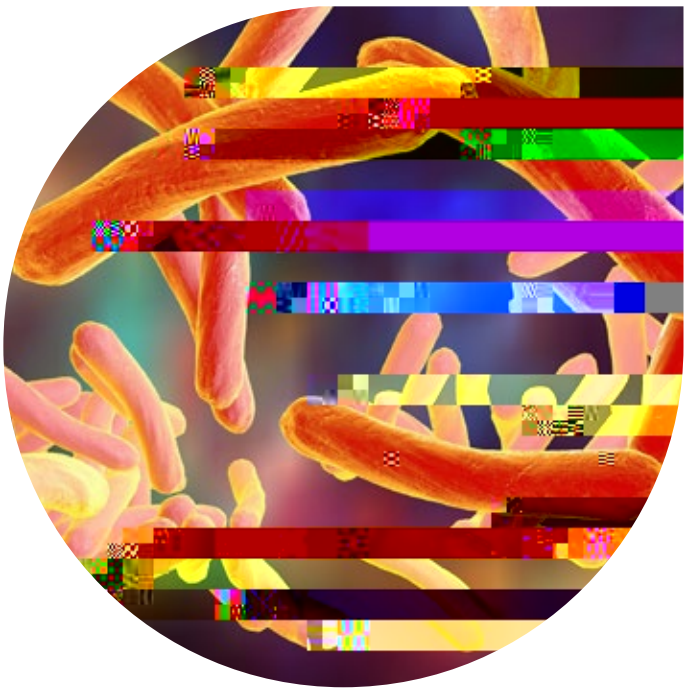
The Bloomsbury SET:

A Knowledge Exchange platform connecting capability to combat the threat from infectious disease and antimicrobial resistance (AMR)



THE BLOOMSBURY SET®

Science | Economics | Technology

WHO WE ARE

The Bloomsbury SET (Science, Economics, Technology) innovation partnership brought together HEIs with a strong reputation in creating enduring impact from their research. This £6.9 million programme, awarded through Research England's Connecting Capability Fund, was led by The Royal Veterinary College, University of London.

The programme aimed to tackle the challenges of infectious disease, and the increasing resistance to antimicrobials that poses a major threat to human health. With particular attention to the rise of zoonotic diseases (diseases that jump from animals to humans), the focus was on improving our ability for early detection in animal populations and to assess the risks to human health. This requires low-cost, portable diagnostic tools, especially in low and middle-income countries. Likewise, disease control is hindered by a lack of suitable vaccines, and by data scarcity, leading to large uncertainties in mathematical models of pathogen spread and persistence, both in humans and livestock.

The Bloomsbury SET has adopted a multidisciplinary approach. Connecting expertise in comparative biological sciences, human and veterinary diagnostics, epidemiology, vaccine development, health economics including antimicrobial resistance (AMR), mathematical modelling of infectious disease, disease surveillance and public health. We integrated this with the knowledge and skills of social scientists in health economics, international development, governance, evidence-based policy-making, linguistics and agricultural economics.

PARTNERS IN THIS PROGRAMME:

THE ROYAL VETERINARY COLLEGE (RVC), with over 200 years of innovation and leadership in veterinary medicine and science, and with a commitment to improving human and animal health and welfare.

THE LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE (LSHTM), a world leading centre for research and postgraduate education in public and global health.

THE LONDON SCHOOL OF ECONOMICS AND POLITICAL SCIENCES (LSE), one of the foremost social science universities in the world (2018-21 only).

SOAS UNIVERSITY OF LONDON, THE WORLD'S LEADING INSTITUTION FOR THE STUDY OF ASIA, Africa and the Middle East.

LIVERPOOL SCHOOL OF TROPICAL MEDICINE (LSTM), the first institution in the world dedicated to research and teaching in the field of tropical medicine (2021-22 only).

ALSO WORKING CLOSELY IN CONJUNCTION WITH:

THE LONDON INTERNATIONAL DEVELOPMENT CENTRE (LIDC), a consortium of seven University of London institutions shaping the future of international development.

BUILDING ON THE PAST, STRENGTHENING THE FUTURE

The Bloomsbury SET was designed to complement existing research and teaching partnerships between its members, as well as progressing a range of exciting new ventures and strengthening the partners' commitment to collaborative working in the area of human and animal health.

- £1.7 million BBSRC-DSTL-DIFD-ESRC-MRC and NERC-funded 'Behavioural Adaptation in live poultry trading and farming systems and zoonoses control in Bangladesh project' - RVC and LSHTM

- £3.7 million HEFCE-funded London International Development Centre - LSHTM, RVC and SOAS £4035 million Epean & Develo

AWARDS

A multi-disciplinary approach to optimize, evaluate social uptake, and mathematically

CREATING OPPORTUNITIES TO MAKE A DIFFERENCE

Aimed to harness creative thinking and innovative ways to approach a problem, our sandpit events brought together academics and industry professionals from different disciplines. Fostering new connections and collaboration, these intensive discussions connected capability across our partners to uncover innovative solutions.

HARNESSING THE POWER OF BIG DATA

Data are one of the most important resources in our world today. The use of AI techniques has the potential to discover patterns from a large data-set, to generate new knowledge and narrative, identifying hitherto unseen connections, and supporting the decision-making process when tackling infectious disease.

WHILE SOME DATA-SETS ARE EASILY ACCESSIBLE, THEY MAY NOT BE SUFFICIENTLY WELL UTILISED.

We are developing a data-linkage machine learning methodology for the knowledge hub 'VetCompass', a lead primary care practice programme that collates de-identifed electronic patient record data from 1,800 primary-care veterinary practices in the UK for epidemiological research. We are also working with the Infectious Diseases Data Observatory using cutting edge statistical approaches to analyse individual participant data on responses to treatment for neglected tropical diseases, connecting expertise between the LSHTM and RVC.

BIG DATA CAN BENEFIT FROM AUTOMATION, USING COMPUTERS TO PERFORM ANALYTICAL TASKS WITH LITTLE OR NO HUMAN INTERVENTION.

By using next-generation sequencing technologies, the DNA of micro-organisms can be accurately characterised, with potential to provide drug-resistance predictions. We are building an automated genomic data curation and collection pipeline of next-generation sequencing data for Mycobacterium tuberculosis. The pipeline uses machine-learning methods to cluster organisms according to their genetic makeup to understand the pathogen's evolution and resistant populations, supporting treatment options.

Drugs that block mosquito-borne transmission of malaria from person to person are effective in halting the spread of malaria. These drugs can induce extreme changes in the shape of Plasmodium parasite cells that can be analysed to identify how the drugs work. We are evaluating commercial off-the-shelf solutions for automated cell isolation and identifcation of drug-treated parasites from microscope images. The automation will accelerate analysis of a high volume of images and could inform the mode of action of these drugs.

Find out more at: www.bloomsburyset.org.uk/awards/data-studies/

BRINGING ALTERNATIVE PERSPECTIVES TO GLOBAL HUMAN AND ANIMAL HEALTH

Using approaches from the arts, humanities and social science to better understand the historical, cultural and socioeconomic diversity that connects people, animals and ecosystems can be vital for tackling the complex challenges of infectious disease and antimicrobial resistance. Interdisciplinary teams from the programme's partner Colleges have been awarded grants to focus a social science lens on these issues through knowledge exchange projects that utilise innovative visual art, design and storytelling methods.

VISUAL ARTS FOR LOCALISED EVIDENCE AND DECISION-MAKING (LEAD)

Researchers from SOAS and LSE, in collaboration with Positive Negatives, are collaborating with African artists to visualise the LEAD project's research findings to enable greater knowledge exchange and impact between local stakeholders. Reflecting the project's mixed methodologies, the artists are using a variety of different media such as animation, posters, murals and short films to visually document different perspectives on the prevention of schistosomiasis and helminth infection for local audiences in Uganda and Malawi.

Working with oral history testimonials and other collected data, artists are also producing comics to narrate local issues such as water use and the experiences of village health workers for use amongst community populations with varying levels of literacy. Visual and interactive materials are [illegible] especially around topics such as infectious disease.

TARGETING EVIDE322.2t06

interventions, such as “Mass Drug Administration” for schistosomiasis and soil-transmitted helminths, is especially important in the context of antimicrobial resistance, with the mass distribution of tablets within child and maternal health for malaria, HIV, and other neglected tropical diseases potentially encouraging the emergence of resistant microbes, among other health concerns.

In recent years, there has been a focus on the utilisation of evidence-based decision-making in global health. While an emphasis on the localisation of this approach is often part of the rhetoric, its realisation has been challenging in practice. The processes of decision-making at different localities is inherently diverse and the evidence needs of local practitioners are not well understood. Further, the most prominent methods used to synthesise knowledge about global health interventions only permit the inclusion of a very narrow, specifc type of information and produce results that are not generalisable for needs of local decisionmakers.

The Localised Evidence And Decision-making (LEAD) project addresses these issues in relation to the transmission and control of schistosomiasis and soil-transmitted helminths in Kenya, Malawi, Tanzania, and Uganda with a synergistic approach to evidence development between local public health practitioners and researchers at LSE and LSHTM. Using a complex systems approach, the LEAD Project aims to identify and respond to the evidence needs of local health practitioners by integrating a series of participatory modelling workshops with locally-relevant evidence development, while taking advantage of recent advances in technological and computational capabilities.

Antimicrobial resistance (AMR) is one of the biggest threats to global health today.
The excessive and inappropriate use of antibiotics is causing some infections

antibiotics are widely available without prescription.

Antibiotics are used to treat bacterial infections in humans and animals. When exposed to low levels of antibiotics for prolonged periods, bacteria evolve to become resistant to that drug. The new resistant bacteria may then pass resistance genes to other bacteria, which also develop AMR. These bacteria are found in farm effuent or untreated human sewage which then contaminate groundwater and the wider ecosystem.

We are taking a ‘citizen science’ approach to our research in Sri Lanka. Using our Nature Citizen app, developed specifcally for the project, volunteers are helping with wildlife identifcation and data collection. By engaging with ordinary people in this way, we are also educating local communities about the problem and its potential solutions.

We are investigating three areas in Sri Lanka, taking photos and faecal samples to establish the occurrence of resistant bacteria in selected mammals and wildlife. One study area has a high density of poultry farms and one, aquaculture sites. The third is a remote location without large-scale commercial farms or human habitations.

Our objective is to establish and compare the prevalence of AMR in these areas and to see if wildlife species aid transmission of resistance genes. We hope our research will provide data that shows AMR spreads through environmental contamination to innocent bystanders and thus enable the community and policy-makers to better address the threat of AMR.

OUR GLOBAL REACH

- Examining options for farmers to diagnose infectious cattle disease faster and investigating pneumonia in calves
- Assessing social acceptability and economic impact of centralised antibiotic usage data collection in cattle farms
- Developing data-linkage machine learning methodology to add individual patient data and improve accuracy of predictions
- Building an automated genomic data curation and collection pipeline of next-generation sequencing data and evaluating solutions for automated images analysis.

SOUTH AFRICA, INDIA & CHINA

- Combining social science, mathematical modelling, epidemiology and health economics to estimate the expected future impact of TB vaccines

AFRICA & ASIA

- Developing a new drug to target enzymes that are highly potent inhibitors of malaria parasites in Africa and Asia
- Developing an assay to improve testing for Crimean Congo Haemorrhagic Fever (CCHF)
- Developing an oral therapeutic for tropical snakebite

- Developing a novel platform diagnostic technology with the potential to revolutionise the detection of tuberculosis in humans and animals
- Creating more effective and potent vaccines using new method of making glycoconjugate vaccines inside safe laboratory bacteria
- for chickens to support increasing global demand for food
- Using nanotechnology to develop antiTd/Sp376.52/Sp37oTJ0 -1. 1 Tf0.945 22 Td[dema}-TjEMC /C2_91 6.52/e00460050agie1000alosi4004D005204 /[•)c3pc uc0460050C004D0000520C90480003005C904n.iM0050a9056005 c4.te

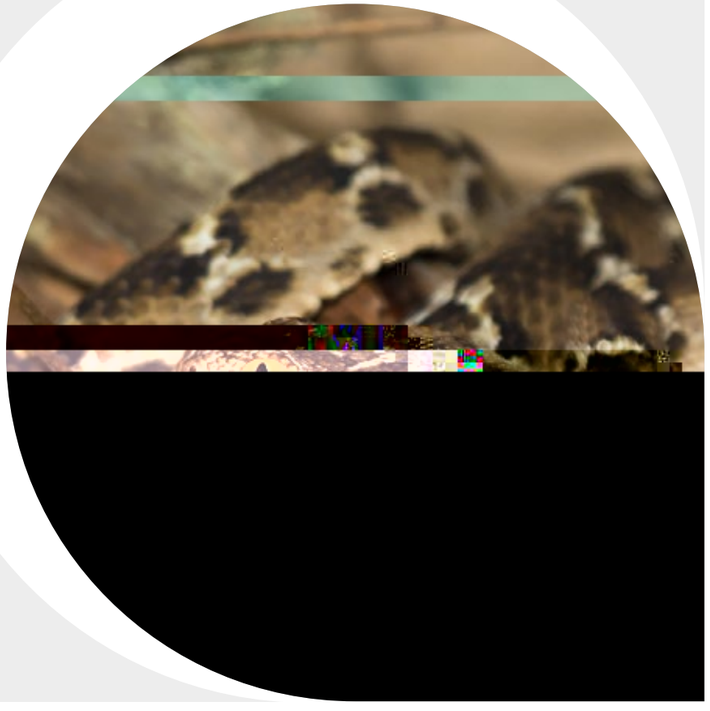
- Using whole genome sequencing technologies of global malaria samples sourced worldwide to gain a deeper insight into parasite biology to develop new diagnostics

SNAKEBITE INTERVENTIONS IN LMICS

Snakebite is a life-threatening neglected tropical disease that causes more than 130,000 deaths annually. Current treatment is restricted to intravenous antivenom, which has to be delivered in a clinical environment, resulting in delays and poor patient outcomes.

Previous work demonstrated that the orally available, licensed, heavy metal poisoning drug Dimaval® showed preclinical efficacy against African/Asian snake venoms rich in metalloproteinase toxins, and that early oral delivery followed by later antivenom administration conferred increases in efficacy in mouse models over antivenom alone. Thus, Dimaval® had potential as a valuable early therapeutic intervention, via oral delivery in a community setting soon after a bite, against certain snakebites.

First, we propose to perform pharmacokinetic analyses to define drug levels collected from healthy volunteer patient cohorts receiving escalating oral doses to define optimal human dosing regimens. This will enable the transition of Dimaval® for snakebite from TRL4 laboratory-scale validation, through TRL5 via small scale safety testing, ready for entry into a Phase II clinical trial (i.e. larger-scale testing in relevant environment, TRL6), thus overcoming a major clinical and regulatory milestone. Simultaneously, we will conduct in vitro and in vivo preclinical research, backfilling the TRL4 space, to investigate the efficacy of Dimaval® against other snake venoms. This enabling strategy will allow the commercial partner leverage of additional markets, where a tangible return on investment exists, to facilitate clinical and regulatory progression while simultaneously prioritising an LMIC access plan.



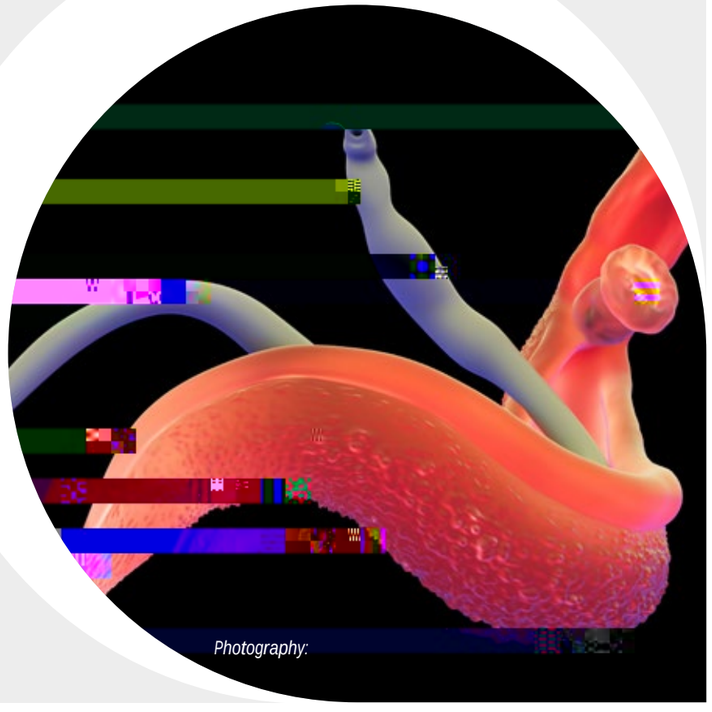
NEW TREATMENTS FOR SCHISTOSOMIASIS

for elimination as a public health problem in all endemic countries and highlights that an integrated approach in which therapeutic intervention will play an important part.

There are three main Schistosoma species that can infect humans with three stages - schistosomula, juvenile and adults - in its complex life cycle present in humans. Infection leads to acute and chronic disease, with current treatment relying on a single 45-year-old drug – praziquantel, which has significant limitations as a therapeutic. With signs of resistance emerging and a vaccine still a distant prospect, discovery of novel anti Schistosoma drugs is of ultimate importance.

This project built on an international interdisciplinary partnership founded under a MRC Newton Award (short-listed for the Newton Prize 2018) bringing together a unique skill set focused on Schistosomiasis drug discovery. This had developed an innovative pipeline for schistosomiasis drug discovery, combining new techniques for target identification, the latest developments in structure-guided drug discovery, advanced high content imaging and new methods in computational chemistry using machine learning/AI techniques.

The team used a combination of computational and experimental techniques to screen a large library of commercially available compounds, and to identify those that inhibit the activity of a protein (smCD1) shown to be crucial for the parasite's survival. This protein was cloned, expressed and purified as a recombinant protein from Schistosoma mansoni, one the main species that infect humans. By X-ray crystallography the atomic three-dimensional structure was determined for the first time, and we saw promising compounds from the initial screen we co-crystallized with smCD1 . We aimed to develop these promising new compounds, improving their efficacy and demonstrating their effectiveness at killing the parasite.



Photography:

Poultry is the world's primary source of animal protein with chickens providing the largest quantity (meat and eggs) consumed by humans. Chicken products are generally affordable, provide high-quality protein and face few religious and cultural barriers. Necrotic enteritis (NE) is a global disease of poultry, which causes damage to the intestines, diarrhea and death in chickens.

REFLECTIONS ON THE BLOOMSBURY SET

Since the start of The Bloomsbury SET programme in April 2018, we have nurtured new partnerships, fostered new knowledge exchange, and facilitated the generation of new ideas. We have achieved wide ranging impacts from developing highly skilled, well-connected people and a portfolio of technologies moving to higher levels of technology readiness, to partnerships with industry and engagement with policymakers on public health interventions for infectious diseases.

The intellectual property portfolio arising from our translational research projects provides many opportunities for collaboration and/or further investment to accelerate the commercialisation of research. We have established connections with industry partners interested in helping fnd routes to market for the solutions being developed by researchers at the partner Colleges.

In addition to more than £5 million in grants translational research, The Bloomsbury SET has further supported academics through mentorship schemes, standalone masterclasses, and a training programme to further their understanding of knowledge exchange and commercialisation.

The Bloomsbury SET has organised a number of events, including our virtual conferences held in 2021, which brought together UK and global partners to explore the concepts and challenges of responding to emerging and infectious diseases, and antimicrobial resistance.

The programme has established and developed strong collaborative relationships between academics and knowledge exchange professionals across the partner Colleges.

Find out more online: www.bloomsburyset.org.uk

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A Knowledge Exchange platform bringing together partner Colleges, together with the London International Development Centre, to accelerate the delivery of innovative scientifc and technical solutions to help safeguard human and animal health.

Research England's Connecting Capability Fund (CCF) supports university collaboration in research commercialisation through allocation of £100 million for competitive projects and formula funds. It aims to share good practice and capacity internally across the higher education sector, forge external technological, industrial and regional partnerships, and deliver the Government's industrial strategy priorities.

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