



SCHOLARSHIP REPORT

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SECTION 1 PERSONAL AND AWARD DETAILS			
Title	Dr	PID	56611
Surname	Smith	Forename(s)	Christopher
Scholarship/award awarded	College Travelling Fellowship	Amount awarded	£2000

SECTION 2 PROJECT/VISIT DETAILS	
Name/Title	Clinical Research Internship
Location	Malawi-Liverpool-Wellcome Trust (MLW) Clinical Research Programme
Aims and objectives	<ol style="list-style-type: none">1. Undertake a one-year voluntary clinical research internship in Blantyre, Malawi at MLW, one of the Wellcome Trust's renowned Major Overseas Programmes.2. Act as study coordinator for 2 independent research studies conducted within the Salmonella and Enteric Disease Group, under the supervision of Principal Investigator Professor Melita Gordon.3. Develop study protocol for both studies.4. Submit ethics applications for both studies to local (COMREC) and international (University of Liverpool; Johns Hopkins University) ethics boards.5. Provide grant management for both studies.6. Assist in research staff recruitment and training for both studies.7. Receive formal training in health economics research methodology.8. Deliver regular research group meeting presentations on the preparation and conduct of both studies.9. Gain skills and experience required to effectively conduct research studies in a low-income, resource-poor global health setting.10. Plan protocols for data collection, processing and analysis, including planning for data dissemination locally and in peer-reviewed open access resources.

Summary

Include methodology, results and conclusions if applicable

1. 'Estimating the economic burden of typhoid fever in children and adults in Blantyre, Malawi: a costing cohort study.'

Typhoid fever affects an estimated 12-27 million people worldwide annually, resulting in 129,000-223,000 deaths. At present, there is a significant lack of longitudinal data detailing the economic impact of typhoid on Malawian families, the healthcare system and society as a whole.

Recently, a new generation of Vi-conjugate vaccines have become available and human infection models show the vaccine to have an efficacy of 87% against clinical disease. Data describing the economic burden of typhoid, coupled with data on the potential cost of future typhoid vaccination programmes, would allow modelling of typhoid vaccine cost-effectiveness. This is urgently needed to guide policy makers and direct the implementation of typhoid vaccination campaigns in Malawi. This costing study aims to evaluate the costs of typhoid to households and the healthcare system in Blantyre District, Malawi, and is the largest costing study of typhoid disease burden in Sub-Saharan Africa to date.

S. *Typhi* blood culture positive participants will be identified and interviewed for detailed information on cost of illness. Subsequent follow-up visits at 30- and 90-days after discharge will be conducted to collect post-discharge costs and assess household income and expenditures. Detailed individual health facility costing is important to calculate the full cost to the healthcare system and important for cost-effectiveness evaluation from a government provider perspective. These data will allow us to determine household costs associated with the illness episode, information that is critical for calculating the full societal cost of illness potentially avertable by vaccination.

Recruitment is taking place at 3 sites:

- Queen Elizabeth Central Hospital, a large national referral hospital in Blantyre which provides free health care to residents of the Southern region of Malawi.
- Ndirande Health Centre, the largest health centre in Blantyre, which includes onsite first referral level inpatient capacity. Services a highly-dense population centre in Blantyre, and is the source of much typhoid in existing surveillance.
- Zingwangwa Health Centre, moderately sized urban primary clinic, servicing a large dense population surrounding the clinic.

Over the course of my internship, I have constructed the study protocol for this study in conjunction with the international PI (Dr N Bar-Zeev, Johns Hopkins University). This has been a multi-stage process, with regular communication with other partners conducting similar cost of illness work in Bangladesh and Nepal (as part of the TyVAC consortium). This process has been difficult, as I am new to the area of health economics research, and has been a steep but rewarding learning curve. At present, we have secured ethical approval locally and internationally, pending minor alteration to the study recruitment procedures. We are currently recruiting and training study staff including research nurses and field workers for data collection. Training is being delivered with the assistance of a Malawian health economist colleague, currently undertaking a PhD through LSHTM. Recruitment is intended to continue over the coming 12 months, during which we aim to recruit approximately 250 study participants. This sample size is anticipated to be more than adequate for our intended primary and secondary objectives. Upon study completion, I will hold responsibility for data management, analysis and summary for dissemination by means of submission to international conferences, and a manuscript for submission to an open-access peer-reviewed journal.

2. Cryptosporidium Diarrhoea Amongst Adults in Blantyre District, Malawi.’

This prospective case-control study aims to investigate the prevalence of Cryptosporidium diarrhoea within a cohort of adults presenting with a primary diagnosis of diarrhoea (3 or more loose stools in 24 hours). Comparing diarrhoeal patients with matched controls, we aim to determine the prevalence of Cryptosporidium amongst symptomatic and healthy individuals. Furthermore, by means of multiplex-qPCR (TAC cards), we will assess for 18 other potential bacterial, viral or parasitic causes of diarrhoea and asymptomatic carriage within this cohort.

This study has been developed on the background of a previously conducted cross-sectional survey (2016), during which the case-participants were recruited and analysed. Results from this study revealed a complex-array of organisms detected, with multiple participants having >1 organism detected by qPCR. In some instances, as many as 13 separate organisms were detected, and this complexity showed no correlation with HIV status or WHO disease staging. This case-control study therefore aims to further clarify the likely organisms responsible for symptomatic disease, by means of stool analysis from asymptomatic matched controls.

Recruitment is taking place at QECH and Ndirande Health Centre, the characteristics of which are mentioned above. Healthy controls will be age and sex-matched, in addition to matching for proportion of HIV positivity (80% in original cohort). There remains difficulty in matching by HIV stage, as chronic diarrhoea is in itself a WHO staging criteria. Recruitment of healthy participants has also been purposefully postponed until July-Sep 2018, in order to match the previous recruitment cycle, to account for the seasonality of diarrhoeal illness. Our recruitment inclusion and exclusion criteria have been adopted from the GEMS study (Global Enteric Multicentre Study), a landmark case-control study which investigated the leading causes of moderate-severe diarrhoea in children at 7 sites in Africa and Asia.

We have gained ethical approval for the study protocol amendment and have study staff recruited and trained ready to commence recruitment at the appropriate time point. I have also been actively involved with preparations with the MLW laboratory staff for sample collection, storage, transport and analysis, having written the laboratory procedures and SOPs.

Upon completion of sample lab analyses, I will hold responsibility for the final data analysis and drafting of manuscript for dissemination of data and findings.

Learning outcomes

Detail here how the aims and objectives were met

My internship at MLW has been an immensely rewarding experience, which has enhanced my commitment to pursuing a clinical academic career in infectious diseases and tropical medicine. I have gained a wealth of experience in the conduct of clinical research studies in a low-income global health setting.

The primary benefit of this year has been the opportunity to take ownership of a study, from inception through to protocol development, ethics application and study set-up. Although neither study has reached completion, I am now able to maintain regular contact with the study teams based in Malawi and provide an active role with data collection and analysis. I will also aim to travel back to Blantyre over the coming year at key points to maintain my role as study coordinator.

I have gained an appreciation for the vast amount of work required to provide oversight for all aspects of day to day management of a research study, including the importance of

	<p>judicious time management, clear communication, and clearly defined objectives and aims which are achievable.</p> <p>Throughout this post, I have worked closely with an international group of collaborators from Liverpool, Malawi, the US and Asia. This has provided strong networking skills and given me an appreciation of how particular problems can be approached from different perspectives to achieve a solution.</p> <p>I have also delivered regular presentations to both my immediate research group, and the wider MLW organisation, enhancing my presentation skills and ability to develop scientific problem solving.</p> <p>Finally, although this internship has primarily been an academic post, I have managed to maintain 1 day a week clinical commitment as a medical registrar in Queen Elizabeth Central Hospital, the co-located tertiary care facility. This has provided excellent clinical experience in managing patients with a range of tropical infections (HIV, TB, Malaria) and non-communicable diseases in a low-income poorly resourced facility with limited diagnostics or therapeutics.</p>
<p>Evaluation <i>How has this scholarship/award impacted on your clinical/NHS practice or equivalent?</i></p>	<p>I have gained a wealth of new academic and clinical experience throughout this venture, confirming my aspirations to work as an infection clinical academic. I have worked with an inspirational group of colleagues and academic leaders and received exceptional mentorship from both local and international staff.</p> <p>Based on this experience, I have gained first hand insight as to how research conducted in Africa can benefit the local population, and drive to improve outcomes for those affected by conditions less commonly seen in UK practice.</p> <p>Several colleagues at MLW were undertaking global health PhD fellowships via the Wellcome Trust and other research funders. I am now certain of my goal to obtain such a fellowship in future to return to Malawi and build upon the work I have started.</p> <p>I am immensely grateful to the RCPSG for their generous support, without which this internship would not have been possible. I would also like to extend my gratitude to all my supervisors and colleagues from MLW, Liverpool School of Tropical Medicine and international collaborators.</p>



Malawi-Liverpool-Wellcome Trust Clinical Research Programme Campus



Salmonella and Enteric Disease Research Group



Working with Dr Nedson Kamwana in the Medical Department of Queen Elizabeth Central Hospital

SECTION 4 | EXPENDITURE

Breakdown of expenditures	<p>Visa – USD 150 (x2) – re-entry after 6 months</p> <p>Malawi Medical College registration – USD 300</p> <p>Return Flights GBP 800 (x2)</p> <p>Rent in Country – USD 2500 (10 months)</p>
<i>Please demonstrate how the scholarship/award funding was used to support your project/visit</i>	

SECTION 5 | PUBLICATION

Scholarship/award reports may be published in College News. Please tick here if you agree to your report being published.	<p>Yes - I give permission for my report to be published in College News</p> <p><i>If your report is selected for publishing, the editor of College News will be in touch to discuss this with you.</i></p>
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