controlled clinical trials and factors associated with recrudescent failures were investigated. We will discuss the impact of the dosing in clinical outcomes and explore risk factors associated with failure.

Drivers of resistance: Why do drug levels matter and why should we measure them?

Bernhards Ogutu
KEMRI-Wellcome Trust, Kenya

The whole mark of antimicrobial drug resistance is the ability of the pathogen to propagate in the presence of adequate drug levels that were previously able to kill the pathogen. The blood drug level is affected by several factors such as host, clinician and product factors. The host factors can be disease status that either enhances or reduces the absorption and/or distribution of the active drug. These can be food substances or other drugs ingested along with the target drug, status of the plasma proteins which bind the drugs and homeostasis of the patient i.e dehydration or blood loss. The drug blood concentration can also be affected by pharmaceutical factors such as reduced quantities in the tablet, inappropriate excipients or solvents used that interfere with dissolution of the product, water and lipid solubility of the drug. A large part of sub-therapeutic levels can be due to dosing error by the patient and clinician. In the event that there is lack of clinical response to a drug there is a need to determine that the expected blood therapeutic level of the active drug was achieved to presume resistance. Relying on the presence of genetic markers or clinical response alone can be misleading as pathogen clearance such as in malaria is multifactorial with the host immune status playing a major role. The role of therapeutic monitoring in the antimalarial drug resistance remains an integral part of the malaria management, but establishing the drug levels in each patient is also critical.

Transmission, selection and the potential for resistance

Edwin Kamau
Walter Reed Army Institute of Research, United States of America

As we enter the malaria elimination era, monitoring, evaluation, and surveillance will be critical for countries to measure how well public health programs operate over time and achieve their goals. Understanding malaria transmission dynamics and especially as it related to transmission of drug resistance traits will be critical in the elimination agenda. It is important that we invest in research and control including sharpening our tools and knowledge on methodologies for estimating and tracking the malaria burden, new strategies to measure transmission, better understanding of immunity, and increased knowledge of the mechanisms and effects of resistance to drugs. Here, we will discuss malaria drug resistance, specifically artemisinin resistance from an African perspective and how transmission dynamics of these resistance traits will impact the malaria elimination effort.

S30: Strengthening the use of data for malaria decision making.

Chair: Dr Thomas Teuscher

Speaker 1: Dr Abdisalan Noor, Compiling evidence for informed decision making, KEMRI, Kenya.
Speaker 2: Dr David O. Soti, Revising malaria control policy and strategy in Kenya , Kenya National Malaria Control Program, Kenya
Speaker 3: Dr Ezeiggwe Nneena, Prioritizing strategies for malaria control in Nigeria, Nigeria National Malaria Control Program, Nigeria
Speaker 4: Dr Mohamed Ali, Malaria stratification and operational options for malaria control in Tanzania,Tanzania National Malaria Control Program, Tanzania
Speaker 5: TBC, Mainstreaming the availability of quality health information through the African Health Observatory, World Health Organisation, Regional Office for Africa.

To maintain current levels of malaria control and its impact on reducing Under 5 mortality depends on continued investments. The Roll Back Malaria (RBM) Partnership pursues two strategies to ensure continued financing for malaria control: i) the mobilizing of additional international and domestic resources through its Harmonization Working Group and ii) the enhancing of national program effectiveness enhancing value for money of investments. Improved use of data from a wide variety of sources is used to develop subnational malaria stratifications that allow the development of targeted subnational operational strategies enhancing value for money. The closure of knowledge gaps is essential if improvements in economy, efficiency, effectiveness or equity are to enhance value for money in malaria programming. The challenge remains the creation of functional partnerships between research and academia and malaria control programs at country level. The symposium will challenge the science community in Africa to more accountably and transparently engage with NMCPs. The symposium will use a facilitated panel discussion to i) provide the methodological background of mapping diverse datasets into policy relevant summaries, ii) provide three country examples of how a more refined malaria stratification can lead to more efficient resource allocation within a fixed ODA envelope, iii) discuss the means of mainstreaming the data driven malaria control prioritization in future and iv) present a series of knowledge gaps that have potential to enhance control program effectiveness significantly.

S31: Nobody should die from malaria today: the significance of public-private partnerships

Chairs: Dr Kileken ole-MoiYoi and Dr Ambrose Talisuna

Speaker 1: Dr Ambrose Talisuna, National Malaria Control Program Best Practice Sharing Workshops: A Public Private Partnership yielding results, KEMRI-Wellcome Trust, Kenya
Speaker 2: Dr Rene Ziegler, SMS for Life: Improving ACT Stock Management and Malaria Surveillance, SMS for Life.
Speaker 3: Dr Doreen Ali Sustainably improving access to quality-assured ACTs in the private sector, National Malaria Control Programme, Malawi.
Speaker 4: Dr Hannah Bowen, Power of One: Engaging the private sector and the general public to in the fight against malaria, Malaria No More, The Netherlands.

S32: TDR Alumni Network – building blocks

Chairs: Prof John Reeder and Dr Fabio Zicker

This is an invitation-only workshop among alumni of TDR, the Special Programme for Research and Training in Tropical Diseases. Participants will provide input and help develop a new alumni platform that will allow for better tracking of career progression, promotion, and discuss ways to increase opportunities for collaborations with other researchers and funders. This is part of TDR's new strategy to increase support for research capacity building.

All MIM participants will also have an opportunity to provide input through a questionnaire, which will be available at the TDR booth, and at a cocktail reception open to all TDR friends immediately following this workshop (17:30 – 19:00).

S33: Indoor Residual House Spraying (IRS) old and new tool for rapid malaria control and elimination

Chairs: Dr Shiva Murugasampillay and Dr Manuel Lluberas

Speaker1: Dr John Govere, Indoor Residual Spraying State of Science and Art of for Malaria Control/Elimination, Public Health Entomology and HD Hudson.
Speaker 2: Dr Constance Bart-Plange, Building effective private public partnership for scaling up IRS in Ghana- The Achievement of the AngloGold Ashanti- Ghana Health Service, National Malaria Control Programme, Ghana
Speaker 3: Dr Michael Okia Universal Indoor Residual Spraying (IRS) in reducing high malaria transmission in northern Uganda districts, IRS Project Phase II, Uganda.
Speaker 4: Stephen M. Magesa, Decentralisation and Capacity building in national indoor residual spraying (IRS) programme: The Tanzanian experience. RTI International, Tanzania.
Speaker 5: Dr Abdullah Ali, Targeted IRS for malaria elimination in Zanzibar, Zanzibar Malaria Program, Zanzibar
Speaker 6: Dr Robert Sloss, New tools for IRS-Long lasting chemicals and robust application equipment, IVCC, United Kingdom.

Indoor Residual Spraying State of Science and Art of for Malaria Control/ Elimination

John Govere & Manuel Lluberas
Public Health Entomology and Hudson

Malaria is curable and preventable. It has been eradicated or reduced to a point where it is no longer a serious health or economic burden to a large number of countries. Almost without exception, eradication was reached by combining active vector population suppression methods and techniques and involving the local population to make their immediate environment less conducive to the proliferation of mosquito populations
Indoor residual spraying (IRS) is the oldest vector control method to be used at large scale for malaria control and elimination. The combination of IRS with DDT and treatment with chloroquine during the 1960's gave the global community the greatest hope ever to eradicate malaria. Malaria was eliminated in Europe and North America and significantly reduced in South-East Asia and parts of Africa. More significantly, every country that achieved eradication did so more than two decades ago, long before the establishment of many of the current anti-malaria initiatives and without the benefit of a vaccine

IRS continued to be the primary method of malaria vector control when the global malaria goal shifted from eradication to control. Some countries in North, Eastern and Southern Africa and in South-East Asia continue to use IRS to control malaria and prevent epidemics . However, recent events point to the uncertainty of the role of IRS in malaria control and elimination. The development and spread of insecticide resistance is a major challenge to continued use of IRS for malaria vector control. All malaria endemic countries now receive global support to achieve LLINs universal coverage. The GPIRM recommends non-pyrethroid IRS in areas with full LLINs coverage. Successful and sustained IRS programs are government driven and enhanced by donor support and the GPIRM recommendation to rotate IRS insecticides of different mode of action annually is beyond the the financial reach and practicality of many endemic countries that have relied on the use of DDT and pyrethroids. Countries that use IRS and apply for global funding are now requested to justify the continued need for IRS. IRS donor support that started very well in the mid-2000 is decreasing, with some IRS projects in some countries closing up. Some governments that had shifted their resources from IRS to other programs are now finding it difficult to reconstitute the IRS programms as donor support is dwindling.

Examples of well organized and systematic indoor residual spray campaigns (IRS) that focus on the vector and include good medical surveillance and treatment systems have been instrumental in eliminating or reducing malaria to a point where it does not overwhelm continuously diminishing public health resources are provided. Unless governments invest into and take absolute charge of IRS programs, IRS will soon be eradicated before the eradication of malaria

Building effective private public partnership for scaling up IRS in Ghana- The Achievement of the AngloGold Ashanti- Ghana Health Service

Bart-Plange, Constance[1], Segbaya Sylvester[2], Aba Baffoe-Wilmot
[1]National Malaria Control Programme, Ghana; [2]AngloGold Ashanti;NMCP-Ghana

Malaria is a major challenge in Sub-Saharan Africa and in Ghana the disease continues to be the cause of significant morbidity and mortality in the country. In 2012, there were over 7,000,000 cases and about 22,000 deaths attributed to malaria in Ghana. The NMCP's Strategic Plan highlights the use of an integrated approach to reduce the disease burden.

Of all the vector control interventions, Indoor Residual Spraying (IRS) is known to have the biggest potential impact for reducing the incidence of malaria in a community. In practice, the effectiveness of IRS for malaria control depends on adherence to the specified criteria of the insecticide application procedure, community acceptance, the availability of well maintained equipment, availability of well-trained personnel, efficient supervision and strong financial support, all of which AngloGold Ashanti (AGA) together with the Ministry of Health (MOH)/Ghana Health Service (GHS) have had. This paper describes the building of effective partnership and the achievement of the AGA-MOH/GHS IRS experience.

AGA and MOH/GHS partnership started in 2005 with the introduction and planning of AngloGold Ashanti's IRS operations in Obuasi (Ghana). The Mine Hospital in 2005 registered 6,800 malaria cases each month, 2,500 of which were mine workers. An integrated malaria control program was introduced with an objective of reducing the malaria burden by 50% within 2 years. In 2007, the malaria cases at the Mine Hospital dropped by 76% with reduced work absenteeism, reduced monthly cost of malaria treatment and increased school attendance.

The AGA success led to a continued partnership with the MOH/GHS and the Global Fund to scale up Indoor Residual Spraying to 40 districts in Ghana. The Ghana Health Service is providing warehouses for insecticide storage and offices in districts. It is envisaged that 8 million people in Ghana will benefit from IRS protection by 2015, a job creation of 3,800 and capacity building in many communities for malaria prevention. The "Obuasi model" has become an International Gold Standard for malaria control programmes.

Coordination of IRS activities in Ghana are done by the Malaria Vector Control Oversight Committee (MaVCOC) chaired by NMCP.There is significant engagement of research institutions in monitoring and evaluation of the project's implementation.

Universal Indoor Residual Spraying (IRS) in reducing high malaria transmission in northern Uganda districts

Michael Okia, J.B. Rwakimari[1]; Peter Okui[2]
[1]Uganda IRS Project Phase II; [2]NMCP Program Manager

According to the *Uganda Malaria Indicator Survey*, 2009, *Plasmodium falciparum* is responsible for 99 percent of malaria cases in country. As confirmed by microscopy, the prevalence of malaria parasitemia in children aged 6 to 59 months was 63 percent in northern Uganda, compared to the national average of 45 percent. Since 2009, Abt Associates has implemented the USAID/PMI funded IRS project, and is currently implementing Phase II of the project in 10 northern districts. Target districts show a decrease in confirmed malaria cases, thereby establishing IRS as a viable control strategy.

The project works in collaboration with the district health teams, to conduct two rounds of spraying every year, achieving more than 85 percent coverage in the target districts. The most common malaria vectors in these IRS target districts are *Anopheles gambiae s.l.* and *Anopheles funestus*, both of which are endophilic and endophagic. To assess the quality of spraying, the project conducts routine entomological monitoring, both pre and post spraying, using pyrethrum spray catches and wall bioassays.

Since the start of spraying, the prevalence of malaria cases in the IRS districts has reduced significantly from 63 percent to less than 20 percent. Similarly, in the majority of these districts, the vector population has dwindled to almost zero. The decrease in malaria prevalence among the population has also led to greater agricultural productivity, and most of these districts which prior to IRS used to suffer from periodic food shortages, are now producing adequate quantities, and at times are even supplying the World Food Program. The cost efficiencies achieved by the project is also evident from the low cost per person protected (in the $1.81 - $2.26 range). This is lower than previous cost estimates, which were in the $2-$6 range.

Sustained high IRS coverage above 85 percent is a cost effective way of significantly reducing malaria incidence, thereby resulting in better socio economic conditions.

Decentralisation and Capacity building in national indoor residual spraying (IRS) programme: The Tanzanian experience

Stephen M. Magesa[1], Mwalimu, DC[2], Makono, A[2], Mcha J[3], Khatib, BO[3], Ali, AS[3], Amier, K[3], Rashid, A[3], Lalji, S[1], Rutta, J[1], Nyange, A[1], Mohamed, M[1], Mutagahywa, J[1], Mandike, R[2] and J. Ngondi[1]

[1]RTI International, Dar es Salaam, Tanzania; [2]National Malaria Control Programme, Dar es Salaam, Tanzania; [3]Zanzibar Malaria Control Programme, Zanzibar, Tanzania

When indoor residual spraying (IRS) was re-introduced in Africa less than a decade ago, there were limited skills within countries in terms infrastructure as well as skills for planning, management and implementation of IRS. These had to be built from scratch in most of countries, particularly those receiving support from the Presidents' Malaria Initiative. As a necessary component of IRS sustainability and exit plans, capacity building in terms of human resources, infrastructure and systems has been implemented by IRS programmes. This paper discusses the experiences, opportunities, challenges and lessons learnt by RTI International while implementing IRS in Tanzania.

A set of manuals were developed for training of IRS personnel. A desk review was undertaken to explore experiences with IRS as documented in periodic reports to PMI from 2006 to-date. Records from end of spray review meetings that bring together district and national stakeholders from target districts implementing IRS were included in the reviews. Decentralization to district level has led to direct involvement of district health personnel in the planning, implementation and supervision of IRS programmes. The District health management teams have been able to build a cadre of staff that are capable of technically managing IRS. Periodic tailored training using customized national curriculum has enhanced the capacity of the district teams. Spray operators and community mobilisers recruited from target villages and trained currently make up a formidable team of reserved skills for hands-on spray operations. Collaboration with national research institutions have built entomological capacity that is important in supporting IRS. The process has succeeded in building adequate technical capacity required for IRS at national and district levels. However, there has been enormous challenges in leveraging capacity for supportive cross-cutting areas such as procurement, logistics and financial management as well as programme management.

Targeted IRS for malaria elimination in Zanzibar;

Abdullah Ali[1], & Fabrizio Molteni[2],

[1]Zanzibar Malaria Program, [2]Swiss TPH

Zanzibar introduced ACT for uncomplicated malaria and SP for IPTp in 2003 and 2004 respectively. LLIN campaigns were conducted for vulnerable groups in 2005 and for the entire population in 2010 and 2012. Universal IRS has been conducted from 2006 and 2011 followed by progressive scale down. This comprehensive package of interventions led to decrease in malaria prevalence from mesoendemic levels to <1% since 2008.

In Zanzibar progression to pre-elimination phase is an attractive option, while intensified efforts are still needed to consolidate the achievements. Since 2010 malaria transmission become extremely seasonal and focalized. In 2001, 70% of cases occurred in 10 weeks and half of cases occurred in two out of ten districts.

The role of different interventions should be considered according to the programme goal and the current epidemiological profile. Targeted IRS is an essential intervention especially after the universal LLIN coverage and the establishment of surveillance system. Timely IRS to prevent seasonal transmission and reduction of transmission foci is ideal in the current epidemiological context. Due to the excellent status of preparedness, preemptive IRS is also an attractive option.

Several options have been considered to select areas to be targeted by IRS. According to epidemiological and entomological considerations and due to limited resources a cut off of 2 cases per 1000 population has been adopted. Targeted IRS was conducted in 25% of households in 2012 and 2013. The scale down of IRS didn't affect the overall malaria incidence.

In Zanzibar there is evidence of changing vector population dynamics: *A.funestus* and *A.gambiae ss*, have been virtually eliminated while the more ubiquitous *A.arabiensis* is becoming more prevalent. Introduction of larval source management is becoming a strategic option to reduce outdoor transmission. It has been demonstrated a reduced susceptibility to pyrethroids. A judicious use of insecticide rotation in the context of insecticide resistance mitigation measures is advocated. Selection of the appropriate insecticide, among the very few available options, should be taken into consideration. Optimal residual duration, effectiveness in different spray surfaces and, finally, costs are the guiding principle to select the insecticide to be used for IRS.

New tools for IRS-Long lasting chemicals and robust application equipment

Robert Sloss[1] & Iñigo Garmendia[2]
[1]Public health product development- IVCC; [2]Product Engineer-Olaker

Indoor Residual Spraying (IRS) is one of the two most important vector control interventions together with long-lasting insecticidal nets (LLINs) for global malaria control and elimination efforts. Historically, IRS was largely responsible for the tremendous accomplishments of malaria programs in Europe, Asia and the Americas in the 20th century. However, the strategy around IRS management and the context in which it is deployed has changed tremendously in recent years.

The challenges facing modern IRS, are the development of resistance to insecticides by *Anopheles* mosquitoes in more than 60 countries worldwide and the timely implementation of high coverage and high quality IRS programs. There is a pressing need for the development of new vector control tools, especially new insecticides and more efficient spraying equipment, to meet and ultimately overcome this challenge.

Long Lasting Insecticides for IRS

Today there is more and more need for development of long lasting formulations of insecticides for IRS, both using pyrethroids, other WHOPES recommended insecticides and new insecticides for vector control. The focus is the benefits in cost effectiveness of being able to carry out effective IRS with only one spray round a year.

The long development process for long lasting IRS formulations should be understood and planned for , including the importance for the developer of a clear target product profile and the importance for Vector Control product development in having fully quality assured trial sites. Finally there will be a discussion of the current portfolio as well as gaps in the portfolio

Robust application equipment

The objective of IRS operations is to apply uniformly the recommended dosage of insecticide active ingredient on all the inside walls of the dwellings. For that purpose, the correct selection and maintenance of spraying equipment is crucial.

Latest developments in technology such as advanced designing software, new materials and manufacturing processes has enabled to develop new spraying tools in order to improve the cost-effectiveness of IRS operations. A new generation of low pressure control flow valve increases remarkably the uniform application of the recommended insecticide dosage on the walls reducing substantially the risk of spray operator contamination. New low erosion nozzles increase significantly the lifespan of nozzles in intensive labor conditions saving money not wasting insecticide. New nozzle protectors avoid considerably nozzle blockages during spraying operations avoiding frequent interruption and loss of time. New advanced materials reduce extraordinarily the fatigue of spray operators reducing 40% the weight carried in their shoulder.

All these new developments offer Malaria Control programs better tools to fight against transmission of Malaria more efficiently.

S34: Tracking artemisinin resistance

Chairs: Dr Corine Karema and Dr Elizabeth Ashley

Speaker 1: Prof Arjen Dondorp, Artemisinin resistance – what we know and what we don't know. Mahidol University, Thailand

Speaker 2: Dr Reupam Tripura, The tracking resistance to artemisinin collaboration – results of a multicentre clinical trial to map the spread of artemisinin resistance, Mahidol University, Thailand

Speaker 3: Dr Shunmay Yeung, Understanding behavioural factors and drug resistance, London School of Hygiene and Tropical Medicine, United Kingdom

Speaker 4 Dr Cally Roper, Migration and the disperal of drug resistance in Africa, London School of Hygiene and Tropical Medicine, United Kingdom

Speaker 5: Dr Ambrose Talisuna, Artemisinin resistance in Africa – can we avert another malaria disaster? WWARN, United Kingdom.

DESCRIPTION OF SYMPOSIUM CONTENT: In this symposium we will give an update of the global situation of artemisinin resistance including the search for a molecular marker. The results of a multi-centre trial in 10 countries in Asia and Africa looking for evidence of spread of resistance will be presented. The findings of an investigation into these patients' illness and treat-seeking behaviour will be described and how these could relate to the geographical distribution of resistance. A geographic description of the emergence and dispersal of resistance mutations across Africa will be presented and what we can learn from this about likely routes of spread of artemisinin resistance in the African continent, in particular the influence of population movement. Finally the threat the emergence of artemisinin resistance poses to malaria control in Africa will be discussed and priorities for action.

S35: Whole-organism pre-erythrocytic malaria vaccination strategies

Chairs: Dr Miguel Prudencia and Dr Stephen L Hoffman

Speaker 1: Dr Stephen L Hoffman, Progress Toward Development of the PfSPZ Vaccine for Use as a Tool for Eliminating *Plasmodium falciparum* Malaria, Sanaria Inc., United States of America.
Speaker 2: Prof Robert Sauerwein, Experimentail vaccination of humans under chloroquine prophaylaxis with sporozoites, Radboud University Medical Centre, The Netherlands
Speaker 3: Dr Shahid Khan, Preclinical development of genetically attenuated malaria parasites for vaccine development, Leiden University Medical Center, The Netherlands
Speaker 4: Dr Miguel Prudencio, A rodent Plasmodium-based strategy for vaccination against human malaria, Instituto de Medicina Molecular, Portugal

Progress Toward Development of the PfSPZ Vaccine for Use as a Tool for Eliminating *Plasmodium falciparum* Malaria

Stephen L Hoffman,
Sanaria Inc, United States of America

The ideal, single stage vaccine for elimination of *Plasmodium falciparum* (Pf) would prevent infection at the pre-erythrocytic stage of the parasite life cycle, thereby preventing all Pf-caused disease and transmission from humans to mosquitoes. The only approach to immunization that consistently induces greater than 90% protection against infection, and protection sustained for at least 10-28 months, has been immunization by mosquito bite with whole Pf sporozoites (SPZ). Most available data are for radiation-attenuated PfSPZ: these parasites invade hepatocytes and express new proteins, but cannot replicate. Sanaria was founded to develop PfSPZ vaccines. The first vaccine developed and tested by Sanaria has been the PfSPZ Vaccine, which is composed of aseptic, purified, radiation-attenuated, cryopreserved PfSPZ. The vaccine was safe and well-tolerated when administered intradermally, subcutaneously, or intravenously. To date, 120 volunteers in the USA have received the vaccine. Recently at the Vaccine Research Center, National Institutes of Allergy and Infectious Diseases, NIH (USA), the PfSPZ Vaccine was administered 4-6 times intravenously (IV) to 40 adults. 0/6 subjects receiving 5 doses of $1.35x10^5$ PfSPZ, 3/9 subjects receiving 4 doses, and 5/6 non-vaccinated controls developed malaria following controlled human malaria infection (p=0.015 in the 5-dose group and p=0.028 for overall, both versus controls) (R. Seder et al., *Science*, 2013). PfSPZ-specific antibody and T cell responses were dose-dependent. These data indicate that there is a dose-dependent immunological threshold for establishing high-level protection against malaria that can be achieved by IV administration of a vaccine that is safe and meets regulatory standards. During the next 9 months, trials will be initiated in Tanzania, USA, Mali, Germany and Equatorial Guinea to demonstrate reproducibility of safety and efficacy, establish durability of protection and protection against heterologous Pf, optimize the immunization regimen and begin the process of determining operational requirements for mass administration campaigns in all age groups.

Experimental vaccination of humans under chloroquine prophylaxis with sporozoites

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A unique tool to study malaria immunology and efficacy of immunisation strategies form Controlled Human Malaria Infections (CHMI) and has proved to be a reproducible, predictable and safe method of inducing *Plasmodium falciparum* (Pf) malaria. An efficient method for induction of complete protection in humans was achieved by us in a CHMI setting by exposing human subjects to Pf-infected mosquitoes while taking blood-stage suppressive chloroquine prophylaxis. When tested in clinical trials, this protocol induced dose-dependently 100% clinically and parasitologically sterile protection against a standard homologous CHMI. Preliminary data, also suggest the presence of heterologous protection . In addition, we showed that CPS-induced protection was long lasting and primarily mediated by immunity to sporozoite and liver stages rather than to asexual blood-stages. Cellular and humoral responses to *Plasmodium falciparum* parasites play an important role in anti-malarial immunity.

Our approach appears to utilize the Pf parasite's clinically salient replicative phase of liver stage development to induce fully protective immune response against sporozoites and liver stages. It opens opportunities to explore mechanisms of protective immunity, allowing the search for immune correlates/signatures of protection and clinical development of a whole sporozoite based vaccine.

Preclinical assessment studies on genetically attenuated malaria parasites suitable for vaccination

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Immunization with Plasmodium irradiated-sporozoites that invade and arrest inside hepatocytes can induce long-lasting sterile protective immunity against malaria in rodent models and in humans. Recently gene deletion mutants, or genetically attenuated parasites (GAP), have been created in rodent malaria parasites which similarly arrest during liver-stage development that provoke strong (in some cases even stronger) protective immunity, in mice. By examining GAPs in rodent-malaria parasites in multiple mice strains, we describe robust and stringent screening approaches to establish GAP safety (do not produce a blood-stage infection) and GAP potency (immunity with the fewest parasites/doses). Using information derived from rodent GAPs we have created a multiple gene-deletion P. falciparum GAP and describe its evaluation during blood-, mosquito- and liver-stage development and have tested its safety by examining its attenuation in cultured primary human hepatocytes and mice engrafted with human liver tissue. This P. falciparum GAP is now being prepared for evaluation in Phase I/II human trials.

A rodent *Plasmodium*-based strategy for vaccination against human malaria

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Whole organism pre-erythrocytic (WOPE) vaccines against malaria are among the most promising immunization strategies against this disease. Currently, such strategies are based on the attenuation of *Plasmodium falciparum* sporozoites. We developed a bold new approach to WOPE vaccination, based on the use of rodent *P. berghei* parasites as the immunizing agent. We demonstrated that this strategy meets the basic requirements for safety and for effective antigen presentation to liver hepatocytes. We are investigating the degree of cross-species protection conferred by *P. berghei* against *P. falciparum*, as well as the added protection afforded by the genetic engineering of *P. falciparum* immunogens onto the *P. berghei* platform. Data will be presented regarding cellular and humoral responses resulting from immunization with the rodent parasite-based vaccine, as well as their ability to specifically recognize and inhibit infection by *P. falciparum*. Finally, the pros and cons of the use of *P. berghei* as a vaccination platform against human malaria will be discussed in the context of currently available alternatives.

S36: Seasonal malaria chemoprevention – a broader picture

Chairs: Prof Christopher V Plowe and Dr Martin De Smet

Speaker 1: Dr Alexander Dodoo, The need, relevance and feasibility of pharmacovigilance, WHO, Switzerland
Speaker 2: Dr Jean Louis Ndiaye, Implications for antimalarial drug resistance, University of Cheik Anta Diop, Senegal
Speaker 3: Dr Alassane Dicko, When should a switch to another drug regimen be considered and what options do we have?, University of Bamako, Mali.
Speaker 4: Dr Chris Drakeley, Malaria prevalence and alternative preventive strategies, London School of Hygiene and Tropical Medicine, United Kingdom

The World Health Organisation issued a recommendation on Seasonal Malaria Chemoprevention (SMC) in March 2012. The recommended SMC strategy is administration of monthly courses of a full therapeutic dose of Sulphadoxine/Pyrimethamine (SP) and Amodiaquine (AQ) to children between 3 to 59 months, in areas of the Sahel with high seasonal transmission and where the efficacy of SP + AQ remains above 90%. Strengthened pharmacovigilance and monitoring of the efficacy of SP and AQ are also part of the recommendation.

The recommendation is well supported by evidence on the impact of SMC on malaria morbidity, yet several questions remain. First, both SP and AQ have documented rare severe adverse effects and the feasibility and methodology of pharmacovigilance in this often challenging context need careful consideration.

Second, an increase in resistance to SP and/or AQ may result from SMC, and surveillance is needed to quantify and report any changes in efficacy as a result of the intervention. It is critical that policy makers are informed and prepared to choose alternative drugs if resistance to either drug is shown to be increasing. Moreover, adoption of SMC is likely to influence the prescription practice for the first line ACT's, so the direct and indirect impact of SMC on the broader issue of ACT and artemisinin efficacy must be part of these discussions.

Third, some regions outside of the Sahel sub-region have a similar seasonal profile and might benefit from SMC strategies. However, already high resistance to SP and/or AQ precludes use of this combination in many areas, and possible options will require careful consideration.

Finally, a better understanding of each local epidemiologic context is still needed. The prevalence of malaria parasites, symptomatic or asymptomatic, is a critical element in the discussion of long term strategies to control the malaria burden. Alternative strategies can include SMC with different molecules, intermittent screening and treatment, or intermittent presumptive treatment.

To maximize the effectiveness of SMC now and prolong its useful life, we need to consider all of these issues as the strategy is expected to be implemented widely in the Sahel and considered elsewhere.

S37: Insecticide treated nets, intermittent preventive treatment and intermittent screening and treatment for preventing malaria in pregnancy in sub-Saharan Africa: results for the MiP consortium

Chairs: Dr Kassoum Kayentao and Dr Meghna Desai

Speaker 1: Dr Patrick Walker, Impact of IPTp-SP and ITNs on placental malaria and low birth weight: Results from modelling studies, Imperial College London, United Kingdom.

Speaker 2: Dr Feiko O ter Kuile, Impact of sulphadoxine-pyrimethamine resistance on the effectiveness of intermittent preventive therapy for malaria in pregnancy (IPTp) in Africa: A systematic review and meta-analysis, Liverpool School of Tropical Medicine, United Kingdom.

Speaker 3: Dr Julie Gutman, Impact of sulfadoxine-pyrimethamine resistance on effectiveness of intermittent preventive therapy in pregnancy: Methodology and protocol development, CDC, United States of America

Speaker 4: Dr Harry Tagbor, A trial of intermittent screening and treatment as an alternative to intermittent preventive treatment with sulfadoxine-pyrimethamine for the control of malaria in pregnancy, Kwame Nkrumah University of Science and Technology, Ghana.

Speaker 5: Dr Clara Menendez, Efficacy and safety of mefloquine as malaria intermittent preventive treatment in pregnancy (IPTp): Results from two multicenter randomised controlled trials in HIV positive and negative African women, University of Barcelona, Spain.

Update on the impact of sulphadoxine pyrimethamine (SP) resistance on intermittent preventive treatment (IPTp) effectiveness, modelling of the impact of intermittent preventive treatment (IPTp) and insecticide treated nets (ITNs) on low birth weight, and results of multi-country clinical trials in sub-Saharan Africa to evaluate alternative drugs or strategies to replace IPTp with SP.

Impact of IPTp-SP and ITNs on placental malaria and low birth weight: results from modelling studies

Patrick Walker[1], Feiko ter Kuile[2,3], Jamie Griffin[1], Clara Menendez[4], Azra Ghani[1]

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BACKGROUND: *P.falciparum* infection during pregnancy leads to a number of adverse outcomes including low birthweight (LBW). Women acquire immunity to malaria in pregnancy over consecutive pregnancies and are most susceptible during their first pregnancy. Current interventions aimed towards preventing this burden focus upon the provision of insecticide treated nets (ITNs) and intermittent preventative therapy (IPTp).

METHODS: An existing model of the progression of placental infection and the development of immunity to malaria in pregnancy was extended to incorporate patterns of the risk of low birthweight by parity and histological stage of infection. This was then used to investigate how different schedules of IPT-SP and ITN use are likely to affect the burden of malaria in pregnancy in terms of the likelihood and duration of infection and risk of LBW attributable to malaria.

RESULTS: The model suggests that a large proportion of the exposure to placental infection can be attributed to infection acquired before or early during pregnancy, before the placenta is sufficiently developed to become parasitized. Although the overall modelled impact of IPT-SP upon birthweight depends upon the assumption made about how clearing parasites reduces the burden of infection, the estimated impact of the intervention is greatest when the first dose is received as early as possible during pregnancy. For similar reasons, ITNs, which have an entirely prophylactic mechanism of action, are estimated to be much more effective when used prior to pregnancy rather than received during an antenatal clinic visit. The incremental value of using ITNs prior to pregnancy is similar when used in conjunction with IPT-SP, as the latter intervention reduces the impact of infections later in pregnancy.

CONCLUSIONS: These results suggest that providing pregnant women with adequate protection from malaria as early as possible during pregnancy should be a priority. In particular, our estimates of the role of parity-dependent immunity and the progression of placental infection imply that ITN use in young women prior to their first pregnancy, the period during their reproductive lifespan when they are least likely to use a net, would have a large impact upon the risk of malaria-attributable low birthweight.

Impact of sulphadoxine-pyrimethamine resistance on the effectiveness of Intermittent Preventive Therapy for malaria in pregnancy (IPTp) in Africa: A systematic review and meta-analysis

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Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, United Kingdom

BACKGROUND: Sulphadoxine-Pyrimethamine (SP) is the only antimalarial currently recommended for Intermittent preventive therapy in pregnancy (IPTp) in sub-Saharan Africa. However, high level resistance threatens its efficacy. To support WHO with the design of a molecular policy decision tool for IPTp, we conducted a meta-analysis to determine the potential modifying effects of SP resistance on the association between IPTp and the risk of low birthweight.
METHODS: IPTp-SP sources included Demographic Health Surveys, Malaria Indictor Surveys, Multiple Indicator Cluster Surveys, AIDS indicator surveys, observational studies and randomized trials with IPTp-SP mono-therapy. Data on molecular markers of SP resistance were obtained by matching spatiotemporal maps of the annual prevalence of the *Pf*dhps-A437G and K540E mutations between 2000 and 2010 to the IPT effectiveness studies. Random-effects meta-analysis was used to estimate of summarized dose-response data with SP dose categorised as 0, 1, 2 and 3+. The primary endpoint was low birthweight (LBW).
RESULTS: The results of the aggregated study and trial data showed a linear trend towards lower effectiveness with increasing resistance (26 studies) when comparing areas with low resistance (<=50% *Pf*dhps-A437G, all in west Africa), moderate resistance (>50% *Pf*dhps-A437G or >10% *Pf*dhps-K540E & <1% *Pf*dhps-A581G) and high resistance (>1% *Pf*dhps-A581G) (P-value for linear trend P=0.02, and P=.008 when one outlier was excluded). Individual-level survey analysis was restricted to areas >80% *Pf*dhps-K540E. A linear decrease in effectiveness with increasing prevalence of *Pf*dhps-K540E was observed (P=0.065), but even in areas with >95% *Pf*dhps-K540E, IPTp-SP remained associated with significantly less LBW. By contrast in areas defined as super resistance (>10% Pfdhps-A581G), no protective association was evident.
CONCLUSION: The effectiveness of IPTp-SP in reducing LBW decreases with increasing population prevalence of the resistant *Pf*dhps-A437G mutation in West Africa and of the *Pf*dhps-K540E mutation in East and Southern Africa. A dose response towards a lower risk for LBW associated with each incremental dose of SP remains evident even in areas with >95% prevalence of pfdhps-K540E; however, the effectiveness of IPTp-SP is compromised if the additional mutation in *Pf*dhps-A581G is prevalent at >10%. Use of molecular policy decision tools are potentially useful to guide IPTp-SP implementation.

Impact of sulfadoxine-pyrimethamine resistance on effectiveness of intermittent preventive therapy in pregnancy: Methodology and protocol development

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BACKGROUND: WHO recommends the use of intermittent preventive treatment in pregnancy with sulfadoxine pyrimethamine (IPTp-SP) to prevent the adverse effects of malaria in Pregnancy (MiP). There is a good correlation between the prevalence of molecular SP resistance markers in *dihydrofolate reductase (dhfr)/dihydropteroate synthetase (dhps*) and the effectiveness of IPTp in reducing low birth weight. Even in the presence of high levels of the quintuple mutant (>90%) IPTp is associated with reduced risk of LBW, but this declines with increasing prevalence of the sextuple mutant (quintuple mutant plus an additional mutation at *dhps* A581G). Practical methods for malaria programs to monitor SP resistance and determine the resistance levels at which IPTp-SP is no longer recommended are lacking.
METHODS: A series of studies were conducted between 2009–2012 in six countries across sub-Saharan Africa with varying degrees of SP resistance to assess the relationship between molecular markers of SP resistance and both the *in vivo* efficacy in asymptomatic infected pregnant women and birth outcomes. The results from these studies, and review of existing literature, were used to inform the development of a protocol for monitoring the impact of SP resistance.
RESULTS: The protocol is under development. Preliminary results will be presented. A stratified and staged approach to monitoring is recommended. In areas with low SP resistance, periodic monitoring of the prevalence of molecular markers of resistance to SP is recommended, with increasing frequency of monitoring as resistance increases to moderate levels. In areas with high resistance (molecular thresholds to be defined), the additional use of delivery cross-sectional surveys with individual-level genotyping of parasites is recommended.
CONCLUSIONS: This protocol aims to provide a practical method of monitoring SP resistance and aiding countries in determining when IPTp-SP is no longer effective so that alternate strategies for prevention of MIP can be deployed.

A Trial Of Intermittent Screening And Treatment As An Alternative To Intermittent Preventive Treatment With Sulfadoxine-Pyrimethamine For The Controlof Malaria In Pregnancy

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BACKGROUND: The incidence of malaria, including the incidence in pregnant women, is declining in some African countries, and resistance to sulfadoxine-pyrimethamine (SP) is widespread. Thus, intermittent preventive treatment in pregnancy with SP (SP-IPTp) may no longer be appropriate in certain situations, and alternative strategies are needed.
METHODS: A multi-centre, randomised controlled non-inferiority trial was undertaken in four west African countries, including 5354 pregnant women who slept under an insecticide treated bed net. The standard SP-IPTp regimen (two to three courses of SP in the second and third trimester) was compared to intermittent screening and treatment (IST) of parasitaemia using a rapid diagnostic test at scheduled antenatal clinic visits in the second and third trimester. The primary end points of the trial are prevalence of low birth weight (LBW), mean maternal haemoglobin measured at the final follow-up visit expected to occur at 38 ±2 weeks of gestation and prevalence of placental malaria. Other outcomes affecting mothers (anaemia, parasitaemia, clinical malaria) and children (still births, perinatal mortality) were also analysed.
RESULTS: A total of 6611 eligible pregnant women were screened and 5354 were randomised into one of the two study arms (2679 into the IPTp arm and 2676 into the IST arm). About 88% of them were aged below 25 years; 54.1% primigravidae and the rest secundigravidae. More than half of them slept under an insecticide treated net the night before enrolment. At the end of follow up, 2511 and 2508 in the IPTp and IST arms respectively had evaluable delivery outcomes. The analysis of the impact of the two interventions on clinical outcomes (birth weight and maternal haemoglobin) is on-going and preliminary results will be presented at the MIM conference in October.
CONCLUSIONS: The study will provide information to national malaria control programmes in countries with seasonal malaria transmission on whether there are alternative, safe and effective methods to the WHO recommended SP-IPTp regimen for managing malaria in pregnancy. The results may also have implications for the control of malaria in pregnancy in areas with high levels of SP resistance and in areas with reduced malaria transmission.

Efficacy and safety of Mefloquine as malaria Intermittent Preventive Treatment in pregnancy (IPTp): results from two multicenter randomized controlled trials in HIV positive and negative African women

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BACKGROUND: The current recommendation by the World Health Organisation (WHO) to prevent malaria infection in pregnancy in areas of stable malaria transmission relies on: i) the prompt and effective case management of malaria illness, ii) the administration of intermittent preventive treatment (IPTp) with sulfadoxine-pyrimethamine (SP) at each scheduled antenatal clinic (ANC) visit and iii) the use of insecticide treated nets (ITNs). However, the spread of parasite resistance to 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 IPTp. The evaluation of alternative antimalarials for IPTp is thus urgently needed in HIV-negative and positive pregnant women. Of all the current available alternative antimalarial drugs, mefloquine (MQ) is the one that offers the most comparative advantages to SP.
METHODS: Two randomized multicenter controlled trials were conducted.
Trial 1: Open-label superiority 3-arm trial conducted in four African countries (Benin, Gabon, Tanzania and Mozambique) to compare the efficacy and safety of two-dose MQ *versus* two-dose SP for IPTp in the prevention of the adverse effects

of malaria during pregnancy in HIV-negative women. MQ tolerability of two different MQ administration regimens was also assessed. The three arms of the study were: 1) IPTp with SP, 2) IPTp with MQ given as full dose on 1 day, 3) IPTp with MQ split dose given over 2 days. All participants received an ITN at recruitment and were followed-up until the infants reached age one.
Trial 2: Double-blind placebo-controlled trial conducted in three African countries (Kenya, Tanzania and Mozambique) to compare the efficacy of three doses of MQ as IPTp with three-dose placebo-IPTp in HIV-infected pregnant women receiving Cotrimoxazole prophylaxis. All participants received an ITN at recruitment.
RESULTS: Trials 1 and 2 enrolled respectively 4749 and 1071 pregnant women. The results obtained on the efficacy and safety of MQ as IPTp in both trials shall be presented.

S38: Analytic challenges in measuring impact of malaria control programmes: Methodological approaches, confounders and lessons learned from the multi-agency malaria control impact evaluations

Chairs: Dr Yazoume Ye and Dr Lia Florey

Speaker 1: Dr Lia Florey, Trends analyses of nationally-representative survey data: What story can be told and what is missing? CF International, United States of America
Speaker 2: Dr Madeleine Thomson, Use of climate information in the assessment of impact of malaria interventions, Columbia University, United States of America
Speaker 3: Dr Absisalan Noor, Preparing for the future: Health systems strengthening for better outcomes and better data to better inform future impact evaluations, KEMRI-Wellcome Trust, Kenya
Speaker 4: Prof Tom Smith, Methofological challenges in evaluating malaria control programme impact: How do we ever find out what worked? Swiss Tropical and Public Health Institute, Switzerland

Trend analyses of nationally-representative survey data: What story can be told and what is missing?

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In the absence of reliable, good quality data on malaria control interventions and malaria-specific health outcomes from health information systems, malaria control programs are often forced to rely on national survey data for monitoring and evaluation. National survey data are valuable in that they provide a snapshot of the level of intervention coverage and child morbidity throughout the entire population, not limited to health facility users. However, surveys rely largely on self-report which can lead to reporting or recall bias. Surveys are also cross-sectional and include limited information on malaria-specific outcomes thus hindering causal attribution. Finally, surveys are limited in scope, omitting many variables relevant to the context of malaria epidemiology.

Following the plausibility model described by Rowe and colleagues, the President's Malaria Initiative and other partners have completed several impact evaluations of malaria control in sub-Saharan African countries. The plausibility argument entails measuring trends in intervention scale-up, trends in malaria-related morbidity and mortality, and trends in other factors that could have influenced outcomes and assessing whether it is plausible to conclude that the scale-up of interventions could have resulted in the trends in malaria-related outcomes. Through the multi-agency impact evaluation work several challenges with this approach have been identified: survey data are not always available for the relevant time periods; malaria control policies and indicators have changed affecting comparability over time, surveys are not always sampled to capture diverse malaria risk within a country, and trends in measurable outcomes are not always easy to interpret due to multifactorial etiologies. Although some of these challenges are insurmountable certain approaches can help strengthen the plausibility argument. Additional questions about trends in survey data can be assessed such as: were interventions deployed in areas of greatest need; was implementation strong enough to reasonably expect an impact; which approaches in implementation led to rapid increases in coverage; was sustained and equitable coverage achieved; and do any alternative explanations exist for observed trends in outcomes. Other approaches include using district-level data from surveys (when available) in ecologic models, and using subnational or demographic surveillance system (DSS) data as supplemental evidence.

Use of climate information in the assessment of impact of malaria interventions.

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BACKGROUND: National level evaluations of malaria control programs are notoriously difficult given the diversity of confounding factors that affect malaria epidemiology. One important, but often overlooked, factor when evaluating impact is pre and post-intervention changes in climate. Malaria is a complex disease: its transmission, via vector mosquitoes (*Anopheles* sp.) can be highly climate sensitive. Temperature is a significant driver of the development rates of both the mosquito vector and plasmodium parasite while rainfall and humidity provide essential environmental characteristics for juvenile mosquito development and adult survivorship respectively.

Here we present new data, methodology and tools for factoring in climate variability and trends into the evaluation of the impact of national malaria control programs.

The confounding effect of climate on malaria impact evaluations in Ethiopia and Tanzania was investigated using newly available high resolution, quality assured, national climate databases. Three tools for climate analysis were used to assess: (1) whether malaria in a given area is climate sensitive, (2) whether rainfall in a given locale is more or less suitable for malaria transmission pre and post intervention; and (3) whether long term trends in the temperature and rainfall exist and are likely to confound malaria impact evaluation.

In Ethiopia country-wide declines in malaria, if observed, cannot be attributed to climate changes (drought) since the intervention period 2006-2010 was generally wetter than the baseline 2000-2005 in most highly populated regions. However, in Tanzania the intervention period (2000-2009) was substantially drier (~15%) than the baseline period used (1995-1999) and drought is likely to have contributed to the observed decline in malaria morbidity and mortality as well as other indices of malaria transmission. In both countries significant warming was observed in highland regions during the last 30 years (>0.15^{c}/decade).

CONCLUSIONS: We conclude that if climate is not taken into account, then the measurement of achievements of national malaria control programs may be overly pessimistic in years that experience an elevated climate risk for malaria in relation to the baseline period. Conversely, measurements may be overly optimistic when climate risk from malaria is low. Therefore, data, methodologies and tools for incorporating climate analysis must be included in routine assessment of malaria interventions in order to more accurately gauge their impact.

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Preparing for the future: Health Systems Strengthening for better outcomes and better data to better inform future impact evaluations.

Abdisalan Noor

KEMRI-University of Oxford-Wellcome Trust Research Programme, Kenya

Very few malaria endemic countries in Africa have sufficient data to assess trends in the disease burden over time and to evaluate the impact of the substantial scale up of malaria control in the last decade on mortality and morbidity.

Nonetheless, evidence shows that several African countries are currently experiencing low levels of malaria transmission with a few aiming for elimination. Integral to malaria control under such low levels of risk is highly accurate malaria data. However, the improvements in health information systems appear to have been outpaced by reductions in transmissions and national ambitions for elimination limiting the ability to track progress and evaluate impact.

Here we provide an assessment of the state of HMIS in Africa and its readiness to explore malaria impact evaluation. We explore alternative sources of data to estimate malaria control in the last decade and suggest ways forward to ensure reliable tracking of progress into the future.

Methodological challenges in evaluating malaria control program impact: how do we ever find out what worked?

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In recent years, substantial reductions have been recorded in the amount of malaria in many endemic countries, especially in East Africa, but it is unclear what are the contributions to this, of ACT use, LLIN scale-up, or other external factors, such as urbanisation, improvements in housing, or evolutionary changes in parasites or vectors.
It is critically important to understand which factors account for the improvements, since the consequences of further scale-up or of withdrawing interventions depend critically on which elements of existing programs account for the effects. Many malaria control programs under-invest in program evaluation, and so do not know how well their program is working.

Observational data on scale-up of interventions and of contemporaneous malariological trends do not, on their own, provide a basis for attributing causality. Simulation modelling can be used to support decisions about which interventions are likely to be most cost effective in given settings, and to predict what a program should be achieving has some potential value. However such modelling should be seen as a complement to, rather than a substitute, for the capture of data on coverage or access from the field.

In general, new interventions cannot be introduced to a whole country all at once. Stepwise introduction of interventions provides the opportunity of estimating the impact of scale-up by comparing areas with the intervention with other areas where it has not yet been introduced. The inclusion of elements of randomisation in the order of introduction to different geographical areas, is critical for inferring causality from such data, and the importance of this should be stressed to program managers.

S39: Mating Biology of Anopheles

Chairs: Dr Jeremie RL Gilles and Prof Mark Q Benedict

Speaker 1: Dr Abdoulaye Diabate, Ecological and physiological correlates of mating in *Anopheles gambiae*, Centre Muraz, Bobo-dialoasou, Burkina Faso
Speaker 2: Dr Flamina Catteruccia, Molecular determinants of reproductive success in *Anopheles gambiae* males, Harvard University, United States of America and University of Perugia, Italy
Speaker 3: Dr Frederic Tripet, Behavioural genetics of assortative mating in *Anopheles gambiae* complex, Keele University, United Kingdom
Speaker 4: Dr Gabriella Gibson, The role of circadian rhythms in the mating behaviour of *Anopheles coluzzii* and *An. gambiae s.s.*, University of Greenwich, United Kingdom

Ecological and physiological correlates of mating in *Anopheles gambiae*

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Recent advances in insect's biotechnology has opened several options for malaria control among which the release of genetically modified mosquito rendered refractory to pathogen infection. Another approach that may be effective is based on sterile male release. However availability of these tools does not necessarily guarantee ultimate success. Field and laboratory studies designed to dissect the mating biology of mosquitoes are needed to provide a foundation for predicting the potential utility of genetic control and that this study is addressing.

Swarms were surveyed and collected in Vallée du Kou, Burkina Faso in 2011 and 2013. A complete map of swarm distribution across the study site was constructed and overall 300 swarms were spotted across the village. Swarms strongly responded to specific man-made markers within the village. The number of swarms/compound varied from 3 to 20 and the distribution did not follow normal expectations and exhibited substantial variations suggesting heterogeneity in ecological factors that account for swarm occurrence between compounds. Analysis of the spatial structure of swarms based on Monte Carlo simulations of random distributions indicated that swarms were clustered. Nearest-neighbor distance between swarms was significantly smaller if swarms were randomly distributed over space and the kernel density estimation (KDE) indicated hotspots where most of the swarms aggregate as a response to specific environmental cues. A multivariate analysis allowed identifying a subset of environmental parameters that best correlate to swarm structures and that includes, the number of swarm markers/surface unit, the exposition of the makers to sunlight, the contrast pattern and the openness of the marker to air circulation. These preliminary results have significant meanings towards the achievement of genetically modified mosquito strategies because they suggest that swarms respond to specific environmental cues, hence can be predicted and manipulated.
KEY WORDS: swarms, Anophes gambiae, ecological factors, genitically modified mosquitoes

Molecular determinants of reproductive success in *Anopheles gambiae* males

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The possibility of manipulating fertility to control field populations of malaria-transmitting *Anopheles gambiae* mosquitoes represents a valid alternative to the use of insecticides. As an example, genetic control strategies based on the release of sterile males over large areas have been advocated to reduce the size of natural mosquito populations. Genetic control measures rely on the ability of released males to mate competitively with field females and induce complete sterility, however the genetic determinants of male reproductive fitness and success are not known.

During copulation males transfer seminal secretions in the form of a gelatinous mating plug that is digested by the female over a period of 24-48 hours. Seminal secretions are produced by the male accessory glands (MAGs), and upon transfer during sex are believed to trigger important changes in female behavior, including switching female receptivity to further copulation, increasing the rate of egg production and inducing egg laying. In recent years we have started analyzing the biology of the MAGs and unraveled the identity of the proteins and lipids produced in these tissues and transferred to females during mating. Using a combination of molecular and cellular approaches, we have identified factors that play a key role in male reproductive success. Interfering in vivo with the function of these factors results in major alteration of the normal post-mating behavior and affects storage of sperm, severely affecting fertility. Our findings reveal possible targets for the design of new tools for the control of vector populations.

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Behavioural genetics of assortative mating in the *Anopheles gambiae* complex

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Anopheles gambiae exhibits complex populations and a number of cryptic taxa have been described. Genome-wide studies have shown that speciation in this species occurs through the divergence of a few loci characterized by reduced recombination and divergent selection. Such 'islands of speciation', located in pericentromeric regions of chromosomes X, 2L and 3L are thought to contain genes responsible for the assortative mating observed in complex An. gambiae populations. We selectively introgressed the island of speciation located on the X chromosome from the S form into an M Mopti form genetic background resulting in pairs of recombinant strains differing only in the molecular form of their X-island. Using this approach, we identified two recombinant strains that mated consistently assortatively thereby broadly mapping assortative mating genes to the X-chromosome island of speciation. These results constitute fundamental steps towards the identification of genetic determinants of pre-mating reproductive isolation in this important species complex.

The role of circadian rhythms in the mating behaviour of *Anopheles coluzzii and An. gambiae s.s.*

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The swarming behaviour of Anopheles coluzzii and An. gambiae Giles s.s. (formerly know and M and S molecular forms of An. gambiae s.s.) was investigated in two villages in Burkina Faso (West Africa). Although the habitats of these villages differ markedly, sympatric populations of the two species occur in both places periodically, but hybrids have never been found. The main aim was to assess the factors that contribute to assortative mating. Out of 90 swarms monitored over 2 years, 60% were single-species swarms of necessity, as the species were segregated either spatially or seasonally (i.e., did not occur in the same villages during the same months), 23% were single species swarms even though both species were present. Therefore, 83% swarming occurs when the two species are physically separated. Only 17% of swarms consisted of a both species, and yet, of the 33 females caught as copulae in these mixed-species swarms, all were found to be inseminated by males of their own species.

To address the question as to how the two species mate assortatively in mixed swarms observations of the time of day at which the males of each species start and stop swarming was recorded under natural condition in wild swarms and under controlled conditions in an actograph (measures the timing of spontaneous activity in individual mosquitoes). The results show that the timing of swarming and spontaneous activity at dusk are primarily under circadian control, with the phase linked closely to sunset throughout the year. The mating activity of these two species was found to be temporally segregated for 15-20% of the swarming period, which may contribute to the observed reproductive isolation of these species in mixed-species swarms.

S40: How intervention effects depend on the setting: insights from mathematical models

Chairs: Prof Tom Smith and Dr Gerry Killeen

Speaker 1: Dr Samson Kiware, Simplified models of vector control impact upon malaria transmission by zoophagic mosquitoes, Ifakara Health Institute, Tanzania

Speaker 2: Dr Angelina M Lutambi, Clustering of vector control interventions has important consequences for their effectiveness: a modelling study, Ifakara Health Institute, Tanzania

Speaker 3: Dr Fredros O Okumu, Mathematical evaluation of community level impact of combining bed nets and indoor residual spraying upon malaria transmission, Ifakara Health Institute, Tanzania

Speaker 4: Dr Oliver JT Briet, Repeated mass distributions and continuous distribution of long lasting insecticidal nets: modelling sustainability of health benefits from mosquito nets depending on case management, Swiss Tropical and Public Health Institute, Switzerland.

Simplified models of vector control impact upon malaria transmission by zoophagic mosquitoes

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BACKGROUND: High coverage of personal protection measures that kill mosquitoes dramatically reduce malaria transmission where vector populations depend upon human blood. However, most primary malaria vectors outside of sub-Saharan Africa can be classified as "very zoophagic", meaning they feed occasionally (<10% of blood meals) upon humans, so personal protection interventions have negligible impact upon their survival.

METHODS: We extended a published malaria transmission model to examine the relationship between transmission, control, and the baseline proportion of bloodmeals obtained from humans (human blood index). The lower limit of the human blood index enables derivation of simplified models for zoophagic vectors that: (1) Rely on only three field-measurable parameters. (2) Predict immediate and delayed (with and without assuming reduced human infectivity, respectively) impacts of personal protection measures upon transmission. (3) Illustrate how appreciable indirect communal-level protection for non-users can be accrued through direct personal protection of users. (4) Suggest the coverage and efficacy thresholds required to attain epidemiological impact.

RESULTS: The findings suggest that immediate, indirect, community-wide protection of users and non-users alike may linearly relate to the efficacy of a user's direct personal protection. Therefore, high levels (≥80%) of protective coverage and efficacy are important to achieve an epidemiologically meaningful impact. Non-users are indirectly protected because the two most common species of human malaria are strict anthroponoses. Therefore, the small proportion of mosquitoes that are killed or diverted while attacking humans can represent a large proportion of those actually transmitting malaria.

CONCLUSIONS: Results from the simplified models of malaria transmission by very zoophagic vectors may be used by control practitioners to predict the impacts of interventions using three field-measurable parameters; the proportion of human exposure to mosquitoes occurring when an intervention can be practically used, its protective efficacy when used, and the proportion of people using it.

Clustering of vector control interventions has important consequences for their effectiveness: a modelling study

Angelina M. Lutambi[1, 2,3], Nakul Chitnis[1, 2], Olivier J.T. Briët[1, 2], Thomas A. Smith[1, 2], and Melissa A. Penny[1, 2]

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BACKGROUND: Vector control interventions have resulted in considerable reductions in malaria morbidity and mortality. When universal coverage cannot be achieved for financial or logistical reasons, the spatial arrangement of vector control is potentially important for optimizing benefits. This study investigated the effect of spatial clustering of vector control interventions on reducing the population of biting mosquitoes.
METHODS: A discrete-space continuous-time mathematical model of mosquito population dynamics and dispersal was extended to incorporate vector control interventions of insecticide residual spraying (IRS), larviciding and insecticide treated bednets (ITNs). Simulations were run at varying levels of coverage and degree of spatial clustering.
RESULTS: At medium to high coverage levels of larvicidal and adultcidal interventions, especially insecticide treated nets (ITNs), it was more effective to spatially spread these interventions than to cluster them. When resources are limited, clustering of larviciding was more effective than unclustered distribution. Although it is often stated that locally high coverage is needed to achieve a community effect of ITNs (or indoor residual spraying (IRS)), our results suggest that if the coverage of ITNs or IRS are insufficient to achieve universal coverage and there is no targeting of high risk areas, the overall effects on mosquito densities are much greater if they are distributed in an unclustered way, rather than clustered in specific localities. Also, given that interventions are often delivered preferentially to accessible areas, and such clustered, our model results show this may well be inefficient.
CONCLUSIONS: This study provide evidence that the effectiveness of an intervention can be highly dependent on its spatial distribution. Given logistical and financial constraints, vector control plans should consider the spatial arrangement of any intervention package to ensure effectiveness is maximized, and in the case of high achievable coverage, in the absence of information that allows targeting, that the distribution is as equitable and as evenly spatially spread as possible as this will maximize benefits.

Mathematical evaluation of community level impact of combining bed nets and indoor residual spraying upon malaria transmission

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BACKGROUND: Indoor residual insecticide spraying (IRS) and long-lasting insecticide treated nets (LLINs) are commonly used together even though evidence that such combinations confer greater protection against malaria than either method alone is inconsistent.
METHODS: A deterministic model of mosquito life cycle processes was adapted to allow parameterization with results from experimental hut trials of various combinations of untreated nets or LLINs (Olyset®, PermaNet 2.0®, Icon Life® nets) with IRS (pirimiphos methyl, lambda cyhalothrin, DDT), in a setting where vector populations are dominated by Anopheles arabiensis, so that community level impact upon malaria transmission at high coverage could be predicted.
RESULTS: Intact untreated nets alone provide equivalent personal protection to all three LLINs. Relative to IRS plus untreated nets, community level protection is slightly higher when Olyset® or PermaNet 2.0® nets are added onto IRS with pirimiphos methyl or lambda cyhalothrin but not DDT, and when Icon Life® nets supplement any of the IRS insecticides. Adding IRS onto any net modestly enhances communal protection when pirimiphos methyl is sprayed, while spraying lambda cyhalothrin enhances protection for untreated nets but not LLINs. Addition of DDT reduces communal protection when added to LLINs.
CONCLUSIONS: Where transmission is mediated primarily by An. arabiensis, adding IRS to high LLIN coverage provides only modest incremental benefit (e.g. when an organophosphate like pirimiphos methyl is used), but can be redundant (e.g. when a pyrethroid like lambda cyhalothin is used) or even regressive (e.g. when DDT is used for the IRS). Relative to IRS plus untreated nets, supplementing IRS with LLINs will only modestly improve community protection. Beyond the physical protection that intact nets provide, additional protection against transmission by An. arabiensis conferred by insecticides will be remarkably small, regardless of whether they are delivered as LLINs or IRS. The insecticidal action of LLINs and IRS probably already approaches their absolute limit of potential impact upon this persistent vector so personal protection of nets should be enhanced by improving the physical integrity and durability. Combining LLINs and non-pyrethroid IRS in residual transmission systems may nevertheless be justified as a means to manage insecticide resistance and prevent potential rebound of not only An. arabiensis, but also more potent, vulnerable and historically important species such as *Anopheles gambiae* and Anopheles funestus.

Repeated mass distributions and continuous distribution of long lasting insecticidal nets: modelling sustainability of health benefits from mosquito nets depending on case management

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BACKGROUND: After global successes in reducing malaria, stagnating funds have spurred interest in the problem of sustaining the gains of recent malaria control successes with long lasting insecticidal nets (LLINs) and improved case management (CM).
RESEARCH QUESTION: This simulation study looked at the malaria dynamics in scenarios with sustained interventions with LLINs and CM, and tried to determine what LLIN distribution rates would be optimal. Also, effects of abruptly halting LLIN distribution were examined.
METHODS: Dynamic simulations of malaria in humans and mosquitoes were run on the OpenMalaria modeling platform. LLINs were distributed in a range of transmission settings, with varying case management coverage levels and varying distribution rates.
RESULTS: In the short term, LLINs were beneficial over the entire transmission spectrum and reduced transmission and the disease burden. Also in the long term, they sustainably reduced transmission in all settings. However, because of the resulting reduction in the acquisition of immunity, after initially being reduced, the malaria disease burden gradually increased and eventually stabilized to a new level. This new level was above the pre-intervention level in previously high transmission settings, if there is a maximum in the relationship between transmission and disease burden at intermediate transmission levels. This result might lead one to conclude that, sustained distribution of LLINs might not be cost effective in high transmission settings in the long term. However, improved CM rendered LLINs cost effective at higher transmission settings than without improved CM coverage and the great majority of the African population lives in areas where the sustained combination of both CM and LLINs is cost effective. The effects of changes in LLIN distribution rate on cost effectiveness were relatively small compared to effects of changes in transmission setting and CM. Abruptly halting LLIN distribution led to temporary morbidity peaks, which were particularly large in low to intermediate transmission settings.
CONCLUSIONS: Planning for optimal combinations of malaria vector control and CM tools will need to take both the pre-intervention potential for transmission, and existing CM levels into account.

S41: The final decade of malaria in Africa: planning for the endgame

Chairs: Dr Jo Lines and Dr John Chimumbwa

Speaker 1: Dr Fatoumata Nafo-Traoré, Roll Back Malaria, Switzerland
Speaker 2: Professor Sir Brian Greenwood, Looking in the crystal ball – the future of malaria, London School of Hygiene and Tropical Medicine
Speaker 3: Dr Alan Magill, How can we accelerate to elimination, Bill and Melinda Gates Foundation, United States of America
Speaker 4: Dr Roly Gosling, University of California – San Francisco, United States of America
Speaker 5: Dr Robert Newman, World Health Organisation, Switzerland.

Dr Jo Lines

OVERVIEW

This symposium starts with the premise that malaria will eventually be eliminated from tropical Africa, probably more than two decades but less than a century from now. The aim of the symposium is to speculate about the period leading up to this happy event - the endgame:

- What will Africa look like by this time?
- What will have happened, between now and then, to make elimination possible?
- Will malaria disappear quickly or slowly?
- Can elimination be stable in tropical Africa, without insecticides and despite the occasional arrival of imported cases? Or will we have to maintain continuous and intensive chemical vector control until worldwide eradication has been achieved? Scientific debate about malaria is quite rightly dominated by short-term questions: what is needed to win the battles of today and next week and next year? However, it is also important to plan for the longer-term: what is needed to win the war? In this Symposium, therefore, we will put these critical short-term concerns aside, and try to avoid adversarial debate about alternative short- and medium-term strategies, or a talent show for promising new technologies. The speakers will present their visions of the end-game. They have been asked to consider a range of contingencies, optimistic and otherwise: not only how elimination might be made possible by a decisive new intervention, but also how it can still be achieved if those hopes are never fully realised. We will then have a panel discussion with selected (and perhaps pre-submitted) questions from the audience. We expect to hear a wide range

of opinions and visions from speakers and audience. The aim is not to develop a shared vision, but to canvas a broad range of opinions. We don't want to reach any conclusions, but to start the debate - and we expect the debate to continue unresolved until the very end.

S42: MMV colaborations in antimalarial drugs development from discovery to access and delivery.

Chairs: Dr Stephan Duprac and Dr Pierre Hugo.

Speaker 1: Prof. Kelly Chibale, MMV 390048, UCT
Speaker 2: Dr Issaka Sagara - Longitudinal repeat-dose study to evaluate the safety and efficacy of repeated administrations of pyronaridine-artesunate, Malaria Research and Training Centre University of Bamako, Mali
Speaker 3: Prof Azra Ghani - Evaluating the Modeling Effects of Implementing Multiple First Line/MFL ACT Treatments Versus Real Life Data, Imperial College, United Kingdom
Speaker 4: Prof. Antoinette Tshefu, Collaboration with the University of Kingshasa, NMCP of DRC and Swiss TPH: Treatment of swere malaria with injectable artesunate - implementation of non-controlled longitudinal introductions in the DRC, University of Kinshasa, DRC
Speaker 5: Dr Robert Newman - Treatment of Severe Malaria with Injectable Artesunate - Implementation of Non-Controlled Longitudinal Observational Study to Support Artesunate Introduction in the Democratic Republic of the Congo (DRC), World Health Organisation, Switzerland.

OVERVIEW

Medicines for Malaria Venture (MMV) is a Product Development Partnership (PDP) that aims to discover, develop andrfacilitate access to new drugs for malaria that will help save the lives of under-served populations living under the threat of this terrible disease. The symposium will present MMV's partnership model in action, providing examples of its collaborations with universities and institutions from Africa and Europe, all working towards the same goal. The first presentation profiles a collaboration with the University of Cape Town on the early stage development of a new promising molecule, MMV 390048, a novel chemical series with potential new mechanism of action against *Plasmodium*. This compound is on track to progress to a "first time in human study in 2014. The second presentation focuses on a collaborative work with the University of Bamako and the European & Developing Countries Clinical Trials Partnership (EDCTP) on a phase IIIb/IV clinical trial carried out in Mali, Burkina Faso and Guinea with 4 different ACTs. Assessment of the "real world" safety and efficacy of pyronaridine-artesunate, one of the four ACTs tested in this trial, which received a positive opinion from EMA article 58 in February 2012, will generate data enabling the malaria community and regulators to better understand the safety profile of this drug combination in cases of repeated administratio. – something that is not covered under the current investigation. The third presentation gives an example of an alliance with the Imperial College in London, focused on modeling and evaluating the effects of implementing multiple first line antimalarial treatments versus real life data. The final talk presents a collaborative work with the University of Kinshasa, the National Malaria Control Programme of Democratic Republic of the Congo (DRC) and the Swiss TPH in Basel, Switzerland on a post-registration, implementation study regarding the treatment of severe malaria with injectable artesunate.

S43: Investing in quality surveillance for malaria (pre-) elimination programmes.

Chair: Dr Claudia Vondrasek

Speaker 1: WHO Elimination Team, Surveillance as the key to malaria pre-elimination, World Health Organisation, Switzerland.
Speaker 2: JHSPH Malaria Research Institute, Surveillance techniques used in Zambia, John Hopkins School of Public Health, United States of America
Speaker 3: Dr Abdul-wahid Al-mafazy, Fit for purpose: Novel surveillance systems for malaria in pre-elimination settings in Zanzibar, Zanzibar Malaria Control Programme, Zanzibar
Speaker 4: South African National Malaria Programme, How South Africa is improving its surveillance techniques, South African National Malaria Programme, South Africa
Speaker 5: Data Dyne, Individual surveillance techniques using mobile phones, Data Dyne, United States of America

Fit for purpose: Novel surveillance systems for Malaria in pre-elimination settings of Zanzibar

Abdul-wahid Al-mafazy[1], Abdullah S. Ali[1], Fabrizio Molteni[2], Issa A. Garimo[3], Michael McKay[4], Mohammed Ali[1], Wahida Hassan[1], Mahdi M. Ramsan[3], Uche Ekenna[5], Richard Reithinger[4], Jessica M. KafUnited Kingdomo[6], Ritha Willilo[2], Stephen Magesa[3], Jeremiah M. Ngondi[3]

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BACKGROUND: In 2008, Zanzibar established the Malaria Epidemic Early Detection System (MEEDS) for electronic reporting and analyzing weekly malaria cases. In 2012, electronic malaria case notification (MCN) was established to enhance timely investigation of individual malaria cases and response activities. We report results of MEEDS and MCN surveillance systems in the malaria pre-elimination settings of Zanzibar.
METHODS: By 2013, MEEDS reported weekly malaria data from 160 (75%) health facilities. Weekly-summary data were transmitted via Unstructured Supplementary Service Data (USSD) mobile phones from health facilities to a remote server. For MCN reporting, a massage for each case is sent from Health Facility to the server where the server generates an alert SMS to the District Malaria Surveillance Officer's (DMSO) mobile phone and tablet. DMSO follows up patients (index cases) to their households. All case-household members are tested for malaria using rapid diagnostic tests (mRDT). People with positive malaria test results are treated with artemisinine-based combination therapy (ACT).
RESULTS: Representativeness has gradually improved as MEEDS was implemented from 10 (7%) primary health care health facilities in 2008 to 52 (37%) in 2009, 90 (63%) in 2010, 142 (100%) of public facilities and 18 (29%) of tertiary and private clinics by 2013. Completeness of submitted data was maintained at 100% since 2010 though technical problems prevented data transmission from some health facilities affecting timeliness of submission. Between 2011 and 2012, the number of malaria tests increased from 266,407 to 275,669. There was a reduction in malaria positive tests from 1.2% to 0.9% ($p<0.001$).

Results of MCN between September 2012 and June 2013 shows that a total of 1,439 index malaria cases were notified, of whom 1,013 (70.4%) were followed up at the household level. Of 4,627 household members tested with mRDT, 7.5% were positive for malaria.
CONCLUSION: The MEEDS and MCN systems provide timely reporting of malaria data and support timely programmatic decision making. Through MEEDS, ZMCP detects abnormal increases in cases and undertake appropriate response. Follow-up of malaria cases through MCN enables active detection of malaria cases and timely treatment of asymptomatic cases to reduce potential for malaria transmission.

S44: Interactions between ACTs for malaria and ARVs for HIV – cause for concern?

Chairs: Prof David Schellenberg and Prof Lasse Vestergaard

Speaker 1: Prof Karen Barnes, Pharmacokinetic interactions between artemether-lumefantrine and drugs used in the treatment of HIV-infected patients, University of Cape Town, South Africa
Speaker 2: Prof Lasse S Vestergaard, Efficacy and safety of artemether-lumefantrine for the treatment of uncomplicated malaria in HIV-positive adults receiving first-line antiretrovirals in Tanzania. University fo Copenhagen, Denmark.
Speaker 3: Dr Jane Achan, Efficacy and safety of artemisinin-based combination therapy in HIV-infected children in Uganda, Makerere University College of Health Sciences, Uganda
Speaker 4: Dr Peter Mangesho, Perceptions and experiences of taking ACTs concomitantly with ARVs among patients with malaria and HIV in Tanzania, National Institute for Medical Research, Tanzania

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Prof David Schellenberg and Lasse Vestergaard

OVERVIEW

OBJECTIVE: This symposium will present findings from recent clinical and qualitative studies conducted in Tanzania and Uganda looking at the problem of concomitant treatment of malaria with artemisinin-based combination treatments (ACTs) and HIV with antiretrovirals (ARVs) in co-infected patients.

RATIONALE: Malaria and HIV both remains major public health problems in large parts of the world. WHO recommends artemisinin-based combination treatment (ACT) for malaria and antiretrovirals (ARVs) for treating HIV/AIDS. Although there is a potential for drug-drug interactions as these agents share common metabolic pathways, limited information is yet available regarding how such interactions might affect the efficacy and safety of these treatments when used concomitantly. Increased metabolism of artemether-lumefantrine (AL), the most commonly used ACT, could lead to decreased drug concentrations and thus reduced antimalarial efficacy and the selection of resistance. In contrast, decreased metabolism could cause increased blood concentrations leading to poorer tolerability or toxicity. Pharmacokinetic studies looking at various combinations of ACTs and ARVs have so far provided conflicting results, and most have been conducted in health volunteers in whom the impact on treatment efficacy cannot be detected. Further efficacy, safety and pharmacokinetic studies are needed in patients with HIV/AIDS andmalaria to assess the clinical significance of any interactions, inform treatment policies and guide safe and effective case management. In addition, a better understanding of how patients perceive and cope with such concomitant drug taking is needed.

CONTENT: The ACT Consortium was formed with the goal of developing and evaluating delivery mechanisms to improve ACT access, targeting, safety and quality. The purpose of this symposium is to present some of the findings of the Consortium's studies addressing co-infection with malaria and HIV and concomitant administration of ACTs and ARVs. Two Consortium studies have addressed the question of ACT-ARV interactions: The SEACAT Study in South Africa looking at PK effects in HIV-patients without malaria, and the InterACT Study in Tanzania looking at efficacy and safety of ACT-ARV interactions in co-infected adults. The study in Tanzania also involved a qualitative study looking at perceptions of concomitant ACT-ARV drug taking. Apart from the ACT Consortium, the Makerere University in collaboration with University of California has conducted a series of studies addressing HIV and malaria co-infection and ACT-ARV interactions, also involving PK and clinical studies. Symposium panelists will present a brief summary of currently known ACT-ARV PK interactions, followed by presentations of results from recent clinical studies in Tanzania and Uganda on how potential drug interactions may affect malaria treatment efficacy and safety, discussing the potential need to revise current treatment recommendations, and how to support patients in receiving most optimal concomitant treatment for malaria and HIV.

Pharmacokinetic interactions between artemether-lumefantrine and drugs used in the treatment of HIV-infected patients

Karen I Barnes
University of Cape Town, Cape Town, South Africa

BACKGROUND: Potential drug interactions need to be considered when treating malaria in people living with HIV/AIDS. Artemether-lumefantrine is currently the most widely used artemisinin-based combination therapy (ACT). As it is generally well tolerated with a wide-therapeutic index, it is expected that interactions that reduce exposure to artemether and or lumefantrine are more likely to be clinically significant than those that increase drug exposure. A decrease in ACT exposure is of particular concern in HIV-infected individuals as they tend to have higher baseline parasitaemias, an independent risk factor for antimalarial treatment failure.

METHODS: A literature search was conducted in PUBMED using the terms "artemether" or "lumefantrine", and "pharmacokinetics" or "concentrations", and "HIV". Articles were reviewed for any evidence of pharmacokinetic drug interactions with artemether-lumefantrine.

RESULTS: Artemether / dihydroartemisinin exposure was decreased by rifampicin, nevirapine, efavirenz, lopinavir/ritonavir, darunavir/ritonavir and etravirine. Lumefantrine exposure was decreased by rifampicin and efavirenz, but was increased by nevirapine, lopinavir/ritonavir and darunavir/ritonavir. However, some inconsistency between studies was found for the effect of nevirapine on lumefantrine exposure, with 2 studies finding increased lumefantrine

exposure and another finding similar lumefantrine exposure with nevirapine co-administration. In one study, artemether/lumefantrine reduced nevirapine exposure. Among the few studies conducted in malaria-HIV co-infected patients, the co-administration of lopinavir/ritonavir decreased the risk of recurrent malaria following artemether-lumefantrine treatment of uncomplicated malaria in Ugandan children, but also increased the number of serious adverse events. Limitations of some studies included small sample sizes, administration of a single artemether-lumefantrine dose, the co-administered drug not reaching steady state during the study, and conduct in healthy volunteers precluding assessment of the effect of the observed drug interaction on therapeutic efficacy.
CONCLUSIONS: Further clinical data from carefully designed population pharmacokinetic and pharmacodynamic field trials are urgently needed for evaluating the clinical significance of these drug interactions, particularly for guiding the management of uncomplicated malaria in patients on efavirenz-based antiretrovirals or rifampicin-based tuberculosis treatment. As resistance emerges and spreads, other drug interactions that increase the risk of artemether-lumefantrine treatment failures may become detectable.

Efficacy and safety of artemether-lumefantrine for the treatment of uncomplicated malaria in HIV-positive adults receiving first-line antiretrovirals in Tanzania

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INTRODUCTION: Although there is concern of drug-drug interactions between artemisinin-based combination treatment (ACTs) for malaria and antiretrovirals (ARVs) for treating HIV/AIDS, very limited information is available about the clinical importance of such interactions. The aim of this study was to examine the efficacy and safety of artemethemter-lumefantrine (AL), the most commonly used ACT, for the treatment of uncomplicated falciparum-malaria in HIV-positive adults recieving first-line ARVs in Tanzania.
METHODS: The InterACT Study was conducted from July 2009 to September 2012 at Muheza District Hospital in northern Tanzania. HIV-positive adults (>15 years) receiving either nevirapine- or efavirenz-based ARVs were enrolled and followed-up for 42 days using WHO standard protocols. Three additional groups of patients were included for comparison: 1) HIV-positive malaria patients not receiving ARVs but treated with AL, 2) HIV-negative malaria patients treated with AL, and 3) HIV-positive patients receiving ARVs but without malaria.
RESULTS: A total of 17,269 patients were screened for malaria, amongst whom 385 HIV-positive patients with confirmed malaria were enrolled into the study and followed-up successfully for 42 days. The therapeutic efficacy of AL after parasite PCR-correction was 99% in HIV-positive patients receiving ARVs (total n=193; 106 on nevirapine, 87 on efavirenz), 100% in HIV-positive patients not on ARVs (n=43) and 98% in HIV-negative patients (n=149). Rates of malaria re-infection within 42 days of AL treatment was low and did not differ significantly between the groups. Mild adverse events were commonly recorded in all four patient groups. Severe adverse events were more commonly observed in HIV-positive versus HIV-negative patients, irrespective of ARV treatment. Day 7 lumefantrine levels are currently being analyzed.
CONCLUSIONS: Clinically significant drug interactions between AL and nevirapine- and efavirenz-based ARVs were not observed, supporting the current treatment guidelines for malaria and HIV co-infection in adults.

Efficacy and safety of artemisinin-based combination therapy in HIV-infected children in Uganda

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BACKGROUND: Artemisinin-based combination therapies (ACTs) are now widely recommended as first line drugs for the treatment of uncomplicated malaria in nearly all African countries. However data on the safety and efficacy of ACTs in HIV-infected populations are still limited
METHODS: We evaluated malaria treatment outcomes in the setting of two cohort studies of in HIV infected children

- Promote and the TCC studies. All children received insecticide treated bed nets, trimethoprim-sulphamethoxazole prophylaxis and antiretroviral therapy when indicated. Children were followed up for their medical care at a dedicated study clinic that was open daily. Children with uncomplicated malaria were treated with artemether-lumefantrine (AL) in the Promote study, AL or dihydroartemisinin- piperaquine (DP) in the TCC study. All children were followed up for 28 days and thick blood smears were done on day 2, 3, 7, 14, 21 and 28 of malaria follow-up. Treatment outcomes and adverse events were assessed over the 28 day follow-up.
RESULTS: There were 184 and 57 HIV-infected children in the Promote and the TCC studies respectively. One hundred twenty three and 43 children in the Promote and TCC studies respectively had at least one episode of malaria. In the Promote study, 527 episodes of uncomplicated malaria were treated with AL while 201 episodes and 165 episodes in the TCC study were treated with AL and DP respectively. During follow-up, all children in the Promote cohort were on ARVs while 52 (91%) children in the TCC were on ARVs. By day 3 of malaria follow-up, only 5 (0.9%) of AL treatments in the Promote study, 2 (1%) of AL and 2(1.2%) of DP treatments in the TCC study still had parasitemia. After 28 days of follow-up, 399 (69.8%) AL treatments in the Promote study, 127(63.2%) AL and 149(90.3%) DP in the TCC study had adequate clinical and parasitological response (ACPR). The rate of late parasitological failure (LPF) with AL treatment was 21.5% in the Promote study and 26.4% in the TCC study. DP had a lower rate of LPF (6.7%). The risk of recurrent parasitemia was significantly lower with DP compared to AL in the TCC study (8.6% Vs 36.2%, P<0.001). The rates of grade 3 or 4 adverse events were low in both studies.
CONCLUSION: AL and DP were efficacious and safe in treatment of uncomplicated malaria in both studies but DP had a less risk of recurrent parasitemia compared to AL in the TCC study.

Perceptions and experiences of taking ACTs concomitantly with ARVs among patients with malaria and HIV in Tanzania

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BACKGROUND: Co-infection of HIV and malaria is common in Sub Saharan Africa. The InterACT clinical trial in Muheza in northern Tanzania sought to understand how drugs for the two diseases may interact. However, little is known about how those with HIV perceive malaria or its treatment. It is important to understand whether risks of co-infection or risks of drug interactions are perceived and whether this affects prevention or treatment practices.
METHODS: This qualitative study explored how HIV-positive people conceptualize malaria and antimalarial medication, in comparison with HIV-negative people. We conducted the study using focus group discussions with people receiving treatment for HIV and/or malaria, and in-depth interviews with health workers responsible for HIV care.
RESULTS: Results suggest that people living with HIV saw malaria as unavoidable, and perceived the disease to be more harmful due to their compromised immune status. However, this did not seem to translate into extra efforts to prevent malaria infection. For those enrolled in a clinical research study, taking antimalarials together with ARVs was largely seen as unproblematic, with health workers' advice and endorsement of concomitant drug taking influential in reported adherence. However, perceptions of drug strength compelled some people, mainly those not enrolled in clinical research, to take the drugs at separate times to avoid anticipated harm to the body. Many reported self-medication with antimalarials, in spite of being aware that clinicians advise assessment prior to any additional treatment. This self-medication practice was in part due to lack of funds but also appeared to relate to the perception that there was no problem with mixing ARVs with antimalarials.
CONCLUSION: The social and material dynamics of clinical research may have influenced attitudes towards concomitant medication. Interventions are required to increase awareness of malaria risks, access to prevention strategies and to support diagnosis and treatment of malaria for people living with HIV.

S45: Roll back malaria impact series for South Africa.

Chairs: Prof Lucille Blumberg and Dr Patrick Moonasar

Speaker 1: Prof Maureen Coetzee, Malaria in South Africa: 110 years of learning to control the disease, University of Witwatersrand, South Africa
Speaker 2: Prof Rajendra Maharaj, Epidemiology of malaria control in South Africa: From control to elimination. South African Medical Research Council, South Africa
Speaker 3: Dr Basil Brooke, Malaria vector vontrol in South Africa, NCID, South Africa
Speaker 4: Prof John Frean, Case mangement of malaria: Diagnosis, NCID, South Africa.
Speaker 5: Prof Karen Barnes, Case management of malaria: Treatment and chemoprophylaxis, University of Cape Town, South Africa
Speaker 6: Dr Natalie Mayet, Health promotion: From malaria control to elimination, CDC/NICD, South Africa.
Speaker 7: Dr Patrick Moonasar, What will move malaria control to elimination in South Africa, Department of Health, South Africa

OVERVIEW

From Malaria Control to Elimination in South Africa

Professor Lucille Blumberg[1] and Dr Devanand Moonasar [2]
On behalf of the members of the South African Malaria Elimination Committee
[1]Deputy Director, National Institute for Communicable Diseases, National Health Laboratory Service Johannesburg, South Africa; [2]Director, Malaria, National Department of Health, Pretoria, South Africa

South Africa is one of thirty-four Malaria-endemic Countries globally that are currently targeting elimination of the disease. In the southern African region this includes Namibia, Swaziland and Botswana. The goal for South Africa is to achieve zero local malaria cases by the year 2018. The objective of this Symposium is to share the successes of the Malaria Control Programme in South Africa, and to highlight the key lessons learnt and the priorities for elimination of the disease. The historical account of Malaria Control Interventions over 110 years details the significant roles played by South Africans in the fight against malaria locally, regionally and internationally. Presentations on vector control and the epidemiology of malaria highlight the period 1995 to 2012, with significant reduction in reported cases since 2001. The contributory factors include: the re-introduction of DDT for Malaria Vector Control a change to Artemisinin-containing Combination Treatment (ACT), and the adoption of Regional Malaria Control Strategies in South Africa, Swaziland and Mozambique through the Lubombo Spatial Development Initiative (LSDI). Effective case management, including both Diagnosis and Treatment, is key to reducing malaria-related morbidity and mortality in South Africa and quality assurance for diagnostic tests is pivotal to good case management and for accurately measuring programme indicators and interventions. Evidence-based Drug Policy has guided chemotherapy and has been critical in reduction of malaria morbidity and mortality in South Africa. As the continuum moves towards Malaria Elimination, a number of different strategies need to be adopted: strengthening of health promotion in partnership with communities to prevent and encourage early treatment-seeking behaviour; active case surveillance; consideration of the use of gametocytocidal drugs; increased vector surveillance and focusing Vector Control on 'hot spots'; monitoring for mosquito insecticide resistance and parasite drug resistance; and intensifying cross-border initiatives.

S46: Implementing seasonal malaria chemoprevention: putting research into practice

Chairs: Prof Ogobara Doumbo, Dr Paul Milligan and Prof Daniel Chandramohan

Speaker 1: Dr Claude Emile Rwagacondo, Update on SMC in the West Africa Region, West African Roll Back Malaria Subregional Network, West Africa.
Speaker 2: Dr Jean L Ndiaye and Dr Mady Ba, Scaling-up SMA for children under 10 yrs of age in Senegal, Unversity of Chiekh Anta Diop and PNLP, Senegal
Speaker 3: Dr Estrella Lasry and Prof Allassane Dicko, Implementation and evaluation of SMC in Mali, Tchad, Niger and Togo, MSF, United States of America and University of Bamako, Mali.
Speaker 4: Dr Ebenezer Baba, Introducing seasonal malaria chemo-prevention into northern Nigeria, Malaria consortium, Nigeria.
Speaker 5: Dr Aleksandra Misiorowska, Improving access to drugs for SMC: The role of the Medicines for Malaria Venture, MMV, Switzerland
Speaker 6: Prof Oumar Gaye and Dr Peter Olumese, Closing remarks, Unversity of Chiekh Anta Diop, Senegal and World Health Organisation Switzerland

OVERVIEW

In 2012, WHO recommended that children living in areas of highly seasonal malaria transmission in the Sahel and sub-Sahel should receive Seasonal Malaria Chemoprevention with sulfadoxine-pyrimethamine plus amodiaquine, an implementation guide has been published, SMC has been included in country strategic plans for malaria control, and six Sahelian countries with common borders (Gambia, Mauritania, Mali, Senegal, Niger, Tchad) have produced a joint strategy for SMC. In 2013 SMC is being implemented in parts of Mali, Senegal, Togo, Tchad, Niger, and Nigeria. The purpose of this symposium is to share experiences of implementing SMC in these countries, with a view to understanding challenges to scaling up SMC, and coordinating approaches to monitoring and evaluation of impact.

S47: Science of Eradication: Global Lessons

Sponsored by: Malaria Eradication Scientific Alliance (MESA)

Chairs: Prof Pedro Alonso and Dr Grace Matsinhe

Speaker 1: Dr Arturo Sánchez López, Advances toward malaria elimination in Mesoamerica and Hispaniola Island,
Speaker 2: Dr Ashwani Kumar, Integrated Vector Management in Malaria Elimination: Implementation, Evidence and Impact Assessment, National Institute of Malaria Research, India.
Speaker 3: Dr Shuisen Zhou, Landscaping and Agenda for Malaria Operational Research on Elimination (mORe), World Health Organisation, China
Speaker 4: Dr Hoda Atta, Malaria Elimination in the Eastern Mediterranean Region: Lessons learned, World Health Organisation, Eastern Mediterranean Region.

This MESA-organised symposium will open a dialogue around what "science of eradication" means in different parts of the world battling malaria and will provide challenging and inspiring topics for debate as our experts present their different perspectives. Highlighting the growing evidence base, it will showcase the approaches of intervention mixes and surveillance, operational research, emerging results and lessons learned from countries and regions eliminating malaria around the globe.

S48: Towards Sustainable Country-owned Financing for Malaria Elimination

Chair: Dr Robert Brinckman

Speaker 1: Mr Steve Knowles, The Corporate Sector's role in malaria control, former Director of Malaria Control, AngloGold Ashanti, Ghana
Speaker 2: Dr Robert Brinckman, Rewarding Impact in Malaria through Cash on Delivery Aid, Clinton Health Access Initiative, United States of America
Speaker 3: Dr. Mohamed Dahoma, Advocating for Hypothecated Levy on Tourism Arrivals: the Zanzibar MOH Experience, Ministry of Health, Zanzibar.

DESCRIPTION OF SYMPOSIUM CONTENT: How can countries attaining low levels of malaria transmission, and targeting malaria elimination, plan to sustainably and independently finance their malaria elimination programs and the subsequent prevention of resurgence? Given the changing nature of development financing, how can countries attract novel kinds of capital beyond the traditional donor landscape? Is there a smarter way to deliver aid to the high performing country governments that cuts down on the often inefficient and time-consuming traditional aid model? This session will introduce alternative models that can support country transitions to sustainable financing; these include cash on delivery aid for malaria, endowment funds, and hypothecated taxes for malaria.

Cash on Delivery (COD) is an innovative approach based on the premise of paying for, and thus rewarding, results. By focusing on one carefully selected impact indicator, which triggers payment upon independent verification, countries are empowered to determine the optimal method of achieving the pre-agreed upon impact, and will be fully accountable for results. COD is being tested in the education sector in Ethiopia and Rwanda by DFID, and has the potential to become a new feature within malaria financing, particularly for countries with high capacity and foreseeable path to exit donor dependency.

Endowment funds for malaria similarly represent a country-owned solution that provides perpetual financing to support sustaining the gains pre and post elimination. Endowments also have the potential to attract new kinds of financing from private investors, moving away from reliance on traditional donors.

Hypothecated taxes are a policy solution that – although not altogether new - has promise to bolster and amplify domestic financing for malaria. For example, in Zanzibar, the government is in advanced stages of considering a tourism tax in support of malaria control, based on economic analyses of tourists' willing to pay.

The models are currently in advanced stages of design and implementation in some countries. The speakers

(offering both donor and country perspectives) will provide an in-depth discussion of the feasibility of the financing models in different country settings, as well as their potential to support elimination financing.

S49: Primaquine: from *P. vivax* radical cure to *P. falciparum* malaria elimination?

Chairs: Dr Andre Tchouatien

Speaker 1: TBC, Efficacy of primaquine in *P. vivax* radical cure.
Speaker 2: Prof J Kevin Baird, G6PD deficiency and primaquine, current status, Eijkman Oxford Clinical Research Unit, United States of America
Speaker 3: Primaquine as a tool for P. falciparum malaria elimination. World Health Organisation, Switzerland.

OVERVIEW

Primaquine has been used for over 60 years, particularly in *P. vivax* endemic areas with relative success. The recent perspective of malaria elimination has attracted renewed interest in its ability to provide radical cure for liver-stage infections and to potentially reduce malaria transmission. Primaquine prevents relapses of *P. vivax* malaria by eliminating the dormant liver stage parasites (hypnozoites). It also kills mature sexual stage parasites (gametocytes) which may, in some circumstances, decrease transmission of *P. falciparum* malaria. These features may be important in regions of sub-Sahara Africa currently reaching low malaria endemicity levels.

Primaquine has one considerable drawback which is the potentially severe side effect of haemolysis in Glucose-6-phosphatase dehydrogenase (G6PD) deficient patients.

A group of experts recently reviewed the WHO treatment guidelines and recommended adding to a cure of artemisinin combined therapy (ACT), a single dose of 0.25mg/kg body weight of primaquine to kill gametocytes of *P. falciparum* and thus decrease transmission. This low dose is expected to be safe in G6PD deficient patients, but studies are ongoing to explore even further reduced dosing.

This symposium will address several pending issues. How to optimize the use of primaquine for *P. vivax* radical cure? What is the current state of the use of primaquine in G6PD deficiency patients? What is the optimal dose of primaquine to safely eliminate *P. falciparum* gametocytes? What is the impact of reduction in the number of *P. falciparum* gametocytes on malaria transmission? How can implementation of primaquine be planned in pre-elimination countries?

S50: From sustainable malaria control to elimination: An African approach

Chairs: Prof Tiaan de Jager and Prof Lyn-Marié Birkholtz

Speaker 1: Prof Lyn-Marié Birkholtz, Sustainable targeting of Plasmodium parasites for malaria control, University of Pretoria, South Africa
Speaker 2: Dr Taneshka Kruger, Slow release pyrethroid-impregnated indoor linings: A novel approach to safer and sustainable malaria vector control? University of Pretoria, South Africa
Speaker 3: Prof Leo Braack, Using vector biting behaviour as a tool for malaria control, University of Pretoria, South Africa
Speaker 4: Prof Clifford Mutero, Multi-sectoral development of malaria decision analysis support tool (MDAST) to optimize integrated vector and disease management, University of Pretoria, South Africa

Sustainable targeting of Plasmodium parasites for malaria control

L Birkholtz
Department of Biochemistry, University of Pretoria, Pretoria, South Africa.

BACKGROUND: Malaria parasite control is still fully reliant on anti-malarial drugs, both for prophylactic use and for treatment of the disease. However, current control programmes are threatened by the rapid development of drug-resistant forms of the malaria parasite. To ensure sustainability in malaria chemotherapy, a continuous pipeline of new new anti-malarials are needed that are: 1) effective against erythrocytic stages and exo-erythrocytic stages of the parasite; 2) effective against resistant forms of the parasite; 3) chemically distinct and with new mechanisms of action; 4) safe without associated toxicities; 5) pharmacokinetically amenable to once-daily oral dosing; and 6) economically viable. Target product profiles for anti-malarials that meet these criteria and support the malaria-elimination strategy are have been identified and are broadly grouped into three areas: 1) control of the disease (treatment of infected patients); 2) blocking the transmission cycle; and 3) radical cures for malaria. One of the areas that could have the biggest impact in sustainable malaria control and malaria elimination is interruption of the transmission of the

parasite between humans and mosquito vectors. Several aspects of current programmes aimed at identifying novel chemotypes will be discussed.
CONCLUSIONS: Surprisingly little is known about basic biological processes governing the parasite's pathogenesis, development and replication and a better understanding thereof could provide opportunities to target the parasite for sustainable malaria control and elimination in the context of multi-disciplinary approaches.

Slow release pyrethroid-impregnated indoor linings: A novel approach to safer and sustainable malaria vector control?

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BACKGROUND: In sub-Saharan Africa, malaria vector control programmes have mainly focused on Indoor Residual Spraying (IRS) and Long Lasting Insecticide-Treated Nets (LLINs) usage. With LLINs, a chemical barrier is added to an often imperfect physical barrier causing a killing effect, whilst inhibiting the mosquito's feeding pattern. LLINs only work when people sleep under the net. Sustained IRS has been carried out in Southern Africa for decades, remaining the backbone of malarial control in the region. Insecticides are applied to inner surfaces of dwellings where malaria vectors often rest after a blood meal. Quality of spraying and high coverage affects IRS effectiveness. IRS should commence before the transmission season but operational and financial delays often occur. Repeated application is sometimes needed, which adds to the increase in cost. The use of DDT during IRS is regarded as the most effective vector control tool, retaining its efficacy for up to twelve months. However, it's a known persistent organic pollutant and research has identified potential negative health impacts. DDT residue levels are present in indoor air for about three months after spraying. Continued malaria prevalence in high disease areas is mainly due to inadequate measures and many countries can't afford the costs to ensure sustainability throughout the transmission season.
DISCUSSION: Safer and more sustainable vector control methods should be considered as opposed to IRS. Certain polymers can be used as slow release insecticide carriers for vector control. Insecticide is incorporated into the fibre during production, remaining stable for longer and is slowly made available for longer. Netlon® (pyrethroid-containing mesh) produced at the Institute of Applied Materials, University of Pretoria, South Africa, yielded positive results in a pilot field trial in Vhembe district, South Africa, over a six month period. Linings were installed in 40 households, and user acceptability and perceived effectiveness was looked at, whilst efficacy was tested every two months via laboratory-based bioassays.
CONCLUSIONS: Slow release pyrethroid-impregnated indoor polymer linings could provide protection against indoor resting mosquitoes between blood feeds, would reduce exposure to insecticidal residues thereby promoting a safer environment, and could potentially lower the cost of sustainable vector control.

Using vector biting behaviour as a tool for malaria control

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BACKGROUND: The current over-reliance on IRS and ITN's to achieve malaria eradication is likely to fail in many African countries. IRS and ITN's impact only those mosquitoes that enter and seek hosts indoors, which represent a subset of infected mosquitoes biting humans. Most rural Africans remain outdoors for several hours after dark, where they are bitten by outdoor-feeding vectors. We studied the biting behaviour of Anopheles arabiensis, An gambiae s.s. and An funestus to explore the use of such behaviour to reduce biting intensity on humans and thereby reduce malaria incidence.
METHODS: We studied outdoor human landing catches on volunteers in South Africa (*An. arabiensis*) and Uganda (*An. arabiensis*, *An. gambiae s.s.*, and *An. funestus*). Three situations were tested (a) In seated position, where on the body do the three vectors bite, (b) If the preferred bite sites were rendered unavailable for feeding, do the vectors then move elsewhere on the body, and (c) if people lie down, do the same findings hold as for when people are seated.
RESULTS: At standing or seated subjects with feet on ground, 100% of An arabiensis, An gambiae s.s. and An funestus bite below mid-calf level, the vast majority on the ankles. When subjects lie down, biting occurs widespread on the body. This suggests that feeding is strongly influenced by height above ground.
CONCLUSIONS: For people engaged in normal night-time outdoor activities, wearing repellent-impregnated anklets to discourage vectors holds the potential to lower malaria incidence. Small children who often sleep at ground level indoors or outdoors and without effective bednets, would benefit by having repellent-impregnated bedmats or bedcovers.
This work was funded by a grant from the Bill and Melinda Gates Foundation through the Grand Challenges Explorations initiative.

Multi-sectoral development of malaria decision analysis support tool (MDAST) to optimize integrated vector and disease management

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BACKGROUND: Policy decisions for malaria control are often difficult to make as they must balance the needs of a large number of stakeholders. Different vector and disease control options may require difficult tradeoffs among competing health, economic and environmental objectives. The objective of this study was to assess how and by whom malaria control policy decisions are currently made, as a crucial first step towards developing an inclusive malaria decision analysis support tool (MDAST) for use at the level of national malaria control programs (NMCPs).
METHODS: Country-specific MDAST activities were carried out in Kenya, Uganda and Tanzania. They included engaging a wide range of stakeholders and conducting a survey to compile feedback to be used in the informed and responsive development of the tool. Those engaged were drawn from a non-random purposeful sample of stakeholders, targeting individuals in ministries, non-governmental Organisations (NGOs), universities and research institutes whose policy decisions and actions are likely to have an impact on the status of malaria or influence malaria control decision-making in the respective countries. Analysis included summary measures of the survey data, comparing results by country as well as aggregated across all three project countries.
RESULTS: Respondents on average thought that most relevant objectives were not being given enough consideration in malaria decision-making. There was also a belief that donor preferences and agendas were exerting too much influence on malaria policies.
CONCLUSION: The results revealed important trends in stakeholder knowledge that influenced further development of the initial MDAST, particularly in the need for integration of research with stakeholder perspectives.

S51: Malaria RDTs: when it is and when isn't malaria

Chair: Dr Hellen Gelband

Speaker 1: Dr Valerie D'Acremont, The causes of fever and fever management in low-resource settings, Swiss Tropical and Public Health Institute, Switzerland.
Speaker 2: Dr Joseph B Babigumira, Malaria diagnosis and febrile illness management: A cost-effectiveness model, University of Washington, United States of America
Speaker 3: Dr Edmund Rutta, The accredited drug dispensing outlet (ADDO) model in Tanzania: A platform for appropriate malaria and non-malaria fever case management, Management sciences for Health, United States of America
Speaker 4: Dr Debbie Burgess, Prospects for rapid diagnostic tests for non-malaria fevers: The pipeline, Bill & Melinda Gates Foundation, United States of America

The Causes of Fever and Fever Management in Low-Resource Settings

Valérie D'Acremont
Swiss Tropical Institute and World Health Association

Since 2010, when WHO recommended that all patients suspected of malaria be tested before treatment, rapid diagnostic tests (RDTs) have been used more and more, laying bare the challenge of proper management of febrile illness when the test result is negative. Better guidance on managing non-malaria febrile illnesses is needed not only to reduce unnecessary use of antimalarials (because many RDT negatives tests still elicit malaria treatment) but to improve the treatment and referral of patients to reduce morbidity and mortality from other conditions.

Recent studies on fever etiology demonstrate that, although the distribution varies by geography, season, age, immunity of the patient, and level of care, there are broad similarities across settings. More than half of young children at the peripheral level suffer from ARI, but radiological pneumonia is rare. Besides malaria, 10-25% have gastroenteritis, with other localized infections accounting for <5%. In the remaining children, fever is due to urinary tract infection (1-6%), enteric fever (2-10%), and rarely, occult bacteremia (<2%). Viral infections cause a large proportion of febrile illnesses in outpatients. In hospitalized older children and adults, fevers are often associated with HIV; in addition to ARI, several diseases related to environmental and occupational exposure such as leptospirosis, rickettsiosis, scrub typhus and brucellosis, are also found. Dengue is an important cause in Asia, less so in Africa.

WHO has produced several guidelines for fever management in different age groups and at different levels of care. A new electronic algorithm integrating the latest research findings has been tested recently in Tanzania, illustrating the advantages and difficulties of adding clinical elements to the IMCI algorithm without the aid of additional rapid point-of-care tests (POCTs). New POCTs for pathogens and/or host biomarkers are essential, and their eventual integration into clinical algorithms must be driven by evidence of clinical benefit, not simply availability or diagnostic performance. Precise guidance on which patients to test with new tools should be developed, along with incentives for health workers to adhere to guidelines and test results.

Malaria diagnosis and febrile illness management: a cost-effectiveness model

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BACKGROUND: We modeled the cost-effectiveness of different strategies for managing febrile illness, with RDTs, ACTs and antibiotics for children under five in Tanzania.
METHODS: A decision-analytic model comparing 2 presumptive and 4 diagnosis-based strategies: (1) P-1— presumptive antimalarials only for all children (2) P-2 — presumptive antimalarials for all and presumptive antibiotics for all severely-ill children (3) RDT-1—antimalarials for test-positive children and no treatment for test-negative children (4) RDT-2 —antimalarials for test-positive children and presumptive antibiotics for severely-ill test-negative children (5) RDT-3 — treatment with antimalarials for test-positive children and presumptive antibiotics for all test-negative children (6) RDT-4 — antimalarials for test-positive children and presumptive antibiotics for severely-ill children.
RESULTS: P-2 led to the highest survival (95.66 %) and RDT-1 led to the lowest (95.16 %). P-1 was the least costly strategy ($25.35 per child) and RDT-4 was the most costly ($26.34 per child). RDT-1, RDT-2, and RDT-3 were dominated. RDT-4 was both more costly and less effective than RDT-2, RDT-3 and P-1. P-2 increased costs by an average of $0.49 per child over P-1 and increased survival by an average of 0.40% leading to an incremental cost-effectiveness ratio (ICER) of $122 per life saved.
CONCLUSION: P-2 was the optimal strategy across a broad range of conditions. Contrary to WHO recommendations, presumptive treatment with antimalarials and antibiotics for severely ill children might be a rational choice for febrile illness management in Tanzania.

The Accredited Drug Dispensing Outlet (ADDO) Model in Tanzania: A Platform for Appropriate Malaria and Non-Malaria Fever Case Management

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BACKGROUND: In Tanzania, like other malaria-endemic settings, the private retail sector constitutes a major source of treatment for fever—40-60% of caregivers of children in many countries first seek treatment in drug shops and pharmacies. Recognizing the role the drug shops play in care seeking, but understanding their limitations, the government (through the Tanzanian Food and Drugs Authority) with support from partners launched the ADDO program in 2003. The ADDO model takes a holistic approach to addressing problems through a package of interventions that builds private sector capacity, provides business incentives, enhances drug availability, helps ensure pharmaceutical product and service quality, and increases consumer awareness. Over a decade, the ADDO program was scaled up nationally, over 119 districts in 21 regions of Tanzania.
METHODS: A descriptive study to document how the ADDO program offers the opportunity for appropriate malaria case management in rural and semi-urban communities in Tanzania and beyond.
RESULTS: Tanzania's National Malaria Control Programme adopted the ADDO platform as part of its national strategy in 2006 to increase access to malaria treatment, paving the way for ADDOs to distribute subsidized artemisinin-based combination therapy (ACT). In 2009, the Affordable Medicines Facility for malaria (AMFm) demonstrated that it significantly increased ACT availability in Tanzania, including in remote drug shops. In 2010, a study followed up ADDOs accredited in 2004 in Ruvuma region to assess the sustainability of improved services beyond the pilot year. The study found that the percentage of ADDOs dispensing malaria treatment according to treatment guidelines rose from 24% in 2004 to 63% in 2010. NMCP is currently piloting the introduction of mRDT in the ADDOs.
CONCLUSIONS: The ADDO model provides a mechanism to increase access to essential medicines in the private sector while ensuring quality of services and products that safeguard public health. At the same time, the private sector shops have demonstrated sustained improvements without donor support. An intervention such as the ADDO program provides a platform to integrate new approaches to care such as developing a management strategy for non-malaria fevers and the use of mRDTs.

Prospects for rapid diagnostic tests for non-malaria fevers: the pipeline

Debbie Burgess
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Pneumonia and malaria remain leading causes of child mortality globally. In many developing countries, treatment decisions must be made without reference to confirmatory laboratory tests. Management of pneumonia and malaria is complicated by overlap in their symptoms, which may include cough, fever and tachypnea. In the case of pneumonia, the etiology of infection may be of bacterial or viral origin—the difference between whether an antibiotic is called for or not. Use of a cost-effective point-of-care diagnostic test, either to differentiate bacterial vs. viral infection or malaria vs. pneumonia has the potential to significantly improve health outcomes in these populations. However, development of such diagnostic tests is dependent on the availability of appropriate biomarkers, with demonstrated specificity for the condition under consideration. Proteomic, whole gene expression and metabolic approaches have helped accelerate this area of research over the last few years, with several candidate markers having been identified and ready for further validation or field evaluation. The leading candidates and issues related to their testing and deployment in the field will be discussed.

S52: Burden and control of Plasmodium falciparum and Plasmodium vivax malaria in pregnancy in Asia, the Pacific and Latin America: Results from the MiP consortium

Chairs: Prof Rose Ieke and Dr Norma Padilla

Speaker 1: Dr Azucena Bardaji, The burden and impact of P. vivax and P. falciparum malaria in pregnancy in low transmission settings and the role of sub-microscopic infections: Results from a multi-country collaborative project, University of Barcelona. Spain.
Speaker 2: Dr Irene Kuepfer, Incidence and consequence of microscopic and sub-microscopic malaria in pregnancy in India: A cohort Study, London School of Hygience and Tropical Medicine, United Kingdom.
Speaker 3: Dr Alfredo Mayor, Physiopathology of P. vivax infection in pregnancy: Placental histopathology, cytoadhesive features and pregnany-specific immune responses, University of Barcelona. Spain
Speaker 4: Dr Holger Unger, Sulphadoxine-pyrimethamine plus Azithromycin to prevent low birth weight in Papua New Guinea, University of Melbourne, Australia
Speaker 5: Dr Anupkumar Anvikar, Efficacy of two ACTs for the treatment of malaria in pregnancy in India: A randomised controlled trial, National Insitute of Malaria Research, India.

OVERVIEW

The burden of malaria in pregnancy on maternal anaemia and low birth weight in Asia and Latin America, including the role of sub-patent infections, and results of clinical trials in areas where *P. falciparum* and *P. vivax* co-exist.

The burden and impact of p.vivax and p.falciparum malaria in pregnancy in low transmission settings and the role of sub-microscopic infections: results from a multi-country collaborative project

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BACKGROUND: It is widely recognised that pregnant women have an increased risk of *P.falciparum* malaria infection and disease. However, very little is known about the burden of *P.vivax* in pregnancy and its impact on maternal and child health.
METHODS: This study makes part of the multicentre collaborative cohort study [PregVax, funded 7th FP-HEALTH-201588, the Spanish Government-EUROSALUD Programme, and the Malaria in Pregnancy Consortium] that aims to estimate the burden of *P.vivax* infection in pregnancy in Brazil, Colombia, Guatemala, Papua New Guinea (PNG) and India. Pregnant women

were enrolled at routine antenatal care (ANC) and followed up until delivery. Blood samples were collected for detection of malaria parasitaemia by microscopy (and by PCR methods in a subsample of women), and anaemia determination at different time points.
RESULTS: A total of 9487 pregnant women were enrolled and 52% (4948) of them followed-up until delivery. Preliminary data on the average prevalence of microscopic *P.vivax* infection was of 0.9% and 0.5% at recruitment and delivery, respectively. The average prevalence of submicroscopic *P.vivax* infection was of 8% and 6,6% at recruitment and delivery, respectively. Data on the prevalence of microscopic *P.falciparum* infection was of 1.3% and 0.5% at recruitment and delivery, respectively. The prevalence of submicroscopic *P.falciparum* infection was of 7.4% and 4% at recruitment and delivery, respectively. Further data on the impact of *P.vivax* and *P.falciparum* infections on maternal anaemia and low birth weight will be presented.
CONCLUSIONS: These findings show that the prevalence of microscopic *P.vivax* and *P.falciparum* infections was low across sites but that of submicroscopic infections was significantly higher. This evidence may contribute to better understand the burden and impact of malaria during pregnancy in low endemic areas where *P.vivax* predominates and may be of help to guide development of effective malaria control and surveillance strategies.

Incidence and consequences of microscopic and sub-microscopic malaria in pregnancy in India: a cohort study

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BACKGROUND: As part of a clinical trial to assess the efficacy and safety of two artemisinin-based combination therapies (ACTs) for the treatment of malaria in pregnancy, we screened a cohort of pregnant women monthly for malaria.
METHODS: Women attending routine antenatal care clinics with a gestational age between 12 and 36 weeks were requested to take part in the study. Those who were enrolled in the cohort were visited once a month. At each visit, blood slides and filter paper samples were collected. If women had fever or history of fever, a rapid diagnostic test (RDT) for malaria was done. RDT positive cases were treated for malaria. For all samples collected during a full calendar year, microscopy was done on all blood slides from all visits. Diagnostic PCR analysis was done on dried blood spots collected at the first and last visit of each woman. If the PCR was positive at the first visit, PCR was done in the blood samples collected in the subsequent visits. If the PCR was positive at the last visit, PCR was done in the sample collected at the previous visits.
RESULTS: The incidence of microscopic and sub microscopic infections during pregnancy and their effects on birth outcomes in a cohort of 2494 pregnant women from three ecological zones in India will be presented. The options of control of burden of MiP in the Indian context will be discussed.
CONCLUSIONS: The current policy of passive case detection is inadequate to control the burden of malaria in pregnancy. The incidence of sub microscopic infections should be taken into account when selecting new interventions to control malaria in pregnancy in this low endemic setting.

Physiopathology of P. vivax infection in pregnancy: placental histopathology, cytoadhesive features and pregnancy-specific immune responses

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BACKGROUND: Evidence of the presence of Plasmodium vivax in the placenta and its cytoadhesive mechanisms is scarce and inconclusive. In addition, phenotypic and functional characteristics of immune cells during vivax malaria in pregnancy have been poorly studied. This information is relevant to understanding whether P. vivax affects placental

and immune function and how infection may contribute to poor pregnancy outcomes.
METHODS: Placental biopsies from 80 Papua New Guinean (PNG) pregnant women were examined by histopathology/ immunohistochemistry and PCR. Peripheral blood mononuclear cells from 50 PNG women and a group of non pregnant women were phenotyped by flow cytometry for T regulatory and B cell subpopulations, and data compared to pregnant women from non-endemic areas. P. vivax isolates from peripheral blood of 12 pregnant women, 24 non-pregnant women and 23 men from Manaus (Brazil) were tested for cytoadhesive phenotypes.
RESULTS: P. vivax mono-infection with parasitized erythrocytes in the intervillous space but no hemozoin in macrophages nor increased intervillous inflammatory cells was observed in 3 of the 80 placentas tested. Binding to placental and brain sections, CSA, CD36 and ICAM1 was observed in 2-15% of the P. vivax isolates, with no association found between these adhesion properties and pregnancy. Rosetting (35/55 [64%]) was associated with a higher risk of anemia (p=0.047). Pregnancy and P. vivax exposure differentially affected the phenotypes of circulating Treg and B cell populations.
CONCLUSIONS: P. vivax can be associated with placental infection and altered immune cell function but placental inflammation is not common. P. vivax infected erythrocytes from peripheral blood of pregnant women do not show a prominent binding to placental receptors used by P. falciparum.

Sulphadoxine-Pyrimethamine plus Azithromycin to prevent low birth weight in Papua New Guinea

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BACKGROUND: Low birth weight (LBW) is common in malaria-endemic Papua New Guinea, and contributing factors may include malaria, anaemia, reproductive tract infections, and maternal undernutrition.
METHODS: We investigated whether the combination of sulphadoxine pyrimethamine (SP, 3 tablets) and azithromycin (AZI, 1 g twice daily for 2 days), given three times during pregnancy, was more efficacious than a single dose of SP plus chloroquine (CQ) in preventing LBW.
RESULTS: 2793 women were randomised equally to each arm, and birth weight data were available on 2012 live births. At enrolment, 7.2% of participants had microscopy-detected malaria parasitaemia, 6.2% of which were due to *P. falciparum*. At delivery, parasitaemia by peripheral and placental microscopy or by histology was less common in women receiving SP + AZI (p=0.02-0.05), but parasite rates were generally low (smear 3.1%, histology 7.4% in SP + CQ group). Factors significantly associated with low birth weight in univariate analyses included baby's sex, gravidity, enrolment site, bed net use, maternal height and mid upper arm circumference and ethnic origin, and partner's employment status. After adjusting for these variables, women receiving three doses of SP + AZI had babies that were significantly less likely to be LBW (aRR 0.72, CI 0.59-0.89; p=0.002) than women receiving SP + CQ. Mean birth weights were 52.7 g higher (CI 13.6-91.8; p=0.008). The low malaria prevalence suggests that SP + AZI improves birth weight through mechanisms additional to its antimalarial effect. Maternal anaemia and mean maternal haemoglobin levels did not differ by treatment arm. Both treatments were well tolerated, with similar rates of adverse events and no drug related SAEs in either arm.
CONCLUSIONS: SP + AZI appears to be safe and efficacious in reducing LBW and increasing mean birth weight in an area with relatively low malaria prevalence. This combination is a promising intervention to improve pregnancy outcomes.

Efficacy of two ACTs for the treatment of malaria in pregnancy in India: a randomised controlled trial

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BACKGROUND: In India, national policy for treatment of malaria in pregnancy in second and third trimesters is artesunate+sulfadoxine-pyrimethamine (AS-SP). However, data on safety and efficacy of Artemisinin based combination therapy in pregnancy is scarce. We assessed the safety and efficacy of AS-SP and artesunate+mefloquine (AS-MQ) for treatment of *falciparum* malaria in pregnancy in India.
METHODS: An open-label, randomised clinical trial was conducted at three sites (Ranchi and Jamshedpur, Jharkhand state and Rourkela, Odisha state). Women attending antenatal care (ANC) clinics with a gestational age between 12 and 36 weeks were screened for malaria at each ANC visit. Pregnant women having *P. falciparum* mono-infection of

any parasite density with or without fever were randomised to either AS-MQ or AS-SP arm of the trial. Blood slides and filter paper samples for PCR were collected on day 0,1,2,3,14,28,42 and 63 post treatment and the participants were followed up until day 42 postpartum.
RESULTS: Between October 2010 and June 2013, two hundred and fourteen women were found to have *P. falciparum* mono-infection among 6684 pregnant women. They were randomised to receive either AS-MQ or AS-SP. There were no therapeutic failures based on blood slide results on day 28, 42 or 63 in both arms of the study. There were twenty one serious adverse events during the study. None of the severe adverse events were deemed to be related to the study drugs.
CONCLUSIONS: Both artesunate+SP and artesunate+mefloquine are safe and effective for treatment of uncomplicated malaria in pregnancy in India.

S53: The Updated Malaria Vaccine Technology Roadmap

Chair: Dr Vasee Moorthy

Speaker 1: Dr Vasee Moorthy, WHO's activities under Priority Areas of the Technology Roadmap, World Health Organisation, Switzerland.
Speaker 2: Dr David C Kaslow, The PATH Malaria Vaccine Initiative's portfolio and strategy, and activities since 2006 within the Roadmap Priority Areas, PATH, Switzerland.
Speaker 3: Dr Michael Makanga, EDCTP's malaria vaccine activities by Roadmap Priority Area, EDCTP, South Africa.
Speaker 4: Dr Lee Hall, NIAID's malaria R&D activities by Roadmap Priority area, National Institutes of Health, United States of America
Speaker 5: Dr Odile Leroy, EVI's malaria vaccine activities by Roadmap priority area, European Vaccine Initiative, Switzerland.

OVERVIEW

WHO and the malaria vaccine funders group coordinated a process to update the 2006 Malaria Vaccine Technology Roadmap, the multilateral strategic framework underpinning malaria vaccine research and development. The process focused on expanding the Roadmap's vision and strategic goals to reflect substantial changes in malaria epidemiology and to encompass the current goals of prevention of malaria transmission, disease, and deaths. The funders group also has documented the progress made in 11 priority areas that support achievement of the Roadmap's vision and strategic goals. In this symposium, the progress made since 2006 will be presented.
Representatives from leading malaria vaccine funding agencies will give presentations on their contributions in the 11 priority areas and current funded activities, setting the stage for the forthcoming updated Malaria Vaccine Technology Roadmap.

S54: Beyond corporate social responsibility: building partnerships for health in Ghana: the AngloGold Ashanti malaria control programme

Chairs: Dr Sylvester Segbaya and Dr Frank Amoyaw.

Speaker 1: Dr Amadu Salifu, Community participation and engagement processes for efficent donor grant implementation, AngloGold Ashanti, Ghana
Speaker 2: Dr Rhoda Reneo Cundo, Managing labour recruitment in large scale IRS specific setting: A case study best practices, AngloGold Ashanti, Ghana
Speaker 3: Dr Frank Amoyaw, Malaria passive case surveillance: Methodology and approach, AngloGold Ashanti, Ghana
Speaker 4: Dr Dominic B Dery, Indoor residual spraying in Ghana: Baseline insecticide susceptibility studies to select appropriate insecticides for spraying in ten districts in Ghana, Ghana Health Service, Ghana

OVERVIEW

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INTRODUCTION: AngloGold Ashanti is a mining company with operations in 20 countries globally. The economic impact of malaria on its operations and the communities in Ghana inspired the initiation of a malaria control program in 2005 with a goal of reducing the disease burden by 50% over the first two years. The overwhelming success of this program led to the company's selection by the Country Coordinating Mechanism as the Principal Recipient of the Global Fund Round 8 Malaria Grant to scale up Indoor Residual Spraying to 40 districts in Ghana.
PARTNERSHIPS: AngloGold Ashanti from the programme inception has been working in partnership with the National Malaria Control Program, the Ghana Health Service, District Assemblies, Environmental Protection Agency, Research Institutions, communities and other stakeholders to scale up this intervention at the national level.

RESULTS: These partnerships have resulted in enhanced local capacity for IRS operations, selection and use of appropriate insecticides, quality improvement in health facility data collection, increased community awareness and acceptance of malaria interventions and a record of drastic reduction(76%) in malaria cases at the Obuasi Mine Hospital since 2005.

In Obuasi, the program has reduced the burden of malaria in the community, increased school attendance, won the gratitude of the community, recognition of the Government, reduced absenteeism at the mine, increased productivity and reduced expenditure on malaria medication to employees and their dependants. At corporate level it has a return on investment and has the backing of the shareholders.

Community Participation and Engagement Processes for Efficient Donor Grant Implementation

Amadu Salifu, Eric Obu Buetey, Sylvester Segbaya, Frank Amoyaw,
AngloGold Ashanti Malaria Control Limited, Box 10, Obuasi Mine, Obuasi, Ashanti Region, Ghana

A community based programme such as the AngloGold Ashanti malaria control programme has been successful and widely accepted by the beneficiary communities. This acceptance is significantly due to the participatory approach adopted during the programme design phases, with the establishment of an engagement process that brought together all stakeholders, interest groups and the recipient communities. It is empirical that large scale community intervention programmes adopt a community centred approach to enable the programme obtain the social license to operate in the host communities.

One of AngloGold Ashanti's core value is treating each other with dignity and respect. It is our believe that individuals who are treated with respect and who are entrusted to take responsibility respond by giving their best.
The programme continues to work towards the preservation of community and householders' dignity, their sense of self-worth in all our interactions, respecting them for who they are and valuing the unique contribution that they have made to our programme success.

Managing Labour Recruitment in Large Scale IRS Specific Setting – Case Study on Best Practices

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BACKGROUND: AngloGold Ashanti Malaria Control Limited as part of its scale-up activities in the 35 districts of Ghana recruits able-bodied individuals for the implementation of the IRS activity in all respective districts.
Per the six-month schedule period for the addition of districts in each spray season, recruitment is done to enable the spray teams prepare to execute their mandate of spraying. The programme has up to date engaged about 1800 individuals to undertake the spraying activity.
Recruitment of labour under the programme is based on good HR planning which involves defining job roles and the associated competencies, as well as developing an understanding of the labour demands and market trends (both internal and external); in order to match the availability of potential labour to Organisational needs.
RATIONALE FOR INCLUSIVENESS: The underlying principle in the recruitment of workforce for deployment at the respective districts and communities is based on an all-inclusive approach where the working populations are sourced directly from the local communities.
The workforce is categorized into the middle level managers and junior level staff. The junior level category includes all auxiliary staff supporting the operations at the various districts.
The rationale for this approach is to promote stewardship, encourage community acceptability and enhance the outcome of spray operations at implementing districts. The community becomes a part of the programme with a rippling effect of flow of funds to the grass root level.
SELECTION PROCESS: The 'best practice/high commitment' approach to our engagement process is the adoption of a sophisticated set of selection processes, rather than relying on a single source of information on which to base decisions about an applicant's suitability for a specific job role. One way that the programme has minimized perceived biases associated with such community based recruitment was to ensure that the scheme is supported by a fair selection process.
BEST PRACTICE: The effective recruitment and selection of employees is a fundamental HRM activity, one that have been managed well and has resulted in significant positive impact on our Organisational performance leading to a more positive Organisational image and stakeholder acceptance.

Malaria Passive Case Surveillance: Methodology and Approach

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AngloGold Ashanti Malaria Control Limited, Box 10, Obuasi Mine, Obuasi, Ashanti Region, Ghana

BACKGROUND: Impact evaluation is an important component of any health and community intervention since it enables evidence-based decision-making. As part of the impact evaluation strategy of the Malaria Control Program, the AngloGold Ashanti Malaria Control Programme has partnered with select Sentinel Health Facilities (SHFs) in the districts of operation to undertake a Passive Case Surveillance (PCS) activity.
The main purpose of this partnership and process approach is to provide a surveillance methodology to monitor the malaria-related trends in the districts, and to use such simple but robust approach to support measurement of programme impact.
METHODS: Test positive data is collected on a monthly-basis at the health facility level upon contact with clients accessing the facilities. Other related information is primarily on the number of cases of malaria treated at each sentinel facility, the treatment prescribed, demographic & medical characteristics of the clients, and their malaria history. Household GPS coordinates are registered on each house within the implementing districts to facilitate spatial mapping of all tests positive cases within the implementing districts. This further provides a comprehensive tool for identifying hotspots within the IRS implementing districts.
RESULTS: A test positivity measurement as an important criterion is estimated at each implementing district facility. This measurement index does not require a defined population denominator to estimate the required rates for impact evaluation purposes, but rather, a convenient denominator derived from the total out patients' records (OPD) is used for estimating the measurement index. This is very relevant in settings where population figures are not disaggregated to the community level, and demographic surveillance systems virtually doesn't exist.
CONCLUSION: This provides very useful information for determining the impact of the indoor residual spraying (IRS) programme within the intervention areas vis-a-vis the number of households protected; and benefiting from the health intervention.

Indoor Residual Spraying in Ghana; baseline insecticide susceptibility studies to select appropriate insecticides for spraying in ten districts in Ghana

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BACKGROUND: Indoor Residual Spraying with appropriate insecticides is a key intervention which can reduce vector populations in a given area and interrupt transmission. We determined insecticides susceptibility of *Anopheles* vectors in order to recommend appropriate insecticides for spraying operations in ten selected districts in Ghana.
METHODS: Between October 2012 and January 2013, immature *Anopheles* were collected and reared to adults. Mortality from tarsal contact of females was assessed with 11 insecticides in four chemical classes: i) organochlorines, ii) organophosphates, iii) carbamates and iv) pyrethroids. Four replicates of 25 unfed *Anopheles gambiae* females, aged 3 days, were exposed to insecticide papers for 1 hour (Fenitrothion was 2hrs). The number knocked down was recorded every 10 minutes and mortality 24 hours post exposure. Pyrethrum Spray Collections (PSC) were performed in 60 randomly selected rooms in each district.
RESULTS: Of 2,038 PSC collections, species compositions were *An. gambaie* s.l (64%), *funestus* (22%), *Culex* species (9%), *Aedes* (4%), *Pharoensis* (1%) and few *Mansonia* and *rufipes* species. Sporozoite rate was 0.036 and Malathion was identified as the most appropriate insecticide for spraying in seven districts (in Upper East, Upper West and Western regions). Fenitrothion was identified most appropriate in three districts (in Upper East and Upper West regions) and Propoxur in one district (in Western Region). Of 483 Polymerase Chain Reactions, *An. gambiae* s.s was prevalent (475) and few *arabiensis* (5) detected in savannah arid communities in the northern districts. The M-form was dominant (143) with no hybrids detected. The S-form was detected across the country though in low numbers (21). Few *kdr* susceptible strains were detected (14) but majority were homozygous kdr^{RR} (120) resistant species and heterozygous were moderate in number (32).
CONCLUSIONS: Organophosphate was found to be the most effective class of insecticide for Indoor Residual Spraying in the selected districts in Ghana. Rotation of insecticides is recommended as it offers a practical solution for resistance management. Though reported that *Kdr* mutation is widespread in West Africa, results contrast observation that, frequency within S-form is much higher and the distribution is more widespread than within the M-form.
KEYWORDS: *Organophosphate, IRS, Anopheles gambiae, Ghana*

S55: Malaria, surveillance, epidemic detection, epidemic preparedness and response: Zanzibar experience following increase in malaria cases in 2013 transmission season

Chair: Dr Jeremiah M Ngondi

Speaker 1: Dr Abdul-wahid Al-mafazy, Fit for purpose: Novel surveillance systems for Malaria in pre-elimination settings of Zanzibar, Zanzibar Malaria Control Program, Zanzibar
Speaker 2: Dr Abdullah S Ali, Epidemic preparedness and response in Zanzibar: detection of increased seasonal malaria cases and response activities in 2013, Zanzibar Malaria Control Program, Zanzibar
Speaker 3: Dr Jeremiah M. Ngondi, What works: evaluation of response activities following increased cases of malaria in Zanzibar in 2013, RTI International,Tanzania
Speaker 4: Dr Mwinyi Msellem, Where do we go from here: Lessons learnt from 2013 response activities and future strategies, Zanzibar Malaria Control Program, Zanzibar

Fit for purpose: Novel surveillance systems for Malaria in pre-elimination settings of Zanzibar

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BACKGROUND: In 2008, Zanzibar established the Malaria Epidemic Early Detection System (MEEDS) for electronic reporting and analyzing weekly malaria cases. In 2012, electronic malaria case notification (MCN) was established to enhance timely investigation of individual malaria cases and response activities. We report results of MEEDS and MCN surveillance systems in the malaria pre-elimination settings of Zanzibar.
METHODS: By 2013, MEEDS reported weekly malaria data from 160 (75%) health facilities. Weekly-summary data were transmitted via Unstructured Supplementary Service Data (USSD) mobile phones from health facilities to a remote server. For MCN reporting, a massage for each case is sent from Health Facility to the server where the server generates an alert SMS to the District Malaria Surveillance Officer's (DMSO) mobile phone and tablet. DMSO follows up patients (index cases) to their households. All case-household members are tested for malaria using rapid diagnostic tests (mRDT). People with positive malaria test results are treated with artemisinine-based combination therapy (ACT).
RESULTS: Representativeness has gradually improved as MEEDS was implemented from 10 (7%) primary health care health facilities in 2008 to 52 (37%) in 2009, 90 (63%) in 2010, 142 (100%) of public facilities and 18 (29%) of tertiary and private clinics by 2013. Completeness of submitted data was maintained at 100% since 2010 though technical problems prevented data transmission from some health facilities affecting timeliness of submission. Between 2011 and 2012, the number of malaria tests increased from 266,407 to 275,669. There was a reduction in malaria positive tests from 1.2% to 0.9% ($p<0.001$).
Results of MCN between September 2012 and June 2013 shows that a total of 1,439 index malaria cases were notified, of whom 1,013 (70.4%) were followed up at the household level. Of 4,627 household members tested with mRDT, 7.5% were positive for malaria.
CONCLUSION: The MEEDS and MCN systems provide timely reporting of malaria data and support timely programmatic decision making. Through MEEDS, ZMCP detects abnormal increases in cases and undertake appropriate response. Follow-up of malaria cases through MCN enables active detection of malaria cases and timely treatment of asymptomatic cases to reduce potential for malaria transmission.

Epidemic preparedness and response in Zanzibar: detection of increased seasonal malaria cases and response activities in 2013

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BACKGROUND: Following increased seasonal transmission of malaria in May 2013, Zanzibar Malaria Control Programme (ZMCP) implemented a number of enhanced interventions to interrupt transmission and mitigate risk of

potential malaria outbreak. We describe the identification of increased cases and response activities undertaken in May and June 2013 in Zanzibar.
METHODS: Increased seasonal transmission of malaria was detected by comparing trends of malaria cases over the same period in 2013 and 2012, based on weekly reports from malaria epidemic early detection system (MEEDS). Using data from malaria cases notification (MCN) the number of cases were monitored on a daily basis to identify emerging malaria hotspots at the Shehia level. Hot-spots were defined as Shehia reporting at least 4 or more weekly cases and a 1.5 fold increase in weekly cases compared to the average from previous three weeks. All potential hot-spots were investigated prior to implementing enhanced response interventions. Enhanced interventions were undertaken in 13 Shehias.
RESULTS: In 2013, compared to 2012, there was increased seasonal transmission of malaria starting in week 17 (44 vs. 22 cases) with a peak in week 25 (199 vs. 50 cases). Between week 19 and 25 of 2013, a total of 12 Shehias were prioritized for enhanced response interventions. The response activities included; 1) mass screening and treatment (MSAT) in 10 Shehias where 0.6% of 17,320 people tested positive for malaria; 2) behavior change communication (BCC) in 5,710 households and distribution of 9,345 long lasting insecticidal nets (LLIN); 3) larval source management in 11 Shehias; 4) pilot of mass drug administration (MDA) in four Shehias where over 90% of target population was treated with artemisinine-based combination therapy; and 5) indoor residual spraying (IRS) in one Shehia where 92.6% of 521 house structures were sprayed.
CONCLUSION: This response demonstrates ZMCP capacity for timely detection of increase in malaria cases, malaria epidemics, epidemic preparedness and response. ZMCP will continue to strengthen response from lessons learned. To enhance response efforts in the future, implementation of interventions should be devolved to district response teams.

What works: evaluation of response activities following increased cases of malaria in Zanzibar in 2013

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BACKGROUND: In May to July 2013, Zanzibar recorded increased seasonal transmission of malaria compared to 2012. The increase in cases was detected through the Malaria Epidemic Early Detection System (MEEDS), a passive surveillance system that reports weekly malaria cases through health facilities. Following the increase in cases, a number of enhanced interventions were undertaken in 13 hot-spot Shehias, including: mass screening [with mRDT] and treatment [with ACT] (MSAT) in 10 Shehias; behavior change communication and long lasting insecticidal net distribution (BCC/LLIN) in 10 Shehias; larval source management (LSM) in 11 Shehias; pilot of mass drug administration (MDA) in 4 Shehias; and indoor residual spraying (IRS) in one Shehia. We report the evaluation of the impact of the response activities on malaria incidence.
METHODS: Malaria incidence data in each 'hot-spot' was monitored on a weekly basis using the malaria case notification (MCN). Trends of weekly malaria incidence from the hot-spot detection week to 5 weeks post-detection were calculated and compared between: Shehias receiving pilot MDA (including BCC/LLIN and LSM); Shehias with MSAT (with or without BCC/LLIN and LSM); and hot-spot Shehias that did not receive any response activities.
RESULTS: In Shehias where pilot MDA, BCC/LLIN and LSM was undertaken, the weekly incidence of malaria declined drastically and remained sustained at very low levels, post intervention. In hot-spots with MSAT, the decline in trends of weekly incidence was less marked compared to pilot MDA hot spots. In hot-spots where no response activities were undertaken, the overall trend of weekly incidence was comparable to the hot-spots with MSAT; however, incidence was higher.
CONCLUSION: The package of enhanced response activities undertaken appear to have impact of on malaria transmission compared to hot-spots where no enhanced response was undertaken. Compared to MSAT, the pilot MDA hot-spots had greater declines in incidence with sustained low levels of malaria post intervention. MSAT with mRDT does not appear to be an effective approach to responding to increased seasonal transmission of malaria in pre-elimination settings. The MDA, BCC/LLIN and LSM approach has showed promising results and requires more investigation.

Where do we go from here: Lessons learnt from 2013 response activities and future strategies

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BACKGROUND: Zanzibar is in malaria pre-elimination phase. To leverage universal coverage with long lasting insecticidal nets (LLIN), early testing and treatment with artemisinine-based combination therapy (ACT) and passive surveillance; additional malaria prevention measures are required. We explore strategies that have potential to enhance progress towards malaria elimination phase in Zanzibar.

FUTURE STRATEGIES: Combination of primaquine and ACT for radical cure of malaria is being proposed. Primaquine is active against both sexual and asexual stages, hepatic and erythrocytic stages and also have an effect to immature and mature gametocytes.

Malaria case notification (MCN), follow-up and screening of case-households has been in place for over a year. Completed follow-up of index cases was about 70%. Strengthening MCN to ensure timely and complete follow-up of all cases is a priority. Evidence suggests that targeted treatment with ACT for members of case households is an effective intervention.

Mass testing and treatment in hot-spots has been in place for two years. Results of mass testing of 17,320 people with malaria diagnostic test (mRDT) in 10 Shehia in May and June 2013 showed 0.6% tested positive. Effectiveness of intervention could be enhanced by use of more sensitive testing methods.

Behavior change communication (BCC) at community level to promote net use, early testing and treatment. Use Shehia health custodian teams to sensitize communities on importance of malaria prevention, especially consistent net use.

Epidemic response and preparedness of district level response teams to implement epidemic response interventions.

Focal indoor residual spraying (IRS) and larval source management (LSM): use of passive and active surveillance to refine malaria transmission and implement timely IRS and LSM interventions.

Screening of visitors at port of entry: This will involve assessment of the human population movement to and from malaria endemic hot-spots; provision of prevention, and screening and treatment for travelers; and evaluation of malaria control in visitors.

Zanzibar pilot of MDA in 2013 demonstrates that MDA was highly accepted by communities at high risk of malaria and was effective in interrupting malaria transmission. Further randomized controlled trials will help may strengthen evidence base of MDA in malaria elimination settings.

S56: What role can schools play in the control and elimination of malaria in Africa?

Chairs: Professor Sir Brian Greenwood, Dr Moussa Sacko and Dr Don Mathanga

Speaker 1: Dr Sian Clarke, Treatment based approaches for malaria control in school children: a review, London School of Hygiene and Tropical Medicine, United Kingdom
Speaker 2: Dr Joanita Nankabirwa, The impact of malaria on cognition and learning in school children across the transmission spectrum: the evidence base, Makarere University College of Health Sciences, Uganda
Speaker 3: Dr Seybou Diarra, The role of schools in supporting community-wide malaria control efforts, Save the Children, Mali
Speaker 4: Dr Katherine Halliday, Schools as surveillance and monitoring platforms, London School of Hygiene and Tropical Medicine, United Kingdom.

Treatment based approaches for malaria control in school children: a review

Sian Clarke
London School of Hygiene and Tropical Medicine, United Kingdom

Malaria control has usually focused on pregnant women and children under five years, in whom the risk of malaria-related mortality is greatest. Yet within the last decade an increasing number of randomized trials of preventive treatment in school children have provided strong evidence of the negative impact that malaria can also have on health outcomes in this older group of children, and the benefits of improved control. This review will examine the available evidence to date, drawing on data from various trials of intermittent preventive treatment and seasonal malaria chemoprevention in school-aged children in Kenya, Uganda, Mali and Senegal (including several recent as yet unpublished studies) to illustrate the substantial reductions in the incidence of clinical attacks, prevalence of asymptomatic parasitaemia, and malaria-related anaemia that can be achieved using treatment-based approaches in different transmission settings. Priorities for future research to improve our epidemiological understanding of malaria in this age group, to inform policy and practice, and the role that schools can play in improving malaria control in this age group will be discussed.

The impact of malaria on cognition and learning in school children across the transmission spectrum: the evidence base

Joanita Nankabirwa
Makarere University College of Health Sciences, Uganda

In addition to the benefits for health, improved malaria control during the school-aged years has the potential to also improve education though the combination of reduced school absenteeism and improved cognitive function. In contrast to the long-term neurological sequelae of cerebral malaria, which are already widely recognized by the public health community, our understanding of the impact of uncomplicated malaria and asymptomatic infection on cognition and learning remains less clear cut. Recent studies in schoolchildren however provide increasing evidence to substantiate a deleterious effect. This talk will present an overview of the data on malaria and cognition and learning available to date, focusing particularly on recent findings from in a number of randomized trials of malaria control in schools in Kenya, Uganda, Mali and Senegal, spanning the epidemiological transmission spectrum from intense perennial transmission to highly-seasonal malaria. The presentation aims to stimulate discussion on the implications of this growing body of evidence for practice: including the benefits of intensified malaria control in schoolchildren for education, as well as health; remaining gaps in knowledge; and the roles of the education and health sectors in working towards the common goal of improved child development in Africa.

The role of schools in supporting community-wide malaria control efforts

Seybou Diarra
Save the Children, Mali

School age children represent 26% of Africa's population, most of whom are attending school. The primary net enrolment rate in low income countries has increased by 64% since 1999, with over 80% of school age children now enrolled in school. The reach of the education system, with its network of teachers, school community associations and school children (nearly 133 million in Sub Saharan Africa), is greater than ever before and exceeds any other state structure. It provides a unique opportunity to reach into communities in support of national malaria control efforts.

TWO CASE STUDIES WILL BE PRESENTED: In Mali, Save the Children worked with schools and school children to promote and monitor the use of mosquito nets during and after a community-wide distribution campaign of Long Lasting Insecticide Treated nets (LLINs). Teachers were trained to conduct simple participative malaria prevention education sessions, drawing on the Child-to-Child approach, form child malaria clubs and organize a School malaria day, open to all community members. These school-led actions increased community awareness, increased malaria knowledge, as well as increased and sustained the use of nets by primary school children. A further study is currently underway to also explore the role that schools and pre-schools can play in supporting the new community-based strategy of seasonal malaria chemoprevention.
In Malawi, schools are supporting the National Malaria Control Programme's goal of providing universal access to malaria diagnosis and treatment. With the increasing use of malaria rapid diagnostic tests (mRDTs), including training of health surveillance assistants (HSAs) to diagnose and treat on the basis of mRDTs in the community, there is a potential role for teachers to support this malaria case management strategy. Teachers are being trained to diagnose uncomplicated malaria using mRDTs and treat using Artemether Lumefantrine in school, alongside other common health problems as part of a first aid kit. It is expected that school children, who are generally less likely to seek treatment, will be tested and treated more promptly and return to school sooner, reducing their levels of absenteeism.

Schools as surveillance and monitoring platforms

Katherine Halliday
London School of Hygiene and Tropical Medicine

In an era of declining malaria transmission with expanding roll-out of interventions, heterogeneity of infection is increasing and the need to identify and target interventions at localised regions of high transmission is becoming ever more critical. Schools can act as an accessible platform for establishing baseline risk of transmission, identifying foci of high transmission for targeted control, and monitoring the impact of subsequent interventions.
In contrast to the traditional metric used to estimate infection prevalence - household cluster surveys - school surveys have the potential to provide an operationally more efficient measure of *Plasmodium* transmission across a range of spatial resolutions. The benefits of using the existing school infrastructure and sampling children assembled at a central location from a broad catchment area means that school surveys are less costly and logistically expensive than community surveys. Hence there is a strong case for the use of schools in depicting heterogeneities in current *Plasmodium* transmission, which can then potentially be extrapolated to the local communities they serve.
In the last five years, a standardised school survey protocol has been employed across a range of countries in Sub Saharan Africa at National regional and local levels including Kenya, Mali, Malawi, Ethiopia, Mozambique, Senegal, Gambia and Uganda. We shall present findings from a selection of these and discuss the ways in which country level control programmes can be guided with regards to fine scale targeting of interventions to specific communities on the basis of transmission "hotspots" detected during school surveys. Additionally we shall discuss the potential for repeated school screenings conducted every 2 to 4 years to aid in monitoring and evaluating the progress of targeted control initiatives implemented.

S57: Improving access to malaria treatment in rural Tanzania: Multiple interventions for lasting improvements

Chairs: Prof Christian Lengeler and Dr Hassan Mshinda

Speaker 1: Dr Flora Kessy, Addressing access to malaria care through strengthening the health system and patient resources – the ACCESS project, Ifakara Health Institute, Tanzania
Speaker 2: Mr Christopher Mshana, Promoting prompt health seeking behaviour through social marketing campaigns, Ifakara Health Institute, Tanzania
Speaker 3: Dr Dominick Mboya, Improving quality of malaria care in health facilities through supportive supervision, Ifakara Health Institute, Tanzania
Speaker 4: Dr Angel Dillip, Improving quality of malaria services in private drug dispensing outlets, Ifakara Health Institute, Tanzania
Speaker 5: Prof Christian Lengeler, Measuring outcomes and impact of the ACCESS interventions, Swiss Tropical and Public Health Institute, Switzerland
Speaker 6: Dr Alex Schulze, Conclusions and outlook for research and interventions, Novartis Foundation for Sustainable Development, Switzerland

S58: Malaria elimination: identifying and targeting the residual parasite pool

Chairs: Mr Simon Kunene and Dr Davis Mumbengegwi

Speaker 1: Dr Davis Mumbengegwi, Performance of RDTs in an active case detection pilot in Namibia, University of Namibia, Namibia
Speaker 2: Mr Nyasatu Ntshalintshali, Implementing LAMP to rapidly evaluate field diagnostics in Swaziland, Clinton Health Access Initiative, United States of America
Speaker 3: Dr Badara Cisse, Targeted mass drug administration to hit hotspots, London School of Hygiene and Tropical Medicine, United Kingdom
Speaker 4: Mr Simon Kunene, Integrating primaquine into national policy in Swaziland, Swaziland National Malaria Control Programme, Swaziland.

OVERVIEW

Eliminating malaria requires identification and treatment of the residual parasite pool. This process is complicated by the fact that many infections are asymptomatic, meaning individuals do not seek treatment, yet can transmit to mosquitoes. Active case detection, whereby programmes actively seek out infections in the community and treat where necessary, is one method to overcome the challenge of asymptomatic infection. It is, however, becoming clear that infections are often of very low density, frequently below the detection limit for RDTs and microscopy. Recent evidence suggests that if untreated, these low density infections remain infectious to mosquitoes. A key question is, therefore, how to deal with this sub-patent, hidden infectious reservoir. This symposium will cover identification of Plasmodia parasites in symptomatic and asymptomatic patients, within at risk communities in Northern Central Namibia by reactive case detection using RDTs. The use of LAMP to evaluate the performance of RDTs in Swaziland, as a tool to help identify infections that may have been missed during active case detection in Swaziland will be discussed. The results of recent field studies on targeted Mass Drug Administration as a measure to remove all Plasmodia reservoirs in Senegal will be presented as will the opportunities and challenges of implementing primaquine therapy into national malaria policy with Swaziland as a case study.

Malaria Case Surveillance Using Mobile Phone Technology in Swaziland

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BACKGROUND: Case-based passive surveillance and case tracking are necessary to achieve malaria elimination. Prior to embarking on an elimination campaign in 2009, the majority of cases in Swaziland were clinically diagnosed and reported monthly by health facilities through a paper-based system, delaying the entry and analysis of malaria case data up to 6 weeks after initial presentation of a case. To achieve elimination, Swaziland required an immediate case reporting system that could trigger a robust active surveillance response among malaria at-risk communities.
METHODS: In August 2010, Swaziland introduced an immediate disease notification system (IDNS), where data on 15 notifiable diseases, including confirmed malaria cases, are reported by healthcare workers to a central toll-free hotline and captured in real-time by a data entry clerk. Following data entry into the database, an automated short-message-service (SMS) text is immediately sent to the mobile phones of the entire National Malaria Control Programme (NMCP) surveillance team alerting them of the case and the reporting health facility. Information collected on each malaria case through the IDNS includes the name, gender, date of birth, contact information, directions to household, and condition details. Following case notification, the NMCP surveillance team attempts to visit the household of the case to confirm demographic details, collect travel history to determine source of infection, and identify potential risk factors associated with infection.
RESULTS: Between the 2008/2009 and 2011/2012 seasons, malaria cases reported to the health management information system (HMIS) decreased 91%, from 7507 to 643, while uptake in the use of the IDNS increased steadily over time. This decrease was both the result of the improved passive surveillance system as well as an increase in the confirmation rate of malaria cases through the introduction of diagnostic capacity at all health facilities. The proportion of cases investigated by the NMCP surveillance team, a system non-existent prior to 2010, is now 85%.
RECOMMENDATIONS: Countries aiming to achieve elimination must implement case-based reporting for passive surveillance at health facilities. Utilisation of mobile phone technology can expedite the reporting and follow-up of malaria cases. Health care worker sensitisation and training will facilitate the uptake of any new reporting system.

S59: Evaluating the impact of malaria control interventions on under-five mortality in sub-Saharan Africa

Chairs: Dr Achuyt Bhattarai and Dr. S. Rene Salgado

Speaker 1: Dr Abdullah S. Ali, Evaluation of Impact of malaria control interventions in Zanzibar, Zanzibar Malaria Control Program, Zanzibar
Speaker 2: Dr Daddi Jimma, Evaluation of the impact of malaria control interventions in Ethiopia, Ethiopian Health and Nutrition Research Institute, Ethiopia
Speaker 3: Dr Doreen Ali, Evaluation of the impact of malaria control interventions on all-cause under-five mortality in Malawi, Malawi National Malaria Control Program, Malawi
Speaker 4: Dr Emmanuela Gakidou, Evaluation of the effectiveness of malaria control interventions on all-cause under-five mortality in Zambia and Uganda, Institute for Health Metrics and Evaluation, Uganda
Speaker 5: Dr Thomas Eisele, Comparative approaches to evaluating the impact of malaria control interventions on all-cause mortality in sub-Saharan Africa - Lessons learned, Tulane University, United States of America.

S60: EVIMalaR research highlights in vector and systems biology

Chairs: Prof Lars Hviid and Prof Flaminia Catteruccia

Speaker 1: Prof Lars Hviid, Introduction – EVIMalaR malaria vector and systems biology research, University of Copenhagen, Denmark
Speaker 2: Prof Flaminia Catteruccia, Sex and reproduction inAnopheles: novel targets for vector control, University of Perugia, Italy
Speaker 3: Mr Julien Pompon, Clonal-dependent killing ofPlasmodium falciparum by the new Tgase2-AP1/Fos axis in Anopheles gambiae, University of Strasbourg, France
Speaker 4: Dr Alexandra Marie, Towards immuno-epidemiological biomarkers for evaluating the human exposure to infectiveAnopheles bites, IRD, France
Speaker 5: Dr Janet Midega, UnderstandingAnopheles mosquito populations during a period of malaria epideiological transition, Imperial College, United Kingdom

S61: Multiple First Line Therapies (MFT) and Protecting the ACT class of medicines: science, modeling and current practices

Chair: Dr Georger Jagoe and Dr Ramanan Laxminarayan

Speaker 1: Dr Keziah Malm, Introduction of MFT as a national treatment strategy in Ghana: Opportunities, challenges and progress to date, Ghana National Malarial Control Programme, Ghana
Speaker 2: Dr John Amuasi, Exploring the feasibility of MFT options: The role of choice in public-private blended MFT strategies and a review of different segmentation approaches, Public health researcher, Ghana
Speaker 3: Dr Ramanan Laxminarayan, Prospective strategies to delay the evolution of anti-malarial drug resistance: Weighing the uncertainty, CDDEP, India
Speaker 4: Dr Ian Hastings, Policy options for deploying anti-malarial drugs in endemic countries: A population genetics approach, University of Oxford, United Kingdom.

OVERVIEW

The use of Multiple First-line Therapies (MFT) has been debated since 2008 as an approach to delay the emergence of resistance for malaria medicines. Proponents argue that using different ACT combinations nationwide can better protect this drug category versus overreliance on a single ACT. Critics are concerned with implementation challenges of MFT, and with proving that MFT delays the emergence of resistance. All agree that protecting ACTs is a public health imperative, given that no non-ACT alternatives will be launched during the next 5-to-8 years for uncomplicated malaria.

Today, Ghana is the only country that officially endorses MFT as a malaria treatment policy. However, in several countries, the private and informal sectors offer a wide variety of ACTs to consumers, making MFT the *de facto* reality. As more countries may emulate the AMFm model, thereby increasing the availability of ACTs in the private sector, new questions arise regarding the potential of MFT throughout Africa.

We will explore why Ghana adopted MFT as a policy and how it is implemented and monitored. Ghana's experience is instructive for other countries considering MFT options, and offers a live platform to help answer questions about the contribution of MFT to national policy.

In assessing MFT, we consider the degree of choice that exists between antimalarials in different settings (e.g. public *vs.* private sector, rural *vs.* urban, paediatric *vs.* adult formulations.) MFT's implementation costs, procurement requirements, and implications for inventory management must also be carefully considered.

Various epidemiological models have been designed comparing the benefits of different treatment strategies to cope with drug resistance. Since the spread of drug resistance is, fundamentally, a genetic process, we consider various drug deployment policies and then consider how genetic factors (e.g. cost of resistance), epidemiology factors (e.g. intensity of transmission), and clinical factors (e.g. proportion of infections treated) affect drug resistance and determine optimal deployment strategy in different clinical/epidemiological settings.

Given that MFT is already practiced in different ways in many malaria endemic countries, there are timely opportunities now to assess its role, its potential impact, and its possible implementation pathways as part of national malaria policy.

S62:Adaptability and the State of Monitoring and Evaluation Systems: Measuring Malaria Now and in Changing Contexts

Chairs: Dr Yazoume Ye and Dr Leopoldo Villegas

Speaker 1: Dr Jean-Marie Ngbichi, Harnessing mHealth to monitor different epidemics within one country: Experience from Mali, MEASURE Evaluation/ICF International, United States of America
Speaker 2: Dr Ali Sie, Designing effective training and tools to streamline malaria M&E efforts in Burkina Faso,Centre de Research en Santé de Nouna, Burkina Faso
Speaker 3: Jui Shah, Developing a framework for in-country impact evaluations of malaria control efforts, ICF International, United States of America
Speaker 4: Dr Eric Eckert,New perspectives in M&E within changing changing contexts of civil and political instability, UNAID,United States of America

Harnessing mHealth to monitor different epidemics within one country: Experience from Mali

Jean-Marie N'Gbichi
Senior Monitoring & Evaluation Specialist, ICF International

Mali has divergent malaria epidemics because of the variation in climate and ecosystems within the country that range from the arid Sahara desert to subtropical flood plains of the Niger River. As a consequence, risk of infection and immunity vary across the Malian population. Population movement, especially in response to recent political events, has led to the increased risk of infection for many displaced persons. The National Malaria Control Program

with help from MEASURE Evaluation has set up a mobile- and web-based reporting system to study and track these epidemics more closely, help detect and mitigate outbreaks, and improve the availability and timeliness of malaria data. The new system generates data that has been analyzed and validated each month, allowing users to access the data by inputting a password as quickly as three weeks after the end of the month. This is a significant improvement over waiting for an annual report generated by the System National information Sanitaire (SNIS), and has shown local health information specialists how to integrate new technologies that will improve data management.

Designing effective training and tools to streamline malaria M&E efforts in Burkina Faso

Ali Sié
Director, Centre de Recherche en Santé de Nouna

Malaria remains a major public health issue in sub-Saharan Africa (SSA), which bears a high burden of morbidity and mortality, mostly within the most vulnerable populations. The current set of efforts to address malaria in SSA is jeopardized by several bottlenecks that prevent the success of these efforts. Lack of coordination as well as lack of capacity at the national level to meet the challenges of designing and implementing effective malaria control and prevention plans (UN, 2005) are major challenges to tracking progress in malaria control.
Monitoring and evaluation (M&E) of malaria programs are now being promoted to fill the gap as effective tools for fighting malaria and strengthening health and community systems. MEASURE Evaluation's capacity building activities aim to establish partnerships with selected universities and training and research centers in developing countries. This includes offering M&E training programs and strengthening partner institutions' capacities to conduct M&E activities. To pursue this objective in SSA, MEASURE Evaluation entered into a partnership with the Centre de Recherche en Santé de Nouna (CRSN) in Burkina Faso in 2011.
Under this partnership, CRSN and MEASURE Evaluation cooperated in the design and implementation of an M&E workshop focused on building the capacity of professionals involved in malaria M&E programs in SSA. The training provides an overview of M&E tools and guidelines as well as concepts and practices used in the development and implementation of malaria M&E plans. It also covers recent developments in M&E tools and techniques. The Regional Workshop on M&E of Malaria took place in Ouagadougou and over three sessions, 51 participants from 13 countries benefited. This is a continuous venture, and an additional curriculum for formal graduate training in M&E is planned.

Developing a framework for in-country impact evaluations of malaria control efforts

Jui Shah
M&E Associate, ICF International

Over the past decade, funding for malaria control programs has increased significantly, especially in sub-Saharan Africa (SSA). This has led to the scale-up of four key interventions: insecticide-treated nets, indoor residual spraying, intermittent preventive treatment for pregnant women, and treatment with effective drugs. Rowe and colleagues proposed a plausibility design in 2007 to measure the impact of malaria control programs. Since then, new measurement needs and evidence have emerged, requiring an update to the approach initially proposed. Several partners are working to develop a new framework document that will provide recommendations for evaluating the scale-up of malaria control interventions in malaria endemic countries. It draws upon the recent experience of the President's Malaria Initiative, which is leading impact evaluations in 15 priority countries in SSA. The framework document is currently under development and is expected to be launched in January 2014.

New perspectives in M&E within changing contexts of civil and political instability

Erin Eckert
Epidemiologist, USAID

When the Roll Back Malaria (RBM) Partnership was launched in 1998, it the global malaria community needed a consistent means to measure scale-up and impact across countries. The RBM MERG, with support from USAID, developed standardized malaria survey modules to collect this information. These tools have been the primary mechanisms to track progress in malaria control in sub-Saharan Africa. Over the past decade, many countries have made tremendous progress in controlling malaria, reducing transmission and all cause child mortality (ACCM). In this rapidly changing environment, new M&E tools and methods are needed for RBM and its partners to monitor continued progress and show impact.
As transmission is pushed into smaller geographic zones or sub-groups of the population (i.e. Senegal, Rwanda) M&E tools must target smaller populations and collect data across national borders. Parasitemia markers from cross-

sectional surveys do not track timely information on trends in disease burden nor correlate well with scale-up of interventions. ACCM will lose its sensitivity as an impact marker as malaria constitutes less of proportional mortality over time, and emphasis is placed on detecting and treating cases.
As countries reduce transmission, M&E efforts should shift focus from broad national surveys to more targeted approaches. Population-based surveys will continue to be necessary to monitor sustained control efforts such as universal coverage with bednets. At the same time, there will be increased need for more frequent programmatic and epidemiologic data at the facility and community levels. PMI and partners are developing facility survey instruments to monitor availability of commodities and provider performance. Epidemiologic data should be derived from both passive surveillance of diagnosis and treatment in facilities and active surveillance of cases and contacts in the community. Such surveillance must also be accompanied by improved laboratory capacity in identifying parasite genetics in low-level transmission dynamics. In high burden countries, ACCM will continue as a macro-level indicator of health sector development, with enhanced modeling to estimate the proportional decrease in mortality due to malaria. However, in countries approaching the goal of 'near-zero deaths' and elimination, measurement efforts should shift to morbidity and markers of transmission to show sustained impact.

S63: Towards strengthening the MIM into an organisation

Chair: Prof Peter de Vries.

S64: Africa taking Leadership in Research Networks

Chairs: Dr Sam Kinyanjui and Dr Sylvie Kwedi-Nolna

Speaker 1: Prof Bassirou Bonfoh, Success of the One Health initiative albeit cultural diversity within Africa, One Health Initiative - African Research Consortium for Ecosystem and Population Health, Côte d'Ivoire:
Speaker 2: Prof Rose Leke, What types of incentives should be adopted for a more prominent African leadership in network? University of Yaounde I, Cameroon:
Speaker 3: Prof. Sharon Fonn, , What does effective partnership mean to an African researcher? Consortium for Advanced Research Training in Africa (CARTA)
Speaker 4: Dr. Margaret Gyapong, Women in leadership roles within Research Networks Africa Institute for Infectious Diseases of Poverty (IIDP), Tanzania
Speaker 5: Prof Francine Ntoumi: Tips from private sector funding to enhance the design of a more successful research capacity strengthening funding scheme? Fondation Congolaise pour la Recherche Médicale, DRC
Speaker 6: Prof Mbacham Wilfred, Challenges for the new generation of health research Leaders in Africa, Poverty Related Disease college, Cameroon

OVERVIEW

BACKGROUND: During the current period of financial crisis, Africa needs to develop new models for research funding schemes that encourage African leadership and are geared towards efficiency, synergy and collaboration. Such models could contribute to eliminate or mitigate the diseases that have contributed to its socio-economic stagnation despite an apparent economic growth. As such, funding opportunities for research and training of the next generation of young African scientists need to consolidate the role of science in the overall development of Africa. Though human capacity development has been prioritized in most capacity building funding schemes, research culture is still poor and women are generally still under-represented in most grant actions. Many institutions are currently interested in discussions on how to increase the number of women in research. Through this symposium ISHReCA aims to bring out tips to guide African decision makers and interested Organisation to increase the number of women becoming scientists and recommend new approaches that could be explored to increase African researchers' leadership in research and development partnerships.
OBJECTIVE & METHOD: This symposium is organized by ISHReCA in collaboration with research for health scientists who are current and former grantees of flagship capacity strengthening funding schemes (such as the Wellcome Trust African Institutions Initiative, WHO/TDR MIM grants and NIH grants, etc…) where African leadership is/was paramount. Panelists representing their field of expertise and initiatives will share their experience about the topic through "exploring challenges of south - south networks which have diverse levels, geographic, language culture, and financial accounting abilities". They would bring out the pattern of problems, potentials and make recommendations for future schemes that wish to give African researchers a leadership role in global partnerships.
The session would be structured as a round table discussion co-moderated by Dr Sam Kinyanjui and Dr Sylvie Kwedi-Nolna. Questions to each panelist would be around the topics outlined below.
EXPECTED OUTCOME: Recommendations will be articulated in order to:

1. Guide the design of more successful African-led and vastly interactive research capacity strengthening funding schemes that are geared towards building both individual and institutional capacity.
2. Motivate more Africa researchers especially young and women to take up leadership positions in Networks,
3. Strengthen African researchers to reach out to and leverage key global health partnerships, resources from multilateral Organisations as well as from the private sector.

KEY WORDS: Africa, Leadership, Research capacity and partnerships

S65: Financing community driven malaria control

Chair: Prof Peter de Vries

Basic health is a human right. This right does not exclude inequalities in health status between individuals or populations (e.g. young versus old). But, inequity, i.e. differences of access to available health services, and the resulting differences in health risks, is not acceptable. Emancipation refers to the sociological mechanisms that aim to reduce inequity (of groups of individuals). With respect to health, emancipation aims at changing socioeconomic and ecologic conditions in order to reduce the differences in health risk for respective populations. These changes, or improvements in health care, cannot be implemented individually; it is a joint effort of people and their institutions. Malaria control is one of the efforts by which people try to provide equal health to all. The majority of investments made in malaria control are traditionally organized through national malaria control programs , health services, NGOs etc. It has been estimated that with the current level of investments malaria cannot be properly controlled let alone be eliminated. Extra investments are needed.

We argue that the resources available in malaria endemic communities are under exploited. Social mobilization to eliminate malaria is a form of emancipation that reduces health inequity. Ownership and investment are the intrinsically connected drivers of the socioeconomic changes needed for an integrated community driven approach to malaria control and elimination. Key to these changes is the return on investment.

In this workshop we will discuss how a community can invest in its own malaria control, how return on investment should be assessed and how ownership should be divided.

S66: Pharmacovigilance in Africa

Chairs: Prof Rachida Souleymani and Prof Alex Dodoo

Speaker 1 : Prof. Rachida Souleymani, Malaria, as an entry point for pharmacovigilance in Africa? Centre Anti Poison et de Pharmacovigilance de Rabat - MoroccoSpeaker 2: Prof. Alex Dodoo, Training courses and pharmacovigilance network in Africa, WHO Collaborating Centre for International Drug Monitoring (Africa Office) Accra - Ghana

Speaker 3: Prof. Christophe Rogier, Challenges in designing and implementing a pharmacovigilance study in Africa; the example of a malaria field monitoring study in Côte d'Ivoire, Institut Pasteur de Madagascar, Madagascar.

OVERVIEW

Malaria medicines represent an important part of the drugs circulating in sub-Saharan Africa, with over the counter access in several countries, and increasing community-based delivery of antimalarial drugs. Clinical studies performed for registration do not address many real-life situations such as repeated dosing, use in patients with no proven malaria, concomitant use of traditional remedies, etc. In addition, quality of circulating medicines is often doubtful. Pharmacovigilance reports generated from this large consumption are scarce. Pharmacovigilance is still an area to be developed in Africa. Medical practitioners often do not know about it and health authorities struggle to put in place effective pharmacovigilance reporting systems.

This symposium will discuss how malaria could be a good entry point for pharmacovigilance in malaria endemic areas of Africa, thanks to training courses, networks that are developed and innovative studies on ACTs.

S67 : Scalable innovations for improved malaria control in the era of elimination

Speaker 1 : Mr Edmound Kertho, Using mobile health (mHealth) for resistance containment and improved quality of care of malaria at community level, Malaria Consortium, Uganda

Speaker 2 : Dr Sandrine Martin, Critical ingredients for community engagement in malaria prevention : A case study, Malaria Consortium, Africa

Speaker 3 : Dr Eric Wetzler, A two-tiered system for effective supervision of community health workers, Save the children, Mozambique.

Speaker 4 : Dr Yasmin Chandani, Improving the availability of medicines for malaria and other childhood infections at the community level : Experiences scaling and institutionalising promising supply chain innovations in Malawi and Rwanda, John Snow International

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Using mobile health (mHealth) for resistance containment and improved quality of care of malaria at community level

Edmound Kertho
Malaria Consortium Uganda

There is a growing body of evidence demonstrating the potential mobile technology have to radically improve healthcare services even in some of the most remote and resource-poor environments. Though the mHealth field is still in its early stages, it has already begun to transform health delivery with projects throughout the developing world demonstrating concrete benefits.
Malaria Consortium is using affordable mobile phone solutions to strengthen the flow of information and data, increase communication between health providers , create accountability and early warning systems to improve elimination efforts, and as motivation and education tools for various levels of health workers.
In Cambodia, where efforts to contain spread of artemisinin resistance in the region are being intensified, real time data is critical for achieving its goal of malaria elimination by 2025. To support this process, Malaria Consortium has developed a diverse set of surveillance tools to improve malaria surveillance and provide national and district staff with the information they need to manage the national malaria programme, respond to malaria outbreaks, respond to individual cases as they move towards elimination and monitor, in real time, levels of critical malaria supplies at health facilities. For example, Village Malaria Workers (VMWs) send rapid diagnostic test (RDT) results through open source software on mobile phones to the Malaria Information System (MIS), where Google Maps can identify and support the containment of hotspots. Similarly, short message service (SMS) reporting tools have also been piloted for monitoring malaria drug stock outs in a number of health centres in Cambodia and it is expected to be scaled up to all health facilities in the coming years.
In Mozambique and Uganda, mHealth innovations are being used to positively impact on community health worker (CHW) motivation, performance and retention in order to increase the quality and coverage of their work in treating malaria, pneumonia and diarrhoea in children under five. Custom made applications are being used to address some of the key challenges faced by CHWs who are now able to send their weekly reports to their supervisors, receive instant feedback and monthly motivational messages; they are also connected to their supervisors and peers through a free to use closed user group. Supervision, as a result, will be targeted based on performance and feedback messages provide reminders and key information for improved diagnosis, treatment and prompt referral. In Mozambique specifically, images and audio are included in the software to refresh the skills in illness identification and treatment.
mHealth projects that provide solutions to key challenges and addressing critical needs, have an extensive role to play in the push towards malaria elimination.

Critical ingredients for Community Engagement in malaria prevention: a case study

Sandrine Martin
Malaria Consortium Africa

Community involvement has been recognised as one of the key features for successful health interventions at community level. Despite consensus among field practitioners that community involvement is essential, few health programmes have formally developed models for implementing effective strategies.
The objective of this presentation will be to describe the key features and preliminary results from two approaches developed and implemented by Malaria Consortium in three African countries to engage local communities in Integrated Community Case Management (ICCM) and address barriers to timely and appropriate management of children with malaria and other infections: the MIM Pan-Africa Malaria Conference Symposium title: Scalable innovations for improved malaria control in the era of elimination
Community Dialogue (CD) approach and the Village Health Club (VHC) intervention. Both interventions were designed in 2011 with the ultimate goal to empower care-givers and communities with knowledge and skills to make improved choices for children's health and survival through individual and collective actions.
The VHC approach, being implemented in Uganda, seeks to improve child health through a community led model with the community health worker (CHW) as its focal point. VHC meetings provides a forum where CHW and club members work together to identify child health and CHW challenges. They also address them using village networks, knowledge, creativity and assets. VHCs are implemented through a four-step learning, planning and action cycle facilitated by the CHW. Throughout the cycle the VHC monitors and reports on their progress. The approach has been implemented in 8 districts in mid-Western Uganda where 880 VHCs have been formed.
The CD approach is a form of community mobilisation and empowerment process aimed at providing communities with information, skills and confidence to gain control over decisions about their own lives. Malaria Consortium adapted and implemented this approach inthree African countries where ICCM is being implemented to trigger genuine dialogue within local communities about the management of selected childhood diseases. The intervention is based on a socio-ecological approach, not only looking at individual behaviours but also seeking to address social norms around health care seeking and prevention practices around child health.
The presentation will draw some initial lessons from the early stage of implementation of both approaches to highlight the critical ingredients for effective community empowerment towards malaria prevention and control at community level.

Improving the availability of medicines for malaria and other childhood infections at the community level: experiences scaling and institutionalizing promising supply chain innovations in Malawi and Rwanda

Yasmin Chandani/Mildred Shieshia
John Snow International

BACKGROUND: SC4CCM is a learning project that identifies simple, affordable solutions to address the unique supply chain challenges faced by community health workers (CHWs). In Malawi and Rwanda, CHWs provide treatment for malaria and other illnesses to children under five in their villages. Baseline assessments in 2010 identified a lack of visibility into CHW logistics data and weak coordination between CHWs, health centers, and districts as barriers to community level availability of medicines including ACTs. To improve data visibility in Malawi the project tested a mHealth solution while in Rwanda a simplified paper-based reporting system was introduced.
METHODOLOGY: The project designed, implemented, and continuously improved interventions for 12 to 18 months, culminating in mixed method midline evaluations in early 2013. The results were presented in country during data validation workshops where stakeholders agreed on components for scale up. Participants completed an exercise using The Pathway to Sustainability Tool to assess program readiness to take innovations to scale, identify areas where support is needed, and guide planning for scale-up and institutionalization. Comprehensive action plans were developed that address all aspects of sustainability from roll out trainings to long term institutional capacity. The same tool will be used in 6-9 months to evaluate progress and readjust action plans.
RESULTS: The workshops highlighted priority activities for institutional capacity building and a timeframe for achieving this. Ministries of Health in both countries are currently scaling up successful solutions with the support of partners; by September 2013 Malawi will have scaled up to 20 of the 29 districts. In both countries a fora has been identified for coordinating scale up efforts and to monitor the transition of operations to the MOH. MIM Pan-Africa Malaria Conference Symposium title: **Scalable innovations for improved malaria control in the era of elimination**
DISCUSSION: This presentation will provide an overview of the two main innovations and key evidence of their success in improving supply chain performance. It will discuss in detail the challenges and considerations for scaling up these innovations and review the tools and coordination mechanisms that SC4CCM has used to engage stakeholders and plan for sustainable scale-up. The presentation will specifically highlight some of the lessons learned in how to achieve effective coordination among stakeholders.

S68 : New tools for management of insecticide resistance

Chairs : Prof Hilary Ranson and Prof Fred Binka

Speaker 1 : Prof Hilary Ranson, A review of Insecticide Resistance in Vector Control, Liverpool School of Tropical Medicine, United Kingdom

Speaker 2: Dr Charles Wondjii, Mechanisms of Insecticide Resistance, Liverpool School of Tropical Medicine, United Kingdom

Speaker 3: Professor Diabate Abdoulaye, Malaria Vector Control in Africa, current strategies and challenges for the future, Institute de Recherche en Science de la Centre Muraz, Burkino Faso

Speaker 4 : Dr Frederic Baur, Development of New Products for Insecticide Resistance Management, Bayer Crop Science, France.

A review of Insecticide Resistance in Vector Control

Prof Hilary Ranson
Liverpool School of Tropical Medicine, United Kingdom

This presentation will give an overview of the current understanding of insecticide resistance in African malaria vectors. The first part will focus on resistance monitoring and will include:

- Examples of the rapid spread of pyrethroid resistance across the continent
- The emergence of Anopheles populations resistant to all major insecticide classes
- The need for more quantitative measures of assessing resistance and its impact

Part two will review the major mechanisms responsible for resistance and include:

- An overview of the key cytochrome P450 enzymes responsible for pyrethroid resistance
- Evidence of cross-resistance caused by metabolic mechanisms
- Discussion of the potential role of a newly detected kdr mutation in conferring higher resistance levels
- Preliminary data describing the role of the cuticle in conferring resistance.

Mechanisms of Insecticide Resistance

Dr Charles Wondjii
Liverpool School of Tropical Medicine, United Kingdom

Metabolic resistance to insecticides is the biggest threat to the continued effectiveness of existing malaria vector control interventions. But its underlying molecular and genetic basis, crucial for successful resistance management, remains poorly characterised.

In this study, using a genome-wide transcriptional analysis, we show that the up-regulation of the glutathione-S transferase gene GSTe2 is strongly associated with DDT resistance. Using a GAL4/UAS transgenic expression of this gene in Drosophila, we showed that over-transcription of this gene alone was necessary and sufficient to confer DDT resistance but more importantly also cross-resistance to pyrethroids. We showed that besides quantitative differences, qualitative changes in GSTe2 were also significantly contributing to the high DDT resistance as In vitro metabolic assays demonstrated that the resistant allele was more active in metabolizing DDT than the susceptible alleles. For the first time in mosquitoes, we identified an amino acid change (L119F) that strongly associates with DDT resistance and designed a molecular diagnostic assay that accurately detects the resistance in field populations. Structural analysis of the GSTe2 indicated that L119F located in the DDT-binding pocket confers the high DDT resistance by significantly increasing the size of the DDT binding cavity allowing more binding of the DDT molecule leading to its increased metabolism. The distribution of this L119F mutation across Africa shows a strong correlation with known patterns of DDT resistance.

Furthermore, we showed that GSTe2 is under strong directional selection in resistant populations, and a restriction of gene flow is observed between African regions, enabling the prediction of the future spread of this resistance.
This study represents a comprehensive and detailed dissection of the genetic, molecular and structural basis of metabolic resistance to insecticides and provides the first resistance marker for metabolic resistance in mosquitoes.

Malaria Vector Control in Africa, current strategies and challenges for the future.

Diabate Abdoulaye
Institute de Recherche en Science de la Centre Muraz, Burkino Faso

Current Malaria vector control strategies in Africa rely on the use of Insecticide Treated Nets (ITNs) and indoor residual spraying (IRS) with insecticides. Over the last years a vast campaign of ITNs distribution in many endemic countries was undertaken towards achievement of universal coverage. Though ITNs and IRS have helped alleviate the burden of malaria in many endemic countries, vector control in Africa is challenged by a number of threats. If we were to achieve elimination/eradication of malaria, these threats need to be addressed.

The first major obstacle is the development of insecticide resistance which is widespread in anopheline mosquitoes. It becomes critical to preserve or recover the efficacy of existing insecticides. Attainment of this goal will require a greatly improved capacity to predict the emergence and dynamics of insecticide resistance in time and space and unfortunately we are far from being there yet.

The second major issue is community acceptability of nets. A few studies have reported a big gap between net ownership and its usage. While the paucity of effective tools in controlling malaria vectors is a big threat, availability of the best tool is of no value if not well implemented by the end-users. Consistent and persistent work to disseminate relevant information is needed to ensure greatest uptake. Another challenge is the question of sustainability. A global effort in investing domestic funds in malaria control is seen in some countries, however malaria control is still largely supported in most if not all cases by international donors. Given the funding prospect for the next few years, countries need to be thinking ahead of sustainable ways of supporting the control if we want to preserve the major achievements reached so far. Finally, though current tools have cut down the malaria burden in many settings, there is growing concern that malaria eradication will not be achieved without introduction of novel control tools. Hence, research is required to accelerate the discovery of new vector control tools that can supplement and help improve the effectiveness of currently available tools.

The third major issue vector control is facing is the change in the biting behavior of malaria vectors after the implementation of current control strategies. Indeed malaria vectors have been reported to bite early before people are going to bed as well as biting frequently outdoor when people are not protected by their nets. Urgent and additional tools are needed to complement ITNs in some settings and this issue needs to be addressed. The fourth issue is the problem of sustainability. In most situations if not all, vector control is implemented thanks to international donor funds. If these funds were to stop today, many countries would not be able to sustain their control program. While advocacy must be done to support malaria vector control, each country should find ways to sustain its control program in absence of international funds.

Development of New Products for Insecticide Resistance Management

Frederic Baur
Bayer Crop Science, France.

Established resistance in Anopheline mosquitoes to pyrethroids and emerging resistance to other classes of insecticides is a significant threat to the continued effectiveness of efforts to eliminate malaria. The Crop Science industry is currently the only sector that can develop new mode of action insecticides based on its experience in the development of Crop Protection products and its R&D capacity. Several companies are working hard to try and come up with solutions. It is nevertheless a challenge to mobilize sufficient resources considering the very high development costs: Sustainable vector control should be supported by sustainable business. For some projects, IVCC is a partner to help overcoming the challenge of developing innovative formulations, and supporting the screening pipeline to discover new chemistry. For other projects, the Crop Protection industry engage its own resources only. But several major hurdles are limiting and delaying market entry of the new solutions including : speed of approval, cost of development trials, lack of data protection and the WHOPES equivalence process

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S69:Pan-African mosquito control association: Networking and paving the way forward for the future of mosquito control in africa and beyond

Chairs: Dr Chiomah Amajoh and Dr Tessa B Knox

Speaker 1: Dr. Charles Mbogo, PAMCA: Introduction & Perspectives, PAMCA, Kenya
Speaker 2: Prof Maureen Coetzee,The future of mosquito control in Africa and beyond, University of Witwatersrand, South Africa
Speaker 3: Dr Michael Macdonald,Global partnerships for public health entomology, World Health Organisation, Switzerland.
Speaker 4: Dr Magaran Bagayoko, PAMCA African Network on Vector Resistance &World Health Organisation Afro-region.
Speaker 4: Dr. Sam Awolola, PAMCA Nigerian Chapter: Society for Mosquito Control in Nigeria (SMCN), Society for Mosquito Control in Nigeria (SMCN), Nigeria
Speaker 5: Major Dhillon, Lessons from the American Mosquito Control Association (AMCA), World Mosquito Control Association
Speaker 6: Yvonne Chaka Chaka, Goodwill Ambassador for the Roll Back Malaria Partnership.
Speaker 7: Dr Abraham Mnzava, Closing Remarks,World Health Organisation, Switzerland