MRC Unit The Gambia

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Annual Report

Annual Report 2018

Leading health research in West Africa to save lives and improve health across the world.

Contents

Foreword

Professor Umberto D'Alessandro

Unit Director

The most important event in 2018 is, without doubt, the formal transfer of the Unit to the London School of Hygiene and Tropical Medicine (LSHTM), a move that builds on existing strong relationships between the two institutions. LSHTM has been ranked among the first 200 Universities in the world; and for the proportion of its total publications ranking in the top 10% of most cited research, it is first in Europe and eighth in the world for research impact in sciences. This is why we are confident that being part of this leading academic institution would provide fantastic opportunities for scientific collaboration, training and career development to our staff. An example of such opportunities is the possibility for our scientific staff to apply for academic titles according to established protocols and procedures; four of them have already done so, and I am sure others will follow soon. Moreover, we have been discussing the possibility of setting up some of the LSHTM short courses in The Gambia; in November 2019, we will have the 3-week epidemiology and statistics course offered by the LSHTM here in The Gambia.

The Unit is continuing to expand its technical capacities. We have established a genome core facility which would allow us to carry out most of the genomic analyses on site, without the need of sending biological samples abroad. Together with the building of the new molecular biology laboratory, still under construction, and the High-Performance Computing Facility, the Unit is establishing high-tech facilities close to the field and will be equipped to carry out world-class research on diseases of public health importance in sub-Saharan Africa. Our capacity in entomological research has also been strengthened with the building of a new insectary that will be used for investigating malaria transmission. It is also important to stress the move towards green technologies. We are installing the biggest solar power generation facility in The Gambia, and probably West Africa, within our premises, which will substantially reduce our carbon emission.

We have continued to expand our activities in West Africa by continuing to work with our Senegalese partners, namely the University Cheikh Anta Diop and the Institut de Recherche en Santé de Surveillance Epidémiologique et de Formation, in Dakar, through the West Africa Global Health Alliance (WAGHA). Dr Melisa Alvarez Martinez, a senior social scientist working on Maternal and Neonatal Health, is now based in Dakar, working directly with our WAGHA partners. In addition, we held a meeting with scientists from the Institut Pasteur Dakar (IPD) with the aim of exploring synergies and potential collaborations. This resulted in the signature of a Memorandum of Understanding between the Unit and IPD.

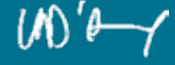
Maternal and Neonatal Health remains an extremely important research area for the Unit. We are part of the PRECISE (PREgnancy Care Integrating translational Science, Everywhere) network funded by the GCRF (Global Challenges Research Fund) UK whose aim is to investigate three important complications of pregnancy, namely high blood pressure (hypertension), babies who are smaller than they should be before birth (fetal growth restriction) and babies who die before birth (stillbirth). The study, besides The Gambia, will be implemented in Kenya and Mozambique. We are implementing PRECISE in Farafenni and surrounding villages where the Unit manages a Health and Demographic Surveillance System that covers a population of about 50,000. This project has also offered the opportunity to finalize an agreement with the University of The Gambia (UTG) for the use of the Farafenni field station that was donated to UTG in 2009. The Unit can now use the facilities in Farafenni as a part of a collaborative agreement.

Antimicrobial resistance is also an important area of research for the Unit and this is the reason why we have dedicated a special section of this annual report to this topic. Within this section we have also inserted information on our work on antimalarial drug resistance.

Training remains an essential activity of the Unit. In 2018, 264 staff benefited from training support, most of them Gambians. In addition, our internship program has been followed by hundreds of young and enthusiastic students who are looking for experiences that would help them in choosing their career. The Unit is also supporting early and mid-career post-doctoral researchers as illustrated by the key research and development achievements shown in this annual report. The important contribution to capacity building provided by the Unit has been recognized and quantified: during the period 2012-2017, the Unit hosted the highest number of externally-funded postgraduate grantees among 11 African institutions which collectively hosted almost half of all grantees (Morel et al. Globalization and Health (2018)14:77 https://doi.org/10.1186/s12992-018-0395-0).

The Gambian Government, and more specifically the Ministry of Health and Social Welfare, is an essential partner for The Unit. We contribute, with our expertise to several technical committees at the Ministry of Health and Social Welfare, and also provide health care services in selected health facilities where our research projects are implemented.

We have started thinking to our quinquennial plan (2021-2026) and budget to be submitted next year for review. We will continue our current lines of research as they reflect public health priorities in West Africa, but may add other areas of research given the opportunities offered by being part of the LSHTM.



OUR YEAR IN PICTURES





















Who We Are

Over 1300 Staff

including **40** Post Docs and **167** laboratory staff based in The Gambia

£20 Million Budget

The Unit has successfully reacquired ISO 15189 accreditation, following an assessment by the Kenya Accreditation Service (KENAS).

For the first time, our laboratories in Keneba and Basse were assessed for inclusion in the accreditation, and are all in compliance with the Good Clinical Laboratories Practices (GCLP).

Clinical Trials Support Office have facilitated the successful conduct of

19 clinical trials

4 clinical trials in start-up stage

46 clinical trials monitored

83 Research Projects

264 Staff

trained in academic and skills development

WHO Collaborating Centre for New Vaccines Surveillance

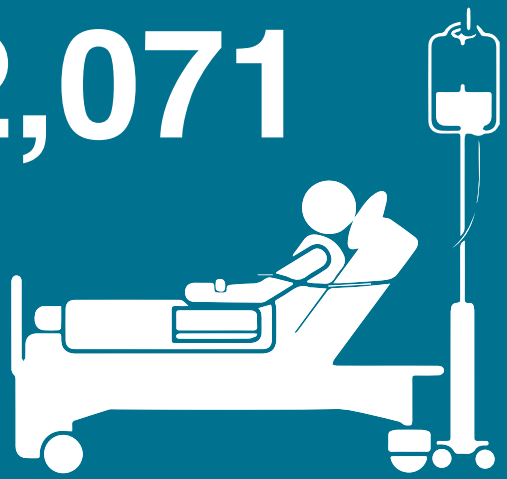
We are now a World Health Organization Regional Reference Laboratory for Invasive Bacterial Diseases.

Our Collaborators in Africa

Institut Pasteur de Dakar

Partnership agreement signed with Institut Pasteur Dakar in September 2018.

Up to **2,071** Patients admitted



Gate Clinic **32,000** Patients

Outpatients **31,000** Patients

In our Fajara and Keneba clinics

Strategy

Strategy

The Unit aims at contributing significantly to the post-2015 sustainable development agenda by producing the evidence base to improve health in West Africa and beyond. This is the reason for focusing our research on health issues that already are - or will probably become - in the next decade, a considerable burden for the local population, specifically infectious diseases, maternal and neonatal health, nutrition-related diseases, and non-communicable diseases. Such research is supported by the core funding provided by MRC UK, and by research grants awarded by a variety of donors. The latter shows that the Unit can compete internationally for research funds, thanks to an enabling environment that includes highly performing research platforms, like our genomic platform, and highly trained staff; proximity to the field and the strong relationship we have built with the local populations. The integration within the London School of Hygiene and Tropical Medicine, on February 1st, 2018, has opened the door to new research topics and collaborations.

As part of our strategy to increase our activities and collaborative links within West Africa, we continue to collaborate with our Senegalese partners, the Université Cheikh Anta Diop and the Institut de Recherche en Santé de Surveillance Epidémiologique et de Formation, within the West Africa Global Health Alliance (WAGHA), with whom we have several research and capacity building projects supported by several funding agencies, i.e. the West Africa Node of Excellence on TB AIDS and Malaria (WANETAM) supported by the EDCTP. We have also started a collaboration with the Institut Pasteur Dakar, and have a senior scientist permanently based in Dakar.

Training and career development of young African scientists remain an essential activity of the Unit. It is extremely encouraging to see that several of our young scientists have been able to secure prestigious fellowships from a variety of sources. In addition, the integration within the London School of Hygiene and Tropical Medicine creates new opportunities for the training of our staff and for setting up courses in The Gambia that would benefit the wider West African region.

Our collaboration with the Gambian Government is essential to carry out our research activities. Members of the Gambian Government, and more specifically of the Ministry of Health and Social Welfare, are active collaborators in our research projects. We continue to have the Gambian Government/MRC Unit The Gambia Joint Committee Meetings where we can have an open dialogue and discuss any issues that may arise during the implementation of research activities. The Unit contributes significantly in terms of expertise to several technical committees at the Ministry of Health and Social Welfare.

Professor Umberto D'Alessandro with the Prince of Wales

Dr Uduak Okomo explaining her work to his Royal Highness Prince of Wales, Fajara Main Site, The Gambia

MRCG at LSHTM Staff with the Prince of Wales

Our research is also enriched by the open partnership and collaboration of communities across The Gambia. The Unit continues to engage with the public through various platforms, to share our work, gauge perceptions, and improve our public engagement strategies for better results.

Leadership Board

Prof. Umberto D'Alessandro
Unit Director
&Theme Leader DCE

Joan Vives Tomas
Director of Operations

Dr. Assan Jaye
Head of Research Training
& Career Development

Dr. Anna Roca
Deputy Theme Leader DCE

Karen Forrest
Head of Clinical Services

Dr. Jonas Lexow
Research Governance &
Support Services Manager

Dr. Davis Nwakanma
Head of Laboratory Services

Prof. Beate Kampmann
Theme Leader VIT

Prof. Andrew Prentice
Theme Leader Nutrition

MRC Festival - TB Stand

MRC Festival Nutrition Theme

MRC Festival cross section of the participants

Our Operations

We are creating and adopting new innovations to support our research and deliver excellent results.

Our Genomics Core Facility: A Bold Step For The Unit

The Genomics Core team at work in the new facility

The establishment of a Genomics Core Facility at our Fajara site represents a bold undertaking for the Unit, and aligns with our agenda to build a strong core genomics capability, and become a stronger partner in the emerging “southern” genomics alliances, particularly in West Africa.

The Unit has already secured and will be investing on the infrastructure to host a state-of-the-art, international standard molecular biology laboratory, and will play a critical role in training scientists from sites and collaborators in West Africa, facilitating West African capacity-building in Genomics. Our mission is to make these complex technologies accessible and biologically interpretable for all research scientists at the MRCG at LSHTM, through the provision of state-of-the-art genomics technology, with the best possible service at the lowest cost.

The Genomics Core Facility, headed by Dr Abdul Karim Sesay, enables investigators with little experience in sample preparation, quality control or analysis to interrogate the genome. It will be developed to become the largest genomics facility in Sub-Saharan Africa, and will help to lead the way in high-speed, comprehensive genomic. It will also ensure that the Unit remains at the forefront of research beyond Africa.

The Genomics Core facility is equipped with a range of high-tech sequencing equipment including: GenomeLab XP, SeqStudio Genetic Analyzer, Illumina MiSeq and Ion Torrent benchtop sequencers, a Pyrosequencer, MinION portable real time sequencers and associated laboratory devices, the first GridION sequencer in Africa. The services on offer cover the whole spectrum of applications utilising first, second and third generation sequencing platforms, at small to medium throughput.

In collaboration with Professor Martin Antonio, Director of World Health Organisation Regional Reference Laboratory for Invasive Bacterial Diseases, the lab successfully sequenced culture isolates from patient specimens collected from the field of suspected meningitis cases during a recent outbreak in a remote region in Northern Nigeria. The lab is currently working towards sequencing directly from patients CSF and will apply it in a field base workflow.

A Changing Landscape for Efficient Research

New Molecular Biology Laboratory

To ensure quality standards, promote growth, and ensure the successful implementation of our mission to deliver innovative, world-leading research aimed at reducing the burden of illness in low- and middle-income countries, we are constantly introducing new and innovative systems, structures and platforms to maintain an enabling research environment.

The Unit is championing some key structural and operational changes for effective delivery across all our sites, and the changing landscape promises to contribute to outstanding research and professional service delivery.

Recognising our growing scope, the Unit identified the need for a dedicated facility to carry out molecular biology work, including molecular biology clinical diagnostics and molecular research work, which includes genotyping, transcriptome studies, proteomics/metabolomics and training.

The new 3000 square meters state-of-the-art building with functional laboratory, office and collaboration spaces is designed to be energy-efficient, distinctively Gambian, and adaptable for future science, with ease of maintenance and connectivity between parts of the building and other buildings on the site.

This molecular biology laboratory project is directly linked to the genomic strategy and the High Performance Computing (HPC) facility, and construction is expected to be completed by November 2019.

Installing the Biggest Solar Power Generation System in The Gambia

In line with our Unit's overall strategy to make our facilities and operations more energy-efficient, and our need to evolve and with the latest green technologies, we have begun the installation of the biggest solar power generation facility in The Gambia, starting with the Fajara campus, where power consumption is currently over 240,000 kilowatts per month.

In October 2018, the Unit applied for, and received, a grant of $200,000 from UNIDO to cover 30% of the installation cost for this project, which consists of installing solar panels which generate up to 65 kilowatts per hour. We expect to optimally produce 120 megawatts per annum, saving up to 5% of our energy bill, and increasing our overall capacity as we grow. The project will also help to reduce our carbon emissions by a significant amount, progressively working towards our target of a 50% reduction across our sites.

The installations are being carried out by Azimut 360, and the company has partnered with M'bolo Association, a women's skills development and training centre in Tujereng, with projects to empower young and vulnerable women with literacy, financial management, and life skills. Their participation in the solar installation at the Unit gives them practical knowledge to become professional solar installers, and develop their technical skills.

M'bolo Association installing the panels

MRCG Director's Awards 2018

Honouring our hardworking and dedicated professionals for their outstanding contributions.

MRCG Director's Awards 2018

Our Unit's 'Oscars' are presented to outstanding staff, recognising excellent research and professional service-delivery in five main categories. The 2018 Director's Awards honoured staff members for their contributions to the growth and advancement of the Unit, and our work in leading health research in West Africa to save lives and improve health across the world.

The winners were honoured at the Annual Staff Dinner in December 2018, with award presentations done by members of the Leadership Board.

Inspirational Leader
Dr. Adedapo Bashorun
Trial Coordinator, PNEUMOSIL

G.E.M (Going the Extra Mile) Award, Amadou T. Jallow
Scientific Officer, IHAT

Research Leader of Tomorrow
Alfred Ngwa, Malaria Scientist

Science Support
Amulai Touray, Theme Project Manager, Nutrition

Outstanding Team
BRIGHT Team

Year In Review

Discover key highlights of our research, activities, and achievements during the year.

Year in Review

January

MRCG donates equipment to the Gambia Government

Through the TEKNON project, we donated equipment worth GBP 50,000 to the Gambia Government, through the Ministry of Health and Social Welfare, to aid in the prevention of pneumonia related deaths. The donated items included a TEKNON Solar Prototype A and TEKNON Mains Power Prototype for Soma site, TEKNON Solar Prototype B, TEKNON Mains Power Prototype for Farafenni, TEKNON Mains Power Storage Prototype for Basse and Spares (Elite Oxygen Concentrator) for Fajara site.

Study shows that nutritional requirements are higher during adolescence than during the prepubescent stage and during adulthood

A study on delivering an action agenda for nutrition interventions for adolescent girls and young women was recently published in the Annals of the New York Academy of Sciences. The study describes evidence-based nutrition recommendations and the current global guidance for nutrition actions for adolescents, as young people undergo major anatomical and physiological maturational changes in preparation for adulthood.

MRCG wins Business Continuity Award

At the 19th Annual Business Continuity Awards, the Unit was awarded the Business Continuity Award in the Resilient Workforce category, in recognition of our management of the political impasse in The Gambia in December 2016 and January 2017. This period demonstrated the Unit's preparedness to function as a referral centre for patients, while complementing the efforts and skills of the Red Cross and other healthcare providers locally.

February

MRCG joins the London school of Hygiene and Tropical Medicine

On 1st February, the Unit formally joined the London School of Hygiene and Tropical Medicine, building on existing strong relationships between the two institutions, and ensuring stronger scientific collaboration as well as new career opportunities for researchers. The Unit and LSHTM have a well-established working relationship and have collaborated on numerous trials and projects for nearly 70 years. The transfer means the Unit is now called the Medical Research Council Unit The Gambia at the London School of Hygiene & Tropical Medicine (MRC Unit The Gambia at LSHTM).

Celebrating the International Day of Women and Girls in Science

The Unit invited 350 students from 17 schools to an Open Day under the theme Opening Doors, Closing the Gender Gap, to commemorate the International Day of Women and Girls in Science. The event aimed to educate youth – both boys and girls – about the significant accomplishments of female leaders in global health in sub-Saharan Africa and to illustrate the career opportunities that are available in science.

MRCG at LSHTM wins highly competitive MRC Foundation Award

The Vaccines and Immunity Theme Leader, Professor Beate Kampmann, and co-investigator Dr Uzochukwu Egere, have recently been awarded a highly competitive Medical Research Council Foundation award to pursue translational research on "Evaluating novel diagnostics and enabling preventive measures for childhood tuberculosis between the United Kingdom (UK) and partners in Sub-Saharan Africa". The Foundation Award represents the MRC's first phase of research funding anticipated from the £1.5bn Global Challenges Research Fund.

March

Bill and Melinda Gates Foundation Pneumonia Division Team Visits MRCG at LSHTM

Over 5 days, senior members of the Bill and Melinda Gates Foundation Pneumonia Division visited the Unit, specifically exploring the Pneumococcal Vaccine Schedules study sites in Kulari and Sabi, where they interacted with staff and inspected the procedures and facilities. They were also taken on a tour of the Basse District Hospital, where they saw procedures for clinical evaluation of patients and the study's electronic medical record system.

National Robotics Competition Finals

The Unit hosted the National Robotics Competition finals at the Fajara campus, in addition to funding support provided for the competition. Five schools: Marina International, Gambia High School, Methodist Academy, SBEC International and SOS High School competed in the finals, and were tasked to build a robot to mass produce vaccines, using Vex kits with the support of a mentor. Gambia High School emerged winners, and were set to represent The Gambia at the Pan African Robotics Competition (PARC) in Rwanda in March 2018, accompanied by their mentor Bai Lamin Dondeh, Head of Data Management at the Unit.

CSD embarks on quality improvement in healthcare delivery

The Unit's Clinical Services Department recently launched a quality improvement programme, to continuously provide systematic changes to work that enables healthcare to be safe, effective, patient-centered, timely, efficient and equitable. The improvements cover several aspects, including a patient satisfaction survey, the production of guidelines to standardize care and two specific projects – one to introduce sepsis alerts and early treatment; and the other to introduce the usage of an Early Warning Score (EWS) to highlight deteriorating patients.

62nd Joint Annual Meeting between The Gambia Government and MRCG at LSHTM

The Unit held its 62nd Joint Annual Meeting with The Gambia Government and other key stakeholders. The Unit Director, Prof Umberto D'Alessandro, presented an overview of activities that took place over the past year, including the Unit's scientific output, data on the clinical care offered in Fajara and Keneba, and trainings carried out within the Unit.

April

World TB Day 2018 Commemorations

The Unit partnered with the National Leprosy and Tuberculosis Control Program (NLTP) to commemorate World TB Day 2018 in Sukuta. The event featured a procession by students, government officials and community members, as well as presentations highlighting the Unit's research on TB diagnosis and treatment, and our partnerships with government to create awareness on TB.

New Blood Test Found to Predict Onset of TB Up to Two Years in Advance

A new blood test has been found to more accurately predict the development of tuberculosis up to two years before its onset in people living with someone with active TB, according to research published online in the American Journal of Respiratory and Critical Care Medicine (AJRCCM), an American Thoracic Society journal. The most significant finding was that prediction of progression to active tuberculosis in household contacts of active TB cases up to two years before the onset of the disease is possible through measurements of a specific combination of a four-gene signature in the blood.

BRIGHT Open Day at Keneba Field Station

A Participant Open Day for the Brain Imaging for Global Health (BRIGHT) project was held at our Keneba field station, bringing together over 70 mothers, fathers and infants, representing every village from which the study has recruited participants. Several workshops were offered, with participants getting the chance to creatively explore how babies use their brains during daily tasks. The team guided participants through activities focused on the brain, the technology used to collect data in BRIGHT, and the importance of mental health. .

May

Dr Madikay Senghore wins ISPPD-11 Robert Austrian Research Award

Dr Madikay Senghore, Post-doc Research Fellow in Microbial Genomics, has been awarded a 25,000 USD Robert Austrian Research Award for his research project on "Understanding the pathogenesis and virulence traits of a novel clade of vaccine preventable streptococcus pneumoniae with outbreak potential". As a postdoctoral fellow in microbial genomics, Dr. Senghore mentors junior scientists, and co-chairs the invasive bacterial disease writing group at the Unit.

7th Multilateral Initiative on Malaria (MIM) Conference in Dakar

Scientists from the Unit participated in the 7th Multilateral Initiative on Malaria Pan African Conference in Dakar, which served as an opportunity to review MIM's 20 years of contribution to the global goal of ending malaria in Africa, to better address current malaria research and control priorities. Over 2500 malariologists attended the conference, which also created a platform for young African scientists to interact with malaria experts. .

June

MRC Festival 2018: showcasing the achievements of our young scientists

The Unit opened its doors to showcase the achievements of our young scientists during the 2018 MRC Festival, held at the Fajara campus. The event also created a unique platform for over 200 local and international collaborators to explore our research activities through interactive demonstrations and innovative infographics.

MRCG at LSHTM donates beds and mattresses to MoHSW

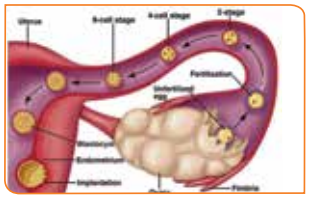
The Unit donated 34 hospital beds and mattresses to the Ministry of Health and Social Welfare, as part of our efforts to support the development of the health system in The Gambia. The representative from the MoHSW, Balla Jatta, thanked the Unit for the donation, and noted that items will help bridge the need gap in the medical field.

July

DNA marks in adults tracked back to changes in earliest days of life

A research team, led by scientists at the Unit, have gained a glimpse of how marks on our genes that could be linked to adverse health outcomes in later life behave differently in the first few days after conception, according to new research published in Science Advances. The study is an important step in understanding a mechanism by which the embryo responds to its early environment, with the potential to influence health in later life.

Understanding how a mother's nutrition around conception time leads to changes in her developing embryo's epigenome



In a series of studies carried out across The Gambia, our researchers have seen that epigenetic marks at key regions of the genome appear to be influenced by seasonal changes in a mother's diet around conception. This work gives a vital insight into how and when a mother's diet might impact her offspring's epigenome. These epigenetic changes have the potential to affect how the offspring's genes are regulated later in life which could in turn affect health and disease susceptibility throughout the life course.

August

New Data Center and Entomology Laboratory inaugurated

The Unit inaugurated a new Data Center and Entomology Laboratory at our main site in Fajara. The Data Centre is equipped with network and storage upgrades that will address the information needs of our science and all new activities in alignment with our quinquennial plan. The laboratory will support research in malaria control and other vector-borne diseases. In recognition of their valuable service to the Unit, the new Data Centre was named after Dr. Maimuna Mendy, and the Entomology Laboratory after Ida Secka.

MRCG at LSHTM scientists win NIH H3 Africa Scheme grant

Professor Martin Antonio and Dr Brenda Kwambana-Adams won a competitive grant from The National Institutes of Health (NIH) under the H3 Africa Scheme. The grant is to be use in understanding the impact of inhaled environmental exposures on the microbiota of the upper airways of African children.

GCLP Accreditations for our Fajara, Keneba and Basse Laboratories

In March, the Kenya Accreditation Service (KENAS) conducted a re-accreditation assessment against ISO 15189. The successful exercise has led to the Unit's reaccreditation to ISO 15189 for another 3 years, confirming that the Unit's Quality Management System is robust, and that we have maintained the technical competence to perform the accredited tests.

September

RHD remains leading cause of cardiac death and disability in children and young adults worldwide

Dr Annette Erhart from the MRCG at LSHTM and Dr Lamin Jaiteh from the EFSTH, secured a Wellcome Trust Seed Award for a pilot project aiming to generate baseline data on the burden of RHD among high risk groups (children and pregnant women) in The Gambia. This pilot project represents a first step on the roadmap for RHD control in The Gambia, and constitutes the evidence base for the formulation of larger multi-disciplinary studies that will address pending knowledge gaps and bottlenecks for the implementation of an effective RHD control program.

The Reach4Kids Africa meeting – Joining forces in The Gambia

The childhood TB team hosted the collaborating African scientists of the Reach4Kids Africa (R4KA) project, and members of their National TB Control teams from Mali, Nigeria and Tanzania. The R4KA project has two objectives: to Find and Treat children with TB in The Gambia and the partner countries (FaT) and to Screen and Prevent (SaP) new cases amongst young children exposed to a case of TB at home.

Ousubie Jawla wins LSHTM Director's award

Ousubie Jawla was a joint winner of the LSHTM's Director's award for Outstanding Contribution in the Professional Services category. Ousubie is a field supervisor at our Keneba field station, and manages a team of ten field assistants and twenty village assistants to deliver the Methyl Donors and Epigenetics-2 (MDEG2) nutritional supplementation trial.

MRCG at LSHTM hosts WANETAM2 Entomology Training Workshop

The Unit hosted the first Entomology Training Workshop at our Fajara campus, under the umbrella of The West African Network of Excellence for TB, AIDS and Malaria (WANETAM-2). The 10-day workshop, which was led by Dr. Kevin Opondo, Dr. Benoît S. Assogba, and Musa Jawara from the Unit, focused on malaria vector research in the context of malaria elimination. Participants were also trained on theoretical and field-based entomology involving field activities, laboratory techniques, data base management and statistical analysis of entomological data.

OCTOBER

Dr Assan Jaye wins LSHTM Director's Award

Dr Assan Jaye, Head of Research Training and Career Development, is a joint winner of the Director's Award for Excellence and Innovation in Developing Students as Researchers. Dr Jaye was recognised for his immense contribution in supporting Researcher Leadership training, since he took up the post as Head of Research Training and Career Development in 2016.

Sniffer dogs could detect malaria in people

Researchers have found that dogs could scent malaria in samples of socks worn by infected children. These findings could potentially lead to the first rapid and non-invasive test for malaria. Although the research is in its early stages, the scientists hope trained sniffer dogs could help to stop malaria spreading between countries and lead to infected people being spotted earlier and treated quickly.

Dr Leopold Tientcheu Djomkam wins the K43 Emerging Global Leader Award

The five-year K43 award of US$ 539,205 will further Dr Tientcheu's independent career development, research and training plans. The award will allow him to extend his research into how Tuberculosis (TB) has evolved with human populations such that the clades of Mycobacterium tuberculosis complex (MTBC), known to be closely associated with human migratory pathways can affect outcome of treatment.

NOVEMBER

A Royal Visit to MRCG at LSHTM

His Royal Highness, the Prince of Wales visited the Unit as part of his tour to The Gambia. The visit was to celebrate The Gambia's return into the Commonwealth in February 2018, and was the Prince of Wales' first trip to The Gambia after the Commonwealth Heads of Government unanimously decided that he should succeed Her Majesty the Queen as the Head of the Commonwealth. His Royal Highness was taken on a tour of our Fajara site, and witnessed poster presentations from the Unit's scientists.

Dr Julia Mwesigwa wins Young Investigator Award

Dr Julia Mwesigwa won the first-tier position of the Young Investigator Award competition held at the 67th annual Tropical Medicine Conference of the American Society Tropical Medicine and Hygiene (ASTMH). Julia submitted results from her on-going PhD studies on the "Impact of mass drug administration on malaria transmission dynamics in The Gambia" at the ASTMH conference. The competition gave Julia the opportunity to present her research findings and defend the results and conclusions to judges and other scientists.

Good housing with indoor plumbing may be key to eliminating childhood malnutrition and stunting

New research from the Unit, published in the BMC Medicine journal, suggests that improved housing with access to piped water may be the crucial keys to eliminating malnutrition and stunting in children. The new findings suggest that better housing with piped water into the home, and keeping animals away from the domestic space, are the pivotal factors that would lead to improving childhood growth.

4th Annual Midwifery Training Programme

The Vaccines & Immunity Theme hosted the 4th Annual Midwifery Training Programme at our Fajara site, as part of the ongoing initiative of Emergency Midwifery Skills & Helping Babies Breathe which started five years ago and continues to strengthen our collaboration with the governmental facilities. The training focused on midwifery and neonatal wellbeing, and also featured a lecture on healthcare associated infection and the importance of hand hygiene, as well as discussions on topics related to maternal and neonatal care.

DECEMBER

Dr Anna Roca and Dr Uduak Okomo Feature at the 2nd Women Leaders in Global Health (WLGH) Conference

Dr Anna Roca and Uduak Okomo were invited as speakers at the 2nd Women Leaders in Global Health (WLGH) conference, hosted by the London School of Hygiene & Tropical Medicine, bringing together established and emerging leaders from across sectors and cultures to work towards gender equity in health leadership. Several other staff from the Unit also attended the conference.

Think TB: Awareness Campaign and Teachers Pilot Training

The Unit organised an interactive training workshop and pilot training for teachers, as part of public engagement activities to raise awareness on TB. The two events were held at the Gambia Methodist Academy, and sought to equip the teachers and students with adequate information to become TB Ambassadors, and sensitize their communities about TB control in The Gambia.

Dr Uduak Okomo awarded a Pump Priming Grant

Dr Uduak Okomo was awarded a Pump Priming grant of £10,000 to carry out a facility-based evaluation of stillbirths and neonatal deaths in The Gambia, as part of her post-doctoral research activities. The funding for this award is provided by the Institutional Strategic Support Fund (ISSF), supported by Wellcome and the LSHTM.

Research Themes

Our three main research themes provide important opportunities for inter-theme synergy.

Disease Control & Elimination

Overview

Our Disease Control and Elimination (DCE) scientific strategy focuses on investigating the interactions between hosts, pathogens and vectors; and evaluating interventions aimed at interrupting transmission and/or reducing the burden of diseases. Each component can inform the other and provide new opportunities for understanding the dynamics of transmission and identifying new targets for interventions. The multidisciplinary DCE approach comprises a large epidemiological component combined with strong laboratory (mainly diagnosis) support. The core component of epidemiology and laboratory sciences is complemented, whenever possible, by social sciences investigating the human factors influencing the epidemiology of the diseases and the uptake/coverage of interventions.

The theme incorporates health system and health economic research components to some of its projects with the aim of ensuring that the interventions evaluated, when successful, are promptly translated into practice. As the aim of the DCE Theme is to control and eliminate disease, it targets not only the disease itself but also asymptomatic or subclinical infections, as these are key components for maintaining transmission at community level.

The DCE theme currently has a large heterogeneous but coherent research portfolio that includes diseases of public health importance in West Africa, including The Gambia, at different stages of control or elimination. The theme combines both well-established with more innovative research lines; and internally- (malaria, bacterial and viral diseases) with externally-led research (hepatitis B). The research activities span from large epidemiological studies assessing burden of disease to clinical trials (individual or cluster randomized) testing or assessing the effectiveness of new public health interventions.

Prof. Umberto D'Alessandro
Unit Director
& Theme Leader DCE

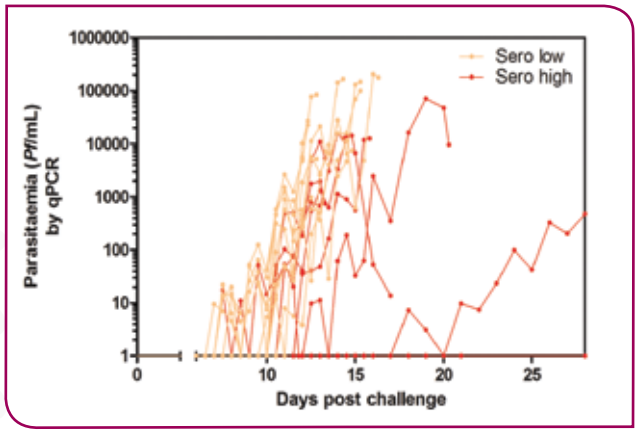
Dr. Anna Roca
Deputy Theme Leader DCE

Highlights

Experimental set-up with a medical detection dog. Sock sample visible in glass jar held in the stand on the right.

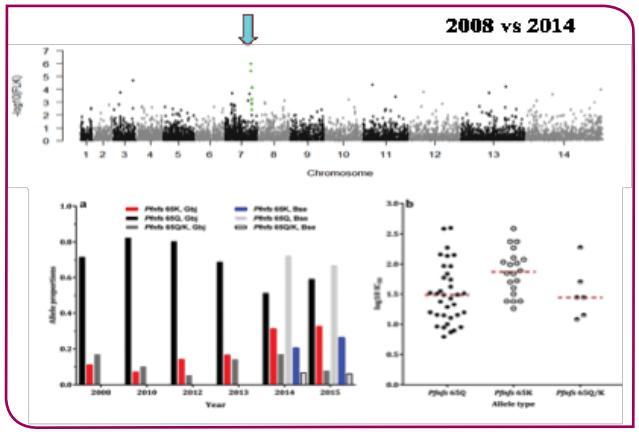
Is it possible to identify people with a malaria infection without taking a blood sample?

Eliminating malaria would be simpler if a non-invasive method was available for detecting infected individuals in populations with low malaria prevalence; then infected individuals could be treated with antimalarials. Dogs have a highly developed sense of smell and may be able to detect volatiles released from people carrying malaria parasites. A proof-of-principle study was done in Basse to determine whether trained dogs could discriminate between infected and uninfected children. Schoolchildren were tested for malaria and at the same time were asked to wear nylon socks overnight to collect foot odour samples. Sock samples from children infected with malaria were used to train two dogs in the UK. After training, a double-blinded study was undertaken to assess the diagnostic accuracy of the dogs. The dogs were able to correctly identify at least 70% of all malaria-infected children. In the future, artificial odour sensors may be able to detect malaria parasites. Until then, trained dogs may be useful at ports of entry to detect asymptomatic malaria carriers entering malaria-free countries.



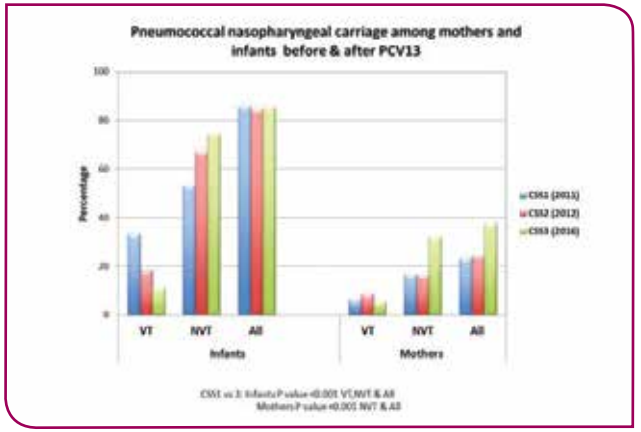
First Controlled Human Malaria infection experiment in The Gambia

Controlled human malaria infection (CHMI) of healthy volunteers by exposure to the bites of infected, laboratory-reared Anopheles mosquitoes or inoculation of infected erythrocytes has been used for nearly 100 years to investigate malaria pathophysiology and immunology and efficacy of vaccines and drugs. During the last decade CHMI studies have been expanded in the US and Europe, and increasingly performed in Africa using injectable, aseptic, purified, cryopreserved, vialed Plasmodium falciparum sporozoites. We set up this experiment for the first time in The Gambia to assess how previous exposure to malaria affected parasite kinetics, clinical symptoms, and immunity. Two cohorts of Gambian healthy adult males with markedly different levels of previous malarial exposure were included in the study, injected with malaria sporozoites, and carefully followed up for the following 28 days. Antimalarial treatment was administered immediately after malaria parasites were detected in the blood stream. Only one volunteer did not become positive for malaria during the follow up. However, malaria infection was detected later in volunteers with previous high exposure to malaria as compared to those with previous low exposure. CHMI was safe and well tolerated in this population opening the possibility to use this model to test new treatments and candidate vaccines.



Plasmodium falciparum retrospective genomics identify new functional mutants against antimalarial, Lumefantrine

We recently reported an increasing proportion of P. falciparum isolates with ex vivo tolerance to lumefantrine in western Gambia. Resistance to sulfadoxine-pyrimethamine and other quinolines remain high, with whole genome scans of the 2008 population showing strong signatures of selection around resistance markers of these drugs. Building on this evidence, we compared these earlier detected genome-wide signatures to those of current populations. We detected sustained selection in genomic regions and new loci under differential selection, possibly due to drug pressure and other antimalarial interventions. There were seven consistent sweeps across all temporal and spatial populations, and these included the strongest known P. falciparum sweep that spans the chloroquine resistance transport (Pfcrt) on chromosome 7.
Based on allele frequencies in single nucleotide variant loci between 2008 and 2014, we identified a significant shift in an allele within the cysteine desulpharase gene that is involved in iron-sulphur metabolism. The allele variant with increasing frequencies is more common in recent P. falciparum isolates with increased tolerance to Lumefantrine, the partner drug in the most widely used antimalarial in The Gambia, Arthemether-Lumefantrine (AL). This is the first evidence of an association between Lumefantrine and genetic variants in natural parasite populations exposed to drugs.



What is the long term impact of PCV13 introduction in The Gambia on transmission of vaccine serotypes?

Serotypes included cross-sectional surveys (CSS) collecting nasopharyngeal samples are a quick way to generate data to understand the circulating pneumococcal strains within a community, within the context of pneumococcal conjugate vaccine (PCV) introduction.

Nasopharyngeal carriage is asymptomatic in most individuals, but the bacteria could spread to local tissues, and cause mild disease or to more distant organs causing severe disease. We conducted a series of surveys among infants who received three doses of a 13-valent PCV and their mothers a) before PCV13 introduction (CSS1), b) 1 year (CSS2) and c) 5 years (CSS3) after PCV13 introduction.

We found a decrease of vaccine serotypes in the vaccinated infants and in their unvaccinated mothers. However, five years after PCV13 introduction, the prevalence of circulating serotypes included in the vaccine was still high and the serotypes not present in the vaccine increased in both the vaccinated infants and their mothers. Genomic analysis showed that the vaccine serotypes were more likely than the other serotypes (non-vaccine serotypes) to lose their ability to express the capsule which may be due to vaccine pressure 1.

Our wealth of data from before during and after vaccine introduction is unique in the sub-region and would contribute immensely to inform new vaccine development.

Nutrition

Overview

The year under review has seen notable highlights, as various large studies have been completed and the results are being published and publicised.

The Early Nutrition and Immune Development (ENID) Trial showed that thymic size, used as an integrated index of adaptive immune function, can be enhanced by providing infants with a multiple-micronutrient-fortified lipid-based nutrient supplement, but that providing similar supplement in pregnancy had no added benefit.

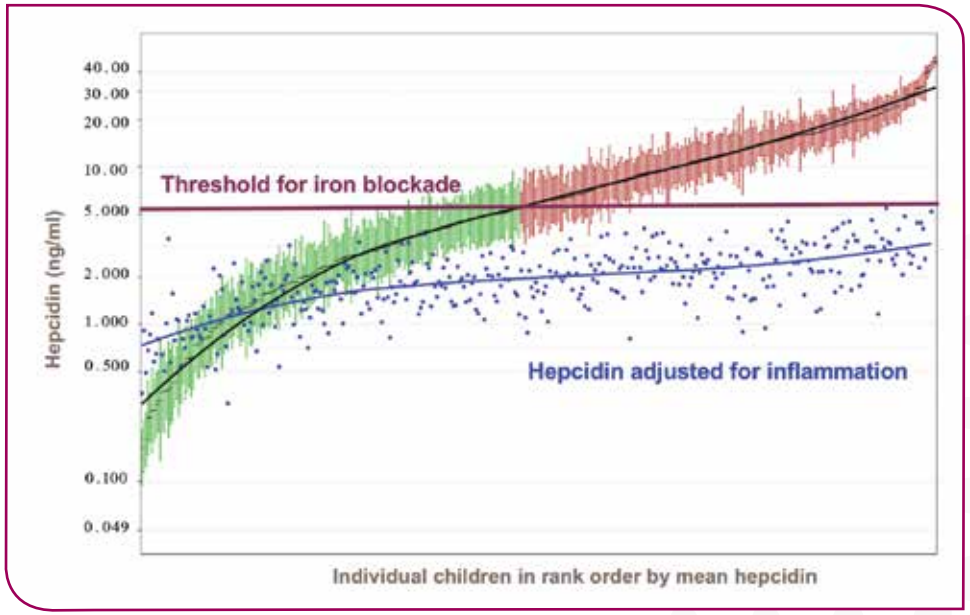
The Hepcidin and Pregnancy (HAPn) Trial showed that, disappointingly, our hepcidin-guided screen-and-treat approach to target iron to the most-needy pregnant women was not more effective than the standard approach of universal supplementation with iron and folic acid. These results support the continued implementation of the WHO recommended regimen.

Our understanding of how a mother's nutrition around the time of conception affects the baby's epigenome has been greatly advanced by our analysis of single-cell data from Chinese IVF human embryos. We have inferred that certain epigenomic regions may have evolved to sense and record nutritional and other influences from the external environment, and to adapt the fetus to be best suited to these conditions. Confirming and exploring this hypothesis is a key focus for our current work.

The Hormonal and Epigenetic Regulation of Growth (HERO-G) Study and Epigenetic Mechanisms linking Pre-conceptional nutrition and Health Assessed in India and Sub-Saharan Africa (EMPHASIS) studies have completed fieldwork, and the Brain Imaging in Global Health (BRIGHT) and Gambian Bone Ageing (GamBAS) have completed recruitment and are following up the participants.

Prof. Andrew Prentice
Theme Leader

Highlights



Many Gambian children maintain levels of hepcidin that block iron absorption – respiratory infections seem to be a major reason.

According to the latest global burden of disease estimates, iron deficiency (ID) and its consequent anaemia (IDA) are by far the most common micronutrient deficiencies worldwide; affecting about 1.25 billion people. The burden falls heavily on mothers and their young children.

A key barrier to solving this problem is the low efficacy of the oral iron in Africa. Our recently published manuscript in Science Advances suggests that as a result of a heavy burden of chronic inflammation, acute infections (particularly respiratory infections) and poor water, sanitation and hygiene conditions, children living in rural areas of The Gambia have anaemia of inflammation in addition to iron deficiency.

We hypothesize that this inflammation is causing further iron deficiency by blocking both non-haem iron absorption and iron utilization by the bone marrow. In the IDeA study, funded by an MRC Project Grant, we are investigating the effects of chronic low-grade inflammation and acute inflammation on iron absorption, iron utilization and anaemia. In addition, we are testing two new strategies for treating anaemia in young children. These strategies are designed to circumvent and modulate the inflammatory blockade of iron absorption and utilization.

New insights into epigenetic changes in the embryonic epigenome at sites sensitive to a mother's nutrition around the time of conception

In a series of studies carried out across The Gambia, we have seen that epigenetic marks at key regions of the genome appear to be influenced by seasonal changes in a mother's diet around conception. The regions known as 'metastable epialleles' (MEs) show characteristic patterns across different tissues, supporting the notion that they are established in the early embryo.

Until recently, these patterns had only been observed postnatally in humans. However, in a unique analysis, Matt Silver and Noah Kessler, bioinformaticians in the Nutrition Theme, were able to track changes at MEs by analysing public data collected from Chinese embryos obtained after in vitro fertilisation. They showed that MEs exhibit highly unusual patterns of DNA methylation at a specific stage in embryonic development, and that these changes were particularly marked at sites shown to be sensitive to season of conception in Gambians.

These changes have the potential to affect how the offspring's genes are regulated in later life which could affect health and disease susceptibility throughout the life course.

The work is published in the journal Science Advances (http://advances.sciencemag.org/content/4/7/eaat2624).

How does methylation at POMC affect the likelihood of obesity?

Obesity is a global public health concern with increasing damaging effects in low and middle-income countries (LMIC), including The Gambia. Obesity interventions are generally expensive and ineffective; therefore, prevention is key.

Pro-opiomelanocortin (POMC) gives rise to melanocortin stimulating hormone (MSH) peptides that mediate the anorectic (appetite suppressing) action of leptin in the hypothalamus. We have previously shown that a child's methylation at POMC is correlated with the mother's nutritional status around conception.

The POMC study led by MRC Clinical Research Training Fellow Dr Toby Candler, recruited nearly 1000 women and children in April 2018 for a year-long prospective study. These participants have been followed up monthly to assess seasonally driven changes in weight and adiposity. From these data, we aim to assess how POMC methylation influences weight-related outcomes and energy balance over a calendar year. We will also assess how mother's diet has influenced POMC methylation by correlating circulating specific maternal metabolites with offspring methylation. This may inform nutritional strategies to break the cycle of obesity across generations.

Capacity building for musculoskeletal sciences in Sub-Saharan Africa – Kate Ward

The Sub-Saharan Africa MuSculOskeletal Network (SAMSON) is a network co-led by Dr Kate Ward and Dr Celia Gregson (U.Bristol) (www.thesamson.org). SAMSON has members from 7 institutions across four partner countries: South Africa, The Gambia, Uganda and Zimbabwe.

SAMSON members recently published a commentary in Lancet Global Health leading a call to action for a focus on fragility fractures in Sub-Saharan Africa. The aims of SAMSON are to

(i) Build sustainable capacity in Muscu loskeletal Health Research by creating a collaborative research platform;
(ii) Share learning in Musculoskeetal Health Research through the lifecourse to reduce burden of disease;
(iii) Inform health policy, promote training, research capacity devel opment, knowledge transfer and public engagement;
(iv) Provide guidance to standardise methods for musculoskeletal assessments across Sub-Saharan Africa.

In 2018, we held two workshops: one capacity building in musculoskeletal health research and scanning methodologies (Harare, Zimbabwe); and the other to build funding applications for collaborative research (Durban, SA). SAMSON is funded through the Academy of Medical Sciences GCRF Networking Scheme (Jarjou, Ward) and from the University of Bristol GCRF funding.

Inaugural meeting of SAMSON partners in Durban, South Africa.

Vaccines & Immunity

Overview

The Vaccines & Immunity Theme (VIT) continues to implement its strategy to add maximum value to clinical trials of new vaccines and observational studies by conducting systems biology research alongside the routine collection of samples.

We are pleased to report that these efforts have already significantly increased our insights into the immune development in the first week of life via the Human Immunology Project Consortium (HIPC), as recently published in Nature Communications. Systems Biology has also helped us to unravel the reasons for the relatively poor performance of a previous version of the live attenuated influenza vaccine (LAIV) in young children (Lancet Respiratory Medicine) and led to the discovery of biomarkers that identify individuals with increased risk of developing tuberculosis (American Journal of Respiratory and Critical Care Medicine).

These projects have also provided the Theme with important training opportunities for staff at all levels, and we are particularly pleased to host prestigious postdoctoral fellowship awards, which will help our current generation of postdocs to develop scientific independence and contribute to the development of the Unit's research agenda as a whole.

Younger Principal Investigators (PI) are developing independent proposals, and are attracting funding, and international links and collaborations not only within the London School of Hygiene and Tropical Medicine (LSHTM), but also with other international partners and networks.

Our reputation for the efficient conduct of clinical trials and the ability to inform future policy decisions remain as strong as ever. We are internationally recognised for setting up a safe and efficient platform for the conduct of maternal immunisation studies. We have also developed several qualitative science studies within our work in both vaccines and tuberculosis, and our community engagement activities continue to prove valuable.

Prof. Beate Kampmann
Theme Leader

Highlights

Dr Mustapha Bittaye, trial obstetrician and Mr Buba Jadama, trial midwife, undertaking a gestational ultrasound scan.

Understanding how immunity changes in the first few days of life- the HIPC project

The Human Immunology Project Consortium (HIPC) team, led by Dr Olubukola Idoko, enrolled over 600 newborns into a systems biology study to understand the ontogeny of neonatal immunity in the first few weeks of life, in the presence and absence of vaccination.

Using just a quarter of a tablespoon of blood, transcriptomic, proteomic and metabolomic signatures are deducted using an optimised protocol which has been implemented by the dedicated team on site.

Analysis will be carried out with our collaborators in the US, Belgium and Canada. We expect to learn how to recognise correlates of protection from early "omic" signatures. Dr Alansana Darboe' s fellowship is embedded in this study and adds additional value by investigating the role of maternal antibody in innate immune signatures in this context.

Bringing a novel conjugated pneumococcal vaccine to licensure

Without doubt, the currently available conjugated multi-valent pneumococcal vaccines have already saved the lives of thousands of children worldwide, but they also represent a serious burden for health budgets.

In collaboration with PATH, recruitment, follow-up and analysis was completed for a phase 3, randomized, controlled, non-inferiority trial of a new 10-valent pneumococcal conjugate vaccine (PCV), manufactured by the Serum Institute of India Pvt Limited. The trial recruited 2,250 6-week-old infants over around 6 months, and achieved over 95% follow-up and over 99% visit window compliance.

The vaccine targets those pneumococcal serotypes most prevalent in low- and middle-income-countries. If successful, the vaccine is expected to be an equally effective but significantly less expensive PCV than those currently available. Results of the trial will be submitted to the WHO for potential prequalification of the vaccine in 2019.

A safe environment to administer vaccines to pregnant women and newborns

Neonatal mortality remains unacceptably high, with over 40% of all deaths in children under the age of five occurring in the neonatal period. The Gambia is no exception. Hence, new interventions targeted at this particularly vulnerable age group need to be tested and implemented, if found safe and effective.

One such intervention strategy is to give vaccines to women during pregnancy, to passively protect their newborns from specific vaccine-preventable infections, thanks to antibody that passes from mother to fetus via the placenta. Our team is pioneering these studies in Africa.

One example is the controlled Propel trial, in which 600 expectant mothers and their newborns have completed recruitment and follow up, with either the mother or the newborn receiving the conjugated pneumococcal vaccine. In addition, a control group of infants were immunised as per regular schedule. The primary endpoint is the acquisition of carriage in the first nine months of life. Follow-up of the newborns for pneumococcal carriage to 9 months of age is completed in early 2019. The trial, led by Dr Ed Clarke, established a safe and reliable platform for the recruitment of mothers to maternal vaccination trials at the Unit, and developed robust procedures for safety follow-up, which will continue to be used in ongoing trials of MenAfriVac and pertussis vaccines (GaPs trial) in 2019.

Rooming in on the "holy grail"- Defining correlates of risk for Tuberculosis (TB)

The TB case-control platform, led by Dr Jayne Sutherland, made a major contribution to the international multi-centre efforts to identify what determines the risk of progression from TB infection to TB disease.

A 12 year project originally funded by the Bill and Melinda Gates Foundation (BMGF) culminated in a series of high impact factor publications which have now delineated prognostic biomarkers to identify people in the community most at risk of developing TB at least 1 year prior to disease onset. The signature derived from the transcriptome was published in the American Journal of Respiratory and Critical Care Medicine (AJRCCM), and a signature derived from the metabolome was published in Nature Communications. These novel signatures are now being tested in clinical trials randomising participants in sub-Saharan Africa to interventions, guided by the signatures.

In addition to applying cutting-edge technologies to identify biomarkers, engagement with the communities affected by TB also took a significant step forward. Dr. Olumuyiwa Owolabi received a public engagement award from the LSHTM for a school-based/adolescent TB awareness campaign.

The Reach4Kids Africa project, which focuses on childhood TB, extended its preventive treatment efforts from The Gambia to sites in Nigeria, Tanzania and Mali in collaboration with their respective National TB programs. The Monitoring & Evaluation materials jointly developed for this research program are now in national use.

Can we improve the delivery methods of vaccines?

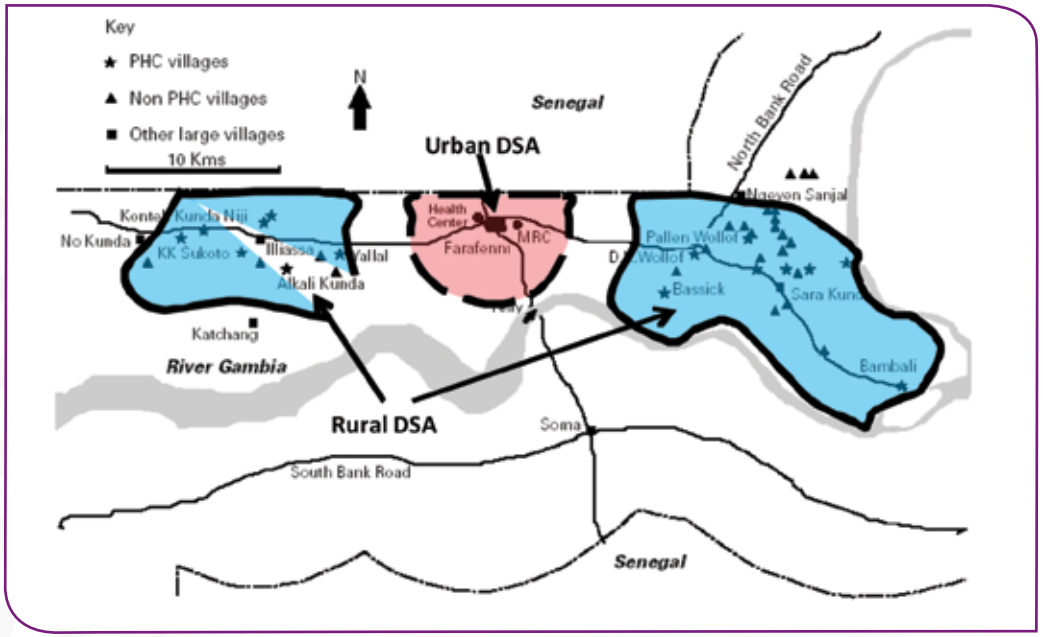
A pragmatic non-inferiority trial comparing different methods for the delivery of fractional dose inactivated poliovirus vaccine (IPV) in a community-based campaign setting was conducted in collaboration with the World Health Organisation (WHO) and the Centre for Disease Control (CDC). This is a follow-up study from our experiences with needle free delivery devices, (published in Clinical Infectious Diseases journal in 2018).

The results of the trial were presented by Dr Adedapo Bashorun to the WHO Polio Research Committee at the Rotary Club International headquarters in Chicago, in October 2018. The trial aimed to provide data to support the polio eradication endgame, and established that the delivery of IPV using the needle free devices is feasible, even in a campaign setting with high numbers of vaccines.

Maternal, Neonatal & Child Health

Promoting synergies to address pressing maternal and neonatal health across our three themes.

PRECISE



Farafenni area is represented in the figure above. Recruitment will take place at the Farafenni hospital and the antenatal care of 3 Health facilities within the Farafenni HDSS area: (i) Ngayen Sanjal, (ii) Illiasa and (iii) Farafenni.

Annually, pregnancy hypertension, fetal growth restriction (FGR), and stillbirth unrelated to intrapartum events are associated with 46,000 maternal and 2.5 million fetal, neonatal and infant deaths. Over 99% of these deaths occur in low and middle-income countries (LMICs), and over half in sub-Saharan Africa.

The PRECISE consortium was established in 2018 to address this area of neglected global health research, with an overall aim to develop a unique cohort of biologically and contextually characterized pregnant and non-pregnant women of reproductive age, to support research into placental disorders (namely hypertension, fetal growth restriction and stillbirth) in sub-Saharan Africa.

The primary objective of the observation study is to develop a unique cohort of pregnant women, to describe the extent of placental disorders in women attending antenatal care in centres representative of urban and rural African communities. Other poor delivery outcomes will also be described as part of the study. Additional objectives include to investigate socio-cultural and health system barriers preventing access, effective management and care pathways; and to investigate the potential for the introduction of novel methods to assist with the diagnosis and management of placental disorders in sub-Saharan Africa. A prospective cohort of up to 10,000 pregnant women from across three countries representative of sub-Saharan Africa: The Gambia (West Africa), Mozambique (Southern Africa), and Kenya (Eastern Africa), will be set up.

The MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine (MRCG at LSHTM) is one of the three recruiting sites of the PRECISE consortium. In The Gambia, 2,000 pregnant women (1,000 in rural Farafenni and 1,000 in Farafenni town) will be recruited during their antenatal care (ANC) visits, and followed-up until 6 weeks post-delivery to determine the prevalence of placental disorders and associated risk factors.

Clinical, epidemiological and demographical information are collected during antenatal visits, labour, and post-labour. Different biological samples are also collected at these time points to create a bio-repository. The Gambian bio-repository is managed, governed and owned by the MRCG at the LSHTM. An additional 600 non-pregnant women of reproductive age will be enrolled in the study and samples will be collected at one time-point.

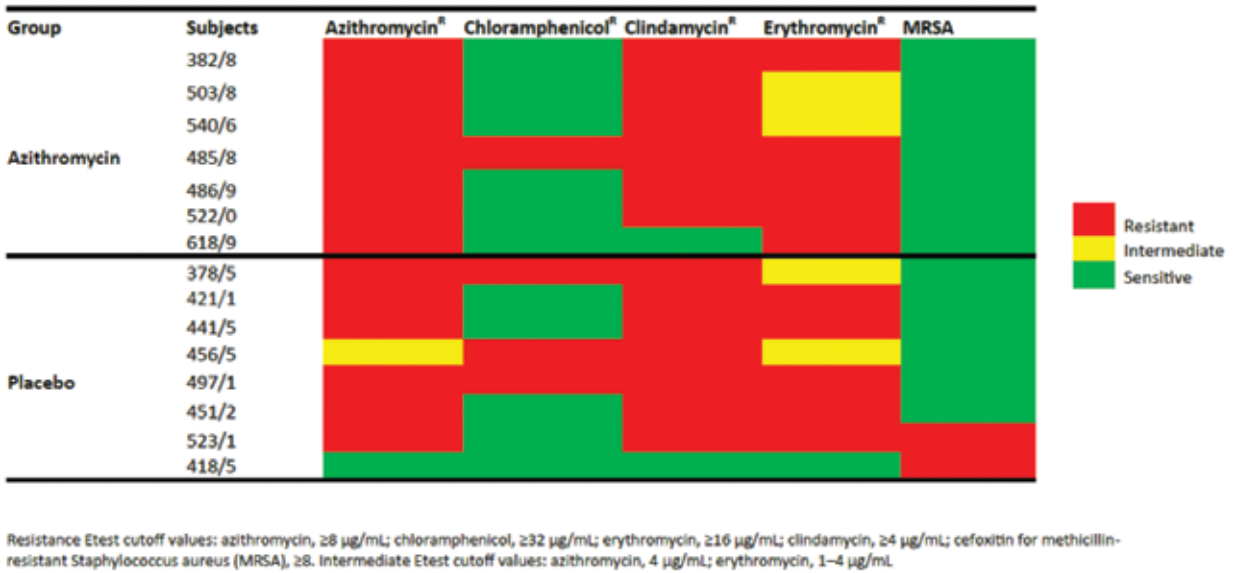
Participants at the PRECISE training

Antimicrobial Resistance

Our work on AMR, one of the greatest threats to human health, is a cross-cutting area among the different Unit themes.

ANTIMICROBIAL RESISTANCE

Azithromycin resistance after the use of prophylactic intra-partum azithromycin – The PregnAnZI trial



Heat map showing pattern of S. aureus isolates resistant to at least 1 antibiotic by trial arm (azithromycin or placebo)

Neonatal and maternal sepsis are major contributors to the high burden of mortality in sub-Saharan Africa (SSA). As the mother is an important source of infection for the newborn, an intervention that is able to decrease vertical transmission of pathogenic bacteria (mother to newborn) should substantially decrease neonatal mortality.

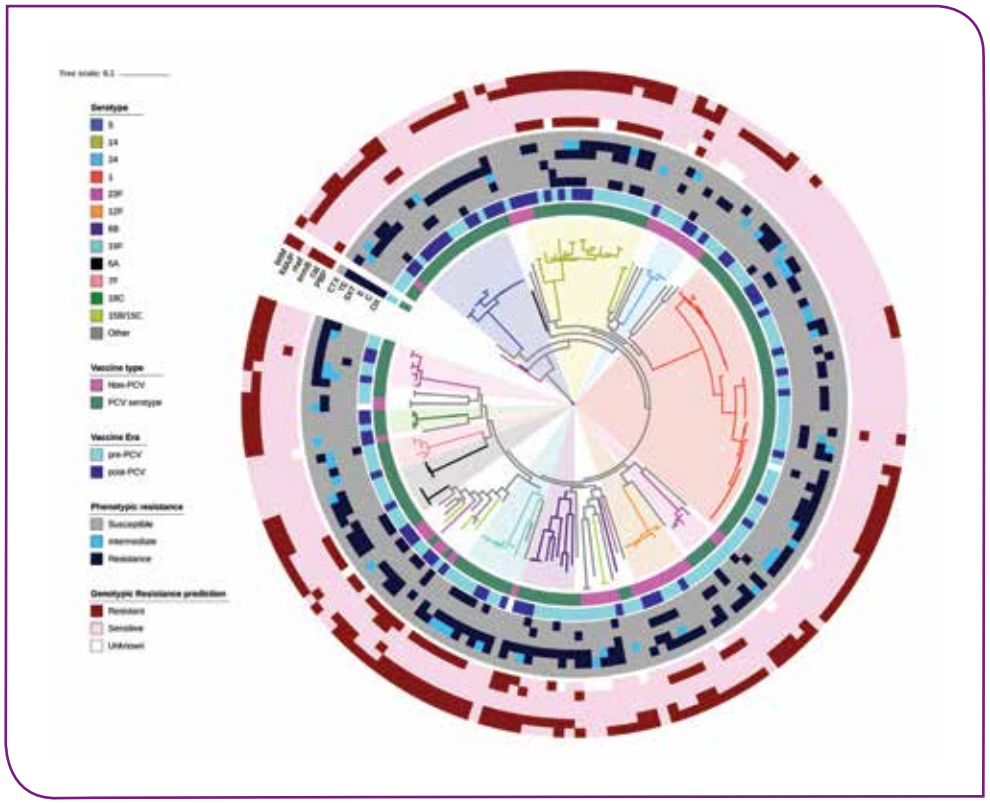
In a multi-country randomized trial, we are assessing the use of intra-partum azithromycin to reduce neonatal mortality and maternal and neonatal sepsis by reducing bacterial colonization, a necessary step for invasive disease. A former proof-of-concept trial showed that intra-partum azithromycin reduced maternal and neonatal bacterial colonization, and the occurrence of infection in both the mother and the babies.

Our proposed prophylactic intervention using azithromycin, a broad spectrum antibiotic has wide potential for additional effects, including off-target consequences, both benefits and risks. As part of the trial results, we observed that the intervention increased rates of azithromycin resistant bacteria during the four weeks following the intervention for *Staphylococcus aureus* and *Streptococcus pneumoniae*, two main bacteria responsible for sepsis.

We later conducted an ad-hoc study evaluating the long-term effect of the intra-partum azithromycin intervention on antibiotic resistance for these two gram positive bacteria (www.ncbi.nlm.nih.gov/pubmed/29608659). For this, we conducted a cross-sectional survey one year after the intervention, collecting nasopharyngeal swabs from 461 children who had participated in the trial. Results of the survey show that the prevalence of *S. aureus* azithromycin resistance previously observed during the neonatal period had returned to baseline levels, with no differences between study arms. This was also true for *S. pneumoniae* azithromycin resistance. In addition, only one isolate (from the azithromycin arm) showed resistance to both macrolides and clindamycin, suggesting constitutive resistance. All clindamycin sensitive macrolide resistant isolates had a negative D-test, indicating no evidence of inducible resistance.

Though the intervention induced a transient azithromycin resistance to S. aureus, this resistance lasted less than 12 months. Although these results for the long-term impact on prevalence of resistance of the two bacteria is reassuring, the short term observations of S. aureus strains warrant further investigation. In addition, similar studies on the effect of the intervention on gram negative bacteria are necessary.

Genomic epidemiology of pneumococcal meningitis in West and Central Africa: a decline of vaccine serotypes and increasing non-vaccine types bearing resistance genes



Antibiotic resistance profiles in the context of the whole genome phylogeny.
A phylogenetic tree with branches coloured by serotype and metadata blocks showing vaccine type, vaccine era, phenotypic antibiotic resistance patterns and predicted antibiotic resistance. Antibiotics studied include to penicillin (PBP, OX), chloramphenicol (cat, C), erythromycin (mef/ermB, E), co-trimoxazole (folP/ folA, SXT), tetracycline (tetM, TE) and cefotaxime (CTX).

Despite contributing to the heavy disease burden in West and Central Africa, little is known about the genomic epidemiology and antimicrobial resistance pattern of Streptococcus pneumoniae causing paediatric bacterial meningitis. The 13-valent pneumococcal conjugate vaccine (PCV13), has been introduced in 39/47 countries in sub Saharan Africa.

We performed a whole genome sequencing on 185 Streptococcus pneumoniae isolates recovered from paediatric meningitis cases as part of the World Health Organisation (WHO) invasive bacterial diseases surveillance in West and Central Africa from 2010 to 2016. Whole genome phylogeny was reconstructed, and antimicrobial resistance patterns were inferred from the genome. Phenotypic antimicrobial resistance testing was performed by disc diffusion.

The distribution of genotypes differed by sub-region, with the largest diversity observed in Central Africa. Phylogeographic clustering was observed within serotypes with isolates from the same sub-region clustering and sharing similar accessory genome content. Resistance genotypes appeared to be conserved within selected sub clades of the phylogenetic tree suggesting clonal inheritance. The proportion of cases due to PCV serotypes decreased from 81% to 64% in the post PCV era compared to the pre-PCV era ($\chi 2$= 8.96, p value 0.011). Among PCV serotypes 72% had at least one resistance gene compared to 85% among non-PCV serotypes. Consequently, in the post PCV era 86% of isolates had at least one resistance gene compared to 70% in the pre PCV era ($\chi 2$= 5.74, p value 0.057).

Our data shows signs that vaccine serotypes are on the decline in the post-PCV era. However, emergence of chloramphenicol resistant serotype 12F strains needs to be carefully monitored.

Antimalarial resistance surveillance and mechanisms in African malaria parasites

Malaria continues to be one of the most important public health problems in Africa. Children and pregnant women are disproportionately affected. There are recent fears that the disease is resurging, despite the increased deployment of insecticide and antimalarial drugs.

The malaria parasites in some regions of the world such as South East Asia have developed resistance to old and new drugs, while resistance to the drugs used for prophylaxis in women and children is also highly prevalent in Africa. If resistance to the new Artemisinin Combination drugs were to emerge or spread to Africa, this will worsen the patterns of increasing prevalence currently being reported in areas where the parasite was previously reported to be declining.

Two studies carried out in collaboration with the University of Ghana and the Wellcome Trust Sanger Institute (UK), are developing sensitive assays and surveying for drug resistant phenotypes and genotypes of the most common malaria parasite in Africa (Plasmodium falciparum).

New antimalarial drugs are also being tested against parasite isolates from across Africa, to determine their potency. This is in collaboration with the Medicine for Malaria Venture. It is expected that these new analyses will provide information on how parasites develop resistance to antimalarials, leading us to develop new approaches to combat them. A total of 1,500 malaria parasite isolates have been tested against 10 common antimalarials. Results have shown that malaria parasite isolates from The Gambia and Senegal are gaining new genetic mutations that are helping them tolerate the partner drugs in Artemisinin Combination Therapies. Specifically, there is increased tolerance of Lumefantrine, and this builds upon resistance to older antimalarials such as chloroquine and sulphadoxine-pyrimethamine. There is a risk of multidrug resistance in malaria in Africa. Molecular markers and benchtop cellular assays that would quickly inform resistance to drugs in infected individuals and communities will, therefore, help to guide control.

We continue to employ NextGeneration sequencing and genomic manipulation approaches to understand this phenomenon and help to identify and develop markers.

West African Collaboration

Creating platforms of resources and infrastructure to promote and develop the next generation of West African scientists.

West African Collaboration

Overview

The West Africa Research Platform (WAP) within the Medical Research Council Unit The Gambia at LSHTM works strategically to increase collaborative research and knowledge exchange between MRCG at LSHTM and partners in West Africa. In the past year, MRCG at LSHTM has signed a Memorandum of Understanding (MoU) with Institut Pasteur de Dakar, thus increasing the partners within the West Africa Global Health Alliance (WAGHA) to four, including Université Cheikh Anta Diop de Dakar (UCAD), Institut de Recherche en Santé, de Surveillance Epidémiologique et de Formation (IRESSEF), and the MRCG at LSHTM.

The key strategies for implementation of WAP include scientific collaborations, capacity building, integration of scientific research platforms (cohorts) and wider scientific engagement, advocacy and policy. The MRCG at LSHTM 2018 workplan for WAP involved reaching out to institutions from Francophone, Anglophone and Lusophone countries. Collaboration with Francophone and Lusophone (e.g. Guinea Bissau) countries is particularly critical, in order to increase research outputs from these countries. The Unit's interactions in West Africa are helping to create greater engagement amongst several research groups in the region.

Dembo Kanteh
West Africa Research Platform Coordinator

Scientific Collaborations

Institutional Alliances

In addition to the WAGHA Alliance, the Unit through the LSHTM signed a Memorandum of Understanding with Institut Pasteur Dakar (IPD), which has been in existence for over 120 years, and provides excellent complementary and additional resources, especially laboratory science. In the past year, IPD collaborated with the Unit's entomology teams to provide training and capacity support to entomology teams across the sub region, within the context of the West African Network on TB, Aids and Malaria (WANETAM) funded skills building programme.

Through the WAGHA alliance, a pump priming seed grants dedicated to intermediate investigators for the entire West Africa has been agreed. This programme will be implemented in 2019, with an aim to facilitate inter- institutional research and grants support for early career scientists and postdoctoral studnets in the sub region.

Programmes and Projects

Dr Melisa Alvarez Martinez took up a post, in March 2018, as a senior social scientist working on Maternal and Neonatal Health. To strengthen institutional collaboration, Dr. Martinez is based at the IRESSEF office in Dakar, where she is leading social work activities across the Unit. She has since built a strong network of people interested in social sciences through the social science interest group. Dr Mareme Diallo, a post-doctoral scientist, is also working with Dr. Martinez.

Dr. Anna Roca continues her work on neonatal and maternal sepsis in The Gambia. The collaboration with Centre Muraz on the PregnAnZI study continued in 2018, with the recruitment of pregnant women in six sites in Burkina Faso.

Professor Beate Kampmann continues her collaborative project with Dr Elhadji Mbaye of IRESSEF, looking at the social factors for the acceptance of vaccinations by communities. This is in addition to her work on childhood TB, with Dr Augustine Ebonyi of Jos University Teaching Hospital.

Professor Martin Antonio runs the WHO Regional Reference laboratory for invasive bacterial diseases in twelve countries in West Africa. This has been a continuous programme since 2009, and it is annually funded by the WHO.

Professor Antonio has also received funding from the National Institutes of Health (NIH)/H3Africa to study the following: the association between indoor air pollutants and the upper airway microbiota, including pharyngeal carriage of meningococcus and pneumococcus; the association between the household dust microbiota and pharyngeal microbiota; and seasonal variation in inhaled exposures and the relationship with the NP and OP microbiota

Dr Alfred Ngwa received funding from the African Academy of Sciences to study the genetic interactions between human populations and malaria parasites in different environmental settings across Africa. Collaborating sites in the sub region are in Mali and Senegal

Integration Of Platforms

The West Africa Research Platform seeks to catalyse the pulling resources aimed at establishing bigger and more efficiently utilised resources across the networks. Professor Andrew Prentice is working with collaborators at the IRESSEF and UCAD to establish a West Africa bio-resource, through the integration of biobank resources from across the institutions.

Dr. Oumar Gaye and Professor Umberto D'Alessandro are collaborating to support the Kerr Soce HDSS site, to ensure that it remains a part of the pool of resources for HDSS resources across the WAGHA Alliance. The Genomics centre and the CAN network are engaged in the development of genomics research competency in the network.

The Biomedical Engineering Team in the Unit continues to provide support for equipment handling, maintenance and acquisition across the Alliance. Within the WANETAM project, Yai-Louise Bensouda from MRCG at LSHTM and Dr Alasane Diaw from IRESSEF are assessing laboratory quality towards accreditation in six partner laboratories spread across the region, in both francophone and anglophone countries.

There is a strong partnership established between the IPD and the Unit in entomology. Staff of the department were involved in the entomology trainings held at MRCG at LSHTM ,and staff of the Unit visited IPD in July 2018 to learn relevant entomological skills. Dr Kevin Opondo had successfully won an African Academy of Sciences (AAS) placement grant to spend 3 months at IPD sometime in 2019.

Achievements

WHO Collaborating Centre for New Vaccines Surveillance (WHO CC NVS)

The Unit is designated as a WHO CC, and supports the West Africa Regional WHO/NHLS external quality control (QC) and quality assurance programme (EQAP) important for vaccine-preventable diseases surveillance.

WHO Collaborating Centre for New Vaccines Surveillance

WANETAM

The Unit's relative strength is being positively leveraged for the sister sites in West Africa. Within the WANETAM grant, a very heavy capacity building programme has been established around the TB and Malaria work packages. In partnership with Université Cheikh Anta Diop, a new World Bank funded centre on the environment, climate change and health, has been created. This programme entails the training of environmental health professionals, as well as programmes linking longitudinal health investigations to the impact of climate change. The Unit also signed up a new collaborative partnership with Institut Pasteur.

Research, Training & Career Development

Nurturing talent for transformational, professional and personal development.

Research Training & Career Development

Overview

Research Training and Career Development (RTCD) Department has been strengthened to professionally and effectively deliver on the strategic training requirements of the Unit. This allows the delivery of the training strategy through the following key objectives:

- Managing resources for targeted trainings to achieve optimal competencies and capabilities;
- Reviewing and developing training and career policies for the Unit to permit optimal use of resources and the development of individuals' career paths;
- Managing our internship program to create unique opportunity within the array of MRC Unit The Gambia expertise for students' exposure to professional pursuits that stimulate individuals' interests; and
- Supporting researcher leadership development program for PhDs and Post-PhDs.

Dr. Assan Jaye
Head of Research Training & Career Development

Highlights

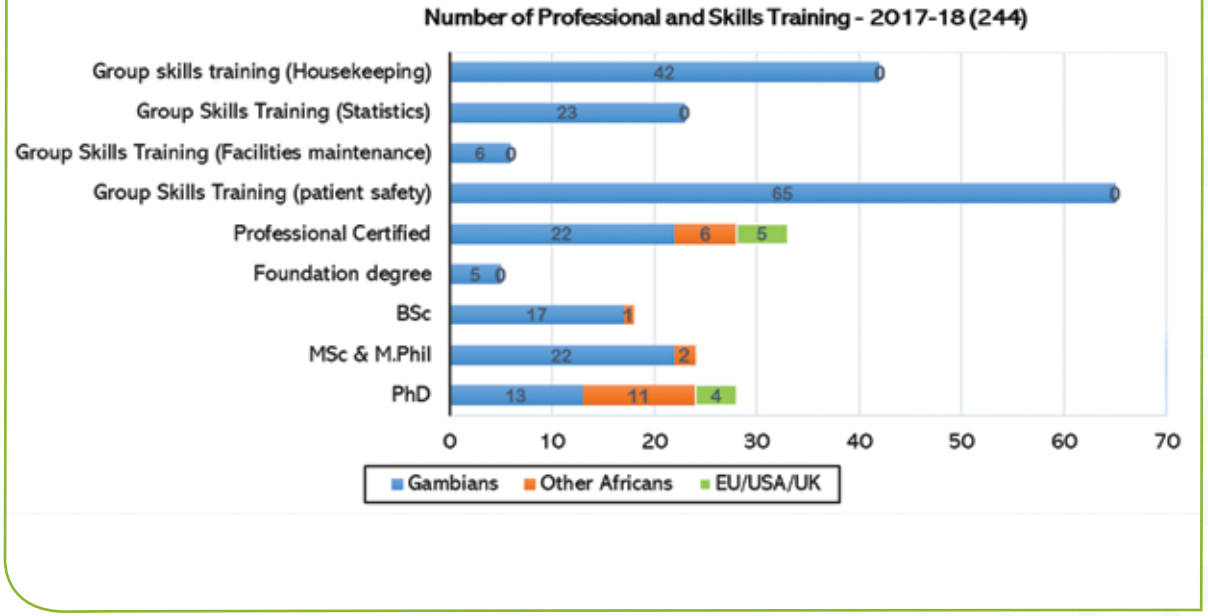


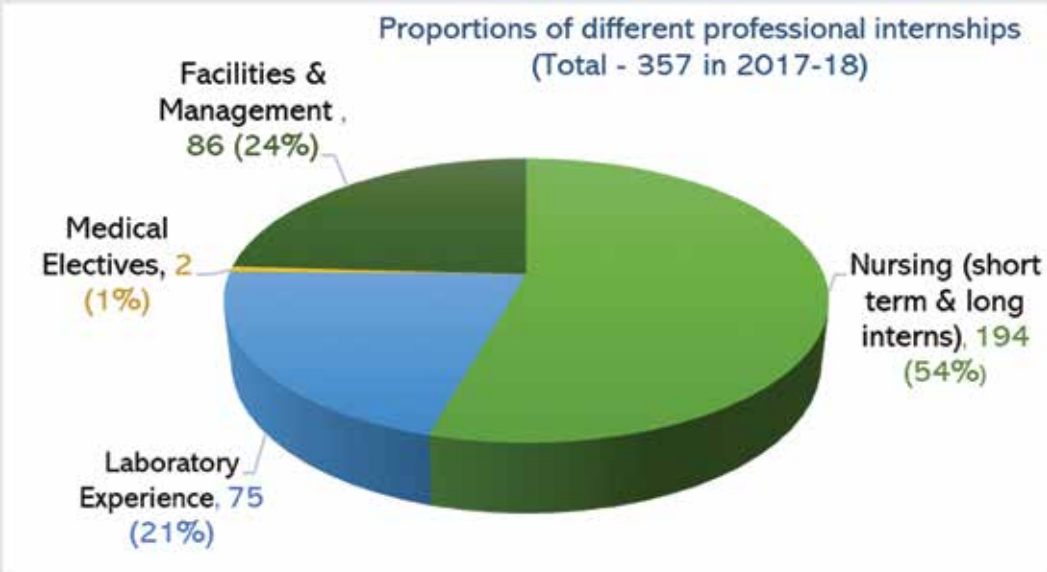
Fig. 1

In 2017-18, there was a considerable increase in the funding support and number of trainings that the Research Training and Career Development (RTCD) department provided for the professional development of staff.

The number of individual staff members who received funding for both specific skills development and academic degree qualifications were 264, higher than the number in 2016-17 (168) and 2015-16 (181) respectively. The annual fully funded PhD studentships of the MRCG at LSHTM Doctoral Training Program (DTP) were however reduced to two in 2018, to provide support to two postdoctoral (PD) 'bridging fund' for an early PD researcher development career. One of the beneficiaries was the West Africa Maternal and Child Health Program.

An average number of 28 ongoing PhD studentships made up our PhD cohort, which MRCG at LSHTM - external collaborative funded-projects added to the cohort by supporting more candidates who were funded from project grants. Eighty percent of staff doing PhDs are Africans, of which 57% are female.

MRCG at LSHTM's contribution to health research capacity in The Gambia and the Continent at large was recently highlighted in the Journal of Global Health: a landscape 2012-2017 mapping by the Special Programme for Research and Training in Tropical Diseases (TDR), as part of externally funded international post graduate trainings across health institutions in Africa. The report states that MRCG at LSHTM supported the highest number of grantees (Morel et al. Globalization and Health (2018)14:77 https://doi.org/10.1186/s12992-018-0395-0).



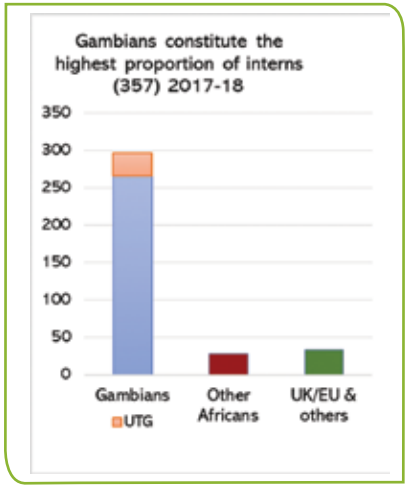
Internship Training Support: To inform Career Choice and/or for Professional Experience

The Unit also increased the number of staff members who were supported for various academic and research support specific skills training, ranging from Medical Statistics (23); Patient Safety (65); Housekeeping [cleaning & environmental maintenance] (42), and Professional Certified Training [Project management, Purchasing; Logistics and Transport; Management studies and HR, ICT and Biobanking] (33).

MRCG at LSHTM continued to offer internship experience as one of its supportive steps to developing careers in Medical and Health for aspiring young students. From 2015 to 2017, an average number of 357 interns spent 3 to 6 months of work experience at the Unit, and 85% of the interns were Gambians.

Management Leadership Training

The RTCD Department organised a 5-day in-house Certified International Business Leader training for 9 MRCG at LSHTM senior managers and researchers in October 2018. The training was conducted by the International Institute for Executive Training, with content including Corporate Strategy, Strategy Evaluation, Project Management, Performance Evaluation, Capital Budgeting, Risk Identification and Quantitative Analyses, Change Management and Implementation tools, Conflict Management and Leadership Styles.



Excellence and Innovation in Developing Students as Researchers

In September 2018, Dr Assan Jaye, Head of Research Training and Career Development, won the LSHTM Director's Award for 'Excellence and Innovation in Developing Students as Researchers' during the LSHTM Week celebrations. The award was in recognition of his role in successfully implementing a strategic approach to support training, and identify and develop bright minds in a researcher development pathway.

Successful PhD Thesis Defences 2017 – 2018

James Jafali (Malawi)
University of Edinburg UK

Computational Deconvolution Analysis of Cellular and Molecular Pathways Associated with Pneumonia Severity in Children under the Age of Five Years, from The Gambia.

Jorjoh Ndure (The Gambia)
Open University, UK

Regulatory T cell and Vaccines: Correlation or Coincidence.

Omar Janha (The Gambia)
University of Leicester, UK

Targeting the Plasmodium falciparum Cyclin-dependent Kinase like kinases (PfCLKs) family of Protein Kinases as Therapeutic Anti-malarial Drug Targets.

MRCG at LSHTM Project-based funded PhD students

Abdou K Sillah (The Gambia)
University of Munich

Impact of Adult Tuberculosis on Household Child Contacts in the Greater Banjul area of The Gambia.

Ya Jankeh Jagne (The Gambia)
Open University, UK

Exploring the interplay between innate and adaptive immune responses to live attenuated influenza vaccine in Gambian children.

Nwongbouwoh Muefong Caleb (Kenya)
Ludwig-maximilians-universität, Munich

Defining the inflammatory pathway and prognostic biomarkers associated with pulmonary morbidity and long-term outcome of patients following TB therapy

MRCG at LSHTM-MRF Gambian funded BSc and MSc - 2017-2018

The MRCG at LSHT- Medical Research Council Foundation (MRF) funded fulltime residential BSc and MSc courses, specifically for supporting Gambians in health research, ended in 2017-2018. The latest awards included the following: BSc in Global Health, and BSc Biological Sciences and Management; and MSc in Data Science, MSc in Biomedical Engineering & Health Technology Management, and MSc in Global Health & Development. The MRF funding has successfully trained a total of 16 MRCG at LSHTM Gambian staff in various aspects of the medical and health discipline, and 3 of these staff members obtained a PhD.

2017

Abdourahman Bah
BSc Global Health
Queen Mary University of London
2018 – 2022

2017

Dominic Arthur
BSc Biological Science and Management
University of Edinburgh
2018 – 2022

2018 - 2019

Mamadou Bah
MSc Global Health & Development
University College London (UCL)

2018 - 2019

Pa Kinteh
MSc Biomedical E ngineering & Health Technology Management
Keele University, UK

2017 - 2018

Pa Modou Cham
MSc Data Science
City University, LondonResearcher Leadership Development

The RTCD Researcher Leadership Development Program is beginning to yield fruits. Following the establishment of our research career structure, researcher development and research methodology frameworks, as well as a culture of mentorship, both mid-career and early career postdoctoral fellows are succeeding in attaining research grants on their own, and moving into a research leader trajectory.

Key Research Leadership Development Achievements 2017-2018

Dr. Alfred Amambua-Ngwa (Cameroon), a mid-career scientist, was awarded a £3 million grant by the Accelerating Excellence in Science in Africa (AESA) for he Pan African Malaria Genetic Epidemiology Network. Alfred is also an International Fellow at the Wellcome Sanger Institute.

Dr. Leopold Tientcheu Djomkam (Cameroon) Global Leader Award (US$ 539,205) from the USA National Institutes of Health (NIH)-Fogarty International Center (FIC). The award will allow him to extend his research into how clades of Mycobacterium tuberculosis complex migratory pathways can affect outcome of treatment.

Dr. Alasana Darboe (The Gambia) got a post-doctoral fellowship shortly after his PhD, from MRC/BBSRC via a grant to IMPRINT (IMmunising PRegnant women and INfants network) at LSHTM. He will investigate how maternal antibodies might affect the immune responses of innate cells in a new born.

Dr. Uduak Okomo (Nigeria) was awarded a Pump Priming Grant from the Wellcome Trust, and in collaboration with UNICEF, she is working on facility-based evaluation of stillbirths and neonatal deaths in The Gambia.

Dr. Madikay Senghore (The Gambia) was awarded a Disease Dynamics under the sponsorship of Professor Bill Hanage. He will continue work on Microbial Genomics focusing on population genomic analysis of bacterial species of the pneumococcus

Dr. Benoit Asogba (Benin) won a second Postdoctoral fellowship, following an MRCG at LSHTM-Deltas PD funding from the GCRF-Crick African Career Accelerator Awards. His program between MRCG at LSHTM and Crick will focus on investigating the potential of blocking mosquito reproductive processes by small molecules, thus giving insights into new ways of targeting the transmission of mosquito-borne diseases.

Dr. Togun Toyin (Nigeria) successfully moved into the position of clinical research fellow in childhood Tuberculosis (TB) at LSHTM. This follows a successful mobility Steinberg PD Fellowship in Global Health at McGill University in Canada, following his PhD at the MRCG at LSHTM. In this new position, he will support the coordination and expansion of research and training elements related to global health and implementation research in childhood TB between the LSHTM and the MRCG at LSHTM.

Dr Eniyou C Oriero (Nigeria) was awarded a Wellcome Trust DELTAS Africa (DELGEME) Postdoctoral Fellowship in 2017, after she completed her PhD at the MRCG at LSHTM. She is currently working on population genomics of Plasmodium malariae in southern Nigeria, with a particular focus on describing the prevalence, genetic diversity and population structure of the parasite species.

Research Publications

Discover the full listing of our publications during the year.

Publications

1. Long read assemblies of geographically dispersed Plasmodium falciparum isolates reveal highly structured subtelomeres. Otto TD, Bohme U, Sanders M, Reid A, Bruske EI, Duffy CW, Bull PC, Pearson RD, Abdi A, Dimonte S, Stewart LB, Campino S, Kekre M, Hamilton WL, Claessens A, Volkman SK, Ndiaye D, Amambua-Ngwa A, Diakite M, Fairhurst RM, Conway DJ, Franck M, Newbold CI, Berriman M. Wellcome Open Res Epub 2018

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4. Functional and Phenotypic Changes of Natural Killer Cells in Whole Blood during Mycobacterium tuberculosis Infection and Disease. Garand M, Goodier M, Owolabi O, Donkor S, Kampmann B, Sutherland JS. Front Immunol. Epub 2018

5. Mother's Milk: A Purposeful Contribution to the Development of the Infant Microbiota and Immunity. Le Doare K, Holder B, Bassett A, Pannaraj PS. Front Immunol. Epub 2018

6. Second-line anti-tuberculosis drug resistance testing in Ghana identifies the first extensively drug-resistant tuberculosis case. Osei-Wusu S, Amo Omari M, Asante-Poku A, Darko Otchere I, Asare P, Forson A, Otu J, Antonio M, Yeboah-Manu D. Infect Drug Resist. Epub 2018

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