

Tackling Global Health Challenges

The NDM Centre for Global Health Research is tackling current and emerging threats to health

We are identifying, increasing understanding of, and developing solutions to some of the world's most serious health challenges through global partnerships. Our world-leading research on infectious diseases and neglected tropical diseases includes immunology, microbiology, diagnostics, therapeutics and vaccines, with established programmes on antimicrobial resistance (AMR) and the management of severe illness within poorly resourced health systems. From these foundations our multidisciplinary work encompasses research on medicines quality, implementation science and broader health systems challenges spanning governance to care quality. The NDM Centre for Global Health Research is using this expertise to develop programmes of work in strategic cross-cutting platforms, which are providing the opportunities for us to tackle the wider issues currently impacting global health together.

Better data and evidence

We actively promote improvements in research practice to ensure all trials and studies can produce and share better data in ethically appropriate ways, as well as fully harness the power of secondary analysis, regardless of their resource level. This enables the development of the highest quality evidence required by decision makers at practice and policy levels.

Innovation and implementation

New health practices, technologies and innovations are being developed all the time. Our research is identifying and evaluating these, as well as examining the mechanisms by which countries can implement them. We are using this knowledge about the most effective, evidence-based practices, technologies and innovations to improve health globally.

Sharing knowledge and strengthening capacity

Working with our partners, we are developing tools and enhancing approaches for sharing knowledge within the global health community. The NDM Centre for Global Health Research currently offers internationally available and recognised training, including our MSc in International Health and Tropical Medicine which is supported by teaching from the Africa and Asia programmes. We are also continuing to evolve more bespoke training and development opportunities, to ensure that capacity strengthening efforts address the current and future needs of different global regions, providing early-career researchers with the foundation they require to launch successful research or policy careers in global health. This includes the huge range of evidence-based online courses offered by The Global Health Network, which are available worldwide.

Enhancing policy and practice

We are working with policymakers and practitioners at all levels, in order to ensure that decision-making related to health is based on the most up-to-date evidence. As part of this our research staff are active members of a range of advisory boards, contribute to policy discussions, as well as regularly provide evidence to bodies such as the World Health Organization. The NDM Centre for Global Health Research is also building understanding more widely for a range of global health issues by developing public engagement and stakeholder engagement activities.

Strengthening health and research systems

The NDM Centre for Global Health Research is strengthening health and health research systems through applied research. We are conducting comparative multi-country research, as well as developing systems and strategies which enable health service redesign, promote appropriate ethical oversight and more effective governance.

Better data and evidence

Antimicrobial resistance and enteric fever

Enteric fever, which includes typhoid fever (caused by *Salmonella Typhi*) as well as in paratyphoid fever (caused by *Salmonella Paratyphi*), is usually spread through contaminated food or water. Globally, there are over 14 million cases of enteric fever every year, resulting in about 135,000 deaths.

Importantly the risk of enteric fever is higher in populations that lack access to safe water and adequate sanitation, with poor communities and vulnerable groups including children at highest risk. The disease is primarily controlled by antimicrobial treatment, but this is becoming increasingly difficult due to antimicrobial resistance (AMR). Therefore, despite the availability of antibiotics, enteric fever continues to be a public health challenge in developing areas of Africa, the Americas, Southeast Asia and the Western Pacific regions.

Antimicrobial resistant infections can have severe consequences, including longer illness, higher mortality, and longer hospital stays. Importantly, enteric fever doesn't just impact individuals. Infection can have consequences for the whole family due to high treatment costs and loss of work due to care commitments for family members who fall ill.

The Global Burden of Disease-AMR (GRAM) project is estimating the burden of antimicrobial resistance (AMR) worldwide by combining data, health statistics and geospatial maps for selected bacterial pathogens including enteric fever. This will be used to build an evidence base of antibiotic resistance which can be used by the global research community and policymakers to tailor interventions at the international, national and local level.

“We wanted to determine how widespread drug resistance is in enteric fever. We found that there have been major increases in drug resistance over almost 30 years, and this has come at a time when typhoid fever went from being relatively easy to treat to being close to untreatable in some parts of the world.

“To combat increasing drug resistance for enteric fever, we need a combination of interventions including: improvements to water, sanitation and hygiene (WASH) infrastructure; ensuring the typhoid conjugate vaccine is incorporated into infant immunisation programmes; and rapid, early diagnosis and treatment to help reduce transmission. We also need to build strong partnerships between the WHO, governments, nongovernmental organisations, academia, the private sector and communities to help control AMR in enteric fever. Importantly, all of these interventions will have wider benefits to health and wellbeing globally

Collaboration enabling international research-driven responses to COVID-19

The Infectious Diseases Data Observatory (IDDO) assembles clinical, laboratory and epidemiological data on a collaborative platform enabling sharing between the research and humanitarian communities. The data are analysed to generate reliable evidence and innovative resources that enable research-driven responses to the major challenges of emerging and neglected infections.

Collecting international clinical data on COVID-19

IDDO hosts one of the largest international collections of clinical data related to COVID-19. The platform enables responsible use of data, allowing researchers to address clinically important questions and generate new evidence that reduces the impact of COVID-19.

The COVID-19 data platform developed in a partnership with ISARIC, addresses the critical need for data sharing and enables responsible access to data for new analyses that address knowledge gaps and accelerate the pandemic response. The platform collates individual patient data from clinical care and follow-up, clinical trials and observational research including those collected by the ISARIC Clinical Characterisation Protocol. Data are made available to researchers, helping them to generate new evidence to improve patient care. The data have been analysed to address a variety of research questions including determinants of patient outcomes, variation in symptoms by age group, neurological complications, and mechanisms of acute kidney injury in COVID-19.

Enabling better coordination of COVID-19 clinical trial research

As the COVID-19 pandemic has progressed, the number of registered clinical trials across the world has increased greatly. However, many of these research efforts overlap and focus on similar questions. While this may help to strengthen potential conclusions, it is also likely to cause inefficiencies due to replication of effort and differing study designs that prevent comparability and large-scale analyses. To ensure that definitive answers can be translated into clinical practice as rapidly as possible, it is crucial that research is coordinated.

Responding to this, IDDO has published the baseline results of a Living Systematic Review, alongside an interactive online tool, which is helping researchers to navigate the increasingly dense COVID-19 clinical trial landscape. The review is an openly accessible, frequently updated resource which summarises the characteristics of clinical trial registrations. Researchers can review the details and differences in studies already underway to help facilitate partnerships, collaborations and harmonisation in study design and data collection.

Responding to COVID-19 in resource-poor settings

IDDO is a member of the COVID-19 Clinical Research Coalition, an international coalition of scientists, physicians, funders, and policymakers from over 220 institutions from over 65 countries responding to COVID-19 in resource-poor settings. The Coalition aims to accelerate desperately needed research in those areas where already-fragile health systems might cause the greatest health impact on at-risk populations by:

- Leveraging global expertise for high-impact COVID-19 research.
- Championing equitable and affordable access to COVID-19 vaccines, diagnostics, and treatments.
- Promoting open sharing of research knowledge and data.

My DPhil in Tropical Immunology, Sandra Adele

Sandra Adele is a DPhil student working on SARS-CoV-2 T cell immunology in the Tropical Immunology research group. She is supervised by Professor Susanna Dunachie.

Could you describe your research?

My research focuses on the magnitude of the T cell responses against SARS-CoV-2 elicited through natural infection and through vaccination. Additionally, I also work on the SARS-CoV-2 emerging variants of concern, and I use bioinformatics and functional assays to address questions regarding T cell escape in these variants.

Why is it important to characterise T cell response?

T cells play a key role in antiviral immunity in several infections. Characterising T cell responses will help us understand their role in immune responses in SARS-CoV-2, which is critical in the development of vaccines. Additionally, characterising T cell responses can help address gaps in scientific knowledge relating to the roles T cells play in immunopathogenesis during acute SARS-CoV-2 infection and the relevance of previous exposure to pre-existing human coronaviruses.

What challenges are there in measuring T cell response in low resource settings, and how is your research addressing this?

T cell responses are measured using a variety of assays which require several reagents to perform the experiments and also equipment to analyse the results. These resources may not be readily available in low and middle income countries (LMIC). The development of a T cell assay that uses reagents and lab equipment that can be readily accessible in LMICs would be helpful in overcoming these challenges. It is also important that the T cell assays are user friendly and involve minimal steps so they can be easily incorporated in different research settings.

Why did you choose to do postgraduate research in tropical immunology?

My background is in Cellular Neuroscience, Pharmacology and Global Health. Before my DPhil I completed the MSc in International Health and Tropical Medicine (MSc IHTM), which made me think about challenges from both a scientific and a public health

perspective. It challenged me to not only focus on the science, but the context in which the science will be applied.

Mapping real-time media reports on the quality of medical products across the world.

Substandard and falsified (SF) medical products, including medicines, vaccines, diagnostic tests and devices are critical global public health issues. They reduce the effectiveness of treatments, cause adverse drug reactions and economic harm, and contribute to antimicrobial drug resistance. This threatens the lives of millions of people. Global investment to improve the prevention and treatment of disease is wasted if the quality of the medical products actually used by patients is poor.

Current SF medical product surveillance in most of the world is extremely limited and incidents relating to poor quality medicines are often not published in peer-reviewed scientific journals. The Medicine Quality Research Group, within the Infectious Disease Data Observatory and the Mahidol Oxford Research Unit, is addressing this.

It has developed the Medicine Quality Monitoring (MQM) Globe – an interactive, online tool which is mapping real-time media reports on the quality of medical products across the world.

The MQM Globe supports national and international organisations to understand and raise awareness of the issue of substandard and falsified medicines. It is filling evidence gaps with customised summaries of national and international newspaper reports in French, Spanish, Mandarin, Vietnamese and English on medical products' quality, with reports available to download. The Globe also includes a system for displaying regulatory alerts webpages. These systems give early warning of new SF incidents, reveal the extent of the problem, how the media perceive and report cases, and may also shed light on how incidents can affect subsequent behaviours and perceptions.

Between 1 January and 15 June 2021 the Globe included 924 incident reports of SF medical products in the press worldwide, and the system is used by multiple international and national organisations to give early warning of problems that need further investigation.

COVID-19

The COVID-19 pandemic poses enormous risks to the global medical product supply, both for non-COVID and COVID medical products due to inequitable access, impaired pharmaceutical production and inspection, and supply chain disruption. There has been a surge over the last year of diverted, substandard and falsified COVID-19 diagnostic tests, PPE, hand sanitisers, vaccines and medicines exacerbating the unmet needs of 7.8 billion people, with great public health harm.

SF medical products jeopardise national, regional, and global attempts to improve access to effective health care because they lead to avoidable morbidity, waste financial resources and contribute to drug resistance. In the context of COVID-19, SF products undermine the global effort to tackle the pandemic.

COVID-19 vaccines are vital interventions to help end the pandemic. However, falsified, diverted and substandard (especially degraded) vaccines are an increasing global public health problem, with 123 reports from 35 countries up to 31 May 2021.

The Medicine Quality Research Group publishes regular reports about diverted and SF-related COVID-19 medical products and COVID-19 vaccines. For all COVID-19 linked product categories combined, there are over 700 different incidents reported in the English lay press alone, highlighting risks to peoples' health in more than 60 countries.

We share these findings internationally to influence health policy for guiding interventions and improve this dangerous but neglected situation.

Innovation and implementation

The world's first human vaccine trial for melioidosis

Melioidosis is a tropical disease caused by the Gram-negative bacterium *Burkholderia pseudomallei*, which is found in contaminated water and soil. Melioidosis is a common cause of illness and death across tropical regions, with an estimated 89,000 deaths occurring annually, chiefly affecting the world's poorest communities in low and middle income countries. Despite its prevalence, it has a relatively low profile compared to other tropical diseases.

Known risk factors for melioidosis include diabetes, alcoholism and renal disease, and the range of presentations includes pneumonia, liver and splenic abscesses and septic shock. Up to two-thirds of people with melioidosis have diabetes mellitus, and a vaccine targeting this well-defined at-risk group is predicted to be a cost-effective public health intervention.

The Tropical Immunology research group will be conducting the world's first clinical trial of a vaccine for melioidosis. The vaccine candidate has been developed by collaborators at the University of Nevada and will be tested in a clinical trial with volunteers in Oxford, with the goal of testing in Thailand.

Professor Susanna Dunachie, Head of the Tropical Immunology research group and Principal Investigator on the project said:

"I have been studying the immune response to melioidosis in Thailand for the past ten years, and I am especially interested in the relationship between diabetes and melioidosis. More than half the people who get ill with melioidosis have diabetes, and up to half the people in low middle income countries who come to hospital with it die. There are treatments, but it's a rapidly fatal disease killing between 10 – 40% of people infected."

"This will be the world's first human vaccine trial for melioidosis and represents a huge step in tackling this neglected but very important disease"

SEREN – affordable diagnostic tests for newborn babies in Tanzania

A research collaboration between AfOx Visiting Fellow Dr Siana Nkya from Muhimbili University for Health and Allied Sciences in Tanzania and Professor Anna Schuh from the University of Oxford has resulted in the development of SEREN, which will be a new social enterprise providing affordable diagnostic tests for newborn babies in Tanzania.

Blood diseases are a major problem in sub-Saharan Africa which has a high incidence of both genetic conditions and blood cancers. While effective and affordable therapies are available in many African countries, a genetic diagnostic test for conditions such as sickle

cell disease (SCD) can cost up to 400 USD and requires highly skilled multidisciplinary staff, equipment and methodologies that cannot easily be maintained.

Siana was working as a laboratory manager at a Newborn screening programme at the Muhimbili University for Health and Allied Sciences (MUHAS) in Dar-es-Salaam conducting early screening for SCD in newborn babies in Tanzania. Working together with Dr Julie Makani from MUHAS and Prof Anna Schuh, from the Molecular Diagnostics Centre, University of Oxford, the three scientists formulated a plan to build local capacity for precise, low-cost, low-maintenance, patient-near DNA diagnostics solutions. To translate their idea into action, Siana applied for the AfOx Visiting Fellowship in 2019. The fellowship was instrumental in enabling her to visit Oxford and work in collaboration with Anna and other colleagues at Oxford's Department of Oncology and the Molecular Diagnostics Centre.

This led to Siana and her colleagues at MUHAS and Anna to co-found SEREN, which will be a social enterprise delivering affordable and accessible diagnostic tests to patients in Tanzania. SEREN will employ 12 full-time staff and provide clinical and laboratory practice training for laboratory technicians, bioinformaticians, nurses and clinicians.

In close collaboration with MUHAS, University of Oxford, the Muhimbili National Hospital and the patient charity Tumaina la Maisha, Siana and Anna have put in place the required infrastructure to facilitate national patient referrals, local sequencing, joint cloud-based data analysis and clinical data collection for the WHO Cancer Registry.

This includes frameworks for parent/patient consent for DNA analysis and to provide diagnostic-grade DNA testing for as low as \$10/test. As of March 2021, 50 children and young adults have undergone testing, and Muhimbili National Hospital has already adopted one of the tests to provide government-funded diagnosis of chronic myeloid leukaemia.

In 2020, SEREN won the University of Oxford's Vice-Chancellor's Innovation Award. Siana and Anna are now in the process of securing additional funding for SEREN and are in discussions with representatives from the Ministry of Health and other stakeholders to secure sustainability for genetic diagnostics that will save the lives of thousands of children and young adults in the region.

"The AfOx Fellowship had a dual benefit. Not only did it give me access to resources and equipment that were then lacking at my home lab, but it also made me think of the social aspect of the diagnostic test. For the first time in my career as a scientist, I thought, how can we create an innovation that will actually work in the community"

Watch a short film about SEREN, and watch Siana talking about her journey.

Sharing knowledge and strengthening capacity

MSc in International Health and Tropical Medicine

This one-year Oxford degree integrates knowledge and skills to better respond to global health challenges in the most affected communities.

Over the past six years, the MSc in International Health and Tropical Medicine (MSc IHTM) has equipped 127 professionals from 51 countries as global leaders for more innovative sustainable solutions.

Recent alumni discuss the skills they have gained from the programme.

Fernando Reis, Brazil

“The ethics module of the MSc IHTM had a deep impact in better preparing me to work with vulnerable populations, and there is no better reward than being able to help those who need it the most.”

After the MSc, Fernando joined the Brazilian National Field Epidemiology Program, where he was involved in investigating an outbreak of diarrhoea in a remote Indigenous village in the Amazon.

“We collected dozens of stool and environmental samples and were able to make them get to a lab almost 2000 km away in 24 hours. The findings were extremely important to help us design recommendations and interventions to stop the outbreak and prevent future ones.”

Mahnaz Hossain Fariba, Bangladesh

“Thanks to the MSc IHTM, I have developed health management skills that are valuable to help serve my country in these challenging times.”

On completion of her MSc, Mahnaz returned to the Bangladesh Civil Service. As an Executive magistrate, she enforces sanitary control measures for the pandemic response strategy.

“I am part of the collaboration and co-ordination process. A road or street is locked down when there is suspicion of COVID-19 infection and executive magistrates are present to ensure the success of the procedure. We are informing people of the importance of staying at home. Most of the shops are closed, and there are not many people on the roads because of this situation.”

Claire Keene, South Africa

“The Masters prepared me for the role in Khayelitsha [a township in Cape Town, South Africa] in general with a good understanding of public health and global health, as well as the background in statistics and epidemiology [which] helped me to be able to understand how to evaluate the programmes that we are implementing”

Following her MSc, Claire joined Médecins sans Frontières (MSF). As a Medical coordinator, she has been involved in managing healthcare provision across a historically underserved urban community.

“Since COVID hit, we have been completely rethinking what we are doing in Khayelitsha, shifting all of our programmes to fill gaps and addressing how we can support HIV and TB patients because those are our focus. So part of that has been supporting the clinics to get them ready to receive COVID patients, screening them, testing people for COVID, as well as making sure that HIV and TB services are integrated.”

Adeniyi Aderoba, Nigeria

“What I really find interesting is the professional training that goes along with [the academic] training. The media training experience is very unique. We’ve had various exposures to different leadership programmes. We were at the Houses of Parliament, we had debates at the Oxford Union, places where prime ministers of the United Kingdom have been to debates.”

Zay Yar Phyo Aung, Myanmar

“I am the second one from my country, Myanmar, to join this course. The very most exciting thing for me throughout this course is to have a connection with people from various parts of the world, and that diversity and the warmth that they provide and by the course – it’s extraordinary. I think we can learn a lot from everyone – sometimes you don’t actually know what’s going on the other side of the world and this is a very unique chance for us to be able to understand.”

The Global Health Training Centre

Building health research skills through free accessible online training at the Global Health Training Centre.

Ecosystem

To tackle disease, we need a connected ecosystem that joins up all types of health research including observational, social science and clinical.

Our eLearning courses are designed to reflect this ecosystem approach

- 132 courses (including 89 translations in 9 languages)
- 2 million online training modules taken

Courses

Our most popular courses reflect recognised knowledge gaps in our global community.

Course	Number of eLearners
ICH Good Clinical Practice.	195,960.
Introduction to Clinical Research.	39,919.
ICH Good Clinical Practice (Spanish).	28,990.
Introduction to Clinical Laboratory Practice.	21,148.
Research Ethics Online Training.	21,612.

Essential Research Skills Training Curriculum

We have designed a three-stage approach to establish an evidence-based Essential Research Skills Training Curriculum.

This work was a collaboration between the World Health Organization's Special Programme for Research and Training in Tropical Diseases (WHO-TDR) and The Global Health Network. The aim was to identify what constitutes the minimum set of skills, knowledge and key principles that would enable those without previous experience in research to undertake high-quality health research.

Stage 1: Gap analysis

Analysis of responses from training needs surveys, session evaluations from research training workshops, and feedback submitted on completion of eLearning. This analysis provides a range of research skills topics and subject areas that are used to generate a core list of research training themes.

Stage 2: Consensus building

Using the Delphi consensus building method with a group of experts and stakeholders to develop a curriculum framework by grouping the themes.

Stage 3: Stakeholder review

Bringing together a diverse group of stakeholders from across the globe to review the suitability of the theme groupings as an accurate reflection of the content, and to evaluate the applicability of the proposed Essential Research Skills Training Curriculum findings to the global research community.

Proposed framework diagram: text is available at <https://www.cghr.ox.ac.uk/research-themes/sharing-knowledge-and-strengthening-capacity/the-global-health-training-centre/research-environment-as-a-system>

Characterising Hepatitis B infection in Vukuzazi, South Africa

Hepatitis B virus (HBV) infection is a significant global public health challenge, causing about 650,000 deaths worldwide each year. Of the 257 million people living with chronic hepatitis B (CHB) infection worldwide, 60–80 million are in Africa.

HBV infection has a substantial impact on disability-adjusted life years (DALYs), due to the disproportionate burden of morbidity and mortality in young adults, caused by inflammatory liver disease, cirrhosis, and hepatocellular carcinoma (liver cancer). This emerging burden of liver disease has substantial economic and social impact on individuals, families and society in many populations. In Africa, prevalence of HBV infection is high (>8% in many settings) and there is a concerning burden of disease in young men.

International Sustainable Development Goals aim for the elimination of hepatitis B virus (HBV) infection as a public health threat by the year 2030. Specific targets focus on reducing incidence, prevalence, and mortality of HBV, and increasing the proportion of all those with chronic infection who are on treatment. To achieve this, increased screening and antiviral treatment are essential.

New research funded through an AfOx Research Development Award (REDA) is starting to develop a detailed picture of HBV infection, immunity and liver disease in a large population cohort in South Africa. The data gathered through this project will help to inform HBV vaccine deployment, provide information about the needs for treatment provision, both for individual benefits and to reduce transmission. The project will also determine the groups most at risk, enabling planning of targeted screening and interventions within the community.

The project is a collaboration between Dr Tongai Maponga from Stellenbosch University and Professor Philippa Matthews from the University of Oxford. The AfOx Research Development Awards (ReDA) are a competitive pump-priming fund aimed at supporting previous AfOx grant recipients from African institutions to follow up on ideas developed during their interactions with Oxford-based colleagues. The Awards are intended to help stimulate larger collaborative projects that will strengthen Africa-Oxford partnerships and make the collaborating partners competitive for future major awards. Tongai and Philippa have worked together to establish a new HBV cohort in Cape Town, with support from the Wellcome Trust. Tongai received an AfOx Visiting Fellowship in August-September 2018 that enabled him to visit Philippa's lab at the Nuffield Department of Medicine in Oxford. Tongai's visit to Oxford provided the opportunity for the researchers to work together on a several collaborations, including a laboratory project to sequence hepatitis B virus (HBV) from their South African patients, and on analysis of HBV viral load data from international cohorts.

Building on this, this new research project is further strengthening the existing collaboration between Tongai and Philippa by characterising HBV infection in a large population cohort, Vukuzazi, established by clinical research teams at the Africa Health Research Institute (AHRI) in KwaZulu-Natal. The aim is to generate a detailed insight into infection and immunity to HBV in this setting, and to describe the clinical characteristics of HBV infection in individuals with and without HIV co-infection.

Developing insights into population-level infection and immunity, together with detailed clinical characterisation to determine the extent and nature of liver disease, will enable the development of recommendations to inform the best deployment of scarce resources in clinical care and public health, as well as providing education, training healthcare workers, and securing longer term investment.

Enhancing policy and practice

Advisory roles

NDM Centre for Global Health Research members are ensuring that decision-making related to health is based on the most up-to-date evidence by being active members of a wide range of advisory boards, working groups, steering groups and committees.

Advisory Roles diagram: text is available at <https://www.cghr.ox.ac.uk/research-themes/enhancing-policy-and-practice/advisory-roles/advisory-role-alternative-text>

Improving the design and delivery of services for those with severe illness including COVID-19

The Health Systems Collaborative, in collaboration with London School of Hygiene and Tropical Medicine, Karolinska Institute, KEMRI-Wellcome, Ifakara Health Institute and the Centre for Global Development with support from Wellcome Innovations, are examining how best to improve outcomes for people with very severe illness in East Africa, with a special focus on severe COVID-19.

Very severe illness can affect anyone, irrespective of underlying diagnosis, age, gender or social status. It includes conditions that are acute and life-threatening but often reversible if patients receive effective emergency and critical care. Despite this, severely ill patients are at high risk of poor outcomes, with mortality rates of up to 82% reported in low-resource settings.

The emergency and critical care challenges we are facing as a result of the COVID-19 pandemic highlight our need to improve care and generate knowledge about feasible, long-term systems strengthening for everyone suffering severe, acute illness. As COVID-19 lacks definitive treatment, essential emergency and critical care to support vital organ functions is needed to reduce mortality. For COVID-19 and other causes of Severe Acute Respiratory Infection, respiratory support is especially important. Improving emergency care so that patients get rapid access to essential forms of critical care could save the lives of many severely ill patients.

The Essential Emergency and Critical Care (EECC) concept is aimed at such patients and includes determining the basic, low-cost actions and treatments required by severely ill patients in a given setting, as well as the system requirements that are needed to successfully deliver them. EECC describes a minimum set of standards that are basic and low-cost, and that can potentially be shared across different health worker groups even in low-resourced, low-staffed settings.

There has been considerable effort by governments and donors to support emergency care and scale up elements of critical care driven by the COVID-19 response. In high income countries, this care is provided in Intensive Care Units (ICU), which require sophisticated equipment and highly skilled staff. However, this can be difficult to quickly scale up in low-resource settings, contributing to inequalities in healthcare for people living in differently developed nations.

The Health Systems Collaborative and KEMRI-Wellcome team are contributing to the POETIC-COVID (Provision of Essential Treatment In Critical Illness in the COVID-19 pandemic) project by leading work to rapidly explore how countries and their partners have mobilised resources and effort to improve and scale up forms of essential emergency and critical care in East Africa during the COVID-19 pandemic. This involves evaluating global and national efforts to strengthen EECC and more advanced critical care services, determining how these efforts have been translated to changes in hospitals and contributing to work estimating the cost-effectiveness of scaling up EECC capacity.

The knowledge we are gaining from this will help design future approaches to optimise the long-term effectiveness of system strengthening in emergency and critical care and positively impact patient outcomes.

An important component of this work includes rapidly communicating findings at national, regional and global levels with decision-makers who are able to act to strengthen care systems. Sharing our findings and using these to build networks and exchange ideas on implementation strategies, will ultimately help learning from the pandemic response, contribute to more effective and equitable health systems in the long-term and improve the outcomes for many severely ill patients worldwide.

Ensuring optimal treatment of malaria infection in children

Malaria medicines are working well in many parts of the world, however, there is serious concern that malaria parasites are once again developing widespread resistance to antimalarial drugs, in particular resistance to artemisinin derivatives and the partner drugs used in Artemisinin-based Combination Therapies (ACTs). The WorldWide Antimalarial Resistance Network (WWARN) is a global collaborative platform that provides research evidence to support international efforts to fight antimalarial drug resistance and is part of the Infectious Diseases Data Observatory (IDDO).

Since 2000, experts have reported dramatic declines in cases and deaths related to malaria. Despite this encouraging news, the decline on morbidity and mortality have stalled since 2015. More than 400,000 people still die from malaria each year, mainly young children in sub-Saharan Africa.

The World Health Organization (WHO) current recommended first and second-line treatments for uncomplicated *Plasmodium falciparum* malaria are ACTs which include a rapid-acting artemisinin component plus a slower-acting partner drug.

Results from WWARN Dose Impact Study Groups have provided evidence for the revised recommendations for optimal use of artemisinin combination therapies included in the updated WHO 'Guidelines for the Treatment of Malaria'.

This contribution is ensuring that young children get the optimal treatment for malaria infection, increasing their chances of survival and lowering their risk of reinfection. Importantly, this is also helping to slow the spread of antimalarial drug resistance.

Revising the recommended dose of DP

The WHO have revised the recommended dose of the ACT antimalarial Dihydroartemisinin-Piperaquine (DP) for young children based on WWARN evidence which has been generated by WWARN analyses.

In 2013, the WWARN DP Dose Impact Study Group published a study suggesting that the dosing regimens for DP should be reviewed. Although DP is still overall a highly efficacious drug, the study highlighted that even when the recommended dose was given, children under five years had a higher risk of treatment failure.

The research showed that a subset of young children were receiving suboptimal doses of DP. The study results suggested that patients receiving a lower than adequate antimalarial dose are slower to respond to treatment, which is less likely to kill all the parasites they have in their bodies, meaning they would be more likely to have malaria again a few weeks later.

Based on the results from the Study Group and pharmacometric simulations for each weight group, the WHO has revised the recommended dose of DP for young children. The changes to the WHO treatment guidelines should limit the risk of treatment failure for young and vulnerable children and prolong the useful lifespan of this important treatment.

Fixed dose combination therapies

In 2015, the ASAQ Dose Impact Study Group found that the efficacy of artesunate-amodiaquine (AS-AQ) can vary due to changes in the formulation of the two parts of the ACT, artesunate and amodiaquine. When both components are combined in a single tablet, this fixed dose formulation shows better treatment efficacy than that observed when separate AS and AQ tablets are just taken at the same time; this is mostly attributed to a lower dosage of AQ in loose AS-AQ formulation. This could be caused by a lower dose of amodiaquine in certain formulas or the need to split tablets for younger patients which can cause inaccuracies in dosing.

Higher dose of AL needed for malnourished children

Research from the AL Dose Impact Study Group in 2015 has confirmed that the current recommended dose of the antimalarial artemether-lumefantrine (AL) is still working very well in patients treated for malaria. However, analyses of data from more than 14,000 patients suggest that therapeutic efficacy was lowest in young children from Asia and young underweight children from Africa.

AL is the most commonly used ACT for treatment of *Plasmodium falciparum* malaria infection in Africa. The research suggests that malnourished children have a higher risk of treatment failure and of suffering reinfections compared to those who are well-nourished, and that a higher dose of AL could potentially improve treatment results for children in this group.

Strengthening health and research systems

Enabling easier, faster and better research by sharing know-how people share what works

The Global Health Network hosts over 50 interconnected knowledge hubs around seven complementary and integrated thematic areas where researchers and teams share data, guidance, methods and experience within their programmes, across networks, between collaborators and with the wider research community.

Each knowledge hub is led and managed by collaborating teams from across the world who foster a community of practice. These are set up in such a way as to provide focussed and highly functional virtual workspaces to facilitate work open, neutral and collaborative workspace where researchers and teams can contribute and others can find examples of good practice to build from.

Thematic areas

- Research Consortia and Networks.

- Social Science, Ethics and Communities.
- Laboratories, Vectors and Diagnostics.
- Infection, Immunity and Resistance.
- Woman and Child Health.
- Research Processes and Methods.
- Non-Communicable Disease.

COVID-19 Research Implementation and Knowledge Hub

Launched in January 2020 in response to the need for robust, collaborative research to immediately understand how to combat COVID-19, the COVID-19 Research Implementation and Knowledge Hub is supporting rapid research implementation in low-resource settings.

The hub enables health professionals and researchers globally to discover the most relevant information, guidance, and resources to their research, role and setting in one place.

- 230,000+ visits to coronavirus.tghn.org
- 140+ countries.
- 40+ workshops.
- 7 working groups.
- 500+ working group members.
- 5,000+ attendees.
- 82 Countries.
- 20,000+ downloads of resources including Case Report Forms, Clinical Characterisation Protocols and ethics approval request templates.

* figures corrects as of February 2021.

Spotlight Professor Sassy Molyneux

Many health innovations and technologies with potential to strengthen global health are already available, but there are major challenges in embedding them into health systems in ways that reach those in greatest need. Incorporating health systems and social science research into global health research programmes can help us understand and work towards overcoming these challenges. Using these research approaches we can explore different stakeholders' perspectives, priorities and practices, examine how policies and interventions are developed and implemented in diverse and complex contexts, and critique how global health research is funded and conducted.

I would describe myself as an interdisciplinary social scientist conducting both health systems and empirical ethics research. My research interests are aimed at strengthening everyday health system resilience and system/provider responsiveness to individual, household and community priorities and concerns. I also study ethical practice in health research and the delivery of care. My role at the NDM Centre for Global Health Research is to support the strategic development of health systems and social science research in global health within the Centre and to strengthen links more widely across the Nuffield Department of Medicine.

We are fortunate that there is a large and strong body of global health research in the NDM Centre for Global Health Research, which involves numerous partnerships with organisations and individuals all over the world, including well-established centres with headquarters in Kenya, Thailand and Vietnam. Across these networks, there is already substantial expertise and experience not only in biomedicine and in developing and testing interventions, but also in research ethics and in understanding the health systems that deliver these interventions. For example there are strong health systems, social science and/or ethics components in studies aimed at strengthening the diagnosis and treatment of dengue and malaria, and in programmes of work aimed at strengthening medicine quality. There is also hospital-based research to determine if and how the introduction of new technologies and service delivery innovations improves the quality of care provided in newborn baby units, and empirical ethics research examining researcher responsibilities when conducting different types of research among vulnerable groups in LMICs. Across all of this research we have been learning about the best ways to plan and conduct research across networks of researchers working in diverse settings.

We are building on this solid platform of health systems and social science research to enhance our knowledge sharing within the department and across our networks. In so doing we aim to continue to embed high quality health systems and social science research into broader interdisciplinary programmes of research. This will enhance our contribution to stronger, more equitable health and research systems, further advancing and protecting the health of those most vulnerable to poor outcomes.

Harnessing innovation to improve quality and outcomes of care

Essential technologies could improve quality and outcomes of care if successfully adopted but benefits in LMIC are threatened by workforce shortages and implementation that fails to consider context and system complexity. Thus, many technologies fail, wasting valuable resources or worsening care quality.

The Harnessing Innovation in Global Health for Quality Care (HIGH-Q) project is increasing understanding of how technological and human resource interventions can be designed and implemented successfully to enhance the quality of inpatient and post-discharge neonatal care.

This programme of work has a specific focus on neonatal care in low and middle income countries' hospitals and explores the interrelationships between technology adoption, workforce deficits and quality of care. It takes a broad view of quality focusing especially on the effectiveness, timeliness, safety and outcomes of care together with families' and staff experiences.

The HIGH-Q programme directly supports five DPhil students in the Health Systems Collaborative research group.

Abdulazeez Imam

Evaluating the effects of a health workforce intervention on indicators of quality of newborn care in Kenyan neonatal units.

“My research aims to determine the impact of adding extra nurses on the quality of inpatient newborn care in Kenyan hospitals which have a very low staff to patient ratios and other

resource constraints. This DPhil fits into objective 2 of the HIGH-Q project which is evaluating how the introduction of a workforce intervention affects the quality of care, including the experiences of neonatal care delivery.

“I originally trained as a Paediatrician in a resource-constrained setting and have always loved neonatal medicine. Doing a DPhil project which focuses on improving neonatal quality of care in a resource-constrained setting is a dream come true. My long-term goal is to rise to the position of a clinical professor conducting international research and managing a thriving grant portfolio. In the HIGH-Q project, I am surrounded by excellent examples of where I hope to see myself in future.”

Gulraj Grewal

Determine how continuity of care may be better supported by an innovation to improve post-discharge care for vulnerable newborns in Kenya.

“My research looks at improving continuity of care post-discharge for sick newborns (hospitalised within 28 days of birth) using a human-centred design (HCD) approach. Involving people in the design process means that the products and interventions we create fit with the needs of the people they are being designed for, as well as ensure that the context they will be delivered in has been taken into consideration.

“I chose to do a DPhil as I was interested in research – this particular DPhil was of interest because of the focus on HCD, which is something I was keen to learn more about. I want to work in academia – lecturing (ideally in Kenya) and conducting research that informs interventions and policy. My DPhil gives me the opportunity to read and learn about theories, whilst also being very practical.”

Gloria Ngaiza

The role of technologies in shaping the practices and experiences of care in Kenyan neonatal units.

“I am interested in using the experiences of people in making health interventions acceptable and successful. Innovation and technology in health is a promising area with not much research from the angle of implementers or beneficiaries. My project is looking at how to ensure the successful use of introduced newborn technologies in Kenyan hospitals, focusing on health workers and caregivers of sick newborns and how their experiences and practices influence the long-term use of these technologies.

“Before joining the university, I worked in global health in several developing countries, and saw the efforts of introducing and using technologies to improve the quality of care in limited settings. Unfortunately, most of those interventions were not sustainable because of context-specific factors that were not considered. The experience I gain through my DPhil will help me to address this by giving me the skills to prioritise, design, implement and evaluate high-quality health research in limited resourced countries.”

Naima Nasir

Governance arrangements for health technology interventions and innovations in LMICs.

“My research examines the governance arrangements for new and existing health technologies and innovations in low and middle-income countries, focusing broadly on sub-Saharan Africa and more specifically on Kenya. This research will provide recommendations to improve the governance of health technologies and innovations which focus on health system strengthening.

“I have a passion for global health research and practice, particularly health systems and policy research, maternal and newborn health, and health systems strengthening. My DPhil aligns with these interests and presents a unique opportunity to gain critical skills in global health research, which I believe will be invaluable to my career. My hope is that my research will contribute meaningfully to health system governance, health system strengthening, and improved quality of health care delivery in my country and region, as well as globally.”

Asma Shaher Rababeh.

Investigating information tools used in post-discharge care for vulnerable newborns in Kenya.

“My research is focused on the use of information tools in supporting the care for vulnerable newborns post-hospital discharge (to home) in low and middle income countries (LMIC) generally and in Kenya in particular, and how they can be better embedded in care processes. These information tools are used to collect data on health including paper-based, electronic-based and hybrid electronic-paper tools.

“In Arabic, we say that to make a lasting contribution to a field is to leave a fingerprint that will never be forgotten and to strive to be among the top listed changing agent names in that field. This has always been my aspiration in healthcare generally and Health Informatics (HI) area in particular. I am committed to enhancing the healthcare system by applying HI solutions. I believe that there are many innovative solutions which will have a huge positive impact on the quality of healthcare services if applied appropriately. For example, telehealth means using new telecommunication technologies to deliver and facilitate health-related services, education, and information to healthcare providers or/and patients over time and distance barriers. The implementation of such a solution will help healthcare providers and their patients in rural and poor places to advance healthcare services.”

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