

In this issue:

- Thank you for attending our first Investigators' Meeting
- Updates since the meeting
- Welcome to our colleagues from Liverpool!

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Thank You!

Thank you to everyone who attended the launch meeting one month ago. It was great to have nearly everyone in Gaborone and to learn more about each AMBITION partner. We had some fruitful discussions and are looking forward immensely to the months and years ahead!

Updates since the meeting:

- We now have a **finalised protocol**: thanks to all for your comments.
- **Full LSHTM Sponsorship** has been obtained, and AMBITION has been registered on the ISRCTN database. The registration number will be circulated shortly.
- We hope that LSHTM will issue **ethical approval** on 15 July, following which the regulatory applications for other sites will be made. Nabila will liaise with sites to help draft these applications.
- We are making progress with **building the database**, and are looking forward to planning SIVs for the coming months.
- The **Consortium Agreement and Clinical Trial Agreements** are almost ready to be signed by all partners, following which we will transfer the pre-financing payments. Thank you very much to those who have finalised their input. If you have queries outstanding, please do liaise with LSHTM's Contracts Office (Luzia.deAlmeida@lshtm.ac.uk) as soon as possible.



Thank you to all who attended the first Investigators' Meeting at Sanitas Nurseries & Garden Centre!



European & Developing Countries
Clinical Trials Partnership



The Liverpool School of Tropical Medicine (LSTM)

The Liverpool School of Tropical Medicine was established in 1898, with a donation from shipping magnate Sir Alfred Lewis Jones following a number of people being admitted to local hospitals with 'tropical' diseases. The site has occupied its current location since 1920, and in 1921, an affiliated laboratory was established in Sierra Leone. Today LSTM continues its tradition of developing strong links with and supporting research overseas institutions, including the Malawi Liverpool Wellcome Trust Clinical Research Programme, which will be an AMBITION recruiting site.



LSTM offers a varied postgraduate programme covering taught Masters, short courses and research degrees. Research spans basic laboratory work, translational research and policy interventions. LSTM recently announced plans to join forces with the University of Manchester's Humanitarian Conflict & Response Unit to establish an educational programme to enrich the skills of field-based personnel working for Médecins Sans Frontières.

Here is the LSTM AMBITION team:

Professor David Laloo (Senior Investigator)

I am Professor of Tropical Medicine and Dean of Clinical Sciences and International Public Health at the Liverpool School of Tropical Medicine. I am also Director of the Liverpool Glasgow Wellcome Trust Centre for Global Health Research and the Wellcome Trust Clinical PhD Programme, and am heavily involved in guiding and supporting the careers of young UK and African scientists. I am an academic clinician in Tropical Medicine and Infectious Diseases with a major research interest in clinical trials in resource poor settings, particularly in HIV and associated infections, malaria and envenoming. I also run a number of multidisciplinary research projects in HIV and malaria. I have a longstanding interest in treatment and prophylaxis of cryptococcal disease, and will be responsible for the Blantyre site for AMBITION. I will also sit on the Trial Steering Group.



Professor Shabbar Jaffar (Senior Investigator)

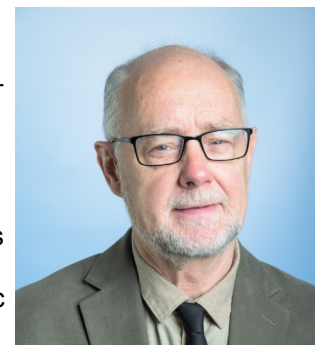
I am a Professor of Epidemiology and the Head of International Public Health at the Liverpool School of Tropical Medicine, where I have been for a whole two years. I was at LSHTM for over 20 years before this. I have lived in The Gambia for 3 years and in Uganda, Malawi and South Africa for about a year each.

I am a HIV clinical trialist. I trained in maths and statistics and then did a PhD on the natural history of HIV-infections in Africa. I have worked with Tom Harrison, Angela Loyse, Sile Molloy and Joe Jarvis for longer than I can remember, including supporting them on the AC-TA trial, and with the early phase Ambition study. With St George's and colleagues in Tanzania and Zambia, we did the large trial of cryptococcal antigen screening combined with pre-emptive antifungal treatment, which published in the Lancet in 2015. Before that, I worked on a large trial of home-based HIV care in Uganda for 5-6 years. I have started to drift a bit and now have an interest in diabetes and cardiovascular disease control but my focus will always remain HIV, particularly prevention of late-stage mortality.



Professor Louis Niessen (Senior Health Economist)

Professor Niessen's research focusses on the importance and contributions of tropical medicine and international health from the societal perspective, across the globe, addressing infectious and chronic diseases, well-being, and poverty. Professor Niessen leads research and teaches on effectiveness, efficiency & equity impact of health system interventions & health services. This is to support social policy, environment, public health, and health care policies, including inequalities, in international health and health technology assessment. His research includes real-life experiments, statistical / mathematical models, systematic reviews and covers epidemiology, public health & population research, economics & economic evaluation, including preference research.



He is the founding professor of the LSTM economics group and collaborates with over ten country teams in Sub-Saharan Africa and in the Hopkins and Erasmus universities, the Karolinska Institute, and other academic groups. He is a lead author of a new Lancet Series on Poverty and Disease. Prof. Niessen is a professor in international health and holds a LSTM Chair in Health Economics and is an Adjunct Professor at the Johns Hopkins School of Public Health and a former NIH-funded Centre Director at icddr, Bangladesh. His postgraduate students include economists, social scientists, and health professionals.

Professor Duolao Wang (Senior Statistician)

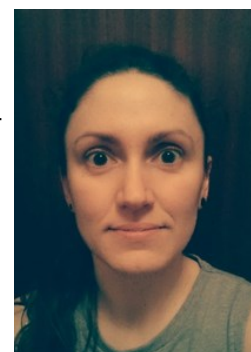
I am Professor of Biostatistics at the Tropical Clinical Trials Unit, Liverpool School of Tropical Medicine. I have over 30 years' experience in pharmaceutical trials and clinical research. I have designed and/or analysed more than 50 Phase I/II trials including first-in-man, pharmacokinetic, pharmacodynamic, bioequivalence, food interaction, bridging, dose-escalation, dose proportionality, thorough QT, dose finding studies, etc. I have also been involved in over 50 Phase III/IV trials including CHARM programme (Cardiovascular drug), RECORD (Diabetic drug, published in NEJM), PARTNER Cohort B and A trials (Cardiovascular devices, three publications in NEJM), Beating Heart Study (Surgery, published in NEJM), ACE (Diabetic drug), CHAMP trial (Cognitive behaviour therapy, published in the Lancet), ZACTIMA trials (Anti-cancer drug, published in the Lancet Oncology), PLACIDE trial (Probiotics, published in the Lancet), WHO Abortion trial (Medical abortion drug and services, published in the Lancet), CAPS trial (Cooking Stove, Published in the Lancet), Pyramax trials (Malaria drug), and Tafenoquine trials (Malaria drug).



As Senior Statistician for AMBITION I will work alongside Shabbar and Laura to conduct the statistical work and analyses for the clinical trial.

Ms. Laura Collett (Statistician)

I recently joined Liverpool School of Tropical Medicine as Medical Statistician within the Tropical Clinical Trials Unit. My research interests have included the statistical design and analysis of clinical trials, particularly multi-stage multi-arm designs, with emphasis on survival analyses. As a trial statistician on AMBITION, I will participate in the TMG, providing statistical advice on the case record form and database development, provide safety and toxicity monitoring to the DMC, carry out statistical analysis, and input into the reporting of trial results.



The University of Liverpool (UoL)

The University of Liverpool was founded in 1881, and has a long history of collaboration with other research-intensive institutions. Its alumni include Nine Nobel Peace prize winners, and it is currently ranked in the top 1% of universities worldwide. It is home to 33,000 students, including those studying at The Liverpool School of Medicine, which predates the University itself, and which is one of the largest medical schools in the UK. The University is home to many collaborative scientific Centres of Excellence, including the North West Cancer Research Centre, the North West Hub for Trials Methodology and the Wellcome Trust Liverpool Glasgow Centre for Global Health Research.



Professor William Hope (Senior Investigator)

William Hope (BMBS, FRACP, FRCPA, PhD), is Professor of Therapeutics and Infectious Diseases at the University of Liverpool in the UK. Professor Hope is a Fellow of the Royal Australasian College of Physicians and a Fellow of the Royal College of Pathologists of Australasia. Professor Hope qualified in Medicine in 1991, before undertaking specialist training in infectious diseases and clinical microbiology. He completed his PhD in antimicrobial pharmacology in 2006, while undertaking fellowships at the University of Manchester, UK, and the National Institutes of Health, Bethesda, USA. He was an NIHR Clinician Scientist, and this award focussed on individualised antimicrobial therapy. Professor Hope leads the newly formed Centre for Antimicrobial Pharmacodynamics, which provides the pharmacodynamic packages for new antibiotics. Areas of special interest and research are antimicrobial pharmacokinetics and pharmacodynamics, antimicrobial drug development and individualisation of antimicrobial therapy. He is a Fellow of the American Academy of Microbiology and is Medical Guideline Director for the European Society of Clinical Microbiology and Infectious Diseases.



The Antimicrobial Pharmacodynamics and Therapeutics laboratory will help in the design, conduct and analysis of the pharmacokinetic-pharmacodynamic sub-study to help characterise dose-exposure-response relationships.

Dr. Katharine Stott

I am a specialist medical registrar in clinical pharmacology and therapeutics in Liverpool, UK, but will be based in Malawi as of the autumn. I am currently undertaking a PhD funded by the Wellcome Trust and supervised by Professors William Hope and David Lalloo. My PhD will investigate the mechanism of action of abbreviated amphotericin B in the treatment of cryptococcal meningitis and will include a pharmacokinetic/ pharmacodynamic substudy of the AMBITION trial. I plan to construct a pharmacodynamic model to understand the contribution of each AMBITION trial drug to fungicidal activity using data from clinical samples collected at the Malawi trial site. I will also address my study question by examining cryptococcal subpopulations in the cerebrospinal fluid of patients with cryptococcal meningitis and by using an animal model to assess the tissue distribution of amphotericin B.



My colleague **Sarah Whalley** is the Bioanalyst based at UoL who will work on AMBITION sample analysis.