22 November 2019

Review of the Joint Global Health Trials funding scheme

Final Report
Review of the Joint Global Health Trials funding scheme

Final Report

technopolis [group], November 2019

Peter Varnai
Maike Rentel
Anoushka Davé
Kelly Simpson
Costanza Tiriduzzi
Emma Pottinger
# Table of Contents

1 Executive summary ........................................................................................................... i

2 Introduction ......................................................................................................................... 1
   2.1 Context and the case for intervention .............................................................................. 1
   2.2 The Joint Global Health Trials Initiative (JGHT) .......................................................... 4
   2.3 Objectives for the JGHT evaluation .............................................................................. 7

3 Evaluation methodology ..................................................................................................... 8

4 The JGHT Funding Scheme Evaluation Framework .......................................................... 9
   4.1 Impact logic model .......................................................................................................... 9
   4.2 The JGHT scheme evaluation framework .................................................................... 11

5 Evaluation of the JGHT funding scheme .......................................................................... 13
   5.1 Inputs and activities - the JGHT portfolio ................................................................. 13
   5.2 Stakeholder engagement ............................................................................................. 33
   5.3 Challenges to trial implementation ............................................................................. 37
   5.4 Outputs ......................................................................................................................... 40
   5.5 Scientific outcomes ...................................................................................................... 49
   5.6 Policy and health outcomes ....................................................................................... 56
   5.7 Impact on health ........................................................................................................... 64
   5.8 Progress towards health-related SDGs ......................................................................... 64
   5.9 Impact case study – summaries .................................................................................. 66
   5.10 Value for money .......................................................................................................... 74

6 The global health trials funding landscape ...................................................................... 77
   6.1 Organisations funding global health trials ................................................................... 77
   6.2 Outputs, outcomes and impacts of other funding global health programmes ........... 80
   6.3 Advantages / disadvantages of the JGHT compared to other funding programmes .... 82
   6.4 Current gaps in the global health trial funding landscape ........................................... 83

7 JGHT funding scheme - design and management ............................................................. 84
   7.1 The design of the JGHT funding scheme ................................................................... 84
   7.2 Additional activities to improve impact ........................................................................ 87
   7.3 Options for changes to the design of the JGHT .......................................................... 89
   7.4 Promotion of the scheme ............................................................................................ 90
   7.5 The review process ...................................................................................................... 90
   7.6 Perceptions of how the JGHT has evolved over time .................................................. 91
   7.7 Added value of a partnership of funders ..................................................................... 92
   7.8 Project monitoring & evaluation ................................................................................ 93

8 Conclusions and recommendations ................................................................................ 94
8.1 Conclusions ............................................................................................................................................ 94
8.2 Recommendations .................................................................................................................................... 95
1 Executive summary

The Joint Global Health Trials funding scheme (JGHT) was established in 2009. It is a partnership of four funders, the UK Medical Research Council (MRC), the Department for International Development (DFID), Wellcome and the Department for Health and Social Care (DHSC). The overall aim of the JGHT is to support the best proposals to generate new knowledge about interventions that promise to contribute to the improvement of health in low- and middle-income countries (LMICs), addressing a major cause of mortality or morbidity.

The funders commissioned an external review to understand the impact of the JGHT scheme, its potential for future impact and to inform the design of future funding programmes. The review was carried out by Technopolis from October 2018 to October 2019, information by desk research, database analysis, and consultations through surveys and interviews with Principal Investigators (PIs), co-investigators, and global health experts and funders (‘Key opinion leaders’).

The evidence reviewed demonstrates that the JGHT is delivering on its core aim and has achieved tangible outcomes and impacts: JGHT-funded research has generated new knowledge about interventions which in turn are starting to contribute to improving health in LMICs.

Overview of the JGHT portfolio

The scheme includes two strands of funding through annual calls: Full trial awards, which support late-stage and health intervention trials (Phase III/IV) to evaluate efficacy and effectiveness, and – starting from Call 5 – Development awards, which enable studies to carry out formative work preparing for a full trial.

In Calls 1-7, the JGHT scheme funded a portfolio of 63 full trial and 33 development awards (of which 28 and 22 had closed by June 2019, respectively), representing an investment of £138.8m. Research addressed a broad range of health issues, with strong emphasis on infectious diseases in the earlier calls, and an increase in mental health research from Call 5. Trial sites are located in 47 countries; 75% of trials include sites in Africa, 30% of trials have sites in Asia, and 8% in Central and South America.

The largest share of full trial awards (63%) were led by principal investigators (PIs) affiliated with institutions located in high-income countries (HICs), compared to 13% of awards led by researchers from LMIC institutions and 24% led by researchers at ‘joint units’ (programmes or institutes funded by organisations from HICs located in LMICs). Around one third of awards was led by female PIs.

The majority of PIs engaged with policy makers during the design and/or implementation of the project (87% of PIs of full trials and all development awards surveyed). 39% of PIs interviewed had engaged with community groups and advisory boards, community leaders, and individuals such as patients who shared their experiences. Several researchers highlighted the importance of joint units in this respect, as these have established engagement structures which researchers are able to draw on.

The JGHT is delivering against its policy and health objectives

Research funded by the JGHT has influenced policy and led to health outcomes.

Of the 28 closed full trial awards, 32% have resulted in policy influence, and a further 36% have a high potential for success, based on the trials’ findings and the level of stakeholder engagement by the study team. Three of these trials provided important evidence by informing decisions to not change a policy or implement an intervention. In addition, three active full trials have already influenced policy. Policy outcomes included direct influence on the World Health Organisation (WHO) guidelines; addition of

1 Joint units include: KEMRI Wellcome Trust Research Programme, Kenya; Mahidol Oxford Research Unit, Thailand; Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Malawi; Mwanza Interventions Trials Unit, Tanzania; MRC Unit The Gambia; MRC/UVRI Uganda Research Unit, Uganda; Oxford University Clinical Research Unit, Vietnam.
products to the WHO Essential Medicines list; influence on WHO policies in other ways, e.g. lending confidence to a guideline under scrutiny, uptake into a best practice strategy paper; influence on national policies; and influence on strategy of international donors and shifting funding priorities.

Nine full trials and one development award likely led to the implementation of a health intervention. Four interventions were recommended by WHO guidelines, at least two of which have been purchased by governments via the Global Fund. Four further interventions have been, or are starting to be, implemented by national governments as part of public health programmes. One intervention is being implemented by an NGO with support from the national government.

In addition, the implementation of JGHT-funded research itself has led to direct and indirect benefits, e.g. through improved standard of care and access to care, education and awareness, for study participants and the wider community. For example, two trials alone have led to direct health benefits for around 450,000 trial participants.

Four key enablers of policy and health outcomes arising from JGHT-funded research were identified:

1. The topic of the trial is timely and under debate in the policy arena, and hence key policy makers have strong interest in the research evidence.
2. The trial addresses a neglected health issue, and little research evidence was available before the trial. The trial thus substantially increased the level of robust evidence on which to base policy decisions.
3. Collaboration with policy makers and key stakeholders in the health system during research planning and implementation, e.g. by embedding the trial within local health programmes.
4. Active engagement with policy makers to inform and influence relevant policies. This is facilitated by researchers holding advisory functions, e.g. as members of guideline committees, or key policy makers holding advisory functions related to the research, e.g. as members of the trial steering committee.

The JGHT is funding high-quality research, leveraging additional funding, building capacity, and fostering collaboration

The majority of the 28 closed full trial awards have either published the main trial findings (20), submitted them for review (3), or are in the final analysis stage, indicating a high trial completion rate of 89%. 60% of JGHT awards reported on ResearchFish that they had received substantial additional funding (co-funding and follow-on funding), capturing around £160m in total. Most of this funding was provided by Wellcome, EDCTP, NIHR, BMGF and US NIH3 (in order).

Of 22 closed development awards funded so far, at least 23% have led to full trials - one funded by the JGHT, and four by other funders, including DFID, US NIH and EDCTP.

JGHT-funded research has built capacity, in HICs and LMICs, and fostered collaboration. 82% of co-investigators from full trial and development awards (140 of 170) felt that the JGHT-funded project had positively impacted their scientific knowledge, and 50% indicated their knowledge of local health needs had improved. Publications of main findings of full trial awards named investigators affiliated with 106 distinct institutes; over half of these institutions were located in LMICs (57), indicating a high level of involvement in the delivery of the trials. The lead authors of a quarter of publications (27%) were based at LMIC institutions, comparable to the shares of lead authors affiliated with joint units (31%), and institutions in HICs (27%). JGHT awards have also led to new collaborations (e.g. as reported by 50% of co-investigators) and allowed researchers to start participating in collaborative networks (30%).

---

2 i.e. relating to the primary outcome of the trial
3 European & Developing Countries Clinical Trials Partnership; National Institute for Health Research; Bill and Melinda Gates Foundation; US National Institutes of Health
The design and promotion of the JGHT are appropriate

Researchers and key opinion leaders were predominantly positive regarding the design and promotion of the JGHT, and no major issues emerged in the consultation. A range of additional activities were highlighted by PIs and co-investigators which the JGHT could support to help it achieve its aims. These included funding for training and other types of research such as implementation and laboratory studies; dissemination and knowledge exchange. Key opinion leaders highlighted the potential for additional support for applicants from LMICs. While researchers appreciated the ‘light-touch’ monitoring arrangements, many researchers felt that reporting beyond ResearchFish® should be put in place to improve tracking of outcomes and impacts.

Of PIs who described a weakness, 29% considered the amount of funding available insufficient, both in terms of the size of awards and the lack of funding for additional aspects such as dissemination, capacity building or student fellowships (e.g. as provided by the EDCTP and US NIH). Despite the fact that the JGHT calls for proposals do not state a budget or time limit, comments by several researchers indicated that the JGHT is perceived to provide funding of about £2-3m for a duration of 3 years.

The partnership of JGHT funders provides added value

The partnership of JGHT funders is working well. It has resulted in a variety of benefits to both funders and researchers, such as the ability to pool budgets and de-risk investment, closer cooperation and sharing of expertise between funders, and a de-fragmentation of the funding landscape. The partnership is considered to have helped maintain the UK’s international leadership in producing high quality research of relevance to LMICs. However, international funders consulted were not aware of the scheme.

The JGHT represents value for money (VfM) in a variety of ways, thereby maximising the impact of the investment

The JGHT represents value for money (VfM) in a variety of ways, maximising the impact of the investment by its funders. The scheme is acknowledged to fill a gap in the global research landscape and delivers research with strong relevance to health issues of disadvantaged populations in LMICs. This is achieved through a partnership of funders, leading to sharing of expertise and risk and to efficiency gains. Its flexible scheme management approach has enabled trials to complete and thus avoid ‘research waste’, leading to 80% of closed awards completing trials and publishing their main results. The value generated by the JGHT includes scientific knowledge and capacity, which has contributed to further scientific work and strengthened the wider research ecosystem. In addition, financial benefits have already been achieved or are anticipated based on current award monitoring data:

- Research cost savings achieved from development awards de-risking full trials
- Additional research funding leveraged on the basis of the JGHT award
- Anticipated cost savings for LMIC health systems and improved health outcomes, partly due to increased education and awareness of health issues
- Direct employment effects of researchers, trial staff and supply chains for the UK and LMIC

Recommendations to increase the value gained from JGHT-funded research

The review concluded that the JGHT is delivering on its core aim and has achieved tangible outcomes and impacts. Underpinned by the evidence gathered, five recommendations to further increase the value gained from the JGHT-funded research have been developed:

1. Keep the overall design of the JGHT, but clearly communicate the scheme’s award parameters to potential applicants, and re-focus researchers on applying for appropriately sized budgets to answer the research question (rather than fitting to the perceived funding envelope).

2. Provide additional support for stakeholder engagement, both pre- and post-award, to avoid challenges during trial implementation and enable pull-through of research findings into policy and practice. This could include small grants for ‘partnership workshops’ and/or an expansion of the
development award scheme, as well as additional funding to cover engagement activities after the award has closed. Funders should explore options for how to maximise opportunities for dissemination and engagement for findings with high potential for policy influence and health impact. This could involve taking an active role in these efforts, e.g. by targeting media and convening meetings, or providing support for a team of specialists for this function.

3. Increase support for LMIC researchers, including resources to assist with proposals, providing detailed feedback to unsuccessful LMIC applicants, promotion of JGHT calls in LMICs, and ‘match-making’ activities to facilitate access to expertise and infrastructure.

4. Agree on key criteria for project selection among JGHT funders, defining how to balance between the size of the health need addressed, the risk of interventions tested not proving effective, and the likelihood that a trial leads to policy influence and health outcomes.

5. Launch additional project monitoring, enabling better tracking of progress and outcomes and identify options to support dissemination of findings and engagement with policy makers.
2 Introduction

2.1 Context and the case for intervention

2.1.1 Global health trends and impact on economic growth

A recent analysis of global mortality rates concluded that between 1950 and 2017, life expectancy increased from approx. 48 years to 71 years for men and from 53 years to 76 years for women (Dicker et al. 2018). Despite this overall progress, there remains substantial variation in life expectancy at birth in 2017, with a gap of nearly 40 years between men in the Central African Republic (at 49.1 years) and women in Singapore (at 87.6 years). And while the greatest progress across age groups was for children younger than 5 years, with mortality of under-5s dropping from 216 deaths per 1000 livebirths in 1950 to 39 deaths per 1000 livebirths in 2017, an estimated 5.4 million children younger than 5 years died in the world in 2017. In addition, progress in life expectancy has been less pronounced and more variable for adults. Much progress has also been made reducing the impact of poverty-related neglected disease. These included a 40% reduction in new HIV infections, 37% reduction in the malaria incidence rate, and a 41% reduction in TB prevalence rates over the 2000-2015 period.

Health also underpins economic growth. A lack of effective health systems, including effective, affordable and accessible treatments and products, can affect the ability of individuals, communities and societies to achieve growth and develop. A recent study confirmed previous analyses that population health has positive and significant effect on both real income per capita as well as its growth. Around 11% of economic growth in low- and middle-income countries (LMICs) from 1970-2000, as measured in their national income accounts, was due to reduction in mortality. Enhanced investments to scale up interventions and health technologies is expected to lead to a fall in infectious, child, and maternal mortality rates in LMICs, matching those presently seen in the best-performing middle income countries. Relative to a scenario of stagnant investments and no improvements in technologies, this would prevent around 10 million deaths in 2035. In addition to new technologies, there is a need to (re-)assess the safety, efficacy, and efficiency of existing interventions, as many treatments, drugs, vaccines and diagnostics do not work as anticipated.

Despite progress, further efforts are still sorely needed. Children born into poverty are almost twice as likely to die before the age of five as those from wealthier families. The proportion of mothers that do not survive childbirth compared to those who do in developing regions is still 14 times higher than in the developed regions, and only half of women in developing regions receive the recommended amount of health care they need. At the UN Summit in September 2015, the Sustainable Development Goals (SDGs) were formally adopted, including goal 3, to: ‘ensure healthy lives and promote well-being for all at all ages’. Some of the stated targets are, by 2030, to:

- reduce the global maternal mortality ratio to less than 70 per 100,000 live births
- end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births
- end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases
- reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being
- strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol
- halve the number of global deaths and injuries from road traffic accidents (by 2020)

References:

• support the research and development of vaccines and medicines for the communicable and noncommunicable diseases that primarily affect developing countries

There is a large unmet need for effective, affordable and safe treatments to achieve these goals. If progress against health-related SDG targets were to continue at the same rate as for the 1990–2017 period, most countries are projected to have a higher health-related SDG index in 2030 than in 2017 (a measure of progress against 41 of 52 health-related SDG indicators)9. However, country-level probabilities of attainment by 2030 vary widely by indicator: Goals related to under-5 mortality, neonatal mortality, maternal mortality ratio, and malaria indicators are projected to be achieved by a high proportion of countries (with at least 95% probability of target attainment). For other indicators, including mortality from non-communicable disease and suicide mortality, no countries are projected to meet the corresponding SDG targets if progress continues at the current pace. For some indicators, including child malnutrition, several infectious diseases, and most violence measures, the annualised rates of change required to meet SDG targets far exceeded the pace of progress achieved by any country in the recent past.

2.1.2 Trials to address health needs in LMICs

Many unanswered questions remain about the efficacy10, effectiveness11, safety and cost-effectiveness of new as well as some existing interventions. Randomised controlled trials (RCTs) are the gold standard method of assessing health interventions, producing clear and numerical measures of their benefits - or the lack thereof. Almost all new advances in health have to be tested employing a rigorous trials methodology and within the required ethical, legal and regulatory frameworks. Trials are hence a core component of later stage development of health innovations and an essential step before implementation of a change in practice, or commercialisation of a new technology, providing definitive answers to the trial question. They can also lead to cost savings when providing evidence that an intervention does not work, and answer questions of cost-effectiveness by demonstrating that cheaper alternatives are equivalent to more expensive interventions (most cost-effectiveness and cost-benefit analyses in healthcare rely on trial data12).

Under-representation in global health trial platforms continues to contribute to sustained health inequity in LMICs, despite the fact that the shortage of funds in developing countries increases the need for reliable healthcare evidence to prioritise the use of their scarce resources. Diseases of relevance to high-income countries are investigated in trials seven to eight times more often than diseases whose burden lies mainly in LMICs13. In addition, researchers in developing countries face a number of barriers (on top of those their developed country counterparts encounter). A recent literature review on barriers facing clinical researchers in LMICs for conducting trials identified the following factors14:

• lack of financial and human capacity (both, lack of skilled personnel and lack of awareness and of motivation to participate)
• ethical and regulatory system obstacles, especially long delays in the review process
• lack of suitable research infrastructure, research materials for conducting trials, and/or a conducive scientific atmosphere (including policy)
• operational barriers, such as an administrative environment characterised by lengthy and complex logistic and financial systems that hamper the conduct of trials
• competing demands on research staff

10 Performance of an intervention under ideal and controlled circumstances. Efficacy trials can overestimate an intervention’s effect when implemented in clinical practice.
11 Performance of an intervention under ‘real-world’ conditions, accounting for external patient-, provider-, and system-level factors that may moderate an intervention’s effect.
12 Department for International Development (2013) Joint Global Health Trials Scheme - Business Case
As trials generally carry a high cost (especially in Phases III and IV), the private sector, as the key actor in product development, has limited incentives to invest given that innovations may be neither patentable nor commercially exploitable. Much of the research in this field has therefore been supported by the public sector and philanthropic sector, through universities and other research institutions, and public-private partnerships. (A more detailed description of other funders and programmes operating in the JGHT’s research funding environment is provided in section 6.1).

2.1.3 Impact on health – requirements for implementation and scale-up

For interventions to have an impact on health, they must be implemented and become readily available to the target population, e.g. through the health service. Here, context plays an important role, as this requires that:

- the intervention is efficacious in the local target population, if different from trial population. Other context-dependent factors include the ability to manufacture and/or transport the intervention under local conditions; local capacity to diagnose the underlying indication; and the availability of any infrastructure/equipment/staff required to deliver the intervention.
- the intervention is affordable to the health system or the individual who needs it.
- the intervention is adopted into policy, e.g. by inclusion in national and international clinical guidelines (recommending which intervention healthcare professionals should employ for specific indications). It thus needs to be visible to and a focus for national policy makers.
- the intervention is taken up into practice, e.g. by health professionals. Such users thus need to be aware of the intervention, trained in its application, and willing to take it up, e.g. recommend a treatment to their patients.
- patients/end users accept, and adhere to, the intervention. Some interventions may come up against social or cultural barriers, either directly on the part of the end user, or the wider community/family (e.g. reproductive health; competing local traditional treatments; lack of patient education). End users also need to be able to access the intervention (which may depend on frequency of administration and distance to treatment site). Other factors affecting adherence include potential side effects of the intervention and the length of treatment course.

To ensure that the trialled interventions have the potential to deliver benefits to end users, these factors need to be taken into account during the planning and implementation of the trial.

Achieving maximum impact requires scale-up of policy influence, implementation and adoption of health interventions, i.e. through the process of expanding their coverage and geographical reach, thus benefitting more people. While some trials may address specific local health needs, most interventions are likely to be suitable for transfer to other locations, potentially with some adaptation to other contexts. This process can be accelerated by conducting multi-site trials, testing the intervention in multiple locations and various contexts (as well as engagement with relevant policy makers in other geographies); however, these trials not only need a larger budget, they also require researchers to navigate multiple administrative, ethical and legal frameworks.

The final level of health benefits will be dependent on a number of factors, including the following:

- The relative prevalence of the problem, disease or condition targeted by the intervention
- The impact of the problem, disease or condition on quantity/quality of life
- The size of the affected population for which the intervention is suitable, acceptable, and accessible
- The effectiveness of the new intervention compared to existing practice
2.2 The Joint Global Health Trials Initiative (JGHT)

2.2.1 History and stated aims of the scheme

The Joint Global Health Trials Initiative (JGHT) was established in 2009, with co-funding from the UK Medical Research Council (MRC), the Department for International Development (DfID), and the Wellcome Trust. Following the launch of the UK’s aid strategy in 2015, which changed the distribution of ODA funding across departments, the Department of Health and Social Care (DHSC) established its global health portfolio in 2016. As part of this effort, the DHSC/National Institute for Health Research (NIHR) joined as a funder of the scheme, with effect from financial year 2016/17.

The partnership was preceded by various joint bilateral relationships between the MRC, Wellcome Trust and DfID. At the time, the global health trials landscape was described as a ‘patchwork’ of opportunities; investigators applied to multiple programmes in order to obtain funding for their proposed trials. The JGHT combined the various funding strands, and brought the review process under a single committee. In addition, this pooling of resources allowed the funders to support larger or more expensive trials, while reducing the risk for individual funders (making it possible to support some trials in new areas / with novel approaches). Joint working has since led to deepening of the funders’ partnership and a better understanding of remaining gaps; e.g. in 2011, the funders of the JGHT at the time (MRC, Wellcome Trust, DfID) and the ESRC came together to address an identified funding gap and develop a ‘sister scheme’ addressing health systems research (the Joint Health System Research Initiative, JHSRI).

The overall aim of the scheme is to support the best proposals to generate new knowledge about interventions that promise to contribute to the improvement of health in LMICs, addressing a major cause of mortality or morbidity. As one funder representative put it: “The aim is to provide clear, definitive evidence if an intervention works or not, and what the next steps should be. […] The ultimate goal is a trial which leads to policy or practice changes.” The scheme hence gives priority to proposals that are likely to produce implementable results and that are designed to address the major causes of mortality or morbidity in LMICs; it is hence focused on late-stage and health intervention trials (Phase III /IV) evaluating efficacy and effectiveness, with the potential for impact over a 5-10 year timeframe. The review process takes into account whether the intervention has the potential to be sustainable and scalable (even if the proposal relates to a single country trial), and whether it shows engagement of local stakeholders, such as local policy makers. The JGHT also considers earlier phase trials of major relevance to the objectives of the call.

Studies funded through the JGHT have to be based in LMICs, with the principal investigator (PI) employed either by a research institution in the UK or in a LMIC; co-investigators can be located in any country. In the specifications for Call 8, the funders highlight that applications can focus on either a single or multi-country assessment as long as research takes place in LMICs. Trials are led by academic groups, but can include collaborations with commercial companies.

The scope of the scheme is broad and includes behavioural interventions, complex interventions, disease management, drugs, vaccines and hygiene and diagnostic strategies. From Call 4, the funders encouraged (but did not require) applications addressing chronic non-communicable diseases and reproductive, maternal and newborn health; from Call 7, mental health was added to this list.

While the scheme is aimed at funding trials, other types of methodologies, such as economic evaluations and social science research, are encouraged alongside the trial to explore implementation and operational issues and to pave the way to implementation and impact. From the outset (i.e. in Call 1), health economics was highlighted as an area to consider in the project design; the Call 3 specifications note that social science and implementation research could be conducted alongside trials (with the aim of providing information relevant for scale up). From Call 7, call specifications encourage applications trial designs other than Randomised Controlled Trials (RCTs), i.e. innovative trial methodologies and adaptive designs that are more complex and can carry a higher risk. The specifications for Call 8 give a stronger steer and set out that applications have to show engagement with the potential users of research (e.g. policy makers) throughout the research process in order to ensure trial results are implementable, scalable and in line with policy needs. Call 8 also emphasises that the funders have an interest in funding complex interventions delivered in community settings, including primary health care.

From 2010, the scheme published annual calls, with up to £20m per year available. In Calls 3 and 4, a number of applications for full trials were considered of high quality and promising, but in need of additional preparatory work. These were awarded smaller ‘development grants’, enabling the
researchers to test the feasibility of interventions and trial design that could ultimately lead to the design of credible, appropriately powered, competitive, full trials. From Call 5, the Development Award programme was fully established as a separate funding track, with generally up to £150,000 available per award. Development awards are aimed at studies to:

- Generate specific data that is needed to inform the trial design, such as to determine the sample size, outcome measures, recruitment strategy, follow-up strategy, appropriate monitoring activities and timings
- Work to understand the likelihood of contamination within the trial e.g. in a cluster randomised trial, and how that contamination might be handled.
- Work to inform design of the trial intervention, for instance feasibility and acceptability issues in a public health intervention

The JGHT was described in an overarching programme model, encompassing the theory of change of the intervention (points 7; 9-12; 14-15), the process elements which allow the programme to be delivered (points 1-3; 5-6; 8; 13), and external factors that may affect the intervention (point 4; other factors) (Figure 1).

**Figure 1 Joint Global Health Trials programme model**

Source: Provided by JGHT funders
2.2.2 Outline of investment to date

The funders committed up to £120m for the first six (annual) calls (2011-2016, with funded projects expected to conclude by 2020/21).

The original agreement between the funders set out that DFID will contribute up to £48m (40%), and each of the other three funders will contribute up to £24m (20% each). In 2017, the four funders signed a new MoU, making available up to £100m in funding for the five-year period from 2016-2020 (Calls 7 – 11, up to £20m per call). The expenditure is to be split evenly between funders, each providing up to £25m. Some of the committed funding can be used to hire two full time support staff, on MRC contracts, to work across both the JGHT and the Joint Health Systems Initiative.

By 2018, seven calls had been completed, and 96 awards were made: 63 full trial awards and 33 development awards.

2.2.3 Scheme management

The funders have taken on different roles to manage the JGHT.

- The MRC is the lead administrative partner, responsible for putting out the calls for proposals, handling preliminary and full applications, arranging external referee reports and providing oversight for studies post-award. Once the proposals have been selected, the MRC administer and account for contributions and manage the grants.

- The Wellcome Trust leads on the administrative arrangements relating to the Joint Funders Review Committee meetings, supports referee selection, and convenes the review panel (which shortlists outlines for invitation to submit full proposals, and selects full applications for funding). The Wellcome Trust, alongside other funders, also provides expertise and due diligence on issues relating to commercial or product development partners, clinical trials sponsorship, insurance and indemnity, intellectual property rights and on regulatory issues.

- DFID and DHSC provide strategic oversight and financial resources.

In addition, all full trials are monitored by a trial steering committee, a data monitoring committee, and an ethics committee, to supervise the trials and ensure they are carried out to the appropriate standards. The outputs and outcomes of JGHT-funded studies are currently monitored through investigators’ submissions to ResearchFish® (required annually for five years after awards completion).

2.2.4 The review process

The review committee meets twice per year, once to review proposal outlines for full awards and development award proposals, and a second time to review the full proposals for the full trial awards. For Call 8, the committee comprised 19 experts in global health and trials.

- The application process for full trial awards is a two-stage process. After review of the outline applications by the review committee, a selection of applicants is invited to submit full proposals. The full trial proposals are sent for external peer review. Full comments are shared with applicants invited to submit full proposals, so these can be adjusted before re-submission to the review committee. Some generic guidance is also shared with applicants that do not pass the outline stage, e.g. on problems that were commonly encountered in unsuccessful proposals.

- The application process for the development award scheme is a single stage process. The application is shortened compared to the full trial form, and there is no external peer review.

The JGHT funding committee panel reviews applications and assigns scores according to pre-set criteria (e.g. see Table 1, Call 8 for full trial awards). For full trial awards, decisions are informed by the external review, but are not bound by the recommendations.

---

56 MoU Amendment letter, February 2018
57 The Medical Research Council (MRC) Guidelines for Good Clinical Practice (1998) define a three-committee oversight structure: the Trial Management Group (TMG), the Data Monitoring Committee (DMC) and the executive Trial Steering Committee. The TMG is responsible for the day-to-day delivery and conduct of the trial; the DMC role is to review safety and efficacy data and make recommendations to an executive group; and the TSC is the executive decision-making group that considers the recommendations from the DMC.
After review of the applications, the funding committee may request additional information or changes to proposals before making a final decision, with the primary focus on funding the best science (e.g. rather than capacity building) and on addressing health needs of LMICs (both, global and local unmet needs). Unsuccessful applicants are provided with more general feedback on proposals, providing the opportunity to improve the project design for future funding applications.

Table 1 Points to consider by JGHT funding committee (full trial proposals)

<table>
<thead>
<tr>
<th>Scoring criteria</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Track record of applicant</td>
<td>Experience of conducting trials to a high standard in the proposed setting. Publication record of outputs from trials, Evidence of uptake of findings; changes in policy and practice, Balance of expertise to undertake the trial (e.g. are clinical, methodological, social, health systems, economics, cultural issues covered), Links with local research/health institutions and involvement of investigators from low and middle income countries</td>
</tr>
<tr>
<td>Importance of the question/need for the trial</td>
<td>Is there a need for such a trial now for this condition or group of patients in the proposed location(s), How important is the problem being addressed? Novelty and innovation: Have similar trials been done previously or are any underway now?</td>
</tr>
<tr>
<td>Study design and feasibility</td>
<td>Is the design of the study appropriate to answer the question? Are the methods and study designs competitive with the best in the field?, Is the recruitment strategy appropriate and feasible?, Is the timeline realistic and achievable?, Are there any ethical concerns?, Have major scientific, technical or organisational challenges been identified, and will they be tackled well?</td>
</tr>
<tr>
<td>Impact</td>
<td>How important an advance would this be? Will the findings be generalizable? What is the likelihood that the findings will be taken up and implemented? Can the intervention be scaled up; is it cost effective? Is it likely to lead to significant improvements in health?</td>
</tr>
<tr>
<td>Financial Aspects</td>
<td>Does the study represent value for money, are the costs realistic and reasonable, do the majority of funds requested support the costs in the low- or middle-income country where the trial will be conducted, are there any financial dependencies e.g. co-funding arrangements</td>
</tr>
</tbody>
</table>

2.3 Objectives for the JGHT evaluation

The funders of the JGHT commissioned an external review to understand the impact of the JGHT programme (retrospective) and its potential for future impact (prospective), and to inform the design of future funding schemes. The study was to gather evidence relating to awards made in Calls 1-7 of the JGHT. It was carried out by Technopolis between October 2018 and October 2019.

The four main objectives for the review were:

1) to assess whether and how the JGHT scheme has delivered on its core aim i.e. the generation of new knowledge about an intervention and its contributions to improving health in LMICs
2) whether tangible outcomes and impacts have been achieved from the funded research
3) to identify ways in which the value gained from this type of research/research programme can be increased
4) to provide guidance on future monitoring of the scheme.

The specification for the JGHT review sets out a range of evaluation research questions to be addressed, falling into six categories:

1) Scientific outcomes of the JGHT
2) Impacts of the JGHT
3) Value for Money (VfM)
4) Location of the JGHT in the wider global health funding landscape
5) Research funding through the JGHT
6) JGHT management and evaluation

In the scoping phase of the review, the funders of the JGHT emphasised that the main objective was to determine the outcomes and impacts achieved by JGHT-funded activities; review activities were focussed accordingly.
3 Evaluation methodology

The evaluation employed a mix-methods approach, involving multiple strands of data collection and analysis which cut across the study’s evaluation questions.

- Scoping exercise

The evaluation started out with a scoping exercise, to allow orientation in relation to the key strategies and parameters of the JGHT, and development of an impact logic model and evaluation framework (evaluation questions set against indicators). This phase consisted of an initial meeting between Technopolis and the JGHT funders, a review of documentation available relating to the JGHT, and scoping interviews with the JGHT funders (7 interviews in total). (A further interview with one of the funding organisations was conducted as part of the key opinion leader programme of interviews.)

- Document review and desk research

**Portfolio analysis**: Information for the portfolio analysis was provided by the funders, including data on both funded and rejected proposals (latter anonymised). Data on funded projects was completed with additional information, such as assigning country, continent, and LMIC status for each research organisation that applied to the JGHT, the indication the award addressed and the target group for each award, the trial methodology employed, and the type of research question addressed. For full trials, the relevant trial registry number was gathered. An extended portfolio analysis is available in Appendix B.

**Funding landscape review**: A review of the funding landscape was conducted. This involved identification of relevant websites and reports in targeted online searches of funders and relevant programmes, including those mentioned in scoping interviews and detailed on G-FINDER. Emphasis was placed on gathering and analysing evaluation reports and evaluation frameworks and indicators to inform the development of an impact evaluation framework for the JGHT review. Extended information is available in Appendix G.

- Database analysis

**Analysis of ResearchFish® data**: 84 of the 96 awards had submitted entries to ResearchFish® in 2019, leaving 12 awards that have not done so (11 full trial awards, one development award). Of the latter, eight are Call 7 awards, and started in 2018. The data was analysed for the following categories: Publications, Further funding, Skills, Dissemination, Policy, Tools, Databases, Software, Artistic products, IP and Products. Where necessary, duplicate entries and outliers were excluded from the analysis. An extended analysis is available in Appendix C.

**Bibliometric analyses**: Data for publications of main findings (i.e. on the primary outcome of the trial) for 22 full trials were extracted from the Scopus database to a) determine the number of citations and b) identify the institutes authors and co-authors are affiliated with.

**Analysis of clinical trials databases**: Clinical trial registration entries were extracted from the World Health Organisation (WHO) ICTRP registry. This database was chosen as it collates entries from several trial registries including clinicaltrials.gov, ISRCTN, EU clinical trials register, Pan-African, and many other national registries. Searches were carried out for trials registered between 1 January 2005 and 31 December 2018 and for specific indications (in the ‘title’ and ‘condition’ fields). Data for all search hits was extracted and duplicates removed. Early-stage (Phase 0 to II) trials and studies other than interventional studies were excluded from the analysis. A full analysis is available in Appendix D.

- Primary data collection: Surveys and interviews

**Survey of all PIs and co-investigators**: Three surveys were developed to gather information from: 1) PIs of open full trial awards; 2) PIs of development awards; and 3) Co-investigators of all awards. The surveys were implemented using an online survey tool, SurveyMonkey. Full questionnaires are available in Appendix A.

The survey was sent to contacts contained within the JGHT grants database (24 PIs of open full awards; 27 PIs of development awards; 556 co-investigators). E-mail addresses where the survey invitation was returned as ‘undeliverable’ were updated through online searches. The survey remained open for 30 days, with non-respondents receiving 2 reminders.
Programme of interviews: Two interview programmes were conducted, aimed at 1) all PIs of completed full trial awards and 2) other key stakeholders.

- Interviews of PIs of completed full trial awards: The objective of this interview programme was to gather information for the impact and process evaluations; for the case studies; and to inform the wider global health landscape review. PIs of completed full trial awards were approached (28 projects). As one researcher was PI of two trials, a total of 27 individuals were contacted. In addition, six PIs of open full trials were contacted, and interviews conducted; five of these had been selected to gather additional in-depth insights from researchers located at institutions in LMICs. Similarly, three PIs of JGHT development awards based in LMICs were contacted. Of the total of 36 individuals contacted, 29 were consulted (23 closed full trial PIs, 6 open full trial PIs, 1 closed development award PI), including three PIs who provided information in writing rather than by interview.

- Interviews of key opinion leaders: The objective of this interview programme was to gather perceptions of the JGHT and its impact, and views of the design and implementation of the JGHT funding scheme; to validate case study findings and provide further context; and to inform recommendations for enhancing the JGHT’s potential for impact. A total of 19 key opinion leaders were interviewed, including international funders (6), review committee members (5), and researchers in leading positions such as Heads of joint units (7).

- Impact case study development
  JGHT-funded projects that had led to impact on policy, practice, and further research were identified from the information gathered in interviews and the survey, and selected for impact case studies. 16 of these were developed through extensive desk research. PIs were consulted directly and given the opportunity to verify the accuracy of the final case study in all cases but one (the Devries case study is based on desk research only). Case study summaries are presented in this report, with the full case studies available in a separate document.

- Analysis and recommendations
  Evidence gathered from multiple sources and perspectives, was used to triangulate and verify findings, and to formulate recommendations.

4 The JGHT Funding Scheme Evaluation Framework

4.1 Impact logic model

A logic model provides a structured approach to look at a programme or intervention. It is based on the idea that there is a linked chain of logic that shows how the inputs to an intervention (e.g. funders’ budget, programme management) and the resulting activities (e.g. research projects, stakeholder engagement) are expected to produce immediate outputs (e.g. new evidence, skills and collaborations). These in turn are connected to medium-term outcomes (e.g. change in local practices) and longer-term outcomes (e.g. change in practices beyond the project site) and eventually the realisation of the objectives - the impacts (e.g. improvement in health of target population). Anticipated outputs, outcomes, and impacts can be linked to a set of indicators that evidence whether, and to what degree, the programme is progressing against its objectives.

In order to describe the intervention of the JGHT funding scheme, we developed an impact logic model, tracing the causal chain of connections between the inputs, activities, outputs, outcomes, and impacts to achieve the stated aims. This was informed by a review of the available policy documents setting out the rationale for the programme, interviews with representatives from the funders (scoping interviews) and an outline of the process through which it was expected to deliver its intended outputs, outcomes and impacts. The logic model expands on the elements related to outcomes and impacts of the JGHT programme model (Figure 1), and is presented in Figure 2.
**Figure 2** Programme logic model for the Joint Global Health Trial funding scheme

- **Needs, Problems, Issues**
  - Unaddressed health-related problems affecting disadvantaged populations in LMICs
  - Health systems, services, and interventions not suitable or too costly for the prevention and treatment of health-related problems in LMIC settings
  - Inequality of access for the most vulnerable populations
  - Insufficient evidence of the best and most appropriate interventions to improve health in LMIC settings
  - Need for large-scale Phase III/IV clinical trials to provide robust evidence, but these are expensive and risky
  - Interest from the private sector limited
  - Fragmented global health trial funding landscape
  - Lack of clinical trial research capacity in LMICs

- **Objectives of JGHT scheme:**
  - To develop and evaluate interventions with potential for significant impact on the health of disadvantaged populations living in LMICs:
    - Generate definitive new evidence of the best and most appropriate interventions in LMIC settings
    - Provide implementable, sustainable and scalable results

- **Inputs**
  - Funding (£)
  - Scheme management & governance
  - Expert review of proposals
  - Active monitoring and evaluation
  - Promotion of scheme

- **Project activities**
  - Implementation of late stage trials in LMICs, potentially including:
    - Social science and health economics expertise
    - Nested studies to support future implementation
  - Training of trial staff
  - Engagement with policy makers, health system, implementing organisations
  - Development grants: pilot studies to inform potential large-scale trials

- **Impacts**
  - Improved population health in LMICs:
    - Decreased levels of mortality
    - Decreased level of morbidity
    - Increased health equality
  - Progress towards health-related MDGs
  - Enhanced economic growth of LMICs

- **Outcomes**
  - Further research informed by trial results
  - New/strengthened international research networks
  - Key decision makers receptive to research evidence, leading to changes in policy
  - Change in policy and implementation of effective health interventions:
    - In trial location
      - Delivered at scale (national and international level)
    - Improved cost-effectiveness of interventions, leading to cost savings for LMIC health systems

- **Evaluation**

- **Social, cultural and economic barriers to implementation**

- **Organisations enabling implementation & access**

- **Communication and dissemination**

In italics: outputs/outcomes in research domain; normal: outputs/outcomes in health domain. In peach: potential barriers to uptake and implementation and JGHT elements addressing these. In green: activities linking outputs to outcomes and impacts, and JGHT elements supporting these. In red: activity and output specific to JGHT development award scheme.
The model also sets out a number of spill-over effects that do not directly relate to the objectives of the scheme, but support the environment within which the programme takes place and can enhance progress towards impact. For example, while capacity building is not an explicit goal of the JGHT, the funded activity can be expected to enhance the skills of researchers and trial staff through their involvement in the project or directly through training courses, which in turn can benefit future research activity. In addition, the model illustrates external factors required to achieve the stated impacts or impeding progress (barriers). While these factors are beyond the remit and scope of the programme itself, funded activity can be informed by, or targeted at, key external factors to facilitate ‘downstream’ effects (i.e. beyond the project outputs).

It should be noted that the linear nature of a programme logic model is helpful for testing causal links and assumptions, but represents a simplification of the actual effects of a programme (e.g. information and learning from outputs and outcomes can be expected to feed back into the programme’s activities).

4.2 The JGHT scheme evaluation framework

The main objective of this review was to determine the outcomes and impacts achieved by JGHT-funded activities to date. To guide the review, the study team developed an evaluation framework setting out indicators for the outputs (Table 2), outcomes (Table 3) and impacts (Table 4) presented in the logic model. Evidence against each of the indicators within the framework was collected, and is presented in this report. (Some of the indicators are annotated with comments in square brackets, […], to indicate any divergence from the original study plan.)

Table 2: Evaluation framework - Outputs of JGHT-funded projects

<table>
<thead>
<tr>
<th>Outputs - Research domain</th>
<th>Indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successfully completed Phase III/IV trials</td>
<td>Number and percentage of completed trials resulting in a definitive answer to the research question; nature of intervention</td>
</tr>
<tr>
<td></td>
<td>Evidence that trial advanced trial methodology*; number of projects using novel trial methodologies, by type</td>
</tr>
<tr>
<td>Evidence on interventions that are appropriate, acceptable and feasible for improving the health of disadvantaged populations and suitable for implementation in LMICs settings</td>
<td>Number of trials with a relevant definitive answer and a clear path to implementation at conclusion of study, including (where relevant) manufacture, access, and implementation [the elements in italics were found to require stakeholder engagement and utility of data, and are covered in the impact section of the report]</td>
</tr>
<tr>
<td>Dissemination of research results</td>
<td>Number of articles published (primary trial results / other project findings)</td>
</tr>
<tr>
<td>High quality research results</td>
<td>Evidence that trials contributed to a shift in the body of evidence and influenced research activity* [this indicator was addressed by outlining the research landscape for four selected diseases]</td>
</tr>
<tr>
<td>Sufficient evidence to design and implement full trials (for development awards)</td>
<td>Number of development awards that have led to successful full trial applications (JGHT / other funding)</td>
</tr>
<tr>
<td>New collaborations between researchers in the UK and LMICs</td>
<td>Number of new collaborative partnerships (UK-LMIC / LMIC-LMIC)</td>
</tr>
<tr>
<td>Enhanced research skills in the UK and/or LMIC [Survey respondents and interviewees were asked to indicate the extent to which skills were developed]</td>
<td>Number of researchers involved in JGHT projects (faculty members, postdoctoral researchers, postgraduate students, technicians)</td>
</tr>
</tbody>
</table>

The definition of ‘definitive answer’ used throughout the evaluation framework is: “A conclusive answer to the research question the trial was designed to address”. This definition does not extend beyond the trial question itself, i.e. it does not require an answer to the question “which is the best intervention to prevent/treat health issue X in target group Y.”
had been enhanced, rather than provide numbers, to allow sufficient time for questions with higher priority)

<table>
<thead>
<tr>
<th>Enhanced research infrastructure and tools in UK and/or LMIC</th>
<th>Number and type of research tools developed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number and type of new/improved research infrastructure established</td>
</tr>
<tr>
<td>New collaborations between researchers and stakeholders relevant for implementation</td>
<td>Number stakeholders engaged during the trial design phase, by type; level and frequency of engagement (descriptive)</td>
</tr>
<tr>
<td></td>
<td>Number of stakeholders engaged during the project phase (by type); level and frequency of engagement (descriptive)</td>
</tr>
<tr>
<td>Key decision makers aware of research and receptive to findings</td>
<td>Level of awareness of key decision makers of JGHT project at the end of project</td>
</tr>
<tr>
<td>Health benefits for trial participants</td>
<td>Number of trial participants that have received health services beyond their usual level of care</td>
</tr>
</tbody>
</table>

*addresses evaluation question set out in the ITT. In italics: Data against this indicator was collected in aggregate form.*

**Table 3 Evaluation framework - Outcomes of JGHT-funded projects**

<table>
<thead>
<tr>
<th>Outcomes - Research domain</th>
<th>Indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Further research informed by research results</td>
<td>Evidence that research findings have informed further work by the research team and/or the wider research community</td>
</tr>
<tr>
<td></td>
<td>Field normalised citation score</td>
</tr>
<tr>
<td></td>
<td>[this score could not be determined as most main trial papers were too recent]</td>
</tr>
<tr>
<td>New /strengthened international research networks</td>
<td>Increased number of collaborative partnerships and expansion of relevant research communities</td>
</tr>
<tr>
<td>Enhanced research environment</td>
<td>Number of joint proposals and funded projects beyond the JGHT award</td>
</tr>
<tr>
<td>[these indicators were added]</td>
<td></td>
</tr>
<tr>
<td>Enhanced research environment</td>
<td>Number of investigators reporting an increase in the priority of health research in their organisation</td>
</tr>
<tr>
<td></td>
<td>Number of investigators reporting an enhancement of research governance structures at the participating LMIC institution</td>
</tr>
<tr>
<td></td>
<td>Number of investigators reporting an increase in LMIC researchers’ research leadership capabilities</td>
</tr>
<tr>
<td></td>
<td>Number of investigators reporting an increased motivation of health professionals at LMIC institutions to become research leaders</td>
</tr>
<tr>
<td></td>
<td>Number of investigators reporting a reduction in cultural or operational barriers to health research</td>
</tr>
<tr>
<td>Outcomes - Health domain</td>
<td></td>
</tr>
<tr>
<td>Change in policy related to health interventions at the trial location(s), and beyond the trial location (scale-up)</td>
<td>Number of trials resulting in a policy change at / beyond the trial location(s); number of organisations/countries involved</td>
</tr>
<tr>
<td></td>
<td>Number of citations in local/national/international clinical guidelines</td>
</tr>
<tr>
<td></td>
<td>Nature of policy change (descriptive)</td>
</tr>
<tr>
<td>Change in implementation of effective health interventions at the trial location(s), and beyond the trial location (scale-up)</td>
<td>Number of trials resulting in the implementation of new effective health interventions at / beyond the trial location(s)</td>
</tr>
<tr>
<td></td>
<td>Nature of the implemented intervention and implementing organisations</td>
</tr>
<tr>
<td></td>
<td>Number of people/patients benefitting from the new intervention</td>
</tr>
<tr>
<td></td>
<td>Level and nature of benefit to the target population (descriptive)</td>
</tr>
<tr>
<td></td>
<td>Number of trials resulting in cost savings for LMIC health system</td>
</tr>
</tbody>
</table>
Improved cost-effectiveness of healthcare provision, leading to cost savings for LMIC health systems

Key decision makers more receptive to research evidence

<table>
<thead>
<tr>
<th>Impact</th>
<th>Indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved population health in LMICs</td>
<td>Decreased levels of mortality and morbidity in relevant LMICs, for health issues addressed by JGHT awards; increase in associated QALYs</td>
</tr>
<tr>
<td>Improved health equality</td>
<td>Availability of interventions addressing the needs of disadvantaged population groups</td>
</tr>
<tr>
<td>Improved health equity</td>
<td>Improved accessibility to interventions for disadvantaged population groups</td>
</tr>
<tr>
<td>Progress towards health-related SDGs</td>
<td>Evidence of progress towards health-related SDGs</td>
</tr>
</tbody>
</table>

Table 4 Evaluation framework - Impacts of JGHT-funded projects

5 Evaluation of the JGHT funding scheme

5.1 Inputs and activities - the JGHT portfolio

5.1.1 Inputs and activities funded

A total of 96 awards were made as part of Calls 1 – 7 of the JGHT, representing an investment of £138.8m. 63 of these awards were for full trials, with a budget of £133.8m, and 33 were development awards, with a budget of £5.06m. 28 full trial awards had closed by the end of May 2019, with 35 remaining active. Of development awards, 22 had closed and 11 remained active (Figure 3). The data provided included three grants with unclear status: ‘payments suspended’, ‘grant suspended’, ‘terminating’. These were classified as ‘closed’ (1) or ‘active’ (2) on the basis of the ‘actual end date’ assigned in the data (i.e. end date before or after June 2019).

Table 5 Number of JGHT awards (Call 1 - 7), by type and status

<table>
<thead>
<tr>
<th>Award status</th>
<th>All awards</th>
<th>Full trial awards</th>
<th>Development awards</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>46</td>
<td>35</td>
<td>11</td>
</tr>
<tr>
<td>Closed</td>
<td>50</td>
<td>28</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>96</td>
<td>63</td>
<td>33</td>
</tr>
</tbody>
</table>

The number of full trial awards ranged from a low of 6 awards in Call 6, to a high of 12 awards in Call 2 (Figure 3). Since the development awards were established as a separate funding stream in Call 5, the number of awards was 10, 7 and 8 (Calls 5, 6 and 7, respectively).
The amount of funding per call allocated ranged between a low of £15.8m in Call 7 / £16.8m in Call 3, and a high of £22.6m in Call 5 (Figure 4).

For full trial awards, the call with the lowest average award size was Call 2, at approx. £1.8m, and the call with the highest average was Call 6, at £3m. The five largest full trial awards amounted to between £4m and £5m (two in Call 1, and one each in calls 2, 3 and 6); the smallest were under £1m (Figure 5a). For development awards, the lowest average award size was in Call 6, at £129,000, and the highest average was in Call 7, at £161,000.

The size of full trial awards was more evenly distributed in Calls 1-4, with around one quarter of awards below £1m, between £1-2m, between £2-3m, and larger than £3m (9, 10, 10 and 8 of 37, respectively) (Figure 5b). In Calls 5-7, the largest share of awards was between £2-3m (38%, 9 of 24), following by 29% (7) between £1-2m, and 28% (6) larger than £3m. This may indicate that researchers are ‘converging’ on proposing trials with a £2-3m budget, or that the review panel considers this size award more competitive.
The average size per full trial award was the same for awards held by institutions in high income countries (HICs) and ‘joint units’ (HIC-funded programmes or institutes located in LMICs20), at £2.2m, and lower for awards held by institutions in LMICs (£1.7m).

**Figure 5**

a) Smallest and largest awards (in £ million), for each call

![Chart showing smallest and largest awards for each call](chart.png)

b) Share of awards by size, comparing awards funded in Calls 1-4 with awards funded in Calls 5-7

![Chart showing share of awards by size](chart2.png)

*Calls 1 and 2 funded one award of under £300,000 each; given that the separate development award scheme had not been established, these awards were omitted from these figures. Source of data: MRC grants database.

---

20 Joint units include: KEMRI Wellcome Trust Research Programme, Kenya; Mahidol Oxford Research Unit, Thailand; Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Malawi; Mwanza Interventions Trials Unit, Tanzania; MRC Unit The Gambia; MRC/UVRI Uganda Research Unit, Uganda; Oxford University Clinical Research Unit, Vietnam. The actual figure for applications from these units may be higher, as the names of investigators for unsuccessful applications were not provided. For awards, each investigator name was checked against the individual’s institution website to determine were the researcher is based (as often only the UK institutions was named, e.g. ‘University of Oxford’ for researchers based at the Oxford University Clinical Research Unit in Vietnam). It is however possible that a number of investigators based at joint units in LMICs were counted as UK-based, as not all websites contained information on location.
5.1.2 Applications and funding requested

The applications process for full trial awards involves two stages, an outline stage followed by a full proposal stage.

Across all 7 calls, the JGHT received a total of 599 project outlines for full trial awards (an average of 86 outlines per call) (Figure 6). Of these, 160 were invited to prepare full proposals (26.7%), 144 full proposals were submitted, and 63 awards were made. This represents an overall success rate of 10.5% from outline to award, and of 43.8% from full proposal to award.

The development award scheme operates a one-step application process. 115 applications for development awards were received for Calls 5-7, at an average of 39 applications per call. Of these, 25 were successful, representing a success rate of 21.6%.

The average number of outlines per call was 85.6, with the largest number of outlines received in Call 1 (142), followed by Call 4 (112), and the smallest number of outlines submitted in Call 6 (55). A total of £910m was requested, ranging between £102m in Call 2 and £169m in Call 4, at a mean of £130m per call. The average award size requested by outlines was relatively steady between Calls 2 and 7, ranging between £1.5m (Calls 2 and 4) and £1.9m (Call 6).

The success rate from outline to award was highest in Call 2 (17.9%), and lowest in Call 1 (7.0%) and Call 4 (8.9%) (Figure 7). Outlines requesting a total of approx. 2.5 times the available budget are shortlisted; the number of invitations to submit full applications is hence under the control of the funders, and ranged between 40% and 50% across the seven calls.

The average number of development award applications for Calls 5-7 was 38.7, with success rates between 17.9% in Call 6 and 27.8% in Call 5. Since the introduction of the Development award scheme, the amount of funding requested under this strand has steadily increased, from £4.4m in Call 5, to £5.3m in Call 6 and £6.8m in Call 7.

21 For Calls 3 and 4, a separate Development Award scheme had not yet been established, and all applications followed the same application process. At the decision meetings of these calls, it was determined that while some of the full trial applications were of high quality, they were not yet ready for a full trial award. These applications were provided with 'development award' funding (8 awards in total), at an apparent 'success rate' of 100%, and are hence not included in Figure 7.
Two full trial proposals that had been rejected at the second stage of the application process went on to successfully apply for a JGHT development award to gather additional evidence.\textsuperscript{22, 23}

5.1.3 Applications and awards, by lead PI affiliation (HIC, LMIC or joint unit)

More than half (57.6\%) of all full trial award applications (second stage\textsuperscript{22, 24}) were led by PIs affiliated with institutions in high income countries (HICs), compared to 27.1\% of applications led by PIs from institutions in LMICs and 13.9\% from joint units (Table 6). Applications led by PIs at institutions in HICs accounted for the largest share of applications across all calls; the share of applications led by PIs at LMIC institutions (excluding joint units) was highest in Call 4 (41.7\%), and lowest in Call 7 (15.8\%). Applications led by PIs affiliated with joint units had the highest success rate, at 75\%, securing 15 of 63 awards across Calls 1-7. This was followed by PIs from HIC institutions, with a success rate of 48.2\%, leading 64\% of awards. Applications led by PIs from LMIC institutions had an overall success rate of 20.5\% (securing 8 awards); however, none of the applications in Calls 6 and 7 were successful (Figure 8).

The total share of full trial awards led by PIs at HIC institutions was 63.5\% (40), 23.8\% for PIs at joint units (15) and 12.7\% for PIs at LMIC institutions (8).

<table>
<thead>
<tr>
<th>Led by PIs affiliated with institutions in:</th>
<th>Share of applications (n=144 applications)</th>
<th>Success rate</th>
<th>Share of awards (n=63 awards)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIC</td>
<td>57.6% (83)</td>
<td>48.2%</td>
<td>63.5% (40)</td>
</tr>
<tr>
<td>LMIC</td>
<td>27.1% (39)</td>
<td>20.5%</td>
<td>12.7% (8)</td>
</tr>
<tr>
<td>Joint unit</td>
<td>13.9% (20)</td>
<td>75%</td>
<td>23.8% (15)</td>
</tr>
</tbody>
</table>

In parentheses: number of awards; Source of data: MRC grants database

\textsuperscript{22} Data excerpt provided by MRC; a third PI whose full trial application to Call 7 was rejected secured a development award in Call 9 (i.e. outside the scope of this review).

\textsuperscript{23} As information on rejected full trial outlines (stage 1) was not available, the MRC database data does not contain information on the overall number of rejected full trial proposals at outline stage that then went on to apply for a development award.

\textsuperscript{24} This information was not available for outline awards.
For development awards, 50.4% of applications were led by PIs affiliated with institutions based in LMICs, 46.1% in HICs and only 2.6% at joint units (Table 7)²⁵. Lead PIs affiliated with joint units again achieved the highest success rate, with 2 of 3 applications funded (66.7%). 26.4% of applications led by PIs from institutions in HICs were successful, compared to 15.5% of applications from PIs at institutions in LMICs.

Across all three calls, applications led by PIs at HIC institutions had a higher success rate than applications led by PIs from LMIC institutions, ranging between 37.5% and 22.2%, compared to 22.2% and 14.3% for LMICs (Figure 9). PIs from joint units submitted only one application per call, and secured one development award each in Calls 7 and 8.

Including awards made in Calls 3 and 4, the total share of development awards led by PIs at HIC institutions was 54.4% (18 of 33), 36.4% for PIs in LMICs (12) and 9.1% for PIs from joint units (3) (Table 7).

Table 7 Development award applications and success rates, by location of lead PI

<table>
<thead>
<tr>
<th>Led by PIs affiliated with institutions in:</th>
<th>Share of applications (calls 5-7, n=115 applications)</th>
<th>Success rate (calls 5-7, 25 awards made)</th>
<th>Share of awards (calls 3-7, n=33 awards)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIC</td>
<td>46.1% (53)</td>
<td>26.4% (14)</td>
<td>54.4% (18)</td>
</tr>
<tr>
<td>LMIC</td>
<td>50.4% (58)</td>
<td>15.5% (9)</td>
<td>36.4% (12)</td>
</tr>
<tr>
<td>Joint unit</td>
<td>2.6% (3)</td>
<td>66.7% (2)</td>
<td>9.1% (3)</td>
</tr>
</tbody>
</table>

In parentheses: number of awards; Source of data: MRC grants database

²⁵ This excludes awards made in Calls 3 and 4, before the launch of the development award scheme.
5.1.4 Applications and awards, by continent

The largest share of full trial award applications (second stage) was led by PIs affiliated with institutions located in Europe (46.9%), followed by Africa (25.0%) and Asia (15.3%) (Table 8). PIs at institutions located in Europe also led the largest share of full trial awards (60.3%), with a success rate of 46.9% from full proposal to award. Lead PIs at institutions in Africa secured 28.6% of awards (most of whom were affiliated with joint units), with a success rate of 50% from full proposal to award, while applications led by PIs at institutions in Asia had a lower success rate of 22.7%.

The largest share of development award applications (calls 5-7) were also led by PIs affiliated with institutions in Europe (44.3%) (Table 8). 27% of applications were led by PIs in Asia and 21.7% in Africa. Success rates were highest for lead PIs in Europe (27.5%), with success rates for applications led by PIs in Asia at 19.4% and in Africa at 16.0%.

Table 8 Applications and success rates, by continent of lead PI

<table>
<thead>
<tr>
<th>Full trial awards, location of lead PI</th>
<th>Share of applications (n=144)</th>
<th>Success rate</th>
<th>Share of full trial awards (n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>56.3% (81)</td>
<td>46.9%</td>
<td>60.3% (38)</td>
</tr>
<tr>
<td>Africa</td>
<td>25.0% (36)</td>
<td>50.0%</td>
<td>28.6% (18)</td>
</tr>
<tr>
<td>Asia</td>
<td>15.3% (22)</td>
<td>22.7%</td>
<td>7.9% (5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Development awards, location of lead PI</th>
<th>Share of applications (calls 5-7, n=115)</th>
<th>Success rate (calls 5-7)</th>
<th>Share of full trial awards (calls 3-7, n=33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>44.3% (51)</td>
<td>27.5%</td>
<td>51.5% (14)</td>
</tr>
<tr>
<td>Asia</td>
<td>27.0% (31)</td>
<td>19.4%</td>
<td>27.3% (6)</td>
</tr>
<tr>
<td>Africa</td>
<td>21.7% (25)</td>
<td>16.0%</td>
<td>15.2% (4)</td>
</tr>
<tr>
<td>South America</td>
<td>3.5% (4)</td>
<td>25.0%</td>
<td>6.1% (1)</td>
</tr>
</tbody>
</table>

In parentheses: number of awards; Source of data: MRC grants database
5.1.5 Applications and awards, by country

Applications were received from lead PIs affiliated with institutions located in 32 countries, in 27 LMICs and five HICs.26

PIs from research organisations in 21 countries applied for full trial awards (full proposal stage). More than half of these applications (55.6%) were submitted by PIs at institutions in the UK (Table 9). The highest share of applications from LMIC PIs originated in South Africa and The Gambia (7.6% each), latter reflecting the location of the MRC Gambia unit, followed by India (4.9%) and Bangladesh (4.2%). Only one application was led by a PI at an institution in South America.

Lead PIs at institutions in 15 countries were awarded a full trial award, with PIs in the UK receiving the largest number (37 58.7% of all full trial awards), followed by PIs in countries in sub-Saharan Africa: The Gambia (7 awards), Kenya (4 awards) and South Africa (3 awards)27 (Figure 10). Lead PIs in India and Bangladesh did not secure any full trial awards. Of countries with 3 or more awards, applications from lead institutions Kenya had the highest success rate, of 100% (all 4 full applications funded), followed by The Gambia (64%), the UK (46%), and South Africa (27%).

Lead PIs from research organisations in 23 countries applied for development awards. In Calls 5-7, 44.3% of lead PIs were from institutions located in the UK (51 of 115), 17.4% in India (20), 5.2% from South Africa (6), and 4.3% from Nigeria (5) (Table 9). Only three PIs leading applications were from South/Central America (2 from Peru, one from Mexico) (Calls 3-7).

Across Calls 3-7, development award applications led by PIs at institutions in 10 countries were successful, with PIs in the UK holding the largest share (17 of 33 awards, or 51.5%), followed by PIs in India (4 awards, 12.1%). Lead PIs in South Africa, Kenya, China and Peru held two grants each (6.1%). For Calls 5-7 (i.e. when a separate development award scheme was in place), applications led by institutions in the UK had a success rate of 27.5%. Applications led by institutions in India had the lowest success rate, at 15.0%, of ‘funded countries’. Lead PIs at South African institutions submitted 6 applications, of which 2 were funded (33.3% success rate); PIs in China and Kenya achieved a success rate of 100% (2 awards each).28

Table 9 Applications and success rates, per country of lead institution

<table>
<thead>
<tr>
<th>Country of lead institution</th>
<th>Full trial application (stage 2) (n=144)</th>
<th>Full trial awards (n=63)</th>
<th>Success rate</th>
<th>Country of lead institution</th>
<th>Development award application (n=115)</th>
<th>Development awards (n=25)</th>
<th>Success rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>80</td>
<td>37</td>
<td>46.3%</td>
<td>UK</td>
<td>51</td>
<td>14</td>
<td>27.5%</td>
</tr>
<tr>
<td>The Gambia</td>
<td>11</td>
<td>7</td>
<td>63.6%</td>
<td>India</td>
<td>20</td>
<td>3</td>
<td>15.0%</td>
</tr>
<tr>
<td>South Africa</td>
<td>11</td>
<td>3</td>
<td>27.3%</td>
<td>South Africa</td>
<td>6</td>
<td>2</td>
<td>33.3%</td>
</tr>
<tr>
<td>India</td>
<td>7</td>
<td>0</td>
<td>0.0%</td>
<td>Nigeria</td>
<td>5</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>6</td>
<td>0</td>
<td>0.0%</td>
<td>Kenya</td>
<td>4</td>
<td>2</td>
<td>50.0%</td>
</tr>
<tr>
<td>Kenya</td>
<td>4</td>
<td>4</td>
<td>100.0%</td>
<td>Bangladesh, Brazil, Tanzania</td>
<td>3</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Pakistan, Uganda</td>
<td>3</td>
<td>1</td>
<td>33.3%</td>
<td>China</td>
<td>2</td>
<td>2</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

In parentheses: number of awards; Source of data: MRC grants database

26 LMIC: Argentina, Armenia, Bangladesh, Brazil, China, Ethiopia, Georgia, Ghana, India, Kenya, Malawi, Mexico, Nigeria, Pakistan, Papua New Guinea, Peru, Philippines, Senegal, Somaliland, South Africa, Sri Lanka, Tanzania, Uganda, Vietnam; HIC: UK (and ‘UK unit’ in LMIC), Australia, Canada, Singapore, Switzerland

27 All awards in The Gambia and Kenya were to the MRC unit and the KEMRI-Wellcome Trust Research Programme.

28 Both awards in Kenya were to the KEMRI-Wellcome Trust Research Programme.
5.1.6 Applications and awards, by institution

PIs affiliated with a total of 42 institutions led JGHT awards.

PIs at 60 institutions applied for full trial awards (27 in HICs, 26 in LMICs, 6 joint units, and 1 global organisation). Applications led by PIs at 30 institutions were successful (18 in HICs, 7 in LMICs, and 5 joint units).

The largest number of full trial awards were led by PIs based at the London School of Hygiene and Tropical Medicine (LSHTM), with 12 awards (19%)\(^29\) (Table 10). PIs at the MRC Unit in The Gambia secured seven awards (11.1%), and PIs at the Liverpool School of Tropical Medicine led five awards (7.9%). PIs at LSHTM also led the largest number of applications (28)\(^30\), with a success rate of 42.9%.

PIs from LMIC institutions securing full trial awards were at the University of Cape town (2 awards), Makerere University, Uganda; the University of Ibadan, Nigeria; Stellenbosch University; South Africa; the Papua New Guinea Institute of Medical Research; The Aga Khan University, Pakistan; and the University Cheikh Anta Diop de Dakar, Senegal (1 award each).

The largest number of applications led by PIs from LMIC institutions were affiliated with the ICDDR,B in Bangladesh and Stellenbosch University (4 applications each), followed by the University of Cape Town and The Aga Khan University, Pakistan (3 applications each).

---

\(^{29}\) This excludes awards made to LSHTM-associated

\(^{30}\) However, as noted above: Names of PIs for unsuccessful applications were not available, the primary location could not be verified. PIs based at joint units in LMICs are often listed under the associated UK university; the number of applications reported per UK institution here may hence be higher than the actual number, and the success rate lower than the actual success rate.
Lead PIs at 79 institutions applied for development awards in Calls 5-7 (26 institutions in HICs, 50 in LMICs, 2 joint units), and 24 institutions led development awards in Calls 3-7 (12 in HICs, 10 in LMICs, and 2 joint units).

The largest number of development awards was led by PIs based at LSHTM, with 3 awards (9.1%, calls 3-7), and a 18.2% success rate (2 awards of 11 applications made in calls 5-7) (Table 11). All other institutions led one or two awards only.

### Table 11 Development award applications and awards, by lead institution

<table>
<thead>
<tr>
<th>Lead institution</th>
<th>Number of development awards (calls 3-7)</th>
<th>Share of development awards (calls 3-7) (n=33)</th>
<th>Number of applications (calls 5-7)</th>
<th>Success rate (calls 5-7), 25 awards made</th>
</tr>
</thead>
<tbody>
<tr>
<td>London School of Hygiene and Trop Med</td>
<td>3</td>
<td>9.1%</td>
<td>11</td>
<td>18.2%</td>
</tr>
<tr>
<td>Liverpool School of Trop Med</td>
<td>2</td>
<td>6.1%</td>
<td>3</td>
<td>66.7%</td>
</tr>
<tr>
<td>Peruvian University Cayetano Heredia</td>
<td>2</td>
<td>6.1%</td>
<td>1</td>
<td>100.0%</td>
</tr>
<tr>
<td>Sangath, India</td>
<td>2</td>
<td>6.1%</td>
<td>3</td>
<td>66.7%</td>
</tr>
<tr>
<td>University of Birmingham</td>
<td>2</td>
<td>6.1%</td>
<td>3</td>
<td>66.7%</td>
</tr>
<tr>
<td>KEMRI/Wellcome Programme, Kenya</td>
<td>2</td>
<td>6.1%</td>
<td>2</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Source of data: MRC grants database
5.1.7 Trial locations

The 63 full trials were implemented at trial sites located in 47 countries (indicated by their clinical trials database registrations). One third of trials involved sites in more than one country (32%, 20 of 63), with 13% (8) involving sites on more than one continent. The majority of trials included trial sites in Africa (74.6%, 46 trials). Fewer trials included sites in Asia (30%, 19 trials) and Central/South America (7.9%, 5 trials) (Figure 11).

Sub-Saharan countries hosted sites for the largest number of trials, headed by Uganda (14), Kenya (11) and South Africa (9). Countries hosted trials across a range of conditions. Further information on trials addressing malaria, tuberculosis, cryptococcal meningitis and podoconiosis is available in the relevant research landscapes (see Appendix G).

Figure 11 Locations of trial sites (n=63)

Source of data: Clinical trial databases: ISRCTN, ICTRP and clinicaltrials.gov. Two trials received co-funding to conduct parallel trials involving sites in HICs and LMICs (MR/M009211/1 and MR/N006127/1); HIC sites are not included in the map.

Including both, full trial and development awards, 41 countries were cited as trial locations within the ‘Case for Support’ documents (n=93). The original project plans saw Uganda hosting the largest number of projects (19), followed by India (16), Kenya and South Africa (12 each) and Malawi (10). The largest number of studies plans involved sites on the African continent (62; 69%), followed by sites in Asia (37 studies; 39%). 29% of awards planned to involve sites in more than one country (27 of 94). This proportion was higher for full trial awards (35%, 22 trials) than for development awards (16%, 5 awards), as would be expected given the scope and size of full trials. 10 studies (11%) intended to involve sites located on more than one continent.

31 Two trials (MR/M009211/1 and MR/N006127/1) included sites in HICs funded through alternative sources. These sites were excluded from this analysis.


33 Some projects received co-funding to conduct parallel trials in HIC and LMIC countries. For this reason, the registration of these trials listed HIC locations as trial sites, but these were not funded by the JGHT.

34 Case for Support (CfS) documents were available for 62 of 63 full trial awards, and 32 of 33 development awards. One award (MR/M009211/1) indicated only ‘worldwide’ in the CfS, and is hence not included in this analysis. It should be noted that the CfS set out initial project plans and were subject to change as the project is implemented.

35 Studies with sites in multiple countries are counted multiple times.
5.1.8 Trial settings

The largest share of full trials were set in the community (35%, 22 of 63), followed by hospitals (33%, 21) and in the home (10%, 6) (Figure 12).

Figure 12 Trial settings of full trials (n=63)

Source of data: Clinical trial databases - registration data

5.1.9 PIs and co-investigators

In total, 647 individuals (PIs and co-investigators of the JGHT, Calls 1 - 7) were listed in the MRC grant database, affiliated with a total of 212 organisations. 88 individuals were in the role of PI in at least one JGHT award, with 9 individuals PIs of more than one award.

Half of the 212 organisations are located in LMICs (49.1%, 104), 41% (87) are located in HICs, and 5.7% (12) are joint units (Figure 13). The UK hosted the largest share of institutions (21.1%, 45), followed by the USA (7.1%, 15), South Africa (6.6%, 14), Uganda (5.2%, 11) and India (4.7%, 10). Just under 30% of organisations were located in Africa and Europe each, 22.2% in Asia and 9.0% in North America. Across the African continent, countries in East and far West Africa are strongly represented.

Individuals at the London School of Hygiene and Tropical Medicine were involved in more awards than any other organisation (41.7%, 40 awards). This was followed by the Liverpool School of Tropical Medicine and University College London (14.6% each), and KEMRI Wellcome Trust Research Programme in Kenya (10.4%). The LMIC organisations involved in the largest number of awards were The Aga Kahn University, Pakistan, and the University of Malawi, Malawi, each involved in 6 awards (6.3%). Organisations located in high income countries other than the UK were John Hopkins University, USA (involved in 6 awards) and the Institute of Tropical Medicine Antwerp, Belgium (5 awards).

Contact details for PIs and co-investigators of JGHT awards (from the MRC’s grant database) were analysed as an indication of affiliation and geographical location of the individuals involved in delivering JGHT projects. It should be noted that:

- The level of contacts available is likely to differ between awards, with some providing information on all researchers at all sites, whereas others only list the main contributors
- Contact details reflect the planned study team at the start of the award, and are not updated over the course of the project. Any changes to the team composition after the start of the award are hence not reflected.
- The team composition may have changed from the original study plan set out in the CfS: 22% of PIs of full trial and development awards indicated that the study team had changed compared to the CfS (9 of 40).

Botswana Harvard AIDS Initiative Partner, CDC Botswana – BOTUSA, Eijkman Oxford Clinical Research Unit, Epicentre Mbarara Research Base, KEMRI CDC, KEMRI Wellcome Trust Research Programme, Mahidol Oxford Research Unit, Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Mwanza Interventions Trials Unit Tanzania, MRC Unit The Gambia, MRC Uganda, Oxford University Clinical Research Unit Vietnam
An analysis of author affiliation, limited to publications of the main trial findings\textsuperscript{38}, of 22 closed full trial awards\textsuperscript{39} showed a similar distribution. Investigators from a total of 106 institutes were named as co-authors. Over half of the institutions were located in LMICs (53.8\%, 57), 34\% were located in HICs (36) and 11.3\% are joint units (12)\textsuperscript{40} (Figure 14). This indicates that the contribution of investigators at the (many) LMIC trial sites is indeed being recognised.

The largest number of institutes were located in the UK (16\%, 17), followed by Viet Nam (10.4\%, 11), Kenya (7.5\%, 8) and the USA (7.5\%, 8). A third of the institutes were located in Africa (34.9\%), 29\% in Asia, 23.6\% in Europe, 9.4\% in North America and 2.8\% in Oceania.

The London School of Hygiene and Tropical Medicine was listed as an author affiliation on the greatest number of publications (36.4\%, 8 publications). This was followed by the University of Oxford (27.3\%, 6 publications) and Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Liverpool School of Tropical Medicine and KEMRI Wellcome Trust Research Programme (22.7\%, 5 publications each). The LMIC organisation listed as an affiliation on the largest number of publications was Makerere University, Uganda (3 publications). Other HIC institutes listed were Radboud University Medical Centre, Netherlands, Menzies School of Health Research and Charles Darwin University, Australia and University of California, San Francisco (listed on two publications each).

\textsuperscript{38} i.e. a peer-reviewed publication reporting on the primary outcome(s) of a trial
\textsuperscript{39} Publications of main trial findings from a further two awards could not be included as one (very recent) publication had not yet been indexed in Scopus (MR/M009211/1) and co-author indexing was not available for the other (G1100570).
\textsuperscript{40} Eijkman Institute for Molecular Biology, KEMRI, Malawi Epidemiology and Intervention Research Unit, Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Medical Research Council Unit Gambia, Dignitas International Malawi, Infectious Diseases Research Collaboration Uganda, Joint Clinical Research Centre Uganda, MRC UVRI Uganda Research Unit on AIDS, Mwanza Medical Research Centre, Oxford University Clinical Research Units Viet Nam, Mahidol-Oxford Tropical Medicine Research Unit
• PI gender balance

The overall gender balance of the 96 JGHT-funded awards was 67% male to 33% female (63 and 33 of 96, respectively). The balance for full trial awards, with 37% of female-led trials (23 of 63) was similar to that of development awards, with 30% of female-led projects (10 of 33).

Gender balance varied significantly from call to call. The largest share of female-led awards occurred in Call 3 for full trials (71%, 5 of 7), and in Call 7 for development awards (50%, 4 of 8) (Figure 15). The smallest shares were in Call 6 for full trial awards (17%, 1 of 6) and Call 5 for development awards (10%, 1 of 10). The share of female-led full trials was relatively low in Calls 6 and 7, but increased again in Call 8 (43%, 3 of 7).

The share of female PIs was higher for institutions located in HICs (41%, 25 of 61 awards) than for institutions in LMICs (26%, 5 of 19). Only 19% of awards to joint units were led by a female PI (3 of 16).

There were also differences between disease areas: While 43% of awards related to TB and HIV were led by female researchers (6 of 14), this was the case for only 19% of awards addressing malaria (3 of 16).

\[\text{i.e. after the time period covered by this review}\]
5.1.10 Health areas addressed

Across all full trial and development awards, the largest share of awards was in the area of 'Infection', at 44.4% (Figure 16), which was addressed in 48 awards. This was followed by 'Reproductive Health and Childbirth' (15.3%) in 21 awards, 'Mental Health' (9.0%; addressed in 9 awards) and 'Cardiovascular' (8.9%; addressed in 13 awards).

The relative shares of health area addressed varied from call to call: The share of 'Infection' awards was highest in Call 1, at 70%, but fell to around 30% in Calls 5 and 7 (Figure 17). The area 'Mental Health' increased its share, from no awards in Calls 3 and 4, to 36% in Call 7. 'Reproductive Health and Childbirth' and 'Cardiovascular' remained relatively steady.

Health Research Classification System (HRCS) Health codes; see https://hrcsonline.net

For the 'JGHT lifetime' analysis, all shares of HRCS codes were added up per code, and expressed as the percentage of all codes added for Calls 1–7. For the analysis of individual calls, all shares of HRCS code were added up per code, and expressed as the percentage of all codes for the call in question.
For full trial awards, the overall share of awards addressing 'Infection' was even higher, at 61%, and remained between 42% (Call 7) and 79% (Call 6). All other areas remained at 25% or below, except 'Mental Health' in Call 7, at 33%. The health area 'Infection' also received the largest amount of funding for full trial awards over Calls 1-7 accounting for £91.2m (70.6%) (£91,223,769) (Figure 18). This was followed by 'Reproductive Health and Childbirth' (£11.9m), ‘Cardiovascular’ (£8.2m), 'Mental Health' (£5.8m), and 'Injuries and Accidents' (£2.8m). All other areas accounted for 2% of the budget or less.

**Figure 18 Funding allocated per health area (HRCS code)**

- Infection
- Reproductive Health and Childbirth
- Cardiovascular
- Mental Health
- Injuries and Accidents
- Other

Source of data: MRC grants database. HRCS health codes. 'Other' includes Cancer, Generic Health Relevance, Other, Respiratory, Inflammatory and Immune System, Oral and Gastrointestinal, and Metabolic and Endocrine.

For development awards (Calls 3–7), the share of projects addressing 'Infection' was much lower, at only 11%. 'Reproductive Health and Childbirth' accounted for the highest share, at 21%, followed by 'Mental Health', 'Cardiovascular', 'Infection', and 'Oral and Gastrointestinal' at 9%-13%. There was no clear trend in health area coverage over time.

Compared to full trial awards, development awards covered a broader range of health areas, with an average of 8 HRCS codes per call for Calls 5–7. This compares to an average of 4.4 health codes covered for Calls 1-7, and an average of 4.7 codes for Calls 5-7, for full trial awards (Figure 19).

**Figure 19 Number of HRCS health codes addressed, per call**

Methodology: Funding was allocated by share of HRCS Health code share, i.e. if an award was assigned to two codes, the award budget was split equally between the two research areas. Award MR/R006121/1, £2.7m, is not coded, and was hence not included in this analysis.
The Case for Support documents, and registration data in clinical trials databases, provided information on the specific diseases/issues addressed by the proposed research, and the types of intervention tested.

A quarter of all full trial awards were related to malaria (25.4%, 16), mostly concerned with disease transmission (Figure 20). 14.3% of trials addressed aspects of TB. As these awards were on average larger than all other trials, at £3.1m, funding dedicated to addressing TB accounted for around 20% of the total full trial award budget (Figure 21). Other indications addressed by several full trial awards include respiratory disease and HIV-related fungal infections.

**Figure 20 Full trial awards, by issue addressed**

Source of data: Cases for support. Data labels indicate number of awards and total funding allocated. HIV-related fungal infections: Cryptococcal meningitis and talaromycosis; Sexual and reproductive health includes Human Papilloma Virus.

**Figure 21 Share of total full trial award funding, by issue addressed**

Source of data: Cases for support and MRC grants database. Data labels indicate average award size.
The largest number of development awards addressed issues related to nutrition (5 of 33; 15.2%), receiving funding of £689,000, followed by interventions addressing cardiovascular disease, diabetes, and tobacco use (3 awards each; 9.1%) (Figure 22).

**Figure 22 Development awards, by issue addressed**

<table>
<thead>
<tr>
<th>Issue</th>
<th>Awards</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutrition</td>
<td>3</td>
</tr>
<tr>
<td>CVD</td>
<td>3</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3</td>
</tr>
<tr>
<td>Tobacco control</td>
<td>2</td>
</tr>
<tr>
<td>Sexual and reproductive health</td>
<td>2</td>
</tr>
<tr>
<td>Childbirth</td>
<td>2</td>
</tr>
<tr>
<td>Living with disability</td>
<td>2</td>
</tr>
<tr>
<td>HIV</td>
<td>1</td>
</tr>
<tr>
<td>Menstrual health</td>
<td>1</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>1</td>
</tr>
<tr>
<td>Malaria</td>
<td>1</td>
</tr>
<tr>
<td>TB</td>
<td>1</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>1</td>
</tr>
<tr>
<td>Antibiotic prescribing</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>1</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1</td>
</tr>
<tr>
<td>Surgical site infection</td>
<td>1</td>
</tr>
<tr>
<td>Mental health</td>
<td>1</td>
</tr>
</tbody>
</table>

Source of data: Cases for support and MRC grants database. Data labels indicate number of awards. Nutrition includes both prevention of malnutrition and of obesity.

### 5.1.11 Type of research conducted

Over the lifetime of the JGHT (Calls 1–7), the largest share of research fell into the broad area of 'Treatment evaluation' (46.0%), followed by 'Prevention' (34.3%), 'Health and social care services' (9.6%) and 'Management of diseases' (7.4%) (Figure 23). Shares for full trial awards and development awards were broadly similar, with a stronger emphasis on 'Treatment evaluation' in full trial awards (49.6% of full trial awards vs. 39.1% of development awards), and a stronger emphasis on 'Prevention' in development awards (43.8% of development awards vs. 29.4% of full trial awards). While relative shares of research activity differed across the seven calls, no clear trends were discernible.

**Figure 23 Share of research area (HRCS research classification codes, all awards)**

- Treatment evaluation: 46.0%
- Prevention: 34.3%
- Health and social care services: 9.6%
- Management of diseases: 7.4%

Source of data: MRC grants database. HRCS research classification codes
More specifically, the largest share of research fell into the class 'Pharmaceuticals' (32.2%). This was followed by 'Primary preventions interventions to modify behaviours or promote well-being' (16.6%), 'Interventions to alter physical and biological environmental risks' (9.4%) and 'Psychological and behavioural' (8.5%).

The relative shares differed between the full trial award and the development award portfolio: While full trial awards fell predominantly into the 'Pharmaceuticals' research class (42.3%), the share was much lower for development award portfolio (12.5%) (Figure 24). Conversely, one third of development awards addressed the research class 'Primary preventions interventions to modify behaviours or promote well-being' (33.9%), with only 7.7% of full trial awards in this area. Vaccines were part of the full trial award portfolio (8.1%) but not the development award portfolio, while 'Psychological and behavioural' research took a larger share of development awards (14.1%) compared to full trial awards (5.6%).

The share of research class per call varied considerably (Figure 25). The research class 'Interventions to alter physical and biological environmental risks' was represented in Calls 1 - 4, but accounted for only a small share in Calls 5 - 7. On the other hand, 'Psychological and behavioural' received no funding in Calls 1-4, a very small share in Call 5, and substantial shares in Calls 6 and 7 (34.6% and 21.4%, respectively).

---

HRCS research classification codes (i.e. second level of research classification group)
Figure 25 Share of HRCS research classification, per call

In parentheses: number of awards; Source of data: MRC grants database. HRCS research classification codes

- **Project team expertise**

The expertise involved in each project as reported by the PI is illustrated in Figure 26. As can be expected, experts in clinical trial methodology (18 of 20), data management (18 of 20), clinical trial management (19 of 20), and statistics (all trials) were involved in nearly all active full trials. Experts in clinical trial methodology and data management were also involved in most of the development awards (17 of 20). 75% of full trials included experts in health economics, and approximately half of the trials experts in social science and in health policy. Social science was the only expertise represented in a larger share of development awards than full trial awards (75% vs 50%), informing preparatory work such as feasibility and acceptability studies and stakeholder consultation. Approximately one third of full trial awards involved experts in health systems and in knowledge brokerage (e.g. for stakeholder engagement and network building), but less than 20% of development awards did so.
5.2 Stakeholder engagement

Stakeholders are an important factor in the success of a project. By communicating and consulting with stakeholders, researchers can:

- tailor the study to fully address local conditions, needs, and cultural preferences
- generate buy-in to enable the project to progress smoothly and minimise opposition (e.g. participant recruitment)
- raise awareness and understanding of the intervention and its potential for implementation (e.g. among policy makers and healthcare providers)

Engagement can occur in the design and during the implementation of the JGHT-funded activity, and/or through dissemination activities following the funded project. While all trials require approval from the national authorities, e.g. obligatory engagement on trial plan and conduct, a different set of relationships and engagement activities are likely to be required to influence national health policy.

5.2.1 Level of stakeholder engagement

PIs reported they had engaged with a range of stakeholder groups during the design and implementation phases of their projects.

In the design phase, most PIs of active full trials and development awards reported that they had engaged with LMIC health care professionals (71%)\(^{46}\), followed by implementing organisations/NGOs (59%). Fewer PIs pointed to engagement with policy makers from international agencies (32%) and community organisations (29%) (Figure 27). Approximately one quarter of projects included experts in knowledge brokerage, such as stakeholder engagement and network building, which would have supported wider engagement. Stakeholder engagement activity during the project was broadly

\(^{46}\) It should be noted that not all trials involve interventions relevant for health care professionals (e.g. toolkits for violence prevention in schools). In addition, some teams include local clinicians and health care providers who feed directly into the study design (limiting the need for external consultation on study design).
consistent with engagement activity in the design phase, with an additional 5-15% of projects engaging with all stakeholder groups except LMIC healthcare providers.

While engagement with policy makers was reported for 87% of full trials (41 of 47), six PIs of full trials (5 of 25 active, 1 of 22 closed trials) indicated that they had not engaged with policy makers during the design or implementation phases of the study or after the conclusion of the study, and only one of these had engaged with implementing organisations/NGOs. 20% of development award PIs (4 of 20) indicated that they had not engaged with policy makers during the design phase of the project; however; all had done so during the implementation phase.

**Figure 27 Stakeholder engagement by JGHT-funded research projects (n=41)**

All PIs indicated that they had engaged with stakeholders via a direct approach (Figure 28). Other common engagement modes were seminars (54%) and workshops (51%).

**Figure 28 Method of stakeholder engagement (n=37)**

The review team did not receive information on stakeholder engagement of the remaining 16 full trials, predominantly because PIs did not respond to the request for information or because PIs held more than one award (with interviews focussing on the earlier trial). In one case, the shortened interview did not cover this topic.

* It is possible that due to prior work, (some of) these teams are already embedded within the relevant policy arena, or have included policy makers within the study team; this information is not conveyed in the survey responses.
In interviews, PIs provided further detail on stakeholder engagement activity, the rationale for engagement, and engagement modes employed.\(^9\)

### 5.2.2 Engagement with policy stakeholders

Of 28 PIs interviewed, eight PIs reported engagement with international policy organisations, foremost WHO (global offices in Geneva and country offices), with two PIs directly involved as members of WHO guideline committees. Two PIs explained that many countries base their national programmes on WHO recommendations, which warrants that “first, in terms of policy impact we need to [target] the international level. That can then trickle down to local national level”. A smaller number of PIs talked about engagement with the implementation funders, such as The Global Fund, UNICEF, BMGF, and The President’s Malaria Initiative. For example, one trial included representatives from The Global Fund and The President’s Malaria Initiative on the trial steering committee (see Case study 7).

Nearly two thirds of PIs (61%, 17 of 28) stated that they had engaged with government in countries where trial sites were located - predominantly national ministries of health, but also provincial/county government offices. Several PIs had embedded their trials within national public health programmes, e.g. mass drug administration campaigns (see Case study 9) and national malaria control programmes (see Case study 7); others kept relevant policy makers informed in regular targeted meetings (see case Davey) or by setting up dedicated policy liaison groups (see Case study 11 and Case study 13). One PI created an international advisory group headed by a high-profile individual, as well as national advisory committees in each country, with the aim of enabling scale up across countries after the conclusion of the trial. In five cases, PIs or study team members were members of government committees or government employees. One PI explained that the study team had been selected specifically to include collaborators who served on national advisory committees in the trial countries. Where this was not possible, very high-profile senior investigators were approached. PIs from the MRC-LSHTM unit in The Gambia pointed out the institute’s strong relationship with the Ministry of Health, based on a 70-year history of conducting research in the country. This includes frequent exchange with the national health programme managers and regular updates to the Minister for Health.

In general, PIs considered engagement with policy makers important, making national decision makers aware of the research while it was being implemented, rather than ‘surprising’ (and possibly embarrassing) them with the publication of trial findings after the conclusion of the study. However, one PI highlighted that engagement with national public health programmes can also be difficult and potentially counter-productive: Local officers can “sometimes be incredibly conservative, and instead of facilitating your work, they can put blocks in your way”. A co-investigator, commenting on issues encountered during a trial, pointed out that full integration with government health programmes not only paves the way for policy change, but also increases communities’ buy-in: “In hindsight, I would have better engaged with the Ministry of Health, not only to secure their buy-in (which we did secure), but also their active involvement in the trial implementation. This would ensure that the community [the research] as part of government interventions rather than a parallel programme. We would also look at integration with ongoing programmes.”.

Two PIs specifically stated that they had not engaged with policy makers in the design, implementation, or post-trial phases. One of these PI explained that the question the trial addressed would not have been of interest to policy makers, and that the choice to not engage had hence been appropriate. The other PI had not engaged with WHO and national policy institutions during the trial, and did not have the resources to actively engage post-trial. While trial findings were highly supportive of a change in policy (and have been published), policy makers are not aware of the evidence and it has not (yet) been taken up.

---

\(^9\) While an indication of the number of PIs reporting engagement with different stakeholder groups is provided, these represent the minimum (rather than absolute) number. Interview discussions did not always cover all stakeholder groups, focussing in more depth on the groups and engagement modes considered most relevant by the PIs.
Likewise, seven PIs felt there was a need for dedicated funding after the completion of the trial to support dissemination and engagement activities and thus help translate findings into policy change. One PI explained that at the time of the trial, the study team was focusing entirely on “getting the study finished”, with no resources left at the end of the grant. Another PI stated: “I think funders are very unrealistic on the whole about how long dissemination takes and how long it’s going to take to get the results together and get papers out. It’s difficult because the money to do that should come from project funding. But that can be very difficult because you’re under pressure to close the project and terminate the contract.”

Another PI explained that after the trial had completed, she attempted to set up meetings with the regional WHO offices and governments of neighbouring countries to develop a policy statement, which would have increased access and use of the superior treatment (see Case study 1). However, she was unable to identify adequate funding to allow her to engage in these activities, and policy change remains limited to the country in which the trial was conducted.

Key opinion leaders broadly agreed that engagement with policy stakeholders is crucial to achieve impact. As one interviewee explained: “We have to pay much more attention to the political and policy interface. If we do RCTs and pragmatic trials but we don’t bring policy makers with us, we waste a lot of money on interventions that never go to scale because we never spoke to the government or policy makers about these things. [...] It all depends on how good you are at bringing policy makers along. And if you do that the sky is the limit.”.

5.2.3 Engagement with LMIC healthcare providers
Several PIs (6 of 28) specifically mentioned engagement with LMIC healthcare professionals (e.g. see Case study 1). One project organised workshops to develop the intervention involving district health management teams, clinicians, community health workers, and technology partners as part of the JGHT-funded trial; another engaged healthcare providers through Theory of Change workshops. Two PIs engaged with professional bodies in country to secure support.

5.2.4 Community and participant/patient engagement
Engagement with communities and participants aims to generate buy-in and minimise opposition, thus facilitating participant recruitment, and enables researchers to tailor studies to fully address local conditions, needs, and preferences. Supporting this intention, a study on the effect of community sensitisation meetings conducted as part of a JGHT-funded trial found that individuals who went to these community meetings were more interested in participating than those who were completely unaware of the study.

More than a third of interviewed PIs (39%, 11 of 28) reported that they had engaged with community groups and community advisory boards, community leaders, and individuals such as patients who shared their experiences. Several PIs working with culturally sensitive interventions, or in communities that had not previously been exposed to research activity, described how they had prepared their studies through extensive community engagement. Specific examples of successful engagement included the following:

- At the start of one study, the team conducted extensive consultation with community leaders in the area, to discuss the trial, generate buy-in, and uncover potential issues. To this end, the team organised information events in the region, which were well-attended and gave participants the opportunity to ask question about the disease and how to manage it. Once in the implementation stage, the study hired local community health workers, living within the community, to deliver

---

51 Sensitisation meetings are organised by research staff to make information on the research available in the villages from which potential research participants may be recruited.
intervention in primary health clinics - an important aspect as patients had to self-present to the clinics. Given the trial took place in a complex ethical landscape, the team had tailored the consent process to be very clear and transparent, laying out the aim of the study and the ‘safety net’ in place for the control arm (composed of regular check-ups, facilitated referral in case of complications, free of cost treatment). The trial did not encounter issues with recruitment, and few potential participants opted out.

- Another team conducted a Rapid Ethical Assessment (REA) prior to starting the trial, to "map the ethical terrain" of communities that had not previously been involved in health research (see Case study 5). The team gathered local knowledge, e.g. on how the community operates, what the community understands about research, and their views on trial characteristics. Specific suggestions were incorporated into the preparatory phases of the trial or used during the course of the trial itself to avoid potential issues. For example, in one trial location, misinformation spread by a local individual alarmed patients. Acting on suggestions made during the REA, the trial coordinator and data manager arranged an emergency district meeting to negotiate with gatekeepers and prevent further rumours being spread.

Conversely, the PI of a trial which encountered major issues with recruitment and compliance due to cultural barriers felt that these might have been avoided by community engagement through an acceptability study.

Researchers highlighted the importance of joint units in building sustained local relationships. Through their long-term presence, these units established field sites and engagement structures which researchers are able to draw on. As one PI explained: “The value of long-term investment in overseas sites, e.g. by Wellcome Trust and the MRC, was priceless in this context. At the village level, there was an awareness of [the research process], such as the concept of randomisation and why and how data might be collected e.g. by electronic data capture or by devices. These established field sites are very important for quality.”. Another PI compared the relative ease of community engagement for a JGHT-funded trial in a location near a joint unit (with well-established engagement processes), with the challenging situation the study team had encountered when preparing for implementation in a region without these advantages.

One PI outlined the benefits arising from community engagement for the JGHT-funded trial and beyond: “Engagement with service users and carers drove the co-development of the project through a participatory approach, giving those affected the opportunity to have a voice and choice in the development of interventions in their country. In addition to supporting the trial itself, wider engagement with the general public and health professionals has also been a crucial means of tackling stigma and strengthening the research infrastructure within [the LMIC]”.

5.3 Challenges to trial implementation

5.3.1 Overview of challenges to trial implementation

Overall, the main challenges during trial implementation were prolonged and complex administrative processes, particularly in relation to regulatory and ethical approval, difficulties with trial recruitment, and local capacity issues, all of which caused delays and at times required additional budget (Figure 29). PIs of 65% of full trial awards (31 of 48) and 60% of development awards (12 of 20) reported issues with administrative processes and requirements at the trial site(s), including approval processes (35% of full trial PIs, 17; 25% of development award PIs, 5) and contracts/financial transfers (15% of full trial PIs, 7). Both types of awards reported issues with hiring and retaining staff with the required skills at trial sites (35% of full trials, 17; 45% of development awards, 9), whereas recruitment was a challenge for a

larger share of full trial PIs (48%, 23). Civil unrest, such as tribal wars and government coups, and worker strikes had caused challenges for seven full trial awards and 3 development awards (15% each).

In line with the effect of these challenges, nearly half of co-investigators who in hindsight would make changes to the project design pointed to changes to the study timeline (42%, 26 of 62), with many highlighting the challenges and unpredictability of working in an LMIC environment, and the need to allow more time for recruitment of participants.

5.3.2 Complex approval processes and administrative requirements

Several PIs of full trial awards commented that the time required for approval processes and contractual arrangements has increased in recent years. Countries in Eastern and Southern Africa have changed their requirements, leading to prolonged and at times multi-stage applications. One PI reported that approvals can take over 200 days at some sites; others explained that the process of obtaining all required ethical and regulatory approvals can involve three or four separate applications and committees in each country, each with varying capacity, requests, and demands. As one PI commented by survey: “There are so many unexpected extra layers of ‘bureaucracy’ that cannot be anticipated. It takes time to navigate through these things. I could fill a book with the number of unexpected administrative things that come up in projects like this.”.

Two PIs also pointed to delays in obtaining approvals from their UK institutions which were not experienced in dealing with research conducted at sites in LMICs, and two PIs from LMICs highlighted the challenge of knowing how to obtain approval from a UK institution for LMIC-led trials. One PI suggested the funders could help overcome this barrier by providing support, or a centralised process, for UK trial sponsorship. To cope with delays caused by slow approval processes, a few PIs mentioned that they had applied for no-cost extensions (and highlighted the importance of this flexibility in the funding programme). One PIs explained that having a local study team member engage directly with key decision makers had helped to progress the process.

Two PIs partnered with NGOs already set up in-country to handle financial transactions and administration. For example, one PI partnered with an NGO already established in the country and active in the (remote) area where the trial was to be implemented. The NGO was able to oversee all financial transfers, which would have been very difficult and time-consuming to manage directly...
between the UK and the local research institutions. In addition, the NGO supported trial logistics in terms of consumables transport and assisted in hiring of local staff. While comprise had to be found between the NGO’s strict operating processes and the unpredictability of timing in research projects, the PI summarised the partnership with: “It was a real really helpful step. It was easier to go through them, financially and with contracts that needed to be put in place – much easier.” In return, the NGO benefitted from the recognition and the experience of assisting with a research trial.

A few researchers mentioned that insurance can be difficult and costly to obtain, due to change in local requirements or because of a lack of precedence. To mitigate against this problem, one co-investigator suggested the funders arrange for global insurance for all its trials through a central company, securing better rates in this way.

5.3.3 Participant recruitment
Half of full trials (23) reported that recruitment had been slower or more difficult than expected. Where reasons were provided, these mainly related to a lower disease incidence than expected. This was the case especially in trials addressing malaria in low transmission settings, where year-on-year variation and enhanced roll out of transmission control or treatment can reduce the number of infected patients ahead of the trial. In other cases, recruitment was slow due to social stigma attached to the intervention (3), because healthcare staff found it difficult to change routine care to accommodate the intervention (1), or due to individuals opposing the trial in the community (2). PIs were able to address these issues by increasing the number of trial sites (8), scaling down the trial (2), moving sites/shifting recruitment targets between sites (3), or moving to a continuous enrolment model (2). In one case, investigators from different LMICs shared their approaches to recruitment, resulting in an uplift in recruitment at ‘slower’ sites (see Case study 2).

Several PIs (5) working with culturally sensitive interventions, or in communities that had not previously been exposed to research activity, highlighted that they had prepared their studies through extensive community and stakeholder engagement (see section 5.2.4). These tended to report fewer issues with recruitment. One study reported that recruitment for a trial addressing a severely stigmatised condition was initially challenging, but was ultimately achieved by further increasing community engagement, involvement of stakeholders including service users and carers, and awareness raising activities. Conversely, the PI of a trial with major recruitment and compliance issues throughout the study felt that these might have been avoided by community engagement to better understand cultural barriers ahead of trial implementation.

5.3.4 Capacity shortages
Issues with staff at trial sites included both high turnover and a shortage of staff with the required expertise. While a degree of training is expected as part of any trial, PIs commented that high turnover of clinical and field staff at trial sites required frequent re-training (10). Reported capacity shortages at LMIC sites included trial coordinators, social scientists, health economists, and data managers. Especially projects involving new trial centres, with no or little prior experience of implementing RCTs, had to provide substantive training.

A number of PIs provided examples of how they overcame challenges. For example, one project was delayed due to the high turnover of trial staff and the need to retrain new staff members. The project team therefore developed an online training module to facilitate a quicker orientation and training process. In two other projects where staff with the required level of skills was not available, the PIs recruited less qualified individuals with the ‘right’ characteristics (e.g. motivated, committed, smart) and provided ongoing training and mentoring to help them to gain additional skills.

Two PIs specifically called out the important role of UK-supported research units in LMICs (“joint units”) in providing capacity. As one PI explained: “Without [this unit], we would never have been able to conduct the trial, because we do not have this clinical trial unit support in this country. The unit has experts in clinical trial design, in data management, it has clinical trial monitoring teams, clinical research managers...all of these people. It’s like the whole machinery has already been built in the country, and we were now in a position to work with local institutions to deliver the trial. I think that
without such a unit, it would be very tough for an LMIC to deliver on their own because they lack the clinical trial capacity.”

5.3.5 Other challenges
Other challenges facing JGHT-funded projects included:
- Unstable political environment, such as tribal warfare, coups, and workers strikes (10)
- Roll out of national interventions interfering with the trial (2)
- Currency fluctuations (decrease in the value of the GBP), leading to budgetary challenges (2)
- High turnover of government staff, making it difficult to interface with local public health officers and public health interventions (1)
- Challenges relating to suppliers and manufacturers of intervention (4). In two cases, this led to delays in access; in one case, the product was no longer produced and the trial had to make major adjustments.

5.4 Outputs

5.4.1 Completed full trials and main trial finding publications
Main trial findings, i.e. those that relate to the trial’s primary research question, have been published for 24 full trial awards (20 of 28 closed full trial awards; 71.4%) and 4 open full trial awards. One trial followed a 2x2x2 factorial design and has published three papers describing the findings for each of the three interventions tested (see Case study 3), bringing the total number of publications of main trial findings to 26.

Of the eight closed full trials that have not published the main results, three have submitted papers for publication, two are in the final analysis stage, and one trial did not take place due to unforeseeable external circumstances. There is no information on the status or intent to published for remaining two trials.

The majority of findings were published in 2018 and 2019 (7 and 8 publications, respectively) (Figure 30), with six papers appearing between June and October 2019. The short timeframe since publication can be expected to affect the level of outcomes and impacts achieved.

Figure 30 Number of main trial findings published in scientific journals, by year

![Figure 30](image)

Source of data: Desk research - 26 main trial findings publications, stemming from 24 full trial awards (20 closed, 4 active)

5.4.2 Definitive answer to the research question
An analysis of results based on the main trial publication indicates that 12 trials confirmed the trial hypothesis (including two Phase II trials), and 8 trials disproved the hypothesis. The trial testing three interventions confirmed the trial hypothesis for one and disproved it for the other two. The remaining trials were:
• A trial which was stopped as the intervention was found to cause harm to participants (see Case study 2)
• A full trial comparing two interventions (rather than stating a specific hypothesis), and found a significant difference between the two (see Case study 1)
• A feasibility study, funded in Call 1, which led to a full trial award in Call 5 (see Case study 10)

A number of PIs increased the sample size during the implementation of the trial (5), and one of the PIs interviewed reported that in hindsight, they would increase the participant size to increase the power of the trial. For one of the trials which reported a significant difference in primary outcome, one co-investigator nevertheless stated that it was ‘underpowered’.

5.4.3 Trial methodologies
The JGHT has an interest in advancing trial methodologies, and call specifications starting with Call 7 encourage applications trial designs.

Methodologies employed in full trials funded in calls 1-7 were mostly standard two-arm blinded or non-blinded individually randomised or cluster randomised controlled trials. Four trials included four arms, and two trials included three arms. Four trials employed factorial designs (one each of 2x2x2, 2x2, 3x2 and factorial design). While these are not novel, PIs explained that they were not often used in LMIC settings. Two development awards employed stepped-wedge study designs. One trial followed a novel trial methodology, using a multi-arm multi-stage (MAMS) framework (see Case study 14).

5.4.4 Publication of findings
Research projects reported on a variety of study findings in addition to results related to the primary research question (main trial findings). These include the trial protocol developed, social and economic studies, validation of assays and diagnostic tests, and epidemiological studies and surveys. In addition, PIs and co-investigators may publish literature reviews and opinion pieces, as well as conference abstracts and book chapters.

71.4% of closed full trial awards (20 of 28) and 4 open full trial awards have published the main findings of the trials, publications for a further three trials are under review, and one trial is in the final stages of analysis. For development awards, 45.5% of PIs of closed awards (5 of 11) reported that they had published findings; publications of a further four PIs were under review. The remaining two PIs indicated that the project was still ongoing. In addition, one of the nine active awards had published results, and another active award had a publication under review.

The ResearchFish® database contains self-reported outputs and outcomes data on most of the JGHT awards (84 of 96). 70% of award holders (59 of 84) reported 772 publications related to their JGHT-funded research, while 25 awards (including all active development awards) did not report any publication. Notably, 338 of these publications were reported for one award. While this is a very long-running award, it represents an outlier compared to the rest of the data. Hence, we excluded this award to avoid skewing the analysis of remaining data.

After excluding the outlier from the analysis, 434 publications were reported for 58 awards, coming to a mean of 7.5 publications per award (see Figure 31). Of these, the vast majority (94%) are journal articles. As would be expected, the smaller development awards that are funded for a shorter period produce fewer publications on average (mean of 4.1/award) than the full trial awards (mean of 8.6 and 9.1 for active and closed awards respectively). For detailed analysis of publications reported in ResearchFish®, see Appendix C.
Table 12 shows journals (12) in which JGHT awardees most frequently published their research findings (according to ResearchFish®), as well as all journals in which main trial findings of full trial awards have been published. Of these, nine are open access journals; the remaining offer immediate open access to specific articles on the payment of a fee (hybrid open access) and/or to all articles after 6 months (delayed open access).

<table>
<thead>
<tr>
<th>Journal</th>
<th>Open Access?</th>
<th>All publications* (number)</th>
<th>Main trial findings** (number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLoS One</td>
<td>Yes</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>The Lancet</td>
<td>Hybrid/Delayed</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>Trials</td>
<td>Yes</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Clinical Infectious Diseases</td>
<td>Hybrid</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>BMJ Open</td>
<td>Yes</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>The Lancet Global Health</td>
<td>Yes</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Wellcome Open Research</td>
<td>Yes</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>The Lancet Infectious Diseases</td>
<td>Hybrid/Delayed</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>BMC Public Health</td>
<td>Yes</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>International Journal of Tuberculosis and Lung Disease</td>
<td>Hybrid/Delayed</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Malaria Journal</td>
<td>Yes</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>The New England Journal of Medicine</td>
<td>Delayed</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>The Lancet HIV</td>
<td>Hybrid/Delayed</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>PLoS Medicine</td>
<td>Yes</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>EBio Med</td>
<td>Yes</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Source of data: *ResearchFish®; **Desk research
5.4.5  Development awards leading to full trial funding

The aim of the development award scheme is to develop trial application ideas into robust and competitive proposals by conducting feasibility studies and obtaining preliminary data. Following on from a development award, one investigator was awarded a full trial (see Case study 13). A smaller award in Call 1 funded a feasibility study which led to a full trial award in Call 5 (see Case study 10). Six PIs who had led development awards reported that they had obtained funding for further studies, including at least for four full trials, from other funders (see section 5.5.2)\(^{54}\). Hence, of 22 closed development awards funded so far, at least 23% (5) have led to a full trial.

The scheme is also used by PIs who were not successful in securing a full trial award to gather additional data - two full trial proposals that had been rejected at the second stage of the application process went on to successfully apply for a JGHT development award; a third was successful in Call 9.\(^{55}\)

An increase in applications from development award holders (and potentially successes) can be expected in the future: Of the development award PIs consulted who had not yet secured further funding, 40% (6 of 15) indicated that the study had been successful and that they were in the process of applying for a full trial award. At the same time, the scheme is also serving to avoid failure of expensive full trials: Three PIs indicated that the development award had demonstrated that the plans for the full trial needed to be significantly changed, and that further preliminary data needed to be collected.

5.4.6  New collaborations

PIs from active full trial awards and development awards reported working with new partners during their JGHT funded project (86%, 18 of 21 of full trials; 75%, 15 of 20 of development awards). Most projects had started to collaborate with partners located in LMICs (77%, 16 full trial awards; 65%, 13 development awards) (Figure 32). Half of the PIs of closed trials (11 of 22) reported that their project had involved new HIC-LMIC or LMIC-LMIC partnerships.

Figure 32 New collaborations

Full trial awards (n=21)  Development awards (n=20)

- No, I had already worked with this project team
- Yes, new partners from institutions in HICs
- Yes, new partners from institutions in LMICs
- Yes, new partners from institutions in HICs and LMICs

The majority of PIs of active full trial and development awards indicated that they either have plans to collaborate in future (38%, 8 of 21; 15%, 3 of 20, respectively) or do not have currently plans but would be open to future collaborations (62%, 13; 75%, 15, respectively). Most full trial PIs wanted to engage in

\(^{54}\) As information on rejected full trial outlines (stage 1) was not available, the MRC database data does not contain information on the overall number of full award outlines submitted following a development award.

\(^{55}\) As information on rejected full trial outlines (stage 1) was not available, the MRC database data does not contain information on the overall number of rejected full trial proposals at outline stage that then went on to apply for a development award.
'regular information exchange and advice' (71%, 15) and half intended to work on joint proposals (52%, 11). The largest share of development award PIs planned to develop a joint proposal (45%, 9).

Half of co-investigators consulted thought that the JGHT project they were involved in had given them contacts for future work (53%, 92 of 172) and reported that collaborations started through a JGHT project were ongoing, beyond the JGHT-funded research (50%, 86 of 172) (see section 5.5.2).

5.4.7 Enhanced knowledge and skills in the UK and/or LMIC

Investigators are likely to gain knowledge and experience through participating in the design and implementation of a study.

70% (120 of 172) of co-investigators from both LMICs and HICs reported that they had either been involved in all aspects of the design of the project, or had made substantial contributions to some aspects of the study. This share was similar for co-investigators from LMICs and HICs (Figure 33). Nearly three quarters of PIs of UK-led active full trials or of development awards (73%, 16 of 22) also indicated that LMIC researchers had been engaged throughout the project, including project design and implementation.

As reported in section 5.1.9, an analysis of author affiliation of publications of 22 full trial awards showed that investigators from a total of 106 institutes were named as co-authors. Over half of these institutions were located in LMICs (53.8%, 57). While this does not suggest the level to which LMIC researchers were involved in trial design and data analysis, it indicates that the contribution of investigators in LMICs is being recognised. 31% of first authors of these publications (8 of 26) were affiliated with joint units, and 27% (7) with LMIC institutions and HIC institutions, each. Two first authors held dual appointments at institutions in HICs and LMICs, and one was a researcher from an LMIC sponsored to complete a PhD at a UK institution to implement the JGHT-funded trial.

Figure 33 Breakdown of involvement by co-investigator institute (LMIC n = 68, JU n = 25, HIC n = 76)

The majority of co-investigators indicated that the JGHT-funded project had positively impacted their scientific knowledge (82%, 140 of 170). In particular, the research had provided co-investigators in LMICs and HICs with scientific knowledge that they were able to use for their further work (71%, 121 of 170) and on the basis of which they were able to secure additional funding (28%, 48) (Figure 34). A number of PIs reported that LMIC researchers and clinicians were promoted or offered opportunities for career advancement as a result of the experience gained by participating in the JGHT study (11).
Knowledge of the context in which the research was carried out was also enhanced, particularly knowledge of local health needs (reported by 49% of all co-investigators (83 of 169); 60% of LMIC and 45% of HIC investigators) and knowledge related to the local health system (40% of LMIC and HIC investigators).

**Figure 34 Knowledge impacts of JGHT-funded research (co-investigators)**

Source of data: Survey of co-investigators. The number of respondents for each question was: Scientific knowledge LMIC n = 65, JU n = 25, HIC n = 75; context knowledge LMIC n = 66, JU n = 24, HIC n = 74.

39% of co-investigators reported that the JGHT-funded research had influenced the work of others in their organisation (66 of 168). This view was more common among co-investigators from LMICs (55%, 36 of 66) (Figure 35). Other benefits included increased knowledge of LMIC researchers beyond the study team (42%, 67), new contacts made by the institute (33%, 56) and securing of further funding by the organisation (26%, 43). Across all categories (except LMIC researcher skills), a larger share of LMIC investigators reported impacts (and a smaller share of LMIC investigators reported ‘no impact’).

For example, an investigator based in an LMIC reported that “the information gathered and the wealth of experience has made [our] organisation attractive for other research donors and partners and has strengthened the relation with the Ministry of Education and Health”. Another respondent explained that “our research organisation is now recognised at the national level for high quality research that informs policy on maternal and child health programmes in the country”. As a result of a partnership developed through the JGHT-funded research, one investigator reported that a grant application was underway to formally link clinical trial units at an LMIC and a UK institution; another organisation had established a partnership with two of [the country’s] leading medical schools and the local government department of health.
Figure 35 Impact of JGHT-funded project on co-investigator institute

Of closed full trial PIs who discussed skills and knowledge acquired, 65% highlighted that the research had enhanced trial capacity at the trial site(s) (13 of 20), including through training in trial methodology and data management. Five PIs mentioned training of laboratory technicians as part of their trials, and another five emphasised the trial’s extensive training of field workers in the delivery of the intervention and data collection, including via electronic capture. A few PIs pointed out that at many hospital trial sites, doctors and nurses are trained to establish a suitable standard of care in the control arm, and to allow implementation of the intervention to be tested.

Three PIs highlighted that the JGHT-funded research enabled trial sites to build up expertise and networks they can draw on for further research. For example, a trial investigating the effect of cleaner cookstoves on pneumonia in children was able to develop expertise on chronic lung disease at the trial site, which has since been used in other studies. Other trials led to expertise in, and platforms for, studies involving infants and studies on maternal vaccination.

5.4.8 Enhanced research tools and infrastructure

Consulted by survey, 29% of PIs of full trials (6 of 21) and 30% of PIs from development awards (6 of 20) reported that new tools had been developed. Examples included tools such as treatment manuals, consent tools, and tools to assist data collection and patient enrolment.

PIs of closed full trials described a number of tools developed for use in the trial itself which have been used for further research. One trial developed a barcoding system for drug packaging to reduce the risk that the intervention and placebo is interchanged between participants, another developed a survey tool and platform which is now being used by the local health officials, a third improved the design of a

---

56 Novel at the time of the trial, has now been superseded by more advanced approaches
fly trap used for research. There were a few examples of sample collections (e.g. blood and stool samples) which are being used for follow-on research.

More than a third of co-investigators based at LMIC institutions reported by survey that the JGHT award had allowed their institution to establish new infrastructure (38%; 25 of 66) (Figure 35). This share was much higher than for institutions in HICs (8%, 5 of 75) and joint units (7%, 2 of 25) (as can be expected, since by definition, JGHT research is carried out in LMICs). In interviews, PIs provided examples of infrastructure established, including diagnostic equipment and laboratories and research platforms (e.g. processes and systems).

In ResearchFish®, PIs of 44 awards indicated that they had developed at least one new research tool, research method, database or software, with 149 new tools reported (see Appendix C). These included databases/data collections, improvements to research infrastructure and new physiological assessment or outcome measures for trials (Figure 36).

![Figure 36 Type of tools developed by type of award](source)

Examples of databases/data collections reported in ResearchFish® mainly relate to databases of data collected in the JGHT studies. Other examples include a database of SMSs appropriate for pregnant teenage girls, a database of treatment reported for community-based deworming and datasets containing costing or household records. Research infrastructure developed in JGHT awards includes electronic medical record systems, data forms and questionnaires, and establishment of new trial sites. New physiological assessment or outcome measures include a household ventilation assessment method for nurses, a quality of life questionnaire for people affected by TB living in shantytowns and an adapted Internalized Stigma of Mental Illness Scale (ISMIS) to measure TB self-stigma.

Only about a quarter of the new tools, databases and software were available to others outside the research team. While the impact of the tools was largely unknown, some types of impact cited include improvement in skills and knowledge, enabling of research through use of research tools and methods by others outside the research team, and better and more accurate data collection and management through the use of databases.
5.4.9 New collaborations between researchers and implementation stakeholders

45% of active full trial PIs (9 of 20) and 35% development award PIs (7 of 20) reported that they had worked with new policy and implementation partners as part of the JGHT-funded research (Figure 37). The main examples of organisations PIs had started to engage with were WHO, LMIC ministries of health (or equivalent), and NGOs. Most PIs reported either an ongoing partnership with the policy makers and implementation partnerships developed under the JGHT award (50% of full trial PIs; 40% of development award PIs) or the intention to partner again in the future (25% and 30%, respectively). A smaller number reported that they do not envision a future partnership (20% and 15%, respectively). A detailed analysis of stakeholder engagement activity as part of JGHT-funded research is provided in section 5.2.

Figure 37 Policy/implementation partnerships

Source of data: Survey of PIs of full trial awards (active) and development awards

5.4.10 Stakeholder awareness and buy-in

Key decision makers, such as international or national policy organisations, need to be aware of the findings of JGHT-funded trials and understand the implications of the research in order to inform policy decisions and, if suitable, effect policy change.

The majority of PIs of closed, implemented full trials indicated that key decision makers at national level (generally, Ministries of Health), or international level (WHO) were aware of the project and its findings (where available) (75%, 20 of 27). This was a result of stakeholder engagement during the trial (see section 5.2), as well as continued efforts, such as presentations and targeted discussions, following the closing of the award. Only one PI thought that key decision makers were unaware of the trial’s findings. (It should be noted that these findings are limited in strength as they are based solely on the perceptions of PIs, rather than on the views of relevant key decision makers.)

5.4.11 Health benefits to study participants

Health research can have direct as well as indirect benefit on the health of study participants. PIs of both full trials and development awards indicated that this was often a result of participation itself, irrespective of the intervention tested, providing participants with improved access to (standard) care and medication, enhanced monitoring and diagnostics, receiving information pertaining to the condition of interest, enhanced awareness of the problem in the community, and upskilling of those delivering an intervention.

Findings of a further two trials are probably known to key decision stakeholders, indicated by the context information provided by the PI in interview, but was not directly confirmed. The situation for 4 trials is unknown.
Two (large) trials alone have led to direct health benefits for around 450,000 individuals. The TUMIKIA trial reduced the prevalence and transmission of helminths in clusters treated at a community-level, rather than through school-based deworming (see Case study 9). With 100,000 households participating in the effective treatment arms, and an average Kenyan household size of four,8 around 400,000 individuals will have benefited from participating in the trial. Another trial investigated the effectiveness of a novel insecticidal net and indoor residual spray interventions (see Case study 7). A total of 45,000 of the novel bed nets were distributed, reducing the prevalence and transmission of malaria, for those using the nets as well as more widely in the villages. Another trial prevented more than 3 deaths for every 100 people starting anti-retroviral therapy, saving the lives of around 30 participants receiving the intervention as part of the trial (see Case study 3).

Most PIs described indirect benefits for the broader community, through an improved standard of care as a result of training of healthcare providers as part of the JGHT-funded study, due to greater awareness/education about the condition, or as a result of the effectiveness of the intervention. For example, one PI explained that individuals beyond the trial intervention clinics are likely to have benefited because the study had raised awareness of the disease in all of the settings. Another highlighted that 140 health professionals were trained in a technique relevant to the disease the trial addressed, but that this technique could also be applied assist with other clinical problems. A third explained that a lot of training and engagement was carried out locally to ensure an appropriate standard care, as per WHO and national guidelines, for all study participants – a standard that was not generally reached by the trial hospitals prior to the study. On the other hand, a key opinion leader explained that while trials often enhance the standard of clinical care during the trial, this standard suddenly drops after the trial finishes. Additional support would therefore be required to sustain this benefit.

In the survey, 90% of PIs of active full trials (18 of 20) reported that their research had led to health benefits for study participants, with the remaining 10% indicating that benefits had not arisen yet, but were likely to do so over the course of the project. Similarly, 75% of PIs of development awards indicated that the research had led to health benefits (15 of 20), with a further 15% (3) reporting that benefits were likely to arise over the course of the project. Of the 20 PIs who were asked about health benefits to research participants, only one indicated that there had not been any.

5.5 Scientific outcomes

5.5.1 Further research informed by project findings

Nearly all closed full trials have published, or are preparing publication of their main findings (93%, 25 of 27, with one additional trial ongoing). A simple analysis of citation data shows that eight papers published between 2015 and 2018 have been cited more than 20 times, and two papers more than 70 times, indicating that findings are used by the wider research community59.

Given the short time period since most of the trials reported, a full citation analysis comparing citation rates of JGHT publications with those publications in the same research field is not yet possible. Indications are that citation impact is high, as shown by an analysis of the six highest-cited papers60:

- Adjunctive dexamethasone in HIV-associated cryptococcal meningitis, NEJM 2016: Total of 113 citations, Field-Weighted Citation Impact: 23.5
- A cleaner burning biomass-fuelled cookstove intervention to prevent pneumonia in children under 5 years old in rural Malawi, The Lancet 2017: Total of 83 citations, Field-Weighted Citation Impact: 23.2

58 United Nations Department of Economic and Social Affairs (2017) Household size and composition around the world, Popfacts No. 2017/2
59 Status 16 October 2019.
60 Field-weighted citation impact (FWCI) is a metric that compares a given document to similar documents; a value greater than 1.0 means the document is more cited than expected according to the average over a three-year window. It takes into account the year of publication, document type, and disciplines associated with its source. Date of analysis: 14 Nov 2019
• The Good School Toolkit for reducing physical violence from school staff to primary school students, The Lancet Global Health, 2017: Total of 53 citations, Field-Weighted Citation Impact: 8.3
• Enhanced prophylaxis plus antiretroviral therapy for advanced HIV infection in Africa, NEJM 2017: Total of 49 citations, Field-Weighted Citation Impact: 13.4
• Effectiveness of a long-lasting piperonyl butoxide-treated insecticidal net and indoor residual spray interventions, separately and together, against malaria transmitted by pyrethroid-resistant mosquitoes: a cluster, randomised controlled, two-by-two factorial design trial, The Lancet 2018: Total of 39 citations, Field-Weighted Citation Impact: 24.0
• Rapid urine-based screening for tuberculosis in HIV-positive patients admitted to hospital in Africa (STAMP): a pragmatic, multicentre, parallel-group, double-blind, randomised controlled trial, The Lancet 2018: Total of 34 citations, Field-Weighted Citation Impact: 20.3

The Field-Weighted Citation Impact (FWCI) of these six publications is already far above average, despite the fact that only the first publication listed was published more than three years ago (and has hence accumulated the full number of citations). The FWCI of the other publications can be expected to increase as they accrue further citations before they reach the three-year point.

Around one third of PIs of closed development awards (36%, 4 of 11) reported that their project findings or outputs have been taken up by other researchers, while 45% did not know whether the findings had been used (Figure 38). Of active awards, 38% of PIs of full trials (8 of 20) and 22% PIs of development awards (2 of 9) reported that their project findings or outputs have been taken up by other researchers.

![Figure 38 Uptake of research findings](image)

Source of data: Survey of PIs of full trial awards (active) and development awards; Full active trial: n=20, Development award active: n=9, Development award closed: n=11

5.5.2 Follow-on funding

According to ResearchFish®, 50 of 84 (60%) JGHT awards have received substantial additional funding (grants of more than £10,000). However, it was not possible to reliably distinguish between funding received to supplement the JGHT award (co-funding) and follow-on funding within the data available in all cases. Further funding was mainly in the form of research grants (83% of the total). Full awards reported more additional research grants and fellowships/studentships than development awards (Figure 39). JGHT awards captured a total of around £160m in further funding from other organisations. This corresponds to a mean of £3.2m further funding per JGHT award (n=50).
Table 13 shows the funders who have provided three or more grants to JGHT projects. 39 other organisations provided 1-2 grants. The major funders were MRC, Wellcome Trust and BMGF, in that order. Funders did not award more than two grants for the same JGHT award with the exception of the MRC that awarded three additional grants to two full awards. The Wellcome Trust, EDCTP, NIHR, BMGF and the NIH provided on average larger grants than the other funders.

Table 13 Funders providing further funding to JGHT awards

<table>
<thead>
<tr>
<th>Funder organisations</th>
<th>Number of grants awarded</th>
<th>Number of JGHT awards that received grants</th>
<th>Average amount of grant (x 1000 GBP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Research Council (MRC)</td>
<td>18</td>
<td>14</td>
<td>639</td>
</tr>
<tr>
<td>Wellcome Trust</td>
<td>11</td>
<td>10</td>
<td>4932</td>
</tr>
<tr>
<td>Bill and Melinda Gates Foundation (BMGF)</td>
<td>11</td>
<td>10</td>
<td>2395</td>
</tr>
<tr>
<td>Grand Challenges Canada</td>
<td>6</td>
<td>5</td>
<td>78</td>
</tr>
<tr>
<td>National Institute for Health Research (NIHR)</td>
<td>6</td>
<td>6</td>
<td>3338</td>
</tr>
<tr>
<td>European and Developing Countries Clinical Trials Partnership (EDCTP)</td>
<td>5</td>
<td>4</td>
<td>4176</td>
</tr>
<tr>
<td>National Institutes of Health (NIH)</td>
<td>5</td>
<td>5</td>
<td>1413</td>
</tr>
<tr>
<td>International Development Research Centre</td>
<td>3</td>
<td>2</td>
<td>513</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>65</strong></td>
<td><strong>36</strong></td>
<td><strong>269</strong></td>
</tr>
</tbody>
</table>

Nearly half of the PIs of full trials and development awards (48%, 24 of 50; 45%, 10 of 22, respectively) reported in the survey and interviews that they had secured additional funding for research related to the JGHT award. Approximately a quarter were developing or had submitted proposals (26% and 23%, respectively). As for the ResearchFish data, the main funders reported to support work based on JGHT awards were the MRC, BMGF, EDCTP, Wellcome, and NIHR/DfID.

The nature of follow-on funding secured by JGHT award PIs fell into four broad categories:

1) Funding for a full trial following a development award
2) Funding for a further full trial
3) Funding for other types of studies building on the JGHT award
4) Funding for networks and consortia
1) Funding for a full trial following a development award

PIs of seven development awards reported that they had secured further funding. One PI received a full trial award from the JGHT (see Case study 13). At least four of the other six development grants PIs secured funding for a full trial from other funders. For example, the findings of a development award on reducing antibiotic over-prescribing in China informed the design of a larger RCT trial funded by DFID through the Communicable Diseases (COMDIS) Health Services Delivery Research Consortium (see Case study 15). Other follow-on funding was secured from the NIH Research Project Grant Program (USD2,500,000), the EDCTP (€5,977,299), and the Administrative Department of Science, Technology and Innovation (Columbia) (£301,000). (Two of these had originally applied for a JGHT full trial award, but were not successful.)

2) Funding for a further full trial

Following the JGHT project, a number of full trial project teams have been awarded funding to conduct new trials that build upon the work of the JGHT project. This includes six full trial PIs who secured a second (or third) JGHT full trial award. There was one example of a PI being awarded a JGHT development award after the full trial to address a barrier to intervention.

Other examples include:

- The DeWorm3 trial, which is extending the findings generated in the JGHT TUMIKIA trial (see Case study 9). DeWorm3 is funded by the Bill & Melinda Gates Foundation and led by the Natural History Museum London (USD895,068). Funding was also awarded by the EDCTP (€4,899,488) for an additional clinical trial (STOP) that will incorporate the same research team involved in the TUMIKIA trial.
- A trial funded jointly by MRC, DFID and NIHR, taking the same intervention used in the JGHT trial and adapting it for a different population (adolescents instead of adults). The new study will draw on the networks and partnerships developed during the JGHT project.
- The PI of a JGHT-funded trial will be involved in a related trial investigating the effect of the same intervention but targeted to a specific age group. The trial is funded by the BMGF (USD6.5m).

3) Funding for other types of studies building on the JGHT award

PIs reported funding for a range of studies that build on evidence and materials generated during the JGHT project. These studies ranged from smaller funding pots of USD25,000 to larger grants over £1M and varied greatly in nature (Table 14). For example, a development award PI received a small grant from the Arts & Humanities Research Council / MRC to develop qualitative interview tools to explore participants experience of the trial (£41,235). A member of the REALITY trial team received a MRC grant (£813,361) for pathogen testing of blood and faecal samples collected during the trial (see Case study 3). A development grant PI (see Case study 16) is co-investigator on a NIHR grant which provides funding for a stakeholder engagement workshop designed to inform a scale up of the development award.

---

61 In addition, a feasibility study funded before the development scheme was established received a full trial award (see Case study 10).
62 https://gtr.ukri.org/projects?ref=MR%2FR022461%2F1
Table 14 Types and funders of extension studies

<table>
<thead>
<tr>
<th>Study type</th>
<th>Funders</th>
<th>Count of projects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feasibility/additional baseline data, social studies</td>
<td>Wellcome Trust, DFID, Arts &amp; Humanities Research Council (AHRC), UKRI, MRC, NIHR</td>
<td>5</td>
</tr>
<tr>
<td>Community/stakeholder engagement</td>
<td>NIHR, Wellcome Trust</td>
<td>2</td>
</tr>
<tr>
<td>Microbiological studies</td>
<td>NIHR, MRC</td>
<td>2</td>
</tr>
<tr>
<td>Epidemiological studies</td>
<td>Bill &amp; Melinda Gates, MRC</td>
<td>2</td>
</tr>
<tr>
<td>Other - Assessment of case definitions, drug safety</td>
<td>Bill &amp; Melinda Gates, Medicines for Malaria Venture (MMV)</td>
<td>2</td>
</tr>
</tbody>
</table>

Source of data: PI surveys and interviews

4) Funding for networks and consortia

A number of JGHT awards led to funding for research networks and consortia. These were typically large grants to support the development of research collaborations, infrastructure, and largescale stakeholder engagement. The role of JGHT funded projects in securing these grants was less direct than for other types of follow-on funding, but PIs reported that their contribution had been important. In one example, the PI of a full trial reported that networks built during the JGHT project were instrumental in the project team being awarded a £7M grant for the IMPALA project, a research unit on Lung Health and Tuberculosis in Africa under the NIHR Global Health Research Programme. Similarly, JGHT-funded research supported a successful bid by the University of Sussex to establish an NIHR Global Research Unit (for £5.7m, 2017-21) (see Case study 5). A JGHT trial on Severe Acute Malnutrition (SAM) in infants helped to secure funding for the Childhood Acute Illness and Nutrition Network (CHAIN), a global research network funded by the BMGF (USD18.7m).

5.5.3 New /strengthened international research networks

JGHT awards have contributed to the formation of international research networks and helped to secure funding to support these (see section 5.5.2).

Co-investigators also reported an increase is their collaborative partnerships and participation in research networks. Half of the survey respondents, from both LMICs and HICs, indicated that the JGHT project had given them contacts for future work (53%, 92 of 172) and that collaborations formed during the JGHT project had continued after (or outside) the project (50%, 86 of 172) (Figure 40). 30% (52) reported that the JGHT project led them to become active in new research networks; this share is higher among co-investigators from LMICs, at 40% (26 of 66). A high share of LMIC co-investigators also indicated that they had established new collaborations with implementation partners (35%, 23 of 66), compared to 13% of researchers from HICs (10 of 76).
Collaboration and networks impacts of JGHT trial on co-investigators

Referring to the impact on collaborations and networks at the project site, 40% of co-investigators (65 of 161) reported that the JGHT-funded research had built up, or expanded, an international network of researchers, with more researchers in HICs pointing to this effect (50%) (Figure 41). A third of investigators considered that the JGHT award had expanded local researcher networks (34%, 35 of 161).

Enhanced research environment

JGHT research assisted in shaping the environment for health research to facilitate future studies. Both full trial and development award PIs reported that the project had increased the priority of health research within LMIC institutions (50% of full trial PIs, 10 of 20; 30% of development award PIs, 6 of 20), reduced cultural and operational barriers for future health research (45%, 9 of 20; and 30%, 6 of 20, respectively), and convinced decision makers and practitioners of the value of health research (40%, 8 of 20; and 30%, 6 of 20, respectively).

Co-investigators reported a range of effects of the JGHT awards at the research location, i.e. beyond the JGHT-funded study team (Figure 42). Just over one third each thought the research had helped convince practitioners and decision makers of the value of global health trials and health research, and...
increased LMIC researchers’ leadership capabilities (35%, 54 of 161). 28% (45) thought the research had reduced operational barriers to future health research. The share of co-investigators indicating that LMIC institutions’ research governance structures had been improved was twice as high among individuals located in LMICs compared to those in HICs (26%, 17 of 64; vs 13%, 9 of 68). Further explaining the nature of wider impacts, several co-investigators pointed to the building of stronger relationships between researchers and policy makers (12).

Figure 42 Impacts at project site beyond the research questions by institute

Source of data: Survey of co-investigators. Number of respondents: LMIC n = 64, JU n = 25, HIC n = 68

Text: This percentage is likely to be higher, as the survey included co-investigators of studies that started only recently, and who indicated ‘no/not yet’ to answer the question. Some of these projects are likely to lead to impacts as they progress to a later stage.
5.6 Policy and health outcomes

5.6.1 Influence on policy related to health interventions

Eight full trial awards have informed policy and are cited in guidelines or policy documents, with evidence from further three trials incorporated into policies to be soon released.

- Influence on WHO policy

There were ten instances of where JGHT-funded trials influenced WHO policy. Four trials have had a direct influence on WHO guidelines (e.g. see cases Day, Gibb, Rowland), with one other expected to do so in the next weeks. Two trials informed the WHO Essential Medicines list and one has lent confidence to a current WHO recommendation that had experienced concerns over safety (see Case study 3 and Case study 4). A further trial has contributed to a WHO recommendation of a diagnostic test (see Case study 8), and another trial was taken up in a WHO best practice strategy paper (see Case study 6).

WHO guidelines are ‘automatically’ adopted by (many) countries, and do not require a policy scale-up as such. Further research can scale policy impact in terms of the target population; for example, one project team is now working on adapting an intervention developed for primary schools for use in secondary schools (see Case study 6). Further research can also provide evidence to refine the policy recommendation; e.g. one study team is now involved in a further trial to determine the effect of an intervention on a smaller sub-population.

- Influence on national guidelines

Evidence from three trials influenced national guidelines: One trial was taken up into national guidelines in Vietnam, and also cited in a WHO guideline (but did not affect the recommendation) (see Case study 1). Two other trials provided evidence for national strategies, both of which are expected to be published in the coming months (see Case study 5 and Case study 9). All three trials have the potential to scale their policy influence on LMICs, with two PIs actively pursuing this goal. The third PI reported she had no resources (time and budget) to engage policy makers. A researcher involved in a fourth trial reported that it had influenced national strategy. This trial has not yet published the main findings, and no further information is available.

- Other: One trial informed the strategy of WHO and international donors and shifted funding priorities

Factors supporting these trials to achieve policy (‘enablers’) impact fell into four categories:

1) The topic of trial is currently under debate in the policy arena, and key policy makers have strong interest in the research evidence (6 trials)

2) Little researched health area, hence little evidence available on the indication addressed by the trial (e.g. talaromycosis, podoconiosis, cryptococcal meningitis), including a lack of an established standard of care. JGHT studies substantially increase the level of robust evidence on which to base policy decisions (3 trials)

3) Collaboration with policy makers and key stakeholders in the local health system during planning and implementation of the research (3 trials). This includes embedding the trial within local health programmes (see Case study 9)

---

64 Release of one policy expected soon; the policy guidelines on the use of azithromycin as a child survival strategy have not yet been published but review of a late draft suggests that the results of the trial will have had a major influence on the final WHO policy recommendation (personal communication, Prof Brian Greenwood, 21 Oct 2019)

65 "A WHO guideline is any document developed by WHO containing recommendations for clinical practice or public health policy. A recommendation tells the intended end-user of the guideline what he or she can or should do in specific situations to achieve the best health outcomes possible, individually or collectively. It offers a choice among different interventions or measures having an anticipated positive impact on health and implications for the use of resources." WHO Handbook for Guideline Development (2012)

66 Two of these policies are expected to be published in the next months.
4) Active engagement with policy makers to inform and influence relevant policies. This is facilitated by researchers holding advisory functions, e.g. as members of WHO guideline or national strategy committees, or key policy makers holding advisory functions related to the research project, e.g. as members of the trial committee (2 trials).

All trials that influenced policy were underpinned by at least two of these enablers. (Further details on enablers and barriers is provided in Table 15 and accompanying description).

There was no clear difference in the ability to influence policy whether a trial was conducted in one country or more. Two trials addressing issues of people living with HIV involved four or more countries (one of which in Africa and Asia), two trials were conducted in two countries, and six trials in one country. The topics of the latter ranged from diseases with limited geographic distribution, such as talaromycosis and podoconiosis, to violence prevention in schools and clean stoves to reduce childhood pneumonia, to helminth transmission and novel insecticidal malaria nets.

Factors enabling policy scale up were continued engagement of the PI or co-investigators, both in the policy (see Case study 5) and research (see Case study 9) arena.

Barriers to policy scale up were a lack of resources, preventing the PI from actively engaging with policy makers in neighbouring countries (see Case study 1), and the need for further research evidence form multiple countries/contexts and over longer periods of time (see Case study 9).

5.6.2 Implementation of effective health interventions

Eight trials have led to some degree of implementation of health interventions. These are:

- Novel nets to control malaria transmission are being made available in areas of confirmed insecticide resistance across Africa. The Global Fund has placed purchases, e.g. in January 2019 for Burkina Faso, with a transaction value of USD 4.2m. The full extent to which countries have implemented the nets is not known. (see Case study 7)
- In Ethiopia, an estimated 100,000 podoconiosis patients have been trained to self-treat with this a simple, inexpensive care package that reduces the frequency and duration of severe symptoms of podoconiosis. The training was predominantly financed and delivered by an NGO, but also included a financial commitment from the Ethiopian government. In addition, 300 health professionals in Ethiopia as well as neighbouring countries have been trained (see Case study 5).
- In Vietnam, all patients with talaromycosis are now given the superior treatment (amphotericin B), compared to only 30% of patients before the trial. This has cut the death rate in half, saving the lives of around 35 individuals every year (see Case study 1).
- In Kenya, the government’s Breaking Transmission Strategy 2019-2023, which was informed by the JGHT-funded trial, targets soil-transmitted helminths with a new, more effective, package of interventions. The strategy is currently being introduced across three counties, in preparation for national roll-out (see Case study 9).
- The Good Schools Toolkit, an intervention shown to reduce violence in schools, is being used in more than 1000 schools across Uganda, Tanzania, Kenya and Rwanda (see Case study 6).
- A JGHT-funded trial on prevention TB-MDR in children and adolescents developed a paediatric formulation of the drug tested in the trial. This has informed inclusion of the formulation on the WHO Essential Medicines List in February 201867. There is evidence that countries have started to purchase this formulation, e.g. the Global Fund placed purchase orders for Ethiopia, Pakistan, Tajikistan and Tanzania from June 2018 for a total of USD 120,00068.

---

In addition, in some instances, impact was assumed but information to assess the extent of implementation was not available. This was the case where interventions and products tested as part of three JGHT-funded trials were recommended by WHO:

- WHO recommends that the antimicrobials cotrimoxazole and isoniazid are taken as part of preventative therapy against tuberculosis for people living with HIV. However, access to isoniazid remained poor and few people were receiving this treatment. Underpinned by evidence from the JGHT-funded trial, a co-formulated pill combining was added to the WHO Essential Medicines list. The polypill should enhance access and adherence; however, the current level of distribution and use of the pill is unknown (see Case study 4).

- Evidence from a JGHT-funded trial contributed to the body of evidence that led to WHO to recommend a new version of a TB diagnostic test, given its higher sensitivity than the previous version. The level of use of this new test is not known (see Case study 8).

- Similarly, the extent to which recommended changes in treatment strategy are implemented is difficult to ascertain. For example, based on evidence from a JGHT-funded trial, a WHO recommendation included as an option the provision of a package of antimicrobial drugs when people with HIV and low immunity levels start anti-retroviral treatment. The extent to which this option is being used is unknown.

Evidence from a further three trials also informed decisions to not implement an intervention, or to alleviate concerns about a current recommendation:

- Findings of one trial led to the recommendation to not provide cryptococcal meningitis patients with dexamethasone due to safety issues (see Case study 2)

- The finding that cleaner cook stoves provided to rural households with children did not improve children's lung health steered WHO and donor organisations away from focussing solely on this approach and towards a shift to also tackle other sources of air pollution.

- Another trial provided confidence that the recommended intervention was effective and safe, alleviating concerns about the currently recommended anti-retroviral drug class (see Case study 3).

In addition, two trials have led to implementation of an intervention while research is still ongoing, and one development award also reported changes in practice:

- One trial led to the implementation of an intervention before the conclusion of the trial, i.e. before an assessment of the effectiveness of the intervention. The Jamaican government decided to implement a toolbox to prevent violence in schools, developed as part of the JGHT-funded project and tested in the trial. This decision was based on the strong relationships the research team had cultivated, working with the national ministry and providers. For example, as the trial progressed, the team shared information on the toolbox and how it was being applied as part of the trial in ongoing presentations and discussion with these key stakeholders. The study team also developed a one-day teacher-training programme based on the toolbox and trained technical staff of the Jamaican Ministry of Education to conduct this training. It has since been conducted with all grade 1 teachers in 2016 and all grades 2 and 3 teachers in 2017 – a total of approximately 5200 teachers, reaching up to 120,000 children per year.

- Researchers working on another (active) award have developed expertise in conducting patient cost surveys as part of the trial. Publications on this aspect of the study are referenced in the WHO handbook for conducting TB patient costs surveys, and the study team has helped to roll out such cost surveys in 15 countries (see Case study 12).

---

69 MR/M007553/1 The "Irie Classrooms Toolbox": a cluster randomised trial of a universal violence prevention programme in Jamaican preschools. Professor Baker-Henningham, Bangor University
A development award has also led to adoption of an intervention: The research team adapted the WHO Caregivers Training Skills (CTS) programme to educate and support caregivers of children with developmental disorders to the Ethiopian context. CST is now used in Ethiopia’s state-run child mental health clinics and rolled out to all caregivers who attend these (see Case study 16).

PIs of several trials reported that the research led, or contributed, to impact on health beyond trial participants as a result of the implementation of the trial, rather than as a result of the main trial findings. In most cases, training of healthcare staff led to upskilling and a sustained increase in the quality of care. One example is a JGHT-funded trial that, based on the experiences with trial participants, led to the development of resources to help patients with brain infections settle back into their communities and cope with disability after being discharged from hospital. The project, which concluded recently, has modified a major local hospital’s approach to discharge planning, and is now being rolled out by a local NGO (see Case study 2). Meetings with policy stakeholders, started through development award and continued through the following full trial, evolved into a regional forum on NCD (Policy Forum on Hypertension and Cardiometabolic Diseases-Impact on Health Systems in Sri Lanka, Bangladesh, Pakistan, and Regional Countries) where government officials present their countries’ strategies and plans to tackle the burden of NCD. This legacy of the development trial enables governments to learn from each other and supports alignment of actions between countries (see Case study 13).

In summary, enablers of implementation for interventions tested in JGHT trials included:

- Donors covering the cost of interventions recommended by WHO (see Case study 1, Case study 3, Case study 7). PIs of trials that influenced WHO policy did not report that they continued to be involved in promoting implementation of the intervention.
- Involvement of an investigator with an implementing NGO (see Case study 5)
- Embedding of research within the local health programme (see Case study 9)

Barriers to implementation included:

- Lack of funds to cover the cost of interventions, where donors do not take these on. In one case, a change in ODA status of the country concerned (Vietnam) endangered availability of the intervention in the future, as PEPFAR would be withdrawing its support over the next years (see Case study 1).
- The need for further evidence to expand the implementation area (scale-up) (see Case study 9). This was being addressed through additional research, funded by BMGF.

5.6.3 Improved cost-effectiveness of healthcare

The cost-effectiveness of interventions was examined as part of four trials that have published their main findings and have reported policy influence.

For one trial, a preliminary analysis published as part of the findings publication suggested that the intervention would be cost-effective (see Case study 3). The full cost-effectiveness analysis for this trial, as well as two other trials, is currently being prepared for publication.

The potential for improving health equity and equality were specifically determined as part of a trial investigating interruption of helminth transmission through community-wide de-worming treatment. The study found that the community delivery platform tested in the trial resulted in comparable coverage and effects of the interventions across important demographic and socioeconomic subgroups (i.e. equity) (see Case study 9).
5.6.4 Future potential for impact on policy and implementation

The majority of JGHT-funded trials have not yet concluded or published results (38 of 62), or have only published their main findings very recently (e.g. 8 trials in 2019).

Bearing in mind the enablers and barriers reported by trials with outcomes (as described in sections 5.6.1 and 5.6.2), and drawing on further information from consultation and desk research, the 15 trials that have published their main findings were assessed for their potential for policy influence, implementation and scale up. (It should be noted that this assessment is based on a limited level of information, in particular for trials where researchers had no or very limited input into the review.)

- Seven trials which have published their main findings were considered to have clear potential for policy influence, based on the evidence they provide and/or the continued level of engagement with policy makers by the PI or research team. One trial is very close to being taken up in policy, with a draft national strategy awaiting endorsement from the ministry (see Case study 10). Five trials resulted in findings with potential for take-up, but published their findings recently (in 2019); all for PIs continue to engage with policy makers and disseminate the results. One trial saw only a small level of benefit across the entire participant population, but showed stronger benefits in sub-groups. As the PI continues to be engaged with national policy makers, there is opportunity for these findings to inform policy. Findings of one trial, confirming the trial hypothesis, were published very recently (October 2019).

An eighth trial has potential for impact, but uptake into policy is not currently actively pursued. The trial resulted in findings with clear potential for take up (simpler and lower cost intervention was more effective). However, as policy makers had not been engaged during the research, and there were no resources (time or budget) for engagement after the award closed, the finding may have limited influence on, or is at a minimum delayed in influencing, strategy going forward without further action. (The publication is currently being incorporated into an updated Cochrane review, and may influence practice in this way.)

- Seven trials were considered to have limited potential for policy influence. Three trials encountered barriers as a result of research and policy developments outside the trial (e.g. FDA did not approve drug tested, intervention tested for safety was shown to not be effective). The findings of the remaining five trials did not result in a clear option for policy change; four of these reported no difference in the treatment and control arms.

- Six closed full trial awards have not yet published their main findings, but three of these have submitted the main publications for review, and one is in the final stages of analysis. Depending on the results, all three have potential for influencing policy, as the PIs have engaged policy makers throughout the design and implementation of the trials.

5.6.5 Success of the JGHT full trial award scheme in influencing policy

Taking ‘policy influence’ as a key performance indicator, the following estimate of the ‘success rate’ for the closed full trial awards of the JGHT can be made:

- 32% of JGHT-funded closed full trials (9 of 28) have resulted in success: Eight closed trials have achieved, or are about to achieve, policy influence. In addition, one feasibility study is close to influencing policy and has resulted in a JGHT-funded full trial, and was therefore counted within the group.

- 36% of JGHT-funded closed full trials (10 of 28) have high potential for success: Six closed trials were scored as having a high potential for policy influence. In addition, four closed trials for which the main findings have not yet been published were counted towards this group, as all PIs continue to be engaged with policy makers (with level of influence depending on trial outcome).

The final figure could hence be more than 70% of closed full trials resulting in policy influence.
5.6.6  **Enablers and barriers**

Table 15 summarises the enablers of and barriers to policy influence, implementation, and scale-up that emerged from the JGHT researcher consultation. This list only includes factors encountered by PIs and co-investigators of the JGHT so far. As more trials report their results and reach the point where these can be taken up into policy, implemented, and scaled, it is likely that additional factors emerge.

**Enablers of and barriers to policy influence** fell into two broad categories:

- Utility of the research evidence for policy making: This aspect focusses on how useful the evidence generated is, a function of the nature of the research question investigated, the quality and scale of investigation, and existing evidence within the area of research. Interventions in complex (real world) settings, affected by a large number of environmental, systems and cultural factors, were subject to many outside influences on the trial result, and are hence particularly challenging in this respect. The expected level of utility of evidence can be assessed at the start of the research project; however, challenges during implementation and developments in the research or policy fields can have (unexpected) impacts.

- Policy makers’ knowledge of the research evidence and willingness to act on it: This aspect focusses on policy makers, including their level understanding of the research and the implications of the findings for policy and implementation, their attitude to the research (e.g. lack of buy-in), and their awareness of and interest in addressing the health need the research relates to. Some of these aspects can be assessed prior to the start of the research project, and a stakeholder engagement plan can be formulated on the basis of this assessment (and active engagement may need to precede the research).

Some of the enablers and barriers are linked. For example, if policy makers are not aware of a health problem, and it is hence not considered a high priority, it is likely to limit opportunities and willingness to engage on research and policy. In these cases, efforts to raise awareness could help to pave the way for constructive engagement (see cases Phillips-Howard and Davey). Alternatively, strong research evidence demonstrating that a change in policy would be beneficial and/or save costs could be used as an effective tool to generate awareness and engagement. In this case, there is a need for active (and potentially prolonged) policy engagement after the research has concluded. Latter may be hindered by a lack of resources to provide investigators with the necessary time and budget; alternatively, investigators may not be in a position (or willing) to focus on policy engagement due to competing priorities (such as further research projects).

**Enablers of and barriers to implementation** were related to:

- The cost of implementation, including whether the cost is covered by donor organisations (e.g. a barrier where the research has not (yet) influenced WHO recommendations) or is taken on NGOs. Enablers of impact were active engagement, and even involvement, with ‘implementers’.

- The ability of the health system and structures at the site of implementation to take up a change into practise. This was facilitated by close working with local government and embedding trials within local health programmes and delivery structures.

**Enablers of and barriers to scale-up** were similar to enablers and barriers of policy influence:

- The level of knowledge of policy makers in relation to the research evidence, and awareness of / willingness to address the health issue concerned. This is facilitated by active engagement with relevant policy makers.

- The utility of the data in contexts beyond the trial location. This can be addressed through additional research in other settings.
<table>
<thead>
<tr>
<th>Table 15 Enablers and barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Policy influence</strong></td>
</tr>
</tbody>
</table>
| **Utility of research evidence to policy makers (Nature, quality, and scale of research)** | - Research provides a clear evidence supporting or rejecting a policy change, especially if:  
  - Question the trial addresses is actively debated by policy makers ('hot topic'). Policy makers have strong interest in the result of the trial  
  - Little evidence is available for the indication addressed by the trial. JGHT-funded research substantially increases the level of robust evidence on which to base policy decisions. | - Research results not conclusive, and do not point to a clear course of action for policy  
  - Intervention is not compatible with existing policies, or in conflict with other policy concerns  
  - Need for further research, e.g. implementation pilot (delay) |
| **Knowledge of research & willingness to act (Stakeholder engagement)** | PI and/or co-investigators actively engage with policy makers on research (planning and implementation), e.g.  
  - Extensive consultation in planning stages, and regular updates during implementation  
  - Policy makers are part of research team  
  - Trial embedded within local health programme | Low level of engagement with policy makers on research |
| **Implementation**            |
| **Cost** | Donors cover cost of intervention | Cost of implementation (if not covered by donors) |
| **Ability of system to take up change** | PI and/or co-investigators actively engage with ‘implementers’, e.g. NGOs  
  - Full buy-in of policy makers and practitioners, e.g. as a result of engagement during planning and implementation of trial  
  - Trial intervention was delivered through local health programme | Lack of awareness of policy change/intervention  
  - Issues with intervention in practice (e.g. shortened shelf life) |
| **Scale-up**                  |
| **Knowledge of research & willingness to act (Stakeholder engagement)** | PI and/or co-investigators actively engage with policy makers in other relevant countries/regions to scale up policy influence  
  - PI and/or co-investigators actively engage in activities to raise awareness of the health problem at international level | Lack of resources (time/budget) for international policy engagement |
| **Utility of data in different contexts** | PI and/or co-investigators conduct research to expand geographic range of results or to include additional target populations (e.g. additional age groups) | Need for additional research to demonstrate trial findings also apply in other contexts |

*Timeline: Trial results were published only recently; policy makers have not yet been able to consider and act*

Source: PI interviews and surveys, desk research
The conditions enabling policy and health outcomes is further abstracted in a model presented in Figure 43. The model separates enablers into two categories:

- Enablers driven by utility of data and external conditions, dictating whether research evidence ‘can’ (in principle) be used and implemented
- Enablers driven by human factors (awareness, understanding, and buy-in), dictating whether individuals involved in the process ‘want to’ respond to the change warranted by the research evidence

Awareness, understanding, and buy-in of decision makers is hence a key factor for achieving policy and health outcomes. Engagement with research is likely to enhance these aspects not only with the project at hand but also for future research. Indeed, as discussed in section 0, JGHT-funded studies have helped to raise decision makers’ awareness of and in research evidence: 35% of PIs (14 of 40) and co-investigators (54 of 161) surveyed reported that the trial had convinced decision makers of the value of health (including 38% of co-investigators working at LMIC institutions).

**Figure 43 Model of conditions enabling policy and health outcomes**

<table>
<thead>
<tr>
<th>Policy</th>
<th>Implementation</th>
<th>Scale-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Can use”</td>
<td>“Can implement”</td>
<td>“Can scale up”</td>
</tr>
</tbody>
</table>
| Research evidence:  
- Demonstrates conclusive option for uptake into policy  
- Is not in conflict with existing evidence (low level of evidence available)  
OR  
- Is of sufficient strength to demonstrate superior policy option, over conflicting evidence (scale and scope of research findings)  
- To avoid delay in uptake: Is reported at the right point in the policy cycle | Implementing organisation:  
- Can afford the intervention (cost)  
- Can deliver the intervention within the existing health system or other relevant structure, incl.:  
  - community acceptance  
  - availability of necessary infrastructure  
  - healthcare worker skills training  
  - suitability of product, technology or care delivery mechanism for local conditions  
  - secure conditions, e.g. no war, environmental disasters | Research evidence:  
- Is relevant to and can be applied to other contexts (expanded geographic contexts; other target populations) |

<table>
<thead>
<tr>
<th>Stakeholder knowledge and buy-in</th>
<th>“Want to use”</th>
<th>“Want to implement/adopt”</th>
<th>“Want to scale up”</th>
</tr>
</thead>
</table>
| Policy makers:  
- Are aware of / involved in research and understand options for take up into policy  
- Are aware of the health need the research addresses  
- Have prioritised the policy addressed in research, with structures in place  
- Feel a level of ownership over research and policy option (buy-in) | Implementing organisation:  
- Can overcome potential resistance to change within the system (including from practitioners and target population)  
- Has bought into the policy change; feels a level of ownership | Policy makers and implementing organisations outside the study context:  
- Are aware and interested in intervention  
- Can overcome potential resistance present in other contexts |

© The model includes aspects reported to have directly affected JGHT projects, as well as points raised in general discussion in researcher and key opinion leader interviews.
5.7 Impact on health

As reported in sections 5.6.1 and 5.6.2, some of the JGHT-funded research has influenced policy and led to the use of research findings and implementation of interventions tested. At this point in the programme, health impacts are still limited to relatively modest numbers of beneficiaries, and the impact at the level of LMIC populations is too small to be detectable. However, the short timeframe since publication of trial findings has to be borne in mind: half of the main trial publications were published in 2018 and 2019 (13 of 26), with just under one quarter published in 2019 (6 of 26) (see Appendix F). There is potential for impact reflected in population-level statistics once roll-out of interventions and adoption of policy changes into practice have occurred. For example, roll-out of the Kenyan government’s strategy to break transmission of soil-transmitted helminths, which was informed by a trial co-funded by the JGHT, has potential to impact on the prevalence of infection and associated morbidity at national level and, if scaled up as a result of a current larger trial, in multiple countries (see Case study 9). In Ethiopia, 100,000 patients suffering from podoconiosis have already been trained in how to self-treat with a simple foot care package, shown to be effective in reducing severe symptoms of podoconiosis by a JGHT-funded trial. With an estimated 1.6 million Ethiopians affected by podoconiosis, this already represents 6.3% of the patient population; further roll-out can be expected to further decrease the level of disability and social effects as a result of the disease (see Case study 5).

Other trials have the potential to avert a deterioration of the current situation. For example, while ‘standard’ insecticidal nets have led to a dramatic reduction in the burden of malaria across sub-Saharan Africa, this progress is now threatened by an increase in insecticide resistance. The new generation of nets tested in a JGHT-funded trial in Tanzania may help to stem this risk, and there is evidence that governments have started to purchase these (see Case study 7). The final impact will depend on many additional factors, including effective distribution and appropriate use of nets.

To fully determine the level of impact of health interventions to which the JGHT funding scheme contributed, further assessment at a later point is required. As one key opinion leader explained: “A lot of the trials tend to think that inclusion in guidelines, for example if clinical recommendations changed in the WHO guideline, would have extremely high impact. Yet the reality is, as experts in implementation science and knowledge translation will tell you, that it is going to be another 15-20 years before [the change] even makes it into common practice.”. At that point, however, the level of impact will be determined not only by the research evidence and its influence on policy and its utility for implementation, but also by a complex set of external factors (e.g. changes in the local context, sustained focus of decision makers on health need addressed at and beyond the trial location), and is hence beyond the scope and responsibility of JGHT-funded researchers.

5.8 Progress towards health-related SDGs

At the UN Summit in September 2015, the new Sustainable Development Goals (SDGs) were formally adopted, including goal 3, to: ‘ensure healthy lives and promote well-being for all at all ages’ (see also section 2.1.1). SDGs include a broad range of health-related targets, to be reached by 2030. The WHO Global Health Observatory tracks health-related statistics, organised to monitor progress towards the SDGs, including indicators for the specific health and health-related targets of the SDGs. JGHT-funded research has addressed, or is addressing, a broad range of these indicators (Table 16).

The attainment of SDGs is likely to require a variety of interventions, research and otherwise; and is hence a tall order for any one trial, or small number of trials, to achieve. Key opinion leaders considered the JGHT to contribute to progress towards the SDGs by addressing the wider health goals (but could not point to the scheme having specifically addressed gender equality). At the same time, the contribution can be expected to be limited; as one key opinion leader elaborated: “To achieve impact on SDGs, multifactorial problems would need to be addressed. JGHT trials are focused and their design

---

does not easily accommodate multifactorial problems such as environmental destruction, malnutrition, lack of energy in poor communities.”.

Information from the trial database registrations showed that most studies (78%, 49 of 63) enrolled both male and female participants. Of the 14 studies that enrolled only female participants 50% (7) were related to reproduction/sexual health.

Table 16 SDG health targets and WHO statistics on health-related targets

<table>
<thead>
<tr>
<th>SDG health and health-related targets</th>
<th>WHO Global Observatory statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Maternal mortality</td>
<td>Maternal and reproductive health</td>
</tr>
<tr>
<td>3.2 Newborn and child mortality</td>
<td>Child health</td>
</tr>
<tr>
<td></td>
<td>Child mortality</td>
</tr>
<tr>
<td>3.3 Communicable diseases</td>
<td>HIV/AIDS</td>
</tr>
<tr>
<td></td>
<td>Tuberculosis</td>
</tr>
<tr>
<td></td>
<td>Malaria</td>
</tr>
<tr>
<td></td>
<td>Neglected tropical diseases</td>
</tr>
<tr>
<td></td>
<td>Cholera</td>
</tr>
<tr>
<td></td>
<td>Influenza</td>
</tr>
<tr>
<td></td>
<td>Meningitis</td>
</tr>
<tr>
<td></td>
<td>Other vaccine-preventable communicable diseases</td>
</tr>
<tr>
<td></td>
<td>Sexually transmitted infections</td>
</tr>
<tr>
<td>3.4 Noncommunicable diseases and mental health</td>
<td>Noncommunicable diseases</td>
</tr>
<tr>
<td></td>
<td>Mental health</td>
</tr>
<tr>
<td>3.5 Substance abuse</td>
<td>Alcohol and Health</td>
</tr>
<tr>
<td></td>
<td>Prevention and Treatment of Substance Use Disorders</td>
</tr>
<tr>
<td>3.6 Road traffic injuries</td>
<td>Road safety</td>
</tr>
<tr>
<td>3.7 Sexual and reproductive health</td>
<td>Universal access to reproductive health</td>
</tr>
<tr>
<td>3.8 Universal health coverage</td>
<td>Universal health coverage data portal</td>
</tr>
<tr>
<td>3.9 Mortality from environmental pollution</td>
<td>Public health and environment</td>
</tr>
<tr>
<td></td>
<td>Joint effects of air pollution</td>
</tr>
<tr>
<td>3.a Tobacco control</td>
<td>Tobacco control</td>
</tr>
<tr>
<td>3.b Essential medicines and vaccines</td>
<td>Essential medicines</td>
</tr>
<tr>
<td></td>
<td>Priority health technologies</td>
</tr>
<tr>
<td></td>
<td>Immunisation</td>
</tr>
<tr>
<td>3.c Health financing and health workforce</td>
<td>Health financing</td>
</tr>
<tr>
<td></td>
<td>Health workforce</td>
</tr>
<tr>
<td>3.d National and global health risks</td>
<td>International Health Regulations</td>
</tr>
<tr>
<td>2.2 Child malnutrition</td>
<td>Child malnutrition</td>
</tr>
<tr>
<td>16.1 Violence</td>
<td>Violence prevention</td>
</tr>
</tbody>
</table>

[http://apps.who.int/gho/data/node.home](http://apps.who.int/gho/data/node.home) Accessed 13 Oct 2019
5.9 Impact case study – summaries

The following section presents 14 impact case studies to illustrate the range of scientific and health outcomes achieved, and the activities that have enabled the project to be implemented and the findings to be taken up. Two additional case studies were presented in preceding sections (see sections 5.4.3 and 5.5.2). An overview of all 16 case studies is provided in Table 17, cross-linked to the relevant case. The full case studies are available in a separate document (Review of the JGHT – Impact Case Studies).

Table 17 Case studies

<table>
<thead>
<tr>
<th>Case study category</th>
<th>Case study</th>
<th>Award details</th>
</tr>
</thead>
<tbody>
<tr>
<td>JGHT-funded trials with evidence of policy influence</td>
<td>Case study 1</td>
<td>G1100682/1, Thuy Le, Call 1</td>
</tr>
<tr>
<td></td>
<td>Case study 2</td>
<td>G1100684/1, Jeremy Day, Call 1</td>
</tr>
<tr>
<td></td>
<td>Case study 3</td>
<td>G1100693/1, Diana Gibb, Call 1 (2 cases)</td>
</tr>
<tr>
<td></td>
<td>Case study 4</td>
<td>G1100693/1, Diana Gibb, Call 1</td>
</tr>
<tr>
<td></td>
<td>Case study 5</td>
<td>MR/K007211/1, Gail Davey, Call 2</td>
</tr>
<tr>
<td></td>
<td>Case study 6</td>
<td>MR/L004321/1, Karen Devries, Call 3</td>
</tr>
<tr>
<td></td>
<td>Case study 7</td>
<td>MR/L004437/1, M Rowland (active), Call 3</td>
</tr>
<tr>
<td></td>
<td>Case study 8</td>
<td>MR/M007413/1, David Meya (active), Call 4</td>
</tr>
<tr>
<td></td>
<td>Case study 9</td>
<td>MR/N00597X/1, Rachel Pullan, Call 5</td>
</tr>
<tr>
<td>Trials with potential for policy influence, PIs actively engaged</td>
<td>Case study 10</td>
<td>G1100677/1, P Phillips-Howard, Call 1 (and Call 5)</td>
</tr>
<tr>
<td></td>
<td>Case study 11</td>
<td>G1100554/1, Feiko Ter Kuile, Call 1</td>
</tr>
<tr>
<td>Full trials, main trial findings not yet published</td>
<td>Case study 12</td>
<td>MR/K007467/1, Carlton Evans (active), Call 2</td>
</tr>
<tr>
<td></td>
<td>Case study 13</td>
<td>MR/N006178/1, Tazeen Jafar, Call 3 (and Call 5)</td>
</tr>
<tr>
<td></td>
<td>Case study 13</td>
<td>MR/L004356/1 Angela Crook, Call 3</td>
</tr>
<tr>
<td>Development awards with evidence of outcomes</td>
<td>Case study 15</td>
<td>MR/M022161/1, Xiaolin Wei, Call 5</td>
</tr>
<tr>
<td></td>
<td>Case study 16</td>
<td>MR/P020844/1, Rosa Hoekstra, Call 7</td>
</tr>
</tbody>
</table>

5.9.1 JGHT-funded trials with evidence of policy influence

Case study 1

**A Randomised, Open-Label, Comparative Study of Itraconazole vs. Amphotericin B for the Induction Therapy of Penicilliosis (G1100682, Call 1)**

- Funding period: 01/08/2011 - 31/03/2017
- Lead PI: Dr Thuy Le
- Lead institution: Oxford University Clinical Research Unit (OUCRU) Vietnam
- Funding amount: £1,540,178

- The ‘Itraconazole versus Amphotericin B for Penicilliosis’ (IVAP) trial was the first trial to compare the relative effectiveness of two treatments, amphotericin B and itraconazole, for talaromycosis, a common fungal infection among HIV-positive persons endemic to southeast Asia. The trial was conducted at five major referral hospitals in Viet Nam, and was led by Dr Thuy Le, Oxford University Clinical Research Unit (OUCRU), Ho Chi Minh City, Viet Nam.
- Before the trial, international guidelines recommended treatment with amphotericin B but were based on poor evidence. The trial showed that amphotericin was more effective than itraconazole, providing robust evidence to underpin the treatment recommendations. The trial’s findings were taken up into national guidelines in Viet Nam, and also described in WHO guidelines.
- The trial led to health impacts by changing treatment of talaromycosis patients in Viet Nam, where amphotericin B is now provided to all patients, compared to only 30% of patients before the trial. This has cut the death rate in half, saving the lives of around 35 individuals every year.
- Locating the trial within the Vietnamese health system was crucial in securing buy-in from practitioners and enabling changes in policy and practice.

**Case study 2**

**A clinical trial of dexamethasone to reduce mortality in cryptococcal meningitis (CryptoDex) (G1100684/Call 1)**

Funding period: 01/10/2011 - 31/03/2017  
Funding amount: £4,217,875

Lead PI: Prof Jeremy Day  
Lead institution: Oxford University Clinical Research Unit (OUCRU), Ho Chi Minh City, Vietnam

- The Cryptodex trial determined whether addition of dexamethasone to standard treatment would improve survival among adults with HIV-associated cryptococcal meningitis. It was led by Professor Jeremy Day, Oxford University Clinical Research Unit (OUCRU), Ho Chi Minh City, Vietnam, and involved 13 centres in 6 countries (Vietnam, Thailand, Indonesia, Laos, Uganda, and Malawi).
- The trial showed that dexamethasone is unlikely to benefit survival in patients with HIV-associated cryptococcal meningitis and its findings were taken up by WHO in the 2018 Guidelines on Cryptococcal Disease in HIV-infected adults, adolescents, and children.
- During the trial, researchers from participating centres in Africa and Asia were able to exchange experiences and share learning, e.g. on delivering interventions in relatively lower setting and approaches to patient recruitment.
- The CryptoDex trial has also helped to inform improvements in the hospital discharge protocol for patients with brain infections, and developed resources to assist patients to cope with disability and re-integrate into their communities. These resources are now being made available through an NGO, and the Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam has already modified their approach to discharge planning.


**Case study 3**

**Reduction of EARly mortaLITY in HIV-infected African adults and children starting antiretroviral therapy: REALITY trial (G1100693/Call 1)**

Funding period: Oct 2012 - Mar 2018  
Funding amount: £3,986,746

Lead PI: Prof Diana Gibb  
Lead institution: University College London / MRC Clinical Trials Unit

- The REALITY trial aimed to address the question of how to reduce the high early death rates when HIV-infected individuals with low immunity start antiretroviral therapy (ART). The trial tested three different approaches, at trial centres in Zimbabwe, Uganda, Malawi, and Kenya. It was led by UCL / MRC CTU.
- The trial showed that taking a package of antimicrobial drugs at the same time as starting ART reduced the rate of death by 3.3%, from 12.2% to 8.9%, i.e. saving 3 lives for every 1000 patients treated.
- The antimicrobial prophylaxis package was taken up into WHO guidelines as an option - but currently not as a first line treatment recommendation. Work to address concerns about antimicrobial resistance and cost-effectiveness of the intervention is ongoing and is expected to inform the next WHO guideline update.
- The trial also showed that giving extra food to those starting on ART, or adding an integrase inhibitor (a new type of antiretroviral drug) to ART did not have an effect on mortality. Latter alleviated concerns over the safety of integrase inhibitors in HIV-infected individuals with very low immunity and lent confidence to the current WHO guidelines recommending integrase inhibitors as the preferred treatment.


Case study 4

**Reduction of EARly mortaLITY in HIV-infected African adults and children starting antiretroviral therapy: REALITY trial (G1100693/Call 1)**

- WHO recommends preventative therapy against tuberculosis for people living with HIV, including the antimicrobials cotrimoxazole and isoniazid. However, access to isoniazid remained poor and few people were receiving this treatment.
- To increase access and adherence, Cipla Ltd developed a co-formulated pill, combining cotrimoxazole and isoniazid. The enhanced prophylaxis arm of the REALITY trial provided an opportunity to test Q-TIB and gather data on adherence and acceptability, to contribute to submission for WHO pre-qualification.
- In 2017, Q-TIB was included on WHO essential medicines list and its use recommended in WHO guidelines. It is now available on the market.

**Funding period:** Oct 2012 - Mar 2018  
**Funding amount:** £3,986,746  
**Lead PI:** Prof Diana Gibb  
**Lead institution:** University College London / MRC Clinical Trials Unit

Case study 5

**Randomised controlled trial of podoconiosis treatment in northern Ethiopia (GoLBet) (MR_K007211_1/Call 2)**

- Podoconiosis is a form of lymphoedema (leg swelling) in people who walk barefoot on volcanic soil in highland tropical areas. The GoLBet trial was the first trial to measure the effects of a simple foot care package on ADLA, the most severe consequence of podoconiosis, an acute inflammation of skin, tissue, lymphatics, and lymph nodes. The trial was led by Prof Gail Davey, University of Sussex, and conducted in rural communities in the East Gojjam Zone, Ethiopia.
- The trial showed that the simple, inexpensive care package was effective in reducing the frequency and duration of ADLA. The package is now set to be incorporated into the next 5-year Ethiopian Neglected Tropical Diseases masterplan (2020-2025).
- So far, an estimated 100,000 podoconiosis patients have been trained to self-treat with the foot care package in Ethiopia, including through a financial commitment by the Ethiopian government for training in 2018. In addition, the University of Sussex working with NGOs has trained 200 health professionals in endemic areas.
- The GoLBet team have also started working in neighbouring countries, e.g. in Rwanda, where the foot hygiene package will be referenced in the national Strategic Plan for 2020-2025, and in Uganda and Cameroon where approx. 40 health professionals where trained.
- A Rapid Ethical Assessment ahead of the trial was important to lay the groundwork for the trial. Gathering local knowledge through community consultation facilitated patient recruitment and enabled the trial team to effectively address challenges encountered during the trial.


**Funding period:** 01/02/2013 - 30/05/2017  
**Funding amount:** £777,890  
**Lead PI:** Prof Gail Davey  
**Lead institution:** Brighton and Sussex Medical School, University of Sussex
The Good Schools Study: A cluster randomised controlled trial of an intervention to prevent violence against children in Ugandan primary schools (MR/L004321/1, Call 3)

Physical, sexual or psychological violence is a global health problem affecting 1 billion children worldwide every year. The problem is particularly acute in Ugandan primary schools with more than 90% of children reporting some form of physical violence from school staff.

A team led by Dr Karen Devries at the London School of Hygiene and Tropical Medicine tested The Good Schools Toolkit, a behavioural intervention developed by a Ugandan NGO Raising Voices, in primary schools in Uganda in a two-arm cluster-randomised controlled trial. A qualitative study, economic evaluation, and process evaluation were also included in the study.

Trial results showed that the intervention was effective at reducing violence towards children by 42% in the space of 18 months. This evidence informed WHO violence prevention guidelines. Moreover, 434 of the children participating in the trial were referred to Child Protective Services. Thus, the study itself has had an impact on the health and wellbeing of children.

The Good Schools Toolkit is now being used in Tanzania, Kenya and Rwanda in addition to Uganda. It is also being adapted for secondary schools and a randomised controlled trial of this new toolkit is planned for 2020.


Combination interventions for controlling malaria transmitted by pyrethroid resistant mosquitoes: A novel bed net with synergist and IRS formulation (MR/L004437/1/Call 3)

Abundant use of pyrethroid-based insecticides has driven an increase in pyrethroid-resistant mosquitoes, threatening the future success of these control strategies.

The JGHT-funded trial evaluated the use of two alternative control products in the prevention of malaria transmission in Tanzania: insecticidal nets combining pyrethroid with piperonyl butoxide (PBO LLIN) and an indoor residual spray (IRS) formulation of a non-pyrethroid insecticide. The reference arm (the current standard of care) was pyrethroid-only LLIN. The study was led by the London School of Hygiene and Tropical Medicine in collaboration with two research institutes in Tanzania.

The trial demonstrated that both products independently reduced malaria infection and transmission compared to standard control strategies. Use of both prevention tools in conjunction did not provide any additional benefit. It was the first trial to measure the impact of PBO LLIN in humans.

The trial’s findings on PBO LLINs were incorporated by WHO into policy, recommending their use in areas where pyrethroid resistance has been confirmed. PBO LLIN are being made available and scaled up across Africa.

Case study 8

Evaluation of a rapid test for tuberculous meningitis: Adjunctive Sertraline for the Treatment of HIV-Associated Cryptococcal Meningitis (MR/M007413/1, full trial /Call 4)

Funding period: 01/03/2015 - 28/02/2018  
Funding amount: £888,672

Lead PI: Dr David Meya  
Lead institution: Makerere University, Uganda

- The JGHT-funded ASTRO-CM trial aimed to evaluate whether addition of the drug sertraline to standard treatment improved survival of HIV patients with cryptococcal meningitis. The trial was led by Dr David Meya, Infectious Diseases Institute in Uganda. The trial results showed that adjunctive sertraline did not improve survival.

- Data collected as part of a study nested within the trial, but not directly related to the issue the trial addresses, has informed WHO policy: During screening of potential trial participants for Cryptococcal meningitis, the ASTRO-CM team also compared diagnostic TB tests and found that the new TB Xpert Ultra assay detected significantly more tuberculous meningitis than the other tests. This contributed to an update of a WHO recommendation in March 2017.


Case study 9

Interrupting transmission of soil-transmitted helminths: cluster randomised trial evaluating alternative treatment strategies in Kenya (TUMIKIA) (MR_N00579X_1/Call 5)

Funding period: 01/11/2015 - 31/10/2018  
Funding amount: £1,027,818

Lead PI: Dr Rachel Pullan  
Lead institution: London School of Hygiene and Tropical Medicine, UK

- Soil-transmitted helminths (STH) are among the most common infections worldwide and affect the poorest and most deprived communities.

- The TUMIKIA trial investigated whether it is possible to interrupt the transmission of STH, evaluating the impact of school-based and community-based treatment on the prevalence and intensity of STH infection. It was co-funded by the Government of Kenya, the Children’s Investment Fund Foundation, and the Bill and Melinda Gates Foundation. The trial was led by Dr Rachel Pullan, LSHTM and included collaborators from the Kenya Medical Research Institute (KEMRI) and other investigators at LSHTM.

- The trial found that community-wide treatment was more effective in reducing hookworm prevalence and intensity than school-based treatment, with little additional benefit of treating every 6 months compared to once per year.

- The results fed into the development of the Breaking Transmission Strategy of the Kenyan government for 2019-2023, which targets STH, and other NTDs, with a package of interventions. Implementation is currently being piloted to prepare for nation-wide roll-out. TUMIKIA findings are also informing WHO discussions on community- vs school-based treatment, and on effective monitoring and surveillance strategies.

- Broadening coverage is faced with a key challenge: Deworming programmes are mainly driven by donations that are limited to children in their use. Unless donor programmes chose to purchase drugs, only a shift in this limitation will enable broader uptake of community-based deworming.

- A longer-term study in Malawi, Benin, and Sri Lanka - the DeWorm3 trial funded by BMGF and led by the Natural History Museum London - is currently expanding on the trial’s results. Findings are likely to guide BMGF strategy and inform WHO and other international organisations.

5.9.2 JGHT awards with potential for policy influence, PIs actively engaged

**Case study 10**

**Menstrual solutions in adolescent schoolgirls in western Kenya: an acceptability, feasibility and safety study (G1100677/1/Call 1)**

<table>
<thead>
<tr>
<th>Funding period: 01/04/2012 - 30/09/2013</th>
<th>Funding amount: £716,200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead PI: Penelope Anne Phillips-Howard</td>
<td>Lead institution: Liverpool School of Tropical Medicine</td>
</tr>
</tbody>
</table>

- Little evidence is available on Menstrual Health Management (MHM) by schoolgirls in LMICs and its impact on education and health outcomes. The JGHT-funded feasibility study responded to this gap and compared three different approaches to MHM (menstrual cups, sanitary pads, no intervention). The study was led by the London School of Hygiene and Tropical Medicine, with partners in Kenya and the UK.
- The feasibility study provided important evidence for the design of a full trial, subsequently funded by the JGHT (ongoing). For example, the full trial’s primary outcome measure was shifted from the level of absenteeism to the level of school drop-out and level of sexually transmitted infections, as the feasibility study showed this to be a more reliable indicator. The study also stimulated further international research activity on the topic.
- Expertise developed through the JGHT award enabled the study team to contribute to committees and fora addressing issues in MHM, both in Kenya and internationally. This has included feeding into the Kenyan National Menstrual Hygiene Management Policy and Strategy, currently under development by the Kenyan Ministries of Health, Education and Gender.


**Case study 11**

**Intermittent screening and treatment or intermittent preventive therapy for control of malaria in pregnancy in Indonesia (G1100654/1 /Call 1)**

<table>
<thead>
<tr>
<th>Funding period: 01/10/2011 - 30/06/2017</th>
<th>Funding amount: £2,426,004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead PI: Prof Feiko ter Kuile</td>
<td>Lead institution: Liverpool School of Tropical Medicine</td>
</tr>
</tbody>
</table>

- Infection with malaria in pregnancy (MiP) can have severe consequences for both mother and baby. Interventions recommended by WHO for the control of MiP are largely based on findings from sub-Saharan Africa; the Asia-Pacific region on the other hand does not have a standardised strategy for the prevention of MiP.
- The JGHT-funded study was the first trial in Indonesia to determine the effectiveness of several strategies designed to prevent malaria in pregnancy. It was led by the Liverpool School of Tropical Medicine, in collaboration with researchers from institutions in the UK, Indonesia, and Australia.
- Comparing the current strategy with two alternatives revealed that intermittent preventive treatment (IPT) was most effective in a high transmission setting to prevent MiP in Indonesia.
- The Indonesian Ministry of Health was engaged throughout the project and has now requested support from the research team to conduct and evaluate a pilot implementation of IPT in the Indonesian healthcare system (subject to LSTM obtaining funding).
- Nested acceptability and systems effectiveness studies were conducted as part of the JGHT award. These provided additional information that will support the implementation of IPT in terms of key priority areas that need to be addressed in the implementation pilot.

Community randomised evaluation of socioeconomic intervention to prevent TB (MR/K007467/1/Call 2)

Funding period: 01/10/2012 - 01/10/2021  
Funding amount: £3,168,125

Lead PI: Carlton Evans  
Lead institution: Imperial College London

- Tuberculosis (TB), one of the top 10 causes of death worldwide, is associated with poverty. Therefore, socioeconomic interventions have a large role to play in addressing this problem.
- A team led by Professor Carlton Evans (Imperial College London; Universidad Peruana Cayetano Heredia, Peru) is evaluating a combined socioeconomic intervention aimed at tackling TB in the CRESIPT trial in Peru. The intervention comprises household visits, community meetings and conditional cash transfers towards TB-associated costs.
- The findings so far show that households receiving the intervention are less likely to incur catastrophic costs, uptake of preventive therapy among household contacts is increased and TB treatment success in TB patients is improved.
- The trial team has engaged with local, national and international stakeholders; influenced the training of health professionals; empowered recovering patients to become community leaders and contributed to improved understanding of TB in the community. Publications emerging from the project have been referenced in WHO’s handbook for conducting TB patient costs surveys and the team has helped to roll out such cost surveys in 15 countries.

Primary Care Strategies to Reduce High Blood Pressure: A Cluster Randomised Trial in Rural Bangladesh, Pakistan and Sri Lanka (COBRA-BPS) (MR/N006178/1/Call 5)

Funding period: 01/09/2015 - 30/11/2019  
Funding amount: £2,233,623 (COBRA-BPS), £201,806 (feasibility study)

Lead PI: Prof Tazeen H. Jafar  
Lead institution: Duke-National University of Singapore Medical School, Singapore

- Hypertension is a leading risk factor of cardiovascular disease, a major cause of mortality and disability. Many affected people in rural South Asia remain undiagnosed and undertreated and are at risk of serious adverse effects. A potential strategy to reduce rates of hypertension is a multicomponent intervention (MCI).
- Professor Jafar, from the Duke-National University of Singapore Medical School, led a feasibility study funded by the JGHT to optimise the delivery of an MCI designed to be embedded in the existing healthcare infrastructure. It encompassed screening and referral of at-risk individuals, family education on mitigation strategies, training of healthcare providers, and a financing model.
- The feasibility study indicated that a full-scale trial in the rural settings of Pakistan, Bangladesh and Sri Lanka was viable. It also supported the development of training manuals and protocols needed to deliver the intervention. Comprehensive stakeholder engagement ensured the intervention was supported by local and national healthcare officials.
- The full-scale COBRA-BPS trial was undertaken following the feasibility study. The final trial results will be published shortly; however, a number of other publications have already emerged including a qualitative assessment of the barriers to accessing healthcare. The stakeholder engagement, established during the feasibility study, has since developed into a regional policy forum centred on cardiovascular disease and hypertension.
Case study 14

Two-month Regimens Using Novel Combinations to Augment Treatment Effectiveness for drug-sensitive Tuberculosis: the "TRUNCATE-TB" trial (MR/L004356/1 / Call 3)

Funding period: Nov 2014 – Mar 2022  
Funding amount: £5,012,977  
Lead PI: Angela Crook  
Lead institution: University College London, UK

- Tuberculosis (TB) presents a high disease burden worldwide, particularly in LMICs. Furthermore, multidrug resistant TB (MDR-TB) has emerged as a serious threat to health security. Patients often fail to adhere to treatment, leading to poor outcomes and drug resistance. Therefore, alternative management strategies are the need of the hour.
- Dr Angela Crook from University College London is leading a team of researchers from the UK and Singapore to test a new management strategy comprising a variety of novel 2-month combination drug regimens against the current 6-month treatment in the TRUNCATE-TB trial. The trial is being conducted in Indonesia, the Philippines and Thailand.
- The TRUNCATE-TB trial is one of the first trials to use the multi-arm multi-stage (MAMS) design in the context of global health trials. This design allows researchers to test multiple intervention arms against a single control arm and drop unpromising intervention arms as well as add new ones part way through the trial. Hence, this approach is more efficient and cost-effective than a traditional two-arm trial and offers a greater chance of finding an effective treatment.
- The study is still ongoing, and findings are yet to emerge. However, the trial has already contributed to enhancing the scientific knowledge, technical skills and professional networks of the researchers working at the trial sites, and stakeholders are being engaged.

5.9.4 Development awards with evidence of outcomes

Case study 15

Develop an interventional study on reducing antibiotic over-prescribing among children with Upper Respiratory Tract Infections in rural Guangxi, China (MR/M022161/1, Call 5 – Development award)

Funding period: 01/04/2015 - 31/12/2017  
Funding amount: £151,260  
Lead PI: Prof Xiaolin Wei  
Lead institution: Shandong University

- Overuse of antibiotics promotes the development of antimicrobial resistance, a major global health problem. Antibiotic over-prescription is widespread in the treatment of upper respiratory tract infections (URTIs) and this challenge is particularly pressing in LMICs.
- A JGHT-funded pilot study aimed to inform the design of a randomised controlled trial aiming to reduce antibiotic over-prescription in the treatment of URTIs in children in rural Guangxi, China. The pilot study tested the feasibility of a multidimensional intervention consisting of clinical guidelines, training material and workshops in two groups (clinicians only; clinicians and caregivers) against a control group.
- Findings of the pilot study informed the design of a full trial which was funded by DfID. This trial showed that the intervention reduced the antibiotic prescription rate by about a third (29%) and that the effect was sustained for at least a year in the intervention hospitals.
- Implementation of the interventions as part of the feasibility study and the full trial had a positive impact in reducing over-prescription of antibiotics regionally.
WHO’s Parent Skills Training for developmental disorders: Piloting task-shifting to non-specialists in Ethiopia (MR/P020844/1, Call 7)

Funding period: 01/08/2017 - 30/04/2019
Funding amount: £147,849

Lead PI: Dr Rosa Anna Hoekstra
Lead institution: King’s College London

- Developmental disorders are common yet under-resourced in LMICs. To address this gap, WHO has developed a Caregivers Training Skills (CTS) programme to educate and support caregivers of children with developmental disorders. The programme, designed to be delivered by non-specialists, had not been adapted to or tested in the Ethiopian context prior to this study.

- A pilot study led by King’s College London, funded by a JGHT development award, aimed to evaluate whether CST can be implemented in the Ethiopian context and determine if the measures to assess its impact are reliable and appropriate. The full results are not yet published, but the qualitative study indicates that the CST is acceptable and can be implemented in Ethiopia.

- The study team placed emphasis on local stakeholder engagement, ensuring that the project became locally owned. The CST has since been taken up by the community: It is now used in Ethiopia’s state-run child mental health clinics and rolled out to all caregivers who attend these.

- The research team is currently collaborating with a team in Kenya to conduct a full multi-country randomised control trial. Findings from the pilot study will feed directly into this planned work.


5.10 Value for money

The JGHT represents value for money (VfM) in a variety of ways, maximising the impact of the investment.

- Partnership of funders

Delivery of the JGHT through a partnership of funders has represented efficiency gains for both funders and applicants by:

- Reducing duplication of effort. A unified review process avoids unnecessary time investment by researchers in submitting proposals to multiple schemes and avoids duplication of effort by review panels. In addition, funders are able to draw on their respective expertise to inform the review process, ensuring a high quality of projects selected (e.g. as evidenced by the high completion rate of trials, see below). Efficiencies are also achieved through centralised scheme management.

- Enabling a strategic view of the scheme’s direction and the JGHT portfolio funded, ensuring that any gaps or duplications are identified (a risk if individual funders work in silos)

- Enabling large-scale global health trials to be funded from pooled resources and at the same time reducing the risk of investment for individual funders

This view was also expressed by key opinion leaders when asked about aspects that contribute to the scheme’s VfM: half (3 of 6) pointed to the set-up of the programme itself and highlighted the added value achieved by running the JGHT as a partnership of funders.
Flexible scheme management
The flexibility of the scheme’s management is contributing to value for money of the research budget. Research in LMICs is facing a variety of risks, from delayed approval processes to civil unrest, jeopardising researchers’ ability to complete the studies. While an accurate assessment of time and cost at the proposal stage is preferable, the flexibility of the JGHT has ensured that research efforts were not ‘wasted’ by allowing for non-costed, as well as some costed extensions. This aspect has contributed to the high trial completion rate (see below).

Support for high-quality research
The JGHT has funded high quality research projects, including 63 full trials addressing health issues of disadvantaged populations in LMICs. Of the 28 closed full trial awards, the majority have published or are in the process of publishing the main trial results (23) with another two in the final analysis phase, indicating that at least 89% of these trials have completed. This compares favourably with reported figures for trial completion rates in a study of 114 trials in the UK, which indicated that only 31% met enrolment goals, and is in line with a recent analysis of Phase III and Phase IV trial completion rates, at 85% and 87%, respectively.

Filling a gap in the wider global health research landscape
Evidence from desk research and stakeholder consultation underpins the finding that the JGHT fills an important gap in the global research landscape. The scheme is unique in that is provides funding for global health trials across health areas relevant to LMICs and across all countries, and in that it is open to lead PIs from LMICs. While there is overlap between the JGHT and the EDCTP, they also complement each other: JGHT covers areas, both disease and geographical areas, not covered by EDCTP, and EDCTP funds activities not covered by JGHT e.g. capacity building and early stage trials.

Research findings with strong relevance to health issues of disadvantaged populations in LMICs
JGHT-funded research is generating essential evidence that has been, or has the potential for being, utilised world-wide to support development. For example, 39% of JGHT-funded closed full trials (11 of 28) have already influenced policy at a local or international level, with a further 36% (10 of 28) showing high potential for doing so (based on the conclusiveness of the research results and the PIs level of stakeholder engagement) (see section 5.6.1). The final figure could hence be as high as 75% of closed full trials resulting in policy influence.

Despite the relatively short time since completion of most of these trials, some impacts on health have already been achieved (see section 5.6.2). For example, in Ethiopia, 100,000 patients suffering from podoconiosis have already been trained in how to self-treat with a simple foot care package, shown to be effective in reducing severe symptoms of podoconiosis. With an estimated 1.6 million Ethiopians affected by podoconiosis, this already represents 6.3% of the patient population (see Case study 5). Further roll-out can be expected to further decrease the level of disability and social effects as a result of the disease. In addition, the trials themselves have resulted in health benefits, both direct and indirect, to study participants and their wider communities (see section 5.4.11). For example, the TUMIKIA trial reduced the prevalence and transmission of helminths in clusters treated at a community-level, rather than through school-based deworming (see Case study 9). With 100,000 households participating in the effective treatment arms, and an average Kenyan household size of four, a minimum of 400,000 individuals have benefitted from participating in the trial. In addition, research activity has increased participants’ and their communities’ knowledge and awareness of risks factors, health issues and ways to address them, leading to potentially positive behaviour change and health outcomes.

United Nations Department of Economic and Social Affairs (2017) Household size and composition around the world. Popfacts No. 2017/2
Leverage of additional resources and economic benefits

JGHT-funded research has led to a range of benefits for researchers in LMICs and HICs, such as enhanced scientific knowledge which has been used for further work (e.g. as reported by 71% of co-investigators, 121 of 170), strengthening the wider research ecosystem. This has also helped to leverage additional funding, as reported by 28% co-investigators (48 of 170). For example, the findings of a development award on reducing antibiotic over-prescribing in China informed the design of a larger RCT trial funded by DfID through the Communicable Diseases (COMDIS) Health Services Delivery Research Consortium (see Case study 15). Another development award led to funding for a full trial from the EDCTP (£5,977,299).

A recent study of the value NIHR clinical research has added to the UK economy found substantial direct and indirect economic benefits. Economic benefits related to direct employment, effects on the UK and LMIC supply chains, the provision of free-of-cost treatment by commercial organisations, and through spending by trial staff within the economy can also be expected to have accrued as a result of JGHT-funded research, both in the UK and LMICs.

Findings of JGHT-funded research have also led to, or have the potential to lead to, cost savings. This includes:

- Learning from development awards which have ‘de-risked’ full trial awards, both by tailoring the intervention to be tested and building stakeholder support (see Case study 10 and Case study 14).
- Potential cost savings for LMIC health systems. For example, the TUMIKIA trial (see Case study 9) found that the community delivery platform tested in the trial resulted in comparable coverage and effects of the interventions across important demographic and socioeconomic subgroups (i.e. equity). This has implications for the intervention tested (de-worming) as well as for other treatments delivered via the community. Another trial has led to cost savings by steering away from a treatment approach involving a harmful intervention (e.g. see Case study 2). However, most studies are still in the process of completing their full cost-effectiveness assessments (see section 5.6.3), and the potential for cost savings through implementation of JGHT findings is not yet known.

5.10.1 Opportunities to improve VfM

There are a number of opportunities to improve the JGHT’s VfM. These are outlined below, and taken up in more detail in the review recommendations (see section 8.2).

- While researchers appreciated the ‘light-touch’ reporting requirements of the scheme, additional monitoring would enhance the funders’ ability to track outcomes and impacts, identify any patterns (both positive and negative, e.g. in relation to outcomes of, or challenges to, specific research areas or research in particular countries), and pinpoint opportunities for sharing learning more widely to optimise the value derived from funded research.
- Funders could ensure that opportunities for further stakeholder engagement are available, both pre- and post-award, in order to ensure full pull-through of research findings to policy and implementation. This could include partnering with other funders or across funding schemes, e.g. with the EDCTP.
- Expansion of the development award scheme (in overall budget, and size of awards available), to de-risk the larger trial and ensure that the stakeholder environment is conducive to take up of research findings.

KPMG (2019) Impact and value of the NIHR Clinical Research Network
6 The global health trials funding landscape

6.1 Organisations funding global health trials

In interviews, researchers and key opinion leaders noted that in addition to the JGHT scheme, funders and programmes such as the European & Developing Countries Clinical Trials Partnership (EDCTP), Bill and Melinda Gates Foundation (BMGF), US National Institutes of Health (NIH), the MRC and the Wellcome Trust were important sources of funding for global health trials.

6.1.1 European & Developing Countries Clinical Trials Partnership

EDCTP is the closest to JGHT in that it provides funding specifically for global health trials. However, its scope is limited to research on interventions for poverty-related infectious diseases taking place in sub-Saharan Africa. On the other hand, EDCTP funds all clinical trial phases (I-IV) – not only late-stage trials – including research investigating health services optimisation as well as capacity strengthening and networking activities such as PhD, MSc and career development fellowships. Nonetheless, the majority of trials funded are Phase II and III studies (58% in EDCTP279). EDCTP is also a larger scale partnership than the JGHT, both in terms of budget (€655m since 2003; average €5.2m for research grants in EDCTP280) and partners which include the European Union and 16 African and 14 European countries including the UK.

Other funders such as BMGF, NIH, Canada’s International Development Research Centre (IDRC) and the Research Council of Norway (RCN) fund global health trials through programmes or funding mechanisms that have a much wider scope, for example, product development or health innovation to address health-related challenges in LMICs. Moreover, their strategic priorities and aims determine the scope of the activities they fund and the manner in which they are funded.

6.1.2 Bill and Melinda Gates Foundation

The BMGF aims to reducing health inequalities in developing countries. As such, it has adopted a challenge-driven approach and fosters the development of new treatments and strategies to decrease the burden of infectious disease and the leading causes of child mortality. Thus, it funds clinical trials as part of a host of activities including discovery and translational research, therapeutic development, vaccine development and surveillance focussing on high burden diseases and areas of unmet need in LMICs such as enteric and diarrheal diseases, HIV, malaria, maternal and new-born health, neglected tropical diseases, pneumonia and TB. Moreover, there is no specific requirement for BMGF-funded trials addressing global health issues to be conducted in LMICs.

BMGF has a more directed approach towards awarding funding. Ideas for proposals are identified by programme officers in consultation with stakeholders including researchers and policy makers. These ideas are further developed into proposals for research through direct solicitation, discussion with one or more organisations who are then invited to submit a proposal and public/private requests for proposals.

Some BMGF funds for global health research are distributed through specific programmes such as Grand Challenges (USD450m83) and Grand Challenges Explorations. The former started in 2003, is

77 HIV, tuberculosis, malaria, neglected infectious diseases, diarrhoeal diseases, lower respiratory tract infections, emerging or re-emerging infectious diseases of particular relevance for Africa such as Ebola virus disease or yellow fever
79 Among interventional trials funded by EDCTP2. Data provided by EDCTP.
80 Clinical trials and implementation research grants funded 2016 to 2018. Data provided by EDCTP.
funded in partnership with the NIH, Canadian Institutes of Health Research (CIHR) and the Wellcome Trust, and consists of a programme of initiatives wherein each initiative focuses on innovation towards addressing a specific global health or development challenge. The latter was initiated in 2007 and invites high-risk, high-reward proposals from innovators on a biannual basis. Successful applicants are initially awarded USD100k with successful projects potentially receiving up to USD1m of follow-on funding.

6.1.3 The US National Institutes of Health

In contrast to the JGHT and EDCTP, the US NIH does not have specific programmes for funding global health trials. The agency funds global health trials worldwide (including in LMICs) through its standard funding mechanisms and specialist institutes such as the National Institute of Allergy and Infectious Diseases (NIAID). There is no defined remit in terms of trial areas or phases, and thus topics such as bioethics, non-communicable diseases, infectious diseases, implementation science, mobile health, mental health and maternal and child health are all covered.

NIAID funds clinical research in one of two ways:

- through extramural grants, where outside entities (typically universities or academic institutions) are funded to conduct research. This usually takes place in the context of existing NIH/NIAID-funding networks such as the AIDS Clinical Trials Group, the Immune Tolerance Network and the Vaccine Treatment and Evaluation units, which ensures that relevant infrastructure is available (e.g. for regulatory support, biostatistics and training). Proposals can be for investigator-initiated (unsolicited) or NIAID-requested (solicited, in predefined areas) research.

- through intramural grants where NIAID scientists work in partnership with investigators in LMICs. The grant comes from the NIAID scientist’s sustained funding allocation (block grant).

Most NIAID clinical trials are funded in response to solicitations from NIAID where the topic and scope is predetermined (NIAID-requested research). Some calls allow LMIC researchers to apply either independently or in partnership with a US institution. In 2018, NIAID funding for clinical research in LMICs was USD443m.

6.1.4 Other funders

Funders such as IDRC (Canada), Grand Challenges Canada (GCC) and the RCN/Norwegian Agency for Development Cooperation (Norad) fund trials as part of innovation programmes with a global health focus.

- IDRC has two programmes for health-related innovation – Food, Environment and Health (covering nutrition, infectious and non-communicable diseases) and Maternal and Child Health. In addition, the agency has partnered with the Canadian Institutes of Health Research (CIHR) and Global Affairs Canada on a third programme – Innovating for Maternal and Child Health in Africa. These programmes fund projects on a competitive basis through calls with their own specific eligibility requirements and thematic focus. Trials form a small proportion of the activities funded (6 of 438 projects; total spend CAD13m) and include testing of vaccines (e.g. Ebola) and prevention.

---

84 BMGF. Grand Challenges. [https://gcgrandchallenges.org/history](https://gcgrandchallenges.org/history) Accessed 20 Oct 2019
85 BMGF. Grand Challenges. [https://gcgrandchallenges.org/about](https://gcgrandchallenges.org/about) Accessed 20 Oct 2019
86 Personal Communication, Dr Clifford Lane (8 October 2019)
88 Personal Communication, Dr Clifford Lane (8 October 2019)
90 Personal communication, Joyelle Dominique (12 October 2019)
interventions. All trials within these programmes were/are being conducted in LMICs, with half of the trials led by LMIC researchers.

- GCC is an independent, not-for-profit organisation funded by the Canadian government and other partners (including DFID, BMGF, USAID and Johnson & Johnson). It supports innovators in LMICs and Canada to develop innovations that will save and improve lives in LMICs. GCC awards grants and zero interest loans for targeted challenges (e.g., maternal and child health, mental health, hypertension, point-of-care diagnostics), innovator-led proposals and challenges related to scaling up promising innovations. Between 2010 and 2018, GCC spent CAD269m on these programmes; the proportion of funding awarded for trials is not clear. So far, about 150 different interventions have been tested in product development or implementation trials. Grants are solicited through open calls for proposals, each defining the scope of what will be funded. PIs can be based anywhere in the world, but funded activities have to take place in an LMIC.

- The Global Health and Vaccination Research (GLOBVAC) programme is the main global health research programme in Norway, jointly funded by RCN and Norad since 2006. It has an annual income of about NOK122m (about £10m), and primarily aims to support high-quality research with potential for high impact on health and health equity in LMICs. Funding is available for research on interventions to prevent, treat and diagnose communicable diseases and to promote reproductive, maternal and child health, including clinical trials of such interventions. Research can be conducted in Norway or LMICs and proposals are solicited through open calls for proposals.

The research funding landscape, and the JGHT’s role within, was determined for a selection of four conditions: malaria, tuberculosis, cryptococcal meningitis and podoconiosis. JGHT-funded research accounted for a small share of funding for malaria- and TB-related research, funding around 2% of trials registered in these disease areas between 2011 and 2018 (16 of 833 and 9 of 662, respectively). The scheme played a much bigger role in the “smaller” disease areas of cryptococcal meningitis, accounting for 23% of trials funded (3 of 13), and podoconiosis, accounting for one of three trials in this area (33%). A detailed analysis of each disease area is available in Appendix G.

6.1.5 Product development partnerships

Several funders also support development of innovations for prevention, diagnosis, or treatment of infectious diseases through Product Development Partnerships (PDPs). Examples include the International AIDS Vaccine Initiative (IAVI), European Vaccine Initiative (EVI), Medicines for Malaria Venture (MMV) and Foundation for Innovative Diagnostics (FIND). PDPs received USD508m in 2017 mainly from government agencies such as the UK’s DHSC and DFID, the US NIH, USAID, the European Commission, the German Federal Ministry of Education and Research (BMBF), the Australian Department of Foreign Affairs and Trade and the Swiss Agency for Development and Cooperation as well as organisations such as the BMGF and UNITAID. The extent of private sector engagement varies from partnership to partnership.

---

92 IDRC. Available at: https://www.idrc.ca/en/search?f%5B0%5D=type%3Aidrc_project&f%5B1%5D=field_program%3A16837&f%5B2%5D=field_program%3A16836&f%5B3%5D=field_program%3A16826. Accessed 20 Oct 2019
94 Ibid.
PDPs are able to combine the strengths of the public and private sector. The majority of the partnerships work as virtual organisations supporting R&D activities that fit their scope and strategy. They target one or more ‘neglected diseases’ (i.e. HIV/AIDS, tuberculosis, malaria and neglected tropical diseases) and use a portfolio management approach for developing products. Clinical trials are funded as part of the product development pipeline. For instance, EVI conducts early stage clinical trials and hands over promising candidates to partners for mid-stage clinical development.

6.2 Outputs, outcomes and impacts of other funding global health programmes

Most funders undertake monitoring of outputs, outcomes and sometimes impacts at a programme level to assess if they are meeting their objectives. Programme evaluations are also commissioned, often from independent, external groups. Most funders use evaluation frameworks and both qualitative and quantitative indicators for monitoring, gathering evidence via a mixed-methods approach (see Appendix G). However, the variation in objectives and timelines, investment and scope of funded activities between funders and programmes limits the level to which outcomes and impacts can be compared across initiatives.

6.2.1 EDCTP

EDCTP funded 96 grants (€395m) for clinical research (including observational studies) between 2004 and 2018. From these grants, 216 clinical trials (interventional studies) have been funded; however, the proportion of funding spent on clinical trials as opposed to observational and other types of studies is not known. EDCTP1 projects (about 180, 2004–13) have generated over 750 peer-reviewed publications (between 2005 and 2019). In addition, four regional Networks of Excellence and a Pan-African Clinical Trials Registry were established. Some examples of impact achieved from EDCTP include the following:

- The CHAPAS trials (CHAPAS-1, 2005–09, €1.2m; CHAPAS-3, 2010–11, €5m) contributed to the approval of specific HIV medicines (Triomune Baby/Junior) by the US Food and Drug Administration in 2007, WHO recommendations on optimal drug ratios for fixed-dose combinations and on appropriate dosage according to weight, the WHO recommendation of abacavir-containing combinations for first-line antiretroviral therapy in children, and applications for regulatory approval for new scored efavirenz tablets.
- The Kesho Bora study (2006–10, €2.7m including €1.1m EDCTP funding) informed the development of revised WHO guidelines, which recommended more extensive use of antiretrovirals in pregnant and breastfeeding women. More generally, the results highlight the potential achievability of elimination of mother-to-child transmission.
- The WANECA trial (2009–14, €9.3m including €4.8m EDCTP funding) showed that two antimalarial drug combinations, dihydroartemisinin–piperaquine (DP, Eurartesim®) and pyronaridine–artesunate (PA, Pyramax®) remain safe and efficacious even when used repeatedly. Trial results were used to support successful applications to the European Medicines Agency to extend use of PA to treatment of multiple episodes of malaria.

---

99 EVI. Available at: http://www.euvaccine.eu  Accessed 20 Oct 2019

100 Technopolis (2014) Assessment of the performance and impact of the first programme of the European & Developing Countries Clinical Trials Partnership (EDCTP)

101 EDCTP2 data provided by EDCTP

102 EDCTP1 data provided by EDCTP

Accessed 20 Oct 2019

Accessed 20 Oct 2019
and for a paediatric formulation; both formulations are now on the list of WHO-prequalified medicines

The European Commission’s interim evaluation of the second phase of EDCTP (from 2014-2016) noted a number of successes related to researcher participation from Sub-Saharan Africa which included (but were not limited to) the following:

- More than 40 countries in Sub-Saharan Africa were involved in activities initiated by EDCTP participating states (14 European and 14 African countries). 50% of these activities involved up to 4 countries and approximately 10% involved a minimum of 10 countries
- Scientists from nearly 30 sub-Saharan countries were represented in applications for funding
- 73% of funded grants (including research grants, fellowships, coordination and support grants) were led by scientists from sub-Saharan Africa

While EDCTP has many similarities with JGHT and has had some notable successes, outcomes are not directly comparable owing to the difference in scope in terms of disease areas, geography and trial phases. Moreover, a comparison of the enablers of outcomes between the JGHT and EDCTP would require further research and analysis to understand differences between the research and stakeholder engagement carried out by these programmes.

6.2.2 Product development partnerships

A selection of PDPs has also been evaluated on behalf of individual funders (DFID/BMBF\textsuperscript{106}, the Australian Government\textsuperscript{107} and the Dutch Ministry of Foreign Affairs\textsuperscript{108}). Findings on outputs and outcomes that emerged from these evaluations and from desk research (PDP websites) are as follows:

- Since 2003, FIND has developed 24 new diagnostic tools for neglected diseases, 17 of which have been recommended by WHO\textsuperscript{109}. It has supported 71 clinical trials and published 241 scientific articles\textsuperscript{110}. Over 50 million FIND-supported products have been provided to 150 LMICs since 2015\textsuperscript{111}. The total expenditure for research activities was USD55m in 2018\textsuperscript{112}.
- Since its inception in 1999, MMV and its public and private partners have brought forward 10 new antimalarials and have helped save an estimated 1.9 million lives through medicines they have supported\textsuperscript{113}. MMV’s expenditure in 2017 and 2018 totalled USD159m which covers all R&D activities including clinical trials.
- The TB Alliance is currently conducting three Phase III trials and one paediatric Phase IV trial\textsuperscript{114}. It previously funded two Phase III studies. In 2018, TB Alliance submitted its first new drug

\textsuperscript{105} Evaluation of the Second European and Developing Countries Clinical Trials Partnership Programme (2014-2016). Experts Group Report. 2017
\textsuperscript{106} Boulton et al (2015) Evaluation of the Product Development Partnerships (PDP) funding activities
\textsuperscript{109} FIND. Available at: https://www.finddx.org/ Accessed 20 Oct 2019
\textsuperscript{111} Ibid.
\textsuperscript{112} Ibid.
PDPs cover the whole spectrum of R&D activities from basic research and translation to product development. Clinical trials form a small proportion of these activities. Moreover, the amount of funding that they put towards clinical trials is unclear. Hence, a direct comparison with JGHT is not possible.

6.2.3 GLOBVAC
An evaluation of RCN and Norad’s GLOBVAC programme conducted in 2016 found that GLOBVAC is a reasonably efficient and effective research support mechanism that fills an important gap in the Norwegian funding landscape. Between 2006 and 2015, about NOK900m (approximately £76m) was spent on the programme which had led to:

- 1,239 scholarly publications; 15 products, 42 prototypes and 12 process or service innovations; 12 patents and 1 licensing agreement; 16 new businesses
- creation of new research collaborations and partnerships within Norway and internationally; capacity development in low and lower-middle income countries
- Phase II and III trials that had provided crucial evidence with regard to interventions against, for example, transmission of HIV from mother to baby through breastfeeding, HIV-1 infection (Vacc-4x vaccine), rotavirus (ROTAVAC® vaccine) and Ebola (rVSV-ZEBOV vaccine)

While GLOBVAC has been evaluated, it funded very few large-scale trials, which does not allow a meaningful comparison with the JGHT.

6.3 Advantages / disadvantages of the JGHT compared to other funding programmes
Researchers and key opinion leaders pointed to a range of strengths that set the JGHT apart from other programmes, including the fact that:

- Researchers are driving the research rather than the funders
- A substantial amount of funding is available at a sufficient scale to conduct a large late-stage trial
- The scheme’s remit covers various conditions including NCDs, mental health and violence, and not just infectious diseases
- All LMICs are in scope and the research can be led by an LMIC researcher
- Grant management and reporting requirements are realistic and do not burden researchers

EDCTP was mentioned by all interviewees as a comparator programme to the JGHT, although significant differences between the two programmes were highlighted (see section 6.1.1). Two interviewees commented that the application process for EDCTP is much more cumbersome than that for the JGHT, which they saw as more straightforward. However, the availability of funding from EDCTP for networking and to translate research results into policy was viewed favourably.

BMGF was also seen as a major funder by the interviewees with the main difference being that although it funds very large trials, it does so with a top-down and directive approach, rather than funding an investigator-initiated trial. According to one key opinion leader, this means that BMGF exerts closer control on trials, including in terms of monitoring progress and milestones and sitting on the trial.

---

117 Technopolis (2016) Mid-term evaluation of second programme for Global Health and Vaccination Research (GLOBVAC2)
118 Ibid.
steering committees, which “is suboptimal and inhibits flexibility”. BMGF’s end-to-end approach was seen as an advantage in that all the questions that need to be answered before a policy decision are identified in advance and policy makers (e.g. WHO and country level policymakers) are involved before a clinical trial is even started. This means that the research undertaken is directly relevant to the needs of the health systems in LMICs. In addition, qualitative research and research for countries to identify what will be required for implementation is often undertaken in parallel to the trials, which shortens the timeline for implementation and impact.

The NIH was described as being very ‘US-centric’ in its approach. However, one interviewee stated that its large resources, better costing models and trial networks in LMICs offer distinct advantages over the JGHT. In addition, its other capacity building efforts e.g. through the Fogarty International Center allows early career researchers from LMICs as well as the US to build professional networks and gain the necessary skills and experience to apply to international global health research programmes.

Opportunities offered by other funders and programmes to engage with policy stakeholders in LMICs were a key distinction for a few interviewees. Examples cited included

- Wellcome Trust, where researchers can apply for public engagement funds when applying for a grant, which can be useful to bring relevant LMIC stakeholders together
- DFID, where programmes are tailored to local needs and local stakeholders are engaged, increasing the likelihood of getting implementable results from the research funded
- NIHR, which has recently offered small development grants to hold consultations with ministries of health in LMICs to identify the priority research questions in the local context

The lack of a specific disease focus in JGHT in contrast to both EDCTP and BMGF was viewed very positively by several interviewees. A disease focus was seen as somewhat limiting as research proposals falling outside the funders’ areas of interest will not be funded, leaving gaps in the funding landscape. It was also noted that as individual funders are pooling their resources in the JGHT, researchers are able to access larger amounts funding, and hence can deliver larger trials.

6.4 Current gaps in the global health trial funding landscape

Researchers and key opinion leaders reported a number of gaps in the research funding landscape.

The majority of PIs (89%, 34 of 38) and co-investigators (94%, 124 of 132) surveyed indicated that there were critical gaps in the global health funding landscape, with 30-40% of researchers referring to a gap in the type of research funded, a gap in funding for critical research infrastructure, and a gap in funding for capacity building and training. PIs of development awards (67%, 8 of 12) more commonly held the view that their health field/intervention was underfunded compared to PIs of full awards (24%, 4 of 17). 17% of PIs (5) and 30% of co-investigators (22) indicated a gap in follow-on funding to support implementation of trial findings, policy engagement, and funding during the manuscript writing stage. This was seen as a barrier to impact; as one respondent summarised: “In many, cases studies are funded and have to operate on stringent budgets. After the end of the trial there are minimal funds left for publication. As such, policy makers may receive results alongside the international community. They are often very minimally engaged in the analysis and interpretation of these results. This may impact ownership as well as utilisation of results moving forwards”.

Gaps reported by researchers and key opinion leaders in interviews fell into four categories:

- Implementation research, taking results from a successful trial and understanding how to scale up the intervention across different locations
- Lack of sufficient funding for research on NCDs in LMICs
- Capacity building in LMICs, e.g. support for junior PIs, funding for graduate students and training in statistics and health economics
- Funding for smaller Phase II trials, to enhance the design of Phase III trials: “These are very valuable and cheaper (i.e. more value for money), but there are few mechanisms to support these. It means that some researchers jump prematurely into Phase III trials in order to secure funding.”
7 JGHT funding scheme - design and management

7.1 The design of the JGHT funding scheme

7.1.1 Overall impressions of the design

Researchers and key opinion leaders were predominantly positive regarding the design of the JGHT. Positive aspects mentioned included:

- The broad range of topics funded under the scheme, e.g. 69% of PIs (24 of 35) and 53% of co-investigators (55 of 104) surveyed expressed positive views of the type of research funded.
- The researcher-led, bottom-up approach to funding, e.g. 81% of key opinion leaders (13 of 16) felt this was a crucial aspect of the scheme.
- The substantive level of funding available, e.g. several researchers and key opinion leaders (5) specifically highlighted that the JGHT was one of a handful of schemes that supported (expensive) RCTs.
- The opportunity for LMIC institutions to apply directly.
- Geographical coverage, without limitation to specific countries or continents, including support for multi-country trials.
- The focus on impact, with projects positioned ‘at the implementation-end of the research spectrum’.

The scheme’s emphasis on stakeholder engagement (such as policy makers) throughout the research process and involvement of social science and health economics experts in the trial team were commended, as both elements were seen to facilitate policy influence and health impact. However, a small number of PIs explained that the requirement for health economic and social science studies as part of the project was not appropriate for all trials. For example, one researcher explained: “We did it because it was required, but it wasn’t really necessary in our situation.” A key opinion leader commented that the cost of some interventions can be driven down after an intervention has been shown to be effective; current costs should hence not dictate whether a piece of research is undertaken or not.

Nearly all PIs (97%, 37 of 38) and the majority of co-investigators (84%, 121 of 144) surveyed agreed that the design and requirements of the JGHT enabled the scheme to attract high-quality proposals, and more than half of PIs (57%, 21 of 37) and three quarters of co-investigators (79%, 115 of 146) felt there were no aspects of the JGHT design or requirements that could be improved. Researchers and key opinion leaders consulted in interviews were also mainly positive about the scheme.

Conversely, 29% of PIs (8 of 28) and 18% of co-investigators (15 of 83) surveyed stated that the JGHT did not have any obvious weaknesses when specifically asked about these. 29% of PIs (8 of 28) considered the amount of funding available a weakness, both in terms of the size of awards (3) and the lack of funding for additional aspects such as dissemination, capacity building or student fellowships (4). 18% of PIs highlighted issues pertaining to administrative factors (e.g. timeline, fund transfer logistics) (5).

Among co-investigators, the most common weaknesses reported were related to award administration, such as lengthy processes and limited communication with funders (24%, 18 of 76). A higher share of co-investigators working at LMIC institutions (40%, 12 of 30) considered these problematic compared to respondents from HICs (Figure 44). Other issues raised were the lack of funding for capacity building and follow-on studies (18%, 14 of 76), and the JGHT’s bias towards established and UK-based PIs (16%, 12; 20% of co-investigators from LMIC institutions). A number of interviewees added that this bias may (at least partially) be due to a lower level of English language skills, less experience in and precedents for writing a ‘polished’ proposal, and a low level of knowledge of the UK research system (including its ethical review process).
7.1.2 Size of awards

Several researchers and key opinion leaders raised issues with the size and length of JGHT awards. While the JGHT was appreciated as one of few funding programmes that provide substantial grants to finance RCTs, the grant sizes were nevertheless too small to appropriately cover the cost of full global health trials. In addition, a few researchers and key opinion leaders considered that the awards were of insufficient duration. Other funders – the EDCTP, US NIH and BMGF - were cited as offering much larger awards and (at least in the case of the EDCTP) over longer periods of time.

Comments by a number of researchers implied that they perceived the JGHT to fund a certain size of award (£2-3m, possibly £4m), over a certain period (around 3 years). In order for the proposals to be competitive, two interviewees reported that they had scaled down their original trial designs to reduce trials costs and enhance their chance of success. As one researcher explained: “You’ve always got to try to squeeze [the research] into what you think is going to be the correct funding envelope. So there’s never enough dedicated time at the end for writing up. It’s always trying to do things on the cheap. [...] I think the expectations of funders in terms of how much money trials should cost is unrealistically small”. On the same point, two other researchers asked for more clarity around the budget range and funding ceiling for full grants. Other aspects mentioned were a clarification of the preferred duration of trials, and the need to include a health economics and qualitative study. On this point, one PI expressed the view that health economics and qualitative studies may not be beneficial as part of the trial in all cases and could be realised at a later stage.

7.1.3 Design of the development award scheme

Researchers and key opinion leaders were overall positive about the development award scheme. All but one of the 14 key opinion leaders who discussed this funding stream were complimentary of it (93%), highlighting its importance in preparing the ground for full trials: By collecting baseline and feasibility data, the awards were expected to underpin the design of the full trial, giving confidence to sample size, outcome measures and implementation aspects. In addition, it could serve to forge strong relationships with stakeholders.

Two interviewees proposed the scheme be expanded, both in its overall budget to allow a larger number of awards to be funded, as well as in the size of individual awards, e.g. to include Phase II trials. A third interviewee advocated for an extended timeline for these awards to allow iteration of research approaches and learning. A suggestion was to offer a larger, longer grants for new interventions, allowing careful development of interventions before testing in a full trial.
However, there were a small number of researchers and key opinion leaders who raised issue with the scheme. Four interviewees felt the two-step approach dragged out the timeline; another did not think this type of research should be a priority for the JGHT.

Two interviewees felt that decisions on development award proposals should take into consideration potential funding through the full trial award scheme. As a key opinion leader explained: “I think we have to be very careful. Sometimes there’s a good idea, and we fund it. But when it comes around to the time of funding the full trial, we realise that it’s not one of our top priorities. So we have to find a way to be able to look at the development grant application with the eye to ‘would we fund a larger trial if this comes up positive’.” Accordingly, a small number of researchers who had applied for a full trial following a development award expressed some frustration that they had not been successful.

7.1.4 The application process

When asked to compare the JGHT’s application process and requirements with those of related funding programmes, nearly all PIs surveyed held a positive view (97%, 29 of 30), with the majority (63%, 19 of 30) describing the JGHT as “simpler than other schemes” and “straightforward”. A smaller share of co-investigators (31%, 24 of 78) considered the process simpler or advantageous, while 35% (27) felt that the process was similar to that of other funders. There were no major differences in the opinions raised between co-investigators from LMIC and HIC institutes and joint units.

A few researchers (from both LMICs and HICs) explained that the application process was less burdensome in comparison to similar programmes, and in particular when compared to the EDCTP. A small number of interviewees (3), all from LMICs, had found it difficult to understand and complete the (many) required forms and UK ethical approval process, and a number of suggestions were made to facilitate this for potential LMIC applicants (see section 7.2.5).

It was noted that the timeframe from application to award, especially for the two-stage full trial awards, was almost a year, during which the research field and conditions at the proposed trial location may already have changed.

7.1.5 Award administration

26% of PIs (9 of 35) and 34% of co-investigators (35 of 104) surveyed pointed to the administrative processes as a key strength of the programme. Programme staff was described as approachable and friendly. A few PIs from LMICs would have liked to more frequent communication and interaction with programme management.

Most interviewed researchers who raised the point of administrative processes also expressed a positive opinion on the monitoring arrangements for JGHT projects. These were described as ‘light-touch’, allowing PIs to dedicate more time to research. As one PI summarised: “In this particular scheme, they treat you like adults: they give you the money, they trust you to do the work, they ask you to publish, they want you to be advocates and get [your research] out there. Then you fill in your ResearchFish® and it’s perfect.”. However, the predominant view among key opinion leaders and representatives of the JGHT funders that current monitoring arrangements were insufficient to capture the scheme’s outcomes and impacts (see section 7.8).

Researchers also commented positively on the JGHT’s flexible approach to funding and openness to accommodating changes in case of unexpected changes in project circumstances. The most frequent changes in projects funded concerned the timeline of the project (projects started late needing a no-cost extension), budget allocation (projects needing to allocate funding differently from the proposal stage) and budget amount (costed extensions).
7.2 Additional activities to improve impact

When asked which additional activities the JGHT could support that would help it achieve its aims, 21% of PIs (7 of 33) and 31% of co-investigators (43 of 139) considered training an important area - especially for early/mid-career researchers and researchers from LMICs. Support for other types of research and for dissemination and knowledge exchange were both highlighted by approximately 21% of PIs (7 of 33) and 22% of co-investigators (30 of 139). Training was more commonly reported by co-investigators from LMICs (39%, 23 of 59) than co-investigators from HICs (25%, 13 of 53) (Figure 45). Conversely, a smaller share of co-investigators from LMICs (14%, 8 of 59) suggested support for other types of research compared to 23% (12 of 53) of co-investigators from HICs.

Figure 45 Additional support activities suggested by co-investigators (LMIC n = 59, JU n = 22, HIC n = 53)

Source of data: Survey of co-investigators

38% (14 of 37) of PIs and one quarter of co-investigators (25%, 36 of 143) surveyed were aware of additional activities covered by other funders that are effective to achieve impacts and health outcomes. Examples provided mainly related to the support for dissemination of results and policy engagement (e.g. as provided by EDCTP, Wellcome Trust and BMGF), for implementation or scale-up (e.g. as provided by BMGF), and for capacity building (e.g. EDCTP, Wellcome Trust-Newton Fund Collaboration, GCRF).

7.2.1 Training and capacity building

Survey respondents highlighted training and capacity building as an important element the JGHT could support to achieve impacts and health outcomes (see above).

While many PIs reported that a lack of capacity had been a challenge for trial implementation, only one of the PIs and one of the key opinion leaders interviewed felt that funding should be provided as part of the JGTHI. Others explained that while capacity building is an important outcome of the research, it should not be a major focus of the JGHT.

Two other key opinion leaders suggested that the funders encourage LMIC institutions to include junior investigators in the project, and require evidence that LMIC researchers are fully involved in developing and implementing the research, and analysing the data gathered. As one representative of a funding organisation explained: “The main way the JGHT could help build capacity is by having scientists train under the scheme and improve their scientific knowledge and skills to take forward in their career. There are many other schemes that target capacity building and meet this need, and they are better designed as capacity building schemes.”
7.2.2 Funding for dissemination and engagement post-award

Interviewees broadly agreed that research impact could be enhanced by providing more support for dissemination and stakeholder engagement after the trial has concluded. With many projects overrunning, the planned timeframe shifts, leading to dissemination and engagement activities having to take place after the grant has closed. This poses a problem for investigators, who for financial reasons need to move on to a new grant and new project. This is particularly difficult for investigators working at LMIC institutions. As one key opinion leader summarised: “Researchers from LMICs don’t have any institutional support via core support or tenure. […] In LMICs, income is tied more heavily to the project grant; [investigators] do not have the flexibility and luxury to work on engaging stakeholders and writing papers once the grant closes.”.

Seven PIs specifically recommended the JGHT provide funding for these tasks. The majority of key opinion leaders (70%, 7 of 10) also supported this approach. Of these, four suggested a separate funding stream (within the JGHT) that PIs could apply for. However, two key opinion leaders in favour of additional support for post-trial stakeholder engagement also cautioned that this should not become added to the responsibilities of researchers but could instead involve funders’ policy departments.

Two PIs suggested a ‘phased approach’ to project funding, whereby “just the PI and project manager are funded right at the beginning, for the first six months. When the trial starts, the amount of funding increases. It then has a long tail at the end, just funding the PI and a project manager or someone to close out [the trial] and do all the dissemination.”.

7.2.3 Support for other types of research

Several key opinion leaders and researchers suggested that the JGHT could broaden the types of funding provided to include smaller trials (Phase II), implementation pilot studies, ‘bolt on’ laboratory-based work, and aspects of health systems research. There was no consensus on the additional type of research to be supported.

7.2.4 Dissemination of results through the funders’ existing networks

Key opinion leaders were asked to comment on the option of disseminating research results through the funders’ existing networks, i.e. funders taking an active role. The majority of key opinion leaders had a positive view of this option (86%, 6 of 7). Three interviewees felt this should not be a blanket approach, but on a case-by-case basis. Two interviewees suggested meetings with the relevant stakeholder audience to present results, and one proposed a joint forum with the EDCTP.

7.2.5 Supporting LMIC investigators during the application stage

Several interviewees pointed to a ‘monopoly’ of a few institutions in securing awards, with few LMIC researchers – with good and innovative ideas - able to compete. This was put down to a number of factors, including a language barrier, a lack of experience dealing with MRC application forms, and a lack of methodological and statistical expertise.

The majority of key opinion leaders (82%, 9 of 11) supported additional efforts funded by the JGHT to assist LMIC applicants in principle, but also cautioned against lowering the quality bar of the review process or awarding funding to LMIC institutions that do not have the necessary capacity and infrastructure to lead a full trial. As one key opinion leader explained: “There is no point if nice grants are written with help, but then there is not capacity to support the delivery of the trial. Support with proposals is great, but it should be done with caution.”.

A number of concrete suggestions for improvement were made by key opinion leaders and researchers:

- A proof-reading service for LMIC applicants, as part of the application, to identify cases in which vocabulary from the call for applications has been misunderstood. For example, one UK-based full trial PI explained that: “I recently encountered somebody who didn’t know what safeguarding really was. They would have been able to do what was necessary, if they’d understood the term. But they thought it was more about financial due diligence.”.
• Providing detailed feedback to unsuccessful applicants to enable them to learn the skill of grant writing as relevant to UK-funded projects. One interviewee suggested this could be targeted towards grants that received high scores and came close to being funded.

• Make available supporting resources, such as examples of successful applications and webinars explaining how to fill in the various forms.

7.2.6 Increased communication between JGHT funders and PIs

Two PIs from LMICs would have also liked to see more involvement of JGHT funders with individual projects. They expressed that, while donor representatives were present on each trial's steering committee, they were not as involved as donors in other funding programmes during the course of the project. As a PI of a full closed trial explained: “It's felt quite hands off so it would be nice to have a bit more of an ongoing dialogue about these studies on the challenges that we have been experiencing, and maybe having early opportunities for discussion”.

7.3 Options for changes to the design of the JGHT

A number of options for changes to the JGHT were discussed with key opinion leaders and representatives of JGHT funders in interviews:

7.3.1 Prioritisation of health issues

Funding calls invite applications restricted to one or a small number of health issues, leading to a ‘critical mass’ of research in the specified area(s) to increase the potential for impact.

The majority of key opinion leaders and representatives of JGHT funding organisations disapproved of this option (81%, 13 of 16). The wide remit was described as a key strength of the scheme; restrictions would limit the flow of new ideas and lower the overall quality of funded projects. Interviewees also highlighted the fact that health needs in LMICs change and cannot be predicted; researchers and public health experts on the ground have the best understanding of the issues to be addressed. As one key opinion commented: “I think it's much better to do it this way [response-mode]. [...] I think it's very close-minded to think that a relatively small team [the prioritising committee] can put together all the important global health questions and then limit the rest of the world to that. I think that's totally the wrong way around. Being open to whatever comes through the door is the right way to do it. Too many other funders are going the other way, believing that they're the ones who know how to save the world.”

However, several interviewees supported that calls continue to encourage researchers to submit applications in certain areas, felt to be important and under-represented in the current grant portfolio.

7.3.2 Commissioned funding stream for research high priority questions

Research addressing a key question for policy makers is commissioned, leading to a definitive answer with immediate policy implications.

Views on this option were more evenly distributed, with 40% of key opinion leaders and representatives of funding organisations (4 of 10) in favour of this option, alongside the response-mode funding stream, to enable a focus on key questions. Of the six interviewees opposed to this suggestion, three are not in favour of top-down approaches (see above), two thought that commissioned research is more suitable to be picked up by other funding programmes, and one held the view that the budget of the JGHT is too low to accommodate both types of funding.

119 7 representatives of JGHT funders were interviewed as part of the scoping phase, using a different interview guide. Where comments addressing the JGHT options were made, these were incorporated into the analysis.
7.3.3 Focus funding on larger, more definitive trials

To provide the strength of evidence required as a basis for global policy making, the JGHT should focus on funding larger trials that result in a definitive answer across a range of contexts.

The majority of key opinion leaders and representatives of JGHT funders were not in favour of increasing the scheme’s focus on larger trials (62%, 8 of 13). Of these, three interviewees were actively opposed to larger trials, pointing to the need for multiple studies in multiple contexts and timeframes rather than one large trial to robustly inform policy. As one interviewee explained: “I’m not necessarily in favour of grants for huge trials that are definitive, because I don’t actually think that science is that simple. I think it is more powerful to have multiple trials that show signals and show smaller signals than one trial as a big signal.”. Five considered the flexibility of award sizes a key strength of the JGHT that should not be changed, and explained that the main focus should remain whether the study will answer the research question. This does not exclude larger awards – as one interviewee explained: “If a proposal clearly demonstrates the needs for a larger budget to answer an important question, then there would not be barriers to funding.”. Another key opinion leader suggested a multi-step scheme: If a trial is successful in one location, the scheme can have a built-in option for trialling in other countries.

Of those supporting an explicit shift to larger trials, two would like to see this coupled to prioritisation of research questions to be addressed, one would like to see more multi-country trials, and another favours multi-arm trials. Three recommend that larger trials are supported by smaller Phase II studies and policy engagement support.

7.4 Promotion of the scheme

For researchers in the UK and LMICs to be aware of the JGHT and to attract the ‘right’ proposals, the funders need to undertake promotional activities.

Award holders broadly agreed that information on the JGHT is communicated through the right channels and that information reaches the relevant research communities. This view was expressed by 92% (35 of 38) of PIs and 73% (110 of 149) of co-investigators surveyed. However, several PIs and co-investigators, both from LMIC and HIC institutions, reported that they had not known about the scheme until collaborators had made them aware of it.

Researchers and key opinion leaders interviewed did not feel they were in a position to comment on whether the JGHT was sufficiently promoted. While the level of awareness in the UK was considered high, interviewees were not certain about the level of awareness globally. Most had the feeling that it was ‘probably’ adequate, with researchers in LMICs who are likely to be successful in applying being aware, but thought difficult to judge the full extent.

When asked about the scheme’s promotional activities, one closed award PI based at an LMIC institution noted that he had not seen information on recent calls for proposals, and that the scheme had “somehow dropped off my radar”; another PI from an LMIC institution had heard of the scheme from a mentor but did not think others at the university were aware. A further PI commented that: “I suppose [the JGHT is communicated through the right channels], but I don’t think they’re very prominent. Only very well-established investigators would dare to go for those awards.”.

Suggestions for improvements in communication of the scheme included sending calls to all previous PIs and co-investigators, dissemination of calls via the medical literature, and activities specifically targeted at increasing awareness in LMICs and outreach to health ministries and special interest groups.

7.5 The review process

Current and former review panel consulted considered the review process to be fit for purpose, and to ‘work well’. A number of PIs of full trial awards also called out the review process as one of the JGHT’s strength. As one PI explained: “A major comment was made about the study design that we were proposing in Stage 1 and we changed, radically. And I appreciated that input. So I think to have two stages is great and to have really robust reviewing is important. And we all benefit from it in the end.”
Committee members were described as ‘very collaborative and respectful’, despite a range of opinions across the panel. The meetings are well run, but broadly perceived as pressed for time. As one committee member commented: “At the end of the review process, when all of the studies are ranked, and the decision needs to be made where the cut-off should be: This step can be somewhat hurried, because it takes place at the very end of the meeting and people need to leave to catch planes etc. Ideally there should be more time dedicated to this step although it may be difficult to work out logistically how this could be done.”.

Committee members highlighted that the number of proposals to review had burgeoned in recent calls, and that it was now a challenge for reviewers to master the workload this represents. Some of the forms were also considered difficult to work with, placing additional burden on the reviewer.

Views on whether the committee encompassed the required expertise varied. Provided the broad range of topics covered by the JGHT, two committee members felt that “sometimes, we don’t have the right experts in the room”. Others explained that this was well covered by the selection of external peer reviewers, but one nevertheless would welcome “the option to co-opt someone in, just for that particular application, so that there is a person who is knowledgeable of the subject in the discussion.”. A researcher felt that more focussed programmes would have more subject-specific experts on the committee, and that this was a challenge for the JGHT due to its broad scope. However, another committee member was very positive about the trial expertise of the panel, and felt the committee was better suited than those of other schemes: “Normally, the funding committee is made up of a mixed group of people. Only a few, if any, may have any expertise in trials. The great strength of the JGHT committee is that virtually everybody on the assessment panel has expertise in trials, so they are the best group to evaluate these.”.

A few committee members and representatives from funders suggested that decision making by the panel take into account additional aspects, such as gender balance, the share of LMIC-led awards, or the level of contribution of LMIC researchers to the proposed research, and a stronger emphasis on the potential of impact of the proposed research on the top causes of mortality and morbidity.

Committee members agreed that the quality of the majority of proposals from LMIC researchers tended to be lower. Two specifically pointed to the lack of experience in proposal writing. Another highlighted that a small number of institutions were ‘monopolising’ the scheme, having an excellent track record of submitting ‘polished’ applications, but not necessarily innovative approaches.

A few researchers felt there was a lack of transparency in the review process and criteria. As two researchers explained: “As an applicant you get preliminary feedback from reviewers. And then you get a decision from a panel. And the preliminary feedback can sometimes be completely contradictory to the final decision feedback. For instance, you can get preliminary feedback that says: “I think you might have too big a sample, you should reduce it”. And then you can get turned down with one of the chief criticisms being the sample size is too small.”. Another pointed to an example where an application had received amazing reviews but did not get funded.

It was also suggested that the review committee appoint more women and experts from LMICs.

### 7.6 Perceptions of how the JGHT has evolved over time

The overarching aim of the JGHT has not changed over the past 10 years: Support for trials generating evidence which ultimately lead to policy or practice changes. Researchers and key opinion leaders alike continued to support this aim, and many key opinion leaders pointed to the scheme’s successes in supporting the highest quality science to inform a broad range of health needs, and in achieving policy influence (in a number of areas they were aware of).

The JGHT was considered to fill a clear gap in the research landscape:

- At the time the it was established, sources of funding for researcher-led global health trials were limited; funding tended to be more focussed on individuals (e.g. fellowships) and awards were
smaller. Pooling of resources as a partnership of funders allowed for a cohort of 6-10 full trials to be funded.

• Today, the JGHT continues to fill a gap, notwithstanding developments in the funding environment over the past decade, such as a broadening of the scope of the EDCTP (see section 6). It is considered to be ‘unique’, combining a response-led approach without a focus on specific health needs and the ability of LMIC researchers to apply. In the words of a key opinion leader: “It is the only scheme with response-mode calls to fund single large Phase III-type clinical trial with the aim of changing policy.”. Others highlighted specific research gaps the JGHT fills, such as research on repurposing of drugs and effectiveness studies. One interviewee summarised with “I feel [the JGHT] fills an important gap in the middle, between products being developed and then evaluated in field studies and more efficient use of existing products.”

In interviews, key opinion leaders were aware that the earlier JGHT calls had supported more ‘traditional’ trials on infectious diseases. The (welcome) impression was that over time, the scheme had become more innovative, and expanded to address a broader range of health issues as well as more implementation-focussed trials. As one interviewee explained: “The JGHT became a signalling device that types of projects that did not perfectly fit any individual funders could receive funding. This was particularly important for some of the health systems type trials but also some of the larger trials that would be a risky for one funder to support alone.”.

However, key opinion leaders also raised a number of aspects of the JGHT they felt needed addressing:

• Enhanced focus on implementation trials: The scheme was described as “still having a tendency to focus on possibly too simple interventions, as opposed to some things which are a little bit more embracing of the complex reality of health systems”. While these trials are more difficult to conduct, and require a broader range of partners, they are “critical to turn research outcomes into health outcomes.”. Funding for implementation research was also highlighted as a gap in the research funding landscape.

• Re-focus on definitive studies: Several interviewees (key opinion leaders and funders) felt that the scheme had ‘stagnated’ and needed to refresh. Researchers were writing proposals to fit the scheme (and hence maximise chances of success) rather than to conclusively address the research question and aim. There were concerns that this represented a barrier to impact, as a single trial at a single location is too small and context-specific for scale up.

7.7 Added value of a partnership of funders

The four funders, committee members, and researchers had an overall positive view of the partnership. While differences in the organisations’ scopes and expertise were acknowledged, some interviewees saw this as a strength, ensuring an informed, coordinated approach across all four organisations. No other issues were raised, but a range of benefits were cited:

• Pooling budgets and de-risking investment: Pooling of budgets has allowed a larger portfolio to be supported, and de-risking investment for each organisation. This has enabled funding of larger trials as well as some more ‘novel’ - and hence riskier - areas of investigation, such as menstrual cups and interventions to reduce violence in schools.

• De-fragmentation of the funding landscape: The JGHT has provided a single point of call for researchers looking to run a global health trial. It has unified the review process under a single review committee; as one interviewee explained, in this way applications from across health fields can be compared to each other and the best ones selected for funding, raising the quality of UK-funded trials. A unified review process also avoids duplication and competition between funders for the ‘best’ projects. This is more efficient for researchers and funders alike, and funders can draw on their respective expertise to inform the review process.

• Closer cooperation between funders: Rather than each pursuing their own priorities, the JGHT allows funders to discuss and coordinate strategies. This has also led them to identify and address
other funding gaps on the path to implementation. For example, the JGHT led to a new joint scheme (health systems research), and a second scheme (implementation research) is currently in pilot stage (via the Global Alliance for Chronic Diseases, GACD). A few interviewees mentioned some tensions between the funders, as each has a different mandate. One key opinion leader alignment between the four funders might mean that certain types of research outside the JGHT are unable to access funding.

- **Sharing of expertise:** Several key opinion leaders highlighted that the partnership enabled funders to bring their respective expertise to the table, e.g. Wellcome for technical aspects of trial design, MRC with strong scientific background, DFID for working in LMICs and policy translation, and DHSC with a strong understanding of the UK network.

- **Broadening areas of research and the research community:** The establishment of a separate Development Award scheme helped to provide funds for pilot studies in global health. This is not only de-risking follow-on research, but also serves as an entry point to global health research and trials for less experienced PIs, and an avenue for preparing the ground in areas not previously involved/addressed (both geographic and in terms of health needs).

Key opinion leaders and representatives from the funders broadly agreed that the partnership had helped to maintain the UK’s reputation and international leadership in producing high quality research of relevance to LMICs. As one interviewee explained: “It helps the reputation very much. We come in at scale and do the job properly.”. Another pointed out that each funder has a different sphere of influence; by working together, the overall reach of the scheme is expanded.

However, it was notable that of the seven international funders interviewed, the representatives of the four North American organisations had not heard of the JGHT. Similarly, a key opinion leader reported that contacts at the US CDC did not know of the scheme. These instances may be down to the individual consulted or may indicate a general lack of awareness of the JGHT on the North American continent.

### 7.8 Project monitoring & evaluation

Most key opinion leaders and funders pointed to 1) research publications and 2) policy influence as the key indicators to track for JGHT awards. The small number of interviewees who mentioned measuring health impact as an indicator, e.g. changes in morbidity and mortality in the trial location and beyond, thought that this would be too difficult to track (and outside the knowledge of the PI).

In line with the MRC’s reporting requirements for all funded research, award holders have to annually report outputs and outcomes via the ResearchFish platform. This includes reporting on publications and policy influence, as well as other indicators such as funding secured, dissemination activity, and tools, databases, software, IP and products developed.

Many key opinion leaders expressed the view that monitoring via ResearchFish was ‘better than nothing’, but that additional reporting should be put in place to track outcomes and impacts. Suggestions for enhanced monitoring included:

- An end-of-grant report, which is reviewed by the review panel and scored, including for aspects such as dissemination and post-trial stakeholder engagement and thus incentivising researchers to focus on these aspects. The end-of-grant could also be used by funders’ communication teams to showcase some of the outcomes.

- Use of ResearchFish to identify potentially interesting trials, and develop case studies for these

- Keeping in touch with the PIs after the trial, and potentially beyond the five-year ResearchFish reporting period. One suggestion was to have a regular short phone call with PIs to discuss any developments.
This review's experience with ResearchFish® mirrors the view that it is good starting point, but it provides neither a complete nor a rounded picture. Regarding the two key indicators of publications and policy influence:

- The category ‘Publications’ suffered from a ‘deluge’ of reporting, making it difficult to identify whether the trial has published its main findings, and a lack of clarity on the degree to which reported publications have a direct link to the funded project. Details on the main trial paper are often included clinical trial registries – but not always.

- The category ‘Policy’ provided some valuable information, but without additional investigation, it was difficult to understand the level of influence achieved and the implications thereof. Of the ten instances in which findings from JGHT-funded trials had influenced WHO policy, six were reported on ResearchFish®, while four were not captured. Latter related to one WHO recommendation (see Case study 7), two instances where data on products used in the trial had informed WHO policy (see Case study 4 and Case study 8), and one instance where the trial had lent confidence to a contested WHO recommendation (i.e. not change). Also not reported was one instance where trial findings had informed national policy (see Case study 1).120.

On the basis of this experience, and resource permitting, we recommend additional monitoring of key outputs and outcomes. This could take the form of a) engaging with and developing case studies from trials reporting of outcomes in ResearchFish®, b) a light-touch end-of-grant report, and/or c) a follow-up survey requesting key information to update on progress and outputs/outcomes. Any additional monitoring has to be supported by resource on the part of the implementing funder; e.g. development of case studies. Recommendations for monitoring are further detailed in section 8.2.5.

8 Conclusions and recommendations

8.1 Conclusions

This review of the JGHT was guided by four overarching objectives:

1) To assess whether and how the JGHT scheme has delivered on its core aim i.e. the generation of new knowledge about an intervention and its contributions to improving health in LMICs

2) Whether tangible outcomes and impacts have been achieved from the funded research

The JGHT has delivered on its core aim and achieved tangible outcomes and impacts: JGHT-funded research has generated new knowledge about interventions which in turn are starting to contribute to improving health in LMICs. Eleven trials - 39% of JGHT-funded closed full trials - have informed, or are about to inform, WHO and national policies. Nine full trials and one development award have led to the implementation of a health intervention. A further 10 trials - 36% of JGHT-funded closed full trials - have high potential for success, as indicated by the nature of the finding and the level of policy engagement by the study team. As more trials complete, further outcomes can be expected.

3) To identify ways in which the value gained from this type of research/research programme can be increased

Key enablers and barriers to policy influence and implementation identified centred around two main aspects: a) the utility of data and external conditions, and b) awareness, understanding, and buy-in by those who are to take up the evidence. Section 8.2 provides a range of recommendations for how the value gained from JGHT-funded can be increased, in relation to both the type of research conducted, and the level of stakeholder engagement prior to, during, and after the award.

120 Other national strategies informed by JGHT awards are still awaiting release.
4) To provide guidance on future monitoring of the scheme

Most researchers welcomed the ‘light touch’ monitoring requirements of the scheme. However, while information reported in ResearchFish® indicates outcomes ‘in short-hand’ for many (but not all) awards, it does not enable a full understanding of the implications for health in LMICs, nor does it identify findings with potential for policy influence / health impact that would benefit from additional support to engage with the relevant stakeholders. Section 8.2.5 makes a number of suggestions to improve future monitoring, depending on resources available: Engagement with trials identified through ResearchFish® submissions, a requirement for an end-of-grant report, and annual requests for information to complement reporting through ResearchFish®.

8.2 Recommendations

Based on evidence and opinions gathered throughout the review, five recommendations have been formulated. These are presented in Table 18 and set out in more detail in the following sections.

Table 18 Summary of recommendations for the JGHT

<table>
<thead>
<tr>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Keep the overall design of the JGHT, but clearly communicate the scheme’s award parameters to potential applicants</td>
</tr>
<tr>
<td>2) Provide additional support for stakeholder engagement, both pre- and post-award</td>
</tr>
<tr>
<td>3) Increase support for LMIC researchers, including resources to assist with proposals, promotion of JGHT calls in LMICs and ‘match-making’ activities to facilitate access to expertise and infrastructure</td>
</tr>
<tr>
<td>4) Agree on key criteria for project selection, defining how to balance between the size of the health need addressed, projects’ risk of interventions not proving effective, and their likelihood of policy influence</td>
</tr>
<tr>
<td>5) Launch additional project monitoring activities</td>
</tr>
</tbody>
</table>

8.2.1 Keep the overall design of the JGHT, but clearly set out the scheme’s award parameters

The majority of researchers and key opinion leaders supported the current design of the JGHT, and the scheme has enabled trials that have achieved a variety of policy influence and health outcomes. An overarching change in design is not required.

However, the issue of under-funded projects and unrealistic timeframes was raised repeatedly. Delays and issues with cost were mainly due to prolonged ethical approval processes and slow recruitment. The delays then impacted on the level of engagement post-trial, as no time remained at the end of the trial. To some degree, this issue is the result of a perceived ‘time and budget limit’ for full trial awards, with PIs ‘squeezing’ their proposed trial timelines and budgets – and possibly methodologies and scale of trial - in order to be competitive.

To avoid this approach, funders should clearly communicate that time and budget are truly flexible and re-focus researchers on asking the right questions and proposing appropriately sized approaches to answer them. This clarification could be provided within the call text.

8.2.2 Provide additional support for stakeholder engagement

The review showed that stakeholder engagement in the design and implementation of the trial, as well as post-award, is an enabler of policy influence and health outcomes. In addition, engagement with communities affected before the trial helps to avoid challenges during its implementation. To maximise the potential for policy and health outcomes and impacts, the JGHT should consider options to further support pre- and post-award stakeholder engagement:
Pre-award

- The JGHT could support joint working between different trial institutions, and between researchers and relevant policy makers, by offering small grants for ‘partnership workshops’, similar to the NIHR’s Proposal and Partnership Development Awards (funding of up to £10,000 to support partnership development), for applicants invited to submit full trial award proposals. This will allow trial plans to be optimised and ensure that all partners are fully informed, with the opportunity to provide input and local perspectives.

- The development award scheme is acknowledged as an important source of funding to build community and policy engagement and awareness, test (and adapt) the proposed intervention, and develop a better understanding of the local context in relation to the health need (e.g. associated risk factors), the proposed intervention (e.g. acceptability), and structures for implementation of the trial (e.g. societal decision making processes). As proposed by several researchers and key opinion leaders, the JGHT could consider an expansion of the development award scheme, both in terms of the amount of funding available per call, and in terms of the size of the individual awards. While its effectiveness in preparing for full trials is not yet clear (see section 5.4.5), this could to be monitored going forward and considered when more information becomes available. If shown to be effective at de-risking full trials, an expansion of this scheme would also avoid ‘costly’ research mistakes, contributing the JGHT’s VfM; this may be particularly important when addressing complex diseases across cultural contexts and health systems.

Post-award

- The JGHT could provide opportunities for PIs or other members of the team to apply for additional funding to cover engagement activities after the award has closed, as some awards are likely to require sustained engagement with policy makers and implementing organisations after the trial has closed in order to realise their full potential for policy influence and take up.

- The funders should explore options for maximising opportunities for dissemination and engagement for trials with high potential for policy influence and health impact. PIs may not always be in a position to continue engagement beyond the trial or may not have the right network of connections to optimise dissemination. To enhance dissemination and learning, efforts could be combined for multiple trials addressing the same health need but in different geographic locations (need-specific research-policy networks), or for multiple trials in the same geographic location but addressing different health needs (geographic networks, working within similar contexts). Meetings could also involve trialists funded from other sources, e.g. working with the EDCTP secretariat. (To enable this approach, the funders need to be informed of, or monitor, the outcomes of JGHT-funded projects – see recommendation on monitoring.).

Funders could take an active role in these efforts, e.g. by targeting media and convening meetings. Alternatively, a team of specialists could be supported to provide this function. For example, the Knowledge Translation Network Africa (KTNet Africa) was a initiative funded by the Dutch Research Council (NWO) which provided a shared platform for health systems knowledge translation in sub-Saharan Africa coordinated by the Makerere University School of Public Health.121.

8.2.3 Increase support for LMIC researchers

Researchers from LMICs were described as having good ideas that address local health needs, but many lacked experience with the JGHT application process and had poor English language skills. To level the playing field and enable full participation of LMIC researchers, the JGHT could:

- Support the proposal writing process by:

---

121 Technopolis Group (2018) Final evaluation of the Netherlands Global Health Policy and Health Systems Research (GHPHSR) programme
- Offering **online resources to assist with proposals**, such as a sample proposal (to show the type of information and level of detail required), and a webinar (to explain requirements for the various forms to be completed)
- Offering a **proof-reading service** at the full application stage to correct grammar and choice of vocabulary
- Providing **detailed feedback to unsuccessful applicants from LMICs** to improve grant writing skills as relevant to UK-funded projects

- **Promote JGHT calls in LMICs** by sending an email to LMIC contacts (or all contacts) in the grants database. This will enable researchers involved in JGHT-funded research to alert LMIC colleagues and share their experience. The option of disseminating calls via the medical/scientific literature could also be explored.
- Offer **small grants for ‘partnership workshops’** for those invited to submit full trial proposals (stage 2) to facilitate full LMIC participation in UK-led trials, similar to the NIHR’s Proposal and Partnership Development Awards (see also recommendation 2 / section 8.2.2).
- Consider **“match-making” activities** in research areas where LMIC researchers submitted interesting ideas, but where the proposed team lacked the knowledge and infrastructure to conduct a trial. This could take the form of workshops or meetings centred on priority health areas, bringing together LMIC researchers and local / UK trials expertise.

8.2.4  **Agree on key criteria for project selection (wider strategic discussion)**

The partnership of funders was viewed as very positive across the board. However, it is clear that the different remits of the four organisations creates a certain level of tension, and the funders have not (yet) reached a consensus on future strategy.

The current stated aim of the JGHT is “to support the best proposals to generate new knowledge about interventions that promise to contribute to the improvement of health in LMICs, addressing a major cause of mortality or morbidity”. In the review process, this aim is currently operationalised by taking into consideration (Table 1):

1. **The scientific quality of the proposal**: Scoring criteria ‘Track record of applicant’ and ‘Study design and feasibility’
2. **The size of the health need**: Scoring criterion ‘Importance of the question/need for the trial’ - “Is there a need for such a trial now for this condition or group of patients in the proposed location(s), How important is the problem being addressed?”
3. **The potential level of impact on the individual**: Scoring criterion ‘Impact’ – “How important an advance would this be? [...] Is it likely to lead to significant improvements in health?” [here, interpreted as relating to the level of improvement seen by the individual; ‘cure’ vs ‘incremental improvement’]
4. **The potential level of impact on the population**: Scoring criterion ‘Impact’ – “Will the findings be generalizable?”
5. **The likelihood of impact**: Scoring criterion ‘Impact’ - “What is the likelihood that the findings will be taken up and implemented? Can the intervention be scaled up; is it cost effective?”

As a programme focussed on research, rather than capacity building, the first of these factors – scientific quality – is a pre-requisite for the success of the scheme. The development award scheme is available to applicants (increases track record score) or for projects in research areas with a lower level of knowledge (improves study design and confidence in feasibility).

Factors 2-5 – size of the health need, potential level of impact of the research on the individual and at population level (i.e. ‘cure’ vs ‘some improvement’), and likelihood of impact – vary in degree between awards funded. Figure 46 presents a simplified model of these factors, and the types of JGHT-funded trials within each category.
### Figure 46 Model of characteristics of funded trials

<table>
<thead>
<tr>
<th>Category 1: Issue widespread, intervention ‘simple’</th>
<th>Category 2: Issue widespread, intervention ‘complex’</th>
</tr>
</thead>
<tbody>
<tr>
<td>e.g. infectious diseases such as malaria</td>
<td>e.g. non-communicable diseases such as CVD</td>
</tr>
</tbody>
</table>

- Widespread issues that can cured/much improved with a single intervention/change
- Interventions focussed on drugs / products; low(er) context-dependency (i.e. generalisable)
- Research focusses on effectiveness; delivery within existing health programmes can help to test implementation
- A large body of research evidence already exists; trial needs to be of sufficient scale to ‘compete’ with existing research evidence
- Research is lower risk as the problem and tested intervention are strongly linked

A single trial can result in policy influence and health impact, as long as it is definitive

For global policy change, trials need to be large (and hence costly) to provide definitive answers across countries

Opportunity to partner with other funders

<table>
<thead>
<tr>
<th>Category 3: Issue less common, intervention ‘simple’</th>
<th>Category 4: Issue less common, intervention ‘complex’</th>
</tr>
</thead>
<tbody>
<tr>
<td>e.g. endemic diseases such as podoconiosis</td>
<td>e.g. CVD in patients with rare predisposing genetic variant.122</td>
</tr>
</tbody>
</table>

- Issues with limited range (endemic) and of low public awareness, can be improved with a single intervention
- Low level of research activity to date, baseline data may not be available
- Standard of care may not have been established
- Research focusses on effectiveness; smaller trials
- Research is generally lower cost and risk, as any findings will substantially increase the body of evidence on which to base policy decisions
- A single trial can result in policy influence and health impact
- Policy makers need to be engaged and interested in addressing the issue; awareness raising and stakeholder engagement are crucial

<table>
<thead>
<tr>
<th>Category 2: Issue widespread, intervention ‘complex’</th>
<th>Category 4: Issue less common, intervention ‘complex’</th>
</tr>
</thead>
<tbody>
<tr>
<td>e.g. non-communicable diseases such as CVD</td>
<td>e.g. CVD in patients with rare predisposing genetic variant.122</td>
</tr>
</tbody>
</table>

- Widespread, complex issues that cannot be ‘cured’ with a single, simple intervention
- Interventions focussed on behaviour/lifestyle, education and care; strongly context-dependent (i.e. not generalisable)
- Research focusses on local implementation in local context(s) (in addition to effectiveness)
- A large body of evidence already exists (from HICs but not LMICs)
- Research is high risk, as outcomes are subject to many external factors
- Includes issues where the full extent of effects is not yet understood, often in community settings (e.g. menstrual health management, clean stoves)

Large need, but requires multiple trials, embedded in local contexts, to achieve policy and health impact

Benefits from high level of involvement of local researchers and stakeholders

Funders need to accept higher risk of ‘failure’

Research in categories 1 and 3 drive the programme success metrics, as a single trial can result in policy influence and implementation of an intervention. And while category 3 research does not reach the same number of individuals as category 1, its research findings have a high likelihood of influencing policy in affected regions – as long as key decision makers have been engaged and are interested in addressing the underlying health need.

---

122 This is a hypothetical example; none of the trials funded by the JGHT and reviewed in this study fell into this category.
Category 2 includes areas of high need, to which there are no ‘easy answers’; many of these issues are also present in HICs (e.g. cardiovascular disease). Multiple trials are required to make headway against these complex conditions, and each intervention is likely to only have an incremental benefit to the individual who receives it. In addition, areas that have been relatively ‘under-researched’, such as menstrual hygiene management, associated consequences may not be fully understood (e.g. transactional sex and STIs), and interventions tested have to be tailored as the cultural and social components of the issue are emerging.

The funders need to agree on a strategic direction of the JGHT, setting out whether categories 1, 2, and 3 are all, and equally, within the scope of the scheme. Specific types of research, or research specific health needs, can be encouraged by highlighting these as part of the call text. The ‘research categories’ can also be further supported by a number of measures:

- Research in category 1 could be supported by **funding very large ‘definitive’ trials**, answering key research questions to inform specific policies. This could also take the form of commissioned research, and/or coordination and partnership with other funders such as the EDCTP (e.g. co-funding for trial sites in Africa).
- Research in category 2 may influence policy in a specific location, but as these types of interventions can be highly dependent on individuals’ behaviour and cultural context, solutions have to be tested in a wide range of settings. This is supported by a **high level of involvement of local researchers and stakeholders**, who are familiar with the context and health system. In recognition of the vast health need category 2 research addresses, funders have to be willing to **accept a higher risk of ‘failure’** in terms of “generating new knowledge about interventions that promise to contribute to the improvement of health in LMICs” (as interventions tested may not be effective), and a **lower likelihood of health outcomes and impacts**. In addition, many NCD trials required **longer timeframes** to reach endpoint, e.g. compared to infectious diseases; the timeframe of the award needs to be able to accommodate this.
- Research in category 3 is most likely to arise from **response-mode proposals**, with researchers on the ground identifying local needs and potential solutions and delivery mechanisms. For these types of projects, **stakeholder engagement is crucial** to raise awareness of the issue addressed, and has to be an integral part of the trial. While impacts will be limited in scope by the smaller number of individuals affected, the research has a high likelihood of influencing policy (provided there is stakeholder buy-in) – and practice (provided implementation can be financed).

8.2.5 **Launch additional monitoring activities**

ResearchFish provides information on outputs and outcomes achieved, but does not enable an understanding of activities undertaken to achieve these and progress made. **Additional monitoring of progress and outcomes** is advisable, enabling the funders to identify opportunities where additional support for dissemination and policy engagement could lead to policy and health outcomes. The extent of monitoring will dependent on the level of resource the funders have available:

- At a minimum, the funders could actively monitor ResearchFish for evidence of policy influence, and contact PIs to explore opportunities for supporting **scale-up** of influence and implementation, where appropriate. This approach requires little additional resource, but is also unlikely to identify trials with potential for policy influence that have not realised their potential.
- A single-contact measure would be to monitor via an end-of-grant report, requesting additional information as set out in Table 19. This will help funders to understand the policy implications of the trial findings and the research team’s plans with regard to future engagement. Where trial findings have high potential for influence, the funders can support PIs in this.
- Valuable information could be gathered at multiple points, during the trial and after the award has closed, via a short annual survey or request for updates on policy/implementation activity. This could be in the form of additional questions during the annual ResearchFish data collection (similar to NIHR beneficiaries provide additional data). This would also enable a deeper understanding of
the different approaches PIs and their teams take for engagement (and their levels of success), and flag any trials with limited engagement activity. For post-award surveys, trials with findings marked as ‘no potential to influence policy’ and ‘not suitable for implementation’ should provide a short summary of ‘lessons learned’, and can then be removed from the follow-up list.

A structured approach to collecting monitoring data from across awards would also help to assess the overall impact of the JGHT programme, and provide material for case studies to promote the scheme. Information to be collected is set out in Table 19.

### Table 19 Information requested from PIs

<table>
<thead>
<tr>
<th>Suggested monitoring data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Full trial awards</strong></td>
</tr>
<tr>
<td>Clinical trial registration number</td>
</tr>
<tr>
<td>Trial hypothesis: confirmed/disproved/inconclusive</td>
</tr>
<tr>
<td>Summary of key findings to date (with word limit)</td>
</tr>
<tr>
<td>Publication of the main trial findings (actual, with reference/DOI; or expected timeline)</td>
</tr>
<tr>
<td>Policy and/or implementation stakeholder engagement activity, during trial and post-trial</td>
</tr>
<tr>
<td>(yes/no/continuing; brief description)</td>
</tr>
<tr>
<td>Trial findings have potential to influence policy (yes/no/requires further research)</td>
</tr>
<tr>
<td>Nature of achieved/expected policy influence (including reference if achieved), brief narrative of current status</td>
</tr>
<tr>
<td>Trial findings suitable for implementation (yes/no/requires further research)</td>
</tr>
<tr>
<td>Description of implementation (actual/expected)</td>
</tr>
<tr>
<td>Description of barriers encountered</td>
</tr>
<tr>
<td>Other key outcomes/impacts directly linked to JGHT-funded research (with word limit)</td>
</tr>
<tr>
<td>Further funding to progress the same or related research question</td>
</tr>
<tr>
<td>Skills and capacity development (separately in LMIC)</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td><strong>Development awards</strong></td>
</tr>
<tr>
<td>Clinical trial registration number (if pilot study)</td>
</tr>
<tr>
<td>Summary of key findings (with word limit)</td>
</tr>
<tr>
<td>Publication of main findings (actual/expected)</td>
</tr>
<tr>
<td>Intervention tested and conditions are suitable for full trial (yes/no/requires further research), with option to provide brief description</td>
</tr>
<tr>
<td>Full trial application (planned/submitted/status – approved/rejected)</td>
</tr>
<tr>
<td>Other key outcomes/impacts directly linked to JGHT-funded research</td>
</tr>
</tbody>
</table>
22 November 2019

Review of the Joint Global Health Trials funding scheme

Final Report - Appendices
Review of the Joint Global Health Trials funding scheme

Final Report – Appendices

technopolis [group], November 2019

Peter Varnai
Maike Rentel
Anoushka Davé
Kelly Simpson
Costanza Tiriduzzi
Emma Pottinger

www.technopolis-group.com
Appendix A  Data collection tools ..............................................................................................................1
Appendix B  JGHT portfolio analysis (MRC grants database)........................................................................25
Appendix C  Analysis of Research Fish data ...............................................................................................53
Appendix D  Clinical trials registry data analysis .......................................................................................62
Appendix E  Survey analyses.......................................................................................................................66
Appendix F  Main trial publications ...........................................................................................................106
Appendix G  Global health funding landscape & approaches to evaluation...............................................109
Appendix A  Data collection tools

A.1  Questionnaire for interviews with PIs of full JGHT funded trials

1) Project background (pre-implementation)

Project aim
Can you briefly describe the primary aim of the trial, at its outset, and what you hoped to achieve?

• What was the health problem the trial sought to address and type of intervention it tested?
• How did this relate to your previous work?
• Who were the expected main beneficiaries/end users of the intervention?
  – Were there particular demographic sub-groups such as gender, age, disability etc that were expected to benefit?
• What outcomes and impacts did you hope to achieve? Were there any specific policies or practices you sought to improve? How did you plan to influence them?
• What other trials have addressed / are addressing this issue? What is the broader research landscape, who conducts and funds other research in this area?
• Did the trial involve any novel approaches? What was the trial methodology?
• What did you find particularly challenging in the preparation phase?
• What did you think would be the main challenges to the trial? Were you aware of any cultural, political, economic, or other barriers to participation?
  – Did the trial involve working with communities or target populations previously involved in similar research?

Project team

• How was the project/team organised?
  – Please describe the project team: name all institutions involved (including their locations). Had you worked with this team before?
• Where were the trial sites (location, country)? Had you worked with these before? How did they interact with the project team?
• What were the roles of collaborators in the delivery of the project? What skills, infrastructure or capabilities did they contribute to the project?
• Were any new partners brought in to support the delivery of the project, i.e. partners you hadn’t worked with beforehand? Why was this done? How did you identify these partners?
  
  For UK-led projects: How were LMIC researchers involved in the design of the project? How were LMIC researchers involved in the implementation of the project, and in reporting of research findings?

Project design

• What preparations were most important in designing the trial?
• Had you carried out a pilot study to collect additional data on the trial location, context, trial methodology, intervention effect? If yes, what did you find and how did this feed into the JGHT-funded full trial?
• Did you involve stakeholders in the design phase of the project?
Who and where?
How did you engage?
Were these new contacts, or had you been working with these stakeholders before? If no, how did you identify individuals?
In hindsight, which of these preparations was most critical to the trial?

2) Trial experience

Adjustments and challenges
Was the project plan adjusted after the start of the project? If yes, why?
Did the actual project team differ from the team described in the trial application?
Did you encounter any challenges? If yes, what were they?
Were any of these unexpected?

Learning from design and implementation phase
In hindsight, is there anything you would change about how the trial was designed and conducted?
Are there additional activities the JGHT could support that you think would have made the research more effective and increased the potential for impact?

Stakeholder engagement
Did you continue engagement with stakeholders during the project (beyond those directly involved in the research)? If yes, who did you engage with and how?
Which engagement activity do you think was most critical to the trial’s progress, outcomes, and impacts?

Benefits of research project to participants
Health benefits to trial participants - Were there health benefits for participants in the JGHT-funded research project? If yes, how have different sub-groups benefited?
Capacity building – Do you think the award contributed to capacity building at the trial sites and in partner institutions? What were the main skills or capabilities developed in LMIC locations?
Can you describe the scale of this benefit?
Did the award involve any formal training for trial staff?

3) JGHT award outputs and scientific outcomes

Research findings
Did the JGHT-funded project answer the research question(s) it originally set out to address?
Could you summarise the key findings?
If the project did not answer the original research question, why not? What happened?
Has the project yielded any additional findings?
Are you aware if others in the research community have taken up the trial’s findings?
Project outputs

1. *Publications* - Did you publish the findings of the JGHT-funded research project? How many publications stemmed from the project? Which of these do you consider the key outputs?

   If published, could you point me to the **reference for the main trial results**?

2. *Tools and databases* - Were any new research tools or databases developed as part of the JGHT-funded project? Do you know if these continue to be used?

3. *Methodology* - Did the project advance the use of novel trial methodologies?
   - Are you aware if others have **taken up** the findings from your JGHT-funded project, or any tools/methodologies developed?

4. *Infrastructure* - Was new or improved research infrastructure established as a result of the JGHT award? If yes, which type of infrastructure and where?
   - Are you aware if other researchers have **made use** of the established infrastructure?

5. **Collaboration:**
   - *Research collaboration:* Have you collaborated, or are you collaborating, with team members of the trial research team? What has been the effect of the JGHT trial on further collaboration?

   **If joint funding has been secured** for a collaboration that originated with the JGHT-funded project, please specify: Name of collaboration partner(s), Source and amount of funding, and Project title
   - *Other stakeholders:* Have you continued contact with stakeholders you started working with as part of the JGHT award? Has this benefitted your research, and its impact, beyond the JGHT-funded activity?

4) JGHT award outcomes and impact

**Potential for impact**

- Do the findings of the JGHT-funded project have the **potential** for impact on the health and well-being of people living in LMICs?
  - Please explain
  - If no, why not?

In hindsight, what could have increased the JGHT-funded project’s potential for impact?

**Take up by policy makers**

- Have the project’s findings been taken up into policy and/or had an impact on health?
  - **If yes:** Who are the policy makers involved and what was the change? What is the scale of take-up?
  - **If no:** Why not?

In hindsight, what do you think could have increased take up by policy makers?

**Implementation and health impact**

- Have the findings of the JGHT-funded project led to, or contributed to, any changes in practice and been implemented?

  **If no:**
  - Why did relevant findings of the JGHT-funded project not contribute to a change in practice?
- In hindsight, what do you think could have been done additionally to assist in the implementation of the project’s findings / a change in practice?

**If yes:**
- Could you describe the implementation, how the findings contributed to it, and who is implementing the change?
- What is the scale of implementation?
- Were there elements of the JGHT project design or the project activities you consider were essential for this change in practice/implementation?
- In hindsight, what do you think could have been done additionally to further assist in the implementation of the project’s findings / a change in practice?

- Have the findings of the JGHT-funded project led to any health benefits in the target population (beyond research participants)?

**If yes**
- Could you describe the health benefits? What has changed as a result of the research?
- How many people/patients have benefitted? How have different sub-groups benefited?
- Could you share or point me to sources of evidence for this impact?
- In hindsight, what do you think could have been done additionally to achieve health impacts?

**If no**
- Why not? Is the implementation too recent, or are there other challenges that have emerged? Is there future potential for health impact, and if yes, what might this look like?
- In hindsight, what do you think could have been done additionally to achieve health impacts?

**Scale-up**

- Is there potential for further scale-up of the impact of the JGHT-project’s findings?

**If yes**
- Could you outline the potential for scale up? Is this being pursued, and if yes, how?
- Were there elements of the JGHT project design or the project activities you consider were essential for scale up?
- In hindsight, what could have increased the JGHT-funded project's potential for scale up further?

**If no**
- Why can the findings not be scaled?
- In hindsight, what could have increased the JGHT-funded project's potential for scale up further?

**Other impacts**

- Were there any other unanticipated impacts, both positive and negative, the JGHT trial may have achieved?

  Has there been any impact on:
  - operational barriers to future health research and global health trials
  - cultural barriers to future health research and global health trials
  - practitioners’ and decision makers’ views of the value of global health trials and health research
- views relating to the importance of global health trials and health research at LMIC institution(s)
- the motivation of health professionals at LMIC institutions to become research leaders
- LMIC researchers’ knowledge and technical skills to undertake health research and global health trials
- LMIC institutions’ research governance structures
- LMIC researchers’ research leadership capabilities
- building or extension of local networks of researchers with effects on research practice
- building or extension of international networks of researchers

5) Other JGHT awards
If you were, or still are, involved in other JHGTI awards:
- Have any of these led to changes in policy and practice?
- Have there been any impacts on health?
- Within the scientific domain, have there been any main advances now used by others?

6) Global health trial funding landscape
- What sources of funding for late-stage global health trials are you aware of (other than the JGHT)?
- What do you consider are the main strengths of the JGHT, setting it apart from other similar funding programmes?
- What are the advantages of other similar funding programmes over the JGHT?
- Are there currently any gaps in the research funding landscape relevant to global health trials that you think function as a barrier to health impact? If yes, what are the main gaps?

7) Design of the JGHT
- Thinking back to when you applied for a JGHT development award, were there any aspects of the scheme’s design and requirements you feel were problematic and could be improved?
- Are there aspects of the scheme’s current design and requirements that are a barrier to attracting relevant high-quality proposals, both from high income countries and low-income countries?
- How do the JGHT’s application process and requirements compare with those of similar funding programmes?
- Do similar funding programmes provide support for additional activities not covered by the JGHT that you consider particularly effective to achieve outcomes and health impacts?
- Do you think calls for proposals and other information on the JGHT are communicated through the right channels, reaching the relevant research community in the UK and as well as in LMICs?

8) Final comments and close
- Do you have any other comments about the JGHT or any suggestions to the funders?
A.2 Questionnaire for interviews with key opinion leaders

Outline of JGHT

1) Interviewee background
• Could you briefly describe your involvement with and expertise in relation to global health research and global health trials? Which area of research or policy making are you mainly involved in?
  
  If funder: Could you outline the design of related funding programmes your organisation offers?
• How familiar are you with the JGHT? Could you outline what you know about it, or how you have been involved?

2) Global health trial funding landscape
• Is the JGHT filling a gap in the global health research funding landscape?
• What are the alternative sources of funding including follow-on funding after JGHT? What would be the situation without JGHT funding?
  OR: What are sources of global health research funding you are familiar with?
• What opportunities and gaps in global health research funding remain for delivering value/impact?
  Are there currently any gaps in the research funding landscape relevant to global health trials that you think function as a barrier to health impact? If yes, what are the main gaps?
• How could a global health research funding programme, such as the JGHT, further address these gaps?

3) JGHT-funded research and outcomes
• What are your overall impressions of the research funded by the JGHT scheme, in terms of:
  - The types and scale of trials funded
  - The quality of research conducted
  - PIs / teams / institutions involved
  Has this changed over time?
• What is your overall impression of the global health outcomes of the JGHT?
• How do these compare with outcomes obtained through other R&I models/programmes that fund global health trials?
  What factors may contribute to any differences?
• How is the JGHT-funded research contributing to the UK’s efforts to achieve the wider health-related Sustainable Development Goals, and focus on gender equality and disability?
• Do you think the scheme is contributing to value for money of international development funds?
  Compared to other schemes, is the JGHT set up to use ODA funding efficiently and effectively?
• In your area of work/expertise, are you aware of specific trials funded by the JGHT? If yes, could you comment on the contribution these have made within the wider research context?
  What has been their impact, in terms of:
  - scientific progress
  - policy / health practice – influencing key decision makers
patient / health outcomes, incl. delivering interventions at scale and improving health in LMICs

Do you have examples you could share with us?

4) JGHT design

- What are your overall impressions of the design of the JGHT scheme? Are there any aspects that stand out, both positive and negative?
- To what extent does the JGHT’s design contribute to research results that are implementable and scalable?
  Do you think the scheme’s design has led to enhanced achievement of health outcomes and impacts?
- What do you consider the main strengths of the JGHT, setting it apart from other similar funding programmes?
  What are the advantages of other similar funding programmes over the JGHT?
- What have similar trials (funded elsewhere) achieved in terms of impact? Where other trials have made significant impacts, how has this been achieved?
- Can you point to global health research funding programmes similar to the JGHT that include design aspects you consider particularly effective in achieving impact?
  For funders: What are aspects of your global health research funding programmes that have been particularly effective in achieving impact?
- What do you think of the two-step approach to funding global health trials – development award scheme for pilot studies, with potential for a full trial award?
  For funders: Does your programme offer similar development awards?
- How could the JGHT enhance its impact and lead to implementable and scalable results?
  What do you think is the:
    - Potential of prioritising health issues that JGHT could solve/ eradicate rather than contribute a piece of research evidence
    - Potential of conducting fewer and larger trials, including in multiple settings
    - Potential of moving to a commissioned stream of funding, while also keeping the current researcher-led stream
    - Potential of specifically funding multiple trials within a thematic area to reinforce one another and exploit synergies.
    - Potential of making available follow-on funding for activities that ensure research evidence reaches decision makers and is taken up by implementers
    - Potential of providing targeted support for LMIC candidates in proposal process, to increase the proportion of LMIC-led awards
    - Potential for dissemination of results to key stakeholders through funders' existing networks
- JGHT calls are open across all global health research areas but encourage submissions in certain areas of need. How does this model compare to other relevant models in terms of being able to fund the highest quality, most relevant questions in global health?

5) Added value of joint working between funders
• What is the added value of running JGHT through a partnership of funders? (including value for money)
• What in your view are the advantage and challenges in supporting health research through a partnership of funders?
  Does the joint working between funders contribute to a more cohesive and coordinated approach to research funding?
• Does the joint working between JGHT funders help to maintain the UK’s reputation and international leadership in producing high quality research of relevance to developing societies? How?
• How does coordination and cooperation between the funders work? How could this be improved?

6) Review process and experiences
• What are the key steps in the JGHT review process? Is it fit for purpose?
  Does the review appropriately cover considerations of global health needs and priorities, innovative approaches, involvement of community and decision makers, potential for implementation and scalability?
  Does the review involve experts of the specific health research area, including experts from the affected geographical area?
• What is the level of relevance and quality of applications received? Has this changed over the lifetime of the JGHT? If yes, why do you think this might be?
• What is the current experience of funding ‘development’ awards for pilot studies?
  Does it change the way full trials are prioritised and funded?
• Do full trials proposals you have reviewed show evidence that they are aiming for a ‘definitive answer’ to their research questions? Do these proposals provide evidence for implementation and scalability?
• What factors do you think lead to differences in the quality of applications?
• Is there a difference in quality and quantity of applications coming from the UK or outside of the UK?
  What are the reasons for any differences? Are there changes that could be made if the funders wished to achieve a more balanced spread?
• Can you identify any trends in the applications received?
• What aspects of scheme management work well or work less well for committee members?

7) Monitoring and evaluation indicators
• [funders only] How does your organisation monitor outcomes and impacts of funded research? What indicators do you use? How do these feed into your decision making processes?
• What measurement indicators do you suggest funders use to evaluate the programme on a periodic basis?

8) Final comments and close
• Do you have any other comments about the JGHT or any suggestions to the funders?
A.3 Survey of PIs of active full trials and active and closed development awards

1) About you
Last name
First Name
Institution (at time of JGHT grant)
Country [drop-down menu]
Grant number and title (as stated in email)
Grant closing date (month/year) [drop-down menu]

2) JGHT award activity
Project team
1. Does the current project team differ from the team described in the Case for support? (select all that apply) [multiple choice]
   - No - The project team was/is as described in the Case for support
   - Yes - The current project team includes additional members compared to the team described in the Case for support – please explain
   - Yes - The current project team does not include all team members described in the Case for support – please explain
   If yes, please explain

2. Where is the trial/development project taking place?
Number of trial site(s) [drop-down menu]
Location of trial site(s) (country) [drop-down menu] – choose all that apply

Project description
3. The research project relates to which type of intervention? (please select all that apply) [multiple choice]
   - Prevention - vaccine regimen
   - Prevention - vector control
   - Prevention - behavioural
   - Prevention - other
   - Treatment - drug repurposing
   - Treatment - drug dosage/regimen
   - Treatment - psychological intervention
   - Treatment - adherence/behavioural
   - Treatment - other
   - Screening and treatment strategy
   - Other - please specify
4. The research targets which group? (please select all that apply) [multiple choice]
   - New-borns and/or Children
   - Teenagers/young adults
   - Girls only
   - Pregnant or recently-delivered women
   - People affected by HIV
   - People affected by malaria
   - People affected by tuberculosis
   - People affected by CVD
   - General population (public health)
   - Other - please specify

5. We would like to understand the range of expertise involved in the project. Does the study team include experts in the following areas (select all that apply): [multiple choice]
   - Clinical science
   - Clinical trial methodology
   - Clinical trial management
   - Data management
   - Statistician
   - Health economics
   - Social science
   - Health policy - local policy context
   - Health systems
   - Health care - Primary care practitioner/nurse/ pharmacist
   - Patient recruiter
   - Knowledge brokerage (stakeholder engagement, network building)
   - Evaluation/impact
   - Other - please specify

6. [FULL TRIAL ONLY] Prior to your application to the JGHT, had you or others carried out pilot studies at the trial location(s) to inform the full trial? [drop-down menu]
   - No - there was no need for a pilot study, we knew the trial location(s), context, trial methodology and intervention well
   - No – but we would have liked to carry out a pilot study, provided we had funding
   - Yes – we conducted a pilot study for the intervention in the context of the trial location(s)
   - Other – please specify

6. [DEVELOPMENT AWARD ONLY] Did you apply for this development grant after a previous proposal for a full trial award was unsuccessful? [drop-down menu]
   - No, I had not previously applied for any full trial awards relevant to this development award
   - Yes, I first applied for a JGHT full trial award; this development award aimed/aims to obtain additional preliminary data to further develop the full trial plan
Yes, I first applied for a full trial award from a different funder; this development award aimed/aims to obtain additional preliminary data to further develop the full trial plan.

7. Did you involve stakeholders in the design phase of the project (i.e. before submitting the application)? (please select all that apply) [multiple choice]
   - No
   - Yes – I involved policy makers from national government(s) in the design phase
   - Yes – I involved policy makers from international agencies in the design phase
   - Yes – I involved LMIC health care professionals in the design phase
   - Yes – I involved implementing organisations/NGOs in the design phase
   - Yes – I involved community organisations in the design phase
   - Yes – I involved members of the intervention target group in the design phase (people affected by the health problem to be addressed)
   - Yes - other (please explain)

If yes, how were you engaging with these stakeholders? (select all that apply) [multiple choice]
   - Direct approach
   - Presentations/seminars
   - Interactive workshops/feedback sessions
   - Policy briefs
   - Social media
   - Online forum
   - Other – please specify

8. Are you engaging with stakeholders during the project (beyond those directly involved in the research)? (please select all that apply) [multiple choice]
   - No
   - Yes – I am engaging with policy makers from national government(s) during the project
   - Yes – I am engaging with policy makers from international agencies during the project
   - Yes – I am engaging with LMIC healthcare providers (beyond the research project)
   - Yes – I am engaging with key stakeholders in the LMIC research system
   - Yes – I am engaging with implementing organisations/NGOs
   - Yes – I am engaging with community organisations
   - Yes – I engaged / am engaging with members of the intervention target group during the project, beyond the research participants (people affected by the health problem to be addressed)
   - Yes - other (please explain)

Please summarise any stakeholder engagement as part of the project and indicate which you consider the most critical.

9. For UK-led projects: How were/are LMIC researchers involved in the design and implementation of the project? Please outline the level and nature of involvement.

**Challenges encountered and adjustments to project plan**
10. What are the main challenges you have encountered in the implementation of the research project? (please select all that apply) [multiple choice]
   - Governance at trial site(s) – please specify
   - Administrative processes and requirements at trial site(s) – please specify
   - Capacity issues / shortage of trained staff at trial site(s) – please specify
   - Patient/participant recruitment – please specify
   - Lack of infrastructure – please specify
   - Other – please specify

11. Did you have to make a major adjustment to the project plan after the start of the project due to unforeseen circumstances/challenges encountered? (select all that apply) [multiple choice]
   - No, the project aligns closely with the Case for Support.
   - Yes, the project plan had to be adjusted, in terms of:
     - Scope of study
     - Study timeline
     - Type of data collected
     - Site of data collection
     - Method of data collection
     - Recruitment of additional experts to team
     - Training for trial staff
     - Engagement with additional stakeholders / stakeholder groups
     - Level / frequency of stakeholder engagement
     - Other – please specify

   If yes, please describe/explain major changes made and how these have helped to address challenges encountered.

12. In hindsight, are there aspects of the project’s design or implementation you would approach differently? [multiple choice] If yes, please indicate what change you would make:
   - No, I would not make any changes to the project’s design and implementation
   - Scope of study
   - Study timeline
   - I would carry out preparatory data collection / a pilot study, prior to full trial
   - Type of data collected
   - Site of data collection
   - Method of data collection
   - Recruitment of additional experts to team
   - Training for trial staff
   - Engagement with additional stakeholders / stakeholder groups
   - Level / frequency of stakeholder engagement
   - Other – please specify

   Please outline why you would like to make these changes.
Health benefits to trial participants
13. Are there health benefits for participants in the JGHT-funded research project? [drop-down menu]
   - Yes
   - No
   - Not yet
   If yes, please describe these health benefits and the number of people likely to benefit

3) JGHT award outputs and scientific outcomes
Questions in this section may not apply to you if your award is still active, and the research project has not yet completed. However, your active project may already have resulted in some outputs and outcomes. If this is the case, please select the relevant option, or indicate “Not yet, as the project is still ongoing”.

14. [DEVELOPMENT AWARD ONLY] The aim of the development award is to develop future trial application ideas into robust and competitive proposals through conducting feasibility studies and obtaining preliminary data. Did the project achieve this aim? [multiple choice]
   - No - the findings of the development award showed that the plans for the full trial need to be significantly changed and that further preliminary data needs to be collected
   - Not yet - the project is still ongoing
   - Yes - I have not yet applied for a full trial award but am planning to do so
   - Yes - I used the data to apply for a full trial award from a different funder and was successful
   - Yes - I used the data to apply for a JGHT full trial award but was not successful
   - Other - please specify
   If you have successfully applied for a full trial award from a different funder, please state the funding programme name and project title

Research findings
15. Has the research project resulted in any findings to date? [drop-down menu]
   - Not yet, as the project is still ongoing
   - Yes
   If yes, please provide a brief summary of key findings. If no, please explain why not.

16. Were any of the findings unanticipated? (including impacts not directly related to the research question it addresses, and/or beyond your research group) [drop-down menu]
   - Not yet, as the project is still ongoing
   - No
   - Yes - please summarise the findings

Publications
17. Have you published any findings of the JGHT-funded project? (including scientific papers, policy briefs, media reports etc) [drop-down menu]
- Not yet, as the project is still ongoing
- Yes, findings of the JGHT-funded research project have been published.
- No, the project’s findings are not suitable for publication. Please explain

If yes, please provide reference(s) for publication(s) reporting key results of the project.

Tools
18. Have any new research tools or databases been developed as part of the JGHT-funded project? [drop-down menu]
   - Not yet, as the project is still ongoing
   - Yes - please describe
   - No

Methodology
19. Were any new research methodologies developed as part of the JGHT-funded project? [drop-down menu]
   - Not yet, but this is anticipated
   - Yes - please describe
   - No

Infrastructure
20. Was new or improved research infrastructure established as a result of the JGHT award? [drop-down menu]
   - Not yet, but this is anticipated
   - Yes - please describe the location (site; country) and type of infrastructure established
   - No - the project will not establish new or improved infrastructure

Uptake of project findings by research community
21. Are you aware if others have taken up project findings, or are using new tools, databases, or methodologies developed as part of the JGHT-funded project? [drop-down menu]
   - Not yet, as the project is still ongoing
   - No - I don’t know whether findings, tools, or methodologies have been used by others
   - Yes – other researchers have taken up knowledge generated by the JGHT-funded project.

If yes, this related to: [multiple choice]
   - the intervention tested
   - the needs of the target population
   - the policy context relevant to the JGHT project
   - the cultural context relevant to the target population
   - the health system context relevant to the target population
   - research tools developed
   - methodologies developed
   - networks developed
4) Collaboration networks

Research collaboration

22. Does the JGHT project involve research collaboration partners you had not worked with previously? (select all that apply) [drop-down menu]
- No, I had already worked with this project team
- Yes, new partners from institutions in HICs
- Yes, new partners from institutions in LMICs
- Yes, new partners from institutions in HICs and LMICs
If yes, please indicate new collaborations (name of institution; country)

Are you collaborating with these researchers beyond the JGHT-funded project? [drop-down menu]
- No, I have not collaborated with these partners beyond the JGHT-funded project, and I am not planning to collaborate in the future
- No, I have not (yet) collaborated with these partners beyond the JGHT-funded project, but am planning to / may collaborate in the future
- Yes, I have collaborated / am collaborating on other projects

If you are collaborating, please select which describe your ongoing collaboration (select all that apply) [multiple choice]
- Regular information exchange and advice
- Developing joint proposal
- Submitted joint proposal
- Secured joint funding
- Collaboration extended to other research groups at my institution/at the JGHT-funded collaboration partners' institutions
- Collaboration extended to other research groups beyond my / the JGHT-collaboration partners' institutions
- Other - please specify

23. If joint funding has been secured for a collaboration that started with the JGHT-funded project, please specify: Name of collaboration partner(s), Type of project/Project title, Source of funding

Policy / implementation partners

24. Does the JGHT project involve policy / implementation partners you had not been in contact with previously? (select all that apply) [multiple choice]
- No, I had already worked with these policy and implementation partners
- Yes, new partners from organisations in HICs
- Yes, new partners from organisations in LMICs
- Yes, new partners from organisations in HICs and LMICs
If yes, please indicate new partner organisations (type; name; country)

Are you in contact with these policy / implementation partners beyond the JGHT-funded project? [drop-down menu]
- No, I have not been in contact with these partners beyond the JGHT-funded project, and I am unlikely to be in contact in the future
- No, I have not been in contact with these partners beyond the JGHT-funded project, but am planning to continue interactions in the future
- Yes, I am in contact in the context of other projects – please specify

If you are not in contact with these partners and are unlikely to be in contact in the future, please explain why this is the case

5) JGHT award outcomes and impact

Impact on policy and health

25. [FULL TRIAL ONLY] Has the project already led to any changes in policy or health? (We are aware that the trial award has not yet closed and is hence unlikely to have led to any outcomes or impacts at this stage.) [multiple choice]
- Not yet, the project is still ongoing
- No, it is unlikely to lead to changes in policy and practice - please explain
- Yes, project findings have informed or led to changes in policy and practice – please explain

26. [DEVELOPMENT AWARD ONLY] While not the aim of the JGHT development award scheme, did / do the project’s findings have potential for take up into policy and impact on health in their own right? [multiple choice]
- No (but the project’s findings can inform further research)
- Yes, the findings of the development award project have/had the potential to inform changes in policy and practice – please explain

If yes, were these changes achieved?

Other impacts

27. Has the JGHT-funded project achieved other impacts, not directly related to the research question it addresses / beyond your research group? (select all that apply) [multiple choice]
- No / not yet
- Yes – it has helped to *convince practitioners and decision makers* of the value of global health trials and health research for contributing to the evidence base
- Yes – it has given a *higher priority* to global health trials and health research at LMIC institution(s)
- Yes – it has *reduced the operational barriers* to future health research and global health trials
- Yes – it has *reduced cultural barriers* to future health research and global health trials
- Yes – it has increased the *motivation* of health professionals at LMIC institutions to become research leaders (e.g. against competing priorities)
- Yes – it has increased LMIC researchers’ *knowledge and technical skills* to undertake health research and global health trials (e.g. learning of new research methods)
- Yes – it has enhanced LMIC institutions’ research governance structures
- Yes – it has increased LMIC researchers’ research leadership capabilities (e.g. confidence, negotiation and communication skills, team building skills)
- Yes – it has built up or expanded a local network of researchers with associated benefits (e.g. pooling of resources, information exchange)
- Yes – it has built up or expanded an international network of researchers with associated benefits (e.g. ongoing collaboration)
- Yes – other (please specify)

Please give a short description of the impact(s) indicated above and provide any supporting evidence/contacts.

28. If you were/are involved in other JGHT-funded awards: Please provide a brief summary of outcomes and impacts achieved, stating the award title and number

6) Global health trial funding landscape

29. What other sources of funding for late-stage global health trials do you know of (other than the JGHT)?

30. In your opinion, what are the main strengths of the JGHT, setting it apart from other related funding programmes? Please explain.

31. In your opinion, what are the main weaknesses of the JGHT compared to other related funding programmes? Please explain.

32. What are the advantages of other related funding programmes over the JGHT? Please explain.

33. Are there currently any gaps in the global health research funding landscape that you think function as a barrier to health impact? [drop-down menu]
   - No, there are currently no gaps in funding relevant to researchers that could address existing barriers.
   - Yes, there are critical gaps in the research funding landscape

34. Please indicate what you consider to be the most critical gaps relevant to research funding (select up to two): [multiple choice]
   - Gap in the type of research funded (e.g. trial, implementation research, tool development, standards)
   - Gap in geographical coverage / research location (e.g. country, continent)
   - Gap in coverage of health problems addressed (e.g. specific diseases)
   - Gap in resources for stakeholder engagement and dissemination of research findings
   - Gap in resources for critical research infrastructure
   - Gap in resources for training
   - Other gap – please specify

Please outline your selected gaps

7) Design of the JGHT

Application
35. In your opinion, could any aspects of the scheme’s design and requirements be improved? [drop-down menu]
- Yes, there were aspects that were problematic and could be improved – please specify
- No, I did not consider any aspects or requirements of the scheme problematic

36. In your opinion, do the scheme’s design and requirements enable it to attract high-quality proposals? [drop-down menu]
- No, I think the scheme’s design and requirements enable it to attract relevant high-quality proposals; there are no issues.
- Yes, I think there are aspects that limit the scheme’s attractiveness and accessibility for researchers from HIC institutions
- Yes, I think there are aspects that limit the scheme’s attractiveness and accessibility for researchers from LMIC institutions
- If yes, please specify problem and suggestion for improvement

37. How do the JGHT’s application process and requirements compare with those of related funding programmes? Please describe the application process and requirements for funders/funding programmes you are familiar with and outline any advantages or disadvantages.

Support for additional activities

38. What additional activities could the JGHT support to increase the potential of impact from its research? (select your top choice)? [multiple choice]
- Support for other types of research
- Stakeholder engagement
- Dissemination and knowledge exchange
- Network building
- Training
- Infrastructure
- Other - please specify
Please briefly explain your choice

39. Do related funding programmes provide support for additional activities not covered by the JGHT that you consider particularly effective to achieve outcomes (e.g. change in policy) and health impacts (e.g. implementation, scale-up) [drop-down menu]
- Yes – please name programme and describe support
- No - I don’t know of additional activities covered by other programmes that are particularly effective

Promotion

40. Do you think calls for proposals and other information on the JGHT are communicated through the right channels, reaching the relevant research community in the UK and as well as in LMICs? [drop-down menu]
- Yes, I think relevant researchers are aware of the JGHT
No, I think communication about the JGHT could be improved – please specify

Comments
41. Do you have any other comments about the JGHT?

A.4 Survey of co-investigators

About you
Last name
First Name
Institution (at time of JGHT grant)
Country [drop-down menu]
Grant number and title (as stated in email)
Grant closing date (month/year) [drop-down menu]

JGHT Award activity
We are also consulting with the PIs of the JGHT awards; in answering the survey questions, please focus on aspects specific to your research.

1. Please indicate your area(s) of expertise you were / are bringing to the JGHT-funded project (select all that apply) [multiple choice]
   - Clinical science
   - Clinical trial methodology
   - Clinical trial management
   - Data management
   - Statistician
   - Health economics
   - Social science
   - Health policy - local policy context
   - Health systems
   - Health care - Primary care practitioner/nurse/ pharmacist
   - Patient recruiter
   - Knowledge brokerage (stakeholder engagement, network building)
   - Other - please specify

2. What was your level of involvement in the design of the project? [Multiple choice]
   - Very involved across all aspects of the design; member of the core research team
   - Substantial contributions to several aspects of the project design
   - Some input to specific aspects of the project design
   - Provided feedback / advice on the project plan
   - Limited input
- Other – please specify

3. Did your actual role or scale of involvement in the project differ from the planned involvement (e.g. as set out in the application)? (select all that apply) [multiple choice]
  - No, my involvement was/is as planned
  - Yes, my involvement differed in scale - I was / I am more involved than planned
  - Yes, my involvement differed in scale - I was / I am less involved than planned
  - Yes, my involvement differed in nature but not in scale
  - Yes, my involvement differed in nature and scale
If yes, please outline any differences

4. In hindsight, are there aspects of the project’s design or implementation you would approach differently? [Multiple choice]
  - No, I would not make any changes to the project’s design and implementation
  - Yes, knowing what I know now, I would make changes to the project’s design and implementation
If yes, I would make changes relating to: [multiple choice]
  - Type of data collected
  - Method or site of data collection
  - Additional expertise on team
  - Stakeholders engaged / involved
  - Scope of study
  - Other – please specify
Please outline any changes you would make

**Impacts of JGHT-funded project**

**Impacts on your work**

5. Has the JGHT-funded project had an impact on your work? Please select all that apply [multiple choice]

*Scientific knowledge*
  - Yes, it has provided me with scientific knowledge I have since used in my further work
  - Yes, it has changed the direction of my research
  - Yes, I used the tools and methodologies I first used as part of the JGHT-funded project in my further research
  - Yes, it has allowed me to secure additional research funding
  - Not applicable

*Context knowledge*
  - Yes, it has provided me with an enhanced understanding of health needs I have since used to direct my further work
- Yes, it has provided me with an enhanced understanding of the policy context I have since used in my further work
- Yes, it has provided me with an enhanced understanding of the local health system context I have since used in my further work
- Yes, it has provided me with an enhanced understanding of the cultural context I have since used in my further work
- Not applicable

Collaborations and networks

- Yes, it has provided me with important new contacts I have used in my further work
- Yes, I have continued to collaborate with partners I first connected with through the JGHT project
- Yes, I am now actively participating in research networks I was not previously involved in
- Yes, I am now actively participating in policy networks I was not previously involved in
- Yes, I am now working with new implementation partners on other projects
- Yes, it has had a strong influence on my policy work beyond the JGHT project
- Not applicable

Please provide a brief description of the main impact for your research/research group. You may include impacts that were not listed above

Impacts on your organisation

6. Has the project led to any impacts for your organisation or institution/department? Please select all that apply [multiple choice]

- Yes, it has influenced the work of others in my organisation
- Yes, it had an impact on my organisation's priorities
- Yes, it has enabled my organisation to establish supporting infrastructure
- Yes, it has provided my organisation with new contacts
- Yes, my organisation is now actively involved in networks it was not previously involved in
- Yes, it has allowed my organisation to secure further funding
- No, not really
- Other – please specify

Please provide a brief description of the main benefit to your research organisation

Other impacts

7. Did the JGHT-funded project have other impacts at the project site(s) (beyond the research question it addresses)? (select all that apply) [multiple choice]

- No / not yet
- Yes – it has helped to convince practitioners and decision makers of the value of global health trials and health research for contributing to the evidence base
- Yes – it has given a higher priority to global health trials and health research at institution(s) located in LMICs
- Yes – it has **reduced the operational barriers** to future health research and global health trials at the project site(s)
- Yes – it has **reduced cultural barriers** to future health research and global health trials
- Yes – it has increased the **motivation** of health professionals at LMIC institutions to become research leaders (e.g. against competing priorities)
- Yes – it has increased LMIC researchers’ **knowledge and technical skills** to undertake health research and global health trials (e.g. learning of new research methods)
- Yes – it has enhanced LMIC institutions’ **research governance structures**
- Yes – it has increased LMIC researchers’ research **leadership capabilities** (e.g. confidence, negotiation and communication skills, team building skills)
- Yes – it has built up or expanded a **local network of researchers** with associated benefits (e.g. pooling of resources, information exchange)
- Yes – it has built up or expanded an **international network of researchers** with associated benefits (e.g. ongoing collaboration)
- Yes – other (please specify)

Please give a short description of the impact(s) indicated above and provide any supporting evidence/contacts.

8. If you were/are involved in other JGHT-funded awards: Please provide a brief summary of outcomes and impacts achieved, stating the award title and number

**Global health research funding landscape**

9. What sources of funding for late-stage global health trials do you know of (other than the JGHT)?
10. In your opinion, what are the main strengths of the JGHT, setting it apart from other similar funding programmes? Please explain.
11. In your opinion, what are the main weaknesses of the JGHT compared to other related similar programmes? Please explain.
12. What are the advantages of other related funding programmes over the JGHT? Please explain.
13. Are there currently any gaps in the global health research funding landscape that you think function as a **barrier** to health impact? [drop-down menu]
   - No, there are currently no gaps in funding relevant to researchers that could address existing barriers.
   - Yes, there are critical gaps in the research funding landscape

14. Please indicate what you consider to be the most critical gaps relevant to research funding (select up to two): [multiple choice]
   - Gap in the type of research funded (e.g. trial, implementation research, tool development, standards)
   - Gap in geographical coverage / research location (e.g. country, continent)
   - Gap in coverage of health problems addressed (e.g. specific diseases)
   - Gap in resources for stakeholder engagement and dissemination of research findings
   - Gap in resources for critical research infrastructure
   - Gap in resources for training
Design of the JGHT Application

15. In your opinion, could any aspects of the scheme’s design and requirements be improved? [drop-down menu]
   - Yes, there were aspects that were problematic and could be improved – please specify
   - No, I did not consider any aspects or requirements of the scheme problematic

16. In your opinion, do the scheme’s design and requirements enable it to attract high-quality proposals?
    [drop-down menu]
   - No, I think the scheme’s design and requirements enable it to attract relevant high-quality proposals; there are no issues.
   - Yes, I think there are aspects that limit the scheme’s attractiveness and accessibility for researchers from HIC institutions
   - Yes, I think there are aspects that limit the scheme’s attractiveness and accessibility for researchers from LMIC institutions

If yes, please specify the problem and suggestion for improvement

17. How do the JGHT’s application process and requirements compare with those of related funding programmes?

    Please describe the application process and requirements for funders/funding programmes you are familiar with, and outline any advantages or disadvantages. If already covered in the previous question on JGHT strengths and weaknesses, please insert ‘see question 10/11’.

Support for additional activities

18. If there are additional activities the JGHT could support that would help it achieve its aims, which do you think would be most important? (select your top choice) [drop-down menu]
   - Support for other types of research
   - Stakeholder engagement
   - Dissemination and knowledge exchange
   - Network building
   - Training
   - Other - please specify

Please explain your answer

19. Do related funding programmes provide support for additional activities not covered by the JGHT that you consider particularly effective to achieve outcomes (e.g. change in policy) and health impacts (e.g. implementation, scale-up) [drop-down menu]
   - Yes – please name programme and describe support
- No, I am not aware of additional activities covered by other programmes that are particularly effective

**Promotion**

20. Do you think calls for proposals and other information on the JGHT are communicated through the right channels, reaching the relevant research community in the UK and as well as in LMICs? [drop-down menu]

- Yes, I think relevant researchers are aware of the JGHT
- No, I think communication about the JGHT could be improved – please specify

**Final comments**

21. Do you have any other comments about the JGHT?
Appendix B  JGHT portfolio analysis (MRC grants database)

B.1  Awards

A total of 96 awards were made as part of Calls 1 – 7 of the JGHT, representing an investment of £138.8m. 63 of these awards were for full trials, with a budget of £133.8m, and 33 were development awards, with a budget of £5.06m. 28 full trial awards had closed by the end of May 2019, with 35 remaining active. Of development awards, 22 had closed and 11 remained active (Table 1).

Table 1  Number of JGHT awards (Call 1 - 7), by status

<table>
<thead>
<tr>
<th>Award status</th>
<th>All awards</th>
<th>Full trial awards</th>
<th>Development awards</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>46</td>
<td>35</td>
<td>11</td>
</tr>
<tr>
<td>Closed</td>
<td>50</td>
<td>28</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>96</td>
<td>63</td>
<td>33</td>
</tr>
</tbody>
</table>

The number of awards made was highest for Call 5, at 20 awards (10 full trial and 10 development), and lowest in Calls 1 and 3, at 10 awards each (Figure 1). The highest number of full trial awards was made in Call 2, at 12 awards, and the lowest in Call 6, at 6 awards. Since the establishment of the development award funding strand in Call 5, the number of awards was 10, 7 and 8 (Calls 5, 6 and 7, respectively).

Figure 1  Number of JGHT awards, by call

The data provided included three grants with unclear status: ‘payments suspended’, ‘grant suspended’, ‘terminating’. These were classified as ‘closed’ (1) or ‘active’ (2) on the basis of the ‘actual end date’ assigned in the data (i.e. end date before or after June 2019).
The 96 awards represent an investment of £138.8m, £133.8m for full trials and £5.06m for development awards. The amount of funding per call allocated ranged between a low of £15.8m in Call 7 / £16.8m in Call 3, and a high of £22.6m in Call 5 (Figure 2).

**Figure 2 Total amount awarded (in £ million), per call**

![Bar chart showing the total amount awarded per call](chart1.png)

The average award size was £2.1m for full trial awards, and £153,500 for development awards. For full trial awards, the lowest average award size was in Calls 2, at approx. £1.8m, and the highest average in Call 6, at £3m. (The low average in Call 2 is due to one small award, at £270,000).

**Figure 3 Average full trial award size, per call (in £ million)**

![Bar chart showing the average full trial award size per call](chart2.png)
The variation in the size of full trial awards ranged from a minimum of £2.2m in Call 4 to a maximum of £4.3m in Call 3. The value of the lowest and highest awards for each Call are shown in Figure 4. The five largest full trial awards were between £4m and £5m (two in call 1, and one each in calls 2, 3 and 6).

The size of full trial awards was more evenly distributed in Calls 1-4, with around one quarter of awards below £1m, between £1-2m, between £2-3m, and larger than £3m (9, 10, 10 and 8 of 37, respectively) (Figure 4b). In Calls 5-7, the largest share of awards was between £2-3m (38%, 9 of 24), following by 29% (7) between £1-2, and 28% (6) larger than £3m.

*Calls 1 and 2 funded one award of under £300,000 each; given that the separate development award scheme had not been established, these awards were omitted from these figures. Source of data: MRC grants database*
For development awards, the lowest average award size was in Call 6, at £129,000, and the highest average was in Call 7, at £161,000. (Call 3 development awards were larger, at an average of £217,000. However, this was before the introduction of a separate Development Award scheme.) The lowest development awards received £91,100 and £95,400 (both in Call 6), while the largest development award was provided with £254,000 (Call 3, see note above) and around £200,000 (5 awards between £190,900 and £206,100, spanning calls 3, 5 and 7).

B.2 Applications and funding requested

Across all 7 calls, the JGHT received a total of 599 project outlines for full trial awards (an average of 86 outlines per call) (Table 2). Of these, 160 were invited to prepare full proposals (26.7%). 144 full proposals were submitted, and 63 approved. This represents an overall success rate of 10.5% from outline to award, and of 43.8% from full proposal to award (Figure 5). The development award scheme operates a one-step application process. 116 applications for development awards were received for Calls 5-7, at an average of 39 applications per call. Of these, 25 were successful, representing a success rate of 21.6%.

<table>
<thead>
<tr>
<th>Application status</th>
<th>Outlines for full trial award scheme</th>
<th>Full trial applications (2nd stage)</th>
<th>Development award applications (calls 5-7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful</td>
<td>160</td>
<td>63</td>
<td>25</td>
</tr>
<tr>
<td>Rejected</td>
<td>439</td>
<td>81</td>
<td>91</td>
</tr>
<tr>
<td>Total</td>
<td>599</td>
<td>144</td>
<td>116</td>
</tr>
</tbody>
</table>

The average number of outlines per call was 85.6, with the largest number of outlines received in Call 1 (142), followed by Call 4 (112) and the smallest number of outlines submitted in Call 6 (55) (Figure 6). The success rate from outline to award was highest in Call 2 (17.9%), and lowest in Call 1 (7.0%) and Call 4 (8.9%) (Figure 7). The success rate from full proposal to award ranged from between 40% ( Calls 1 and...
6) to 48% and 50% (Calls 2 and 5, respectively). The average number of development award applications for Calls 5-7 was 38.7, with success rates between 17.9% in Call 6 and 27.8% in Call 5.

Since the introduction of a separate Development award scheme in Call 5, the amount of funding requested under this strand has steadily increased, from £4.4m in Call 5, to £5.3m in Call 6 and £6.8m in Call 7 (Figure 8).

Two PIs whose applications for full trial awards had been rejected in Call 6 (second stage) successfully applied for a development award in Call 7. At least one PI who had led a development award was rejected at the second stage for a full trial award. One investigator was awarded a full trial as a follow-

---

1 For Calls 3 and 4, a separate Development Award scheme had not yet been established, and all applications followed the same application process. At the decision meetings of these calls, it was determined that while some of the full trial applications were of high quality, they were not yet ready for a full trial award. These applications were provided with ‘development award’ funding (8 awards in total), at an apparent ‘success rate’ of 100%, and are hence not included in Figure 7.

2 Data excerpt provided by MRC; a third PI whose full trial application to Call 7 was rejected secured a development award in Call 9 (i.e. outside the scope of this review).

3 As information on rejected full trial outlines (stage 1) was not available, there is no indication of the overall number of full award outlines submitted following a development award from the MRC database data.
on from a development award, and a smaller award in Call 1 funded a feasibility study which led to a full trial award in Call 5.

(For full trial awards, outlines requesting a total of approx. 2.5 times the available budget are shortlisted; the total amount requested in the second application stage is hence under the control of the funders. Data for the amount requested in the outline stage was not available.)

Figure 8 Amount of development award funding requested (£ million)

B.3 Applications from and awards to lead institutions, by geographic location

- By location of lead PI institution: LMIC, HIC, or joint unit (in LMIC)

More than half (57.6%) of all full trial applications (second stage) were led by PIs affiliated with institutions located in high income countries (HICs) (83 of 144), compared to 27.1% of applications led by PIs from institutions in LMICs (39) and 13.9% from ‘joint units’ (20) located in LMICs (HIC-funded programmes or institutes located in LMICs) (Figure 9). The share of applications for full trial awards for each call was consistently highest from lead PIs affiliated with institutions in HICs, at between 42% and 67% (Figure 10). The share for lead PIs from institutions in LMICs (excluding joint units) was highest in Call 4 (at 41.7%, 10 of 24 applications), and lowest in Call 7 (at 15.8%, 3 of 19 applications). The share of applications from PIs at joint units was highest in Call 5 (21%) and lowest in Calls 1 and 2 (8% each).

Overall, lead PIs from joint units had the highest success rate at 75%, securing 15 of 63 awards across Calls 1-7 (Figure 9). This was followed by lead PIs from HIC institutions, with a success rate of 48.2% (40 awards). PIs from LMIC institutions secured 8 full trial awards, representing a success rate of 20.5%. (Global organisations submitted two applications, but these were not successful.) The number of awards to PIs at institutions in HICs ranged between 4 (Call 6) and 9 (Call 2); PIs at institutions in LMICs and join units secured between 1 and 3 awards, each (Figure 12).

---

5 As information on rejected full trial outlines (stage 1) was not available, there is no indication of the overall number of rejected full trial proposals at outline stage that then went on to apply for a development award from the MRC database.

6 Joint units include: KEMRI Wellcome Trust Research Programme, Kenya; Mahidol Oxford Research Unit, Thailand; Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Malawi; Mwanza Interventions Trials Unit, Tanzania; MRC Unit The Gambia; MRC/UVRI Uganda Research Unit, Uganda; Oxford University Clinical Research Unit, Vietnam. The actual figure for applications from these units may be higher, as the names of investigators for unsuccessful applications were not provided. For awards, each investigator name was checked against the individual’s institution website to determine were the researcher is based (as often only the UK institutions was named, e.g. ‘University of Oxford’ for researchers based at the Oxford University Clinical Research Unit in Vietnam). It is however possible that a number of investigators based at joint units in LMICs were counted as UK-based, as not all websites contained information on location.
Across most calls, the success rate was highest for applications led by PIs at joint units (except Call 3), followed by applications lead by PIs at HIC institutions (Figure 10). In Calls 6 and 7, none of the full trial awards went to lead PIs at institutions located in LMICs (except joint units). The total share of full trial awards for PIs at HIC institutions was 63.5% (40 of 63), 23.8% for PIs at joint units (15) and 12.7% for PIs at LMIC institutions (8).

The average size per full trial award was the same for awards led by PIs at institutions in HICs and joint units (£2.2m; average of 40 and 15 awards respectively), and lower for awards led by PIs at institutions in LMICs (£1.7m; average of 8 awards).

**Figure 9 Number of full trial award applications (second stage) and awards, by location of lead PI**

**Figure 10 Share of application for full trial awards (second stage), by location of lead PI and call**
For development awards, 50.4% of applications (to Calls 5-7) were led by PIs based at institutions in LMICs (58 of 115), 2.6% were from joint units in LMICs (3), and 46.1% from institutions in HICs (53) (Figure 13). Again, lead PIs from joint units had the highest success rate at 66.7%, securing 2 of 25 development awards, followed by PIs at HIC institutions, with a success rate of 26.4% (14 awards). Applications led by PIs from LMICs secured 9 awards, a success rate of 15.5%.

The share of applications for development awards for each call (5-7) was relatively equal for lead PIs from institutions in HICs and LMICs, ranging between 16 and 18 applications (43.9 – 48.7% share) for HICs and between 18 and 21 applications (48.7% and 51.4% share) for LMICs (Figure 14).

Across all three calls, applications led by PIs from HIC institutions had a higher success rate than those from institutions in LMICs, ranging between 37.5 and 22.2%, compared to 22.2 and 14.3% for LMICs.

*This excludes awards made in Calls 3 and 4, before the launch of the development award scheme.*
(Figure 15). Only one application led by a joint unit was submitted per call (and one development award was provided in Calls 7 and 8).

Including awards made in Calls 4 and 5, the total share of development awards for lead PIs at institutions in HICs was 54.4% (18 of 33), compared to 36.4% for lead PIs at institutions in LMICs (12) and 9.1% at joint units (3) (Figure 16).

**Figure 13** Number of development award applications and awards, by location of lead PI

**Figure 14** Share of development award applications, by location of lead PI and call
Figure 15 Success rate of development award applications, by location of lead PI and call

Figure 16 Number of development awards made, by location of lead PI and call

Key figures for applications and awards are summarised in Table 3.

Table 3 Key figures: Applications and awards, by location of lead PI

<table>
<thead>
<tr>
<th></th>
<th>Share of applications (n=144 applications)</th>
<th>Success rate</th>
<th>Share of awards (n=63 awards)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full trial awards</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIC</td>
<td>57.6% (83)</td>
<td>48.2%</td>
<td>63.5% (40)</td>
</tr>
<tr>
<td>LMIC</td>
<td>27.1% (39)</td>
<td>20.5%</td>
<td>12.7% (8)</td>
</tr>
<tr>
<td>Joint unit</td>
<td>13.9% (20)</td>
<td>75%</td>
<td>23.8% (15)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Development awards</th>
<th>Share of applications (calls 5-7, n=115 applications)</th>
<th>Success rate (calls 5-7, 25 awards made)</th>
<th>Share of awards (calls 3-7, n=33 awards)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIC</td>
<td>46.1% (53)</td>
<td>26.4% (14)</td>
<td>54.4% (18)</td>
</tr>
</tbody>
</table>
• By continent of lead PI

The largest share of full trial applications (second stage) was led by PIs at institutions in Europe (46.9%; 81 of 144 applications), followed by PIs in Africa (25.0%; 36 applications) and Asia (15.3%; 22 applications) (Table 4). Lead PIs at European institutions also secured the largest share of full trial awards (60.3%; 38 of 63), representing a success rate of 46.9%. PIs at institutions in Africa secured 18 awards, with a success rate of 50%, while PIs at Asian institutions had a lower success rate of 22.7% (securing 5 awards).

The largest share of development award applications (calls 5-7) was also led by PIs at institutions in Europe (44.3%; 51 of 115 applications). This is followed by applications led by PIs in Asia (27.0%; 31 of 115), Africa (21.7%; 25 of 115) and South America (3.5%; 4 of 115) (Table 4). Success rates were highest for lead PIs in Europe (27.5%; 14 awards from 51 applications), with success rates for applications from lead PIs in Asia and Africa at 19.4% (6 awards) and 16.0% (4 awards), respectively. One of the four applications led by PIs in South America was successful. The overall shares of development awards (calls 3-7) are 51.5% for lead PIs in Europe, 27.3% for PIs in Asia, and 15.2% for PIs in Africa.

| LMIC | 50.4% (58) | 15.5% (9) | 36.4% (12) |
| Joint unit | 2.6% (3) | 66.7% (2) | 9.1% (3) |

• By country

Applications were received from lead PIs affiliated with institutions located in 32 countries (5 HICs, 27 LMICs).

PIs from research organisations in 21 countries applying for full trial awards (full proposal stage), and PIs from 23 countries led applications for development awards.

Table 4 Key figures: Applications and awards, by continent of lead PI

<table>
<thead>
<tr>
<th>Full trial awards, by location of lead PI</th>
<th>Share of applications</th>
<th>Success rate</th>
<th>Share of full trial awards</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>56.3% (81 of 144)</td>
<td>46.9%</td>
<td>60.3% (38 of 63)</td>
</tr>
<tr>
<td>Africa</td>
<td>25.0% (36)</td>
<td>50.0%</td>
<td>28.6% (18)</td>
</tr>
<tr>
<td>Asia</td>
<td>15.3% (22)</td>
<td>22.7%</td>
<td>7.9% (5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Development awards, by location of lead PI</th>
<th>Share of applications (calls 5-7)</th>
<th>Success rate (calls 5-7)</th>
<th>Share of full trial awards (calls 3-7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>44.3% (51 of 115)</td>
<td>27.5%</td>
<td>51.5% (14 of 33)</td>
</tr>
<tr>
<td>Asia</td>
<td>27.0% (31)</td>
<td>19.4%</td>
<td>27.3% (6)</td>
</tr>
<tr>
<td>Africa</td>
<td>21.7% (25)</td>
<td>16.0%</td>
<td>15.2% (4)</td>
</tr>
<tr>
<td>South America</td>
<td>3.5% (4)</td>
<td>25.0%</td>
<td>6.1% (1)</td>
</tr>
</tbody>
</table>

*LMIC: Argentina, Armenia, Bangladesh, Brazil, China, Ethiopia, Georgia, Ghana, India, Kenya, Malawi, Mexico, Nigeria, Pakistan, Papua New Guinea, Peru, Philippines, Senegal, Somaliland, South Africa, Sri Lanka, Tanzania, Uganda, Vietnam; HIC: UK (and ‘UK unit’ in LMIC), Australia, Canada, Singapore, Switzerland
55.6% of applications for full trial awards (80 of 144) were led by PIs at institutions located in the UK, 7.6% applications (11) were from lead PIs located in The Gambia and South Africa, 4.9% in India (7) and 4.2% in Bangladesh (6) (Table 5).

Lead PIs at institutions in 15 countries were awarded a full trial award, with PIs in the UK receiving the largest number (37 of 63 awards corresponding to 58.7% of all full trial awards), followed by PIs in The Gambia (7 awards), Kenya (4 awards) and South Africa (3 awards). Full trial award applications led by PIs in India and Bangladesh were not successful. Of countries with 3 or more awards, applications from lead institutions in Kenya had the highest success rate, at 100% (all 4 full applications funded), followed by The Gambia, with a success rate of 64%, the UK (46%), and South Africa (27%).

Lead PIs from research organisations in 23 countries applied for development awards. In Calls 5-7, 44.3% of applications were led by institutions located in the UK (51 of 115), 17.4% in India (20), 5.2% from South Africa (6), and 4.3% from Nigeria (5).

Across Calls 3-7, development award applications led by PIs at institutions in 10 countries were successful, with PIs in the UK holding the largest share (17 of 33 awards, or 51.5%), followed by PIs in India (4 awards, 12.1%). Lead PIs in South Africa, Kenya, China and Peru held two grants each (6.1%). For Calls 5-7 (i.e. when a separate development award scheme was in place), applications led by institutions in the UK had a success rate of 27.5% (51 applications leading to 14 awards) (Table 5). Applications led by PIs in India had the lowest success rate at 15.0% (20 applications leading to 3 awards). PIs at South African institutions submitted 6 applications, of which 2 were funded (33.3% success rate); PIs in China and Kenya achieved a success rate of 100% (2 awards each).

Table 5: Applications and success rates, per country of lead institution

<table>
<thead>
<tr>
<th>Country of lead institution</th>
<th>Full trial application (stage 2) (n=144)</th>
<th>Full trial awards (n=63)</th>
<th>Success rate</th>
<th>Country of lead institution</th>
<th>Development award application (n=115)</th>
<th>Development awards (n=25)</th>
<th>Success rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>80</td>
<td>37</td>
<td>46.3%</td>
<td>UK</td>
<td>51</td>
<td>14</td>
<td>27.5%</td>
</tr>
<tr>
<td>The Gambia</td>
<td>11</td>
<td>7</td>
<td>63.6%</td>
<td>India</td>
<td>20</td>
<td>3</td>
<td>15.0%</td>
</tr>
<tr>
<td>South Africa</td>
<td>11</td>
<td>3</td>
<td>27.3%</td>
<td>South Africa</td>
<td>6</td>
<td>2</td>
<td>33.3%</td>
</tr>
<tr>
<td>India</td>
<td>7</td>
<td>0</td>
<td>0.0%</td>
<td>Nigeria</td>
<td>5</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>6</td>
<td>0</td>
<td>0.0%</td>
<td>Kenya</td>
<td>4</td>
<td>2</td>
<td>50.0%</td>
</tr>
<tr>
<td>Kenya</td>
<td>4</td>
<td>4</td>
<td>100.0%</td>
<td>Bangladesh</td>
<td>3</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Pakistan</td>
<td>3</td>
<td>1</td>
<td>33.3%</td>
<td>Brazil</td>
<td>3</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Uganda</td>
<td>3</td>
<td>1</td>
<td>33.3%</td>
<td>Tanzania</td>
<td>3</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>China</td>
<td>2</td>
<td>0</td>
<td>0.0%</td>
<td>Australia</td>
<td>2</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Global organisation</td>
<td>2</td>
<td>0</td>
<td>0.0%</td>
<td>China</td>
<td>2</td>
<td>2</td>
<td>100.0%</td>
</tr>
<tr>
<td>Kenya</td>
<td>2</td>
<td>0</td>
<td>0.0%</td>
<td>Georgia</td>
<td>2</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Tanzania</td>
<td>2</td>
<td>1</td>
<td>50.0%</td>
<td>Ghana</td>
<td>2</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Vietnam</td>
<td>2</td>
<td>2</td>
<td>100.0%</td>
<td>Uganda</td>
<td>3</td>
<td>1</td>
<td>33.3%</td>
</tr>
<tr>
<td>Argentina</td>
<td>1</td>
<td>0</td>
<td>0.0%</td>
<td>Peru</td>
<td>2</td>
<td>2</td>
<td>100.0%</td>
</tr>
<tr>
<td>Canada</td>
<td>1</td>
<td>1</td>
<td>100.0%</td>
<td>Armenia</td>
<td>1</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Malawi</td>
<td>1</td>
<td>0</td>
<td>0.0%</td>
<td>Ethiopia</td>
<td>1</td>
<td>0</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

9 All awards in The Gambia and Kenya were to the MRC unit and the KEMRI-Wellcome Trust Research Programme, respectively.
10 Both awards in Kenya were to the KEMRI-Wellcome Trust Research Programme.
• By institution

PIs affiliated with a total of 42 institutions led JGHT awards.

PIs at 60 institutions applied for full trial awards (27 in HICs, 26 in LMICs, 6 at joint units located in LMICs, and 1 with a global organisation). Applications led by PIs at 30 institutions were successful (18 in HICs, 7 in LMICs, and 5 joint units located in LMICs). The largest number of full trial awards were led by PIs based at the London School of Hygiene and Tropical Medicine (LSHTM), with 12 of 63 awards (19%). PIs at the MRC Unit in The Gambia secured 11.1% of awards (7), and the Liverpool School of Tropical Medicine 7.9% (5). PIs at LSHTM also led the largest number of applications (28), with a success rate of 42.9%.

PIs from LMIC institutions securing full trial awards were at the University of Cape Town (2 awards), and Makerere University, Uganda; the University of Ibadan, Nigeria; Stellenbosch University; South Africa; the Papua New Guinea Institute of Medical Research; The Aga Khan University, Pakistan; and the University Cheikh Anta Diop de Dakar, Senegal (1 award each).

The largest number of applications led by PIs from LMIC institutions were affiliated with the ICDDR,B in Bangladesh and Stellenbosch University (4 applications each), followed by the University of Cape Town and The Aga Khan University, Pakistan (3 applications each).

<table>
<thead>
<tr>
<th>Lead institution</th>
<th>Number of full trial awards</th>
<th>Share of full trial awards</th>
<th>Number of applications</th>
<th>Success rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>London School of Hygiene and Trop Med</td>
<td>12</td>
<td>19.0%</td>
<td>28</td>
<td>42.9%</td>
</tr>
<tr>
<td>MRC Unit, The Gambia</td>
<td>7</td>
<td>11.1%</td>
<td>11</td>
<td>63.6%</td>
</tr>
<tr>
<td>Liverpool School of Trop Med</td>
<td>5</td>
<td>7.9%</td>
<td>10</td>
<td>50.0%</td>
</tr>
<tr>
<td>University College London</td>
<td>4</td>
<td>6.3%</td>
<td>6</td>
<td>66.7%</td>
</tr>
<tr>
<td>KEMRI/Wellcome Trust Research Programme, Kenya</td>
<td>4</td>
<td>6.3%</td>
<td>4</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

11 This excludes awards made to LSHTM-associated units.
12 However, as noted above: Names of PIs who led unsuccessful applications were not available, the primary location could not be verified. PIs based at joint units in LMICs are often listed under the associated UK university; the number of applications reported per UK institution here may hence be higher than the actual number, and the success rate lower than the actual success rate.
In total, for Calls 3-7, 24 institutions led development awards (12 in HICs, 10 in LMICs, and 2 joint units). Lead PIs at 79 institutions applied for development awards in Calls 5-7 (26 HIC, 50 LMIC, 2 joint units in LMICs, 1 unknown).

The largest number of development awards was led by PIs based at LSHTM, with 3 of 33 awards (9.1%, calls 3-7), and a 18.2% success rate (2 awards of 11 applications made in calls 5-7) (Table 7). All other institutions led one or two awards only.

### Table 7 Number and share of development awards, by lead institution

<table>
<thead>
<tr>
<th>Lead institution</th>
<th>Number of development awards (calls 3-7)</th>
<th>Share of development awards (calls 3-7)</th>
<th>Number of applications (calls 5-7)</th>
<th>Success rate (calls 5-7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>London School of Hygiene and Trop Med</td>
<td>3</td>
<td>9.1%</td>
<td>11</td>
<td>18.2%</td>
</tr>
<tr>
<td>Liverpool School of Trop Med</td>
<td>2</td>
<td>6.1%</td>
<td>3</td>
<td>66.7%</td>
</tr>
<tr>
<td>Peruvian University Cayetano Heredia</td>
<td>2</td>
<td>6.1%</td>
<td>1</td>
<td>100.0%</td>
</tr>
<tr>
<td>Sangath, India</td>
<td>2</td>
<td>6.1%</td>
<td>3</td>
<td>66.7%</td>
</tr>
<tr>
<td>University of Birmingham</td>
<td>2</td>
<td>6.1%</td>
<td>3</td>
<td>66.7%</td>
</tr>
<tr>
<td>University of Liverpool</td>
<td>2</td>
<td>6.1%</td>
<td>1</td>
<td>100.0%</td>
</tr>
<tr>
<td>University of Nottingham</td>
<td>2</td>
<td>6.1%</td>
<td>1</td>
<td>100.0%</td>
</tr>
</tbody>
</table>
KEMRI/Wellcome Programme, Kenya 2 2 6.1% 100.0%

CBCI Society for Medical Education
Human Sciences Research Council, SA
ICDDR, Bangladesh
King’s College London
MRC/UVRI Uganda Research Unit on AIDS
National University of Singapore
Pham Ngoc Thach University of Medicine
Public Health Foundation of India
Queen’s University of Belfast
Shandong University, China
Sun Yat-Sen University, China
University College London
University of Oxford
University of Plymouth
University of the Witwatersrand
University of York

1 award each

**Trial locations**

In total, 41 countries were cited as trial locations within the ‘Case for Support’ documents of full trial and development awards. Countries with sites included in the largest number of awards were Uganda (19 awards), India (16), Kenya and South Africa (12 each) and Malawi (10) (Table 8). [Studies with sites in multiple countries are counted multiple times.]

The largest number of studies involved sites on the African continent (62 studies; 69%), followed by sites in Asia (37 studies; 39.3%).

<table>
<thead>
<tr>
<th>Country</th>
<th>All awards</th>
<th>Full trial awards</th>
<th>Development awards</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uganda</td>
<td>19</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>India</td>
<td>16</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Kenya</td>
<td>12</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>South Africa</td>
<td>12</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Malawi</td>
<td>10</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Pakistan</td>
<td>7</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Tanzania</td>
<td>7</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>The Gambia</td>
<td>7</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Peru</td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Vietnam</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Bangladesh</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Indonesia</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

*Case for Support documents were available for 62 of 63 full trial awards (all except MR/R006075/1), and 32 of 33 development awards (all except MR/M017362/1). It should be noted that these are initial project plans and subject to change as the project is implemented (i.e. trial site locations may be added, changed, or dropped).*
28.7% of awards were conducted at sites in more than one country (27 of 94). This proportion was higher for full trial awards (35.4%, 22 of 62 trials) than for development awards (15.6%, 5 of 32). 10 studies (10.6%, 10 of 94) were conducted at sites located on more than one continent.

B.4 PIs and co-investigators

Contact details for PIs and co-investigators of JGHT awards (from the MRC’s grant database) were analysed as an indication of affiliation and geographical location of the individuals involved in delivering JGHT projects. It should be noted that:

- The level of contacts available is likely to differ between awards, with some providing information on all researchers at all sites, whereas others only list the main contributors
- Contact details reflect the planned study team at the start of the award, and are not updated over the course of the project. Any changes to the team composition after the start of the award are hence not reflected.

In total, 647 individuals (PIs and co-investigators of the JGHT scheme, Calls 1 - 7) were listed in the database, affiliated with a total of 212 organisations. Half of these organisations are located in LMICs: 104 LMIC institutions (49.1%) and 12 joint units (5.7%); 87 organisations are in HICs (41.0%); 14. 473 researchers were involved in full trials, from 168 organisations, and 194 researchers in development awards, from 74 organisations.

More than half of the 647 researchers were located in HICs (351, 54.8%), compared to 226 researchers (34.9%) at LMIC institutions and 58 researchers (9.0%) in joint units. The share of organisations in HICs is also lower than the share of researchers in HICs (and vice versa for LMICs), indicating that the number of participating researchers per organisation is higher in HICs compared LMICs. This difference is more pronounced for full trial awards than for development awards (see Table 9).

Joint units were more involved in full trial awards than in development awards, representing 7.1% (12 of 255) and 2.7% of all organisations (2 of 104), respectively. This is also reflected in the higher share of researchers from joint units involved in full trial awards.

Table 9 Share of PI and co-investigators, by location of affiliated organisations

<table>
<thead>
<tr>
<th>Location</th>
<th>All awards</th>
<th>Full trial awards</th>
<th>Development awards</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% of all researchers</td>
<td>% of all organisations</td>
<td>% of researchers</td>
</tr>
<tr>
<td>HIC</td>
<td>53.8%</td>
<td>41.0%</td>
<td>53.9%</td>
</tr>
<tr>
<td>LMIC</td>
<td>34.9%</td>
<td>49.1%</td>
<td>32.1%</td>
</tr>
<tr>
<td>Joint unit</td>
<td>9.0%</td>
<td>5.7%</td>
<td>11.4%</td>
</tr>
<tr>
<td>Other</td>
<td>2.3%</td>
<td>4.2%</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

14 Botswana Harvard AIDS Initiative Partner, CDC Botswana – BOTUSA, Eijkman Oxford Clinical Research Unit, Epicentre Mbarara Research Base, KEMRI CDC, KEMRI Wellcome Trust Research Programme, Mahidol Oxford Research Unit, Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Mwanza Interventions Trials Unit Tanzania, MRC Unit The Gambia, MRC Uganda, Oxford University Clinical Research Unit Vietnam

15 The ‘Other’ category includes 15 individuals from 9 organisations, active globally (e.g. WHO, Epicentre, PATH, Dignitas International) or their location is unclear.
Of the 212 organisations listed in the contacts database, the largest number (21.2%, 45) were located in the UK, followed by the USA (7.1%, 15), South Africa (6.6%, 14), Uganda (5.2%, 11) and India (4.7%, 10) (Table 10). Just under 30% of organisations were located in Africa and Europe, followed by Asia (22.2%) and North America (9.0%).

**Table 10 Location of organisations involved in awards (PIs or co-investigators), by country and continent**

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of organisations per country</th>
<th>% of all organisations</th>
<th>Continent</th>
<th>Number of organisations per continent</th>
<th>% of all organisations</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>45</td>
<td>21.2%</td>
<td>Africa</td>
<td>60</td>
<td>28.3%</td>
</tr>
<tr>
<td>USA</td>
<td>15</td>
<td>7.1%</td>
<td>Europe</td>
<td>59</td>
<td>27.8%</td>
</tr>
<tr>
<td>South Africa</td>
<td>14</td>
<td>6.6%</td>
<td>Asia</td>
<td>47</td>
<td>22.2%</td>
</tr>
<tr>
<td>Uganda</td>
<td>11</td>
<td>5.2%</td>
<td>N America</td>
<td>19</td>
<td>9.0%</td>
</tr>
<tr>
<td>India</td>
<td>10</td>
<td>4.7%</td>
<td>Oceania</td>
<td>14</td>
<td>6.6%</td>
</tr>
<tr>
<td>Australia</td>
<td>7</td>
<td>3.3%</td>
<td>S America</td>
<td>6</td>
<td>2.8%</td>
</tr>
<tr>
<td>China</td>
<td>7</td>
<td>3.3%</td>
<td>Caribbean</td>
<td>1</td>
<td>0.5%</td>
</tr>
<tr>
<td>Indonesia</td>
<td>6</td>
<td>2.8%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kenya, Pakistan, Vietnam</td>
<td>5</td>
<td>2.4%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burkina Faso, Canada, Philippines, Tanzania</td>
<td>4</td>
<td>1.9%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The London School of Hygiene and Tropical Medicine was involved in more awards than any other organisation (40 of 96, 41.7%). This was followed by the Liverpool School of Tropical Medicine and University College London (each involved in 14 awards, 14.6%), and KEMRI Wellcome Trust Research Programme in Kenya, involved in 10 awards (10.4%) (Table 11). The LMIC organisations involved in the largest number of awards were The Aga Khan University, Pakistan, and the University of Malawi, Malawi, each involved in 6 awards.

Organisations located in high income countries other than the UK involved in the JGHT were John Hopkins University, USA (involved in 6 awards) and the Institute of Tropical Medicine Antwerp, Belgium (5 awards).

**Table 11 Involvement of research organisations in JGHT awards**

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Number of awards involved in</th>
<th>Percentage of awards involve in</th>
</tr>
</thead>
<tbody>
<tr>
<td>LSHTM</td>
<td>40</td>
<td>41.7%</td>
</tr>
<tr>
<td>LSTM</td>
<td>14</td>
<td>14.6%</td>
</tr>
<tr>
<td>UCL</td>
<td>14</td>
<td>14.6%</td>
</tr>
<tr>
<td>KEMRI Wellcome Joint unit</td>
<td>10</td>
<td>10.4%</td>
</tr>
</tbody>
</table>
88 individuals were in the role of PI in at least one JGHT award, with 9 individuals PIs of more than one award (Table 12). Four of the 96 JGHT awards listed two PIs.16

Individuals involved in the largest number of awards, as PI or co-PI, are listed in Table 12.

<table>
<thead>
<tr>
<th>Name</th>
<th>Contact organisation</th>
<th>Number of awards involved in</th>
<th>As PI</th>
<th>As Co-PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Umberto D’Alessandro</td>
<td>MRC Unit, The Gambia</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Andrew Weeks</td>
<td>University of Liverpool</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Diana Gibb</td>
<td>Medical Research Council</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Feiko ter Kuile</td>
<td>LSTM</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Kathryn Maitland</td>
<td>Imperial College London</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Duolao Wang</td>
<td>LSTM</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Koen Peeters</td>
<td>Institute of Tropical Medicine, Antwerp</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Paul Milligan</td>
<td>LSHTM</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Peter Olupot-Olupot</td>
<td>Mbale Regional Referral Hospital,</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

16 Call 2, Full trial, closed: Ambrose Talisuna and Dejan Zurovac; both University of Oxford; Efficacy of mobile phone short message service (SMS) on malaria treatment adherence and post-treatment review.

Call 3, Full trial, active: Angela Crook (University College London) and Patrick Phillips (University of California, San Francisco); Two-month Regimens Using Novel Combinations to Augment Treatment Effectiveness for drug-sensitive Tuberculosis: the "TRUNCATE-TB" trial

Call 4, Full trial, closed: Katherine Fielding and Stephen Lawon; both LSHTM; Rapid Urine-Based Screening for Tuberculosis to Reduce AIDS-Related Mortality in Hospitalized Patients in Africa (STAMP) Trial

Call 5, Full trial, active: Mark Loeb (McMasters, Canada) and Antonio Dans (U Philippines Manila); A randomized controlled trial of influenza vaccine to prevent adverse vascular events.
PIs by gender
The overall gender balance of the 96 JGHT-funded awards was 67% male to 33% female (63 and 33 of 96, respectively). The balance was relatively similar for full trial awards, with 37% of female-led trials (23 of 63) and 30% of female-led development awards (10 of 33).

The gender balance varied significantly from call to call. The largest share of female-led awards occurred in Call 3 for full trials (71%, 5 of 7), and in Call 7 for development awards (50%, 4 of 8) (Figure 17). The smallest shares were in Call 6 for full trial awards (17%, 1 of 6) and Call 5 for development awards (10%, 1 of 10).

Figure 17 Gender of PI of JGHT awards: share of female PIs per call

Awards led by institutions located in HICs were more often headed by female PIs (41%, 25 of 61) than awards led by institutions in LMICs (26%, 5 of 19). Only 19% of awards to joint units were led by a female PI (3 of 16).

There were also differences between disease areas addressed: While 43% of awards related to TB and HIV were led by female researchers (6 of 14), this was the case for only 19% of awards addressing malaria (3 of 16).

B.5 HRCS Health codes
Over the lifetime of the JGHT scheme, the largest share of award classification (i.e. taking into account the percentage of awards attributed to a category) was in the area of 'Infection', at 44.4% (Figure 18). This area was addressed to some degree in 44 awards (Figure 19). The area of 'Reproductive Health and Childbirth' accounted for 15.3% of HRCS health area allocation (in 21 awards), followed by 'Mental Health' (9.0%; addressed in 9 awards) and 'Cardiovascular' (8.9%; addressed in 13 awards).
The relative shares varied from call to call (Figure 20). The share of 'Infection' awards was highest in Call 1, at 70%, but fell to around 30% in Calls 5 and 7. The area 'Mental Health' increased its share, from no awards in Calls 3 and 4, to 36% in Call 7. 'Reproductive Health and Childbirth' and 'Cardiovascular' remained relatively steady.

For the 'JGHT lifetime' analysis, all shares of HRCS codes were added up per code, and expressed as the percentage of all codes added for Calls 1-7. For the analysis of individual calls, all shares of HRCS code were added up per code, and expressed as the percentage of all codes for the call in question.

This is the number of trials with any level of HRCS Health area attribution, e.g. 100%, 50%, 25% etc; added up, the total number of awards hence exceeds the actual number of awards (77 vs 63).

For the ‘JGHT lifetime’ analysis, all shares of HRCS codes were added up per code, and expressed as the percentage of all codes added for Calls 1-7. For the analysis of individual calls, all shares of HRCS code were added up per code, and expressed as the percentage of all codes for the call in question.
For full trial awards, the overall share of awards addressing 'Infection' was even higher, at 61%, followed by 'Reproductive Health and Childbirth', at 12.5%, and 'Mental Health' and 'Cardiovascular' (at 7.3% each) (Figure 21). The share of full trial awards in the area of 'Infection' remained between 42% and 79% across all calls. All other areas remained at 25% or below, except 'Mental Health' in Call 7, which increased to 33%.

For development awards (Calls 3-7), the share of projects addressing 'Infection' was much lower, at only 11%. 'Reproductive Health and Childbirth' accounted for the highest share, at 21%, followed by 'Mental Health', 'Cardiovascular', 'Infection', and 'Oral and Gastrointestinal' at 9%-13% (Figure 22).
There was no clear trend in health area coverage over time. However, compared to full trial awards, development awards covered a broader range of health areas, with an average of 6.4 codes for Calls 3–7, and an average of 8 HRCS codes for Calls 5–7, i.e. since full establishment of the Development Award scheme. This compares to an average of 4.4 health codes covered for Calls 1–7, and an average of 4.7 codes for Calls 5–7, for full trial awards (Figure 23).

The health area 'Infection' also received the largest amount of funding for full trial awards over Calls 1–7 accounting for 70.6% (£91.2m) (Table 13). This was followed by 'Reproductive Health and Childbirth' with 9.2% of the budget (£11.9m), 'Cardiovascular' with 6.4% of the budget (£8.2m), 'Mental Health' with 4.5% of the budget (£5.8m), and 'Injuries and Accidents' at 2.2% (£2.8m). All other areas accounted for 2% of the budget or less.

Methodology: Funding was allocated by share of HRCS Health code share, i.e. if an award was assigned to two codes, the award budget was split equally between the two research areas. Award MR/R006121/1, £2.7m, is not coded, and was hence not included in this analysis.
Per allocation, 'Injuries and Accidents' and 'Generic Health Relevance' received the largest amount of funding, respectively at £2.8m and £2.5m (normalised, to reflect an allocation of 100% per classification); however, these areas relate to single full trial awards (in Call 4 and Call 3, respectively) (Table 13). The area of 'Infection' saw an average allocation of £2.4m, whereas the 'Cardiovascular' area received an average of £1.8m, 'Reproductive Health and Childbirth' £1.5m, and 'Mental Health' £1.3m.

Table 13 Funding per HRCS Health area - full trial awards (£)

<table>
<thead>
<tr>
<th>Health area</th>
<th>Total funding</th>
<th>Average normalised funding per award</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>£91,223,769</td>
<td>£2,384,935</td>
</tr>
<tr>
<td>Reproductive Health and Childbirth</td>
<td>£11,862,120</td>
<td>£1,530,596</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>£8,215,676</td>
<td>£1,825,706</td>
</tr>
<tr>
<td>Mental Health</td>
<td>£5,753,001</td>
<td>£1,278,445</td>
</tr>
<tr>
<td>Injuries and Accidents</td>
<td>£2,841,141</td>
<td>£2,841,141</td>
</tr>
<tr>
<td>Generic Health Relevance</td>
<td>£2,489,327</td>
<td>£2,489,327</td>
</tr>
<tr>
<td>Cancer</td>
<td>£2,352,357</td>
<td>£2,352,357</td>
</tr>
<tr>
<td>Other</td>
<td>£2,018,969</td>
<td>£1,009,485</td>
</tr>
<tr>
<td>Respiratory</td>
<td>£1,153,194</td>
<td>£2,306,387</td>
</tr>
<tr>
<td>Inflammatory and Immune System</td>
<td>£1,090,670</td>
<td>£2,181,341</td>
</tr>
<tr>
<td>Metabolic and Endocrine</td>
<td>£103,066</td>
<td>£206,132</td>
</tr>
<tr>
<td>Oral and Gastrointestinal</td>
<td>£103,066</td>
<td>£206,132</td>
</tr>
</tbody>
</table>

The health area 'Reproductive Health and Childbirth' received the largest amount of funding for development trial awards over Calls 1-7, accounting for 20.8% (£1.0m) (Table 14). This was followed by 'Infection', with a 13.2% of total funding for development awards (£640k), and 'Cardiovascular' and 'Mental Health', accounting for 12.7% and 12.0% of the funding, respectively. The average normalised level for development awards ranged between £183,000 for 'Infection' and £132,000 for 'Generic Health'.

Table 14 Funding per HRCS Health area - development awards (£)

<table>
<thead>
<tr>
<th>Health area</th>
<th>Total funding</th>
<th>Average normalised funding per award</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reproductive Health and Childbirth</td>
<td>£1,010,349</td>
<td>£151,477</td>
</tr>
<tr>
<td>Infection</td>
<td>£640,086</td>
<td>£182,882</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>£614,552</td>
<td>£157,577</td>
</tr>
<tr>
<td>Mental Health</td>
<td>£581,404</td>
<td>£145,351</td>
</tr>
</tbody>
</table>

Methodology: Again, funding was allocated by share of HRCS Health code share, i.e. if an award was assigned to two codes, the award budget was split equally between the two research areas. Award MR/R006121/1, £2.7m, is not coded, and was hence not included in this analysis.
### Oral and Gastrointestinal
£369,187
£135,233

### Respiratory
£358,964
£143,586

### Neurological
£340,753
£170,377

### Metabolic and Endocrine
£245,174
£141,719

### Generic Health Relevance
£220,667
£132,136

### Cancer
£124,748
£138,609

### Stroke
£124,748
£138,609

### Renal and Urogenital
£85,962
£171,924

### Blood
£74,454
£148,908

### Inflammatory and Immune System
£66,815
£133,030

#### B.6 HRCS Research classification codes

Over the lifetime of the JGHT scheme (Calls 1–7), the largest share of fell into the research classification group 'Treatment evaluation', at 46.0% (Figure 24). This was followed by 'Prevention' (34.3%), 'Health and social care services' (9.6%) and 'Management of diseases' (7.4%). Shares for full trial awards and development awards were broadly similar, with a stronger emphasis on 'Treatment evaluation' in full trial awards (49.6% of full trial awards vs. 39.1% of development awards), and a stronger emphasis on 'Prevention' in development awards (43.8% of development awards vs. 29.4% of full trial awards).

The relative shares varied considerably from call to call. For example, the share of 'Treatment evaluation' was highest in Calls 6 and 1, at 92.3% and 65% respectively, and lowest in Calls 2-4, ranging between 22.4% and 31.3%. The share of 'Prevention' was steadier, ranging between 30.0% (Call 1) and 48.7% (Call 5), except in Call 6, when its share dropped to 7.7%.

Regarding HRCS research classification codes (i.e. second level of research classification group), the largest share of research supported was classified as 'Pharmaceuticals', at 32.2% (Figure 25). This was
followed by 'Primary preventions interventions to modify behaviours or promote well-being' (16.6%), 'Interventions to alter physical and biological environmental risks' (9.4%) and '6.6 Psychological and behavioural' (8.5%).

The relative shares differed between the full trial award and the development award portfolio: While full trial awards fell predominantly into the 'Pharmaceuticals' research class (42.3%), the share was much lower for development award portfolio (12.5%). Conversely, one third of development awards addressed the research class 'Primary preventions interventions to modify behaviours or promote well-being' (33.9%), with only 7.7% of full trial awards in this area. Vaccines were part of the full trial award portfolio (8.1%) but not the development award portfolio, while 'Psychological and behavioural' research took a larger share of development awards (14.1%) compared to full trial awards (5.6%).

**Figure 25 Share of research classification code**

<table>
<thead>
<tr>
<th>Research Classification</th>
<th>Full Trial Awards</th>
<th>Development Awards</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Primary preventions interventions to modify behaviours or promote well-being</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.2 Interventions to alter physical and biological environmental risks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.3 Nutrition and chemoprevention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.4 Vaccines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.5 Resources and infrastructure (prevention)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2 Evaluation of markers and technologies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.3 Influences and impact</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.4 Population screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.1 Pharmaceuticals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.2 Medical devices</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.4 Surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.6 Psychological and behavioural</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.8 Complementary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.1 Individual care needs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.3 Management and decision making</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.1 Organisation and delivery of services</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.2 Health and welfare economics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.3 Policy, ethics and research governance</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The share of research class per call varied considerably, e.g. for 'Primary preventions interventions to modify behaviours or promote well-being' from around 35% in calls 5 and 7 to 0% in Calls 1 and 6 (Figure 26). The exception was the research class 'Pharmaceuticals', which had a substantial share across all calls, at around 30%. The research class 'Interventions to alter physical and biological environmental risks' secured funding in Calls 1 - 4 (between 8.3% and 23.3%, with an average of 18.3%), but accounted for only a small share in Calls 5-7 (less than 4%). On the other hand, research class 'Psychological and behavioural' received no funding in Calls 1-4, a very small share in Call 5 (2.6%), and a substantial share in Calls 6 and 7 (34.6% and 21.4%, respectively).
B.7 Diseases/issues addressed and types of intervention tested

Information from the Case for Support documents of all funded awards was categorised by the study team in relation to specific diseases/issues the awards addressed, and the types of intervention that were tested.

A quarter of all full trial awards were related to malaria (16 of 63; 25.4%) (Figure 27). Of awards addressing malaria, most were concerned with the prevention and lowering of transmission of the disease (14 full trials). Awards addressing TB accounted for 14.3% of trials (10 of 63). As these awards were on average larger than all other trials, at £3.1m, funding dedicated to addressing TB accounted for around 20% of the total full trial award budget (Figure 28).

Other indications addressed in multiple full trial awards include respiratory disease (6 awards; 9.31%), and mental health and HIV-related fungal infections (4 awards each; 6.3%) (Figure 27). The share of funding for trials addressing cardiovascular disease and sexual and reproductive health (6.1%) exceeds that of trials addressing mental health (4.0%), due to the smaller average size of the mental health full trial awards (Figure 28).
Figure 27 Full trial awards, by issue addressed* (in £; data labels indicate number of awards)

*HIV-related fungal infections: Cryptococcal meningitis and talaromycosis; Sexual and reproductive health includes Human Papilloma Virus; Malnutrition refers to Severe Acute Malnutrition (SAM) in infants

Figure 28 Share of total full trial award funding, by issue addressed (data labels indicate average award size)

The largest number of development awards addressed issues related to nutrition (5 of 33; 15.2%), receiving funding of £689,000, followed by interventions addressing cardiovascular disease, diabetes, and tobacco use (3 awards each; 9.1%) (Figure 29).
A large proportion of development awards (48.5%; 16 of 33 awards) investigated interventions aimed at modifying the behaviour of at-risk individuals or patients to prevent disease or improve health outcomes (e.g. through educational tools or SMS messaging).

More than one third of full trial awards targeted infants, children and adolescents (12; 36.5%), and 13 awards (20.6%) were related to women and girls. These figures are higher for development awards, with 42.5% of awards addressing issues relevant to children (14 of 33), and 24.2% addressing issues relevant to women and girls (8 of 33).

---

21 A number of trials addressing issues relevant to girls fall into both categories.
Appendix C  Analysis of Research Fish data

C.1  Overview

A total of 96 awards were made as part of the JGHT calls 1 to 7, 33 development awards (22 closed and 11 active) and 63 full awards (28 closed and 35 active). Of the 96 awards, only 84 (53 full and 31 development) had provided data regarding project outputs, outcomes and impact through ResearchFish (see Table 15). Of the remaining 12 awards, eight are active awards from call 7.

<table>
<thead>
<tr>
<th>Call number</th>
<th>Full trial awards</th>
<th>Development awards</th>
<th>Total</th>
<th>Awards not reported in ResearchFish and their status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Call 1</td>
<td>10</td>
<td>NA</td>
<td>10</td>
<td>1 Full Closed</td>
</tr>
<tr>
<td>Call 2</td>
<td>12</td>
<td>NA</td>
<td>12</td>
<td>1 Full Closed</td>
</tr>
<tr>
<td>Call 3</td>
<td>7</td>
<td>3</td>
<td>10</td>
<td>1 Full Closed</td>
</tr>
<tr>
<td>Call 4</td>
<td>10</td>
<td>5</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Call 5</td>
<td>10</td>
<td>10</td>
<td>20</td>
<td>1 Full Closed</td>
</tr>
<tr>
<td>Call 6</td>
<td>6</td>
<td>7</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Call 7</td>
<td>8</td>
<td>8</td>
<td>16</td>
<td>1 Development + 7 Full Active</td>
</tr>
<tr>
<td>Grand Total</td>
<td>63</td>
<td>33</td>
<td>96</td>
<td>12</td>
</tr>
</tbody>
</table>

The analysis presented in this section represents only those 84 awards for which monitoring data are available. Further, it should be noted that this data has its limitations since it is self-reported and the various reporting fields are interpreted and completed inconsistently by researchers. Therefore, some of the data needs to be interpreted with caution. Where relevant, the caveats for interpretation are described individually for the concerned impact category in this annex.

C.2  Publications

Data reported in the ‘publications’ category in ResearchFish was cleaned to exclude any publications published prior to the award start date (month and year), since these could not have been outputs of the JGHT award itself. In total, 17 papers were deleted based on this criterion.

From our experience, we also know that researchers often include publications unrelated to the relevant award in their ResearchFish submissions. On scanning through the data available, this also appears to be the case with some JGHT awards. However, it was not possible to reliably clean the publications’ data considering the volume of publications involved and without in-depth knowledge of the grant. Reporting of funding support and grant numbers is not available for publication types other than journal articles and even within journal articles it can be inconsistent. It was also not possible to verify attribution for all the awards with the researchers themselves. Hence, it should be noted that the number of publications resulting from JGHT awards may be an over-estimation.

In total, 59 awards reported 772 publications, while 25 awards (including all active development awards) did not report any publication. However, 338 of these publications were reported for one award. While this is a very long-running award, it represents an outlier compared to the rest of the data. Hence, we excluded this award to avoid skewing the analysis of remaining data.

On excluding the outlier from the analysis, 434 publications were reported for 58 awards, coming to a mean of 7.5 publications per award (see Table 16). Of these, the vast majority (94%) are journal articles. As would be expected, the smaller development awards that are funded for a shorter period produce...
fewer publications on average (mean of 4.1/award) than the full trial awards (mean of 8.6 and 9.1 for active and closed awards respectively).

**Table 16 Number of publications by type of JGHT award**

<table>
<thead>
<tr>
<th>Type of publication</th>
<th>Closed Full (n=24)</th>
<th>Closed Development (n=17)</th>
<th>Active Full (n=17)</th>
<th>Total (n=58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Journal Article</td>
<td>207</td>
<td>65</td>
<td>135</td>
<td>407</td>
</tr>
<tr>
<td>Conference Proceeding/Abstract</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>Technical Report</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Manual / Guide</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Book Chapter</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Policy briefing/report</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Working Paper</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Scholarly edition</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>219</strong></td>
<td><strong>69</strong></td>
<td><strong>146</strong></td>
<td><strong>434</strong></td>
</tr>
<tr>
<td>Mean publications per award</td>
<td>9.1</td>
<td>4.1</td>
<td>8.6</td>
<td>7.5</td>
</tr>
<tr>
<td>Mean journal articles per award</td>
<td>8.6</td>
<td>3.8</td>
<td>7.9</td>
<td>7.0</td>
</tr>
</tbody>
</table>

The table below shows the top 12 journals in which JGHT awardees published their research findings. Of these, seven are open access journals and the remaining offer immediate open access to specific articles on the payment of a fee (hybrid open access) and/or to all articles after 6 months (delayed open access). Preference for some form of open access is most likely due to the JGHT funders’ requirements for their research to be freely accessible by the public at large.

**Table 17 Top 12 journals for publications**

<table>
<thead>
<tr>
<th>Journal</th>
<th>Open Access</th>
<th>Number of Publications</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLoS One</td>
<td>Yes</td>
<td>21</td>
</tr>
<tr>
<td>The Lancet</td>
<td>Hybrid/Delayed</td>
<td>17</td>
</tr>
<tr>
<td>Trials</td>
<td>Yes</td>
<td>17</td>
</tr>
<tr>
<td>Clinical Infectious Diseases</td>
<td>Hybrid</td>
<td>16</td>
</tr>
<tr>
<td>BMJ Open</td>
<td>Yes</td>
<td>15</td>
</tr>
<tr>
<td>The Lancet Global Health</td>
<td>Yes</td>
<td>15</td>
</tr>
<tr>
<td>Wellcome Open Research</td>
<td>Yes</td>
<td>13</td>
</tr>
<tr>
<td>The Lancet Infectious Diseases</td>
<td>Hybrid/Delayed</td>
<td>12</td>
</tr>
<tr>
<td>BMC Public Health</td>
<td>Yes</td>
<td>11</td>
</tr>
<tr>
<td>International Journal of Tuberculosis and Lung Disease</td>
<td>Hybrid/Delayed</td>
<td>11</td>
</tr>
<tr>
<td>Malaria Journal</td>
<td>Yes</td>
<td>11</td>
</tr>
<tr>
<td>The New England Journal of Medicine</td>
<td>Delayed</td>
<td>11</td>
</tr>
</tbody>
</table>
C.3  Further funding

50 out of 84 (60%) JGHT awards reported having received substantial further funding (excluding grants less than GBP 10,000) from a number of organisations (Table 18). However, it is not possible to distinguish between funding received to supplement the JGHT award (co-funding) and follow-on funding. Moreover, three additional grants had been counted against two related JGHT awards to the same PI. To avoid double counting, these grants were attributed to the older of the two awards.

The further funding was mainly in the form of research grants (83% of the total). Full awards reported more additional research grants and fellowships/studentships than the development grants. Overall, JGHT awards captured about £160m of further funding from other organisations. This corresponds to a mean of £3.2m further funding per JGHT award (n=50).

<table>
<thead>
<tr>
<th>Type of funding</th>
<th>Closed Full (n=17)</th>
<th>Closed Development (n=10)</th>
<th>Active Full (n=18)</th>
<th>Active Development (n=5)</th>
<th>Total (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research grant</td>
<td>40</td>
<td>16</td>
<td>36</td>
<td>4</td>
<td>96</td>
</tr>
<tr>
<td>Fellowship/Studentship</td>
<td>6</td>
<td>3</td>
<td>9</td>
<td>1</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>19</td>
<td>45</td>
<td>5</td>
<td>115</td>
</tr>
</tbody>
</table>

The table below shows the organisations which have provided three or more grants to JGHT projects. 39 other organisations provided 1-2 grants. The MRC provided the most additional grants (18) followed by the Wellcome Trust and BMGF (11 each). Except for the MRC none of the funders provided more than two additional grants for the same project. Even the MRC provided a maximum of three additional grants, and that too for only two full awards. However, Wellcome Trust, EDCTP, NIHR, BMGF and the NIH provided on average larger grants than the other funders – to the tune of millions of pounds.

<table>
<thead>
<tr>
<th>Funder organisations</th>
<th>Number of additional grants</th>
<th>number of JGHT awards</th>
<th>Average amount of grant (x 1000 GBP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Research Council (MRC)</td>
<td>18</td>
<td>14</td>
<td>639</td>
</tr>
<tr>
<td>Wellcome Trust</td>
<td>11</td>
<td>10</td>
<td>4932</td>
</tr>
<tr>
<td>Bill and Melinda Gates Foundation (BMGF)</td>
<td>11</td>
<td>10</td>
<td>2395</td>
</tr>
<tr>
<td>Grand Challenges Canada</td>
<td>6</td>
<td>5</td>
<td>78</td>
</tr>
<tr>
<td>National Institute for Health Research (NIHR)</td>
<td>6</td>
<td>6</td>
<td>3338</td>
</tr>
<tr>
<td>European and Developing Countries Clinical Trials Partnership (EDCTP)</td>
<td>5</td>
<td>4</td>
<td>4176</td>
</tr>
<tr>
<td>National Institutes of Health (NIH)</td>
<td>5</td>
<td>5</td>
<td>1413</td>
</tr>
<tr>
<td>International Development Research Centre</td>
<td>3</td>
<td>2</td>
<td>513</td>
</tr>
<tr>
<td>Total</td>
<td><strong>65</strong></td>
<td><strong>36</strong></td>
<td><strong>269</strong></td>
</tr>
</tbody>
</table>

C.4  Skills

Only 23 awards reported skills-related problems. Ten projects encountered problems in recruiting people with clinical trial expertise locally. Five projects reported problems with retaining trained staff, either due to staff moving to new jobs (4 cases) or being unavailable to work on the trial due to maternity leave (1 case).
Other skills-related problems mentioned more than once were: issues recruiting staff with the right language skills (either no English skills or no local language skills) and difficulties recruiting people with data analysis skills locally.

C.5 Dissemination

After cleaning for duplicates, we found that 65 awards reported dissemination of trial findings in expert panels or working groups, press or media releases and talks and presentations, etc. In total, 517 dissemination activities were reported (see Table 20).

Table 20 Number of dissemination activities by type of award

<table>
<thead>
<tr>
<th></th>
<th>Closed Full (n=21)</th>
<th>Closed Development (n=17)</th>
<th>Active Full (n=20)</th>
<th>Active Development (n=7)</th>
<th>Total (n=65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of dissemination activities</td>
<td>210</td>
<td>100</td>
<td>284</td>
<td>23</td>
<td>517</td>
</tr>
</tbody>
</table>

The primary audience for almost half of the dissemination events (n=241, 47%) was professional practitioners (e.g. academics, NGO professionals, schoolteachers, and funders) or health professionals (Table 21). The main mechanism for dissemination was talks or presentations, accounting for nearly half of the dissemination activities (n=243, 47%). This was also the predominant dissemination type for most audiences. About half (53%) of the dissemination activities were targeting international audiences. Notably, the geographical reach of activities targeting study participants, students, schools, patients, carers and patient groups was predominantly local. Overall, the median audience numbers ranged from 51 to 100 people for all dissemination activities.

24 awards, mostly full trials, reported dissemination to policymakers, including parliamentarians and politicians, through a total of 67 dissemination activities (Table 21). The main mechanisms for dissemination were talks/presentations (n=29, 43%) or participation in a working group or expert panel (n=24, 36%). The audience numbers reached tended to be smaller (median range, 11-50 people), which is understandable as this is a smaller community. In addition, dissemination was generally at the international (n=26, 39%) or national (n=22, 33%) level.
### Table 21: Number of dissemination activities by primary audience, dissemination type and reach

<table>
<thead>
<tr>
<th>Primary audience</th>
<th>Type of dissemination</th>
<th>Reach</th>
<th>Total events</th>
<th>No. of JGHT awards</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Chief geographical reach (% events)</td>
<td>Median no. of people reached per event (range)</td>
<td></td>
</tr>
<tr>
<td>Professional Practitioners/Health professionals</td>
<td>Talk</td>
<td>International (60%)</td>
<td>51-100</td>
<td>241</td>
</tr>
<tr>
<td></td>
<td>Activity, workshop or similar</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Working group / expert panel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Press release, conference, etc.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>website, blog or social media channel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>magazine, newsletter or online publication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Broadcast</td>
<td>International (60%)</td>
<td>101-500</td>
<td>106</td>
</tr>
<tr>
<td></td>
<td>Open day/ institutional visit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Public/other audiences/media</td>
<td></td>
<td>International (60%)</td>
<td>11-50</td>
<td>67</td>
</tr>
<tr>
<td>Policymakers</td>
<td></td>
<td>International (39%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Local (44%)</td>
<td>51-100</td>
<td>34</td>
</tr>
<tr>
<td>Study participants or study members</td>
<td></td>
<td>Local (39%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undergraduate/postgraduate students</td>
<td></td>
<td>51-100</td>
<td>28</td>
<td>15</td>
</tr>
<tr>
<td>Third sector organisations/supporters</td>
<td></td>
<td>11-50</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>Industry/Business</td>
<td></td>
<td>International (86%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>51-100</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Patients, carers and patient groups</td>
<td></td>
<td>Local (63%)</td>
<td>51-100</td>
<td>8</td>
</tr>
<tr>
<td>Schools</td>
<td></td>
<td>Local (86%)</td>
<td>101-500</td>
<td>7</td>
</tr>
<tr>
<td>Other academic audiences</td>
<td></td>
<td>International (100%)</td>
<td>NA</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>International (53%)</td>
<td>51-100</td>
<td>517</td>
</tr>
</tbody>
</table>
C.5.1. Outcomes of dissemination activities

PIs were also asked to report the most significant outcomes from their dissemination activity. The most frequently reported outcomes for around one-fifth of the activities each were making plans for future related activity such as next steps for research, collaborations, publications and roll out; change in the views, opinions and behaviours of the audience; and increase in requests for further participation (Table 22). 57 (11%) of dissemination activities were reported to have influenced a decision, for example, decisions related to implementing an intervention, or updating of national or WHO guidelines.

Significant outcomes were not reported for about 6% of the activities and PIs were not aware of any impact for a similar number of activities.

<table>
<thead>
<tr>
<th>Type of most significant outcome</th>
<th>Number of dissemination activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plans made for future related activity</td>
<td>107</td>
</tr>
<tr>
<td>Audience reported change in views, opinions or behaviours</td>
<td>101</td>
</tr>
<tr>
<td>Increase in requests about (further) participation or involvement.</td>
<td>97</td>
</tr>
<tr>
<td>Increase in requests for further information</td>
<td>75</td>
</tr>
<tr>
<td>Decision made or influenced</td>
<td>57</td>
</tr>
<tr>
<td>Not aware of any impact</td>
<td>29</td>
</tr>
<tr>
<td>Colleague/s reported change in views or opinions</td>
<td>20</td>
</tr>
<tr>
<td>Not reported</td>
<td>31</td>
</tr>
<tr>
<td>Total</td>
<td>517</td>
</tr>
</tbody>
</table>

C.6 Policy

Full trial awards reported the most instances of policy influence (85% of all instances). In all, 42 JGHT awards reported policy influence of some kind (Table 23). The main routes to policy influence were ‘participation in an advisory committee’ or ‘membership of a guideline committee’. However, these types of influence were largely absent for development awards as well as local or regional spheres of influence.

About a sixth of the instances of policy influence were through influencing the training of practitioners and researchers at local, national, continental and multi-continental/international levels (Table 23). Another sixth of the policy influence was down to citation in policy documents, clinical guidelines or reviews (Table 23). Their geographical reach was mainly at the national or multi-continental/international level, which would be expected as most guidelines and policies in the global health area are developed at a national or international level.

<table>
<thead>
<tr>
<th>Type of policy influence</th>
<th>Geographical reach</th>
<th>Closed Full (n=20)</th>
<th>Closed Development (n=7)</th>
<th>Active Full (n=13)</th>
<th>Active Development (n=2)</th>
<th>Total (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participation in advisory committee</td>
<td>Local/ Regional</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>National</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Continent</td>
<td>National</td>
<td>Multi-continent</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>-----------</td>
<td>----------</td>
<td>----------------</td>
<td>-------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Membership of a guideline committee</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>National</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continent</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-continent</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenced training of practitioners or researchers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local/Regional</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>National</td>
<td>1</td>
<td>0</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continent</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-continent</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implementation circular/rapid advice/letter to e.g. Ministry of Health</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local/Regional</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>National</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continent</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-continent</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citation in clinical guidelines</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>National</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continent</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-continent</td>
<td>6</td>
<td>0</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citation in other policy documents</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>National</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-continent</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participation in a national consultation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local/Regional</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>National</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continent</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gave evidence to a government review</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local/Regional</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>National</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continent</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citation in systematic reviews</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-continent</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citation in clinical reviews</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-continent</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>67</td>
<td>15</td>
<td>45</td>
<td>131</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

C.6.1. Impact achieved through policy influence

Award-holders can report on impacts achieved from the reported policy influence in ResearchFish. However, for 73 (56%) of the instances of policy influence reported, no impact was stated either because there is no impact as yet or the impact is unknown. Of the remaining 58, 50 report some type of healthcare impact in terms of improved accessibility, efficiency and effectiveness of public services; better skilled workforce and improvements in survival, morbidity or quality of life. However, it should be noted that these are potential impacts and are expected to be achieved via policy and practice changes through for example changes in guidelines, implementation of interventions and workforce training.
C.7 Tools

For the purpose of this study, we have considered submissions to the tools, databases and software categories of ResearchFish, broadly as tools. As such, the analysis presented here is an aggregate analysis of those three reporting fields. Overall, 44 awards indicated having developed at least one new research tool, research method, database or software, reporting a total of 149 new tools (Table 24). After databases/data collections, improvements to the research infrastructure and new physiological assessment or outcome measures for trials are the main tools developed within the JGHT awards.

Examples of databases/data collections developed mainly include databases of data collected in the JGHT studies. Others include a database of SMSs appropriate for pregnant teenage girls, a database of treatment reported for community-based deworming and datasets containing costing or household records. Research infrastructure developed in JGHT awards includes electronic medical record systems, data forms and questionnaires, and establishment of new trial sites. New physiological assessment or outcome measures include a household ventilation assessment method for nurses, a quality of life questionnaire for people affected by TB living in shantytowns and an adapted Internalized Stigma of Mental Illness Scale (ISMIS) to measure TB self-stigma.

Table 24 Type of tools developed by type of award

<table>
<thead>
<tr>
<th>Type of tool</th>
<th>Closed Full (n=13)</th>
<th>Closed Development (n=14)</th>
<th>Active Full (n=10)</th>
<th>Active Development (n=7)</th>
<th>Total (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Database/Collection of Data</td>
<td>13</td>
<td>16</td>
<td>12</td>
<td>6</td>
<td>47</td>
</tr>
<tr>
<td>Improvements to research infrastructure</td>
<td>6</td>
<td>18</td>
<td>12</td>
<td>2</td>
<td>38</td>
</tr>
<tr>
<td>Physiological assessment or outcome measure</td>
<td>3</td>
<td>9</td>
<td>11</td>
<td>2</td>
<td>25</td>
</tr>
<tr>
<td>Software, webtool or application</td>
<td>1</td>
<td>9</td>
<td>8</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>Model of mechanisms or symptoms - human</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>Technology assay or reagent</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Biological samples</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Model of mechanisms or symptoms - mammalian in vivo</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>29</strong></td>
<td><strong>47</strong></td>
<td><strong>57</strong></td>
<td><strong>16</strong></td>
<td><strong>149</strong></td>
</tr>
</tbody>
</table>

Only about a quarter of the new tools, databases and software were available to others outside of the research team. While the impact of the tools was largely unknown, some types of impact cited include improvement in skills and knowledge, enabling of research through use of research tools and methods by others outside the research team, and better and more accurate data collection and management through the use of databases.

C.8 Products

The analysis here combines the products, artistic products and IP reporting field of ResearchFish. 41 awards reported development of one type of product, while 43 reported no products. In all, 58 interventional products and 36 artistic products were reported (Table 25). The interventional products reported in most cases do not represent new drugs, vaccines, diagnostic or other interventions created within the JGHT projects but rather new formulations or combinations as well as interventions being tested for a different purpose or in a different context.
The impact of the interventional products was largely unknown except in 18 cases. In most of these cases (n=12), the impact had been felt as a result of deploying the intervention within the JGHT-funded trial. These impacts were largely in terms of improved skills and knowledge within the research team and healthcare workers participating in the trial. For example, in the CRESIPT study, some of TB survivors who were active community case finders in the trial are now government approved health workers. Similarly, tools developed in a trial looking at reducing antibiotic over-prescribing among children with upper respiratory tract infections in China have led to improved diagnosis and management of patients, improved knowledge of the use of antibiotics among caregivers and doctors, and resulted in more rational use of antibiotics in the hospitals involved in the trial.

In the remaining 6 cases, the interventions tested had contributed to public health guidance or were closer to wider adoption and thus were nearer to achieving potential health impact. Examples included a pharmacometric model which has formed the basis for updating dosing guidance for levofloxacin in children affected by TB, a new paediatric formulation for TB that is close to being licensed in South Africa, and two interventions that are being adopted on a wide-scale – an insecticidal bed net and a tablet combining three drugs for prophylaxis in late HIV presenters.

The artistic products have mainly been used to increase awareness of the disease or the trial among the general public, policy makers and other stakeholders as well as to empower and educate participants and potential participants.

Table 25 Type and number of products developed by type of award

<table>
<thead>
<tr>
<th>Type of product</th>
<th>Closed Full (n=13)</th>
<th>Closed Development (n=9)</th>
<th>Active Full (n=14)</th>
<th>Active Development (n=5)</th>
<th>Total (n=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventional products (n=59)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Therapeutic Intervention - Drug</td>
<td>8</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>Preventative Intervention - Behavioural risk modification</td>
<td>1</td>
<td>3</td>
<td>7</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>Preventative Intervention - Physical/Biological risk modification</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Management of Diseases and Conditions</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Support Tool - For Medical Intervention</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Therapeutic Intervention - Psychological/Behavioural</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Therapeutic Intervention - Vaccines</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Health and Social Care Services</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Diagnostic Tool - Non-Imaging</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Therapeutic Intervention - Medical Devices</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Artistic Products (n=36)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Film/Video/Animation</td>
<td>6</td>
<td>6</td>
<td>7</td>
<td>0</td>
<td>19</td>
</tr>
<tr>
<td>Artwork/Image</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Artefact (including digital)</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Exhibition/Performance</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>23</td>
<td>43</td>
<td>5</td>
<td>95</td>
</tr>
</tbody>
</table>
Appendix D Clinical trials registry data analysis

- **Background**
  Clinical trial registry data was collated for all 63 full JGHT trials over calls 1-7. Data was downloaded from ISRCTN, ICTRP and PACT registries.

- **Trial status**
  The status of each full trial as listed in the clinical trials database is given in Figure 30. As expected, trials in calls 1, 2 and 3 are primarily completed.

![Figure 30 Status of full trials per funding call (n=63)](image)

- **Study participants**
  Most studies (78%, 49 of 63) enrolled both male and female participants. Of the studies that enrolled only female participants 50% (7 of 14) were related to reproduction/sexual health.

  The target age group of patient recruitment varied between studies. The majority of studies enrolled only adults (38%, 24 of 63) with roughly even numbers focussing on children (32%, 20) and mixed ages (29%, 18). One study (2%) recruited seniors only.

- **Trial sites and settings**
  One third of the studies were listed as multi-country (32%, 20 of 63) and 13% (8) were listed as multi-continent. Overall, 55 countries hosted trial sites (Figure 33). The majority of trials included trial sites in Africa (74.6%, 46 trials). Fewer trials included sites in Asia (30%, 19 trials) and Central/South America (7.9%, 5 trials).

  Trials were most commonly set in the community (35%, 22 of 63), followed by hospitals (33%, 21) and other (11%, 7) (Figure 31).

---

22 Two trials received co-funding to conduct parallel trials in developed and LMIC countries; these are included in this analysis (but would not have been funded by the JGHT award).
Trial interventions and types

Drugs were the most common intervention evaluated in the full trials, accounting for almost half of all trials (48%, 30 of 63) (Figure 32). Behavioural interventions (11%, 7), vaccines (11%, 7) and mixed interventions (10%, 6) were also common. Seven trials (11%) had interventions that did not fit into the discrete categories, these were highly varied and included, for example, SMS reminders, diagnostic screening and hygiene.

The majority of studies were classified as treatment (51%, 32 of 62) or prevention studies (41%, 26). The remaining were classified as health services research (5%, 3), diagnostic (2%, 1) or screening (2%, 1). Treatment studies were primarily drug interventions (72%, 23 of 32), whereas prevention studies varied across the intervention types.

Target conditions

The 63 trials targeted 19 conditions. Malaria accounted for the largest share of trials (24%, 15 of 63), followed by tuberculosis (14%, 9 of 63) and sexual/reproductive health (11%, 7 of 63). The full list of conditions is available in Table 26.

The conditions investigated varied between locations with most countries reporting a mixture of conditions (Figure 33).

There were overlaps between some conditions, in particular between HIV and tuberculosis and between HIV and cryptococcal meningitis. In such cases, the condition allocated is based on the condition that is being targeted with the intervention, e.g. in a trial evaluating a TB vaccine in populations with HIV, the trial would be listed under TB.
Figure 33 Map of trial locations listed in clinical trial database and the top 5 countries with the most trials.
### Table 26 List of conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>% (count)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria</td>
<td>24% (15)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>14% (9)</td>
</tr>
<tr>
<td>Reproduction/sexual health</td>
<td>11% (7)</td>
</tr>
<tr>
<td>Mental Health</td>
<td>8% (5)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td></td>
</tr>
<tr>
<td>Cardio-vascular disease</td>
<td>5% (3 each)</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td></td>
</tr>
<tr>
<td>HIV, Prophylactic antibiotics, Violence prevention, Human papilloma virus</td>
<td>3% (2 each)</td>
</tr>
<tr>
<td>Head Injury, Streptococcus, Helminths, Liver fluke, Podoconiosis, Talaromycosis, Hepatitis, Malnutrition</td>
<td>2% (1 each)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>63</strong></td>
</tr>
</tbody>
</table>
Appendix E  Survey analyses

E.1  PI survey analysis

E.1.1. Overview
Responses were received from 88% (21 of 24) of PIs of full active trials and 74% (20 of 27) of PIs of development awards (7 closed, 13 active). Of the PIs of full trials who did not respond, one was not able to be contacted due to an incorrect email address, and another was from a trial with two PIs where only one responded.

- Location of respondents (by country)
Approximately two thirds of respondents were located in the UK for both full trials (66%, 14 of 21) and development awards (65%, 13 of 20). For full trials, two respondents were located in The Gambia, and one respondent each in Canada, Kenya, Papua New Guinea, the Philippines, and Uganda. For development awards, three respondents were located in India, and one each in Bangladesh, Kenya, South Africa, and Vietnam.

- Project overview
The reported number of trial sites per award varied from 1 to 30 (full award) and 1 to 10 (development award). Across all awards, trial sites were located in 32 different countries (Figure 34). The largest number of trials involved sites in Uganda and India (10 each, 25%).

Figure 34 Countries listed as trial sites (n=40)

When asked what the tested intervention of the research project was, most respondents (83%, 34 of 41) selected one intervention, 15% (6) selected two or three and one respondent selected 6 interventions (Figure 35). The largest number of respondents indicated the tested intervention was ‘prevention – behavioural’ (24%, 10), followed by ‘treatment – psychological’ (20%, 8) and ‘treatment - drug dosage/regimen’ (17%, 7). Overall, the interventions were evenly divided between treatment (including screening and treatment) and prevention (58%, 24 and 51%, 21, respectively).
The majority of PIs (70%, 29 of 41) reported only one target population for their award, 17% (7) selected two and 12% (5) selected three or more (Figure 36). The target population varied between projects, with new-borns/children the most commonly selected group (37%, 15). There was a relatively even distribution between the diseases represented with the exception of malaria which represented only 5% (2) of responses. This could be explained by a greater proportion of malaria projects receiving funding during the earlier calls for funding, which would not be reflected in the surveys of active trials.

**Pilot studies**

Responding to the question of whether a pilot study had been carried out at the trial location prior to applying to the JGHT, over half of the PIs of full trials (55%, 11 of 20) reported that there was no need for a pilot study, while roughly one third (35%, 7) indicated that they had conducted a pilot study at the trial location (Figure 37).
Approximately one third of development award respondents (30%, 6 of 20) had previously applied for a full award from the JGHT, 5% (1) reported that they had previously applied to another funder, while 65% (13) reported that they had not applied for a full trial related to this research (Figure 38).

The majority of development award respondents indicated that the intervention was successful and are either in the process of applying for (45%, 9 of 20), or have obtained (5%, 1) further funding for a full trial (Figure 39). Three respondents (15%) indicated that the results of the development award showed that the plans for the full trial need to be significantly changed and that further preliminary data needs to be collected. Of these, two reported that the intervention was shown to be non-effective.

Throughout the survey PIs described some benefits of the development award scheme. One PI stated that participation in the development award had helped to guide the design of the full study. Another PI who has since received funding for a full trial reported that the development trial revealed a lot about the temporal variability of the topic that may otherwise have been mistaken for an effect of the intervention implementation. However, there was also criticism that conducting a pilot RCT is ill-advised, as this requires almost as much work as conducting a properly powered trial: “One still needs study documents, approvals, logistical systems etc to be in place and to conduct the same analyses”.

* Other refers to a trial where the intervention showed significant results, but the regulatory landscape of the intervention is currently under review. The decision to proceed will depend on the nature of the upcoming changes. * One respondent applied for JGHT funding and was unsuccessful but was subsequently successful with an application with another funder. # There were two development awards that have secured JGHT funding for a full trial. The PIs of these awards were interviewed so are not included in the survey results.
E.1.2. Project team

- Change to project team

Most of the PIs (78%, 31 of 40) reported that the project team did not change from the team set out in the Case for Support (Figure 40). Where changes were made, reasons given included a new trial site, career transitions, maternity leave, and the death of a researcher.

Figure 40 Reported change to project team (n=40)

The project team was/is as described in the Case for support
The current project team includes additional members than described in the Case for support*
The current project team does not include all team members described in the Case for support*

*One PI answered yes to both adding and removing team members

- Project team expertise

The expertise involved in each project as reported by the PI is illustrated in Figure 41. The most common expertise involved in the project were clinical trial methodology (88%, 36 of 41), data management (88%, 36) and statistician (85%, 35). Conversely, expertise in health systems (27%, 11), knowledge brokerage (e.g., stakeholder engagement, network building) (27%, 11) and patient recruitment (22%, 9) were the least frequently reported. PIs of full trials reported on average nine different skills, whereas PIs of development awards reported an average of six different skills (Figure 42).

Figure 41 Expertise included in the project (full =21; development n = 20)
**Figure 42 Heatmap of expertise reported by each PI. Each column represents a separate response (n=41).**

<table>
<thead>
<tr>
<th>Respondent</th>
<th>Full</th>
<th>Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical science</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical trial methodology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical trial management</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Data management</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statistician</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health economics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social science</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health policy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health systems</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient recruiter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knowledge brokerage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evaluation/impact</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Full - laboratory skills (n=1), epidemiologist (n=1), entomologist (n=2), early childhood education (n=1); Development – microbiologist (n=1), clinicians (n=1).

**E.1.3. Stakeholder engagement**

PIs reported a range of stakeholder engagement during the design phase of the project. The largest number of survey respondents reported that they had engaged with LMIC health care professionals (71%, 29 of 41), followed by implementing organisations/NGOs (59%, 24). Fewer respondents pointed to engagement with policy makers from international agencies (32%, 13) and community organisations (29%, 12) (Figure 43). PIs of full awards reported engagement with more stakeholders on average (mean=3) compared to PIs of development awards (mean=2) (Figure 44). The number of stakeholder groups consulted was highly variable between different awards: While seven full trial PIs indicated engagement with 5 or 6 stakeholder groups, ten PIs had engaged with 1-2 stakeholder groups. Five full trials (from Calls 4, 5 and 6) did not engage with national or international policy bodies.
Stakeholder engagement during the project was consistent with the stakeholder engagement during the design phase. Again, the largest number of survey respondents reported that they engaged with LMIC health care professionals (66%, 27 of 41), followed by implementing organisations/NGOs (63%, 26) (Figure 45). A larger proportion of full award PIs reported engagement with LMIC research systems compared to development award PIs (76%, 16 and 25%, 5, respectively) and policy makers from international agencies (62%, 13 and 20%, 4) (Figure 46). Reported stakeholder engagement was greater during the project compared to during the design phase for all stakeholders except LMIC healthcare providers. The number of stakeholder groups...
consulted remained highly variable between different awards: Seven full trial PIs indicated engagement with 6-8 stakeholder groups, four PIs engaged with 1-2 stakeholder groups. Only one of the five full trials that had not engaged with national or international policy bodies started engagement during the trial implementation (and none of the remaining four trials included policy makers as part of the study team). It is possible that due to prior work, (some of) these teams are already embedded within the relevant policy arena, but that this information is not conveyed within the survey responses.

Figure 45 Stakeholder engagement during project beyond those directly involved in the research project (n=41)

*Other includes engagement with scientific and technical experts (n=1), policy makers from state government (n=1) and details of how research was disseminated (n=2).

Figure 46 Heatmap of stakeholder engagement during project beyond those directly involved in the project. Each column represents a separate response (n=41)

^Other includes engagement with scientific and technical experts (n=1), policy makers from state government (n=1) and details of how research was disseminated (n=2).
All respondents indicated that they engaged with stakeholders via a direct approach (100%, 37 of 37) (Figure 47). Other common approaches were via seminars (54%, 20) and workshops (51%, 19).

**Figure 47 Method of stakeholder engagement (n=37)**

- LMIC researcher involvement for UK-led projects

Of the respondents who were PIs of UK-led projects, 81% (22 of 27) commented on how LMIC researchers were involved in the trial. The most common response (73%, 16 of 22) was that LMIC researchers were engaged throughout the project including project design and implementation. A smaller proportion (27%, 6) shared that LMIC involvement took on more of an advisory role or that LMIC-based researchers were predominately involved in the design phase of the project. A number of respondents (18%, 4) reported that LMIC researchers led aspects of the project, including economic analysis and the development of culturally appropriate awareness information. LMIC researchers were also reported (23%, 5) to have been important conduits for stakeholder engagement and networking. Nearly a quarter of PIs (23%, 5) reported a pre-existing relationship with LMIC researchers and/or research institutes.

**E.1.4. Barriers and enablers**

- Challenges

When asked what the main challenges were in the implementation of the research project, the largest number of respondents indicated that they had encountered difficulties related to reporting or gaining approvals (68%, 27 of 40), followed by challenges with local capacity (43%, 17) (Figure 48). The impacts of the challenges encountered were most commonly described as delays to the project timeline (30%, 12) and/or challenges with recruitment (20%, 8).

Several PIs (28%, 11 of 40; 33% of full awards, 7 of 20) reported that the approval process (including regulatory and ethical approvals) took longer than expected with one reporting that approvals could take over 200 days at some sites. While 12.5% (5) reported having to obtain approval from more than one institute/site. For example, one PI reported that the process of obtaining all required ethical and regulatory approvals could involve three or four separate applications and committees in each country, each with varying capacity, requests, and demands.
Challenges with local capacity were reported by 43% (17 of 40) of respondents (33% of full awards, 7 of 20). Training requirements varied from basic training (e.g. orientation to trial methods) to more comprehensive training covering multiple aspects of the trial (e.g. basic trial methodology, implementing the intervention and managing data). It was understood that due to the nature of the development award a degree of training would be expected. A development award PI reported that it was the first time running such a trial in their city and country and that many things needed to be learned during the implementation of the trial.

An example of politics included governments rolling out a national intervention that put the control arm at risk. In such cases additional steps needed to be taken (e.g. intensified patient engagement) to maintain the integrity of the project. Other challenges associated with working in countries with sometimes politically unstable environments were retraction of support at short notice, workers strike, conflict, or elections that impacted the running of the trial.

Challenges with patient recruitment were reported by 20% (8 of 40) of respondents. There were slightly more full trial PIs reporting patient recruitment challenges (25%, 5 of 20) than development award PIs (15%, 3 of 20). One PI reported that there were challenges with recruitment associated with stigma of the health condition in the local country.

A number of PIs included examples of how they overcame challenges. For example, in one project there was a high turnover of trial staff which was causing delays due to the need to retrain each new staff.
member. The project team therefore developed an online training module to facilitate a quicker orientation and training process. In another study, the recruitment process was slow due to a lower than expected birth rate. This was resolved by expanding the study site and altering the inclusion criteria.

- **Adjustments**

  Although 44% of respondents (18 of 41) reported there were no major adjustments to the project plan after the start of the project, over a quarter of these (28%, 5 of 18) went on to select areas where they had adjusted the project (Figure 49). In such cases, these responses were recoded and included in the respective ‘adjustment’ categories. Of the 20% of PIs who selected “other” (8), three repeated a category already listed and were recoded to that selection.

  The most common adjustment reported by PIs was to the study timeline (49%, 20 of 41). This is in line with study timeline delays being commonly described as an impact of the challenges above (30%, 12). A number of development PIs reported asking for a no-cost extension (12%, 5, 1 did not state no-cost).

  Overall, adjustments to study design were reported by over half of respondents (56%, 23 of 41). Adjustments to trial team and stakeholder engagement were comparatively less common (15%, 6 and 7%, 3, respectively).

  Figure 49 Adjustments made to study during implementation (n=41)

  ![Adjustments made to study during implementation](image)

  ^Total is the percentage of respondents who selected one or more of the categories within each group.

  Some of the adjustments reported were in response to changes in the policy landscape. For example, one trial needed to adjust the control arm of the trial in light of updated WHO guidance for basic treatment. Other causes for adjustments were the addition of secondary research questions e.g. assessment of drug resistance, longer patient follow-up and sequencing of samples.

  In one case, the trial team conducted more extensive training than initially proposed in order to ensure that those delivering the trial reached the minimum competencies required. Given the extensive nature
of the training, the trial was able to be upgraded from a non-randomised trial to a randomised control trial, in consultation with the funders.

- Lessons learned

Most PIs indicated that, in hindsight, they would have made a change to the study design (71%, 29 of 41), in particular in relation to the study timeline, site and scope (19%, 9; 19%, 9 and 12%, 5, respectively) (Figure 50). A smaller proportion also indicated they would have managed stakeholder engagement differently (14%, 6) or would have carried out a pilot study (7%, 3). The most common reasons given for the above “lessons learned” were to make the study outcomes more translatable into policy, e.g. so results would be more generalisable (45%, 13 of 29), or to build a better relationship with stakeholders to ensure a smoother running of the project (31%, 9).

Figure 50 Changes that PIs would have made to study with hindsight (n=41)

The majority of respondents from full trials reported that there are no findings to date since the project is ongoing (71%, 15 of 21), about a quarter 24% (5) reported the main trial findings and two reported preliminary/auxiliary findings. Conversely, main findings were reported for 70% (14 of 20) of the development awards with 25% (5) projects ongoing (Table 27). This difference is likely due to the mix of both active and closed trials in the development group. The most frequently reported output was publications with 29% (6 of 21) of full and 30% (6 of 20) development trials respondents reporting a publication to date. The type of publications included the main trial paper, trial protocol, social or economic study paper or other paper (e.g. validation of methodology). PIs also reported that they have papers in preparation or submitted to journals.

E.1.5. Impacts, outcomes and outputs

The survey included PIs of active full trials (21) and PIs of closed (7) and active (13) development awards. These results represent a snapshot of the impacts, outcomes and outputs of each trial at the time of the survey and these will naturally change in the active trials as the projects progress. Given the disparity between full and development awards, these responses will be reported separately in this section.

- Outputs and scientific outcomes

The majority of respondents from full trials reported that there are no findings to date since the project is ongoing (71%, 15 of 21), about a quarter 24% (5) reported the main trial findings and two reported preliminary/auxiliary findings. Conversely, main findings were reported for 70% (14 of 20) of the development awards with 25% (5) projects ongoing (Table 27). This difference is likely due to the mix of both active and closed trials in the development group. The most frequently reported output was publications with 29% (6 of 21) of full and 30% (6 of 20) development trials respondents reporting a publication to date. The type of publications included the main trial paper, trial protocol, social or economic study paper or other paper (e.g. validation of methodology). PIs also reported that they have papers in preparation or submitted to journals.
In response to the question if new tools or databases were developed as part of the project, 29% (6 of 21) of full and 30% (6 of 20) of development respondents reported new tools were developed. These tools were either associated with the intervention (e.g. treatment manuals) or were research tools (e.g. consent tool, data collection, patient enrolment).

Table 27 Outputs and scientific outcomes

<table>
<thead>
<tr>
<th>Outputs and scientific outcomes</th>
<th>Full (n=21)</th>
<th>Development (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Findings (did the research answer the primary research questions?)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5 (24%)</td>
<td>14 (70%)</td>
</tr>
<tr>
<td>Yes, preliminary/auxiliary</td>
<td>2 (5%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Ongoing</td>
<td>15 (71%)</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>Social study findings^</td>
<td>1 (5%)</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Publications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main trial publication</td>
<td>3 (14%)</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>In prep/submitted</td>
<td>7 (35%)</td>
<td></td>
</tr>
<tr>
<td>Trial protocol</td>
<td>2 (10%)</td>
<td></td>
</tr>
<tr>
<td>Social/economic paper</td>
<td>2 (10%)</td>
<td></td>
</tr>
<tr>
<td>In prep/submitted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other paper</td>
<td>4 (19%)</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>In prep/submitted</td>
<td>1 (5%)</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>Tools (incl. software)/Databases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tool for delivering/monitoring intervention (e.g. can be used for implementation)</td>
<td>3 (14%)</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>Tool for research (e.g. consent tool, data collection)</td>
<td>4 (19%)</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Database for continued research</td>
<td>1 (5%)</td>
<td></td>
</tr>
</tbody>
</table>

^Results were categorised from “describe main findings” questions

- Collaborations, networks and partnerships

The majority of respondents reported working with new partners during their JGHT funded project (86% (18 of 21) of full trials; 75% (15 of 20) of development trials) (Figure 51). Most projects had started to collaborate with partners located in LMICs (77% of full trial awards; 65% of development awards) and 57% of full trial awards and 35% of development awards included new partners located in HICs.

Figure 51 Collaborations

- No, I had already worked with this project team
- Yes, new partners from institutions in HICs
- Yes, new partners from institutions in LMICs
- Yes, new partners from institutions in HICs and LMICs
The majority of full and development award respondents indicated they either have plans to collaborate in future (38%, 8 of 21; 15%, 3 of 20, respectively) or do not have currently plans but would be open to future collaborations (62%, 13; 75%, 15, respectively). When asked about the ongoing plans for these collaborations, ‘regular information exchange and advice’ was the most common selection for respondents of full trials (71%, 15) (Figure 52). Developing a joint proposal was the most common selection for respondents of development trials (45%, 9) and was the second most common selection for respondents of full trials (52%, 11).

Roughly a third of respondents from full and development awards reported that they have secured funding for the ongoing collaborations (33%, 7 of 21; 30%, 6 of 20, respectively), and one third were planning or had submitted proposals (33%, 7 of 21; 30%, 6 of 20, respectively). Sources of this additional funding are listed in Table 28. Three PIs of full awards (14%, 3 of 21) reported securing further funding from the JGHT for related research (two full awards, one development award). Another full award PI reported securing a £4M grant from the Wellcome Trust to support a collaborative research network incorporating researchers who first worked together on the JGHT project.

Development award PIs reported similar funding outcomes. One PI reported a £2M grant awarded by the NIHR to support the research collaboration that was formed during the JGHT development project. In another three examples, PIs from development awards had secured additional smaller grants (between £25,000 – £200,000) to further support the implementation and feasibility of the trial intervention.

Addresses

Respondents reported that research networks had been developed/expanded during the JGHT funded project. Even numbers of full trial respondents reported a development/expanded of local and
international networks (50%, 10 of 20) whereas slightly more development PIs reported development/expansion of local networks (60%, 12 of 20) than international networks (40%, 8).

In 45% of full trials (9 of 20) and 35% of development awards (7 of 20), respondents reported working with new policy/implementation partners (Figure 53). The majority of new partnerships for both were in LMIC. Examples of new policy/implementation partnerships included NGOs, WHO and local LMIC Ministry of Health (or equivalent).

Figure 53 Policy/implementation partnerships

Full trial respondents (n=20) Development trial respondents (n=20)

- No, I had already worked with these policy and implementation partners
- Yes, new partners from organisations in LMICs
- Yes, new partners from organisations in HICs and LMICs

Most respondents reported either an ongoing partnership (full 50%, 10 of 20; development 40%, 8 of 20) or the intention to partner again in the future (full 25%, 5 and development 30%, 6) with the policy makers/implementation partnerships developed under the JGHT award. A smaller number reported that they do not envision a future partnership (full 20%, 4 and development 15%, 3).

- Other outcomes

Further outcomes of the JGHT funded projects reported by survey respondents included new infrastructure in LMIC institutes, training and building research capacity (Table 29). Building research capacity was the most frequently reported outcome, specifically building capacity in relation to knowledge and technical skills (full 70%, 14 of 20; development 75%, 15 of 20), followed by leadership capabilities (full 60%, 12; development 60%, 12).

Table 29 Other outcomes

<table>
<thead>
<tr>
<th>Other outcomes*</th>
<th>Full (n=20)</th>
<th>Development (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infrastructure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research</td>
<td>6 (30%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Community/health care</td>
<td>4 (20%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Training</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research general (incl. lab skills)</td>
<td>2 (10%)</td>
<td></td>
</tr>
<tr>
<td>Research capacity building at LMIC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motivation</td>
<td>11 (55%)</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>Knowledge and technical skills</td>
<td>14 (70%)</td>
<td>15 (75%)</td>
</tr>
<tr>
<td>Governance</td>
<td>8 (40%)</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Leadership</td>
<td>12 (60%)</td>
<td>12 (60%)</td>
</tr>
</tbody>
</table>
• Impacts

The majority (76%, 16 of 21) of full trial respondents indicated that policy/health impacts had not yet been achieved as the project was still ongoing but that such impacts were anticipated (Table 30). A further 24% (5) reported that the trial had influenced policy, namely WHO recommendations and national programmes. One PI reported that the findings of the research were currently being implemented.

Most (55%, 11 of 20) development award respondents reported that the outcomes of the trial could not be used to inform health or policy outcomes but that they can inform further research. Of those who reported that the results had the potential to lead to health or policy impacts (40%, 8), one reported that the project had influenced healthcare practice, but further research is required before formal policy changes are made and the true health impact understood.

The majority of full trial PIs (11%, 52 of 21) also reported that it was too early to report on the uptake of the scientific outputs of the trial, however 19% (4) reported that further research had taken up the findings of the trial with regards to the intervention tested.

<table>
<thead>
<tr>
<th>Impacts</th>
<th>Full (n=21)</th>
<th>Development (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy/health impacts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not yet, but likely or have potential</td>
<td>16 (76%)</td>
<td>8 (40%)</td>
</tr>
<tr>
<td>Yes, influenced policy/health</td>
<td>4* (19%)</td>
<td></td>
</tr>
<tr>
<td>No, but will inform future research</td>
<td>12 (55%)</td>
<td></td>
</tr>
<tr>
<td>Practise/implementation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Findings practised in study countries</td>
<td>1 (5%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Uptake of scientific outputs (e.g. databases, tools, methods)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not yet</td>
<td>11 (52%)</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>The intervention tested</td>
<td>4 (19%)</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>Research tools developed</td>
<td>3 (14%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Networks developed</td>
<td>1 (5%)</td>
<td></td>
</tr>
<tr>
<td>Policy context</td>
<td>1 (5%)</td>
<td></td>
</tr>
<tr>
<td>Health system context</td>
<td>1 (10%)</td>
<td></td>
</tr>
</tbody>
</table>

*One PI refers to research fish report – substantial volume of information provided includes membership on policy boards, and suggestions that it is in policy – brief investigation reveals policy may still be under review.

• Other impacts

Respondents also reported impacts associated with the process of conducting the trial (Figure 54). The most common impact reported by respondents from full trials was a benefit to the health of the trial participants derived from their participation (60%, 12 of 20), mainly through improved access to healthcare during the trial, enhanced monitoring and diagnostics, and receiving information pertaining to the condition of interest. Respondents from development trials most commonly reported health benefits as a result of participants’ receiving the trial intervention as part of the study, i.e. the intervention itself was beneficial (40%, 8 of 20).
In a small number of cases there was a benefit to the broader community where the trial was being run, for example through improved health care capacity, health screening and greater awareness/education about the condition (10% of full trials, 2 of 20; 5% of development awards, 1 of 20).

JGHT research also assisted in shaping the environment for global health research, facilitating future studies. Both full trial and development award PIs reported that the trial had increased the priority of GH research within LMIC institutes (full 50%, 10 of 20; development 30%, 6 of 20), reduced cultural and operational barriers to GH research (full 45%, 9; development 30%, 6), and convinced decision makers and practitioners of the value of GH research (full 40%, 8; development 30%, 6).

* including awareness of condition and healthcare capacity
• Outputs and impacts survey responses

The range of ‘other’ impacts and outcomes (i.e. impacts/outcomes not directly related to the research question) reported varied extensively between responses (Figure 55). Just under a half (45%, 9 of 20) of full trial respondents reported impacts in seven or more areas and around a third (30%, 6) reported impacts in four or fewer areas. This variation was also observed across development trial responses but to a lesser extent, with only a quarter of respondents (25%, 5 of 20) reporting an impact in seven or more areas and around a third (35%, 7) reporting impacts in four or fewer areas. The most commonly reported ‘other’ impact/outcome was an increase in LMIC researchers’ knowledge and technical skills (full 70%, 14; development 70%, 14) followed by an increase in LMIC researchers’ research leadership capabilities (full 55%, 11; development 60%, 12) (Figure 56).

Figure 55 Heatmap of ‘other’ reported impacts/outcomes.

<table>
<thead>
<tr>
<th>Full</th>
<th>Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Helped to convince practitioners and decision makers of the value of GHT</td>
<td></td>
</tr>
<tr>
<td>Given a higher priority to GHT and health research at LMIC institution(s)</td>
<td></td>
</tr>
<tr>
<td>Reduced operational barriers to future health research and GHT</td>
<td></td>
</tr>
<tr>
<td>Reduced cultural barriers to future health research and GHT</td>
<td></td>
</tr>
<tr>
<td>Increased motivation of professionals at LMIC institutes to become research leaders</td>
<td></td>
</tr>
<tr>
<td>Increased LMIC researchers’ knowledge and technical skills</td>
<td></td>
</tr>
<tr>
<td>Enhanced LMIC institutions’ research governance structures</td>
<td></td>
</tr>
<tr>
<td>Increased LMIC researchers’ research leadership capabilities</td>
<td></td>
</tr>
<tr>
<td>Built up or expanded a local network of researchers</td>
<td></td>
</tr>
<tr>
<td>Built up or expanded an international network of researchers</td>
<td></td>
</tr>
<tr>
<td>No / not yet</td>
<td></td>
</tr>
</tbody>
</table>
Overall, there were more outputs reported or anticipated from full trials than from development awards (Figure 57). Most respondents (75%, 15 of 20) from full trials indicated that there were outcomes that are anticipated but not yet developed. This is in keeping with the understanding that all of these trials were classified as ‘active’ at the time of the survey.

The most common output reported or anticipated by both full and development respondents was publication of findings (full 100%, 20 of 20; development 100%, 20 of 20), followed by health benefits to trial participants (full 100%, 20; development 90%, 18). New research methodology was the least commonly reported or anticipated outcome for both full and development awards (full 40%, 8; development 25%, 5) (Figure 58).
Figure 57 Heatmap of reported outputs. Dark colours represent yes, light colours represent not yet and grey indicates no. White indicates no response. Red denotes full trials and green denotes development awards.

<table>
<thead>
<tr>
<th></th>
<th>Full</th>
<th>Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health benefits for participants</td>
<td><img src="image" alt="Heatmap" /></td>
<td><img src="image" alt="Heatmap" /></td>
</tr>
<tr>
<td>Publication of findings</td>
<td><img src="image" alt="Heatmap" /></td>
<td><img src="image" alt="Heatmap" /></td>
</tr>
<tr>
<td>Research tools or databases</td>
<td><img src="image" alt="Heatmap" /></td>
<td><img src="image" alt="Heatmap" /></td>
</tr>
<tr>
<td>Research methodologies</td>
<td><img src="image" alt="Heatmap" /></td>
<td><img src="image" alt="Heatmap" /></td>
</tr>
<tr>
<td>Research infrastructure</td>
<td><img src="image" alt="Heatmap" /></td>
<td><img src="image" alt="Heatmap" /></td>
</tr>
<tr>
<td>Project findings taken up</td>
<td><img src="image" alt="Heatmap" /></td>
<td><img src="image" alt="Heatmap" /></td>
</tr>
</tbody>
</table>

Figure 58 Reported and anticipated outcomes (full n=20; development n=20)
E.1.6. JGHT and the funding landscape

- Global health funding landscape

When respondents were asked what other sources of funding for late-stage global health trials they were aware of, the US National Institutes of Health (NIH) was most commonly cited (33%, 13 of 39), followed by funding from the Bill & Melinda Gates Foundation (BMFG) (31%, 12), the European and Developing Countries Clinical Trials Partnership (EDCTP) (26%, 10) and Wellcome Trust (26%, 10) (Table 31).

Table 31 Other funders in the global health research landscape. The top 5 funders are in bold.

<table>
<thead>
<tr>
<th>Funder</th>
<th>n = 39</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td></td>
</tr>
<tr>
<td>Wellcome Trust</td>
<td>10 (26%)</td>
</tr>
<tr>
<td>NIHR</td>
<td>6 (15%)</td>
</tr>
<tr>
<td>MRC</td>
<td>4 (10%)</td>
</tr>
<tr>
<td>Global Challenges Research Fund</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>UKRI</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Newton Fund</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Global Alliance for Chronic Diseases</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>US</td>
<td></td>
</tr>
<tr>
<td>NIH</td>
<td>13 (33%)</td>
</tr>
<tr>
<td>Bill &amp; Melinda Gates Foundation</td>
<td>12 (31%)</td>
</tr>
<tr>
<td>USAID</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Presidents Malaria Initiative</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Thrasher Foundation</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>EU</td>
<td></td>
</tr>
<tr>
<td>EDCTP</td>
<td>10 (25%)</td>
</tr>
<tr>
<td>EU</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Horizon 2020</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>National Health Medical Research Council (Australia)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Canadian Institutes of Health Research</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Pharmaceutical companies/in kind</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Others – listed once each: Indian Research Funding Council, Philippine Council for Health Research and Development, UNITAID, WHO, Population Health Research Institute (Canada)</td>
<td>5 (13%)</td>
</tr>
</tbody>
</table>

- Strengths, weakness and advantages of the JGHT

Strengths of the JGHT reported by PIs fall into three major categories:
1) the type of research funded under the scheme, including the scheme’s values and focus on impact
2) the administrative processes, including application and post award interactions with the funders
3) the reputation of the funding organisations.

Most respondents were complimentary of the type of research funded under the scheme (69%, 24 of 35), in particular the broad range of topics that were covered (31%, 11) (Figure 59). Also commended were
the types of trial designs that were funded (e.g. design/size), the focus on LMIC involvement, the flexibility to encompass capacity building and the focus on research that yields implementable results. One respondent commented that a key strength was that the scheme not only addresses major health related problems affecting low and middle income countries, but also encourages involvement and engagement of stakeholders, such as policy makers, throughout the research process in order to ensure trial results are implementable, scalable and in line with policy needs.

About a quarter of respondents (26%, 9 of 35) felt that the application process and administrative procedures during the trial were key strengths of the JGHT, with most explaining that it was a straightforward and supportive process (20%, 7). A few respondents also highlighted the flexibility in the funding (11%, 4).

A smaller proportion reported that the reputation of the funders was a key strength (14%, 5).

Of respondents from development awards, over a quarter (27%, 5 of 18) reported that the development scheme was a key strength of the JHGTI, with one PI highlighting as important “the recognition that it is important to first develop an intervention and test the trial design, before plunging straight into a full RCT”.

Almost a third of respondents stated there were no obvious weaknesses of the JGHT (29%, 8 of 28) (Figure 60). 29% of respondents considered the amount of funding available was insufficient (8), 18% reported issues with administrative factors (e.g. timeline, fund transfer logistics) (5) and 14% a lack of specific funding for dissemination, capacity building and PhD studentships (4).
Of the PIs who responded to the question of whether other funding programmes had advantages over the JGHT, half (50%, 12 of 24) indicated that they were unsure or did not know the landscape well enough to comment. The majority of those that were able to comment (58%/7 of 12) mentioned funding, specifically either the amount of funding available (25%, 3) or the funding of additional aspects such as capacity building or student fellowships (33%, 4).

- **Current gaps in funding landscape**

The majority of respondents (89, 34 of 38) felt there were critical gaps in the global health funding landscape. [Nine respondents indicated there were no critical gaps in the global health research funding landscape; however, five of these went on to select critical gaps. These responses were therefore recoded to ‘yes’.]

The most frequently identified gap was in the type of research funded (44%, 17 of 38), followed by resources for critical research infrastructure (37%, 14) and resources for training (34%, 13) (Figure 61).

When asked to explain the choice of critical gaps, 76% (29 of 38) of respondents who had indicated that there was a funding gap provided further details on the nature of the gap. The majority reiterated the need for funding of their specific health problem/intervention/geography (41%, 12 of 29) or capacity building and training in LMICs (38%, 11). The feeling that their health field/intervention was underfunded was reported more commonly by PIs of development awards (67%, 8 of 12) compared to PIs of full awards (24%, 4 of 17). Overall, the majority reported a need for funding relating to a non-communicable disease (50%, 6 of 12) and/or multidisciplinary research (25%, 3 of 12).

Another gap raised related to the lack of follow-on funding to support further research and implementation of trial findings (17%, 5 of 29). One PI reported that there is a lack of funding continuity when trial outcomes indicate further trials are required. All respondents who discussed this gap were from full awards. Other gaps discussed included a lack of funding for addressing systems-level problems, for stakeholder engagement and for research to better understand local priorities.


Design of the JGHT

Most respondents felt there were no aspects of the JGHT design or requirements that could be improved (57%, 21 of 37). Of those who said there were areas that could be improved, the reasons given were varied. Some general themes included the addition of funding for capacity building, requirements on timelines for administrative procedures, and increasing the available funding amount.

Despite these areas for potential improvement, 97% (37 of 38) of respondents felt the current design and requirements enabled the scheme to attract high-quality proposals.

When asked to compare the JGHT’s application process and requirements with those of related funding programmes, almost all responses were positive (97%, 29 of 30). Most respondents described the JGHT scheme as “simpler” than other schemes or “straightforward” (63%, 19 of 30); others reported that it was similar (30%, 9). One respondent commented that the application timeline was longer than other schemes (3%). Two respondents (7%) wrote that the Je-S system needed to be revamped. Two PIs also expressed appreciation of the low frequency of reporting requirements, feeling it was less burdensome compared to some other schemes (7%).

Most respondents (92%, 35 of 38) considered the JGHT scheme to have been communicated through the right channels, and to have reached the relevant research community in the UK and as well as in LMICs. Of those who indicated it was not communicated effectively, two (6%) suggested the use of social media e.g. Twitter, and one respondent (3%) suggested dissemination via the medical literature.

Additional activities to support impact

More than a third of respondents (38%, 14 of 37) reported that related funding programmes provide support for additional activities that are not covered by the JGHT to facilitate achievement of scientific outcomes and health impacts. The most frequent examples were dedicated funding streams to support implementation and translation of findings into policy (e.g. EDCTP and BMGF), and a focus on capacity building (e.g. Wellcome Trust-Newton Fund Collaboration, GCRF and EDCTP). Other activities that were shared were a workshop on impact (NIHR), funding for results dissemination (Wellcome trust) and funding to embed ancillary studies within a trial (BMGF).

When asked which additional activities the JGHT could support that would help it achieve its aims, equal numbers (21%, 7 of 33) considered training, networking, and dissemination and knowledge exchange.
the most important areas. Infrastructure and stakeholder engagement were less frequently selected (6%, 2 each) (Figure 62).

Figure 62 Additional activities the JGHT could support to increase the potential impact from research (n=33)

*Other included flexibility in funding to account for unexpected events, funding of larger trials, face-to-face interactions with funders and support for policy change and implementation.

PIs who discussed the need for networking support (21%, 7 of 33) suggested the JGHT could facilitate a networking event or structure specifically for JGHT award recipients. Suggestions for training were more varied and included flexibility to use research budget for training, student scholarships, and training in specific skills or methods. Other areas of support mentioned were flexibility in funding to account for unexpected events, funding of larger trials, face-to-face interactions with funders, and support for policy change and implementation.

A.1.1 Final comments

The final comments were mostly positive (87%, 13 of 15) including mentions of how the JGHT is unique in the UK, how the scheme has a great potential for health impact and how the funding has furthered the PI’s area of research.

Roughly half of the comments (47%, 7 of 15) included suggestions for improvements related to the need for networking of grant holders, sustained long-term support to detect longer term impacts, funding for larger projects, a clear contact person within the JGHT and guidance to encourage limiting the proposal to the main project aims.

E.2 Co-investigator survey analysis

E.2.1 Overview

- Summary of responses

The survey invitation was sent to 556 co-investigators. Of these, 17% (94) were unable to respond either because they did not feel they were involved sufficiently in the trial, were on annual leave, did not have a current searchable email address, were retired, on maternity leave or deceased. Of those remaining, responses were received from 38% (175 of 462).

Responses were received from co-investigators representing 85% (81 of 95) of the JGHT funded projects with a median of 2 responses per project.
- **Respondent details**

Country was reported by 98% (172 of 175) of respondents with 41 countries represented. The United Kingdom represented the greatest proportion of responses (33%, 56 of 172) followed by South Africa (5%, 8), Malawi (4%, 7), India (4%, 7) and Australia (4%, 7).

The majority of respondents were from high income countries (HIC) (44%, 77 of 175) (Figure 63). Responses from low/middle income countries (LMIC) made up 39% (68) and joint units (JU) made up 14% (25) of responses.

**E.2.2. Role of co-investigator**

Most respondents (87%, 152 of 174) indicated expertise in 1-4 area(s). The most common areas of expertise reported were clinical trial methodology (50%, 87 of 174), clinical science (43%, 74), and clinical trial management (41%, 72) (Figure 64). Fewer respondents had expertise as a patient recruiter (10%, 17) and knowledge brokerage (8%, 14).

On average, LMIC respondents selected a larger number of expertise areas compared to investigators in HICs. Each of the areas was selected by a larger share of LMIC researchers than HIC investigators, with the exception of health economics (HIC 21%, 16 of 77; LMIC 10%, 7 of 68) and statistics (HIC 16%, 12 of 77; LMIC 10%, 7 of 68) (Figure 65). This may indicate a lesser degree of specialisation (perceived or actual) in researchers in LMICs compared to those active in HICs.

Clinical trial methodology, clinical science and clinical trial management were the most commonly selected areas of expertise for all LMIC, HIC and joint unit respondents. This was most apparent in LMIC and joint unit respondents where, with the exception of LMIC respondents for clinical science, over 50% of respondents selected each of these areas. Patient recruitment was only selected by LMIC and JU respondents (LMIC 21%, 14 of 68; JU 12%, 3 of 25).
When asked about their level of involvement in the design of the project, most co-investigators reported being either very involved (44%, 77 of 174) or having made a substantial contribution (27%, 46) to the design of the project (Figure 66). The reported involvement did not vary greatly between co-investigators from LMIC, JU or HIC with all three reporting most commonly that they were involved in all aspects (HIC 41%, 31 of 76; JU 44%, 11 of 25; LMIC 49%, 33 of 68) (Figure 67). Co-investigators from a LMIC reported higher rates of having a feedback/advisory role compared to HIC and JU (LMIC 13%, 9 of 68; HIC 1%, 1 of 76; JU 0%), whereas JU co-investigators reported the highest rate of limited input (LMIC 3%, 2 of 68; HIC 3%, 2 of 76; JU 12%, 3 of 25).
The majority of co-investigators did not feel that their role in the project differed from what was written in the funding application (82%, 143 of 174) (Figure 68). Of those that did report a change (18%, 30), over half (57%, 17 of 30) reported being less involved than planned. Responses were similar between co-investigators across LMIC, JU and HIC institutes (Figure 69).
E.2.3. Project design and implementation

The majority of co-investigators indicated that, in hindsight, they would not make any changes to the design or implementation of the project (64%, 111 of 173) (Figure 70). Of those that indicated they would make changes, the most commonly reported change was to the study timeline (15%, 26 of 173). One quarter of respondents (25%, 44) outlined the reason for their selected change. Most (89%, 39 of 44) of these comments provided specific details for the selected change within their trial, commonly highlighting the challenges and unpredictability of working in an LMIC environment (23%, 10). A small proportion of these (16%, 7 of 44) indicated additional areas they would change (e.g. better communication across the research team).

The proportion of LMIC and HIC respondents who reported they would not make changes or would change the study timeline was similar (LMIC 59%, 2 of 68; HIC 63%, 47 of 75) (Figure 71). There was a greater proportion of respondents from JUs would not make changes (80%, 20 of 25). No co-investigators from LMIC institutes reported that they would make changes by conducting a pilot study,
change the scope of the study or include more training for staff. By comparison, no co-investigators from HIC reported that they would recruit additional experts to the team.

Figure 71 Changes to the project in hindsight by co-investigator institute (LMIC n = 68, JU n = 25, HIC n = 75)

E.2.4. Impacts for coinvestigators
- Impacts on own work
Co-investigators were asked how the JGHT funded project has impacted their work across three areas: scientific knowledge, collaborations and networks, and context knowledge. Overall, most respondents indicated the project had impacted their scientific knowledge (82%, 140 of 170), in particular that the project had provided them with scientific knowledge that has been used in further work (71%, 121 of 170) (Figure 72).

With regards to collaborations and networks, roughly even numbers of respondents indicated that the JGHT project had given them contacts for future work (53%, 92 of 172) and that collaborations formed during the JGHT project had continued after (or outside) the project (50%, 86 of 172).

The context knowledge impact most commonly reported was that knowledge of health needs had improved as a result of their involvement (49%, 83 of 169).

A number of co-investigators (42%, 73 of 173) provided further details on how their involvement in the trial had specifically impacted their work with one investigator reporting that the trial “had consolidated a successful research collaborative network and enabled a shift from epidemiological and qualitative exploratory work to interventions.”

Co-investigators also explained why there had been no impacts to date (16%, 12 of 73). The most frequently given reason was because the trial was still ongoing and it was too early to report any definitive impacts (75%, 9 of 12).
Figure 72 Impacts of JGHT trial on the work of co-investigators

<table>
<thead>
<tr>
<th>Scientific knowledge (n=170)</th>
<th>Total^</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scientific knowledge for further work</td>
<td></td>
</tr>
<tr>
<td>Secure additional funding</td>
<td></td>
</tr>
<tr>
<td>Tools and methodologies for further work</td>
<td></td>
</tr>
<tr>
<td>Changed research direction</td>
<td></td>
</tr>
<tr>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>Collaborations and networks (n=772)</td>
<td></td>
</tr>
<tr>
<td>New contacts for future work</td>
<td></td>
</tr>
<tr>
<td>Continued collaborations</td>
<td></td>
</tr>
<tr>
<td>Active in new research networks</td>
<td></td>
</tr>
<tr>
<td>New implementation partners</td>
<td></td>
</tr>
<tr>
<td>Influence on policy work beyond project</td>
<td></td>
</tr>
<tr>
<td>Active in new policy networks</td>
<td></td>
</tr>
<tr>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>Context knowledge (n=169)</td>
<td></td>
</tr>
<tr>
<td>Total^</td>
<td></td>
</tr>
<tr>
<td>Not applicable</td>
<td></td>
</tr>
</tbody>
</table>

^ Total indicates the total number of respondents who selected any impact within that theme.

In general, the proportions of co-investigators reporting impacts did not vary greatly between LMIC and HIC locations (Figure 73). There were only two reported impacts where the proportions differed by more than 10%, these were an enhanced understanding of health needs (HIC 45%, 33 of 74; LMIC 59%, 39 of 66) and new implementation partners (HIC 13%, 10 of 76; LMIC 35%, 23 of 66) (Figure 74). A smaller proportion of co-investigators from JU reported impacts across all impacts when compared to LMIC and HIC, instead reporting the highest rate of not applicable in each category.
The number of respondents for each question was: Scientific knowledge LMIC n = 65, JU n = 25, HIC n = 75; Context knowledge LMIC n = 66, JU n = 24, HIC n = 74.

- Impacts for co-investigators institution

The most commonly reported impact on the co-investigators’ institute was that the JGHT funded trial impacted the work of others at the institute (39%, 66 of 168), followed by providing the institute with new contacts (33%, 56) and allowing the organisation to secure further funding (26%, 43) (Figure 75). Over a quarter reported that the project had no impact on their organisation (26%, 44). Of those who selected ‘other’ most (7 of 12) explained that they did not know the impacts on their institution.

Over a third of respondents (37%, 62 of 168) provided further information on how the JGHT trial has impacted their institute, mostly (90%, 56 of 62) providing specific details on the impacts selected. For example, on respondent reported that “The information gathered, and the wealth of experience has made [their] organisation attractive for other research donors and partners and it has strengthened the relation with the Ministry of Education and Health”. One respondent reported that a subsequent grant application was underway and would further strengthen the collaboration between their LMIC institute.
and their UK based partners that was developed as part of the JGHT. A smaller number of respondents (10%, 6 of 62) explained why there were no impacts to date. This was primarily because the project was ongoing (83%, 5 of 6)

Figure 75 Impacts on the co-investigators institute (n=168)

Higher proportions of LMIC co-investigators reported impacts on their institute for all impacts except new networks which was reported at a comparable rate between LMIC and HIC (HIC 25%, 18 of 72; LMIC 24%, 16 of 66) (Figure 76). The greatest difference was in their reported impact on establishing new infrastructure which was reported by 38% (25 of 66) of LMIC respondents compared to 8% (2 of 25) of JU and 7% (5 of 72) of HIC. Similarly, over half of LMIC respondents (55%, 36 of 66) reported that the trial had impacted the work of others in their organisation, compared to 32% and 28% by JU and HIC respectively (JU 8 of 25; HIC 20 of 72). That more impacts were reported in LMIC institutes is further supported by the higher proportions of JU and HIC respondents reporting that there were no impacts compared to LMIC (LMIC 12%, 8 of 66; JU 36%, 9 of 25; HIC 35%, 25 of 72).

Figure 76 Impact on co-investigator institute by institute (LMIC n = 66, JU n = 25, HIC n = 72)
E.2.5. Impact at project site

The most frequently reported impact at the project site, beyond the research question, was an increase in the LMIC researcher’s knowledge and technical skills to undertake health research and global health trials (42%, 68 of 161), followed by the development or expansion of an international researcher network (40%, 65) (Figure 77). There were roughly even numbers of responses indicating the trial had: led to a build-up or expansion of a local network of researchers (35%, 55), helped convince practitioners/decision makers of the value of global health trials and health research (35%, 54), and increased LMIC researchers’ leadership capabilities (33%, 54). Less than one fifth reported there were no impacts or that impacts had not been achieved yet (19%, 30).

Over a third of respondents (39%, 62 of 161) provided further information on the impacts at the trial site, again most commonly expanding on the impacts listed in Figure 77. The most common discussion point was that the project had increased the research capacity of institutes or individuals (37%, 23 of 62). Other themes were stronger relationships between researchers and policy makers (19%, 12) and further funding (13%, 8).

A number of respondents commented that they were unable to answer the question because they were not sufficiently involved at the study site or the study was ongoing (10%, 6).

![Figure 77: Impacts at project site beyond the research questions (n=161)](image)

- Increased LMIC researchers’ knowledge and technical skills to undertake GHT/HR^*
- Built up/expanded international network of researchers
- Built up/expanded local network of researchers
- Helped convince practitioners/decision makers of the value of GHT/HR^*
- Increased LMIC researchers’ research leadership capabilities
- Reduced the operational barriers to future GHT/HR^*
- Given a higher priority to GHT HR at LMICs institution(s)
- Increased motivation of health professionals at LMIC institutions to become research leaders
- Enhanced LMIC institutions’ research governance structures
- Reduced cultural barriers to future GHT and HR^*
- Other
- No / not yet

*GHT and HR = global health research and health trials.

The increase in LMIC researcher’s knowledge was reported consistently between co-investigators from LMIC, JU and HIC institutes (LMIC 42%, 27 of 64; JU 44%, 11 of 25; HIC 43%, 29 of 72) (Figure 78).
The remaining impacts were reported fairly evenly between HIC and LMIC with the proportions of respondents differing by 10% only twice, these were the development or expansion of an international researcher network (HIC 50%, 34 of 68; LMIC 33%, 21 of 64) and enhanced LMIC institutions’ research governance structures (HIC 13%, 9 of 68; LMIC 27%, 17 of 64). JU institutes generally had the lowest proportion reporting each impact. JU also had the greatest proportion reporting that there were no impacts or that impacts had not been achieved yet (JU 20%, 5 of 25) but this proportion was not greatly different from that of LMIC or HIC (LMIC 16%, 10 of 64; HIC 19%, 13 of 68).

Figure 78 Impacts at project site beyond research question, by institute (LMIC n = 64, JU n = 25, HIC n = 68)

E2.6. Other JGHT awards

A small subset of co-investigators (5%, 9 of 175) provided details about their involvement on other JGHT awards, including two who commented that additional funding applications had been rejected. A further two respondents reported that they have ongoing global health projects with the MRC under the Newton Fund.


E.2.7. JGHT and the funding landscape

- Global health funding landscape

When respondents were asked what other sources of funding for late-stage global health trials they were aware of, the Bill & Melinda Gates Foundation was most commonly cited (37%, 43 of 116), followed by funding from the European and Developing Countries Clinical Trials Partnership (EDCTP) (34%, 39), the US National Institutes of Health (NIH) (32%, 37) and Wellcome Trust (24%, 28) (Table 32).

**Table 32 Other funders in the global health research landscape.**

<table>
<thead>
<tr>
<th>Funder</th>
<th>n = 116</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UK</strong></td>
<td></td>
</tr>
<tr>
<td>Wellcome Trust</td>
<td>28 (24%)</td>
</tr>
<tr>
<td>MRC</td>
<td>11 (9%)</td>
</tr>
<tr>
<td>NIHR</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>Global Challenges Research Fund</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>Global Alliance for Chronic Diseases</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>Newton Fund</td>
<td>1 (1%)</td>
</tr>
<tr>
<td><strong>US</strong></td>
<td></td>
</tr>
<tr>
<td>Bill &amp; Melinda Gates Foundation</td>
<td>43 (37%)</td>
</tr>
<tr>
<td>NIH[^]</td>
<td>37 (32%)</td>
</tr>
<tr>
<td>USAID</td>
<td>2 (2%)</td>
</tr>
<tr>
<td><strong>EU</strong></td>
<td></td>
</tr>
<tr>
<td>EDCTP</td>
<td>39 (34%)</td>
</tr>
<tr>
<td>EU</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>IMI</td>
<td>1 (1%)</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
</tr>
<tr>
<td>National Health Medical Research Council (Australia)</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>Grand Challenges Canada</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>UNITAID</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>Pharmaceutical companies/in kind</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>WHO</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Others – listed once each: Against Malaria Foundation, ANRS (France), Canadian Institutes of Health Research, DFID, Foundation Botnar, MacArthur Foundation, Medicines for Malaria Venture, Meningitis Vaccine Project, Swiss Programme for Research on Global Issues for Development (r4d programme), The Global Fund, World Bank</td>
<td>11 (9%)</td>
</tr>
</tbody>
</table>

[^] Includes the various “subs” e.g. national institute of mental health and AIDS clinical trials group.

- Strengths, weaknesses and advantages of the JGHT

Strengths of the JGHT reported by co-investigators fall into two major categories:

1) the type of research funded under the scheme, including the scheme’s values and focus on impact
2) the administrative processes, including application and post award interactions with the funders

Most respondents were positive about the type of research funded by the JGHT (53%, 55 of 104). Specifically, this was due to the broad topics funded by the scheme (15%, 16), the size, design and funding amount (14%, 15), and the focus on LMIC researchers and institutes (14%, 15) (Figure 79). Co-
investigators also complimented the funding process (34%, 35). Many respondents commented that the administrative procedures within the MRC were supportive and straightforward (20%, 21). The flexibility of the funding was also commended (13%, 13). One respondent commented that “It is the only dedicated source for clinical trial funding where you can apply for any trial. It is hugely important for global health. The scheme has had long-lasting health impacts (through high quality research) in Africa. The funding is flexible and grant management is friendly.”.

Of those who felt they could not comment (16%, 17 of 104), most indicated that they did not have sufficient knowledge of the scheme or funding landscape (76%, 13 of 17).

When asked about the main weaknesses of the JGHT, 20% (15 of 76) of respondents felt there were no weaknesses to report. The most common weaknesses reported were funding procedures including lengthy processes and limited communication with funders (24%, 18), followed by a bias towards established and UK-based PIs (18%, 14), and a lack of specific funding for capacity and follow-on studies (16%, 12) (Figure 80).

PIs from LMIC institutes most commonly reported funding processes as a weakness of the JGHT (40%, 12 of 30) (Figure 81). By comparison, views of PIs from HIC institutes were relatively evenly split between a range of weaknesses (between 10-17%, 3-5 of 30). It is of note that no PI from a LMIC institute reported that the types of projects funded was a weakness. About a third of PIs from JUs (31%, 4 of 13) felt that the amount of funding available was a weakness.
Current gaps in funding landscape

The majority of respondents (94%, 124 of 132) felt there were critical gaps in the global health funding landscape. Twenty-nine respondents indicated there were no critical gaps in the global health research funding landscape; however, 21 of these went on to select critical gaps. These responses were therefore recoded to ‘yes’.

The most common gap identified was the type of research funded (46%, 64 of 140), followed by resources for critical research infrastructure (43%, 60) and resources for training (40%, 56) (Figure 82).

When asked to explain the choice of critical gaps, just over half (52%, 74 of 140) of the respondents provided further details on the nature of the gap. The majority reiterated the need for funding of their specific health problem/intervention/geography (53%, 39 of 74). Almost a third (30%, 22) commented...
that there was a lack of funding sources to support the next steps of implementation after the trial, which includes funding for implementation trials, follow-on support to negotiate policy translation, and funding during the manuscript writing stage (particularly for LMIC researchers). One respondent summarised this challenge, reporting “In many cases studies are funded and have to operate on stringent budgets. After the end of the trial there are minimal funds left for publication. As such, policy makers may receive results alongside the international community. They are often very minimally engaged in the analysis and interpretation of these results. This may impact ownership as well as utilisation of results moving forwards”.

The other common gap discussed was the funding for infrastructure development in LMIC to facilitate research (16%, 12 of 74). Comments included that the limited funds to support infrastructure development restricted the types and locations of global health trials with one reporting: “It is not easy to get funding to support development of the research infrastructure needed to run clinical trials in LMICs.”

![Figure 82 Critical gaps reported relevant to global health research funding (n=141)](image)

* Other included gaps in longer term capacity building in LMIC and lack of support for translation of findings into policy.

**Design of the JGHT**

Most respondents felt there were no aspects of the JGHT design or requirements that could be improved (79%, 115 of 146). Of those who felt the design could be improved, 26% (8 of 31) made comments in relation to the application process although the specific comments were varied. A further 16% (5 of 31) reported that there should be more support for capacity and career development built into the scheme, this was most commonly reported by co-investigators from LMIC institutes (4).

The majority of respondents (84%, 121 of 144) felt that the current design and requirements enabled the scheme to attract high-quality proposals. Of those who believed there were barriers for LMIC applicants (10%, 14), a frequent comment by co-investigators from LMIC and JU institutes was that they needed more support during the application process (29%, 4 of 14). A smaller proportion (6%, 9) reported there were barriers to applications from HIC institutions, which was predominately due to the ineligibility for PIs from non-UK HICs to apply.

When asked to compare the JGHT’s application process and requirements with those of related funding programmes, the most common response was that the JGHT was “similar” to other funders (35%, 27 of 78). 31% (24) reported that the process was simpler, more straightforward, or advantageous to other schemes. About one fifth (22%, 17) outlined areas that could be improved. These areas were mixed but
encompassed the turnaround time of applications and the need for more guidance during the application process. There were no major differences in the opinions raised between co-investigators from LMIC, JU or HIC institutes.

The majority (73%, 110 of 149) of co-investigators reported that the calls for proposals and other information on the JGHT are communicated through the right channels and reach the relevant research communities. The major comments for the improvements to the promotion of the scheme were reaching out to Health Ministries or special interest groups, sending calls to all previous grant holders and co-investigators, and more targeted awareness in LMICs. Some reported that they had not known about the scheme before being a co-investigator or only saw the call by chance, this was the reported evenly by researchers from LMIC and HIC institutes.

- Support from JGHT to improve impact

Three quarters of respondents (75%, 107 of 143) were not aware of additional activities covered by other funders that are effective to achieve impacts and health outcomes. Of those who did believe there were additional support activities under different funders (25%, 36 of 143), these were most commonly support for dissemination of results (e.g. EDCTP, Wellcome Trust and Bill & Melinda Gates), support for implementation or scale-up (e.g. Bill & Melinda Gates), and support for capacity building (e.g. EDCTP).

When asked which additional activities the JGHT could support that would help it achieve its aims, the most important areas considered were training (31%, 43 of 139), followed by support for other types of research (22%, 30), and dissemination and knowledge exchange (18%, 25) (Figure 83).

Figure 83 Additional activities the JGHT could support to increase the potential impact from its research (n=139)

<table>
<thead>
<tr>
<th>Activity</th>
<th>% Respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Training</td>
<td>31</td>
</tr>
<tr>
<td>Support for other types of research</td>
<td>22</td>
</tr>
<tr>
<td>Dissemination and knowledge exchange</td>
<td>18</td>
</tr>
<tr>
<td>Network building</td>
<td></td>
</tr>
<tr>
<td>Stakeholder engagement</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

Training was more commonly reported by LMIC respondents (39%, 23 of 59) than by respondents from HIC and JU (HIC 25%, 13 of 53; JU 26%, 6 of 22) (Figure 84). Conversely, a smaller share of co-investigators from LMICs (14%, 8 of 59) suggested support for other types of research compared to 23% (12 of 53) of co-investigators from HICs.

Most of the co-investigators who discussed the need for training emphasised this was needed for early/mid-career researchers and researchers from LMIC. Suggestions for other types of research were more varied and encompassed different project designs and topics.
Figure 8.4 Additional support activities by co-investigator institute (LMIC n = 59, JU n = 22, HIC n = 53)

**E.2.8. Final comments**

The final comments were mostly positive (66%, 19 of 29) and included mentions of how the JGHT is an important contribution to global health.

Less than half of the comments (45%, 13 of 29) included suggestions for improvements related to the need for more funding and an expansion of the types of trials considered.
# Appendix F  Main trial publications

Publications of main trial findings, i.e. findings relating to the primary outcome measure of the trial, for 24 JGHT-funded trials.

<table>
<thead>
<tr>
<th>Grant Reference</th>
<th>Grant Holder</th>
<th>RO</th>
<th>Grant status</th>
<th>Call</th>
<th>Trial results paper</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR/K007211/1</td>
<td>Gail Davey</td>
<td>U Sussex</td>
<td>Closed</td>
<td>Call 2</td>
<td>Negussie H et al. (2018) Lymphoedema management to prevent acute dermatolymphangioadenitis in podoconiosis in northern Ethiopia (GoLBeT): a pragmatic randomised controlled trial. Lancet Glob Health 6:e793–e803</td>
</tr>
<tr>
<td>-----------------</td>
<td>-------------------</td>
<td>----------</td>
<td>--------</td>
<td>---------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
technopolis
Appendix G Global health funding landscape & approaches to evaluation

G.1 The global health funding landscape

Global health trials are mainly supported by the public and philanthropic sector through research grants to universities and other research institutions and public-private partnerships. In interviews, researchers and key opinion leaders mentioned that funders and programmes such as the European & Developing Countries Clinical Trials Partnership (EDCTP), Bill and Melinda Gates Foundation (BMGF), National Institutes of Health (NIH) in the US, MRC and the Wellcome Trust also fund global health trials and provide similar size grants. A few interviewees mentioned funders such as DFID, USAID, AusAID – the Australian agency for foreign aid, the National Health and Medical Research Council (NHMRC) of Australia and the Global Challenges Research Fund (GCRF). The US Centers for Disease Control and Prevention (CDC) and the WHO Special Programme for Research and Training in Tropical Diseases (TDR) were considered smaller funders unable to manage larger trials. An overview of some of the main funders and their funding towards global health trials is provided in the next sections.

G.1.1. European & Developing Countries Clinical Trials Partnership (EDCTP)

EDCTP was established in 2003 as part of the European Commission’s Sixth Framework Programme for Research and Technological Development, and exists as a not-for-profit organisation. The objective of the first EDCTP programme, which ended in 2015, was to accelerate the development of new or improved drugs, vaccines, microbicides and diagnostic technologies, including neglected infectious diseases and emerging or re-emerging infectious diseases, that are prevalent in sub-Saharan Africa. This was executed via partnerships between European and African institutions in collaboration with the pharmaceutical industry and other like-minded and willing organisations. This collaborative endeavour progressively developed into a partnership that includes 16 African countries and 14 European Union member states plus Norway and Switzerland.

The next programme phase, EDCTP2 was approved by the European Parliament and European Council in 2014, with the European Commission allocating a total budget of €683m for a further 10-year period, with the understanding that the Participating States would at least match that contribution. While the overarching strategy has not changed for the second phase, the focus has been extended to include neglected infectious diseases and all clinical trial phases (I-IV) including research investigating health services optimisation.

The EDCTP issues a range of calls for proposals aimed not only at clinical trials in specific research areas or for specified intervention types but also capacity strengthening and networking activities, in order to create a sustainable environment for high-quality medical research. These include PhD, MSc and career R&D development fellowships, and networking grants.

EDCTP1 awarded 254 grants with a total value of €208m. During this time, 102 clinical trials (with a focus on phase II and III) and 13 diagnostic studies were completed in 24 countries, generating over 700 peer-reviewed publications. In addition to this, four regional Networks of Excellence and a Pan-African Clinical Trials Registry were established. By the close of 2018, EDCTP2 had selected 192 proposals with

26 EDCTP. Strategy and work plans. Available at: http://www.edctp.org/see-work/strategy/ Accessed 20 Oct 2019
a funding of €447m. This includes €396m, for supporting large-scale trials. The average funding per clinical or operational research grant is €5.2m. Just over half (58%) are phase II and III trials, and many target key populations, including pregnant women, newborns, children and adolescents. A further 16% of the clinical research grants involve phase IV studies, including product-focused implementation studies. About half the trials (51%) concern drugs, while about a quarter (27%) are for vaccines (Figure 85). Over two-thirds (70%) of the trials are for TB, malaria and HIV/HIV-associated infections.

Figure 85 EDCTP2 clinical trials activity by disease area and intervention type (2016-2018) [1]

Data source: Data provided by EDCTP

G.1.2. Bill and Melinda Gates Foundation (BMGF)

Typically, BMGF collaborates with grantee and partner organisations to develop proposals that align with its strategic priorities. Ideas for proposals are identified by programme officers in consultation with stakeholders including researchers and policy makers. These ideas are further developed into proposals for research through direct solicitation, discussion with one or more organisations who are then invited to submit a proposal and public/private requests for proposals.

BMGF also contributes to global health research via a number of research programmes coordinated through its Global Health Division. However, none of these are specifically for clinical trials. The aim underlying these activities is to reduce health inequalities in developing countries by fostering the development of new treatments and strategies to decrease the burden of infectious disease and the leading causes of child mortality. These broad research areas include discovery and translational sciences, enteric and diarrheal diseases, HIV, malaria, maternal and new-born health, neglected tropical diseases, pneumonia, TB and finally vaccine development and surveillance. The predominant research funding programmes, within the field of Global Health Research, offered by BMGF are Grand Challenges and Grand Challenge Explorations.

Grand Challenges is a programme of initiatives wherein each initiative focuses on innovation towards addressing a specific global health or development challenge. It started in 2003 and is funded in

---

29 Among interventional trials funded by EDCTP2. Data provided by EDCTP.
partnership with the NIH, Canadian Institutes of Health Research (CIHR) and Wellcome Trust. In 2014, the programme was relaunched as Grand Challenges. The initial initiative focussed on 14 specific scientific challenges related to infectious diseases and nutrition, for example, development of therapies to cure latent and chronic infection, of technologies that permit the assessment of numerous conditions and pathogens at point of care and of a plant species capable of providing an optimal range of bioavailable nutrients. A further 12 challenges have been added since covering a number of the research areas such as vaccines development and manufacture, point of care testing and data analysis and modelling techniques. In addition, a number of much broader challenges within the field of maternal and child health such as solutions for achieving healthy birth, growth and development, and the prevention of preterm birth were included along with biomarker discovery for both gut function and tuberculosis. Overall, Grand Challenges in Global Health awarded 44 grants with a total value of USD450m involving scientists and researchers from 33 countries.

As an adjunct to the Grand Challenges programme, BMGF launched Grand Challenges Explorations (GCE) in 2007 committing USD100m over a five-year period. Its purpose was to engage many innovators in a short time frame, maximising the possible benefits of global health research across a broad range of disease and research topics. The programme invites high risk, high-reward proposals on a biannual basis, with a total of 106 GCE initiatives being launched since the programme’s inception. Applications are accepted from any discipline and any organisation including academia, government laboratories, research institutes, not-for-profits and for-profit organisations. Successful applicants are initially awarded USD100k with successful projects potentially receiving up to USD1m of follow-on funding.

G.1.3. US National Institutes of Health (NIH)

The majority of Institutes, Centres and Offices across NIH are engaged in global health research and research training activities to some extent. As such, trials in areas such as bioethics, non-communicable diseases, infectious diseases, implementation science, mobile health, mental health as well as maternal and child health are funded either through NIH’s central funding mechanism or specialist institutes such as the National Institute of Allergy and Infectious Diseases (NIAID). While NIH does not currently have a dedicated programme for testing health interventions, this is within the scope of thematic programmes funded by the Institutes and Centres. The Fogarty International Center that leads NIH activities in global health, predominantly funds basic research, early stage development and research training activities.

NIAID funds clinical research in one of two ways. One is through extramural grants where outside entities, typically universities or academic institutions, are given funding. Often that will be money to US entities partnering with entities in LMICs. Clinical research through extramural grants is usually done in the context of existing NIH/NIAID-funding networks like the AIDS clinical trial group, our immune tolerance network, vaccine treatment and evaluation units, etc. This ensures that the extramural clinical trials are done in the context of larger research consortia that have the relevant infrastructure to do that type of research e.g. regulatory support, biostatistics support, clearly defined training activities, etc. Applications for extramural grants are made in response to Funding Opportunity

34 BMGF. Grand Challenges. https://gcgh.grandchallenges.org/challenges?f%5B0%5D=field_initiative%3A37072 Accessed 20 October 2019
37 Personal Communication, Dr Clifford Lane (8 Oct 2019)
Announcements (Calls for Proposals) and can be for investigator-initiated (unsolicited) or NIAID-requested (solicited, in predefined areas) research.

The other way is intramural grants where NIAID scientists work in partnership with investigators in LMICs. The grant comes from the NIAID scientist’s sustained funding allocation.

NIAID funds most of its clinical trials through networks and collaborations where NIAID determines the research topic and project scope. Clinical trials funded in LMICs always contain an element of capacity building and research training but this is usually not a specific requirement in the solicitation. Eligibility for funding will change from call to call and may allow LMIC researchers to apply independently or in partnership with a US institution. In 2018, NIAID funding for clinical research in LMICs was USD443m.

G.1.4. The Global Fund against Tuberculosis, Malaria and HIV

Founded in 2002, the Global Fund is a partnership between governments (37 countries and the European Commission), civil society, charities and foundations, the private sector and people affected by the diseases. It aims to promote innovative solutions to global health challenges, particularly those presented by AIDS, TB and malaria. The Global Fund raises nearly USD4b a year, 95% from donor governments and 5% from the private sector and foundations. This money is invested in supporting programmes run by local experts in more than 100 countries.

Programmes are funded in three-year cycles. The current funding cycle runs from 2017 to 2019. In each funding cycle, the Global Fund allocates funds to eligible countries. A Country Coordinating Mechanism, which is a national committee that includes representatives of people affected by the three diseases, medical experts, government and civil society submits funding requests for interventions to fight the three diseases on behalf of the country as a whole. After review by an independent panel of experts and approval by the Global Fund’s Board, countries implement their grants through local experts and partners. Evaluation and oversight continue throughout implementation to monitor progress and performance.

While most of the funds go towards implementing solutions known to be effective, the Fund also invests in the discovery of better drugs and new tools for health to bring an end to the epidemics of HIV, TB and malaria. For example, in 2018, the Global Fund and partners supported pilot programs for a malaria vaccine, and helped countries test the next generation of long-lasting insecticidal mosquito nets. In India, IBM, the Global Fund and the India HIV/AIDS Alliance have together developed the eMpower tablet / mobile app to speed up patient reporting, track expenses, expedite payments to health workers, increase stock and commodity traceability (barcode recognition), as well as collect monitoring and evaluation data. However, the amount of funding specifically going into clinical trials is not known.

G.1.5. Product Development Partnerships (PDPs)

Several funders also support development of innovations for prevention, diagnosis, or treatment of infectious diseases through Product Development Partnerships (PDPs). The objective of PDPs is to develop a new medical product for prevention, diagnosis, or treatment. PDPs combine the strengths of the public and private sector. The majority of the partnerships work as virtual organisations supporting

---

39 Personal Communication, Dr Clifford Lane (8 October 2019)
41 Personal Communication, Dr Clifford Lane (8 October 2019)
42 Personal communication, Joyelle Dominique (12 October 2019)
R&D activities that fit their scope and strategy, thereby supporting the development of products suited for use in developing countries

Nonetheless, there are significant differences between the organisational structures of different PDPs and their specific approach to product development. Some PDPs operate primarily as a convenor of partnerships, providing a platform for collaboration between academic scientists, research and clinical trial organisations, pharmaceutical companies, product manufacturers and other stakeholders. Others engage more directly in product development and operate their own research and manufacturing facilities. The extent of private sector engagement also varies.

PDPs received USD508m in 2017 mainly from government agencies such as UK’s DHSC and DFID, US National Institutes of Health (NIH), USAID, the European Commission, the Dutch Ministry of Foreign Affairs, German Federal Ministry of Education and Research (BMBF), the Australian Department of Foreign Affairs and Trade (DFAT), the Swiss Agency for Development and Cooperation (SDC) and Irish Aid as well as charities such as the BMGF and UNITAID, many of whom are represented in the PDP Funders Group. In 2017 (just as in 2016), the three highest-funded PDPs were the International AIDS Vaccine Initiative (IAVI), Medicines for Malaria Venture (MMV) and PATH.

Some of the activities undertaken by individual PDPs are as follows:

- Drugs for Neglected Diseases initiative (DNDi) has clearly contributed to improving access for key drug interventions in malaria, human African trypanosomiasis, Chagas disease, and visceral leishmaniasis. In addition, through disease platforms, it has successfully built capacity in disease-endemic countries with plans to make this sustainable post-DNDi.
- Foundation for Innovative Diagnostics (FIND) is highly competent in supporting the development of new diagnostics for neglected diseases. Since 2003, it developed 24 new diagnostic tools of which 17 have been recommended by WHO.
- European Vaccine Initiative (EVI) has fostered standardisation and harmonisation within European vaccine development efforts and has played an important role in addressing the translational gap between vaccine candidates developed through basic science, and limited industrial production, and early stage clinical trials. Seventeen vaccine candidates have progressed to early clinical development and three candidates have been handed over to partners for mid-stage clinical development.

G.1.6, International Development Research Centre, Canada

The International Development Research Centre (IDRC) funds research in developing countries. It has two health-related programmes – Food, Environment and Health, and Maternal and Child Health. The Food, Environment and Health Programme supports research to develop evidence, innovations and policies targeted at improving health, building healthier food systems and preventing non-communicable and infectious diseases. The Maternal and Child Health programme focusses on developing solutions through implementation research, particularly in relation to health information systems and adolescent sexual and reproductive health and rights. The programmes fund projects on a competitive basis through calls which have their own specific eligibility requirements and thematic focus.

IDRC is partnering with the Canadian Institutes of Health Research (CIHR) and Global Affairs Canada on the Innovating for Maternal and Child Health in Africa programme, a seven-year (2014 to 2020) CA$36m initiative. This programme is currently funding 19 Implementation Research Teams (IRTs) composed of African and Canadian researchers and African health policymakers to develop practical,
cost-effective solutions to health system challenges. The aim is to generate new knowledge about how interventions work, for whom, and under what conditions, to ensure that mothers and their children have better access to the care they need. The programme has four priority research themes: (1) high impact, community-based interventions; (2) quality facility-based interventions; (3) enabling the policy environment to improve healthcare services and outcomes; and (4) human resources for health.

To promote uptake of findings the IRTs are working closely with three health policy and research organisations in East Africa and one in West Africa that facilitate mutual learning among researchers and policymakers and strengthen individual and institutional capacities for research. The expectation is that these efforts will help integrate the evidence generated by researchers into policies and practices concerning maternal and child health in the targeted countries.

G.1.7. Grand Challenges Canada

Grand Challenges Canada (GCC) is an independent, not-for-profit organisation funded by the Canadian government and other partners (including DFID, BMGF, USAID, Johnson & Johnson and DFAT, Australia) that funds innovators in LMICs and Canada to develop innovations that will save and improve lives in LMICs.

GCC awards grants and zero interest loans through a challenge fund mechanism for three types of challenges.

- Targeted challenges for innovation: (1) Maternal, newborn and child health (Saving Lives at Birth Program – in collaboration with USAID and other partners); (2) early childhood development (Saving Brains Program); mental health (Global Mental Health Program). Previous targeted challenges were on Point-of-Care Diagnostics and Hypertension
- Challenges for funding innovators in global health with no pre-identified theme (Stars in Global Health Program)
- Challenges to enable promising innovations to transition to scale (Transition to Scale Program)

From 2010 until the end of the financial year 2017-18, GCC has made CAD269m available for the aforementioned programmes. However, the proportion of funding awarded for trials is not clear. Grants are solicited through Request for Proposals on the website, which define the scope the research areas that will be funded. PIs can be based anywhere in the world, but the country of implementation has to be an LMIC.

G.1.8. Research Council of Norway / Norwegian Agency for Development Cooperation

The Norwegian Ministry of Foreign Affairs and Norwegian Agency for Development Cooperation (Norad) contribute to global health R&D through a number of WHO initiatives and PDPs as well as pooled funding initiatives such as the Saving Lives at Birth Initiative with Global Challenges Canada.

The Global Health and Vaccination Research (GLOBVAC) programme is the main global health research programme in Norway, jointly funded by the Research Council of Norway (RCN) and Norad since 2006. The programme has had an annual income of NOK121.8m from 2013, with the majority of funds originating from Norad.

---

53 Ibid.
55 Technopolis (2016) Mid-term evaluation of second programme for Global Health and Vaccination Research (GLOBVAC2)
The primary objective of the GLOBVAC programme is to support high-quality research with potential for high impact that can contribute to sustainable improvements in health and health equity in LMICs. The programme has a wide scope but gives the highest priority to projects in:

- Prevention and treatment of, and diagnostics for, communicable diseases, particularly vaccine and vaccination research
- Family planning, reproductive, maternal, newborn, child and adolescent health
- Health systems and health policy research
- Innovation in technology and methods development

The table below summarises the funding characteristics of the funders and programmes described in this section.

---

https://www.forskningsradet.no/prognett-globvac/About_the_programme/1224697869303
Table 33 Comparison of global health funders’ global health trials funding activity

<table>
<thead>
<tr>
<th>Funder</th>
<th>Programme/s (if relevant)</th>
<th>Funding modality</th>
<th>Level of funding</th>
<th>Priority disease areas</th>
<th>Types of activities funded</th>
<th>Eligible locations</th>
</tr>
</thead>
<tbody>
<tr>
<td>JGHT</td>
<td>NA</td>
<td>Open calls for proposals</td>
<td>£139m (2011-18)</td>
<td>None</td>
<td>Late stage intervention trials</td>
<td>UK and LMICs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LMICs</td>
</tr>
<tr>
<td>EDCTP</td>
<td>NA</td>
<td>Open calls for proposals</td>
<td>EDCTP1: €208m EDCTP2: €447m</td>
<td>Infectious diseases</td>
<td>Phase I to IV trials; capacity development; health services optimisation</td>
<td>Europe; Sub-Saharan Africa</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sub-Saharan Africa</td>
</tr>
<tr>
<td>BMGF</td>
<td>Grand Challenges (GC)</td>
<td>Commissioned research Open/restricted calls for proposals</td>
<td>GC: USD450m GCE: USD100m (2007-2012)</td>
<td>Infectious diseases Maternal, newborn and child health</td>
<td>Vaccine development; Surveillance; Discovery and Translational Sciences; Innovative Technological Solutions</td>
<td>Worldwide</td>
</tr>
<tr>
<td></td>
<td>Grand Challenge Explorations (GCE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Worldwide</td>
</tr>
<tr>
<td>BMGF</td>
<td>Programmes within individual institutes and centres</td>
<td>Extramural grants for solicited and unsolicited research through calls for proposals Intramural funding</td>
<td>NIAID: USD 443m in 2018 for clinical research in LMICs</td>
<td>Depends on call</td>
<td>Early to late stage trials; capacity development; trial networks</td>
<td>Depends on call – in principle worldwide</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Depends on call – in principle worldwide</td>
</tr>
<tr>
<td>NIH (including Fogarty International Centre and NIAID)</td>
<td>Programmes within individual institutes and centres</td>
<td>Extramural grants for solicited and unsolicited research through calls for proposals Intramural funding</td>
<td>NIAID: USD 443m in 2018 for clinical research in LMICs</td>
<td>Depends on call</td>
<td>Early to late stage trials; capacity development; trial networks</td>
<td>Depends on call – in principle worldwide</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Depends on call – in principle worldwide</td>
</tr>
<tr>
<td>PDPs</td>
<td>E.g. International AIDS Vaccine Initiative (IAVI), Medicines for Malaria Venture (MMV) and PATH</td>
<td>Calls for proposals In-house research and manufacturing</td>
<td>USD508m in 2017</td>
<td>HIV/AIDS, tuberculosis, malaria and neglected tropical diseases</td>
<td>product development across all stages; vaccines, drugs, diagnostics</td>
<td>Worldwide</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Worldwide</td>
</tr>
<tr>
<td>The Global Fund</td>
<td>Country level programmes</td>
<td>Funding requests made by national committees that include medical experts, government and civil society</td>
<td>Nearly USD4b a year</td>
<td>HIV/AIDS, TB and malaria</td>
<td>Predominantly implementation, but also discovery of better drugs, vaccines and tools</td>
<td>LMICs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LMICs</td>
</tr>
<tr>
<td>Global Challenges Canada</td>
<td>Stars in Global Health Transition to Scale Global Mental Health Saving Lives at Birth Saving Brains</td>
<td>Open call for proposals</td>
<td>CAD269m over 9 years</td>
<td>Maternal, newborn and child health, Mental Health, Hypertension</td>
<td>Innovation to address specified challenges, scale-up</td>
<td>Worldwide</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LMICs</td>
</tr>
<tr>
<td>IDRC</td>
<td>Food, Environment and Health Maternal and Child Health Innovating for Maternal and Child Health in Africa</td>
<td>Open call for proposals</td>
<td>CAD 36m for Innovating for Maternal and Child Health in Africa (2014-20)</td>
<td>non-communicable and infectious diseases, maternal and child health</td>
<td>Prevention, implementation research, new technologies, community- and facility-based interventions, health systems research, capacity building</td>
<td>Canada and LMICs</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------------------------------------------------------------------------------------------------</td>
<td>-------------------------</td>
<td>----------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>RCN/Norad</td>
<td>GLOBVAC</td>
<td>Open call for proposals</td>
<td>NOK121.8m annually</td>
<td>infectious diseases; maternal, newborn, child and adolescent health</td>
<td>Prevention, treatment, diagnostics, particularly vaccine research; technological innovation; methods development; health systems and health policy research</td>
<td>Norway and LMICs</td>
</tr>
</tbody>
</table>
G.2 Approaches to programme evaluation

Most of the funders described monitor their funding activities at the organisation or programme level using key performance indicators (KPIs) to see if they are meeting their objectives. In addition, many funders commission independent process and/or impact evaluations at periodic intervals, usually midway or after the programme has been completed (interim and ex post evaluations). An overview of these approaches is provided in this section.

G.2.1. European & Developing Countries Clinical Trials Partnership

EDCTP has undergone a range of internal and external assessments. An independent performance and impact assessment of EDCTP1 was carried out by Technopolis in 2014. Most recently an interim evaluation of EDCTP2 was completed in 2017 based on extensive desk research and document review with a programme of stakeholder interviews, and consultation with an expert group. The key areas of focus for the evaluation were: efficiency, relevance, coherence, effectiveness and added value. The report also noted the indicators that will be used to measure EDCTP2’s ability to meet its very specific targets. These include short term outputs such as the number of supported clinical trials and the number of interventions that have progressed along the clinical trial pathway; medium term outcomes such as the number of publications resulting from funded projects; and longer term impacts such as the number of new interventions, improved policies and guidelines and patents or patent applications.

G.2.2. Bill and Melinda Gates Foundation

At BMGF, the overall aim is to integrate evaluation into the fabric of the work, achieve early alignment with partners, and generate evidence that is useful for future strategy. Therefore, measurable outcomes and indicators of progress and success are defined and agreed on early in the grant proposal process. What is evaluated varies according to what will best inform decision-making. Evaluation is a high priority when programme outcomes are difficult to observe and it is not clear how best to achieve results, but it is a low priority when results are easily observable, and the product does not involve wider distribution products or tools, or creation of new data sets or analyses. Thus, evaluation that will improve the effectiveness of an organisation, programme, innovation, or operating model is a high priority, but evaluation of clinical trials is a low priority. However, where evaluation is undertaken, a range of methods, both qualitative and quantitative; retrospective and prospective designs; experimentation; theory-based evaluation; and systems-based approaches are used as appropriate.

At the programme level, projects outputs and outcomes are monitored to assess their outcomes and impact. However, this is mainly self-reported. For example, Grand Challenges Explorations awardees are required to prepare both a financial and scientific report upon completion of the project. Outputs and outcomes associated with awards are tracked using ResearchFish and awardees have to include a narrative account within the final report.

G.2.3. The Global Fund

Monitoring and evaluation is done by each funded country. Countries are expected to spend 7 to 10% of the grant budget for monitoring and evaluation as per an evaluation plan submitted at the time of grant

---

57 Technopolis Group (2014) Assessment of the performance and impact of the first programme of the European & Developing Countries Clinical Trials Partnership (EDCTP)
59 BMGF: https://www.gatesfoundation.org/how-we-work/general-information/evaluation-policy
61 https://gcgh.grandchallenges.org/grand-challenges-explorations-tracking-outcomes-and-outputs-using-researchfish#FunFacts
signing. The plan sets out how implementers intend to collect, collate, analyse and report on the data resulting from programmes.

Implementers are asked to select relevant programme indicators from a core list of indicators drawn from the latest technical guidance and based on commonly used measures. This promotes a common understanding of monitoring and evaluation and reduces the reporting burden for countries. The indicators can be found in a Modular Framework Handbook and include impact, outcome and coverage indicators at the national level. The modular framework is broken down first by disease area, then type of intervention and indicator.

G.2.4. Product Development Partnerships
In 2007, research funded by BMGF and the Rockefeller Foundation on behalf of the PDP Funders Group (which is chaired by DFID) recommended a common performance measurement approach and led to a new performance measurement framework for PDPs with a comprehensive set of areas (commercialisation, organisational strength, enabling environment and health impact) and dimensions (e.g. reputation, scientific environment, portfolio management, product uptake) to evaluate. The framework is intended to be used by both donors and PDP managers to measure performance and can be tailored to each PDP’s own characteristics.

Individual donors have evaluated the impact of their investment in PDPs, the approaches are not aligned and methodology was defined as per the evaluation questions drafted by the donor organisations.

G.2.5. International Development Research Centre, Canada and Grand Challenges Canada
Evaluation is integral to the IDRC’s work. It conducts formal evaluations for projects, programmes and the organisation as a whole to track results, generate knowledge and remain accountable to funders and other stakeholders including researchers and the general public. While programmes are evaluated externally, the IDRC has also developed a practical tool called Research Quality Plus (RQ+) to effectively evaluate the quality of research that is locally grounded and globally relevant. The RQ+ approach facilitates independent, expert review that is values-driven, inspired by systems thinking, accepting of quantitative and qualitative evidence, and systematic. The tool recognises that scientific merit is necessary, but not sufficient. It acknowledges the crucial role of stakeholders and users in determining whether research is salient and legitimate, and focusses attention on how well scientists position their research for use.

IDRC also led on monitoring and evaluation of the Development Innovation Fund – Health (DIF-H) for Grand Challenges Canada. DIF-H was evaluated in 2015 using a mixed-methods design involving data sources such as programme documents, project databases, academic and grey literature, interviews, focus group discussions, field-based case studies, and an online survey of successful and unsuccessful applicants. The views of consortium staff, applicants and grantees, other stakeholders and external

---

63 Ibid.
68 https://www.idrc.ca/en/about-idrc/accountability/evaluation
experts were gathered. A framework analysis\textsuperscript{73} approach was used to triangulate and analyse the findings to ensure they were robust and sufficiently comprehensive.

**G.2.6. Research Council of Norway / Norwegian Agency for Development Cooperation**

A mid-term evaluation of the GLOBVAC2 programme was conducted in 2016\textsuperscript{55}. This evaluation reviewed the programme from six dimensions – relevance, effectiveness, efficiency, utility / impact, durability and cross-cutting issues such as gender balance. Methodologically, it involved desk research, portfolio analysis, a survey of grantees, stakeholder interviews (with grantees, programme staff, key experts, external stakeholders, etc.), impact case studies and portfolio assessment by an expert review panel.

Portfolio analyses are done using the Health Research Classification System (HRCS)\textsuperscript{74} which classifies all health research along two dimensions: Research Activity and Health Category. The programme also actively incorporates the Health&Care21 monitor\textsuperscript{75}. This monitor helps compile knowledge about the resources, results and impact of research and innovation in the health and care field, and includes relevant indicators.

**G.2.7. US National Institutes of Health (NIH)**

NIH’s individual institutes and centres undertake evaluations of programmes in relation to needs assessments, process and outcome evaluations to inform the planning of their activities. NIAID and Fogarty International Center both follow evaluation-framework based approaches\textsuperscript{76,77}. Evaluation is seen as a routine, continuous quality improvement, review process. Reviews and evaluations are based on measured quantitative outputs, outcomes, and impacts (metrics), as well as qualitative outputs, outcomes and impact, with programmes being assessed against their own goals and objectives, taking into account the financial resources and granting mechanisms that are in place. Where possible, evaluations depend on external peer review and reflection to generate recommendations.

The table below summarises the evaluation approaches and key performance indicators of some of the main funders and programmes.

<table>
<thead>
<tr>
<th>Funder/Programme</th>
<th>Type of evaluation / monitoring (year, if applicable)</th>
<th>Indicator types</th>
<th>Examples of KPIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDCTP</td>
<td>2007 and 2009 independent review</td>
<td>Output Outcome Impact</td>
<td>Number of funded projects</td>
</tr>
<tr>
<td></td>
<td>2009 internal assessment</td>
<td></td>
<td>Number of publications</td>
</tr>
<tr>
<td></td>
<td>2013 internal impact assessment</td>
<td></td>
<td>Number of new interventions</td>
</tr>
<tr>
<td></td>
<td>2014 independent performance and impact evaluation</td>
<td></td>
<td>Proportion of clinical trials with African leadership</td>
</tr>
<tr>
<td></td>
<td>2017 independent interim evaluation</td>
<td></td>
<td>Improved policies and guidelines</td>
</tr>
<tr>
<td>BMGF</td>
<td>Evaluation of clinical trials typically not undertaken</td>
<td>Output Outcome</td>
<td>Defined by project</td>
</tr>
<tr>
<td></td>
<td>Monitoring through self-reporting by grantees e.g. through technical and financial reports, ResearchFish</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


\textsuperscript{74} http://www.hrcsonline.net/

\textsuperscript{75} https://www.helseomsorg21monitor.no/

\textsuperscript{76} Fogarty International Center Evaluation https://www.fic.nih.gov/About/Staff/Policy-Planning-Evaluation/Pages/evaluation-framework.aspx Accessed 20 Oct 2019

\textsuperscript{77} NIAID. Program Evaluation at NIAID. https://www.niaid.nih.gov/about/evaluation Accessed 20 Oct 2019
The Global Fund
Monitoring and evaluation by funded country
Monitoring through self-reporting by grantees
Coverage
Outcome
Impact
Number and percentage of people living with HIV by sex and age
Percentage of adults and children with HIV known to be on treatment 12 months after initiation of antiretroviral therapy by sex, duration of treatment and age

PDPs
2014 Review of the PDPs Fund for the Dutch Ministry of Foreign Affairs
2015 Evaluation of DFID and BMBF’s PDP funding activities
2017 Evaluation of Australia’s investment in Product Development Partnerships
Output
Outcome
Impact (to a lesser extent)
Number of new candidates identified
Number of projects killed
% of partners in endemic countries
% funds raised against annual target
New financing mechanisms
Number of people receiving treatment with counselling

IDRC and Grand Challenges
Canada
External evaluations
Output
Outcome
Impact
Number of funded projects
Number of publications
Funds leveraged by projects
Lives saved/improved
Increased access to innovative health products in developing countries

Research Council of Norway / Norwegian Agency for Development Cooperation
External evaluation
Output
Outcome
Impact
Number of projects funded with partners from international institutions
Number of scientific publications
Number of recruitment positions
Male vs female PI ratio
Number of North-South and South-South collaborations

NIH
Usually internal evaluations
Programme planning
Programme management
Outputs
Outcomes
Relevance to NIH strategy
Review criteria
Quality of feedback to PI
Minority applicants
Success rate
Number of partnerships
Number of publications
Policies adopted or advanced

G.3 Research funding landscapes – selected diseases

Given the diversity of health needs addressed by the JGHT, the research funding landscape was determined for a selection of four conditions: malaria, tuberculosis, cryptococcal meningitis and podoconiosis. Each landscape, and the JGHT’s role within, is presented below.

In summary, as would be expected, JGHT-funded research accounted for a small share of funding for malaria- and TB-related research, funding around 2% of trials registered in these disease areas between 2011 and 2018 (16 of 833 and 9 of 662, respectively). The JGHT played a much bigger role in the “smaller” disease areas of cryptococcal meningitis, accounting for 23% of trials funded (3 of 13), and podoconiosis, accounting for one of three trials in this area (33%).

G.3.1. Malaria
- Current state of play

Malaria is found in more than 100 countries worldwide including parts of Africa, Asia and central America. The highest burden of disease is in Sub-Saharan Africa and India which together account for
80% of the global burden.\(^{78}\) The past years have seen a promising reduction in the number of malaria cases worldwide thanks to increased control efforts. However, challenges with insecticide resistance, treatment regimens and limitations in diagnostics are hindering control efforts so that the rate of reduction has begun to plateau and, in some areas, cases are beginning to rise.\(^{79}\) To address these issues, a number of strategies are in the development pipeline including vaccines, new vector-control products and novel treatment regimens.

Global health trials are a critical step in facilitating the policy uptake of these strategies. The Action and Investment to defeat Malaria 2016-2030 report\(^{80}\) states that translation of trial results into policy is a key action and requires partnerships between researchers and implementing partners such as local and national governments. It also states that there is a need for more qualitative research techniques to ensure the interventions meet the expectations and approval of local communities. Indeed, a recent study investigating the funding landscape of malaria\(^{81}\) concluded that implementation of research findings was strongest where there was sense of local ownership. These needs are being recognised and funders, including the JGHT, are now encouraging researchers to engage with policy makers and conduct parallel social studies.

In 2011, the malaria Eradication Research Agenda (malERA) was published calling for a global coordinated approach to malaria control and elimination while recognising the heterogenous nature of the disease required a response tailored to the local context.\(^{82}\) Given these complexities, a variety of mechanisms are required to combat the disease with trials needed across the disease’s geographical range and transmission cycle. The JGHT malaria portfolio reflects this diverse landscape and includes projects across a range of countries examining vector control, treatment regimes, prevention during pregnancy, vaccination and barriers to transmission.

- **Trial activity**

Between 2005 and 2018 there were 833 trials registered in clinical trials databases.\(^{83}\) Of these, 16 were JGHT-funded making up only 2% of all trials and 6% of trials between 2011-2018 (Figure 86). The number of trials registered each year ranged from 47 to 96 with a median of 56 trials per year. The research into malaria reflects this global spread with 73 countries represented as trial sites across the 833 registered trials. One tenth of trials were multi-country (10%, 83 of 833) and 2% (17 of 833) were multicontinental. Of the JGHT trials, one quarter (25%, 4 of 16) were multi-country and one was multicontinental.

Overall, the country most frequently listed as a trial site was Kenya accounting for 7% (82 of 1101) of trial sites listed in the registry. Despite being the county with the highest burden of malaria, Nigeria\(^{84}\) had less than half the total number of trial sites as Kenya (38 vs 82, respectively). There was, however, an increase in the number of trial sites registered in Nigeria between 2011-2018 compared to 2005-2010. A similar increase was also observed in India, the country with the highest burden of vivax malaria, with the number of trial sites growing from 14 in 2011-2018 to 32 in 2005-2010\(^{85}\).

---


\(^{79}\) Ibid.

\(^{80}\) Action and Investment to defeat Malaria 2016-2030. For a Malaria-Free World. World Health Organization. 2015


\(^{83}\) Data on malaria trials was downloaded from the WHO International Clinical Trials Registry Platform (ICTRP). Duplicates were removed. Trials were excluded if they were deemed not relevant (phase 1 and 2 trials, and observational studies) and if they were registered prior to 2005 or after 2018.


\(^{85}\) The pre-JGHT period is 6 years and the post-JGHT period is 8. The increase in the number of trials should therefore be interpreted with caution.
The number of trial sites in Africa decreased between 2005 and 2009 from 91 trials to 49 (Figure 87). The number remained relatively constant until 2018 where the number of trial sites dropped again to 34. With the exception of 2006-2009 the number of trial sites in Asia has remained relatively consistent with between 20-29 trial sites reported each year. The 16 JGHT trials spanned 14 countries with 5 trials taking place over multiple countries and one taking place over multiple continents. Only two trials took place in Asia, one in Indonesia and the other spanning Afghanistan, Ethiopia, Indonesia, and Viet Nam.

Source: Technopolis analysis of WHO ICTRP data. Locations of the JGHT trials are indicated in blue.
Funding landscape

Excluding funding for basic research, the level of funding for malaria research has remained relatively stable between 2007 and 2017 (Figure 88). This includes all types of research into products (drugs, vaccines, diagnostics, etc.) and not only trials. Hence, funding levels for trials could not be compared over time. The annual amount of funding ranged from USD360m in 2013 to USD500m in 2009. Governments were the largest contributor between 2011 and 2017, funding a total of USD1.2b, followed by philanthropic funding (USD941m) and private sector (USD809m) (Table 35).

Figure 88: Research funding for malaria (excluding basic research, 2007 to 2017)

Source: Technopolis analysis of G-Finder data

Table 35 Research funding for malaria (excluding basic research, 2011 to 2017) by type of funder

<table>
<thead>
<tr>
<th>Type of funder</th>
<th>Amount (1 million USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Philanthropic</td>
<td>1,232</td>
</tr>
<tr>
<td>Private sector</td>
<td>941</td>
</tr>
<tr>
<td>Public sector - Governments</td>
<td>809</td>
</tr>
<tr>
<td>Public sector - Multilaterals</td>
<td>31</td>
</tr>
<tr>
<td>Unspecified</td>
<td>0.05</td>
</tr>
<tr>
<td>Grand total</td>
<td>3,013</td>
</tr>
</tbody>
</table>

Table 36 below shows the top ten public and philanthropic funders of research into malaria-related products (excluding basic research, 2011-17) plus JGHT funders as well as the number of trials they funded (2011-18, where source of support known). These findings should be interpreted with caution as (1) we do not know what proportion of the funding has been allocated to clinical trials and (2) funding sources in clinical trial registries are self-reported by the registrant and funding sources are not uniformly recorded in all clinical trial registries. Moreover, many trial registrations do not include reference to the funding sources of the trial; hence, the number of clinical trials is most likely under-reported.

86 Funding landscape data were extracted from G-Finder. Basic research products were excluded.
Between 2011 and 2017, public and philanthropic funders provided a total of USD2b. The Bill & Melinda Gates Foundation was the largest funder of research addressing malaria, contributing close to USD872m over the 7-year period, followed by the US National Institutes of Health (NIH) and the US Department of Defence (DOD) which contributed USD533m and USD156m, respectively (Table 36). DFID was the largest UK-based funder contributing just under USD129m. The European Commission was the largest funder of trials listed in the ICTRP database with at least 19 trials funded independently of the JGHT scheme.

Table 36: Major public and philanthropic funders and number of malaria clinical trials funded

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bill &amp; Melinda Gates Foundation</td>
<td>872</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>US National Institutes of Health (NIH)</td>
<td>533</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>US Department of Defence (DOD)</td>
<td>156</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>UK Department for International Development (DFID)</td>
<td>129</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td>US Agency for International Development (USAID)</td>
<td>63</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>The Wellcome Trust</td>
<td>53</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>European Commission (EC)</td>
<td>52</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>Indian Council of Medical Research (ICMR)</td>
<td>52</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>French National Institute of Health and Medical Research (Inserm)</td>
<td>36</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>German Federal Ministry of Education and Research (BMBF)</td>
<td>31</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>UK Medical Research Council (MRC)*</td>
<td>28</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>UK Department of Health and Social Care (including NHS and NIHR)*</td>
<td>10</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

*Data on the MRC and DHSC are provided to allow comparison. Source: Technopolis analysis of G-Finder and WHO ICTRP data

Between 2011 and 2017, the largest share of funding by both public and private sector donors supported drug development (public 41%; private 66%), followed by vaccine development (public 35%, private 31%) (Figure 89). Compared to the private sector, the public sector funded a broader range of products overall, e.g. chemical vector control, diagnostics and biological vector control together accounting for 17% of public funding but only 3% of private funding.

Of the 16 JGHT projects, half (8/50%) were investigating drug interventions, three (19%) were investigating chemical vector control and one was investigating a vaccine.

The proportions of funding according to recipient for the top 10 funders and the MRC is shown in Figure 90. The largest share of funding went to PDPs (39%), accounting for 67% and 99% of contributions from

---

The numbers indicate any trials citing the relevant funder as a source of support. Thus, jointly funded trials are double counted. JGHTs are counted against each funder with the exception of DHSC where only projects funded after DHSC joined the scheme are shown.
BMGF and DFID, respectively. Research at academic institutions is predominantly funded by the NIH (USD253m), followed by the Bill & Melinda Gates Foundation (USD174m), and the European Commission (USD36m). Half of the Wellcome Trust funding (50% or USD27m) and almost three-fourths of the MRC funding (72% or USD18m) went towards academic and other research institutions.

Figure 89 (a) Public funding by product (USD2.2b) and (b) Private sector funding by product (USD809m)

Source: Technopolis analysis of G-Finder data

Figure 90 Flow of funding by recipient type (2011-2017)

Source: Technopolis analysis of G-Finder data
Several funders focus specifically on research in malaria or in the Big Three diseases (HIV/AIDS, TB and malaria). These include The Global Fund, medicines for malaria venture (MMV) and President’s Malaria initiative (PMI).

- **The Global Fund** – financing malaria control programmes, innovations and drug discovery

  The Global Fund is a partnership between governments, NGOs and the private sector with a focus on accelerating the end of AIDs, TB and malaria. The scheme contributes 65% of all international financing for malaria programmes and, as of June 2019 had invested over USD12b.88 Currently, the scheme funds 80 malaria projects over 64 locations with a combined budget of USD3.4b.89 The Global Fund also invests in implementation and in 2018 facilitated the distribution of 131 million mosquito nets.

- **Medicines for malaria venture (MMV)** – developing new antimalarial drugs

  Established in 1999 MMV aims to reduce the burden of malaria “by discovering, developing and delivering new, effective and affordable antimalarial drugs”.90 To date this PDP has helped bring forward 10 new antimalarials resulting in an estimated 1.9 million lives saved.91 The majority of MMV’s expenditure is spent on research and development, accounting for 72% of its 2017 spending. MMV is currently working across 30 countries with over 150 partners from public and private sectors, NGOs and clinical trial sites to support a portfolio of 65 projects.

  MMV receives funding from government, philanthropic foundations and private industry, requiring an estimated USD100m annually. The two largest donors to date are Bill & Melinda Gates Foundation and DFID who have contributed 59% and 18% of total donations/pledges from 1999-2024, respectively.

- **President’s Malaria initiative (PMI)** – scaling up malaria prevention and treatment

  The PMI was launched in 2005 with the initial aim of reducing malaria-related mortality across Sub-Saharan Africa by 50%.92 The initiative has since expanded to over 24 malaria endemic countries in Sub-Saharan Africa and across the greater Mekong Subregion in Southeast Asia. The primary aim of reducing mortality has shifted towards the goal of elimination. In 2018 PMI contributed USD 723M towards research and malaria control programmes. PMI works closely with other funders and stakeholders. For example, in 2018 PMI procured 1.5 million insecticide treated nets with a donation from DFID.93

  PMI has 54 research priority areas covering malaria prevention, infection in pregnancy, elimination, health systems, behaviour change communication, and monitoring and evaluation. Since its inception PMI has funded 98 research studies including feasibility projects and clinical trials.94

---

**G.3.2. Tuberculosis (TB)**

- Current state of play

The massive disease burden of TB along with the emergence and rapid spread of drug-resistant TB requires increased focus on the development and evaluation of novel drug regimens that will be more effective, less toxic, and increase adherence. The tuberculosis research community has identified a number of promising compounds in new classes (e.g. the drug development pipeline maintained by the Working Group on New TB Drugs of the Stop TB partnership) that will need clinical evaluation in combination with each other and with standard drugs to identify the best possible regimen.

However, Phase 2 and 3 trials could prove to be a critical bottleneck within this search for a new combination regimen since the traditional approach is to conduct multiple phase 2 parallel-group randomised controlled trials (RCTs) for every potential new drug combination before moving to phase 3 trials. Moreover, current regimens are highly efficient and hence non-inferiority, pragmatic/adaptive trials seem to be the need of the hour. As such, innovative trial designs with treatment selection or screening-adaptive designs comparing several new treatments to a common control, for example, the multi-arm multi-stage (MAMS) trial design are increasingly being considered (including by the JGHT). This push towards innovative approaches is being supported by policymakers as well as regulators as such designs promise to make clinical development faster, more efficient and safer.

Concerted efforts from many stakeholders towards developing shorter, better tolerated and effective treatment regimens has led to steady process in the development of new and repurposed TB drugs, treatment trials and host-directed therapies. As of 2018, several new or repurposed antimicrobial drugs are in advanced trial stages for MDR-TB, and nine antimicrobial drug candidates are in phase 1 and 2 trials. The JGHT is also contributing in this regard, having funded the SURE, SHINE, TRUNCATE-TB and RIFASHORT trials, all of which are looking at shortening TB treatment in different target populations. Furthermore, some drug-based prevention trials are also being conducted. Examples include the V-QUIN and JGHT-funded TB-CHAMP trials which are looking at prevention of TB among household contacts of people with multidrug-resistant TB.

In addition to treatment regimens, more accurate and faster diagnostic assays are also being evaluated to stop the continuing reliance on sputum cultures which take time and can be inaccurate. This includes molecular assays based on mycobacterial DNA (e.g. the Xpert MTB RIF assay), 16S rRNA and the

---

100 Ibid.
105 Ibid.
106 ISRCTN registry: SURE: Short intensive treatment for children with tuberculous meningitis. ISRCTN40829906
107 ISRCTN registry: SHINE study: Shorter treatment for minimal TB in children. ISRCTN63579542
109 Clinicaltrials.gov. (2019) A Randomised Trial to Evaluate Toxicity and Efficacy of 1200mg and 1800mg Rifampicin for Pulmonary Tuberculosis. NCT02581527
110 ANZCTR: The V-QUIN MDR TRIAL: A randomized controlled trial of six months of daily levofloxacin for the prevention of tuberculosis among household contacts of patients with multi-drug resistant tuberculosis. 69817
111 ISRCTN registry: Tuberculosis child multidrug-resistant preventive therapy: TB CHAMP trial. ISRCTN92634082
transcriptome as well as positron emission tomography–computed tomography (PET-CT) based assays. Point-of-care assays such as the mycobacterial lipoarabinomannan (LAM) test using urine samples are also being evaluated clinically and improved upon. The JGHT-funded STAMP and TB Fast Track trials both built on the TB-LAM test. The former tested a TB screening strategy and the latter a TB management strategy among people with HIV.

- Trial activity

Between 2005 and 2018, 662 interventional trials related to TB were registered (see Figure 91), of which 9 (1.4%) were JGHT-funded. This accounted for 1.9% of trials registered between 2011 and 2018, the period when the JGHT has been part of the funding landscape. The number of TB trials registered every year has almost doubled during this period with the median number of trials registered between 2011 and 2018 being 59 (range 49 to 66) compared to 30.5 (range 28 to 37) per year between 2005 and 2010.

Figure 91 Total number of TB trials per year (2005-2018)

Source: Technopolis analysis of WHO ICTRP data

Trial site locations in terms of countries are known for 640 of the 662 TB trials, and these are predominantly in LMICs, especially in Africa, South and East Asia, and Latin America (see Figure 92). Recent trends (from 2011 onwards) suggest that fewer trials are being conducted in Europe and North America compared to earlier (13% versus 25% of trial locations in 2005-2010). At the same time, trial sites in East Asia and the Pacific have increased (from 15% to 26%) largely due to the contribution of China (7 trials in 2005-2010 to 83 trials in 2011-2018). During the same period, the number of trials in Vietnam, Thailand, South Korea and Taiwan have also increased (see Figure 92).

Overall, trials were being conducted in 91 different countries between 2005 and 2018. 86 trials (13%) were multi-country and 55 (9%) were multi-continent. The geographical spread of trial sites also increased during the JGHT period, going from 65 countries between 2005 and 2010 to 85 countries.

114 ISRCTN registry: Rapid urine-based Screening for Tuberculosis to reduce AIDS-related Mortality in hospitalized Patients in Africa (STAMP) trial. ISRCTN71603869
115 ISRCTN registry: TB Fast Track. ISRCTN35344604
116 TB trial entries were downloaded from the WHO International Clinical Trials Registry Platform (ICTRP). Duplicates were removed. Trials were excluded if they were deemed not relevant (phase 0, 1 and 2 trials, and observational studies) and if they were registered prior to 2005 or after 2018.
between 2011 and 2018 (see Figure 92). South Africa, India and Brazil have been among the five most popular trial locations throughout the period (2005 to 2018). However, since 2011 China and Uganda have replaced the US and UK within the top five (see Figure 92). Higher trial activity in these countries may be down to the establishment of the BRICS (Brazil, Russia, India, China, and South Africa) TB Research Network, in addition to various national TB research networks in countries from Thailand to Ethiopia\(^{117}\), and signals that more high-burden countries\(^{118}\) are prioritising TB research.

The JGHT TB trials cover 14 different countries. The majority of these (seven out of nine, 78%) have at least one site in sub-Saharan Africa, with five of the nine trials (56%) being conducted entirely or partly in South Africa (see Figure 92). Overall, five (56%) of the JGHT trials are multi-country, of which three (33%) are multi-continent – two covering South Asia and sub-Saharan Africa and one covering South America, sub-Saharan Africa and Europe.

Figure 92 Location of TB trial sites before (2005-2010, a) and with JGHT (2011-2018, b)

Source: Technopolis analysis of WHO ICTRP data


• Funding landscape

Excluding basic research, research funding for TB amounted to around USD4.6b between 2007 and 2017. This includes all types of research into products (drugs, vaccines, diagnostics, etc.) and not only trials. Hence, funding levels for trials could not be compared over time. The average yearly spend was USD378m between 2007 and 2010 and USD439m between 2011 and 2017. Since 2011, the yearly funding has been relatively stable (Figure 93). The majority of funding (total USD2.2b, 73%) between 2011 and 2017 came from public sector and philanthropic organisations, while the private sector accounted for the rest (total USD821m, 27%) (Table 37). Funding went to research on drugs, vaccines and diagnostics in that order with the public and philanthropic sectors also directing more funding towards biologics and other unspecified products which might include behavioural and educational interventions (see Table 37).

Figure 93 Research funding for TB (excluding basic research, 2007 to 2017)

Source: Technopolis analysis of G-Finder data

Table 37 Research funding for TB (excluding basic research, 2011 to 2017) by type of funder

<table>
<thead>
<tr>
<th>Type of funder</th>
<th>Amount (million USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Public sector - Governments</td>
<td>1,380</td>
</tr>
<tr>
<td>Private sector</td>
<td>821</td>
</tr>
<tr>
<td>Philanthropic</td>
<td>810</td>
</tr>
<tr>
<td>Public sector - Multilaterals</td>
<td>59</td>
</tr>
<tr>
<td>Unspecified</td>
<td>3</td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td><strong>3,073</strong></td>
</tr>
</tbody>
</table>

Source: Technopolis analysis of G-Finder data

Based on G-Finder data
Among the JGHT trials, the majority (5 trials, 56%) are related to drugs, either for treatment or prevention. The remaining four trials concern a vaccine, screening strategy, treatment management strategy and socioeconomic intervention.

Table 38 below shows the top ten public and philanthropic funders of research into TB-related products (excluding basic research, 2011-17) plus JGHT funders as well as the number of trials they funded (2011-18, where source of support known). These findings should be interpreted with caution as (1) we do not know what proportion of the funding has been allocated to clinical trials and (2) funding sources in clinical trial registries are self-reported by the registrant and funding sources are not uniformly recorded in all clinical trial registries. Moreover, many trial registrations do not include reference to the funding sources of the trial; hence, the number of clinical trials is most likely under-reported.

Nevertheless, the data available indicates that the Bill and Melinda Gates Foundation (BMGF) and US National Institutes of Health (including the National Institute of Allergy and Infectious Diseases and Fogarty International Center) are contributing the most money into TB research (not necessarily clinical trials), almost nine times as much as the next highest contributor, the European Commission (Table 38). The European Commission appears to be funding clinical trials mainly under EDCTP, while the majority of the JGHT funders’ funding (except for the Department of Health and Social Care or DHSC) into TB trials seems to be via the JGHT. The Wellcome Trust and DHSC (via the NHS and National Institute for Health Research) have funded at least 8 TB trials each outside the JGHT mechanism. We have attributed only 2 JGHT trials to DHSC (those registered in 2017 and afterwards) as it started contributing to the initiative only from the 2016/17 financial year.

Source: Technopolis analysis of G-Finder data
Table 38 Major public and philanthropic funders and number of TB clinical trials funded\(^{130}\)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bill &amp; Melinda Gates Foundation (BMGF)</td>
<td>759</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>US National Institutes of Health (NIH)</td>
<td>722</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>European Commission (EC) including EDCTP</td>
<td>85</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>US Agency for International Development (USAID)</td>
<td>84</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>UK Department for International Development (DFID)</td>
<td>70</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Indian Council of Medical Research (ICMR)</td>
<td>65</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>US Centers for Disease Control and Prevention (CDC)</td>
<td>58</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Unitaid</td>
<td>54</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>German Federal Ministry of Education and Research (BMBF)</td>
<td>39</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>The Wellcome Trust</td>
<td>35</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>UK Medical Research Council (MRC)</td>
<td>31</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>UK Department of Health and Social Care (including NHS and NIHR)</td>
<td>6</td>
<td>8</td>
<td>2</td>
</tr>
</tbody>
</table>

Source: Technopolis analysis of G-Finder and WHO ICTRP data

The proportions of funding going to different types of recipients from the top ten public and philanthropic funders plus the MRC and UK DHSC are shown in Figure 95. The largest share of funding from these funders (41%) went to academic and other research institutions. Between 70 and 80% of funding from the Wellcome Trust, NIH and Unitaid went to such institutions. 34% of all funding from the 12 funders went towards product development partnerships (PDPs), accounting for all DFID and almost all (99%) DHSC funding. The BMGF also contributed a majority of its funding (66%) for PDPs, while the European Commission mainly funded TB-related product research via academic and research institutions (36%) and PDPs (39%).

\(^{130}\) The numbers indicate any trials citing the relevant funder as a source of support. Thus, jointly funded trials are double counted. JGHTs are counted against each funder with the exception of DHSC where only projects funded after DHSC joined the scheme are shown.
Several funders focus specifically on research in TB or in the Big Three diseases (HIV/AIDS, TB and malaria). These include The Global Fund, Stop TB alliance and PDPs – the TB alliance, TB Vaccine initiative (TBVI) and Foundation for Innovative New Diagnostics (FIND). Founded in 2002, the Global Fund is a partnership between governments (37 countries and the European Commission), civil society, charities and foundations, the private sector and people affected by the diseases. The Global Fund provides 69% of all international financing for TB and has disbursed more than USD6.7b towards TB grants as of August 2019, 95% of which is from governments. While most of the funds go towards implementing solutions known to be effective, the Fund also invests in the discovery of better drugs and new tools for health to bring an end to the epidemics of HIV, TB and malaria. The fund is investing heavily towards developing faster, more accurate molecular diagnostic technology to detect TB and drug resistance and interventions to address human rights and gender-related barriers to TB services. The Global Fund has also supported pilot projects to validate the effectiveness of a shorter treatment regimen (9-12 months versus 18-24 months) for drug-resistant TB and clinical trials on the effect of interventions in the context of TB co-infections and co-morbidities in addition to capacity building, health system strengthening and operational research in countries affected by TB.

124 Ibid.
125 WHO ICTRP database
The Stop TB Partnership operates through a secretariat hosted by the UN and involves over 1700 partners in more than 100 countries, which include international and technical organisations, government programmes, research and funding agencies, foundations, NGOs, civil society and community groups and the private sector. Through the TB REACH mechanism, which is supported by Global Affairs Canada, BMGF, USAID and National Philanthropic Trust (US), the Partnership provides grants of up to USD1m for testing innovative approaches and technologies aimed at increasing the number of people diagnosed and treated for TB, decreasing the time to appropriate treatment and improving treatment success rates. Particular areas of focus are innovation using Xpert MTB/RIF technology to enable large scale and point of care use; interventions for different affected populations such as children, people with HIV and mobile populations; community mobilisation and e-health/m-health interventions.

PDPs have been set up to develop new medical products for prevention, diagnosis or treatment. They use private sector approaches towards R&D and mostly work as virtual organisations. Various PDPs operate in the TB area including the TB Alliance, TBVI and FIND.

Established in 2000, TB Alliance receives funding from government and philanthropic donors such as BMGF, BMBF, EDCTP, UKAID, USAID, MRC and the Global Health Initiative Technology (GHIT) towards developing better, faster-acting and affordable TB drugs. As such, it manages the largest pipeline of new TB drugs in history. The current pipeline includes regimens that are undergoing Phase 1, 2 and 3 trials (3, 1 and 3 regimens respectively) and Phase 4 evaluation of paediatric formulations of standard TB medication. It has previously funded five Phase 2 and two Phase 3 studies. In 2018, TB Alliance submitted its first new drug application, for pretomanid, to the US Food and Drug Administration (FDA).

TBVI is a consortium of 50 partners from academia, research institutes and private industry, and works to develop new TB vaccines and biomarkers. Between 2010 and 2017, the European Commission (82%, €38m) has been the major funder with some funding from BMGF (9%, €4m) and DFID (2%, €1m). About €4m (8%) of the total funding (€47m) has been allocated to clinical trials. To date, it has moved six vaccine candidates from discovery to the preclinical phase, and 4 candidates are going to Phase I trials. One candidate, MTBVAC, has progressed to Phase IIa trials.

FIND focuses on development and delivery of diagnostics for major diseases affecting the world’s poorest populations and its funders include BMGF, BMBF, EDCTP, GHIT Fund, The Global Fund, Stop TB Partnership/TB REACH and WHO among several others. FIND has considerably advanced the field of TB diagnostics and provides diagnostics developers with access to its large TB specimen bank. This includes 12 new TB diagnostic tests recommended by WHO including Line Probe Assays to detect drug resistance, Xpert MTB/RIF and LAM tests as well as the TB LAMP test that provides fast results that can be detected by the naked eye and the TrueNat/TrueLab chip-based assay. Current priority
projects include point-of-care TB-LAM and molecular TB tests and a sequence and treat project using next generation sequencing for drug susceptibility testing. FIND has its own Clinical Trials Unit and a clinical trials network comprising 19 LMICs. This has allowed FIND to train over 6,000 healthcare workers and strengthen 3,000 laboratories and trial sites.

G.3.3. Cryptococcal meningitis

- Current state of play
Cryptococcal meningitis is a fungal brain infection that occurs primarily among people with advanced HIV disease. It accounts for an estimated 15% of all AIDS-related deaths globally, causing more than 600,000 deaths each year. Drugs currently in use are more than 60 years old.

- Trial activity
Between 2005 and 2018, 21 interventional trials related to cryptococcal meningitis were registered (Figure 96), of which 3 (14.3%) were funded by the JGHT. This accounted for close to a quarter of all trials (23.1%) registered since the start of the scheme (2011 and 2018). The largest number of trials funded in any one year was five in 2012, more than double the number seen in any other year.

Figure 96 Total number of cryptococcal meningitis trials per year (2005-2018)

The country of the trial site was known for 20 of the 21 cryptococcal meningitis trials. Trials were conducted in 17 countries, mainly in Africa (80%) with the remainder in Asia. Uganda, Tanzania and South Africa hosted the largest number of trials (5 trials each). In Asia, sites in Thailand and Cambodia were involved in two trials each.

All three of the JGHT funded trials involved more than one country, and spanned across two continents (Asia and Africa). In comparison, only one third of trials funded by other funders were implemented in more than one country.

140 WHO (2016) Guidelines for the diagnosis, prevention and management of cryptococcal disease in HIV-infected adults, adolescents and children
142 Cryptococcal meningitis trial entries were downloaded from the WHO International Clinical Trials Registry Platform (ICTRP). Duplicates were removed. Trials were excluded if they were deemed not relevant (phase 0, 1 and 2 trials, and observational studies) and if they were registered prior to 2005 or after 2018.
Figure 97 Location of cryptococcal meningitis trial sites (2005-2018). Location of JGHT sites indicated in blue

Source: Technopolis analysis of WHO ICTRP data

- Funding landscape

Funding for drug research addressing cryptococcal meningitis amounted to approximately USD30.8m between 2013 and 2017 (Figure 98) (including research other than trials). The average yearly spend was USD6.1m between 2013 and 2017. Funding for cryptococcal meningitis has increased with funding doubling between 2016 to 2017. Governments provided the majority of funding accounting for ~USD30m, the remaining funding was made up by philanthropic funders (Table 37).

Figure 98 Research funding for cryptococcal meningitis

Table 39 Research funding for cryptococcal meningitis by type of funder (2013-17)

<table>
<thead>
<tr>
<th>Type of funder</th>
<th>Amount (million USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Public sector - Governments</td>
<td>30</td>
</tr>
<tr>
<td>Philanthropic sector</td>
<td>1</td>
</tr>
<tr>
<td>Grand Total</td>
<td>31</td>
</tr>
</tbody>
</table>

Source: Technopolis analysis of G-Finder data

Table 40 below shows the major public and philanthropic funders of research into cryptococcal meningitis –related products as well as the number of trials they funded (2011-18, where source of support known). These findings should be interpreted with caution as (1) we do not know what proportion of the funding has been allocated to clinical trials, and (2) funding sources in clinical trial registries are self-reported by the registrant and funding sources are not uniformly recorded in all clinical trial registries. Many trial registrations do not include reference to the funding sources of the trial; hence, the number of clinical trials is most likely under-reported.
The data available indicates that the US National Institutes of Health (including the National Institute of Allergy and Infectious Diseases) has contributed the largest amount of funding to cryptococcal meningitis research – over three times that of the next highest contributor, the MRC. The JGHT, however appears to have become an important source of funding for trials alongside the French National Agency for Research on AIDS and Viral Hepatitis in recent years, having funded three trials each between 2011 and 2018. Two clinical trials received funding from EDCTP in the same period; however, the European Commission did not emerge as a major funder in the G-finder results. Only one JGHT trial has been attributed to DHSC as the other two were registered before the Department had joined the scheme.

<table>
<thead>
<tr>
<th>Type of funder</th>
<th>Amount, x 1000 USD (G-Finder, 2013-2017)</th>
<th>Number of clinical trials other than JGHT (ICTRP, 2011-2018)</th>
<th>Number of clinical trials (JGHT, 2011-2018)</th>
</tr>
</thead>
<tbody>
<tr>
<td>US National Institutes of Health (NIH)</td>
<td>20,316</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>UK Medical Research Council (MRC)</td>
<td>6,473</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>UK Department of Health and Social Care (DHSC)</td>
<td>1,629</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>UK Department for International Development (DFID)</td>
<td>811</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>The Wellcome Trust</td>
<td>801</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>French National Agency for Research on AIDS and Viral Hepatitis (ANRS)</td>
<td>362</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Australian National Health and Medical Research Council (NHMRC)</td>
<td>214</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Swiss National Science Foundation (SNSF)</td>
<td>122</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Merieux Foundation, Fondation Mérieux</td>
<td>75</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td><strong>30,805</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The proportions of funding for different types of recipients from the major public and philanthropic funders are shown in Figure 99. The largest share of funding (69%) went to academic and other research institutions (including 100% of funding from Wellcome and 71% of funding from the US NIH). All cryptococcal meningitis funding from UK DHSC and DFID, and 12.5% of MRC funding went to ‘Other intermediary’.

143 The numbers indicate any trials citing the relevant funder as a source of support. Thus, jointly funded trials are double counted. JGHTs are counted against each funder with the exception of DHSC where only projects funded after DHSC joined the scheme are shown.
G.3.4. Podoconiosis

- Current state of play

Podoconiosis is a form of lymphoedema (leg swelling) in people who walk barefoot on volcanic soil in highland tropical areas. The disease results in oedematous feet and legs and subsequently progresses to elephantiasis. Although podoconiosis is rarely a direct cause of mortality, it greatly reduces productivity, leading to significant stigma from the community and health professionals, and a low quality of life.

Podoconiosis affects an estimated 4 million subsistence farmers globally.144 Most of the highly affected countries are in the African region, with prevalence particularly high in Cameroon, Ethiopia and Uganda.145 In Ethiopia, the national average prevalence is estimated to be 4.0%.146 Another study reported 1.6 million people living with podoconiosis in Ethiopia with 35 million people at risk of the disease in the country.147

In 2011, podoconiosis was recognised by WHO as a neglected condition, but did not appear on the 2018 list of WHO neglected tropical diseases (NTDs). With low knowledge and awareness of the disease, and very few research groups investigating the issue, health interventions addressing podoconiosis are often

grouped alongside lymphatic filariasis (LF) programmes, the ‘better-known’ elephantiasis caused by parasitic worms. However, recent mapping efforts have shown that these diseases are frequently found in different regions of countries, or different countries altogether. Diagnosis and provision of health interventions for people with podoconiosis hence requires a separate programme from LF.

- **Trial activity**

Between 2005 and 2018, only three trials related to podoconiosis were registered, one each in 2013, 2016 and 2018. The trial registered in 2013 was funded by the JGHT; the later trials were funded by Procter and Gamble (2016) and GlaxoSmithKline and DFID (2018). All three trials had trial sites in Ethiopia, with the trial registered in 2018 also implemented in Bangladesh.

- **Funding landscape**

A summary of research funding on the website of the NGO Footwork lists three epidemiological studies, two supported by Wellcome, one by the University of Sussex, and one study investigating genetic factors determining susceptibility to podoconiosis funded by the MRC (MR/J008621/1; £500,000). Footwork was launched by Prof Gail Davey, University of Sussex, in 2012 to work towards the elimination of podoconiosis.

---


151 G-finder does not provide information on podoconiosis.
