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Philippa (LSHTM, London)

Timothée (Institut Pasteur, Paris)

Greetings from Gaborone!

We continue to make excellent progress with ethical and regulatory approvals. Our first Trial Steering Committee call was held on 9 October: it was productive and our four independent members (Professor John Perfect, Drs. Douglas Wilson, Andrew Kambugu and Saidi Kapiga) are very supportive of our trial.

Philippa has paid visits to Gaborone, Blantyre and Cape Town, and will visit Paris, Lilongwe and Kampala in November. She is meeting with PIs and with financial and administrative colleagues to ensure that teams are equipped for effective financial and administrative management of AMBITION funds, and prepared for the first EDCTP periodic report, due 28 February 2018.

In this issue we introduce colleagues from The University of Cape Town and from IDI Uganda —welcome to all! Additional colleagues at both sites will be recruited and introduced soon.

We also had a successful Meningitis Trials Network meeting on 12 October. It was a good introductory call and the Network will meet again in January 2018.

Best wishes, Joe



Ethical submissions and approvals

Most approvals are still in progress as per our last issue. Good news is that we received **full Ethics approval in Botswana**. Regulatory approval is the only outstanding approval before Princess Marina Hospital in Gaborone can start initiation training and procedures!

Our next planned submissions this month are in Malawi and South Africa.

Sub-studies: call for proposals!

We are collating a list of proposed sub-studies using AMBITION trial samples. Thank you to those who have already submitted suggestions! If you have **a pertinent research idea which would involve using the AMBITION samples or data**, please do get in touch with David Lawrence, Lead Clinician, at ambition@lshtm.ac.uk.

A short form will need to be completed to assess the needs and resources of your proposal. The final list of sub-studies will be approved by the Ambition TMG.

AMBITION Meningitis Trials Network

The Steering Committee of the African Meningitis Research Network met online for the first time on Thursday 12th October. Chaired by Dr. Mosepele Mosepele and supported by Network Manager Winnie Baraedi Sento, both in Botswana, representatives from AMBITION sites and other experts working in the field discussed the plans for the Network to share knowledge, expertise and research ideas about meningitis and other infectious diseases.

The first task for the Network is to compile a **situational analysis of how meningoencephalitis** is addressed and treated in each country.

Following this, the Steering Committee hope to formulate research questions and plan how to work together on future trials. Members will meet again in January 2018.

Health Economics Course, Blantyre

Almost all details are in place for the Health Economics Course, which will take place in Blantyre, Malawi, from 20—24 November. The course will be led by Prof. Louis Niessen and will be attended by at least two colleagues from each AMBITION site. Drs. David Lawrence and Nabila Youssouf will also be present

All delegates will be contacted shortly with a full schedule and with requests for dietary requirements.

The University of Cape Town (IDM)



The Institute of Infectious Disease and Molecular Medicine (IDM) was established in 2004 as a trans-faculty postgraduate research institute within the University of Cape Town. The Institute's Vision is to be "an international centre of excellence where world-class scientists work together to tackle diseases of major importance in Africa". Research is focussed upon infectious diseases (in particular HIV/AIDS and TB), non-communicable diseases such as cancers, genetic medicine and molecular medicine, including drug discovery.

The Institute's Mission is as follows:

- ◆ To conduct basic, clinical and public health research that is leading-edge and relevant to the needs of African people
- ◆ To develop indigenous scientific capacity in biomedical, clinical and public health research
- ◆ To influence health policy and practice by translating scientific discoveries and applying them in its communities
- ◆ To build partnerships with other Institutes and Centres in South Africa and elsewhere

The Institute contains 20 highly active research groups, including The South African TB Vaccine Initiative, The Desmond Tutu HIV Centre (DHTC) and the Wellcome Trust-funded Centre for Infectious Diseases Research in Africa (CIDRI-Africa). There are 32 Full, 16 Associate, 15 Affiliate and 15 Adjunct Members, 65 Postdoctoral Fellows and 230 Masters and PhD students.

Research is funded by a wide range of organisations, including the US NIH, the South African Medical Research Council, the Bill & Melinda Gates Foundation and the EDCTP, in addition to industrial partners. **Here is the AMBITION team:**

Prof. Graeme Meintjes (Principal Investigator)

Graeme Meintjes is a Professor of Medicine, an Infectious Diseases Physician, Wellcome Fellow and clinician scientist based at the University of Cape Town in the Institute of Infectious Disease and Molecular Medicine. He obtained his medical degree and PhD from UCT, and a Masters degree in Public Health from Johns Hopkins University. He is a Fellow of the College of Physicians of South Africa and the Royal College of Physicians of Glasgow. His research focuses on improving understanding of pathogenesis, diagnosis and treatment of the clinical complications that affect patients with advanced HIV disease, including HIV-associated tuberculosis, immune reconstitution inflammatory syndrome (IRIS) and cryptococcal meningitis, as well as drug-resistant TB. He has been lead or principal investigator on several clinical trials addressing treatment strategies for these conditions. His work also focusses on improving understanding of the immunopathogenesis of HIV-associated TB, specifically the immunological reactions underlying TB-IRIS and the immune phenotype associated with mortality in patients with HIV and disseminated TB.

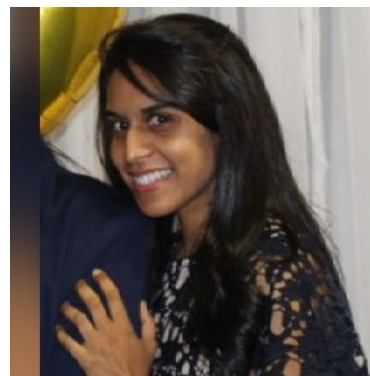


Dr. Sumaya Sayed (Sub-Investigator)

I completed my MBChB degree at the University of Cape Town in 2007. Thereafter I did my internship and community service in Cape Town. Since 2011, I have been employed as a medical officer at GF Jooste and Mitchell's Plain Hospitals - both academic hospitals.

I have been working in the Department of Internal Medicine for the past 5 years, in both a clinical and supervisory role to junior doctors and medical students.

The majority of conditions I see are HIV associated, and I have thus developed a keen interest in infectious diseases. I have obtained the SA Diploma in HIV Management in 2015. I have no prior experience in research, but I am really motivated to learn. I am grateful to have been afforded this opportunity and am really excited to be part of the AMBITION Trial team as a clinical sub-investigator at Mitchell's Plain Hospital.



Dr. Charlotte Schutz (Sub-Investigator)

I am a medical doctor and have worked in clinical research since 2009. I am interested in HIV-infection and specifically in co-infections with opportunistic infections like tuberculosis and cryptococcal meningitis. I hold an MPH in Clinical Research from UCT and I am currently working on a PhD project focusing on the determinants of mortality in HIV-infected patients with tuberculosis.

I was involved in the COAT trial at the Cape Town site as medical officer and will be a sub-investigator on the AMBITION trial. I will assist with preparations of submissions to the relevant regulatory bodies and will be involved in a supporting role for the Cape Town team throughout all the phases of the trial.



Dr. Tom Crede (Sub-Investigator)

I completed my undergraduate training at the University of Cape Town in 1994, and after a brief stint in the UK, returned to South Africa in 1998. I subsequently completed my FCP at Groote Schuur Hospital in 2004, and went on to work as a consultant at the old GF Jooste Hospital, which will be familiar to several of you involved in AMBITION. Subsequently I spent 7 years at Groote Schuur Hospital in charge of the Acute Medical Emergency Unit, before moving to run the Department of Medicine at Mitchells Plain Hospital, which is where I am based now. My main medical interests relate to acute general medicine, as well as infectious disease management in our resource constraint environment. I will be a co-investigator at Mitchells Plain Hospital.



Dr. Tania Morar (Pharmacist)

I hold a Bachelor of Pharmacy degree from Rhodes University and have worked in the UK and South Africa. I have experience in a number of aspects of Pharmacy, having worked in the Public Sector, Import and Distribution, Medical Aid Industry and the Retail Environment. With a keen interest in Infectious Diseases, I was finally able to come on board as the Associate Pharmacist with the UCT eKhayavac Research Team in December 2016 to work on the HVTN702 trial. In June I joined the Predict TB Study and am currently working on the AMBITION Phase 3 trial, having assisted with the ethics application (submitted 4 September 2017) and am busy with the MCC application (due for submission in November). I will be fulfilling the role of AMBITION Trial Pharmacist for the Cape Town site.





Infectious Diseases Institute (IDI), Kampala

The IDI was built through Pfizer funding and opened to the public in 2004. The Institute is part of the College of Health Sciences at Makerere University and runs as a semi-autonomous entity with its own grant management, finance and contractual systems.

Its main mandate is training, research and clinical care as a tertiary HIV care Centre of Excellence.

It currently provides care and treatment services to over 100,000 people living with HIV in urban and rural settings in Uganda (directly through our large clinic, and in partnership with government and non-government health facilities) which amounts to about 10% of the national effort. IDI is a national referral centre for complicated cases of HIV.

IDI has trained over 19,000 health workers from Uganda and 27 other African countries in HIV/AIDS and TB co-infection, malaria, lab services, pharmacy, systems strengthening (data management, monitoring and evaluation, grants management), and research capacity building. It has a research programme comprising over 40 projects (with over 500 articles in peer-reviewed journals to date), and is also committed to major long-term outreach programmes to build capacity across Uganda. IDI has its own comprehensive clinical data system and employs over 900 staff.

IDI's Vision is "a healthy Africa free from the burden of infectious diseases".

AMBITION study participants will also be recruited at Mbarara Regional Hospital, 270km from Kampala.

Here are some of the AMBITION team:

Dr. David Meya (IDI Principal Investigator)

Dr. Meya is a Senior Lecturer in the School of Medicine at the College of Health Sciences, Makerere University, and holds an appointment as adjunct Associate Professor at the University of Minnesota. He has been involved in clinical research of central nervous system infections and complications, with a focus on HIV Immune Reconstitution Inflammatory syndrome (IRIS), an often deadly complication of antiretroviral therapy (ART) in persons living with AIDS with opportunistic infections such as cryptococcal meningitis and tuberculosis. Dr. Meya has led epidemiological and translational research studies as well as randomized clinical trials in Uganda in collaboration with colleagues from the University of Minnesota.

Dr. Meya also has a specific interest in public health interventions to prevent meningitis at population level. He has advocated for cryptococcal antigen (CrAg) screening as a strategy to reduce deaths and hospitalizations from cryptococcal meningitis. He is currently leading efforts to initiate implementation of the national CrAg screening program in collaboration with the Ministry of Health, Clinton Health Access Initiative (CHAI), the Central Public Health Laboratories and U.S. CDC.

Dr. Meya has been the Principal Investigator on NIH R01, CDC U01, and UK MRC grants. Currently, he is a Co-PI on a collaborative clinical trial focusing on improving the clinical outcomes of HIV-infected persons with cryptococcal meningitis, the second most common AIDS-defining opportunistic infection in Sub-Saharan Africa using adjunctive sertraline (Zoloft). For the AMBITION Trial, Dr. Meya will be the lead investigator at the Infectious Diseases Institute in Uganda.



Dr. David Boulware (Co-Investigator)

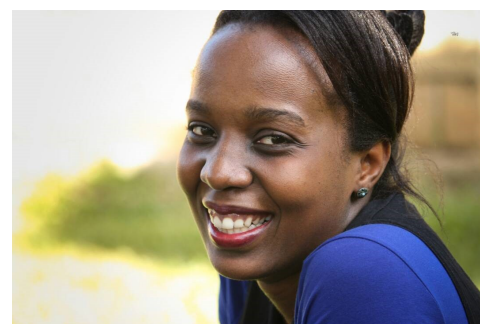
Dr. David Boulware is a Distinguished Associate Professor in Infectious Diseases at the University of Minnesota (USA) with formal training in clinical trials, public health, and tropical medicine. His primary research interests are in meningitis in resource-limited areas including diagnosis, prevention, treatment, and quality improvement initiatives incorporating cost-effectiveness analyses in order to translate knowledge into improved care. Dr. Boulware has worked with colleagues in Uganda since 2005 on cryptococcosis, and will work with AMBITION protocol implementation in Uganda. Dr. Boulware has active research collaborations in Uganda, South Africa, and Ethiopia leading a multidisciplinary, international research team. A notable quotation of his is "Cryptococcus is too neglected to be considered a neglected disease."



Dr. Lillian Tugume (Medical Officer)

I have been working with the "Meningitis group" at the Infectious Diseases Institute since 2014; shortly after I graduated with MBChB from Makerere University College of Health Sciences. I joined the team as a Research Medical Officer for the recently concluded Adjunctive Sertraline for Cryptococcal Meningitis (ASTRO-CM) trial and my major role was clinical. I have a keen interest in developing a career in academia particularly in the field of Epidemiology and Biostatistics. I am currently pursuing graduate training in Public Health to that effect.

My major roles on the AMBITION trial will be screening and enrolling study participants and providing ongoing clinical care alongside the rest of the clinical team.



Dr. Kenneth Ssebambulidde (Study Doctor)

I recently graduated with a Bachelor's degree in Medicine and Surgery (MBChB) from the College of Health Sciences, Makerere University in Uganda. Shortly after my internship training, I had an opportunity to work as a Medical Officer on the Adjunctive Sertraline for the treatment of HIV associated Cryptococcal Meningitis (ASTRO-CM) trial that has just been concluded. As a result, I have gained a wealth of experience in Cryptococcal meningitis clinical care and comprehensive HIV care in general.

I am intrigued by the innate immune responses to *Cryptococcus neoformans* specifically complement system and antigen presentation. I hope to further my immunology interests by delving into the world of vaccine development in the near future.



Abdu Musubire (Study Doctor)

I received my Bachelors of Medicine and Bachelor of Surgery (MBChB) from Mbarara University in 2000. From 2001 to 2005, I served as a medical officer at Kibaale District Health Centre IV clinic in western Uganda, where I participated in several HIV related activities that included a baseline qualitative and quantitative survey for HIV services in Kibaale district. I also trained as a national trainer in the integrated management of Adolescent and Adult Illnesses (IMAI) that paved the way to the national rollout of antiretroviral therapy (ART).

In 2005, I moved to Makerere University where I completed a Masters of Medicine (M.Med) in internal medicine in 2011, and worked on several cryptococcal research studies at IDI, including the COAT and ASTRO-CM trials. Since 2008, I have served as an attending physician on the neurology ward at Mulago National Referral Hospital. As part of this, I teach both medical students and postgraduate physicians in general internal medicine and neurology. I am particularly interested in inflammatory and infectious diseases of the nervous system. I am a former Forgyat fellow and am currently conducting research on the causes and clinical outcomes of patients with non-traumatic spinal cord injury presenting to Mulago National Referral Hospital.



Darlisha Williams MPH (Project Manager)

I have been living and working in Uganda since 2011 as the study coordinator for the University of Minnesota's cryptococcal meningitis clinical trials. I began my time in Kampala working on COAT (the Trial for the Optimal Timing of HIV Therapy after Cryptococcal Meningitis), followed by the ASTRO study, which investigated the utility of using adjunctive sertraline therapy for the treatment of cryptococcal meningitis.

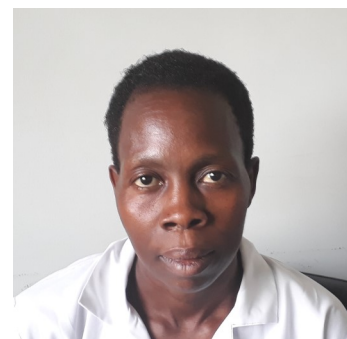
I received my master's in public health and epidemiology from the University of Minnesota and have worked previously with the Centers for Disease Control and Prevention, and the World Health Organization on immunization projects in Tanzania.

As the AMBITION project manager in Uganda, I will oversee the day-to-day activities on site as well as manage the data collection and logistics. I look forward to meeting everyone working on this important study.



Jane Frances Ndyetukira (Study Nurse)

I am a Registered nurse with 19 years of experience in Nursing and Midwifery. I have been working as a senior nurse in Cryptococcal Meningitis clinical studies since 2010. This includes the Cryptococcal Optimal ART timing (COAT) Study from 2010 to 2012 and more recently the Adjunctive Sertraline for Cryptococcal Meningitis (ASTRO-CM) study from August 2013 to October 2017. I have special Interests in counselling and Health Education, and I am currently pursuing a Bachelor's Degree in Public Health to further these interests.



Cynthia Ahimbisibwe (Study Nurse)

I am a Registered nurse with 10 years of experience in Nursing and Midwifery. I have been working as a nurse in Cryptococcal Meningitis clinical studies since 2010. This includes the Cryptococcal Optimal ART timing (COAT) Study from 2010 to 2012 and more recently the Adjunctive Sertraline for Cryptococcal Meningitis (ASTRO-CM) study from August 2013 to October 2017. I have special Interests in counselling and Health Education and a Bachelor's Degree in Community Psychology to assist me to achieve this.

My major roles in the ambition study will be consenting study participants, giving general nursing care including clinical monitoring, administering medications, completion of Case Report Forms and follow up of participants to ensure minimal loss to follow up. Additionally, I will be giving general oversight to ensure that all study procedures are completed accurately at each visit.



Andrew Akampurira (Medical Laboratory Technologist: Microbiology)

I work with Makerere University, College of Health Sciences, the Department of Microbiology and the Infectious Diseases Institute, have been working with College and IDI for 10 years. I have worked as Medical Laboratory Technologist - Microbiology in the following studies: IRIS, COAT, NOAT, ORCAS, ASTRO and now AMBITION. I will act as Medical Laboratory Technologist - Microbiology, performing all microbiology laboratory assays and other laboratory disciplines as per the study protocol. I am interested in prevention, improved care and patient management.



Alisat Sadiq (Study Counsellor)

I have formal training in HIV AIDS related counselling. I kick-started my counselling career as a study counsellor for the Cryptococcal Optimal ART timing (COAT) Study from 2010 to 2012 that was enrolling Anti Retro- viral Therapy (ART) naïve patients only. I later worked as a counsellor in the Adjunctive Sertraline for Cryptococcal Meningitis (ASTRO-CM) study that enrolled both ART naïve and experienced patients from August 2013 to October 2017. Over the years, I have developed an interest in understanding and exploring the unique counselling needs of AIDS patients either failing on ART or presenting late with Stage IV disease including Cryptococcal Meningitis.



My colleagues know me as the person who “never fails to consent a patient!” My major roles in the AMBITION study will therefore be administering consent to study participants and ensuring minimal loss to follow up. I will also look out for the overall social welfare of study participants that may interfere with compliance to study procedures.