Strategic Plan

KEMRI–Wellcome Trust Research Programme

2016–2023

KEMRI | Wellcome Trust

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Introduction

The KEMRI-Wellcome Trust Research Programme has delivered internationally competitive research and capacity building for 26 years. We renewed core funding for our next 5-year cycle starting October 2016, and this has been extended in 2021 for a further two years to 2023. Our strategic plan is therefore updated to match. Our scientific themes draw together researchers from different disciplines to work on high priority areas and enhance the rapid dissemination and uptake of findings into policy and practice. Work within and between themes is highly inter-disciplinary and interaction between themes is common. We promote a broad and inclusive approach to scientific themes, providing flexible capacity to respond to emerging health challenges.

We have 850 employees and work across 3 main hubs in Kenya (Nairobi and Kilifi) and Uganda (Mbale) with an international network of collaborating sites (Figure 1).

From Nairobi we coordinate health systems research including networks of hospitals for pragmatic trials, undertake international and national epidemiological work and coordinate malnutrition surveillance. From Kilifi we undertake work across the spectrum of disciplines with a unique resource of linked demographic surveillance of 0.29M residents, clinical phenotyping and molecular biology. From Mbale we coordinate multi-centre clinical trials on malaria and its consequences. Clinical research and social science cut across all three hubs.

Figure 1: Programme Locations

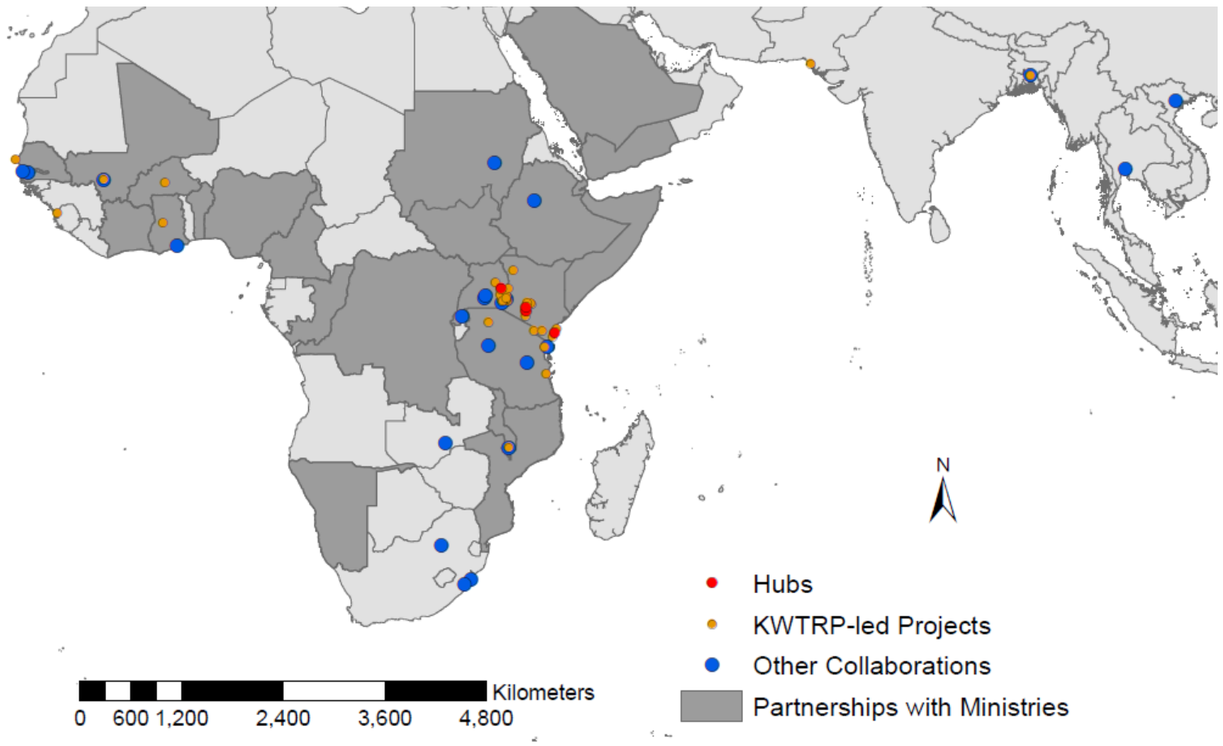


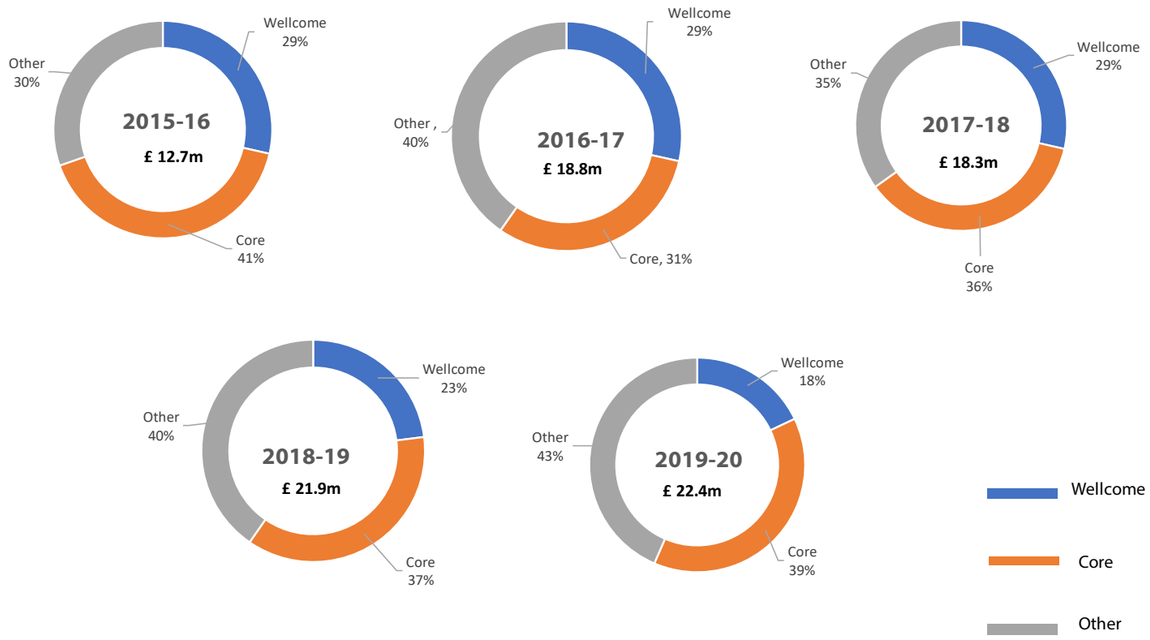
Table: Value of New Awards by Financial Year (£k)

Our funding strategy is to use Wellcome's core funding to provide the basic platform for research, and our scientific outputs are supported by additional project funding including Fellowships from the Wellcome Trust and other funders.

The table (left) and figure (below) show the recent outcomes of this strategy, with new awards by financial year and rates of spend per year, respectively.

	2015-16	2016-17	2017-18	2018-19	2019-20
Wellcome	6,747	3,647	3,684	4,109	11,652
EDCTP	-	1,454	4,892	696	382
MRC	307	1,109	3,360	782	1,266
IAVI	929	860	1,037	784	2,554
U Oxford	500	500	675	550	681
DfID/FCDO	690	316	-	-	2,040
Broad	-	269	432	-	-
DNDi	-	114	-	135	-
BMGF	8,397	86	2,390	1,770	9,965
UK DoH	-	-	98	-	-
GAVI	1,961	-	1,985	-	-
NIHR	-	-	1,434	-	-
LimmaTech	-	-	-	987	-
WHO	-	-	-	451	-
Other	2,174	178	269	618	855
Total	**21,704**	**8,533**	**20,256**	**10,881**	**29,394**

Figure 2: Rates of Spending by Year

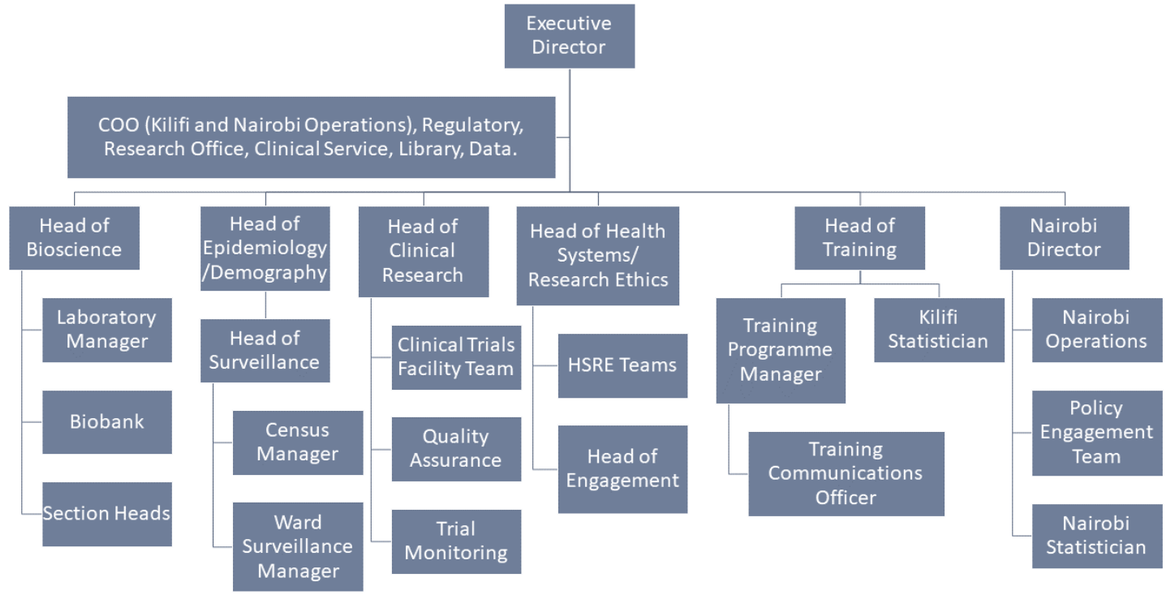


Management

The Kilifi and Nairobi hubs operate as part of a KEMRI centre (the Centre for Geographic Medical Research – Coast). The Programme Director is based in Kilifi, and works with Directors in the Nairobi and Mbale hubs. KEMRI contributes a Deputy Director to the partnership, appointed to the KEMRI – CGMRC Centre. In Mbale, Uganda we collaborate with the Mbale Clinical Research Institute. Our Operational Platform is led by our Chief Operating Officer.

Our work is supported by four Scientific Departments, with science strategy led by a Head with responsibility for an aspect of the core research platform. Our three hubs integrate via the Scientific Themes which run across the Programme (see below). Our Scientific committee, which includes Directors and Heads of Departments, determines and oversees scientific strategy. The Executive Management Committee, chaired by the Programme Director, oversees our operational governance, financial and risk management.

Figure 3: Management Organogram



Vision and Mission

Our vision is high quality, purposeful, and relevant research in human health, building sustainable research capacity and leadership. We undertake cutting-edge and novel research relevant to national, regional and global needs. Our core operational and research platforms include the Kilifi health and demographic surveillance site (DSS), state-of-the-art laboratories, a network of three hubs (i.e. Nairobi and Kilifi in Kenya, and Mbale in Uganda) additional sites including Bagamoyo (Tanzania), a network of 19 Kenyan hospitals (Clinical Information Network), and an engagement team (community, policy and public).

Our strategy is to leverage core for investigator-led funding awards that support a diverse interdisciplinary programme (~£2 investigator-led funding for £1 core funding). Our overarching aim is to inform healthcare delivery in LMIC settings. We address all aspects of the care delivery pathway, beginning with the broad systems perspective that determines the care given (e.g. "Health Systems"), through translational work on preventing or treating illness (e.g. "Vaccines" or "The Sick Child") to discovery of the fundamental biology to develop interventions (e.g. "Pathogen Biology"). These component themes are described below.

Scientific Themes

Health Systems

We generate quantitative and qualitative evidence on health services quality, policy and health economics. **Health Services research** includes work on nursing care and task shifting and on inpatient care of children and neonates. An example is the Clinical Information Network (CIN). CIN is a learning health systems partnership with the Ministry of Health, Kenya Paediatric Association, and University of Nairobi, and captures routine data on admission, quality of care and outcomes in 21 public hospitals across Kenya with rapid feedback to hospital teams. CIN is a core component of the Programme, including a dataset of 180k paediatric admissions and 70k neonatal admissions. In future work we will: 1) work with health workers to co-design and evaluate better approaches to providing care in newborn units in public hospitals; 2) evaluate essential technologies for newborn care.

Governance and accountability research includes evidence to improve the structure, decision making, and coordination of health systems. For instance, previous work has shown that political devolution disrupted health system functioning, with impacts that include health worker strikes and compromised health system resilience. We will further examine: 1) health system responses and resilience to COVID-19; 2) responsiveness of health systems to citizen feedback and; 3) use of evidence to inform healthcare priority setting at the devolved level.

Health economics research provides evidence to inform health system reforms that promote equity, efficiency, and financial risk protection. We conduct microeconomics (e.g. costing diabetes, hypertension and COVID-19 case management), and showing the cost-effectiveness of skill-mix change in neonatal care. We will further: 1) assess the cost-effectiveness of advanced care for COVID-19 and the COVID-19 vaccine and; 2) examine the implementation of cost-effectiveness analysis as a routine healthcare priority setting approach in LMIC settings.

Our macroeconomic focus is on progress toward Universal Health Coverage (UHC). The Universal Health Coverage index is low in Kenya. We will: 1) evaluate UHC reforms in Kenya; 2) assess the health system efficiency and; 3) assess the impact of COVID-19 on health financing and UHC.

Population Health and Surveillance

The integrated Demographic and Surveillance System (DSS) captures vital events among 300,000 residents of Kilifi County, linked to morbidity and mortality surveillance at Kilifi County Hospital and integrated with lab diagnostics. We estimate population-level incidences of common diseases (e.g. malaria, rotavirus diarrhoea, pneumococcal disease, epilepsy), test associations between exposures such as vaccination status or genetic risk factors and outcomes such as infectious diseases or mortality, evaluate Non-Communicable Disease incidence such as stroke, diabetes and cancer, and monitor vaccine coverage using serological surveys.

An example of the value of continuous surveillance was our recent analysis of mortality during health worker strikes. Africa has reported few COVID-19 deaths outside South Africa and Northern Africa, but deaths may be underreported. Our continuous DSS data will allow us to estimate excess mortality compared to previous years. Monitoring effectiveness and safety of COVID-19 vaccines will be a critical challenge for LMICs. We will use the DSS to monitor impact and long-term vaccine effectiveness. We have analytical capacity for National and Global Surveillance, including the social and epidemiological determinants of health states and transitions, and access to services and vulnerabilities at fine scales. Nationally, we have mapped child mortality, malaria and malnutrition, and internationally the first sub-Saharan African maps on access to emergency health services and 115 years of malaria transmission in Africa.

Our hospital-based surveillance (CIN) has generated findings that have helped characterise common clinical syndromes such as childhood pneumonia, diarrhoea, malaria, and neonatal conditions prompting policy discussions at WHO towards revising global policy recommendations. Future directions include linking CIN data on severe malaria to malaria ecologies, increased malaria control in the community and changing epidemiology. Throughout 2020, CIN provided near real-time data to the Public Health Emergency Operations Centre on suspected and confirmed COVID-19 cases, and we are developing a hub-and-spoke approach for bacteraemia surveillance in CIN hospitals that can be scaled and embedded in LMIC health systems.

Clinical Research

Our vision is to answer questions of immediate translational importance, focusing on inpatient care (i.e. "the sick child") and subsequent development (i.e. "the developing child").

We lead international consortia on: a) critical care of **"the sick child"** including trials of blood transfusion and fluid resuscitation, oxygen therapy and treatment of severe malaria; b) management of malnutrition including supportive care, nutritional rehabilitation and clinical/ omic and pathophysiological pathway characterization; c) treatment for sickle cell disease (now 1% of children in East Africa and a growing clinical burden) including trials of hydroxyurea and prophylactic antimalarials; d) antibiotic case management including trials of antibiotic stewardship.

Examples of recent, current and future work (respectively) from these multi-disciplinary programmes are as follows: a blood transfusion trial showing that higher volume blood transfusion reduced mortality in afebrile children but increased mortality in febrile children; a trial of narrow versus broad spectrum antibiotic use in malnourished children to inform antimicrobial stewardship in hospitals; new Fellowships on i) immunological reactions to multiple transfusions in children with sickle cell disease and ii) optimization of breast feeding support for mothers of malnourished infants.

Mental health problems in LMIC settings are common in childhood, adolescence and adulthood and a major challenge to **"the developing child".** We pioneered the use of the Kilifi Development Assessment scale (now widely used across Africa) and conducted will integrate 22 previous cohort studies including epidemiology, neuropsychology and neurophysiology to apply novel approaches to data assimilation and data sharing.

We are establishing a clinic cohort of 3,500 people with epilepsy and other psychiatric disorders. We will further characterize this cohort through deep phenotyping, genetics and biomarker studies and pragmatic clinical trials.

We have identified psychosis as a common presentation to clinic, and depression as an under-recognized illness in the community. Over the next 5 years we will conduct community surveys of common mental disorders.

We have ongoing studies examining the psychosocial impact and health outcomes of aging with HIV and will conduct detailed longitudinal phenotyping and ethnographic studies to understand perceptions of illness in older people.

Vaccines

We will work from early to late phase development, including first-in-human studies in Kenya where this accelerates public health outcomes, providing critical immunogenicity and efficacy data to support licensing and informing health policy with post-vaccination evaluations of effectiveness. We will accelerate progression through early testing by undertaking first-in-human studies in Kenya, providing critical immunogenicity and efficacy data to support licensing and inform health policy with post-vaccination evaluations of effectiveness.

Human infection studies will be used to accelerate and prioritize clinical development of candidate malaria and Shigella vaccines. These studies provide rapid efficacy data in a relevant population. We have established the largest human infection study for malaria to date and are funded for the **first Shigella human** infection study in Africa. We will study vaccine-induced and naturally acquired immunity against infection and transmission for candidate malaria and Shigella vaccines. We engage with national regulatory agencies and with the community to facilitate early-phase vaccine trials including first-in-human studies such as Ebola vaccine trials. We are now undertaking early phase trials of candidate vaccines for non-typhoidal salmonella, HIV, malaria and gonococcal disease.

We will progress with registration for both human and animal use of ChAdOx1 RVF vaccine, undertaking first-in-human studies against the outbreak pathogen rift valley fever (RVF). We will complete safety and immunogenicity evaluations of the ChAdOx1 nCoV-19 vaccine (developed by University of Oxford and AstraZeneca) to provide crucial data relevant to Sub Saharan Africa.

We will examine fractional and alternative dosing schedules of currently licensed vaccines, including for Yellow Fever vaccine (where our recent data on 1/5th of standard doses has immediate impact on the effective global stockpile) and for pneumococcal vaccines where cost is limiting.

Post-licensing effectiveness studies at population-level offer an opportunity to evaluate herd immunity (which augments the effectiveness of vaccination) and serotype or strain replacement (which may offset early benefits). Our epidemiological surveillance is uniquely well-suited to examine these effects, having demographic surveillance of 280,000 residents with fully linked prospective monitoring of clinic vaccinations, phenotyping of cases and mortality monitoring, and a legacy of 25 years of data and samples to contextualize long-term trends and variations in genotype.

We are an evaluation partner for **effectiveness trials** of the RTS,S malaria vaccine (working with WHO) utilizing the CIN, and will participate in the Phase III trials of R21, a cost-effective biosimilar to RTS,S manufactured by Serum Institute India. We also work on the effectiveness of pneumococcal conjugate vaccine (PCV), including cost effectiveness.

Pathogen Biology

Our aim is fundamental discovery of host susceptibility factors to inform vaccine design and informing public health interventions through vector biology and virus transmission models.

Defining the mechanisms of **host immunity** informs vaccine design. We have developed chip-based methods for screening several hundred full-length antigens simultaneously [2] and are conducting these assessments in a) experimental studies using controlled human malaria infection and b) large multi-centre immuno-epidemiological studies with partners in 13 West and East African sites to provide the largest post-genomic integrated assessment of P. falciparum vaccine candidates to date [3]. We are also studying the acquisition of immunity in children who experience recurrent malaria episodes. We will look for evidence of patterns of cellular activation that reproducibly predicts multiple malaria episodes in different cohorts.

A recent example of host susceptibility work is the finding that the Dantu red blood cell variant protects from severe malaria through stiffening the erythrocyte membrane. Future work among longitudinal cohorts will examine correlates of immunity to malaria, arboviruses and respiratory viruses, and specific studies of the naïve B cell repertoire to predict optimal vaccination strategies to HIV and determining the duration of antibody and cellular immunity to SARS-CoV-2.

Our **vector biology** group focusses on residual malaria transmission after scaling up bednet use. An example is future work on ivermectin as a tool to inhibit malaria transmission, including pharmacokinetic studies and a cluster randomized trial.

During the **COVID-19 response,** we supported testing, running 80,000 SARS-CoV-2 PCR tests, with research outputs on pooled RT-PCR testing. We generated and shared over 500 SARS-CoV-2 genomes from Kenya. We validated our own in-house SARS-CoV-2 ELISA, providing the first systematic sero-surveillance in Sub-Saharan Africa using a blood bank donor population. We applied SEIR models with geographical structure to integrate serological and test data, leading to policy briefs to inform the Government response. We will update these models to inform Government on the likelihood of further waves contingent on schools opening, new variants and acquisition of immunity.

Research Ethics and Research Culture

Ethics is central to all our work as an area of scientific enquiry and as a core value. Our academic aims are to contribute to ethics discourse, policy and practice for health and research systems through innovative empirical ethics and normative discourses. The research regulatory office ensures compliance of all research protocols with local, national and international guidelines, providing strategic linkage with relevant review and regulatory bodies and ensuring that research led out of the Programme adheres to the latest guidance as approved nationally. We have a dedicated committee for communication and consent. A Data Governance Commiteee oversees and makes decisions on all data requests, guided by guidelines developed informed by empiric ethics work led out of the Programme. A biobanking policy is in development informed by practical experienced and on-going empirical ethics work.

We are proactive and anticipatory in our **research on ethics,** conducting empirical ethics studies to unpack ethical issues in new fields of scientific enquiry including in emerging technologies (e.g biobanking, open science, gene technologies); ethically complex topics (involvement of vulnerable populations, young persons, people with intellectual disability in health research); new research approaches and designs (e.g. Human Infection studies; pragmatic trials, issues that emerge in epidemic situations including COVID19); and areas that require revisiting using an ethics lens (e.g. decolonisation). Our work feeds into and draws on wider national and global networks that we are members of, and which we continue to strengthen and expand.

To promote the **well-being and equitable treatment of our staff,** we implement an **anti-harassment policy** that outlines clear mechanisms for reporting and handling of reported cases and have undertaken regular training on the policy. Episodes of harassment and actions taken are reported at management committees and, to Wellcome as per Wellcome policy thresholds. We are intentional about gender equity in recruitment, representation in leadership, and the work environment.

We integrate public engagement and policy engagement to enhance the **purposefulness and relevance** of our research. **Capacity development** is central, with continuous professional development for all staff, and a science training strategy that has delivered 283 internships, 224 masters, and 188 PhDs (plus 56 current PhDs) since the programme's inception in 1989. We foster a stimulating inter-disciplinary environment and co-create with policy makers as evidenced by our COVID response.

We encourage open research, for example by our Wellcome Open gateway with 77 publications by June 2021 (i.e. 9% of all Wellcome Open articles), and data shared through our Harvard Dataverse with >7500 downloads of 138 datasets. We leverage ~£2 additional funding for £1 core funding and publish >200 papers per year with 141 papers since 2010 cited >100 times.

Training and Capacity

Our training strategy is to emphasize the full career path with a progressive and long term outlook in the development of local research leadership. We aim to build a critical mass of African researchers who are technically proficient, able to independently lead internationally competitive science, engage with funders and policy makers and act as supervisors and mentors for the next generation.

Our conceptual framework "Attract, Train and Retain" outlines a systematic approach for enhancing the progression of individuals along the research career path. We will provide 36 attachments and internships per year (including Masters projects from local universities), and recruit from this pool and from external applications to 5 PhD studentships per year. We will support transition from PhD to independent researcher for 2 Early Post-Doctoral researchers per year, and support 4 Mid-Career Fellowships during the next 5 years. A successful outcome will comprise 80% of interns remaining in science at 5 years follow up, 95% of PhD students completing in 3.5 years with 80% of PhD students remaining in science at 5 years and the establishment of a further 5 independent research leaders at 5 years.

Public Engagement

Our engagement strategy has grown over the last 5 years and includes broad areas of: **Community Engagement** (e.g. working with networks of community representatives, programme open days and outreach events within the KHDSS); **Public/Media Engagement** (e.g. conducting journalist/researcher workshops, radio programmes, Media tours); **Schools & University Engagement** (engagement with Primary and Secondary students in Kilifi, and engaging university students in Kilifi and Nairobi); and **Policy Engagement** (working with policy makers at national and county level to input into research planning, implementation, and uptake of findings to policy). Our overarching aim is to strengthen mutually respectful and responsive relationships with communities, stakeholders and policy makers and support co-learning between publics and scientists, achieved through diverse deep and wide interactions using adaptable and responsive approaches.

Our activities are presented under broad long-term outcomes as follows with adaptations for COVID-19:

Outcome 1: High capacity of community members and public to understand and appreciate the value of health research.

- Open Days: targeting individuals from identified gatekeeper groups to visit KWTRP and interact with scientists. We are developing virtual reality laboratory tours, targeting school students and community members.
- Radio Programme: partnering with several local radio stations to host live, interactive radio shows. Radio programmes can be through physical studio visits, or via live telephone call-in between radio presenter and researcher.
- School/University Engagement: annual engagement sessions with primary and secondary students in Kilifi; expansion to Nairobi planned through interactive virtual engagement (Ms Teams or Zoom) sessions. University engagement currently being conducted through virtual workshops with students from Pwani University and several universities in Nairobi). We are developing an inspirational book on African scientists for distribution to students within Kenya (and possibly African region).
- Theatre: We have partnered and trained a local Theatre production company to deliver research themed drama outreaches in the community. Radio drama has been used during the COVID-19 pandemic to deliver interactive drama episodes to publics.
- Media Engagement: Virtual and socially distanced media tours and workshops have and will be undertaken. We have established a Media Advisory Group, which we will continued working with. We will develop animation videos to further engage the public (building on the success of the vaccination video as featured during prime-time TV news in Kenya).

Outcome 2: Researchers responsiveness to community views, fostering people-centred research practice.

- Consultations with networks of KEMRI Community Representatives (KCRs) and Young Persons Advisory Groups (YPAGs) on planned and ongoing research (physical as well as virtual meetings; Q&A through WhatsApp group);
- Consultations include discussions with advisory groups on emerging initiatives such as Biobanking, gene technology and related areas of global health emergencies and technologies.

Outcome 3: Close partnership with policy makers to facilitate translation and policy impact.

- We will strengthen relationships between researchers and policy makers through initiatives including: a) partnership with policy makers to co-produce and implement research; b) formally embedding KWTRP researchers in policy making spaces; c) policy dialogues and; d) reciprocal secondments of MoH and KWTRP researchers.

Our engagement strategy is anchored on a robust monitoring and evaluation theory of change, which guides the conduct of our formative, process and summative evaluation activities. Learning derived from data is used to adjust our engagement approaches, as well as share our experiences with wider local, national and global research communities.

KEMRI-Wellcome Trust Research Programme
CGMRC, PO Box 230-80108,
+254 709 983000/info@kemri-wellcome.org
Kilifi, Kenya

https://kemri-wellcome.org/

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