Drivers of Resistance in Uganda and Malawi: The DRUM Consortium

Grant title: MR/S004793/1

Final Report July 2022

1. Summary of the major outcomes of this award

DRUM was established to transform our understanding of the drivers of Antimicrobial Resistance (AMR) in Southern and Eastern Africa and enable the design of interventions to mitigate AMR spread by determining specific drivers of transmission. The DRUM consortium began as a £3 million interdisciplinary programme of work to address how human behaviour and antibacterial usage in urban and rural Africa leads to the transmission of AMR amongst E. coli and K. pneumoniae in humans, animals and the environment and influences the clinical impact of drug-resistant bloodstream infection (DR-BSI) in humans.

The consortium has since attracted significant further grant funding, including a GCRF AMR Clusters Grant, *Enabling optimal antimicrobial use in East Africa* (reference: EP/T024984/1); total budget of £151,039. Through LSTM's iiCON project, funds were awarded from UKRI and Unilever for *Tracking anti-microbial resistance across care settings in Liverpool (TRACS)*; total value £1,542,068. Prof. Nicholas Feasey's NIHR Professorship grant, *Preventing Healthcare Associated Infection and Antimicrobial Resistance* in Africa, brings additional funding in the total amount of £2,730,579. Another project called *Antimicrobial Stewardship in Hospitals, Resistance Selection and Transfer in a One Health Context* had a total budget of £604,731.

We are currently working with large, complex datasets to develop agent-based models that will enable us to predict how these transmission pathways can be interrupted.

Figure 1: Visual Minutes from the final DRUM Annual Meeting by Claire Stringer

Full version attached in annex 1

2. Achievement against milestones

MS1 Ethical approval to start sampling: complete at all sites

MS2 May 2019 review field sampling: fieldwork complete in Malawi and in Uganda

MS3 Mar 2020 Determine sequencing strategy at consortium meeting & review surveillance data/ decide when to stop field surveillance: First Nagoya Protocol compliant Access and Benefit Sharing agreement between UK and Malawi health sectors signed. All samples shipped to Wellcome Sanger Institute and whole genome sequencing complete.

3. Update of activity within separate work streams

For existing publications for each of the work stands, please see Table 1

a. WS1- Management of Consortium

WS1 was extremely effectively delivered by Senior Programme Manager Beth Hollihead and her team at LSTM, ensuring rigourous governance of the project which included coordination of the regular project management committee meetings. This ensured equitable partnerships, with all DRUM partners being involved in the strategic decision making for the project including decisions around budgets, decisions around project activities, identifying and managing risks, ensuring quality outputs, and making decisions around activities and timings.

An extension was requested and agreed by UKRI to allow time for Sanger to complete the sequencing. The collaboration agreement was amended to reflect this and now all contracting is complete. The final expenditure report has been submitted to UKRI. The financial management of the project was effectively delivered by the LSTM Research Management Services Department with support from the DRUM project management team.

The project management team supported the logistics for the project staff including the recent stakeholder meeting in Malawi. They organised and coordinated the annual consortium meetings; with meetings in person during the early years of the project and then online during the pandemic. The team also worked on keeping the DRUM consortium website up to date with the latest DRUM outputs.

This work strand is now winding down, and its remaining focus is on the final report, but will keep updating Researchfish with future outputs.

b. WS2- Surveillance of humans, animals and the environment

In both Malawi and Uganda, we have completed household recruitment in all 3 regions in 2021, processed all samples and completed DNA extraction. In Malawi, our chemical filter

analyte project which will evaluate antimicrobial contamination, and our community transect walks and market food sampling projects have also completed. All samples (approximately 12,000) have been sequenced at Wellcome Sanger Institute. The lead bioinformatician was awarded a Wellcome International Fellowship and continues with the analysis.

c. WS3-Evolutionary trajectories of AMR development related to local antimicrobial usage

WS3 was designed to explore the evolutionary biology of resistance emergence and determine if there was any optimisation possible in terms of treatment decisions for Enterobacteriaceae infections using the antibiotics co-amoxiclav and gentamycin.

When carrying out evolutionary studies it is important to consider the growth conditions of the bacteria being studied and these differences were rapidly assessed within this work package and published (DOI: 10.3389/fmicb.2019.02001)

Following this initial exploration of the effects of media on the evolution of antibiotic resistance we carried out a large-scale experiment to determine if the order of resistance development affects the ability of the bacteria cells to replicate; this effect is known as the biological cost and a high biological cost affects the fitness of the bacteria in a negative way. Less fit bacteria which have developed resistance are less likely to survive in the absence of the selective pressure of the antibiotics to which they have become resistant. More fit resistant bacteria may well survive longer, and rarely may be more fit than susceptible strains, even in the absence of selective pressure.

Ten independent lineages of two clinical isolates of *Escherichia coli* and two isolates of *Klebsiella pneumoniae* were selected in the presence of sub-inhibitory concentrations of amoxicillin-clavulanic acid (AMC) or gentamicin (GEN). Five independent lineages of each isolate-antibiotic combination for one *E. coli* and *K. pneumoniae* isolates were subsequently selected for resistance to the alternative antibiotic, creating 25 AMC-GEN and 25 GEN-AMC independent lineages per isolate. Comparative fitness and disc diffusion assays of all independent lineages were assessed, as was collateral sensitivity profiles to a range of unrelated antibiotics, and all isolates were whole genome sequenced.

We found that, while fitness effects of antibiotic selection in individual lineages varied, overall, the fitness effect of single selection in AMC or GEN is dependent on the genetic background. Additionally, relative to both the original and immediate single-selected ancestors, sequential selection in GEN-AMC resulted in a larger, overall fitness cost compared to AMC-GEN, which is replicated in both *E. coli* and *K. pneumoniae*. Collateral effects on susceptibility to other antibiotics can be either dependent or independent on the order of antibiotic selection.
This data indicates that the order of antibiotic selection can impact the overall fitness costs of AMR and collateral effects on other antibiotics. This data has been shared with the clinical teams within DRUM and is currently being written up for publication.

d. WS4-Understanding intensity of and reasons for antibiotic use

This workstrand is a qualitative study that focused on 3 research questions:
1. What antibiotics are used in humans, animals and crops; where are they

used and in what quantity?
2. What socio-cultural, economic and health system contexts drive the use of antibiotics in humans, animals and crops?
3. What are the opportunities for changing the context and behaviour?

Data collection
Fieldwork was conducted in a range of sites (rural Chikwawa, urban Ndirande and peri-urban Chileka). We conducted a total of 220 medicine interviews, 115 key informant interviews and 25 stakeholder interviews (with a range of stakeholders across national policy, regulation and academia).

A survey was conducted with 217 households including 1051 household members to understand current antibiotic use. The survey was conducted in Chileka, Ndirande and Chilomoni.

Dissemination of research findings
A total of 6 papers were published in international peer reviewed journals, generating new knowledge on prescribing and use practices within health care facilities and within households for both animals and humans.

See annex 2 for a presentation of the work strand methodologies and findings.

e. WS5-Understanding the drivers of WASH practices and their relation to transmission

WS5 worked hand in hand with the WS2 teams across both Malawi and Uganda to ensure effective value for money, and temporal synergy between the observed infrastructure and behaviours alongside the microbiological sampling at individual and household level.

Throughout the period of the programme the following was achieved:

Malawi

Data collection

- **Households**
  - Related questions in household and individual CRF: 300 households
  - Household checklists: 300 households (885 checklists over study period)
  - Household observations: 195 households (36 hours per household over study period)
  - RANAS survey: 300 households (i.e. 100 households in each study location)

- **Wider Community**
  - Transect walks
    Community wide transect walks were conducted across all three study sites. These were repeated monthly over a 12-month period with associated sampling (WS2) of the wider environment from high risk areas to understand the presence of AMR in wider public areas.
  - Markets

Three markets were examined in detail in each study area (total=9 markets). These were observed for 4 days to understand the practices being undertaken and potential risk pathways. Each market was subject to a Hazard Analysis Critical Control Point (HACCP) assessment which informed the appropriate sampling areas for WS2 in this setting. Market sampling also tested a novel ESBL quantification method using IDEXX Colilert Quantitrays with advice and support from the CDC.

Data analysis

All data from the programmes above have been consolidated, cleaned and where appropriate uploaded to the Dataverse. Analysis of WS5 data is being undertaken in conjunction with data from WS2 to determine temporal and spatial associations. Data from markets and transect walks are being analysed separately to evaluate the risk from these settings using the HACCP and Sanipath tools respectively. Initial findings from data analysis to date can be found in submitted publications.

<u>Uganda</u>

Data collection

- **Households**
    - Related questions in household and individual CRF: 100 households
    - Household checklists: 100 households (100 checklists over study period)
    - Household observations: 54 households - 36 hours per household over the study period (24 households were only observed at recruitment). Observations included having research assistants situated in participants' households for 6 hours to observe general routine WASH activities as well as hand hygiene practices by household members.
    - RANAS survey: 153 households (80 in Kampala and 73 in Hoima) were conducted during the study, 2 transect walks during both dry and wet seasons in Kampala and Hoima over a period of 6 months, active microbiology sampling in certain areas during the transect walks, and 10 key informant interviews conducted.

- **Wider Community**
    - Transect walks were conducted in both Hoima and Kampala in two phases. The first phase was during a dry season and the second during a rainy season over a combined period of six months. The transect walks involved traversing the study sites and observing the various WASH and broader environmental health issues including infrastructure within the environment and public places. Microbiology samples were also collected from some of the sites at the public places to confirm the presence of resistant bacteria. Public areas where WASH observations and sampling were done include markets, schools, health facilities, public toilets, public tap-stands, boreholes and wells, waste dumping sites, open tranches, and places of worship. In markets, the research team did observations for a minimum of 6 hours a day and noted various high-risk WASH-related activities. Each market had samples taken from suspected high-risk WASH sites.

- ○ Key informant interviews (KIIs) were also conducted to obtain views of influential community members regarding WASH. A total of 10 KIIs were conducted in the study sites (5 in Kampala and 5 in Hoima). The key informants included market chairpersons, community health workers, village chairpersons, caretakers of public toilets, a health assistant, a health inspector, and an IPC health facility focal person.

Data analysis

All data from the above activities was consolidated, cleaned and analysed in Microsoft Excel to derive basic understanding as we await the general analysis of the case report form data. Analysis of WS5 data is being undertaken in conjunction with data from WS2 to determine temporal and spatial associations. Data from household observations and transect walks are being analysed separately to evaluate the risk from these settings using the hazard analysis critical control point (HACCP). Data from the KIIs was transcribed, translated to English (for the one collected in the local languages) and analysed manually using thematic analysis.

f. WS6- Dynamical agent-based modelling of AMR in Uganda and Malawi

Agent-based models are used to model the spread of a disease in a heterogeneous population, by defining individual-specific hazard rates at which each individual get infected and subsequently recover from it. We propose a novel Susceptible-Infected-Susceptible model taking into account individuals' location, individuals' covariates, seasonality and environmental effect to model the spread of AMR bacteria in a considered population. We fit the aforementioned model to the data on Extended-Spectrum Beta-Lactamase-producing *E. coli* and *K. pneumoniae* in Malawi using SMC², which also allow to perform model selection. We find *E. coli* to be more persistent in the environment compared to *K. pneumoniae.* We estimate a strong seasonal effect for both bacteria and an effective R showing a transmission of *E. coli* primary driven by within household interactions and by both within and across household interactions for *K. pneumoniae*. We also argue age, gender and income not being influential in the spreading process compared to the dynamic of the individuals.

The pipeline for the study is general, and can be adapted to different location (e.g. Uganda data), different covariates (e.g. WASH data), mixed species (e.g. add animal data). The main steps of the pipeline are:

1. define a stochastic model for the bacteria spread.
2. define a synthetic population to model the unseen individuals and avoid underestimation of the transmission rate.
3. define a likelihood to "connect" the data with the defined model.
4. run SMC² to estimate the parameters of the model.

The findings and the pipeline are going to be submitted for publication on the "Journal of the Royal Statistical Society: Series C (Applied Statistics)", to ensure the procedure to be reviewed by global experts in Statistics. The project was co-funded by EPSRC grant EP/R018561/1 (Bayes4Health) and motivated the work "Approximate optimal SMC proposal distributions in individual-based epidemic models" (https://arxiv.org/abs/2206.05161) currently under revision by "Statistica Sinica".

g. WS7- Understanding the economic implications of antimicrobial resistance

In Malawi, using previously validated data collection tools, we collected data on health provider (direct medical) costs, costs incurred by patients and their families as a result of hospitalisation (direct non-medical and indirect costs) and health-related quality of life outcomes in patients with drug resistant bacterial bloodstream infections. We first used these data to make cost comparisons between resistant and susceptible infections and then applied the generated costs to microbiological surveillance and projected population data for Blantyre and Malawi, to estimate the economic burden of drug resistant bacterial bloodstream infections. We illustrate that drug resistant bacterial bloodstream infections are associated with higher health provider and patient level costs than susceptible infection, as well as poorer HRQoL outcomes. We demonstrate a substantial current and future economic burden to the hospital and society as a result of drug resistant bacterial bloodstream infections.

In Uganda, the DRUM-Uganda team conducted a study to understand cost implications for the management of patients with sepsis who might have antimicrobial resistant (AMR) bacteria as a cause of their sepsis. This study was done as a collaboration between IDI and Walimu, the implementing partner in Uganda for a NIHR-funded grant called the African Research Collaboration on Sepsis (ARCS). The hospital costing study aimed to estimate the resources 'consumed' by each sepsis patient during their hospital admission, ranging from the days of inpatient admission to investigations and treatments given. The study also estimated costs incurred by the healthcare provider in managing patients admitted to hospital with sepsis and assessed whether costs differ by causative organism and resistance to antimicrobial agents. Primary analysis of these data are still underway.

h. WS8- Identifying and addressing barriers between in-country sectors involved in AMR

The project established Ugandan and Malawian sites as sustainable model settings for interdisciplinary study and mitigation of antimicrobial resistance (AMR) by embedding a One Health strategy at the heart of a consortium that would generate outputs applicable to similar communities throughout East and Southern Africa and beyond. The African Institute for Development Policy's (AFIDEP) work as part of the DRUM Consortium was two-fold. The first was policy research through an assessment of the policy platform and the evolution of policy processes in Malawi. The second was policy engagement and communication, through several activities with stakeholders, and the development of policy-relevant communication products thereafter. To assess the policy platform and evolution of policy processes in Malawi the research took a qualitative approach involving key informant interviews with policymakers and other stakeholders engaged with national-level ABR policy development and implementation. Interviews were conducted with stakeholders identified from the animal health, human health, and environmental health sectors. The research revealed misuse of antibiotics is a major concern for stakeholders. The lack of collaborative communication across the relevant sectors was considered a challenge, leading some to perceive antimicrobial resistance as mainly a human health issue. Suggestions to promote engagement and collaboration among sectors were put forward. Evidence from the interviews will be presented in the form of two manuscripts assessing the challenges to policy implementation as well as the experience of drafting a policy agenda for Malawi. A regional policy analysis was conducted, which created the basis for the development of an elaborate policy engagement

and communications strategy. The strategy set the overall direction, objectives and scope of engagement and communication for policy under the Malawi project. A public engagement plan was applied to reach stakeholders interested in AMR using a stakeholder power and interest matrix. A strategic communications approach was used to guide the development and dissemination of communication products as well as to motivate stakeholders to act in making AMR a cross-cutting public health issue. A mix of print, audio-visual and online platforms were used for communication with key stakeholders. The range of engagement products were also used to raise awareness during the World Antimicrobial Awareness Week in 2019, to encourage the conversation on AMR in Malawi. Additionally, to build local capacity, AFIDEP through DRUM and in collaboration with the African Research Collaboration on Sepsis (ARCS) undertook a week-long training to strengthen the capacity in evidence informed policy making (EIPM) among health policy makers, civil society, and researchers in Malawi. This activity was designed to not only equip policymakers with vital knowledge on how to use evidence in the development of policy and engaging policymakers but as a means of fulfilling one of the consortiums' goals of reframing AMR as a health issue with strong linkages to other public health concerns such as sepsis. This report reflects on AFIDEP's implementation of first the policy research and second the policy engagement activities within the DRUM consortium, specifically for Malawi, and it highlights the lessons learned throughout the process.

For full information see annex 3, end of project report from AFIDEP

4. Financial report on spending

Partner	Country	Expenditure to March 2022	Percentage of total expenditure	
LSTM	UK	1,061,172.21	30%	Spend supports activities in UK, Malawi and Uganda
Lancaster	UK	507,143.07	14%	
Strathclyde	UK	262,184.61	7%	
Sanger	UK	367,915.57	10%	
UoL	UK	25,655.81	1%	
CEH	UK	39,590.22	1%	
AFIDEP	Malawi	220,026.94	6%	
MLW	Malawi	377,393.71	11%	
IDI	Uganda	543,114.68	15%	
Makarere	Uganda	100,318.18	3%	
Total		**3,504,515.00**	**100%**	

5. Stakeholder Engagement

Stakeholder engagement has taken diverse forms and engagement with policy makers is a key component of WS8 (see above). Further detail is provided below:

Policy makers: In addition to the description of WS8, in the Malawi context, the national lead for AMR at the Ministry of Health is a co-investigator in DRUM and supported the development of DRUM from the stage of the development award grant writing workshop. Mrs Kasambara is kept up to date with findings from DRUM via interaction with WS8, though monthly PMC meetings, and through Feasey, MacPherson and AFIDEP's membership of the MoH Malawi AMR TWG. In Uganda, Henry Kajumbula (DRUM-Uganda co-I) is the chairperson for the Uganda national AMR task force. From the project's inception, DRUM-Uganda engaged the One Health Technical Working Group (OHTWG) [comprising representatives from the Ministries of Health (MoH); Water and the Environment (MWE); Agriculture, Animal Industry and Fisheries (MAAIF) and Tourism and Wildlife and Antiquities (MTW&A)] and provided periodic updates during the grant period. As well, Dr Shevin Jacob (DRUM-Uganda site PI) has been invited as a member of the One Health AMR Research Technical Working Committee, a sub-committee of the OHTWG.

Practitioners: DRUM is a community-based study evaluating community-based transmission and consequent asymptomatic carriage of ESBL-bacteria, rather than a disease state. Engagement with practitioners predominantly occurred at the end of the study. We have, however, presented summaries of data in Malawi at Project Progress meetings (MLW); hospital Grand rounds (QECH, Malawi); the Malawi College of Medicine Research Dissemination Conference, WASH and Environmental Health sectors stakeholder meetings and directly to the MoH (most recently 19 March 21). In Uganda, DRUM has presented at the 2018 National AMR Conference and the 2019 Global Network of AMR and IPC Symposium. As they become available, final data will be communicated through in country research dissemination meetings, peer reviewed publications and through WS8 engagement work.

Community engagement: As DRUM is a community-based study, extensive work was done in Malawi and Uganda to engage with communities prior to commencing recruitment through district health officers, councils, community advisory groups and village headmen. Results will be communicated back through these channels. In Malawi community dissemination meetings have been held in all three study sites. These were attended by participants, community leaders and community health workers providing feedback on the research findings and tackling questions from participants arising from the findings. Please see results dissemination brief in annex 4.

DRUM has also highlighted the challenge of explaining what AMR is in communities that frequently do not have a grasp of germ theory even in a vernacular sense. This has led to a piece of work being funded by the Wellcome Trust who have developed a method entitled "Public Deliberative Conversations about AMR", a two-way dialogue programme to empower citizens to create local solutions and influence strategies related to AMR. Wellcome have funded this work in Malawi, and it began in September 2020 to strengthen community engagement and involvement around AMR generally and AMR research in particular.

6. UK/HIC-LMIC Engagement

DRUM was designed at a grant writing workshop held in Malawi and further informed by a stakeholder meeting in Kampala. The design and planning began in LMIC countries and continued at the kick off meeting (See response to Q1).

In terms of implementation, the PI of the DRUM Consortium (Feasey) is based full time in Malawi at MLW, a Wellcome Major Overseas Programme institute jointly governed by the University of Malawi the College of Medicine, LSTM and UoL. It is part of MLW's mission statement to improve the health of Malawi and train the next generation of Malawian scientists. Work in Malawi is jointly conducted with the University of Malawi Polytechnic. As per the engagement piece above, Kasambara, the Malawi lead for AMR is a named co-investigator that helped to design DRUM. We concluded DRUM Malawi with national stakeholder meeting in Lilongwe, which was well attended. Here we shared our results and started to consider research priorities for DRUM2.

The Uganda lead (Jacob) is based full-time in Uganda and is a Team Lead for the Global Health Security Department at the Infectious Diseases Institute (IDI), the implementing partner for DRUM in Uganda. IDI is a semi-autonomous organization within the College of Health Sciences at Makerere University, the oldest university in Africa. Kajumbula, Mugisha and Joloba (EAG) are deeply embedded in Ugandan AMR strategy at both the policy and research level.

DRUM has been committed to capacity strengthening through development of research capacity infrastructure in the environmental laboratory it has equipped laboratories in Uganda and Malawi (a key strategic aim of the Malawi College of Medicine) and through development of individuals as evidenced above. In terms of analysis, the bioinformatics lead (Musicha) is a Malawian, who has secured a Tier 1 visa to the UK through DRUM and was based at Sanger during DRUM, and has now returned to Malawi with a Wellcome International Fellowship.

Chidziwisano (WS5 PDRA, Malawi) and Musoke (WS5 lead, Uganda) are emerging WASH leaders in their respective countries, and we have trained a cadre of One Health, interdisciplinary field workers and environmental microbiology technicians in this process. The WASH work was therefore led by LMIC researchers in both Malawi and Uganda, who have presented results at several conferences and taken ownership of the research decisions, plans, implementation and analysis. Papers resulting from this work will all be led by Malawian and Ugandan researchers.

7. Outputs, publications, presentations, workshops.

Table 1

DRUM authors	Title	Journal	Date	Link	Work strand
Andrew C Singer, Claas Kirchhelle, Adam P Roberts	(Inter)nationalising the antibiotic research and development pipeline	Lancet Infectious Disease	18/11/2019	https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(19)30552-3/fulltext	3
Ellie MacPherson, Clare Chandler	The 'Drug Bag' method: lessons from anthropological studies of antibiotic use in Africa and South-East Asia	Global Health Action	24/07/2019	https://www.tandfonline.com/doi/full/10.1080/16549716.2019.1639388	4
Alastair Hubbard, Adam Roberts	Piperacillin/tazobactam resistance in a clinical isolate of Escherichia coli due to IS26-mediated amplification of blaTEM-1B	Nature Communications	01/10/2020	https://doi.org/10.1038/s41467-020-18668-2	3

Claas Kirchhelle, Paul Atkinson, Alex Broom, Komatra Chuengsatiansup, Jorge Pinto Ferreira, Nicolas Fortané, Isabel Frost, Christoph Gradmann, Stephen Hinchliffe, Steven J Hoffman, Javier Lezaun, Susan Nayiga, Kevin Outterson, Scott H Podolsky, Stephanie Raymond, Adam P Roberts, Andrew C Singer, Anthony D So, Luechai Sringernyuang, Elizabeth Tayler, Susan Rogers Van Katwyk, Clare R Chandler	Setting the standard: multidisciplinary hallmarks for structural, equitable and tracked antibiotic policy	BMJ		https://gh.bmj.com/content/5/9/e003091.abstract	2, 3, 4
Levi Kalitsilo AFIDEP	Sepsis and antimicrobial resistance: An urgent call to strengthening health information system	AFIDEP and DRUM website		https://www.afidep.org/sepsis-and-antimicrobial-resistance-an-urgent-call-to-strengthening-health-information-systems/	8
Elissavet Nikolaou, Alasdair T. M. Hubbard, João Botelho, Taylor A. M. Marschall, Daniela M. Ferreira and Adam P. Roberts	Antibiotic Resistance Is Associated with Integrative and Conjugative Elements and Genomic Islands in Naturally Circulating Streptococcus pneumoniae Isolates from Adults in Liverpool, UK	Genes		https://www.mdpi.com/2073-4425/11/6/625	3

AFIDEP	Antimicrobial Resistance Comic	AFIDEP and DRUM website		https://www.drumconsortium.org/sites/drum/files/content/attachments/2020-03-06/DRUM%20Comic%20Strip%20English.png	
AFIDEP	Introduction to the DRUM consortium	AFIDEP and DRUM website		https://www.drumconsortium.org/introduction-to-the-drum-consortium	8
Victory Kamthunzi, Levi Kalitsilo, Claire Jensen and Paul Kawal	Sepsis and Antimicrobial Resistance in the Era of COVID-19: Overcoming Global Health's Triple Crisis	Blog AFIDEP Website	Sep-20	https://www.afidep.org/sepsis-and-antimicrobial-resistance-in-the-era-of-covid-19-overcoming-global-healths-triple-crisis/	8
Musicha P, Msefula L, Mather A, Cain A, Chaguza C, Peno C, Heyderman R, Everett D, Thomson N, Feasey N.	Genomic Epidemiology of Klebsiella pneumoniae in Malawi: acquisition of ESBL determinants across diverse lineages (Poster)	Antimicrobial Resistance – Genomes, Big Data and Emerging Technologies (Virtual Conference)	4-6/11/20		2

Shevin Jacob	IDI Science Fair, took place on Zoom and Shevin Jacob presented DRUM at the fair. The Science Fair attracted participants from over 10 countries, including: U.S., Nigeria, Kenya, UK, Pakistan, India, Ghana and Uganda and had 759 participants		Feb 2021	https://idi.mak.ac.ug/idi-science-fair/	2
David Musoke, Kondwani Chidziwisano, Tracy Morse	The role of Environmental Health in preventing antimicrobial resistance in low- and middle-income countries.	Environ Health Prev Med	2021	https://doi.org/10.1186/s12199-021-01023-2	5
Derek Cocker, Kondwani Chidziwisano, Tracy Morse, Nicholas Feasey	One Health, AMR and WASH: Is the "Apoocalyse" coming? (2021).	Side event held at UNC Water and Health: Where Policy Meets Practice.	Oct 2021	Overview presentation of AMR work followed by Chairing of Panel Discussion with participation from WHO, LSTM (UK), UNC (USA), CDC (USA), UCL Berkley (USA), Makerere (Uganda), MUBAS (Malawi). https://pure.strath.ac.uk/ws/portalfiles/portal/129627847/UNC_presentation_V1.5.pdf	2, 5

Masoamphambe, E., Cocker, D., Feasey, N., Chidziwisano, K.R., Panulo, M., Morse, T.	A novel ESBL Colilert system for environmental surveillance of AMR bacteria at markets in LMICs	Poster presentation at UNC Water and Health: Where Policy Meets Practice.	Oct 2021	https://pure.strath.ac.uk/ws/portalfiles/portal/129785558/Masoamphambe_etal_UNC_2021_A_novel_ESBL_colilert_system_for_environmental_surveillance_of_AMR_bacteria.pdf	2, 5
Mwapasa T., Mphasa, M., Cocker, D., Feasey, N., Morse, T.	Community exposure assessment to anti-microbial resistance (AMR); case study of Malawi.	Poster presentation at UNC Water and Health: Where Policy Meets Practice.	Oct 2021	https://pure.strath.ac.uk/ws/portalfiles/portal/129842485/Mwapasa_etal_UNC_2021_Community_exposure_assessment_to_anti_microbial_resistance.pdf	2, 5
Morse, T., Chidziwisano, K., Musoke, D., Cocker, D., Feasey, N.	Development of a protocol for assessing the role of WASH in AMR distribution in the environment.	Poster presentation at UNC Water and Health: Where Policy Meets Practice.	Oct 2019	https://pure.strath.ac.uk/ws/portalfiles/portal/98568056/Morse_etal_WH_2019_Development_of_a_protocol_for_assessing_the_role_of_WASH_in_AMR_distribution_in_the_environment.pdf	2, 5
Panulo, M., Masoamphambe, E., Cocker, D., Feasey, N., Chidziwisano, K.R., Morse, T.	The role of public markets in food safety in Malawi	Oral presentation at UNC Water and Health: Where Policy Meets Practice.	Oct 2021		2, 5

AFIDEP	Drum end of project report	Report	2022	See annex 3 attached	8
John Mankhomwa, Rachel Tolhurst, Eunice M'biya, Ibrahim Chikowe, Pemphero Banda, Jimmy Mussa, Henry Mwasikakata, Victoria Simpson, Nicholas Feasey, and Eleanor E. MacPherson	A Qualitative Study of Antibiotic Use Practices in Intensive Small-Scale Farming in Urban and Peri-Urban Blantyre, Malawi: Implications for Antimicrobial Resistance	Frontiers in Veterinary Science	2022	Frontiers | A Qualitative Study of Antibiotic Use Practices in Intensive Small-Scale Farming in Urban and Peri-Urban Blantyre, Malawi: Implications for Antimicrobial Resistance (frontiersin.org)	4, 2
MacPherson, E,E, Reynolds, J, Sanudi, E, Nkaombe, A, Phiri, C, Mankhomwa, J, Dixon, J, Chandler, C.I.R.,	Understanding antimicrobial resistance through the lens of antibiotic vulnerabilities in primary health care in rural Malawi,	Global Public Health	2021	https://doi.org/10.1080/1744169 2.2021.2015615	4
Phiri, M, MacPherson, EE, Panulo, M, Chidziwisano,K, Kalua, K, Mahebere Chirambo, C, Kawalazira, G, Gundah, Z, Chunda, P, Morse, T,	Preparedness for and impact of COVID-19 on primary health care delivery in urban and rural Malawi: a mixed methods study	BMJ Open	2022	Preparedness for and impact of COVID-19 on primary health care delivery in urban and rural Malawi: a mixed methods study | BMJ Open	4
MacPherson, E,E, Reynolds, J, Sanudi, E, Nkaombe, A, Mankhomwa, J, Dixon, J and Chandler, C.I.R	Understanding Antimicrobial Use in Subsistence Farmers in Chikwawa District Malawi, Implications for Public Awareness Campaigns.	PLOS Global Public Health 2(6): e0000314.	2022	Understanding antimicrobial use in subsistence farmers in Chikwawa District Malawi, implications for public awareness campaigns | PLOS Global Public Health	4, 5

Mindy Panulo, Jones Chipinga, Effita Masoamphambe, Kondwani Chidziwisano, Derek Cocker, Tracy Morse.	The role of WASH on food safety in marketplaces in rural, urban and peri – urban Malawi	Oral presentation at MEHA conference Malawi	2022		2, 5
Taonga Mwapasa, Madalitso Mphasa, Derek Cocker, Kondwani Chidziwisano, Nicholas Feasey and Tracy Morse	Community Exposure Assessment to Anti-microbial Resistance; case study of Malawi	Oral presentation at MEHA conference Malawi	2022		2, 5
Kondwani Chidziwisano, Derek Cocker, Nicholas Feasey and Tracy Morse	Individual risk perception to antimicrobial resistance (AMR) through environmental pathways in Malawi	Oral presentation at UNC Water and Health: Where Policy Meets Practice.	2022		2, 5
MacPherson, E,E, Reynolds, J, Sanudi, E, Nkaombe, A, Mankhomwa, J, Dixon, J and Chandler, C.I.R.	Understanding Antimicrobial Use in Subsistence Farmers in Chikwawa District Malawi, Implications for Public Awareness Campaigns.	PLOS Global Public Health 2(6): e0000314.	June 2022	https://doi.org/10.1371/journal.pgph.0000314	4
Mankhomwa, J., Tolhurst, R., M'biya, E., Chikowe, I., Banda, P. N., Mussa, J., Mwasikakata, H., Simpson, V, Feasey N., MacPherson, E.	A qualitative study of antibiotic use practices in intensive small-scale farming in urban and peri-urban Blantyre, Malawi: Implications for antimicrobial resistance	Front.Vet. Sci. 9:876513.	May 2022	doi:10.3389/fvets.2022.876513	4

Manyau, S, Dixon, J, MacPherson, E.E., Palanco Lopez, P, Mutukwa, N, Kandiye, F.R., and Chandler, C.I.R.,	A wound down there kills all work!" Antibiotics and the Biopolitics of Sex Work in Zimbabwe	Medical anthropology theory	2022	https://doi.org/10.1080/0145974 0.2022.2037083	4
Palanco Lopez, P, Manyau, S, Dixon, J, MacPherson, E, Nayiga, S, Manton, J, Kirchhelle, C, and Chandler, C.I.R	Antibiotic arrivals in Africa: Case study of yaws and syphilis in Uganda, Malawi and Zimbabwe,	Medical Anthropology Theory	2022	https://doi.org/10.17157/mat.9.3. 5633.	4
MacPherson, E,E, Reynolds, J, Sanudi, E, Nkaombe, A, Phiri, C, Mankhomwa, J, Dixon, J, Chandler, C.I.R.,	Understanding antimicrobial resistance through the lens of antibiotic vulnerabilities in primary health care in rural Malawi,	Global Public Health	2021	https://doi.org/10.1080/1744169 2.2021.2015615	4
Dixon, J, MacPherson E, Nayiga, S, Manyau, S, Nabirye C, Kayendeke, M, Sanudi, E, Nkaombe, A, Mareke, P, Sithole, K, de Lima Hutchison, C, Bradley, J, Yeung, S, Ferrand, R, Lal, S, Roberts, C, Green, E, Denyer Willis, L, Staedke, S Chandler, C.I.R	A Mixed-Methods, Multi-Country Analysis of Household Antibiotic use in Malawi, Uganda and Zimbabwe	BMJ Global Health	2021	doi:10.1136/bmjgh-2021-006920	4
Eleanor MacPherson co-chairing Anthropological approaches to studying antibiotics and their use: methodological challenges and innovations, Full chair list:	Anthropological approaches to studying antibiotics and their use: methodological challenges and innovations,	Royal Anthropological Institute's Mobilising Methods in Medical Anthropology,	January 2022		4

Justin Dixon and Eleanor MacPherson					
MacPherson, E,E, Reynolds, Phiri, C, Mankhomwa, J, Dixon, J, Chandler, C.I.R., (2021)	Understanding antimicrobial resistance through the lens of antibiotic vulnerabilities in primary health care in rural Malawi,	American Society of Tropical Medicine and Hygiene Conference	2021		4
Mangochi, H, Tolhurst, R, Simpson, V, Kawaza, K, Chidziwisano, K, Feasey, N, Morse, T, MacPherson, E,E, (2022) A	Qualitative Study exploring health workers and patient caregivers' hand hygiene practices in a neonatal unit in Blantyre, Malawi, implications for controlling outbreaks of drug resistant infections	Wellcome Open Res 2022, 7:146	2022	https://doi.org/10.12688/wellcomeopenres.17793.1	4

8. Summarise activities, outcomes and evidence of how research capacity has been strengthened.

DRUM has been committed to capacity strengthening with examples of activities include in October 2020 until March 2021, Eleanor MacPherson led a structured writing course for junior Malawian social scientists affiliated with the DRUM study (5 students). The course combined individual mentoring with group learning topics included:

- Creating a work schedule (and being held accountable for it),
- Developing an abstract,
- Identifying an appropriate journal for submission,
- Refining cited works,
- Analysis of evidence and clarifying arguments,
- Making claims of significance,
- Writing cover letters to journals for submission
- Organising and formatting the paper

The approach was successful with three participants submitting and having accepted first-author journal articles (and two had co-author work accepted).

Other capacity strengthening activities in Malawi included:
- Three Malawian Master students have completed their studies and two more have commenced MSc's from a follow on UKRI (NERC) funded project.
- Patrick Musicha has been awarded a Wellcome International Fellowship and is returning to Malawi.
- Kondwani Chidziwisano and Taonga Mwapasa visited South Africa to University of Kwa Zulu Natal for training in Sanipath (approximately Jan 2020)
- Mentoring and support for the Malawi research team in writing manuscripts, briefs, and community engagement tools
- Training of all 8 field staff on the methods for observations, surveys and sampling. This was at Malawi University of Business and Applied Sciences
- Taonga Mwapasa was our field manager and is now progressing through her MSc
- Mindy Panulo led our markets research and is now doing her PhD
- Kondwani Chidziwisano is now leading his own research partnerships with ETH, Zurich and LSHTM
- Mindy Panulo and Taonga Mwapasa attended a Manuscript Writing Workshop, 8th to 13th July, 2021 at the College of Medicine
- Taonga Mwapasa attended a Biostatistics Workshop, 13th to 17th May 2019 at the College of Medicine

Capacity strengthening activities in Uganda included:
- Anne Katahoire worked with a social scientist who was mentored throughout the project in qualitative research. During the project, they collected some of the data together and when it came to the analysis, they worked together to develop a coding frame that was used to code the interviews. The social scientist then wrote up some

sections of the report. The next step now is to write a manuscript and publish the data findings in a Journal.
- WS5 SWARU WASH activities included:
  - The capacity of the data collection teams in Uganda was enhanced in conducting these activities both by the investigators in Uganda and Malawi (who had implemented these activities before the Uganda team). The Uganda data collection teams were trained in conducting RANAS survey and using the WHO Sani path tool to conduct WASH assessments.

Uganda studentships:

Name	Role in DRUM	Institution	Course	Status
Fred Isaasi	Veterinary officer; Deputy Study Coordinator	Makerere University	Masters of Science (Epidemiology)	Co-funded by DRUM and LSTM. Co-supervisors Nick Feasey and Shevin Jacob; currently underway
George Katende	Laboratory technologist	Makerere University	Masters of Science (Clinical Microbiology and Immunology)	Co-funded by DRUM and ARCS; currently underway
Esther Rottenburg	Research Degree Student (anthropology; global health)	London School of Hygiene and Tropical Medicine	PhD	Co-Advisor (Shevin Jacob); currently underway

9. Any other noteworthy outcomes beyond those captured above

Whilst we are not aware of negative outcomes, DRUM has provided a wealth of data to policy makers in Malawi via stakeholder meetings and the AMR technical working group. This has helped inform the implementation of the AMR national action plan in Malawi

In Uganda, the Makerere University-Infectious Diseases Institute (IDI), the DRUM Implementing Partner for Uganda, was awarded a grant (value: $99,347) through the Grand Challenges Africa AMR scheme called "Drivers of antimicrobial resistance among peripartum mothers and children with sepsis in Hoima, Uganda (DRUM+)". The grant leveraged DRUM's field sampling research infrastructure to determine microbiologic linkages between household carriage of ESBL-E and ESBL-K AND patients (peripartum women or neonates/children < 5yo) hospitalized with sepsis who have ESBL-E and ESBL-K blood stream infection or colonization. Primary data analyses are currently underway.