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Review of the Joint Global Health Trials funding scheme

Final Report - Appendices

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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?

Do you think the JGHT funds global health research activities that lead to international development impact?

- In *your area of work/expert*ise, 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
- other impacts

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

- other - please specify

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

- Other gap

Please explain your answer

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

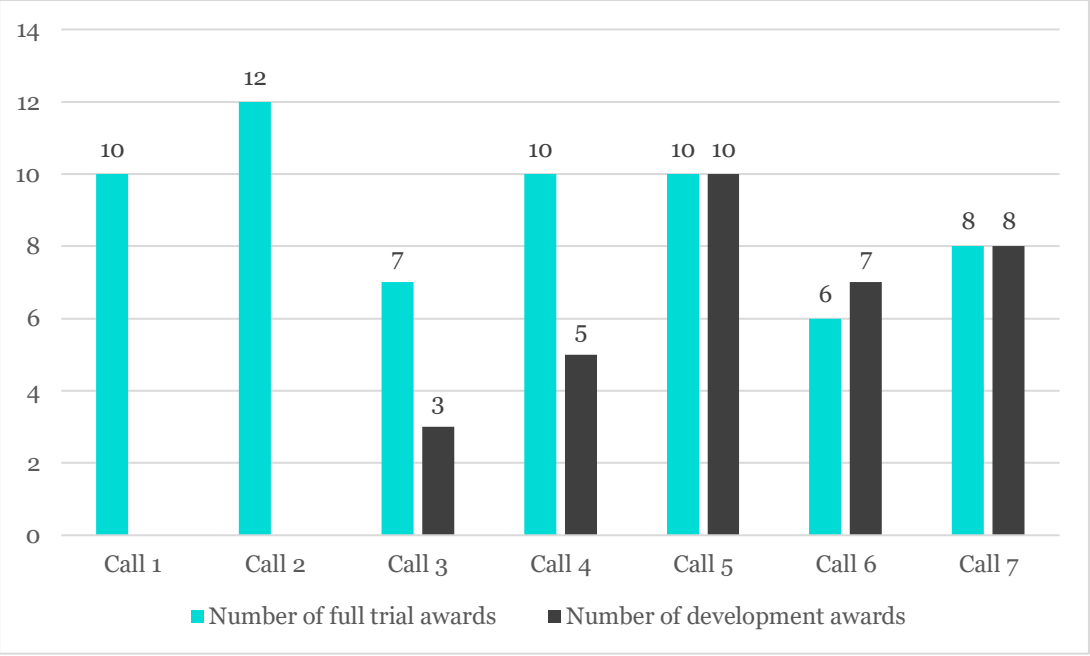
A total of 96 awards were made as part of Calls 1 – 7 of the JGHT, representing an investment of £138.8m. 63 of these awards were for full trials, with a budget of £133.8m, and 33 were development awards, with a budget of £5.06m. 28 full trial awards had closed by the end of May 2019, with 35 remaining active[1]. Of development awards, 22 had closed and 11 remained active (Table 1).

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

Award status	All awards	Full trial awards	Development awards
Active	46	35	11
Closed	50	28	22
Total	**96**	**63**	**33**

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).

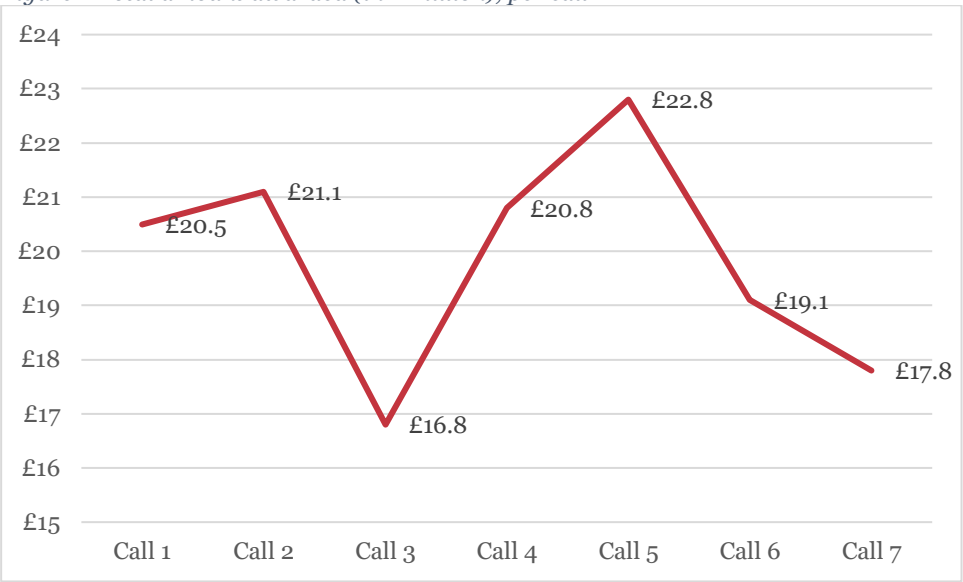
Figure 1 Number of JGHT awards, by call



[1] 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).

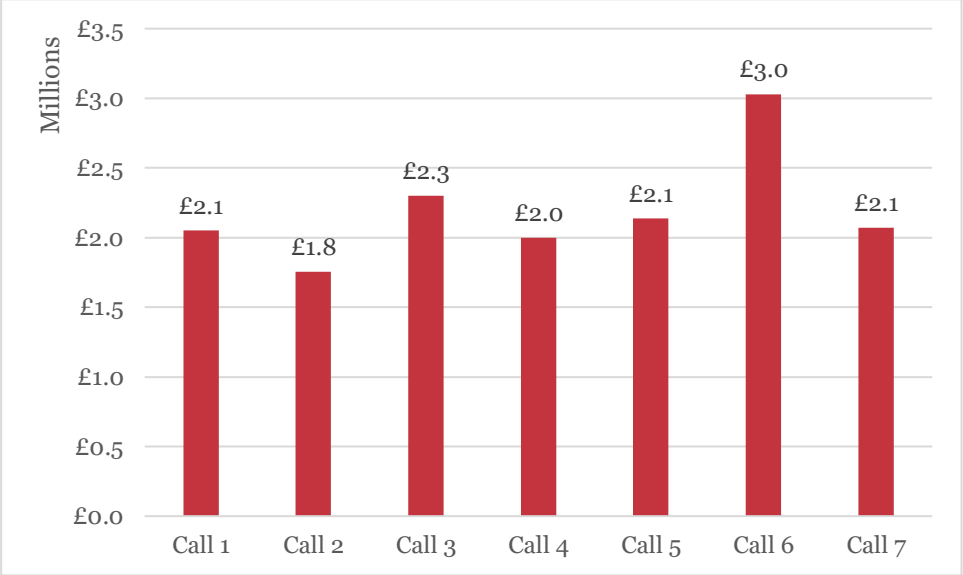
The 96 awards represent an investment of £138.8m, £133.8m for full trials and £5.06m for development awards. The amount of funding per call allocated ranged between a low of £15.8m in Call 7 / £16.8m in Call 3, and a high of £22.6m in Call 5 (Figure 2).

Figure 2 Total amount awarded (in £ million), per call



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).

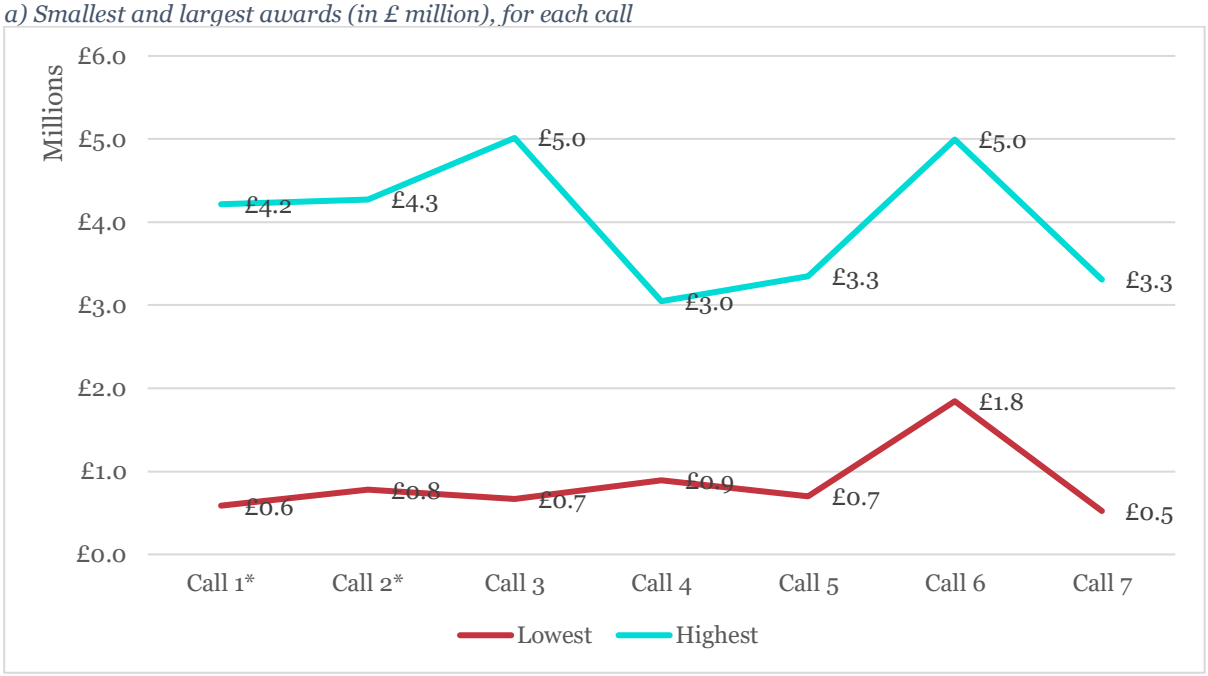
Figure 3 Average full trial award size, per call (in £ million)



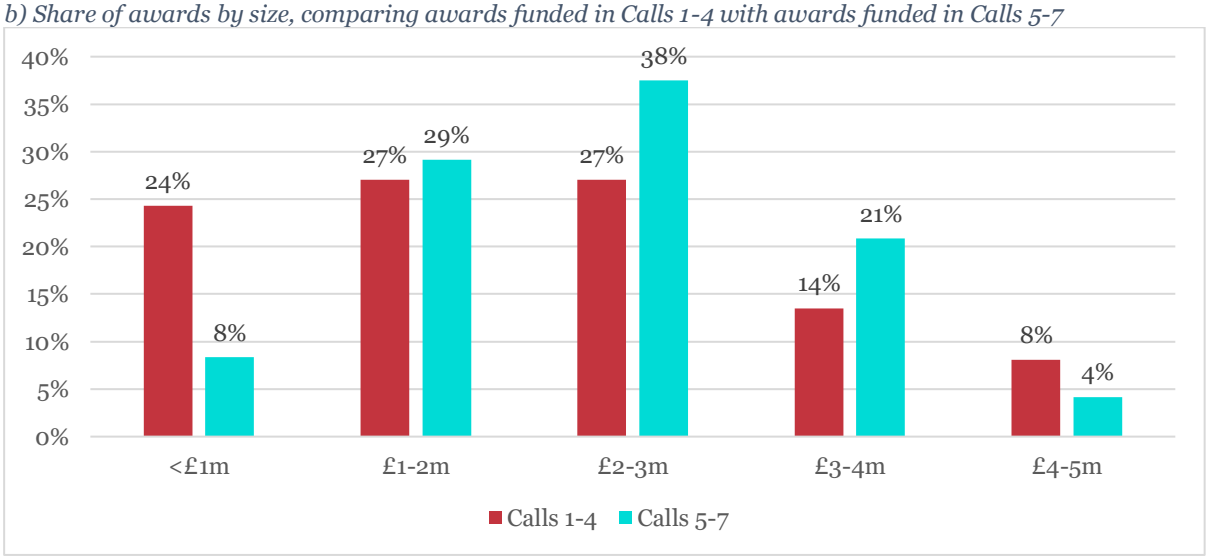
The variation in the size of full trial awards ranged from a minimum of £2.2m in Call 4 to a maximum of £4.3m in Call 3. The value of the lowest and highest awards for each Call are shown in Figure 4. The five largest full trial awards were between £4m and £5m (two in call 1, and one each in calls 2, 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.

Figure 4 Award size per JGHT call
a) Smallest and largest awards (in £ million), for each call



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



*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).

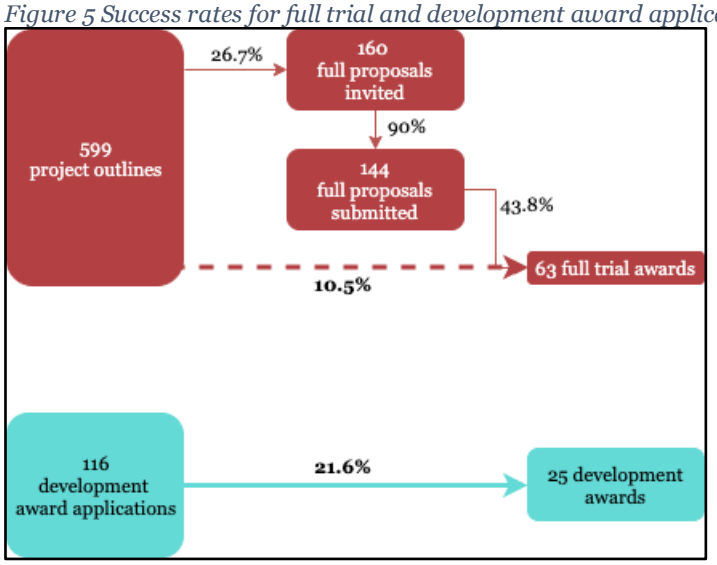
B.2 Applications and funding requested

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 2 Number of applications to the JGHT

Application status	Outlines for full trial award scheme	Full trial applications (2nd stage)	Development award applications (calls 5-7)
Successful	160	63	25
Rejected	439	81	91
Total	**599**	**144**	**116**

Figure 5 Success rates for full trial and development award applications



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[2].

Figure 6 Number of applications to JGHT

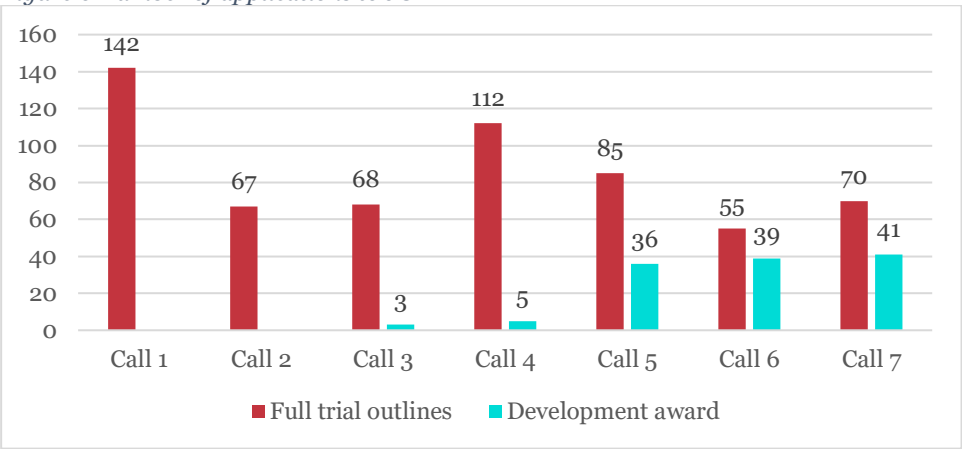
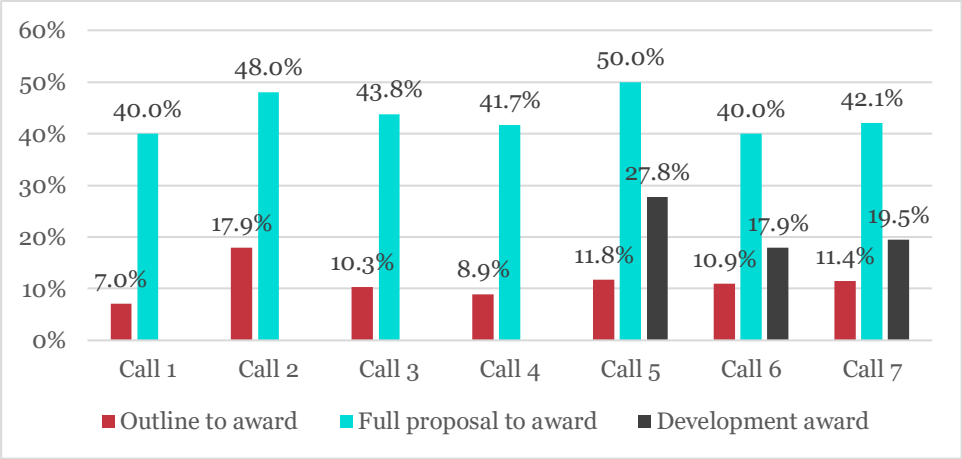


Figure 7 Application success rates



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[3]. At least one PI who had led a development award was rejected at the second stage for a full trial award[4]. One investigator was awarded a full trial as a follow-

[2] 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.

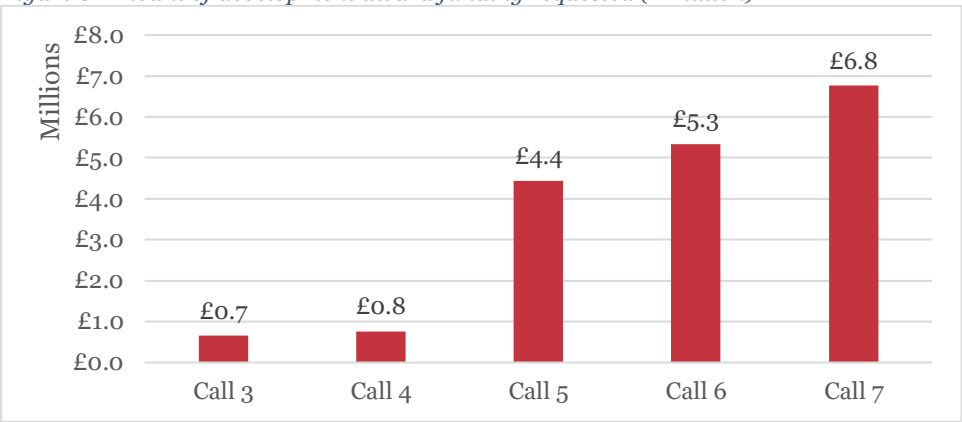
[3] Data excerpt provided by MRC; a third PI whose full trial application to Call 7 was rejected secured a development award in Call 9 (i.e. outside the scope of this review).

[4] 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[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[6]) (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

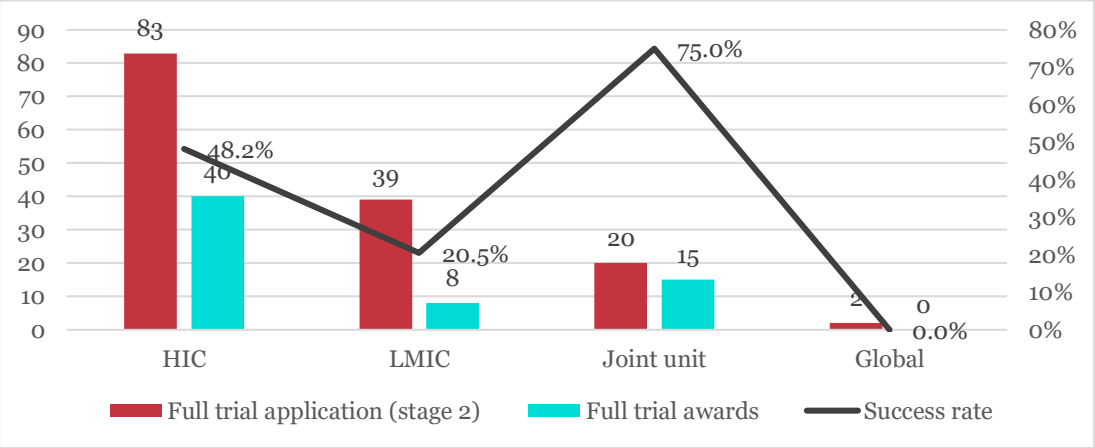


Figure 10 Share of application for full trial awards (second stage), by location of lead PI and call

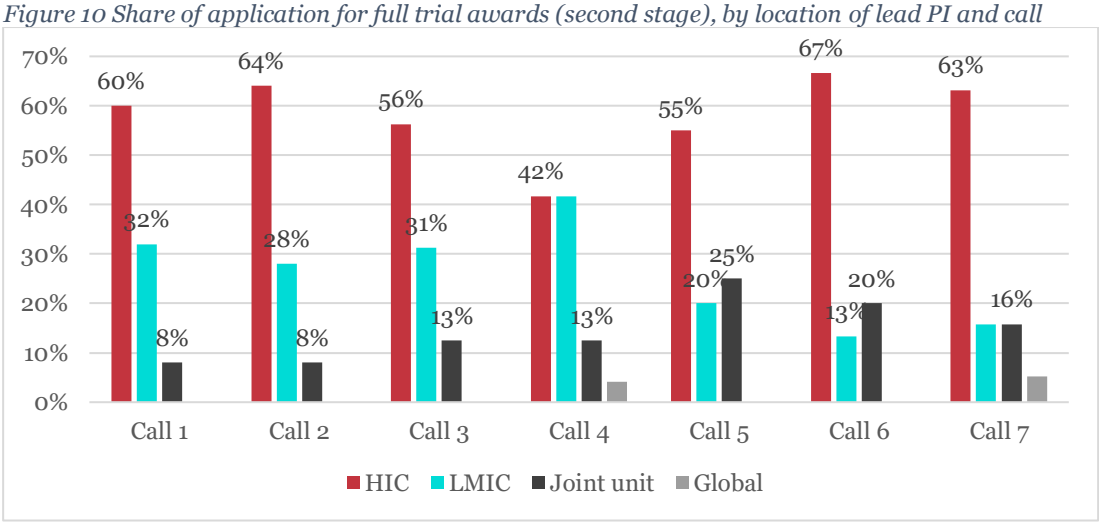


Figure 11 Success rate for full trial applications (second stage), by location of lead PI and call

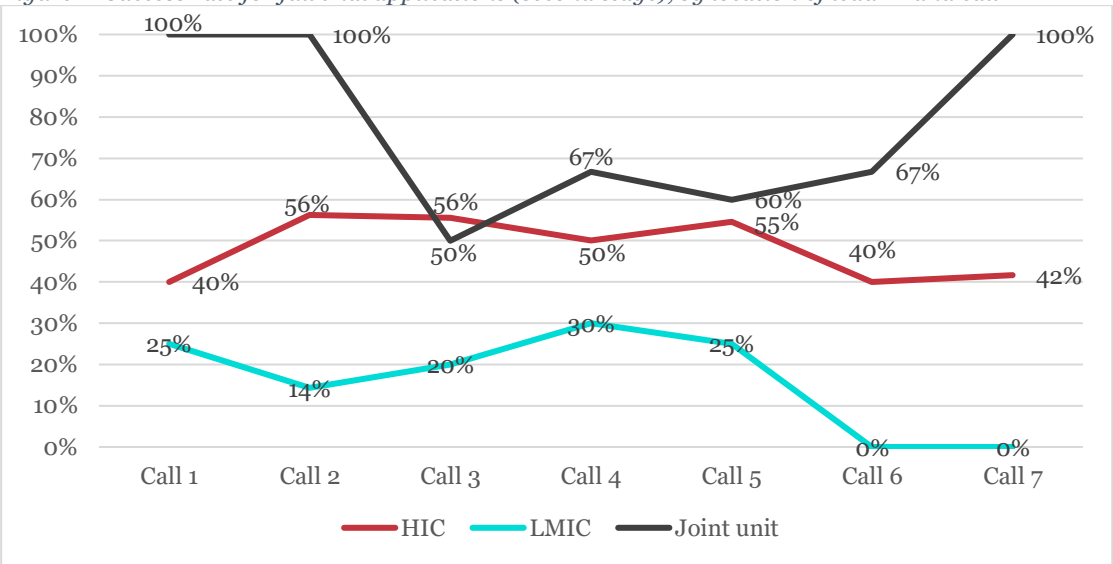
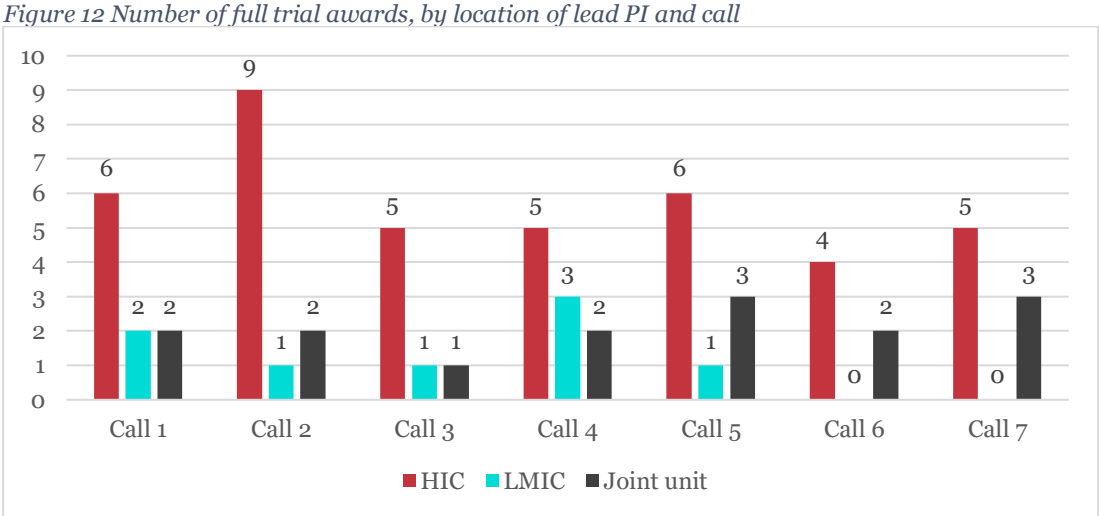


Figure 12 Number of full trial awards, by location of lead PI and call



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)[7]. 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 from 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

[7] 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

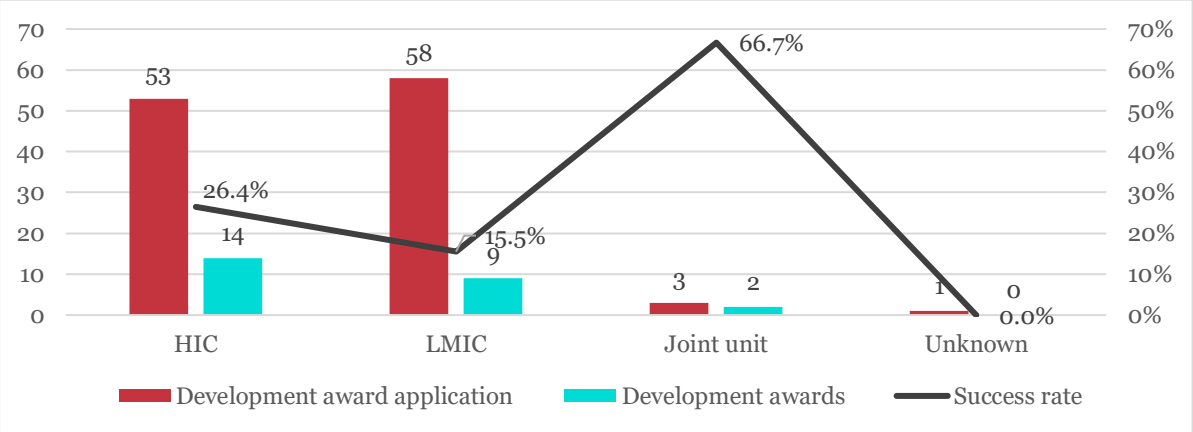


Figure 14 Share of development award applications, by location of lead PI and call

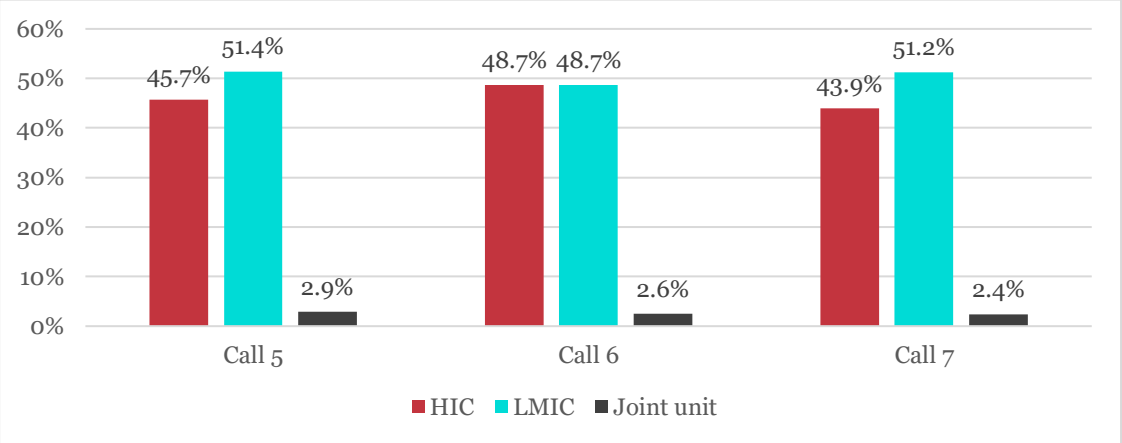


Figure 15 Success rate of development award applications, by location of lead PI and call

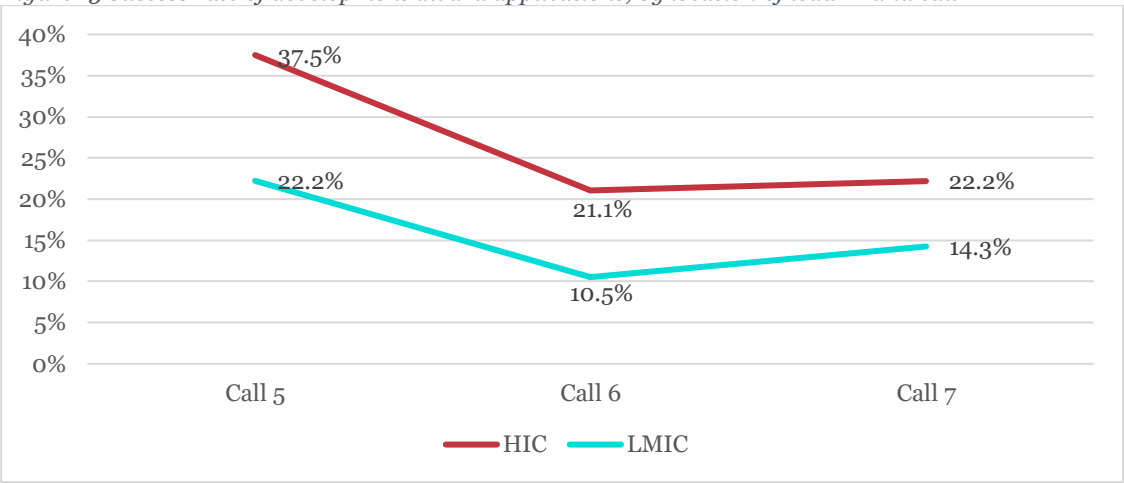
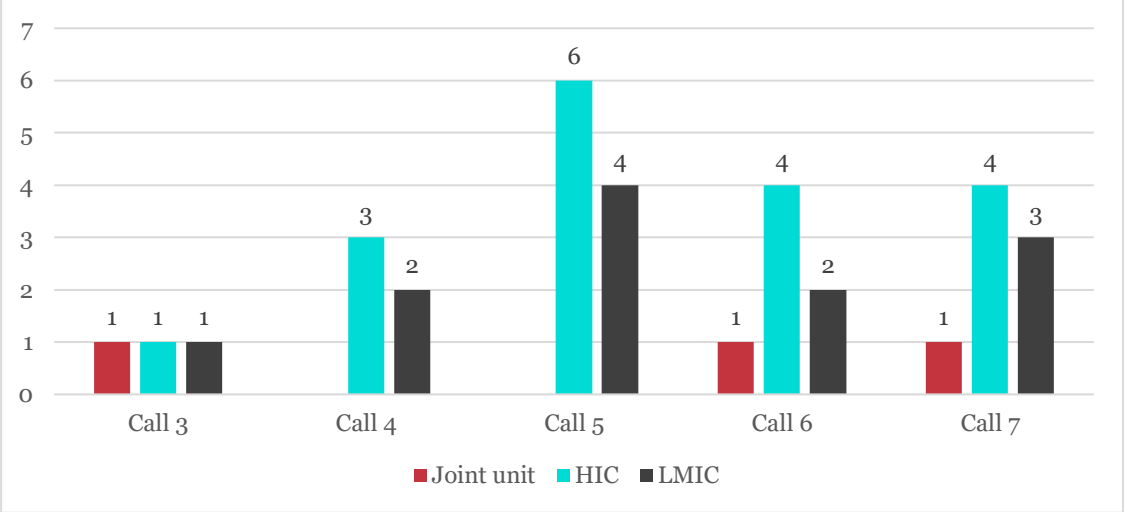


Figure 16 Number of development awards made, by location of lead PI and call



Key figures for applications and awards are summarised in Table 3.

Table 3 Key figures: Applications and awards, by location of lead PI

Full trial awards	**Share of applications** (n=144 applications)	**Success rate**	**Share of awards** (n=63 awards)
HIC	57.6% (83)	48.2%	63.5% (40)
LMIC	27.1% (39)	20.5%	12.7% (8)
Joint unit	13.9% (20)	75%	23.8% (15)
Development awards	**Share of applications** (calls 5-7, n=115 applications)	**Success rate** (calls 5-7, 25 awards made)	**Share of awards** (calls 3-7, n=33 awards)
HIC	46.1% (53)	26.4% (14)	54.4% (18)

LMIC	50.4% (58)	15.5% (9)	36.4% (12)
Joint unit	2.6% (3)	66.7% (2)	9.1% (3)

- 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.

Table 4 Key figures: Applications and awards, by continent of lead PI

Full trial awards, by location of lead PI	**Share of applications**	**Success rate**	**Share of full trial awards**
Europe	56.3% (81 of 144)	46.9%	60.3% (38 of 63)
Africa	25.0% (36)	50.0%	28.6% (18)
Asia	15.3% (22)	22.7%	7.9% (5)
Development awards, by location of lead PI	**Share of applications** (calls 5-7)	**Success rate** (calls 5-7)	**Share of full trial awards** (calls 3-7)
Europe	44.3% (51 of 115)	27.5%	51.5% (14 of 33)
Asia	27.0% (31)	19.4%	27.3% (6)
Africa	21.7% (25)	16.0%	15.2% (4)
South America	3.5% (4)	25.0%	6.1% (1)

- By country

Applications were received from lead PIs affiliated with institutions located in 32 countries (5 HICs, 27 LMICs[8]).

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.

8 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)[9]. 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)[10].

Table 5 Applications and success rates, per country of lead institution

Country of lead institution	**Full trial application (stage 2)** (n=144)	**Full trial awards** (n=63)	**Success rate**		**Country of lead institution**	**Develop-ment award application** (n=115)	**Develop-ment awards** (n=25)	**Success rate**
UK	80	37	46.3%		UK	51	14	27.5%
The Gambia	11	7	63.6%		India	20	3	15.0%
South Africa	11	3	27.3%		South Africa	6	2	33.3%
India	7	0	0.0%		Nigeria	5	0	0.0%
Bangladesh	6	0	0.0%		Kenya	4	2	50.0%
Kenya	4	4	100.0%		Bangladesh	3	0	0.0%
Pakistan	3	1	33.3%		Brazil	3	0	0.0%
Uganda	3	1	33.3%		Tanzania	3	0	0.0%
China	2	0	0.0%		Australia	2	0	0.0%
Global organisation	2	0	0.0%		China	2	2	100.0%
Kenya	2	0	0.0%		Georgia	2	0	0.0%
Tanzania	2	1	50.0%		Ghana	2	0	0.0%
Vietnam	2	2	100.0%		Uganda	3	1	33.3%
Argentina	1	0	0.0%		Peru	2	2	100.0%
Canada	1	1	100.0%		Armenia	1	0	0.0%
Malawi	1	0	0.0%		Ethiopia	1	0	0.0%

[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.

Nigeria	1	1	100.0%		Global organisation	1	0	0.0%
Papua New Guinea	1	1	100.0%		Mexico	1	0	0.0%
Senegal	1	1	100.0%		Philippines	1	0	0.0%
Singapore	1	1	100.0%		Singapore	1	1	100.0%
Switzerland	1	1	100.0%		Somaliland	1	0	0.0%
Thailand	1	1	100.0%		Sri Lanka	1	0	0.0%
Total	**144**	**63**	**43.8%**		Uganda	1	0	0.0%
					Vietnam	1	1	100.0%
					unknown	1	0	0.0%
					Total	**123**	**33**	**26.8%**

- 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%)[11]. 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)[12], 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 ICDDRB 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 6 Number and share of full trial awards, by lead institution (>2 awards)

Lead institution	Number of full trial awards	Share of full trial awards	Number of applications	Success rate
London School of Hygiene and Trop Med	12	19.0%	28	42.9%
MRC Unit, The Gambia	7	11.1%	11	63.6%
Liverpool School of Trop Med	5	7.9%	10	50.0%
University College London	4	6.3%	6	66.7%
KEMRI/Wellcome Trust Research Programme, Kenya	4	6.3%	4	100.0%

[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.

University of Oxford	3	4.8%	9	33.3%
The University of Manchester University of Cape Town University of Liverpool University of Oxford / OUCRU Vietnam	2 awards each	3.2%		
Bangor University Durham University Imperial College London King's College London LSHTM / Mwanza Intervention Trials Unit NIMR Tanzania Makerere University McMaster University Medical Research Council National University of Singapore Papua New Guinea Inst of Med Research Queen Mary University of London St George's University of London Stellenbosch University Swiss Tropical & Public Health Institute The Aga Khan University, Pakistan University Cheikh Anta Diop de Dakar University of Birmingham University of Ibadan University of Oxford / Mahidol-Oxford Tropical Medicine Research Unit, Thailand University of Sussex	1 award each	1.6%		

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

Lead institution	**Number of development awards** (calls 3-7)	**Share of development awards** (calls 3-7)	**Number of applications** (calls 5-7)	**Success rate** (calls 5-7)
London School of Hygiene and Trop Med	3	9.1%	11	18.2%
Liverpool School of Trop Med	2	6.1%	3	66.7%
Peruvian University Cayetano Heredia	2	6.1%	1	100.0%
Sangath, India	2	6.1%	3	66.7%
University of Birmingham	2	6.1%	3	66.7%
University of Liverpool	2	6.1%	1	100.0%
University of Nottingham	2	6.1%	1	100.0%

KEMRI/Wellcome Programme, Kenya	2	6.1%	2	100.0%
CBCI Society for Medical Education Human Sciences Research Council, SA ICDDRB, 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[13]. 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 8 Number of awards including trial sites, per country

	All awards	**Full trial awards**	**Development awards**
Uganda	19	12	7
India	16	8	8
Kenya	12	8	4
South Africa	12	10	2
Malawi	10	7	3
Pakistan	7	4	3
Tanzania	7	6	1
The Gambia	7	7	
China	6	3	3
Peru	5	2	3
Vietnam	5	5	
Bangladesh	4	1	3
Indonesia	4	4	

[13] 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%)[14]; 87 organisations are in HICs (41.0%)[15]. 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

Location	All awards		Full trial awards		Development awards	
	% of all researchers	% of all organisations	% of researchers	% of organisations	% of researchers	% of organisations
HIC	53.8%	41.0%	53.9%	41.1%	53.6%	45.9%
LMIC	34.9%	49.1%	32.1%	47.0%	41.2%	48.6%
Joint unit	9.0%	5.7%	11.4%	7.1%	3.6%	2.7%
Other	2.3%	4.2%	2.5%	4.8%	1.5%	2.7%

[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

Country	Number of organisations per country	% of all organisations	Continent	Number of organisations per continent	% of all organisations
UK	45	21.2%	Africa	60	28.3%
USA	15	7.1%	Europe	59	27.8%
South Africa	14	6.6%	Asia	47	22.2%
Uganda	11	5.2%	N America	19	9.0%
India	10	4.7%	Oceania	14	6.6%
Australia	7	3.3%	S America	6	2.8%
China	7	3.3%	Caribbean	1	0.5%
Indonesia	6	2.8%			
Kenya, Pakistan, Vietnam	5	2.4%			
Burkina Faso, Canada, Philippines, Tanzania	4	1.9%			

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 Kahn 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

Organisation		Number of awards involved in	Percentage of awards involve in
LSHTM	HIC	40	41.7%
LSTM	HIC	14	14.6%
UCL	HIC	14	14.6%
KEMRI Wellcome	Joint unit	10	10.4%

Imperial College London	HIC	9	9.4%
University of Oxford	HIC	9	9.4%
MRC The Gambia	Joint unit	8	8.3%
University of Liverpool	HIC	8	8.3%
Johns Hopkins University, USA	HIC	6	6.3%
King's College London	HIC	6	6.3%
The Aga Khan University, Pakistan	LMIC	6	6.3%
University of Malawi	LMIC	6	6.3%
Institute of Tropical Medicine, Belgium	HIC	5	5.2%
University of Cape Town	LMIC	5	5.2%

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 12 Individual researchers involved in more than one JGHT award

Name	Contact organisation	Number of awards involved in	As PI	As Co-PI
Umberto D'Alessandro	MRC Unit, The Gambia	6	3	3
Andrew Weeks	University of Liverpool	4	3	1
Diana Gibb	Medical Research Council	4	3	1
Feiko ter Kuile	LSTM	4	2	2
Kathryn Maitland	Imperial College London	4	2	2
Duolao Wang	LSTM	4	0	4
Koen Peeters	Institute of Tropical Medicine, Antwerp	5	0	5
Paul Milligan	LSHTM	4	0	4
Peter Olupot-Olupot	Mbale Regional Referral Hospital,	4	0	4

[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 Lawn; 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.

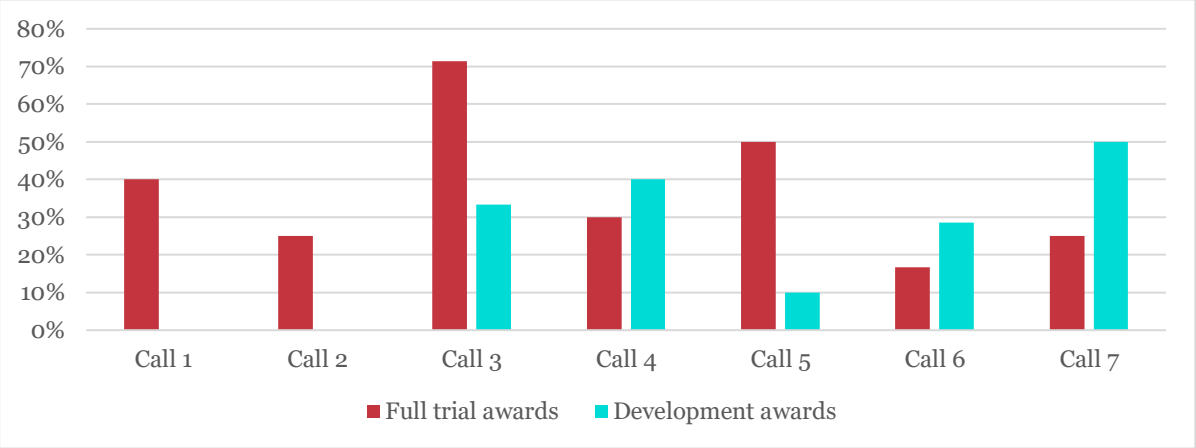
Chris Drakeley	LSHTM	4	0	4

- 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



Source of data: MRC grants database, desk research

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).

Figure 18 Share of HRCS classification[17] (all awards)

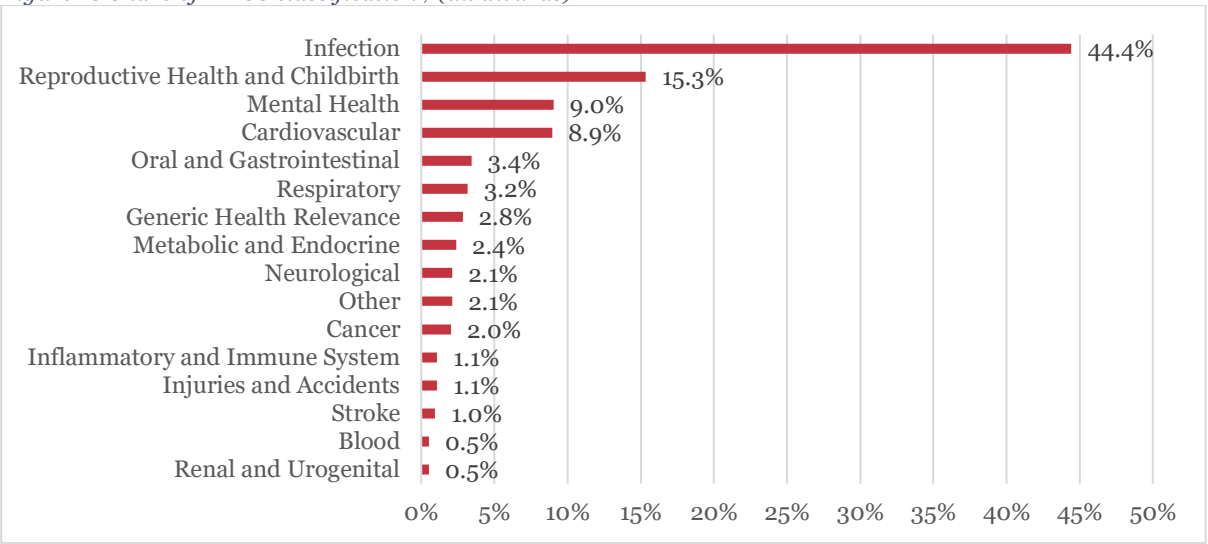
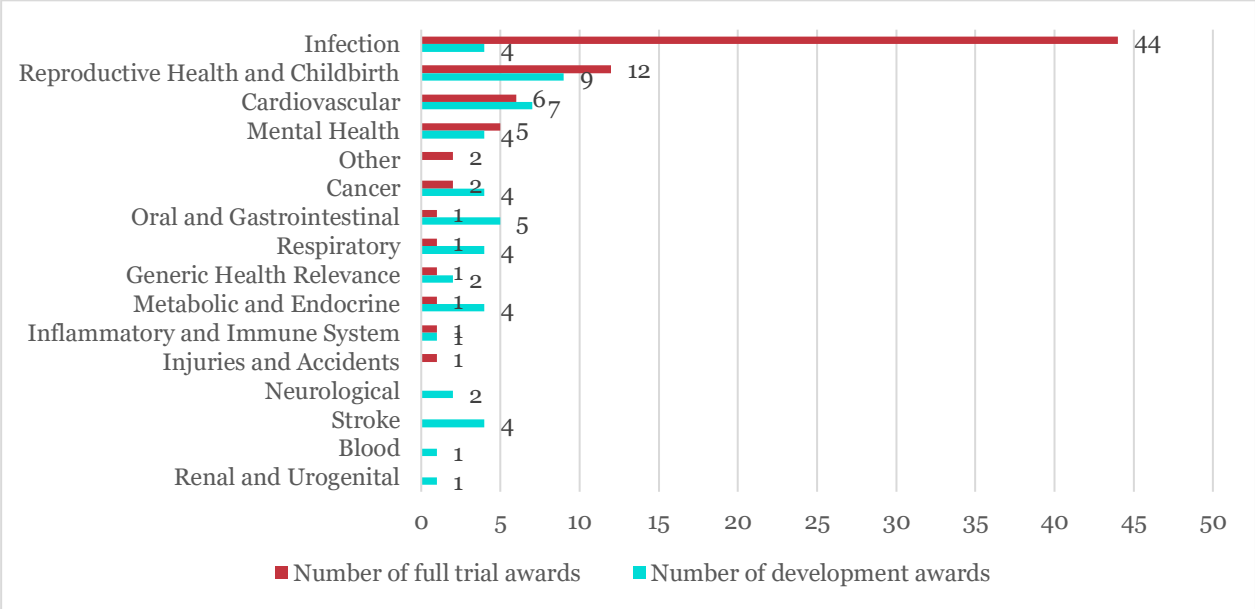


Figure 19 Number of awards addressing HRCS health classifications[18]

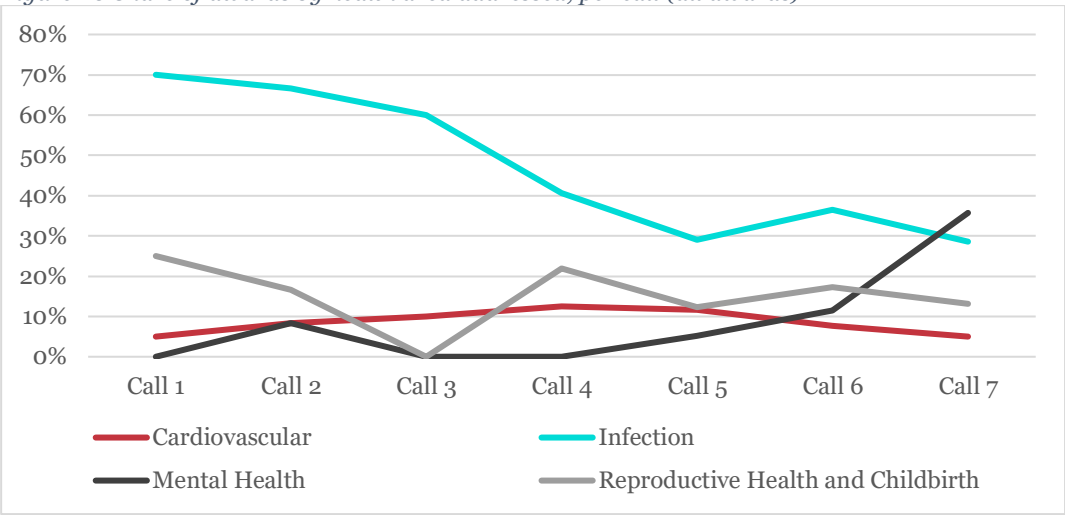


The relative shares varied from call to call (Figure 20). The share of 'Infection' awards was highest in Call 1, at 70%, but fell to around 30% in Calls 5 and 7. The area 'Mental Health' increased its share, from no awards in Calls 3 and 4, to 36% in Call 7. 'Reproductive Health and Childbirth' and 'Cardiovascular' remained relatively steady.

[17] 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*.

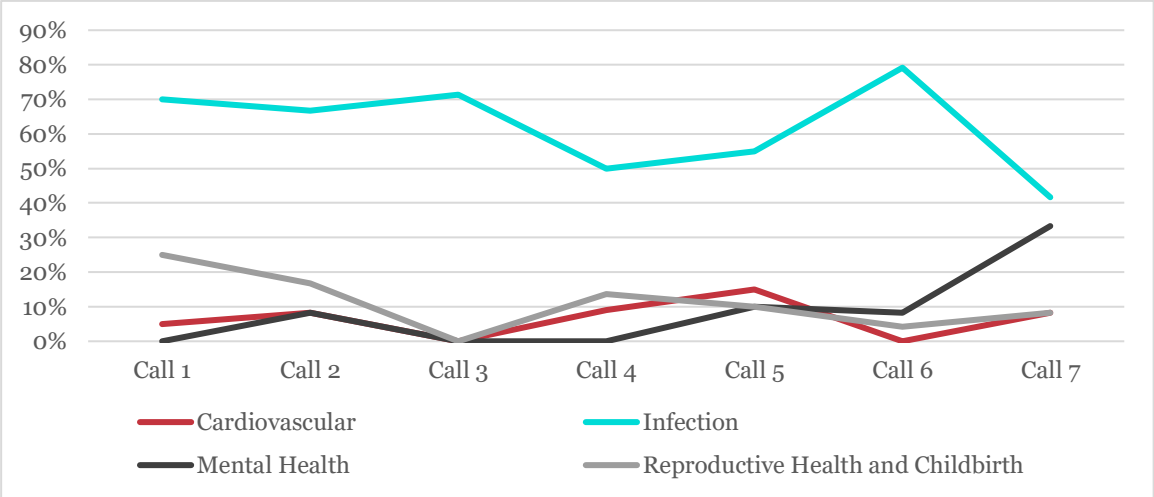
[18] This is the number of trials with any level of HRCS Health area attribution, e.g. 100%, 50%, 25% etc; added up, the total number of awards hence exceeds the actual number of awards (77 vs 63).

Figure 20 Share of awards by health area addressed, per call (all awards)



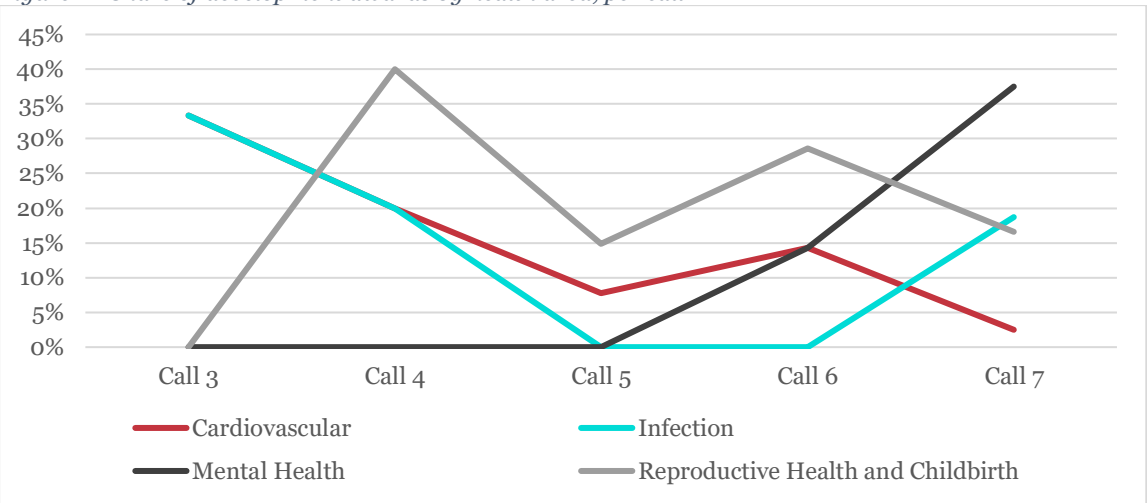
For full trial awards, the overall share of awards addressing 'Infection' was even higher, at 61%, followed by 'Reproductive Health and Childbirth', at 12.5%, and 'Mental Health' and 'Cardiovascular' (at 7.3% each) (Figure 21). The share of full trial awards in the area of 'Infection' remained between 42% and 79% across all calls. All other areas remained at 25% or below, except 'Mental Health' in Call 7, which increased to 33%.

Figure 21 Share of full trial awards by health area, per call



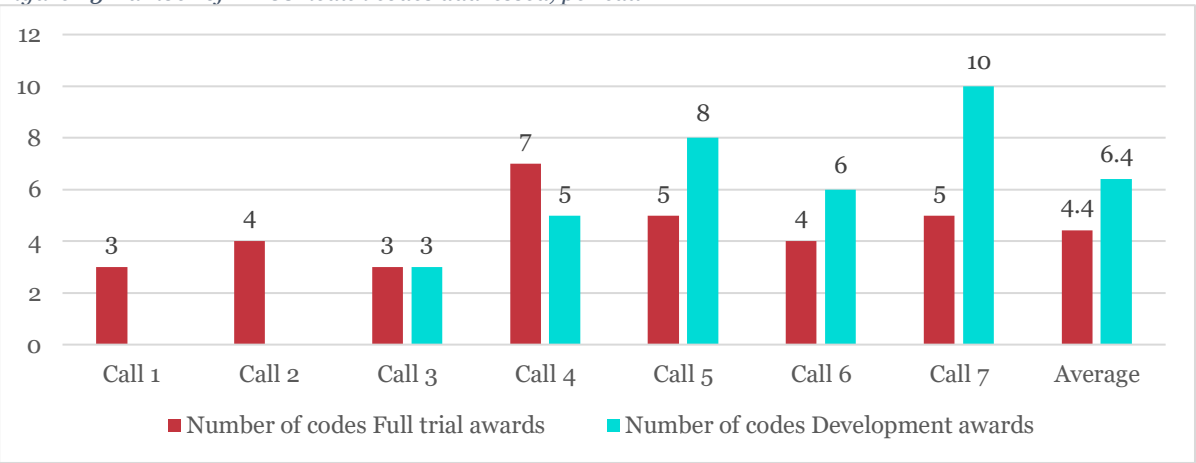
For development awards (Calls 3-7), the share of projects addressing 'Infection' was much lower, at only 11%. 'Reproductive Health and Childbirth' accounted for the highest share, at 21%, followed by 'Mental Health', 'Cardiovascular', 'Infection', and 'Oral and Gastrointestinal' at 9%-13% (Figure 22).

Figure 22 Share of development awards by health area, per call



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).

Figure 23 Number of HRCS health codes addressed, per call



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)[19]. 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.

[19] 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 (£)

	Total funding	**Average normalised funding per award**
Infection	£91,223,769	£2,384,935
Reproductive Health and Childbirth	£11,862,120	£1,530,596
Cardiovascular	£8,215,676	£1,825,706
Mental Health	£5,753,001	£1,278,445
Injuries and Accidents	£2,841,141	£2,841,141
Generic Health Relevance	£2,489,327	£2,489,327
Cancer	£2,352,357	£2,352,357
Other	£2,018,969	£1,009,485
Respiratory	£1,153,194	£2,306,387
Inflammatory and Immune System	£1,090,670	£2,181,341
Metabolic and Endocrine	£103,066	£206,132
Oral and Gastrointestinal	£103,066	£206,132

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)[20]. 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 (£)

	Total funding	**Average normalised funding per award**
Reproductive Health and Childbirth	£1,010,349	£151,477
Infection	£640,086	£182,882
Cardiovascular	£614,552	£157,577
Mental Health	£581,404	£145,351

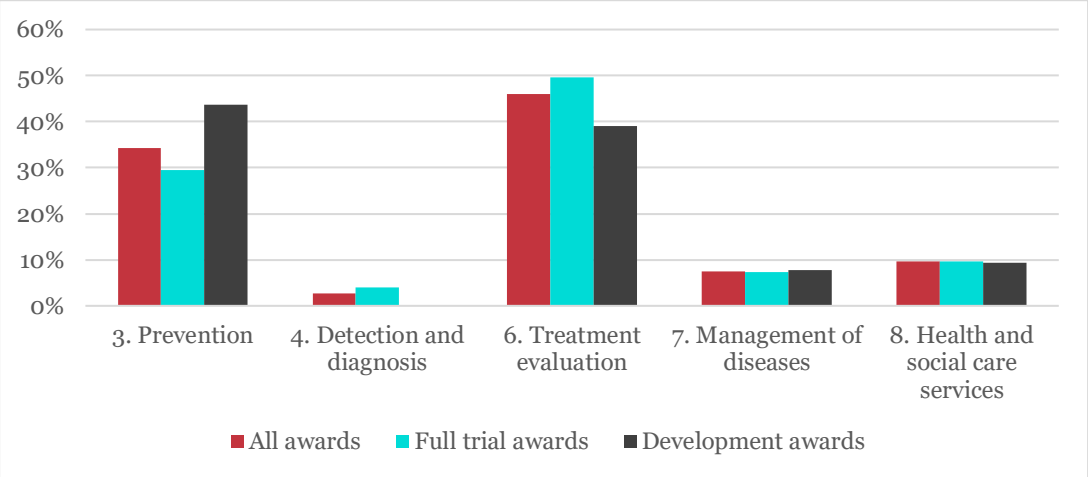
[20] Methodology: Again, funding was allocated by share of HRCS Health code share, i.e. if an award was assigned to two codes, the award budget was split equally between the two research areas. Award MR/R006121/1, £2.7m, is not coded, and was hence not included in this analysis.

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	£133,630

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).

Figure 24 Share of research classification group codes



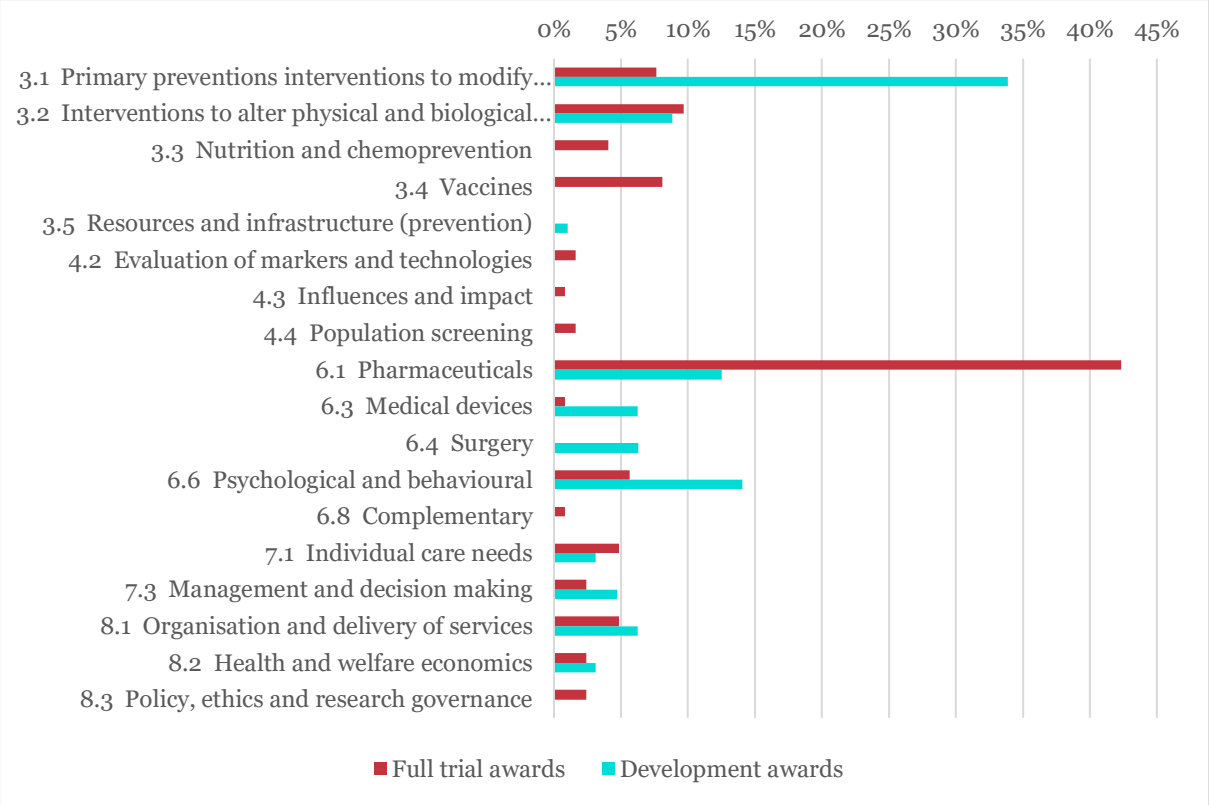
The relative shares varied considerably from call to call. For example, the share of 'Treatment evaluation' was highest in Calls 6 and 1, at 92.3% and 65% respectively, and lowest in Calls 2-4, ranging between 22.4% and 31.3%. The share of 'Prevention' was steadier, ranging between 30.0% (Call 1) and 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%).

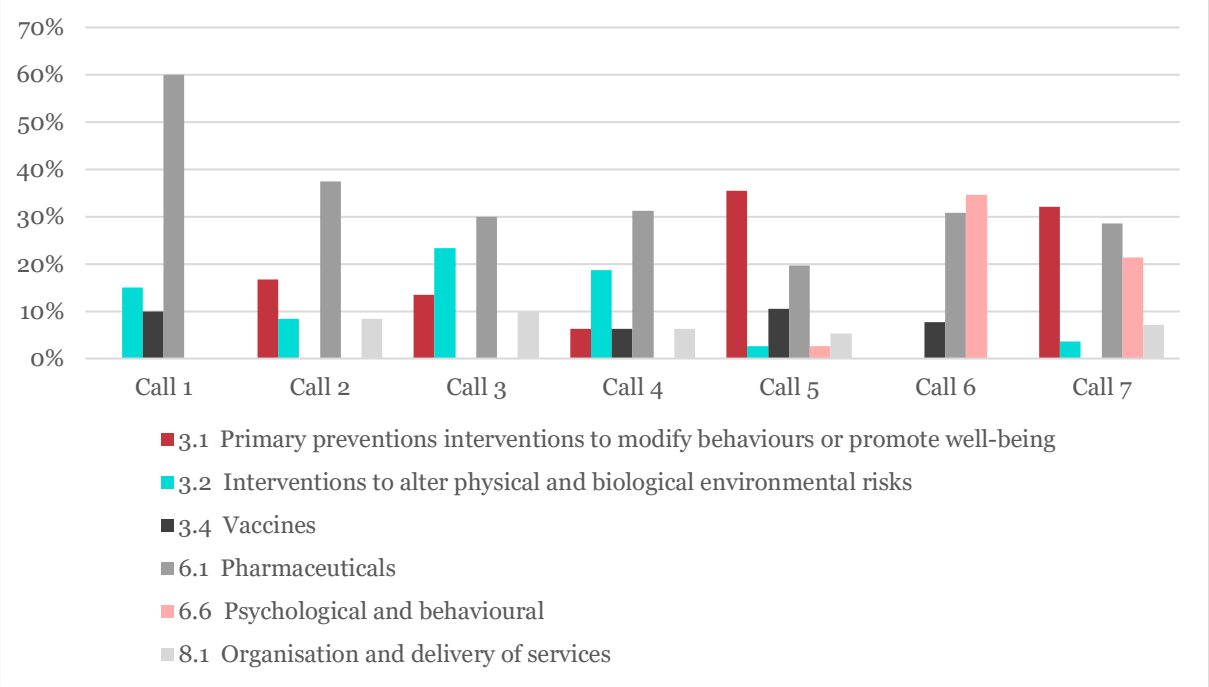
The relative shares differed between the full trial award and the development award portfolio: While full trial awards fell predominantly into the 'Pharmaceuticals' research class (42.3%), the share was much lower for development award portfolio (12.5%). Conversely, one third of development awards addressed 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



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).

Figure 26 Share of research classification, per call



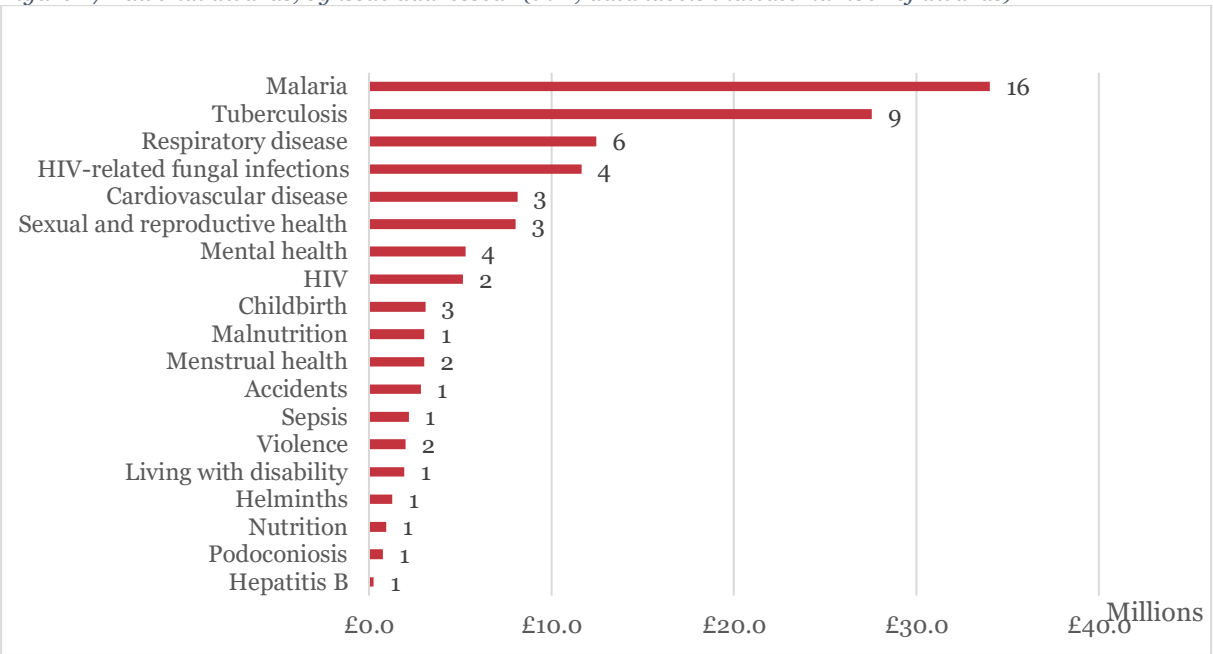
B.7 Diseases/issues addressed and types of intervention tested

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).

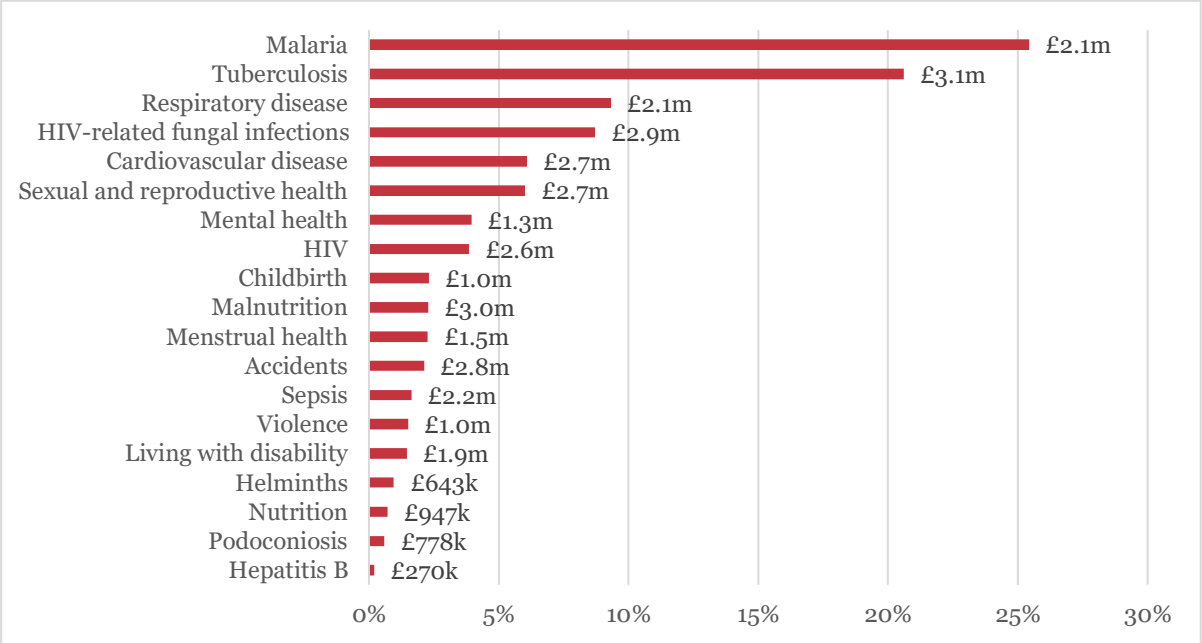
Other indications addressed in multiple full trial awards include respiratory disease (6 awards; 9.31%), and mental health and HIV-related fungal infections (4 awards each; 6.3%) (Figure 27). The share of funding for trials addressing cardiovascular disease and sexual and reproductive health (6.1%) exceeds 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)*



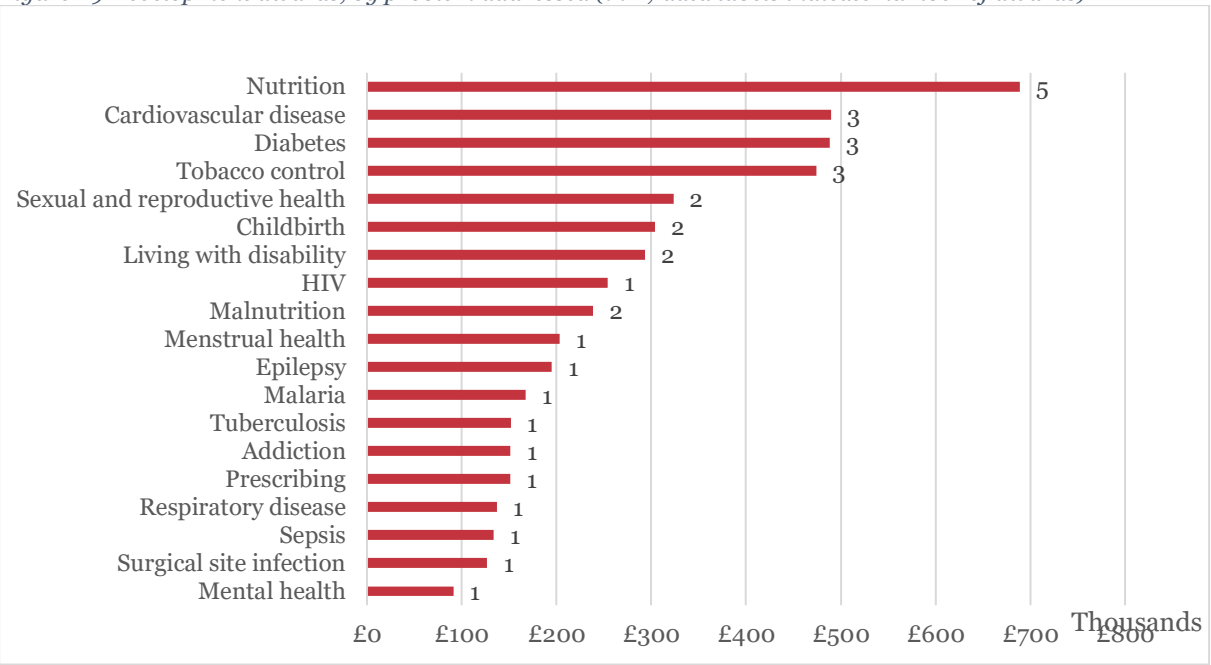
*HIV-related fungal infections: Cryptococcal meningitis and talaromycosis; Sexual and reproductive health includes Human Papilloma Virus; Malnutrition refers to Severe Acute Malnutrition (SAM) in infants

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).

Figure 29 Development awards, by problem addressed (in £; data labels indicate number of awards)



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[21] (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 15 Number of awards by JGHT call

Call number	Full trial awards	Development awards	Total	Awards not reported in ResearchFish and their status	
Call 1	10	NA	10	1 Full	Closed
Call 2	12	NA	12	1 Full	Closed
Call 3	7	3	10	1 Full	Closed
Call 4	10	5	15	0	
Call 5	10	10	20	1 Full	Closed
Call 6	6	7	13	0	
Call 7	8	8	16	1 Development + 7 Full	Active
Grand Total	63	33	96	12	

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

Type of publication	Closed Full (n=24)	Closed Development (n=17)	Active Full (n=17)	Total (n=58)
Journal Article	207	65	135	**407**
Conference Proceeding/Abstract	7	2	0	**15**
Technical Report	1	1	3	**5**
Manual / Guide	0	0	4	**4**
Book Chapter	1	1	0	**2**
Other	2	0	0	**2**
Policy briefing/report	0	0	2	**2**
Working Paper	1	0	1	**2**
Scholarly edition	0	0	1	**1**
Total	**219**	**69**	**146**	**434**
Mean publications per award	9.1	4.1	8.6	**7.5**
Mean journal articles per award	8.6	3.8	7.9	**7.0**

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

Journal	Open Access	Number of Publications
PLoS One	Yes	21
The Lancet	Hybrid/Delayed	17
Trials	Yes	17
Clinical Infectious Diseases	Hybrid	16
BMJ Open	Yes	15
The Lancet Global Health	Yes	15
Wellcome Open Research	Yes	13
The Lancet Infectious Diseases	Hybrid/Delayed	12
BMC Public Health	Yes	11
International Journal of Tuberculosis and Lung Disease	Hybrid/Delayed	11
Malaria Journal	Yes	11
The New England Journal of Medicine	Delayed	11

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 18 Number of additional grants by type of JGHT award

Type of funding	Closed Full (n=17)	Closed Development (n=10)	Active Full (n=18)	Active Development (n=5)	Total (n=50)
Research grant	40	16	36	4	96
Fellowship/Studentship	6	3	9	1	19
Total	46	19	45	5	115

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 19 Organisations who provided further funding to JGHT awards

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

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

	Closed Full (n=21)	**Closed Development (n=17)**	**Active Full (n=20)**	**Active Development (n=7)**	**Total (n=65)**
Number of dissemination activities	210	100	284	23	517

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

Primary audience	**Type of dissemination**								**Reach**		**Total events**	**No. of JGHT awards**
	Talk	Activity, workshop or similar	Working group / expert panel	Press release, conference, etc.	website, blog or social media channel	magazine, newsletter or online publication	Broadcast	Open day/ institutional visit	Chief geographical reach (% events)	Median no. of people reached per event (range)		
Professional Practitioners/Health professionals	137	52	34	1	7	6	3	1	International (60%)	51-100	**241**	**46**
Public/other audiences/media	28	22	8	23	9	10	6	0	International (60%)	101-500	**106**	**39**
Policymakers	29	11	24	1	0	2	0	0	International (39%)	11-50	**67**	**24**
Study participants or study members	10	7	13	0	1	2	0	1	Local (44%)	51-100	**34**	**16**
Undergraduate/ postgraduate students	25	2	0	0	0	0	0	1	Local (39%)	51-100	**28**	**15**
Third sector organisations/ supporters	4	3	5	0	2	0	0	0	International (86%)	11-50	**14**	**6**
Industry/Business	4	1	4	0	0	0	0	0	International (56%)	51-100	**9**	**6**
Patients, carers and patient groups	0	4	1	0	1	0	1	1	Local (63%)	51-100	**8**	**6**
Schools	3	3	0	0	0	0	0	1	Local (86%)	101-500	**7**	**6**
Other academic audiences	3	0	0	0	0	0	0	0	International (100%)	NA	**3**	**3**
Total	**243**	**105**	**89**	**25**	**20**	**20**	**10**	**5**	**International (53%)**	**51-100**	**517**	**65**

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 22 Type of outcome of dissemination activities

Type of most significant outcome	Number of dissemination activities
Plans made for future related activity	107
Audience reported change in views, opinions or behaviours	101
Increase in requests about (further) participation or involvement.	97
Increase in requests for further information	75
Decision made or influenced	57
Not aware of any impact	29
Colleague/s reported change in views or opinions	20
Not reported	31
Total	517

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 23 Instances of policy influence by type, geographical reach and type of award

Type of policy influence	Geographical reach	Closed Full (n=20)	Closed Development (n=7)	Active Full (n=13)	Active Development (n=2)	Total (n=42)
Participation in advisory committee	Local/ Regional	0	1	0	0	31
	National	4	0	1	0	

	Continent	5	0	2	0	
	Multi-continent	9	0	9	0	
Membership of a guideline committee	National	4	0	3	0	25
	Continent	5	0	1	0	
	Multi-continent	6	0	6	0	
Influenced training of practitioners or researchers	Local/ Regional	5	2	0	1	23
	National	1	0	5	0	
	Continent	0	0	3	1	
	Multi-continent	2	1	1	1	
Implementation circular/rapid advice/letter to e.g. Ministry of Health	Local/ Regional	1	4	2	0	17
	National	2	0	0	1	
	Continent	1	1	1	0	
	Multi-continent	2	0	2	0	
Citation in clinical guidelines	National	0	0	1	0	10
	Continent	2	0	0	0	
	Multi-continent	6	0	1	0	
Citation in other policy documents	National	1	0	1	0	8
	Multi-continent	3	0	3	0	
Participation in a national consultation	Local/ Regional	0	0	1	0	8
	National	1	2	2	0	
	Continent	1	1	0	0	
Gave evidence to a government review	Local/ Regional	1	1	0	0	5
	National	1	1	0	0	
	Continent	0	1	0	0	
Citation in systematic reviews	Multi-continent	3	0	0	0	3
Citation in clinical reviews	Multi-continent	1	0	0	0	1
Total		67	15	45	4	131

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

Type of tool	Closed Full (n=13)	Closed Development (n=14)	Active Full (n=10)	Active Development (n=7)	Total (n=44)
Database/Collection of Data	13	16	12	6	**47**
Improvements to research infrastructure	6	18	12	2	**38**
Physiological assessment or outcome measure	3	9	11	2	**25**
Software, webtool or application	1	1	8	3	**13**
Model of mechanisms or symptoms - human	0	0	8	3	**11**
Technology assay or reagent	4	0	4	0	**8**
Biological samples	2	3	1	0	**6**
Model of mechanisms or symptoms - mammalian in vivo	0	0	1	0	**1**
Total	**29**	**47**	**57**	**16**	**149**

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

Type of product	**Closed Full (n=13)**	**Closed Development (n=9)**	**Active Full (n=14)**	**Active Development (n=5)**	**Total (n=41)**
Interventional products (n=59)					
Therapeutic Intervention - Drug	8	0	4	1	13
Preventative Intervention - Behavioural risk modification	1	3	7	1	12
Preventative Intervention - Physical/Biological risk modification	1	3	3	0	7
Management of Diseases and Conditions	2	2	1	0	5
Support Tool - For Medical Intervention	0	5	0	0	5
Therapeutic Intervention - Psychological/Behavioural	0	0	4	1	5
Therapeutic Intervention - Vaccines	1	0	4	0	5
Health and Social Care Services	1	0	2	1	4
Diagnostic Tool - Non-Imaging	0	0	2	0	2
Therapeutic Intervention - Medical Devices	1	0	0	0	1
Artistic Products (n=36)					
Film/Video/Animation	6	6	7	0	19
Artwork/Image	3	3	3	0	9
Artefact (including digital)	0	0	6	0	6
Exhibition/Performance	0	1	0	1	2
Total	**24**	**23**	**43**	**5**	**95**

Appendix D Clinical trials registry data analysis

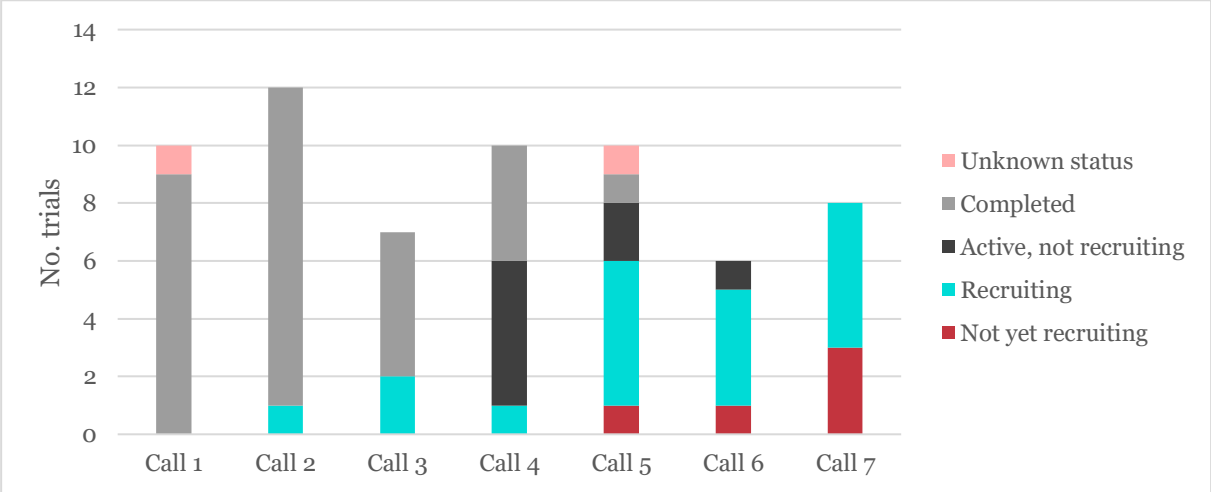
- Background

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)



- 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.

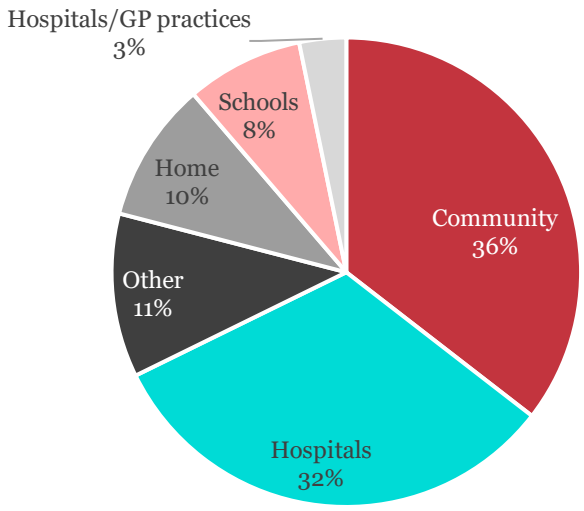
- Trial sites and settings

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)[22]. 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).

Figure 31 Trial settings

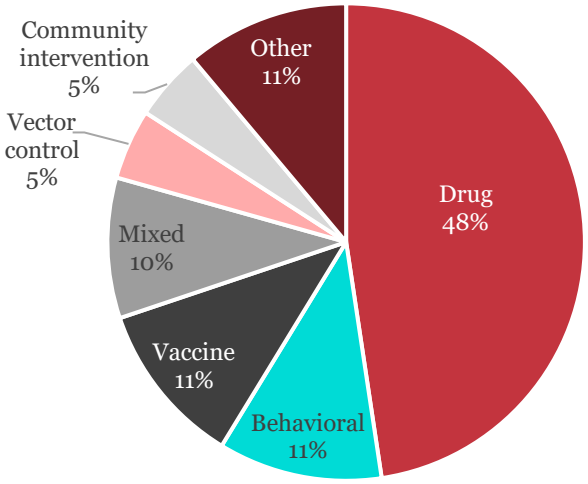


- Trial interventions and types

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.

Figure 32 Types of trial intervention (n=62)



- 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)[23]. 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).

[23] 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

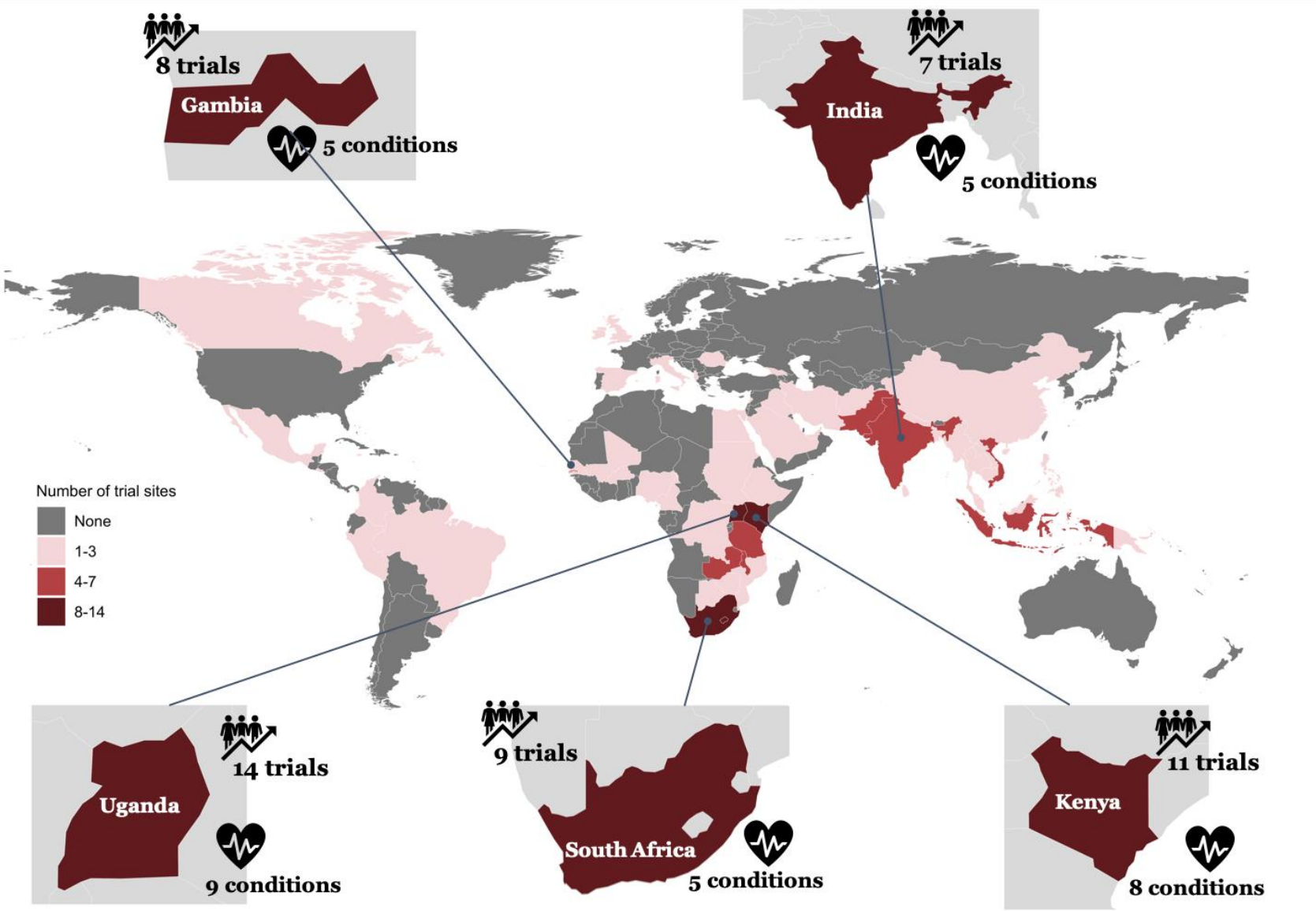


Table 26 List of conditions

Condition	**% (count)**
Malaria	24% (15)
Tuberculosis	14% (9)
Reproduction/sexual health	11% (7)
Mental Health Pneumonia	8% (5)
Cardio-vascular disease Cryptococcal meningitis	5% (3 each)
HIV, Prophylactic antibiotics, Violence prevention, Human papilloma virus	3% (2 each)
Head Injury, Streptococcus, Helminths, Liver fluke, Podoconiosis, Talaromycosis, Hepatitis, Malnutrition	2% (1 each)
Total	**63**

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.

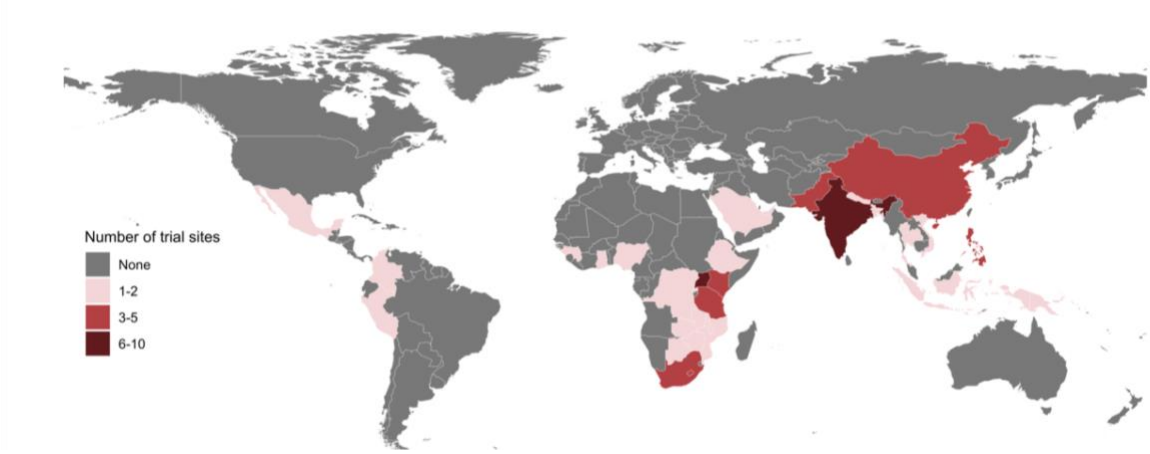
- Location of respondents (by country)

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

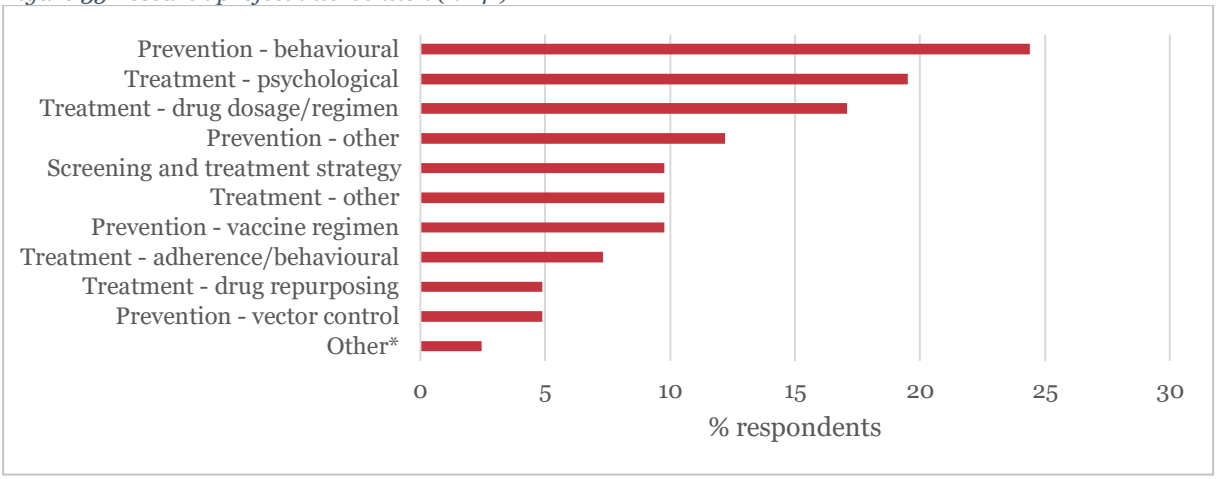
The reported number of trial sites per award varied from 1 to 30 (full award) and 1 to 10 (development award). Across all awards, trial sites were located in 32 different countries (Figure 34). The largest number of trials involved sites in Uganda and India (10 each, 25%).

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).

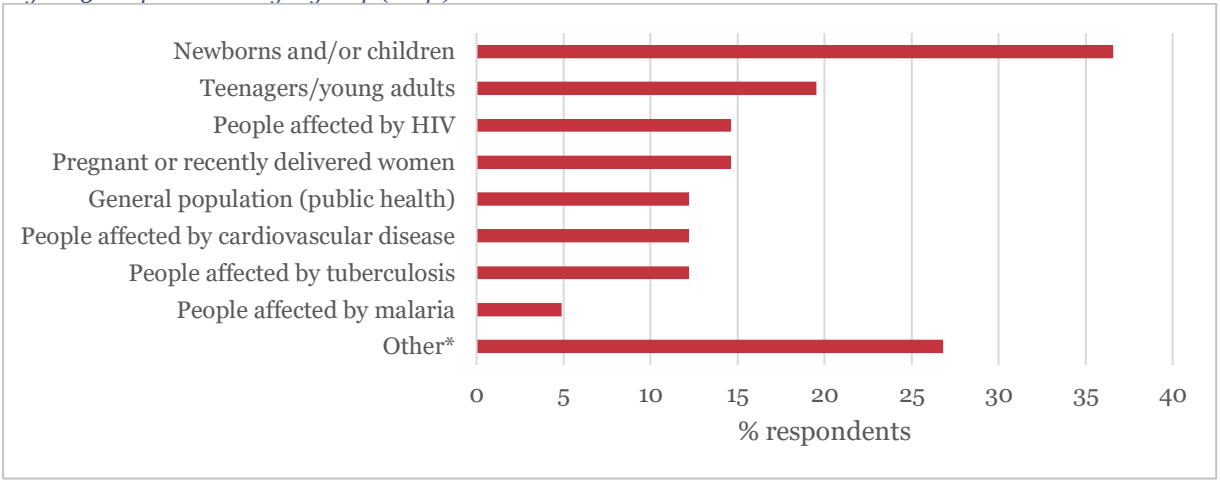
Figure 35 Research project intervention (n=41)



* other included economic intervention and specific details on the selected answer.

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.

Figure 36 Population target group (n=41)

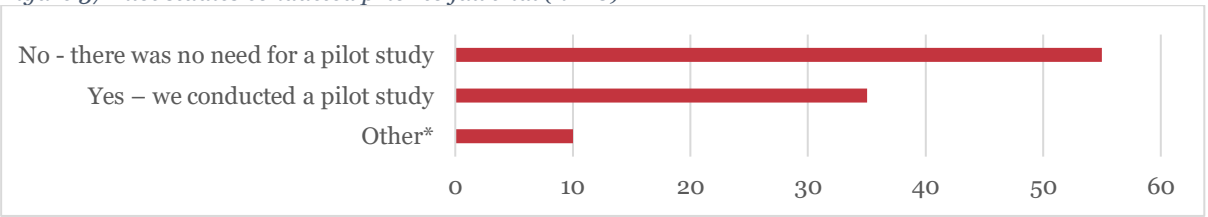


* Other includes people affected by mental illness, diabetes, head injury and hazardous behaviour, the elderly, mothers and women.

- 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).

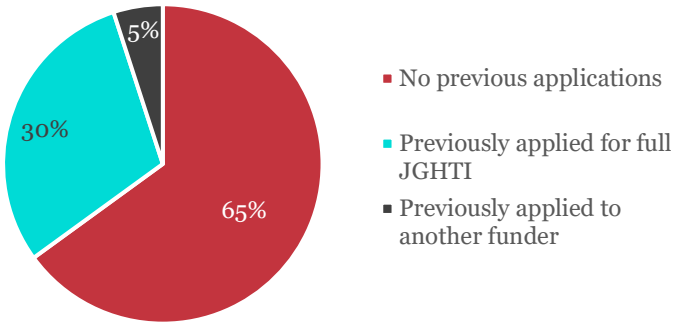
Figure 37 Pilot studies conducted prior to full trial (n=20)



* Other included surveillance to determine baseline endpoints and previous studies that were conducted in other countries.

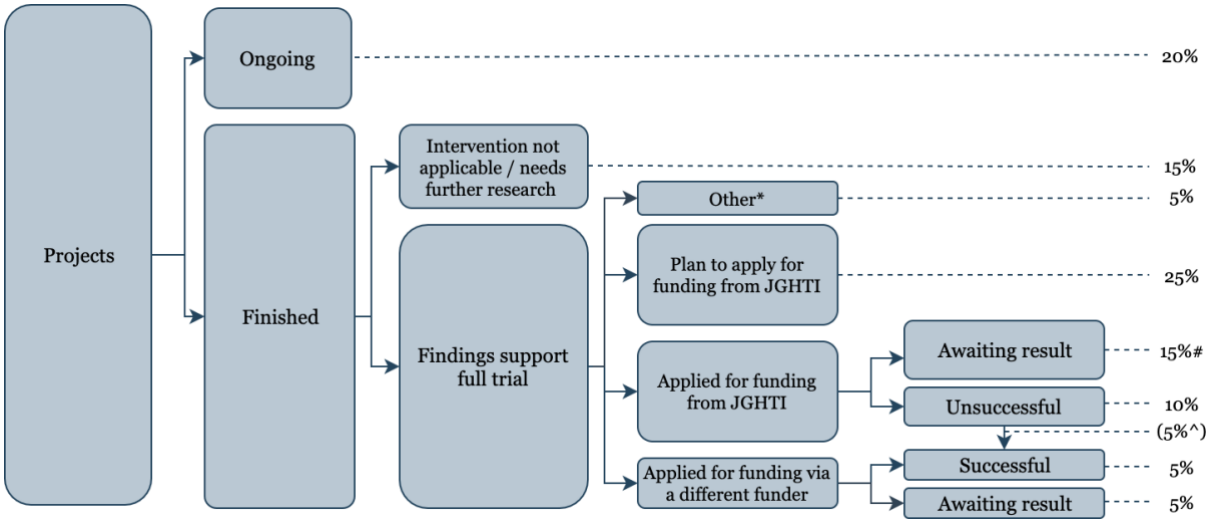
Approximately one third of development award respondents (30%, 6 of 20) had previously applied for a full award from the JGHT, 5% (1) reported that they had previously applied to another funder, while 65% (13) reported that they had not applied for a full trial related to this research (Figure 38).

Figure 38 Application history of development award (n=20)



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.

Figure 39 Evolution of development award projects (n=20)



* 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.

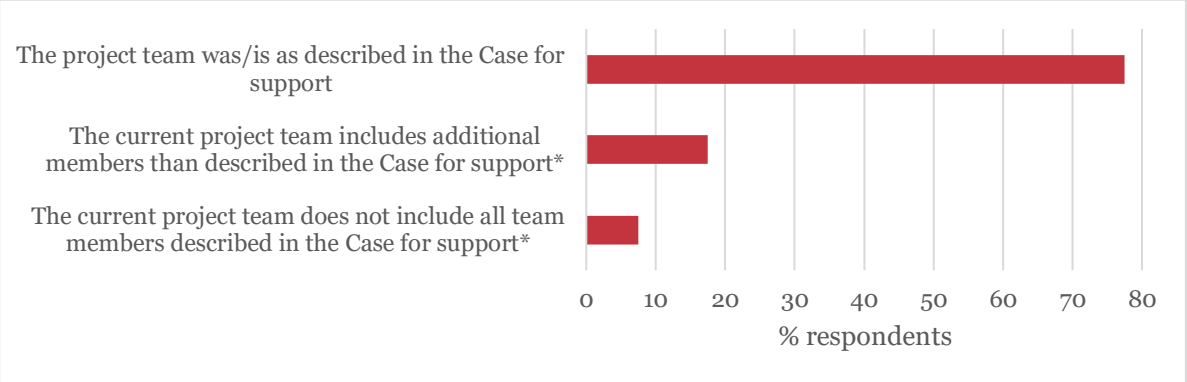
Throughout the survey PIs described some benefits of the development award scheme. One PI stated that participation in the development award had helped to guide the design of the full study. Another PI who has since received funding for a full trial reported that the development trial revealed a lot 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”.

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)



*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)

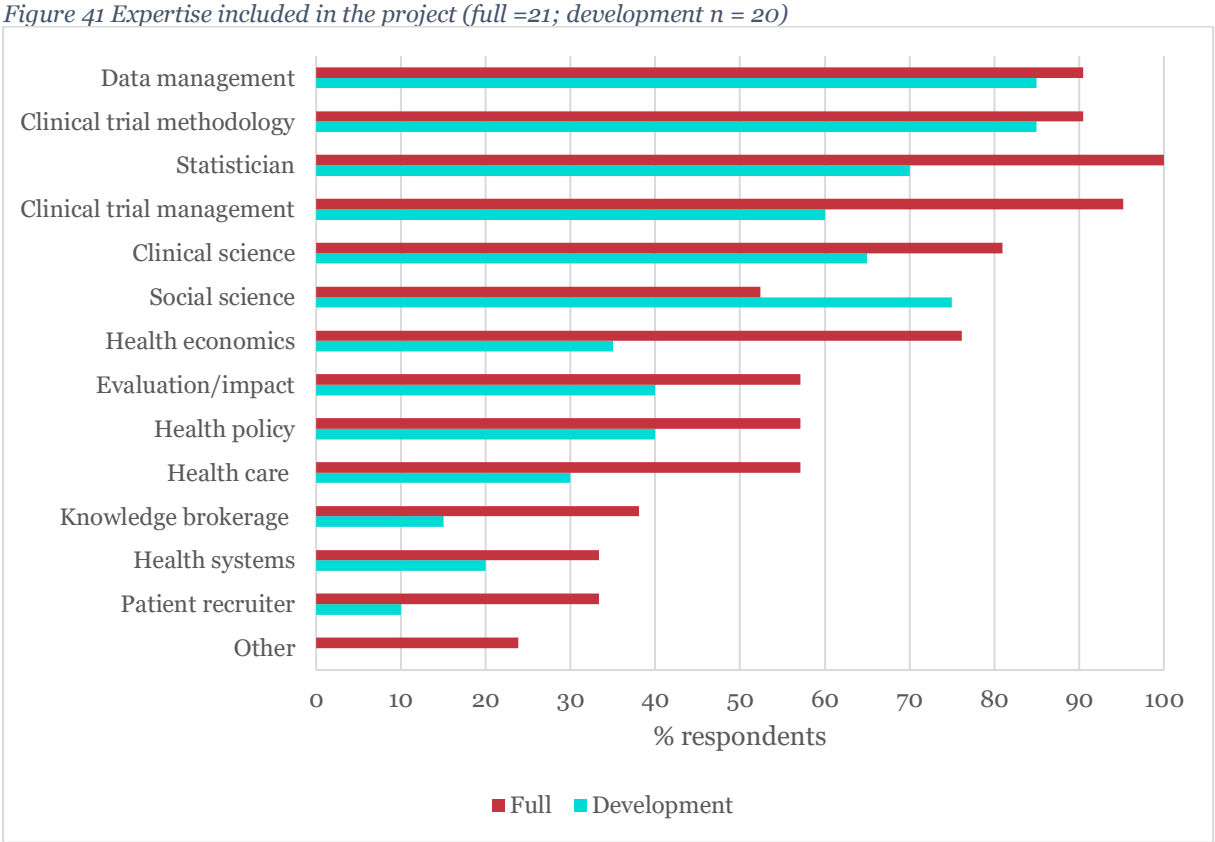
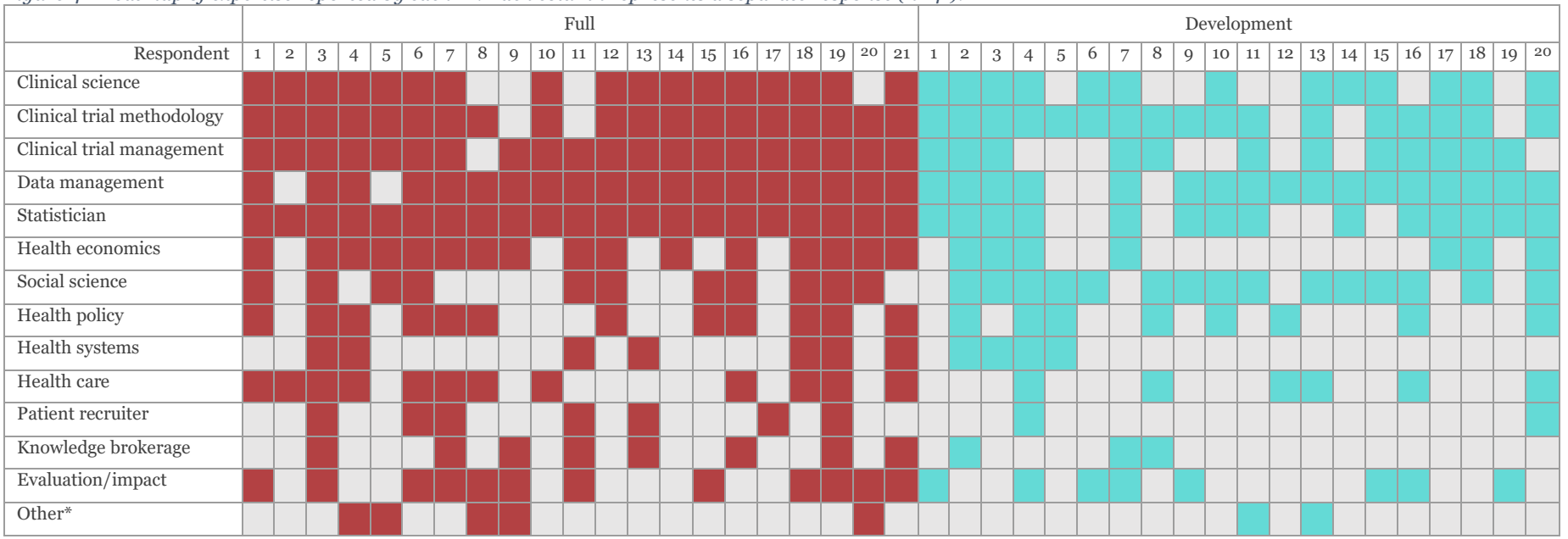


Figure 42 Heatmap of expertise reported by each PI. Each column represents a separate response (n=41).

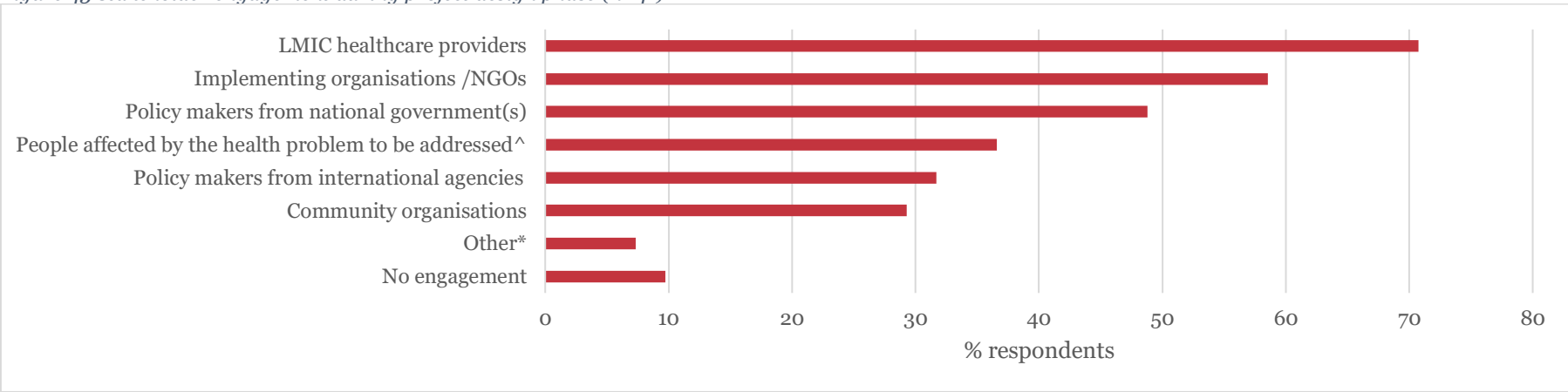


*Full - laboratory skills (n=1), epidemiologist (n=1), entomologist (n=2), early childhood education (n=1); Development – microbiologist (n=1), clinicians (n=1).

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.

Figure 43 Stakeholder engagement during project design phase (n=41)



^Beyond those directly involved in the research project *Other includes mention of a historic partnership with the stakeholders (n=1), national subject experts (n=1), and policy makers from state government (n=1).

Figure 44 Heatmap of stakeholder engagement during project design phase. Each column represents a separate response (n=41)

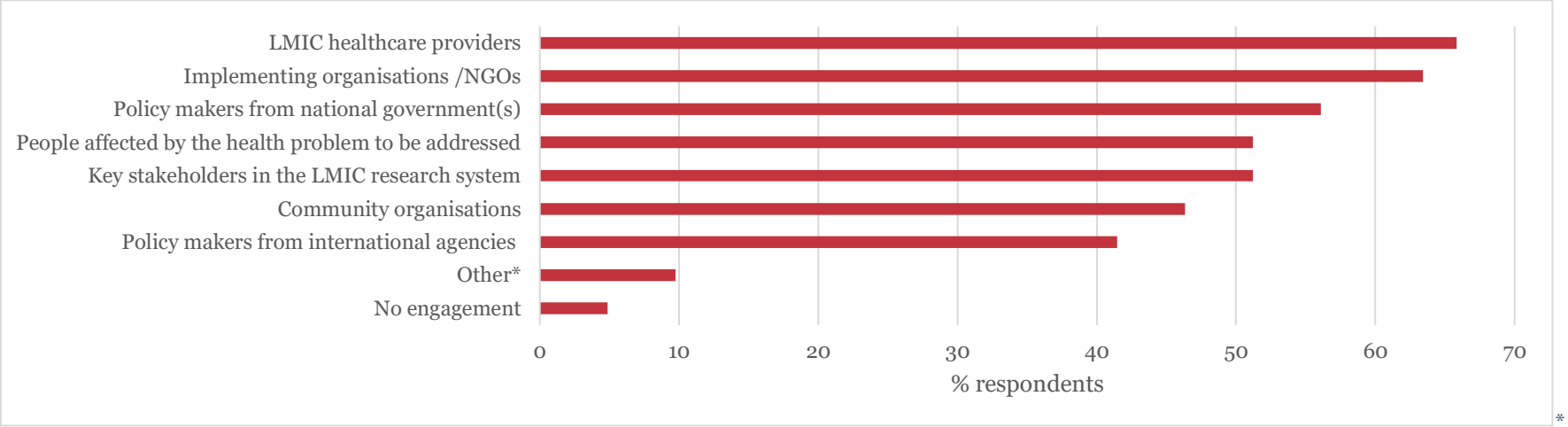
	Full																					Development																				
Respondent	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Policy makers from national government(s)																																									
Policy makers from international agencies																																									
LMIC healthcare providers																																									
Implementing organisations /NGOs																																									
Community organisations																																									
People affected by the health problem to be addressed^																																									
Other*																																									
No engagement																																									

^Beyond those directly involved in the research project *Other includes mention of a historic partnership with the stakeholders (n=1), national subject experts (n=1), and policy makers from state government (n=1).

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).

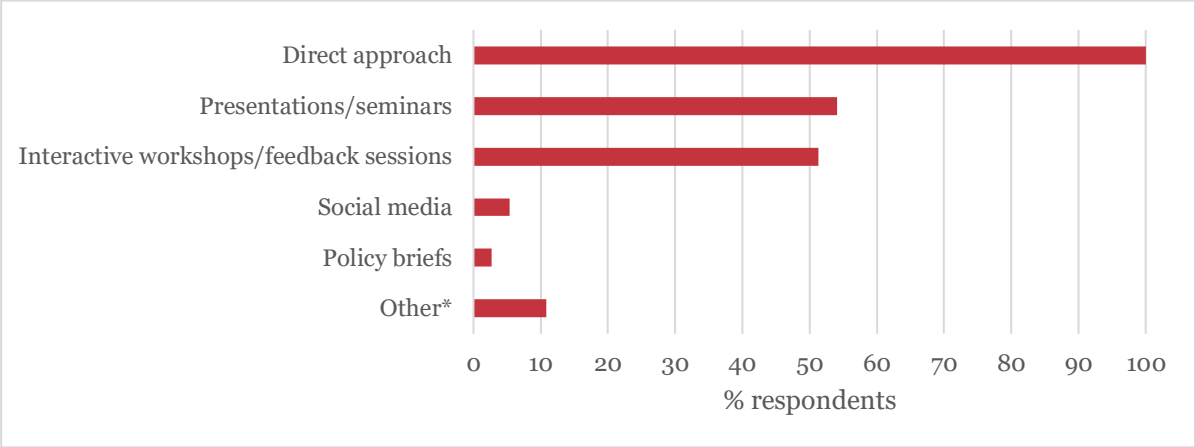
Figure 46 Heatmap of stakeholder engagement during project beyond those directly involved in the project. Each column represents a separate response (n=41)

	Full																					Development																			
Respondent	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Policy makers from national government(s)	■			■		■	■	■	■		■	■				■	■	■	■	■			■		■	■		■		■	■	■		■					■		■
Policy makers from international agencies	■		■	■	■			■	■			■	■	■		■	■	■	■			■							■		■								■		
LMIC healthcare providers[1]	■		■			■	■	■			■	■	■	■	■	■	■	■	■		■	■		■	■	■	■		■		■	■		■		■	■		■		
Key stakeholders in the LMIC research system			■		■	■	■	■	■	■	■	■	■	■	■	■	■	■	■					■			■	■		■						■					
Implementing organisations /NGOs	■		■	■		■	■	■		■	■			■		■	■	■	■	■				■	■	■		■	■	■	■			■	■		■		■	■	
Community organisations			■	■	■	■			■		■		■			■		■	■				■					■	■		■		■	■		■		■		■		■
People affected by the health problem to be addressed			■	■	■	■	■	■	■		■	■				■		■	■	■		■	■	■					■	■			■		■			■			
Other^																		■			■																		■			
No engagement		■																																				■			

^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)



** Other includes participant groups, teleconferences and visits to trial sites.*

- 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.

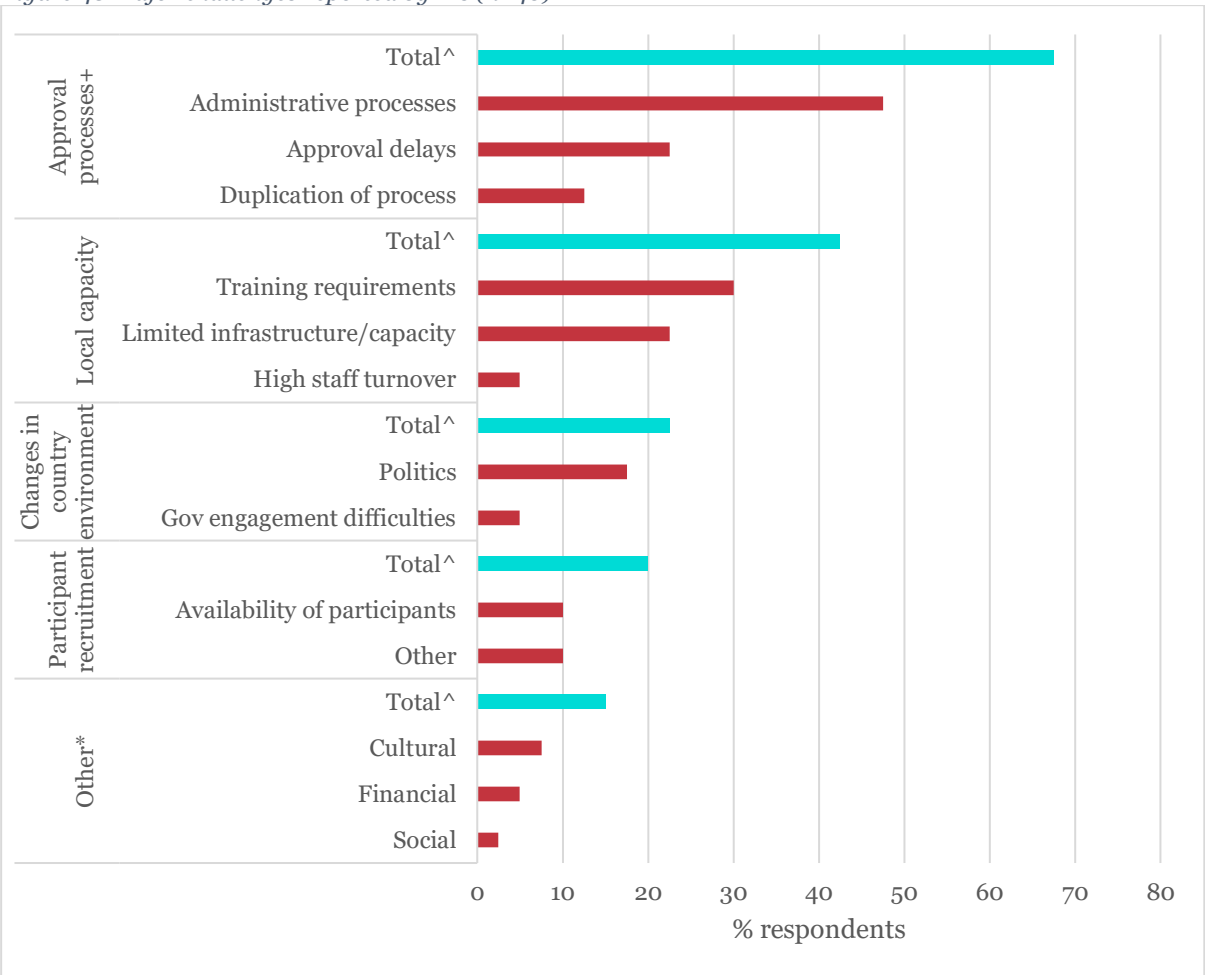
E.1.4. Barriers and enablers

- 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.

Figure 48 Major challenges reported by PIs (n=40)



+ Approval processes include regulatory and ethical approval. *Other included administrative/governance issues at UK site, intervention coverage and issues with local government ^Total is the percentage of respondents who selected one or more of the categories within each group.

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.

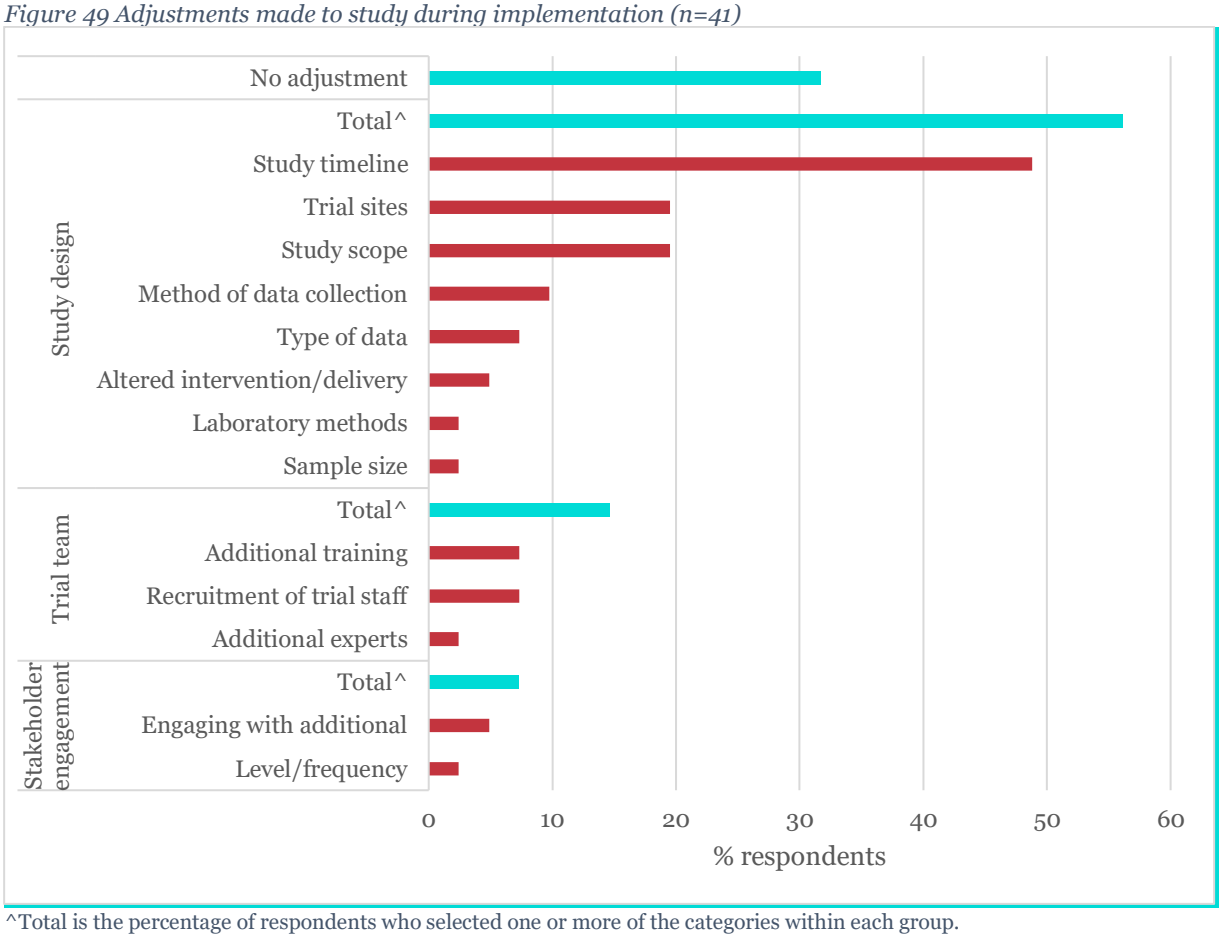
- Adjustments

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)



^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.

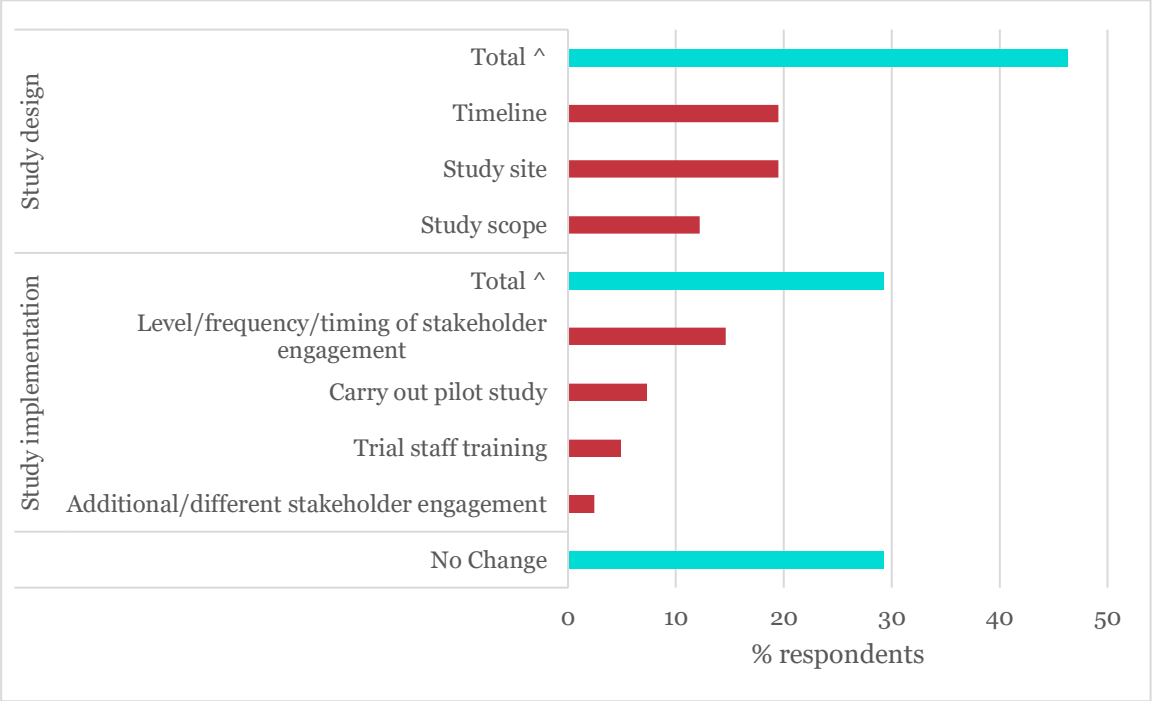
In one case, the trial team conducted more extensive training than initially proposed in order to ensure that those delivering the trial reached the minimum competencies required. Given the extensive nature

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)



^Total is the percentage of respondents who selected one or more of the categories within each group.

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

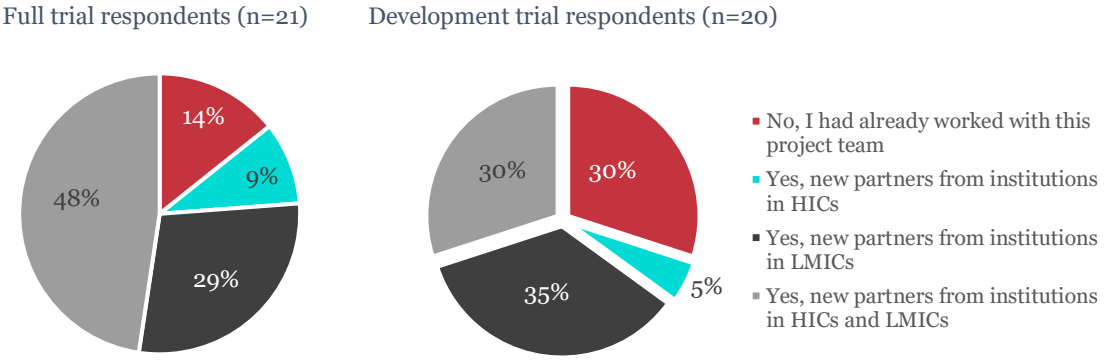
Outputs and scientific outcomes		**Full *(n=21)***	**Development *(n=20)***
Findings (did the research answer the primary research questions?)			
	Yes	5 (24%)	14 (70%)
	Yes, preliminary/auxiliary	2 (5%)	1 (5%)
	Ongoing	15 (71%)	5 (25%)
Social study findings^		1 (5%)	2 (10%)
Publications			
	Main trial publication	3 (14%)	3 (15%)
	In prep/submitted		7 (35%)
	Trial protocol	2 (10%)	
	Social/ economic paper	2 (10%)	
	In prep/submitted		1 (5%)
	Other paper	4 (19%)	3 (15%)
	In prep/submitted	1 (5%)	5 (25%)
Tools (incl. software)/Databases			
	Tool for delivering/monitoring intervention (e.g. can be used for implementation)	3 (14%)	3 (15%)
	Tool for research (e.g. consent tool, data collection)	4 (19%)	4 (20%)
	Database for continued research	1 (5%)	

^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

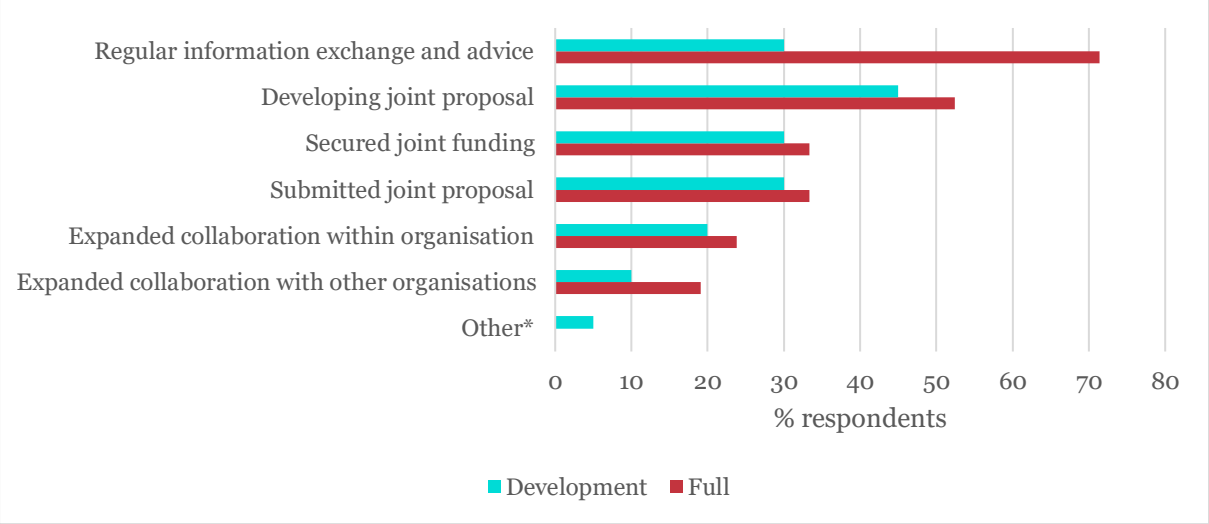


The majority of full and development award respondents indicated they either have plans to collaborate in future (38%, 8 of 21; 15%, 3 of 20, respectively) or do not have currently plans but would be open to future collaborations (62%, 13; 75%, 15, respectively). When asked about the ongoing plans for 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.

Figure 52 Future of ongoing collaborations (full n = 21; development n=20)



* Other = intention to submit a joint proposal subject to changes in the regulatory landscape.

Table 28 Sources of funding for ongoing collaborations

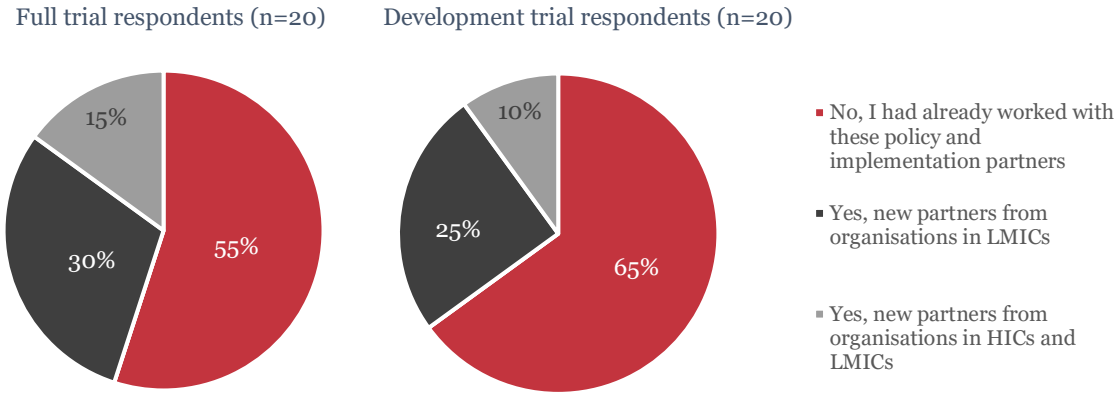
Full trials	Development awards
• JGHT • Wellcome Trust Collaborative Award	• NIH • NIHR • Health Systems Research Initiative • Global Challenges Research Fund • MRC/Arts & Humanities Research Council. MRC-AHRC Global Public Health: Partnership Awards scheme

Respondents reported that research networks had been developed/expanded during the JGHT funded project. Even numbers of full trial respondents reported a development/expansion 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



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

Other outcomes*		**Full *(n=20)***	**Development (n=20)**
Infrastructure			
	Research	6 (30%)	1 (5%)
	Community/health care	4 (20%)	1 (5%)
Training			
	Research general (incl. lab skills)	2 (10%)	
Research capacity building at LMIC			
	Motivation	11 (55%)	7 (35%)
	Knowledge and technical skills	14 (70%)	15 (75%)
	Governance	8 (40%)	4 (20%)
	Leadership	12 (60%)	12 (60%)

- 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 30 Impacts and uptakes

Impacts		**Full *(n=21)***	**Development *(n=20)***
Policy/health impacts			
	Not yet, but likely or have potential	16 (76%)	8 (40%)
	Yes, influenced policy/health	4* (19%)	
	No, but will inform future research		12 (55%)
Practise/implementation			
	Findings practised in study countries	1 (5%)	1 (5%)
Uptake of scientific outputs (e.g. databases, tools, methods)			
	Not yet	11 (52%)	7 (35%)
	The intervention tested	4 (19%)	3 (15%)
	Research tools developed	3 (14%)	1 (5%)
	Networks developed	1 (5%)	
	Policy context		1 (5%)
	Health system context		2 (10%)

*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.

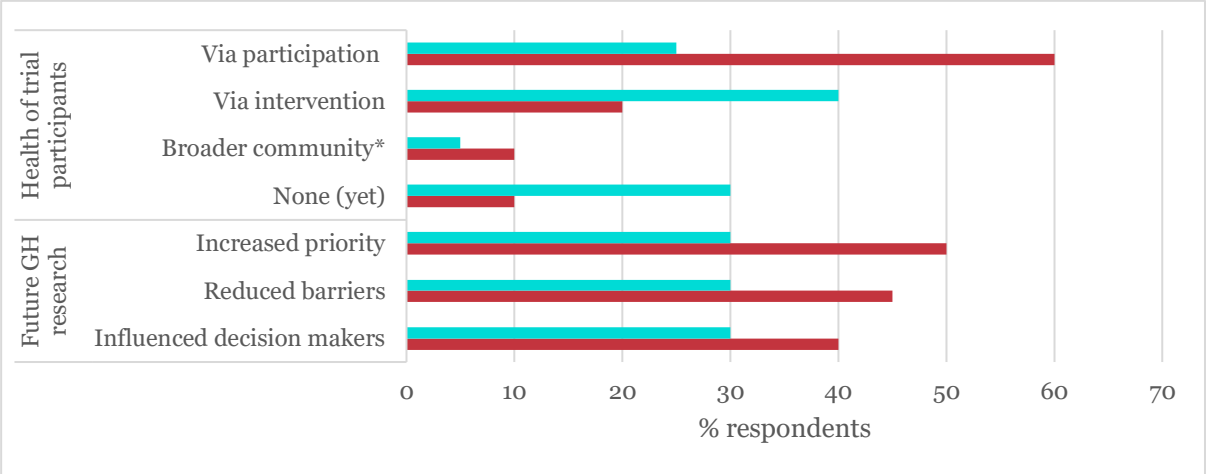
- Other impacts

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 health care 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).

Figure 54 Other impacts of JGHT funded trials (full n = 20; development n = 20)



* 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.

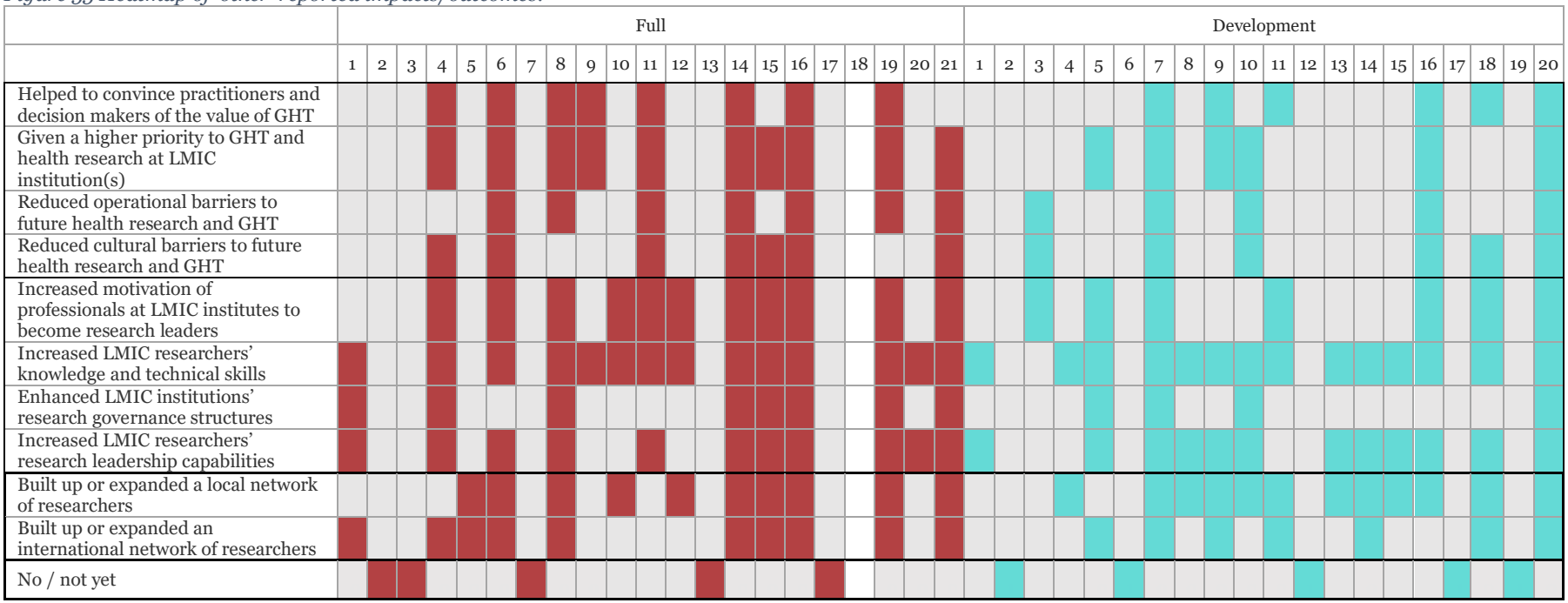
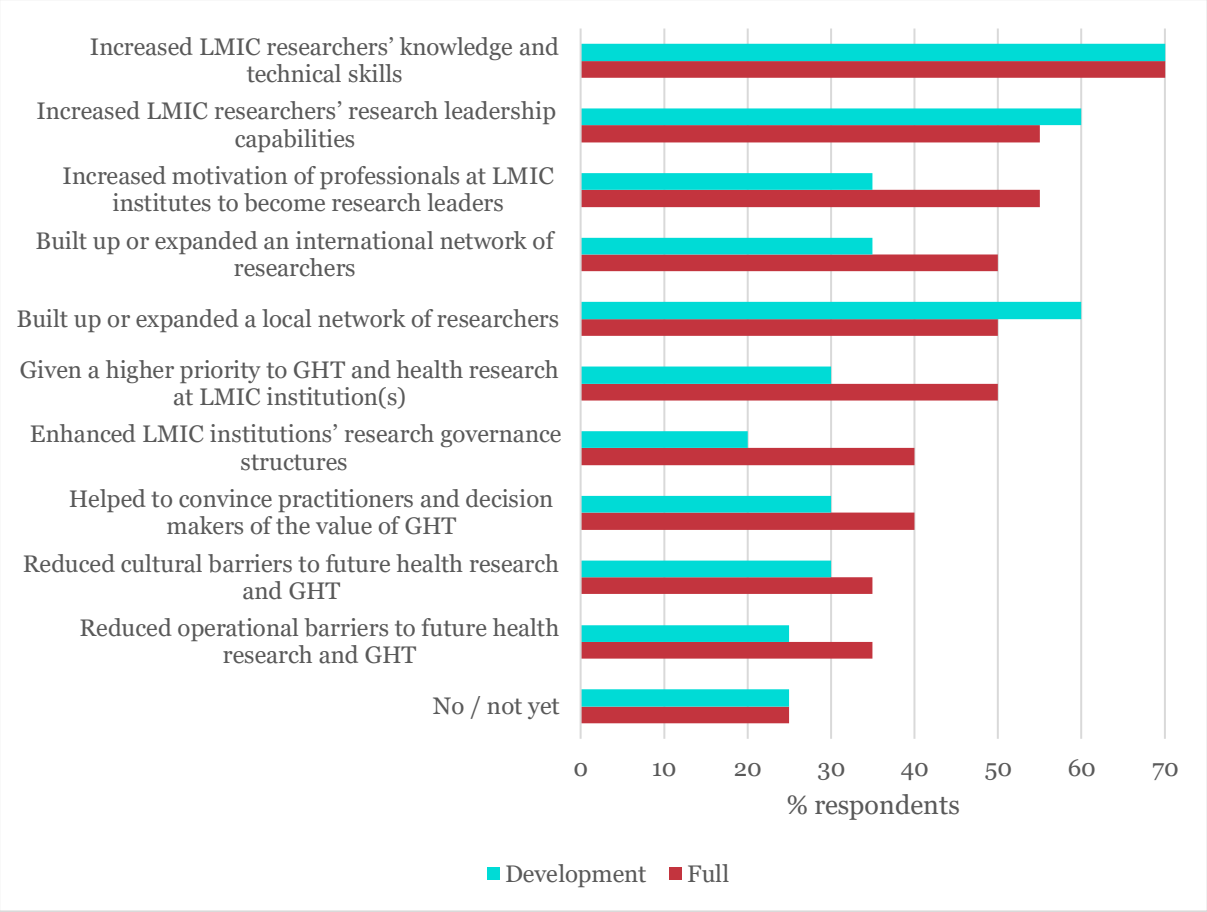


Figure 56 'Other' impacts/outcomes (full n=20; development n=20)



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.

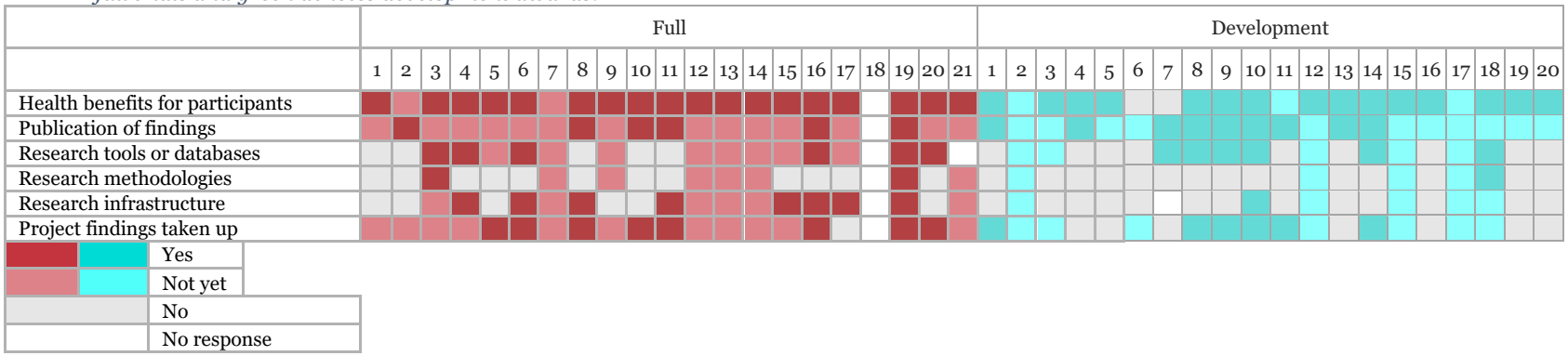
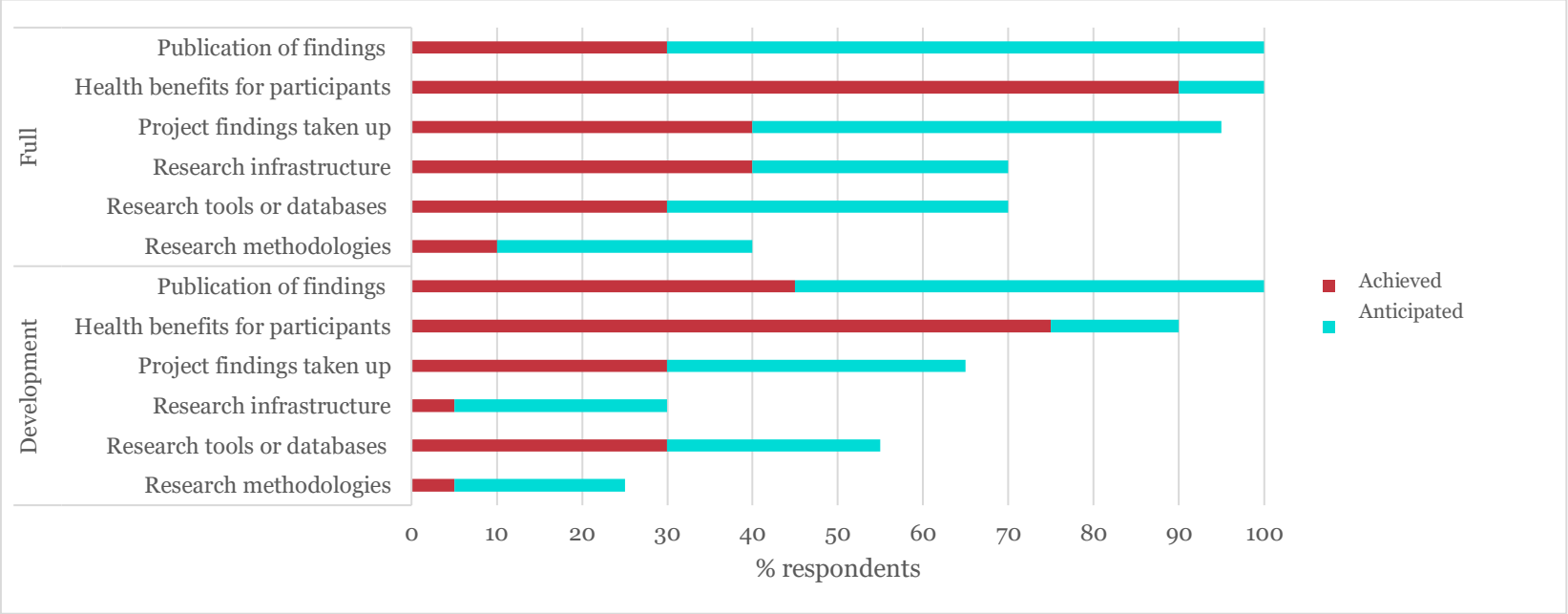


Figure 58 Reported and anticipated outcomes (full n=20; development n=20)



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.

Funder		***n* = 39**
UK	Wellcome Trust	10 (26%)
	NIHR	6 (15%)
	MRC	4 (10%)
	Global Challenges Research Fund	3 (8%)
	UKRI	1 (3%)
	Newton Fund	1 (3%)
	Global Alliance for Chronic Diseases	1 (3%)
US	NIH	13 (33%)
	Bill & Melinda Gates Foundation	12 (31%)
	USAID	2 (5%)
	Presidents Malaria Initiative	1 (3%)
	Thrasher Foundation	1 (3%)
EU	EDCTP	10 (25%)
	EU	3 (8%)
	Horizon 2020	1 (3%)
Other	National Health Medical Research Council (Australia)	2 (5%)
	Canadian Institutes of Health Research	2 (5%)
	Pharmaceutical companies/in kind	2 (5%)
	Others – listed once each: Indian Research Funding Council, Philippine Council for Health Research and Development, UNITAID, WHO, Population Health Research Institute (Canada)	5 (13%)

- 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

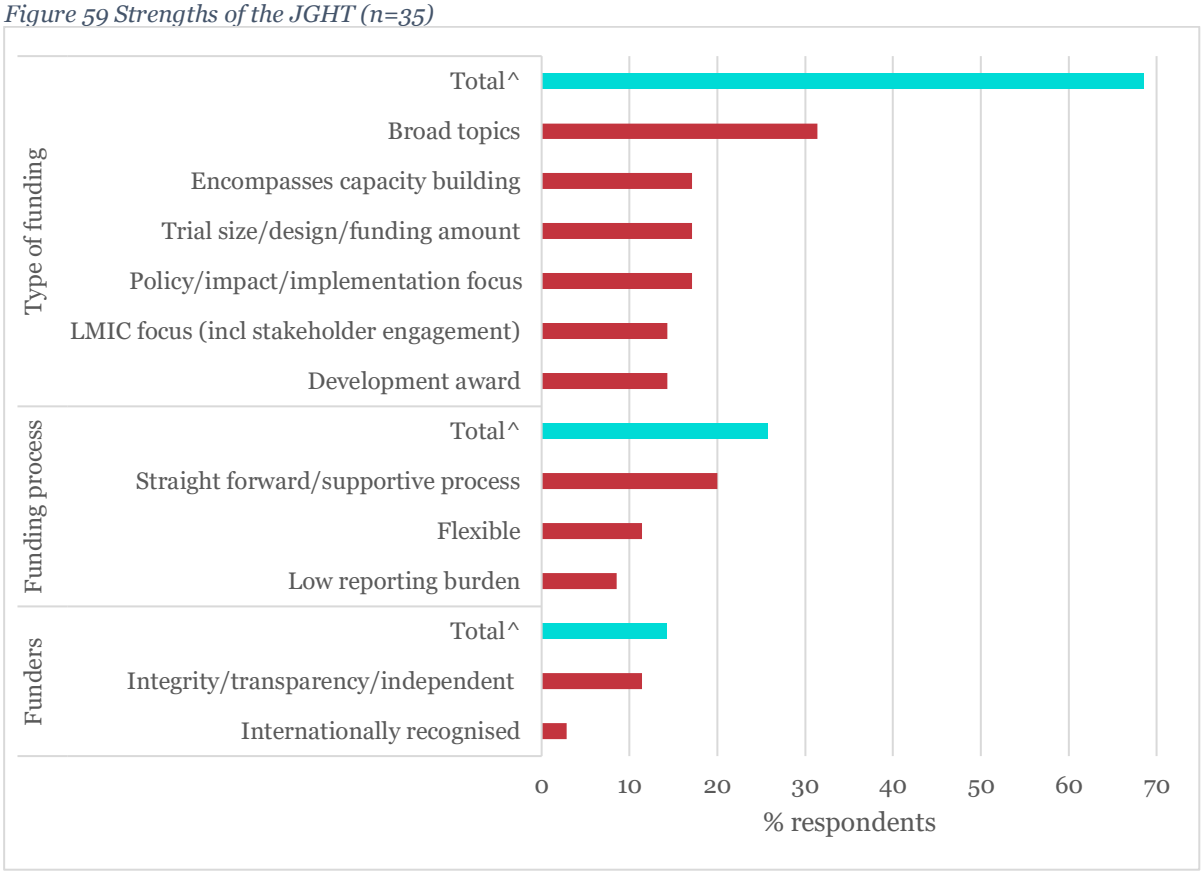
the types of trial designs that were funded (e.g. design/size), the focus on LMIC involvement, the flexibility to encompass capacity building and the focus on research that yields implementable results. One respondent commented that a key strength was that the scheme not only addresses major health related 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".

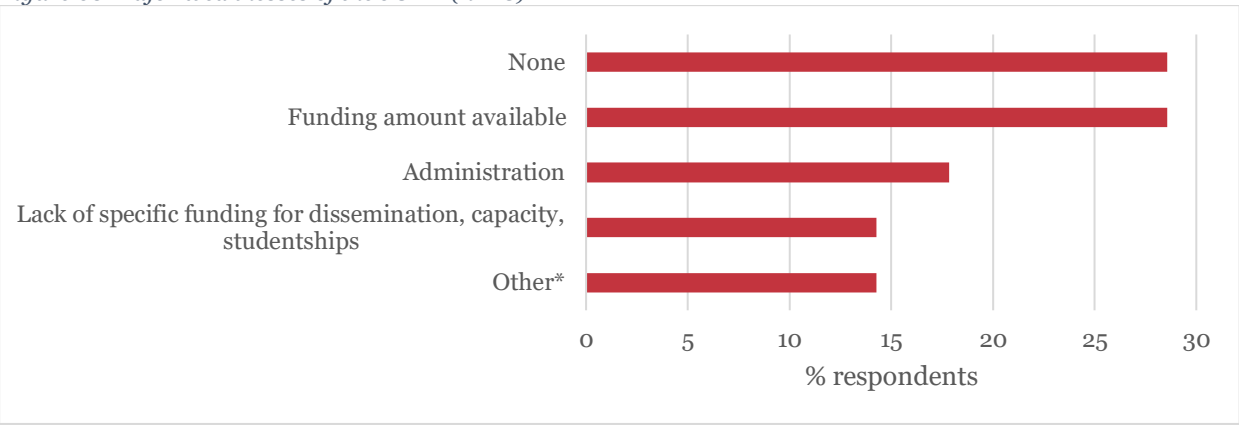
Figure 59 Strengths of the JGHT (n=35)



^ Total is the percentage of respondents who selected one or more of the options within each group.

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).

Figure 60 Major weaknesses of the JGHT (n=28)



* Other included a lack of support for nested studies, infrequency of funding calls, nonspecific nature of calls and not funding non-trial epidemiological studies.

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

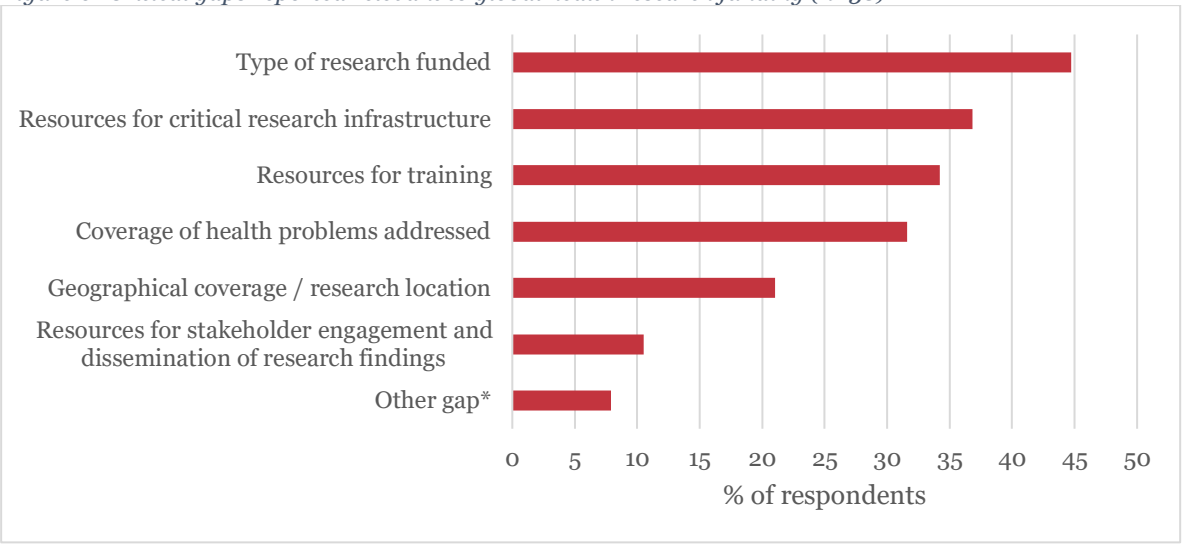
The majority of respondents (89, 34 of 38) felt there were critical gaps in the global health funding landscape. [Nine respondents indicated there were no critical gaps in the global health research funding landscape; however, five of these went on to select critical gaps. These responses were therefore 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.

Figure 61 Critical gaps reported relevant to global health research funding (n=38)



*Other includes disparate requirements of each funder, too much emphasis on track record, and lack of funding for follow-on studies.

- 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.

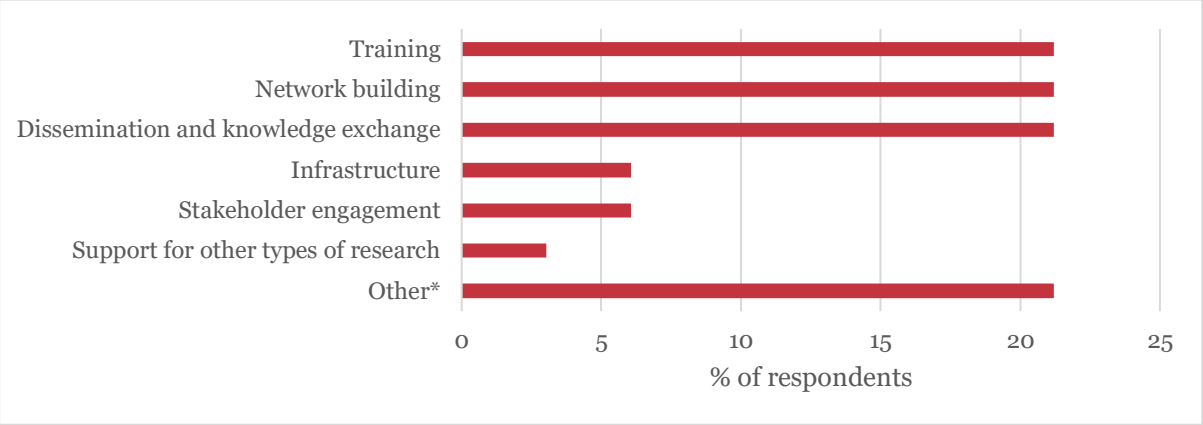
- Additional activities to support impact

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).

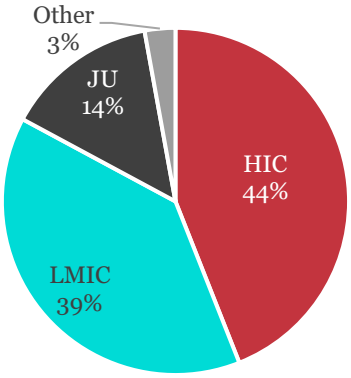
Responses were received from co-investigators representing 85% (81 of 95) of the JGHT funded projects with a median of 2 responses per project.

- 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.

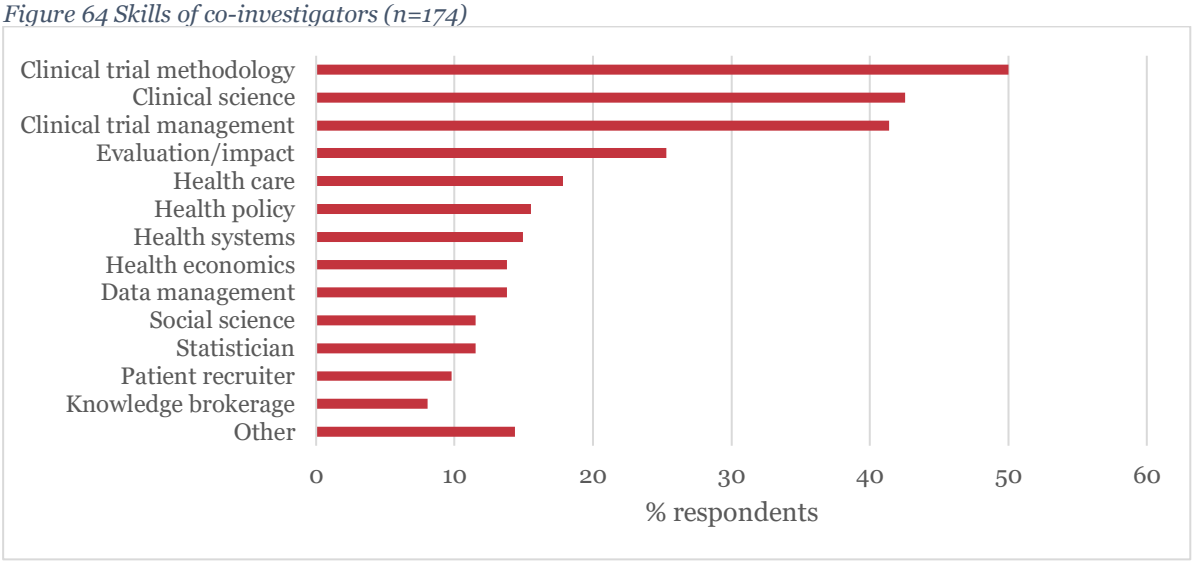
Figure 63 Proportion of respondents by institute location



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).

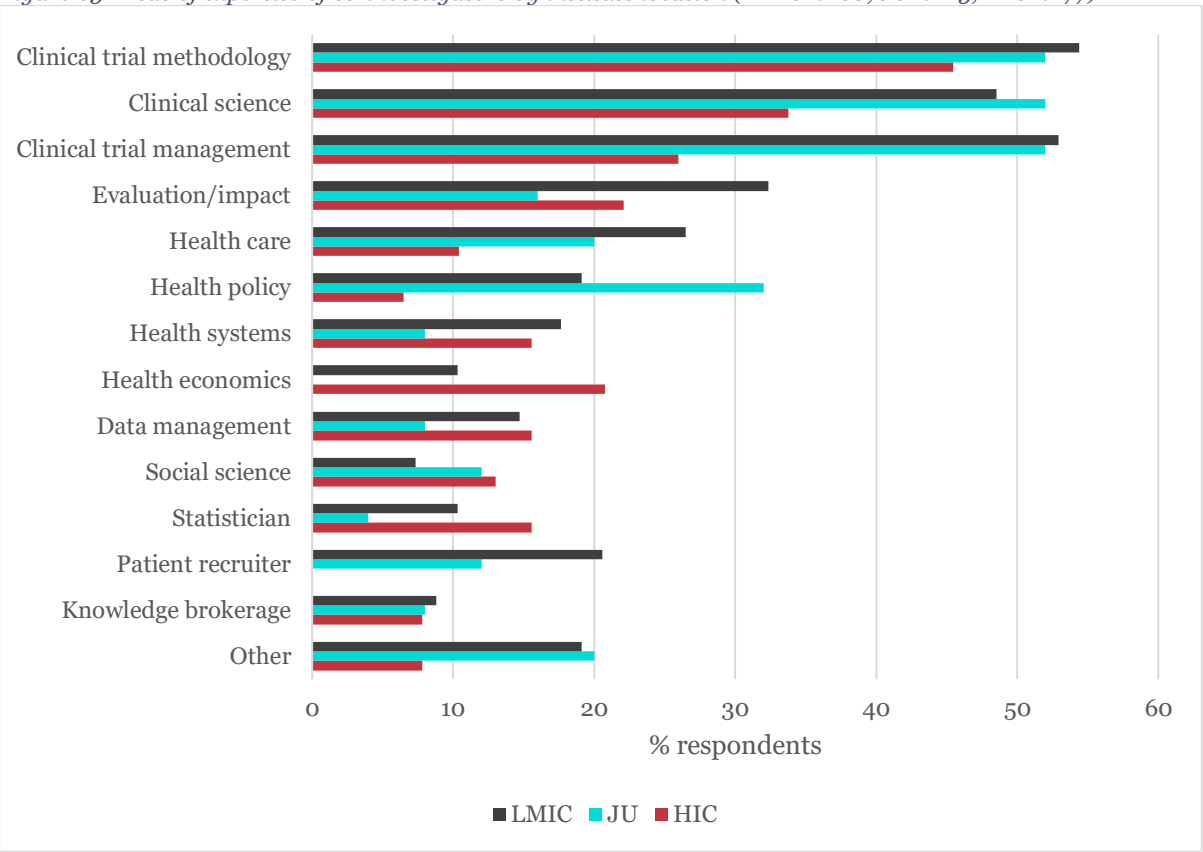
Figure 64 Skills of co-investigators (n=174)



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).

Figure 65 Areas of expertise of co-investigators by institute location (LMIC n=68, JU n=25, HIC n=77)



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).

Figure 66 Level of involvement in design of project (n=174)

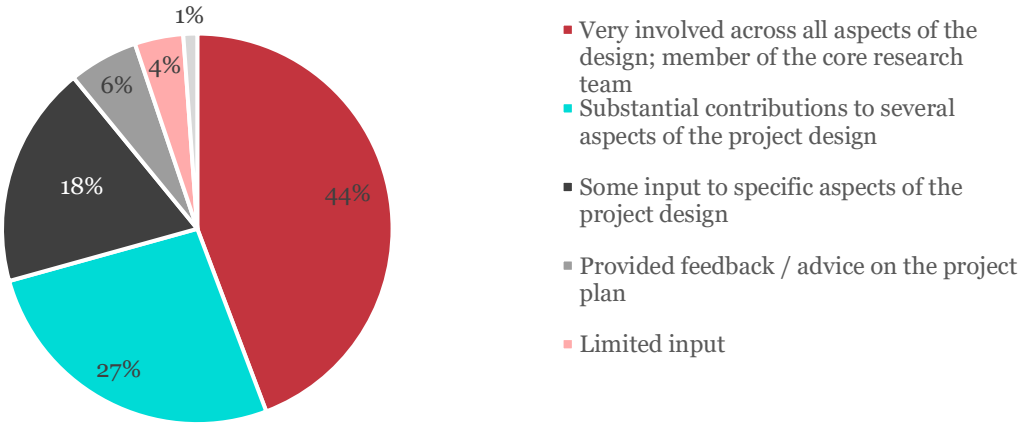
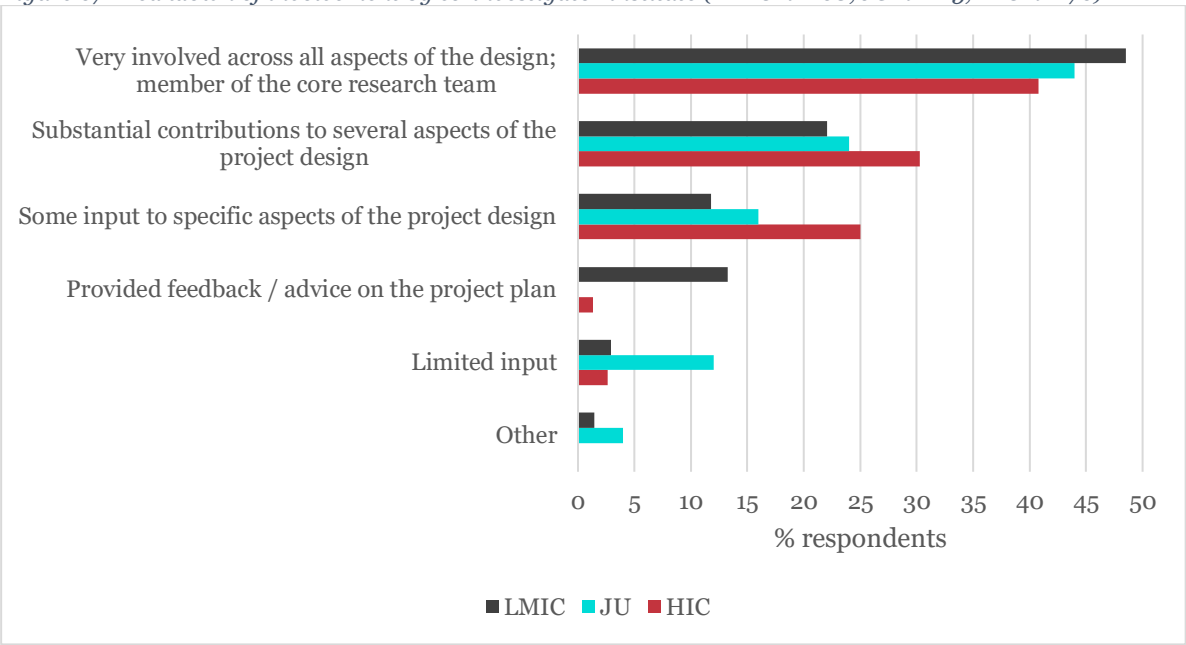


Figure 67 Breakdown of involvement by co-investigator institute (LMIC n = 68, JU n = 25, HIC n = 76)



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).

Figure 68 Changes to role or scale of involvement in project compared to funding application (n=174)

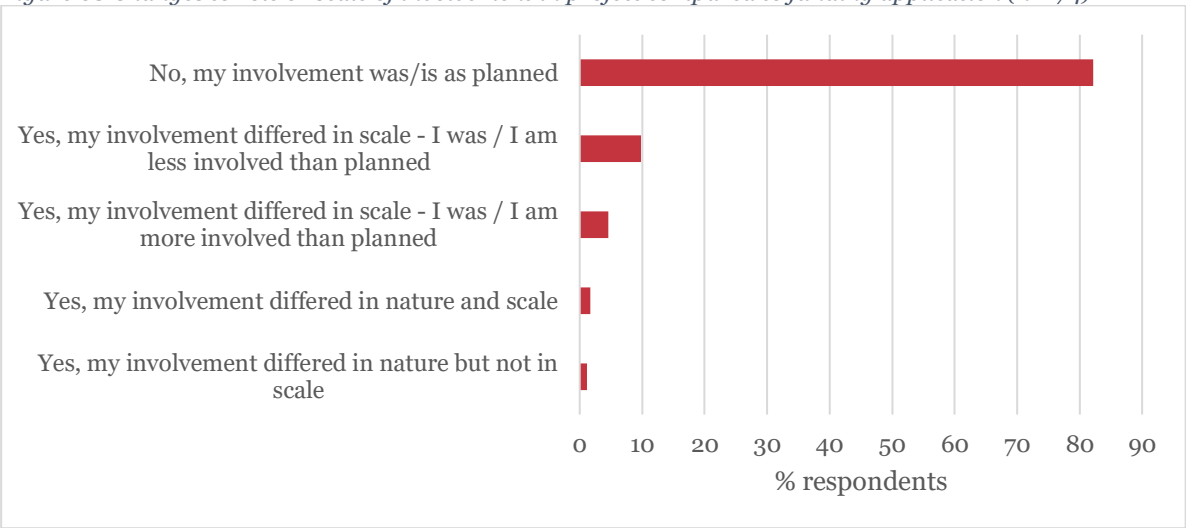
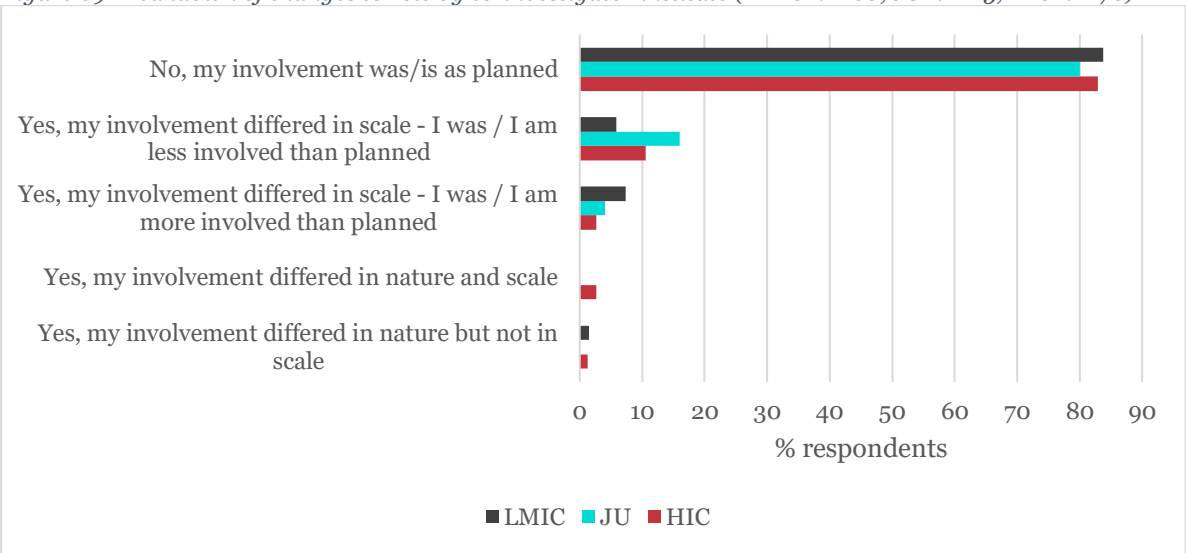


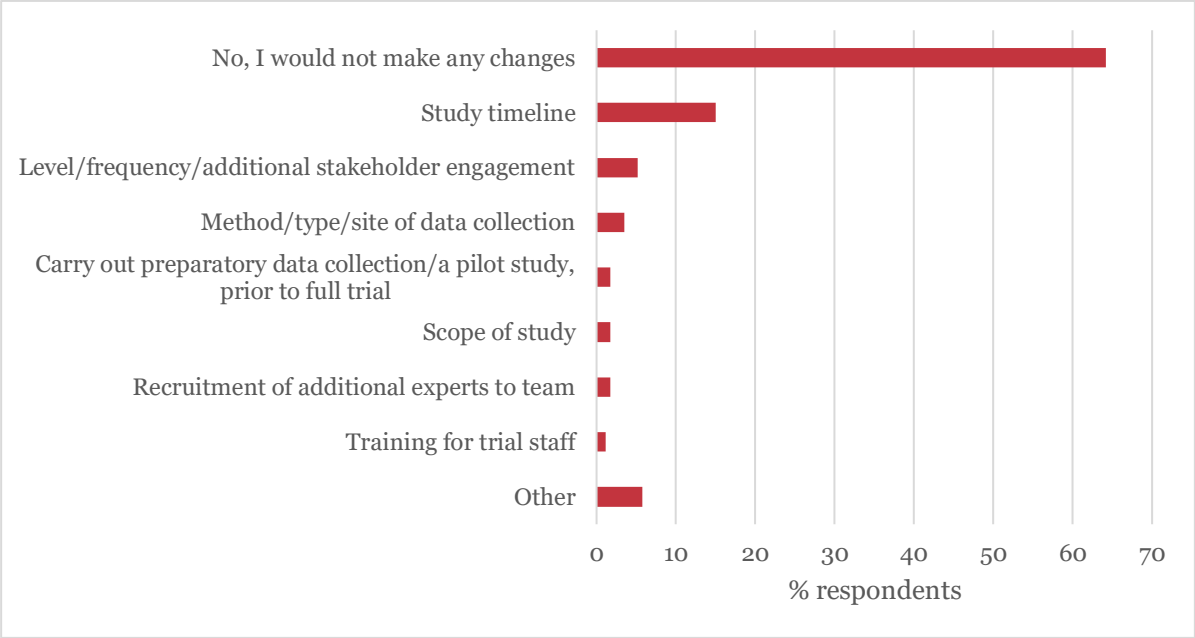
Figure 69 Breakdown of changes to role by co-investigator institute (LMIC n = 68, JU n = 25, HIC n = 76)



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).

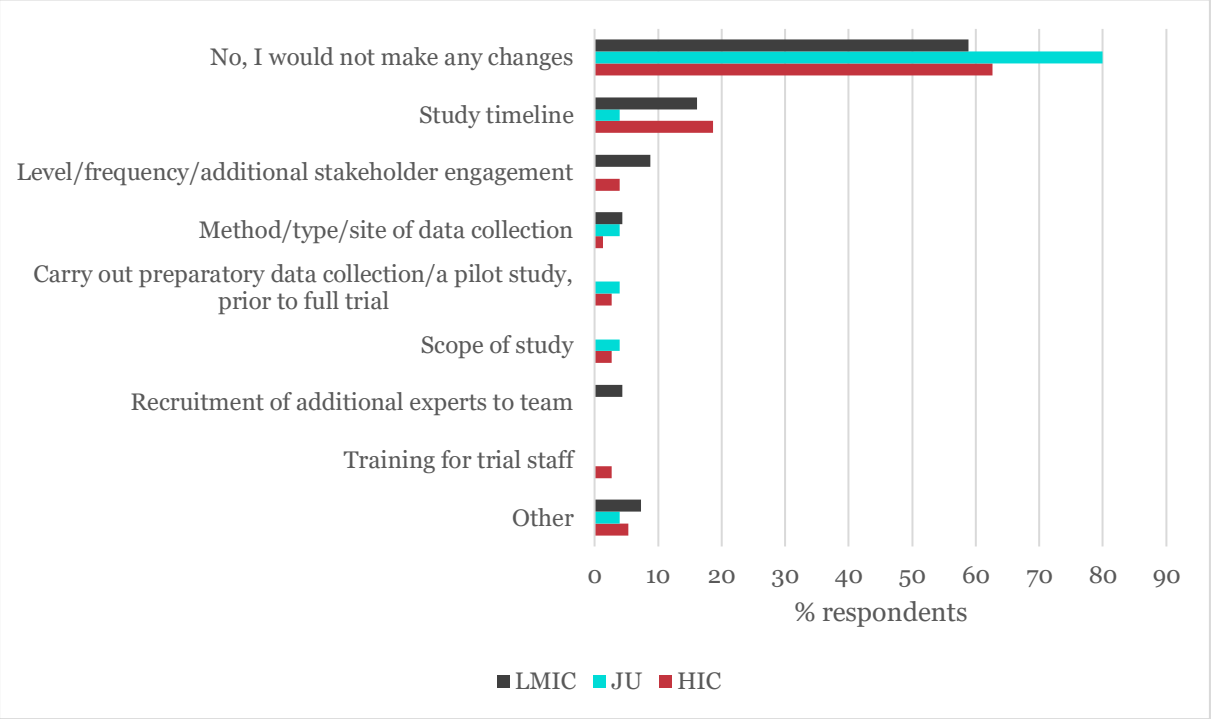
Figure 70 Changes that would be made to the project in hindsight (n=173)



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).

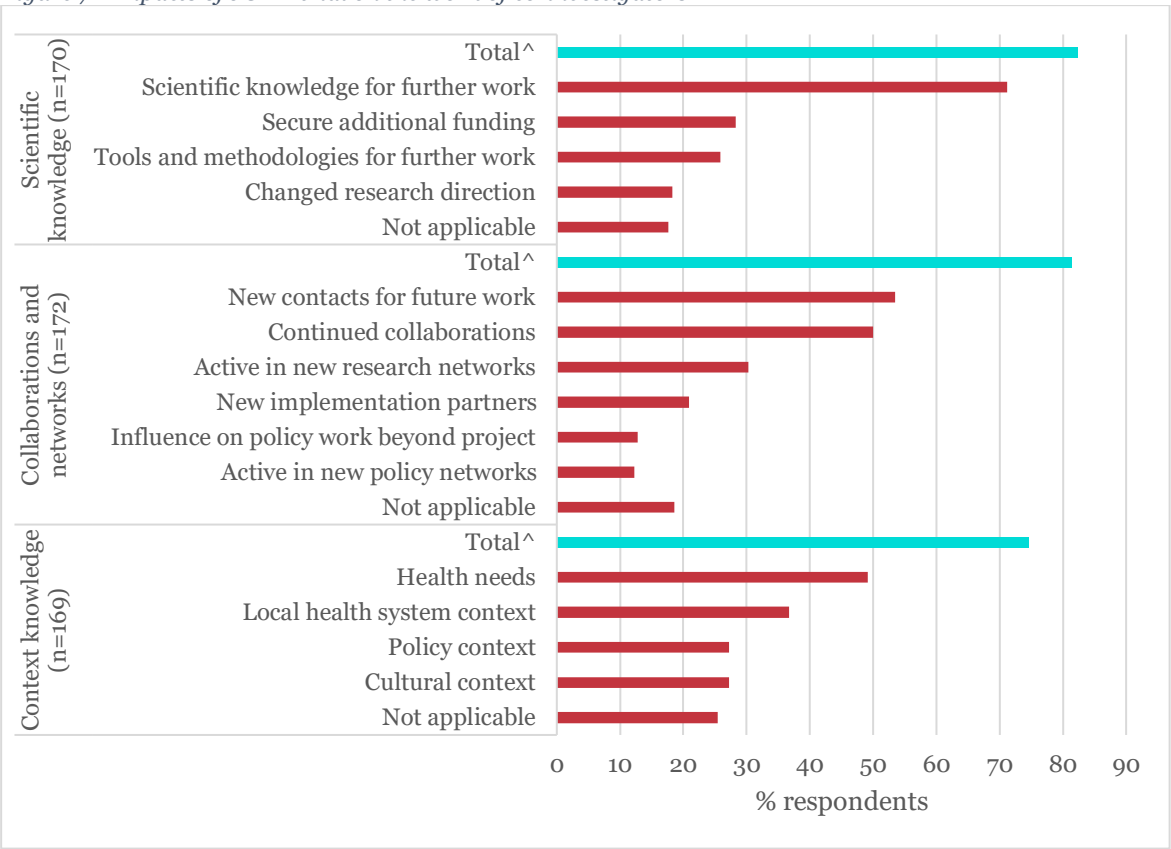
With regards to collaborations and networks, roughly even numbers of respondents indicated that the JGHT project had given them contacts for future work (53%, 92 of 172) and that collaborations formed during the JGHT project had continued after (or outside) the project (50%, 86 of 172).

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).

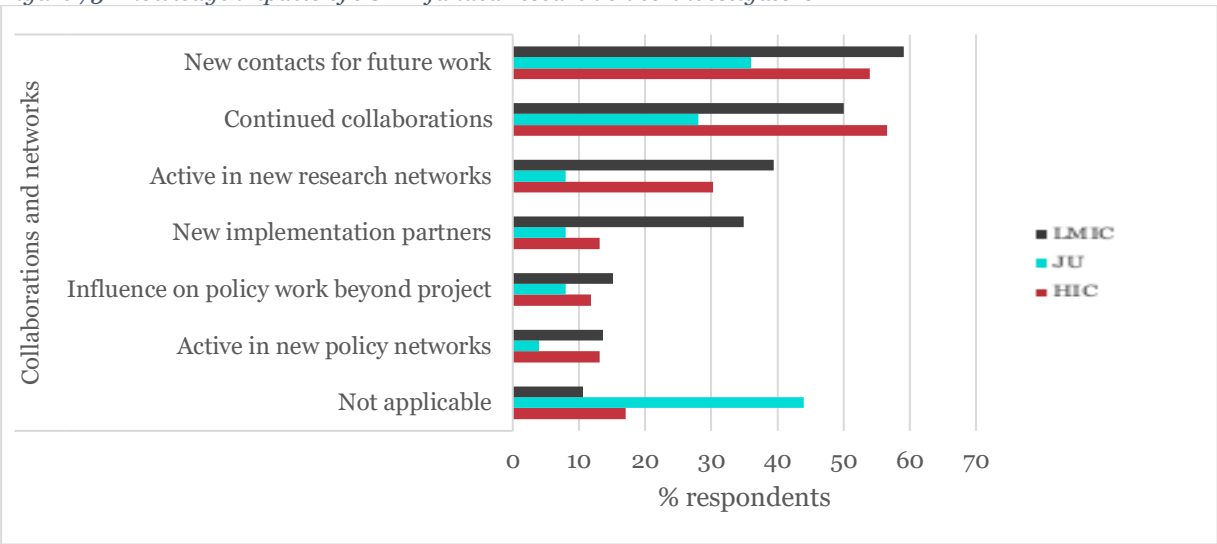
Figure 72 Impacts of JGHT trial on the work of co-investigators



^ Total indicates the total number of respondents who selected *any* impact within that theme.

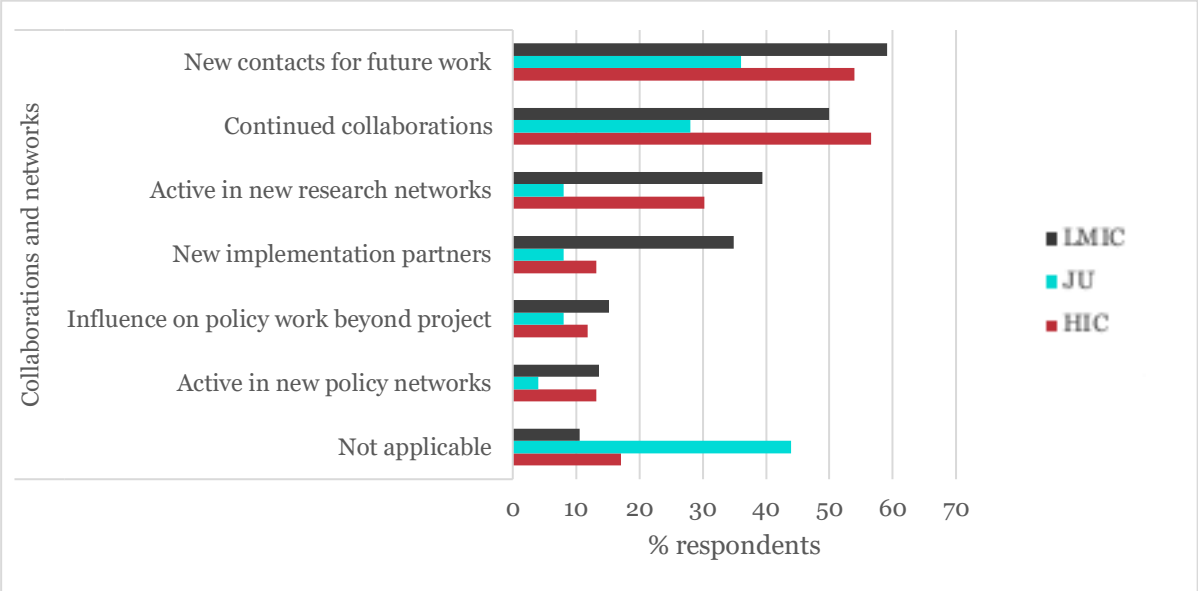
In general, the proportions of co-investigators reporting impacts did not vary greatly between LMIC and HIC locations (Figure 73). There were only two reported impacts where the proportions differed by more than 10%, these were an enhanced understanding of health needs (HIC 45%, 33 of 74; LMIC 59%, 39 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.

Figure 73 Knowledge impacts of JGHT-funded research on 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.

Figure 74 Collaboration and networks impacts of JGHT trial, co-investigators (LMIC n = 66, JU n = 25, HIC n = 76)



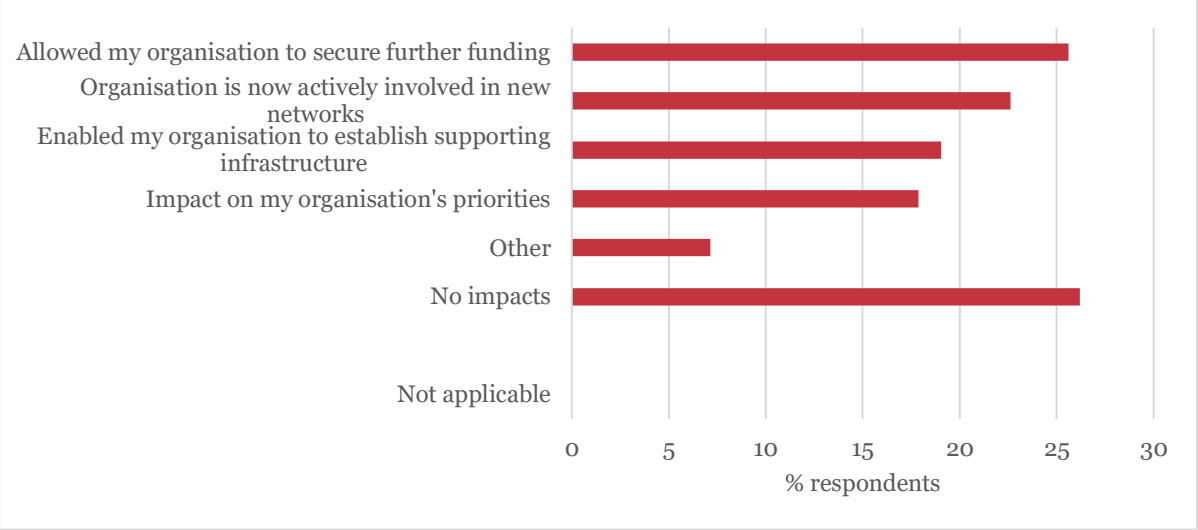
- Impacts for co-investigators institution

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

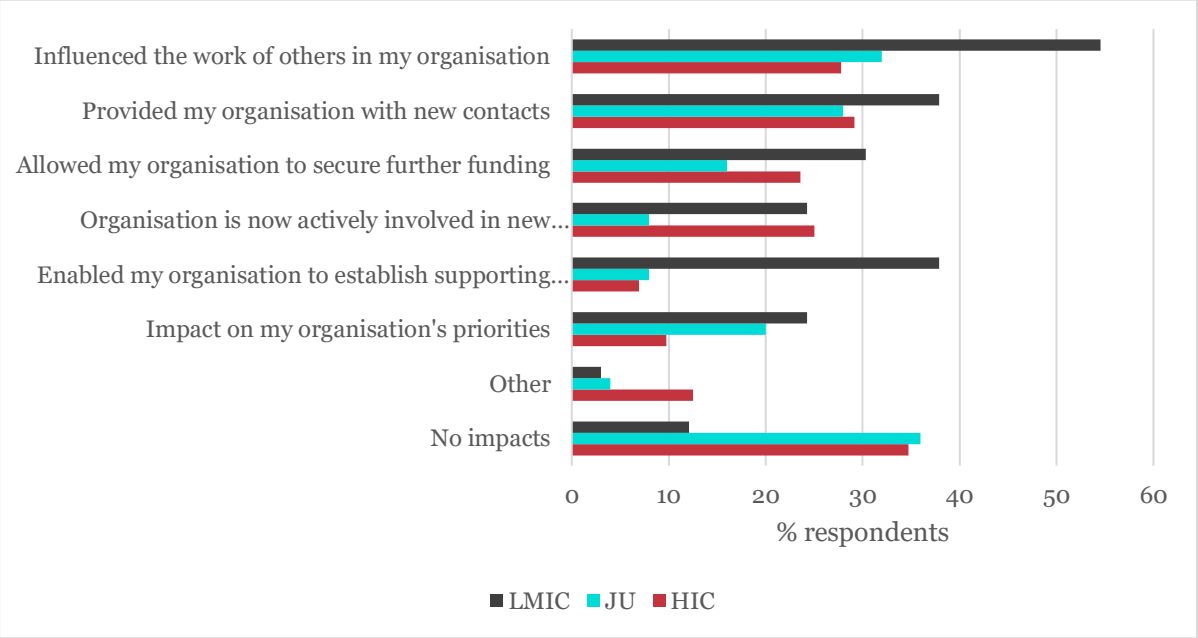
and their UK based partners that was developed as part of the JGHT. A smaller number of respondents (10%, 6 of 62) explained why there were no impacts to date. This was primarily because the project was ongoing (83%, 5 of 6)

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)



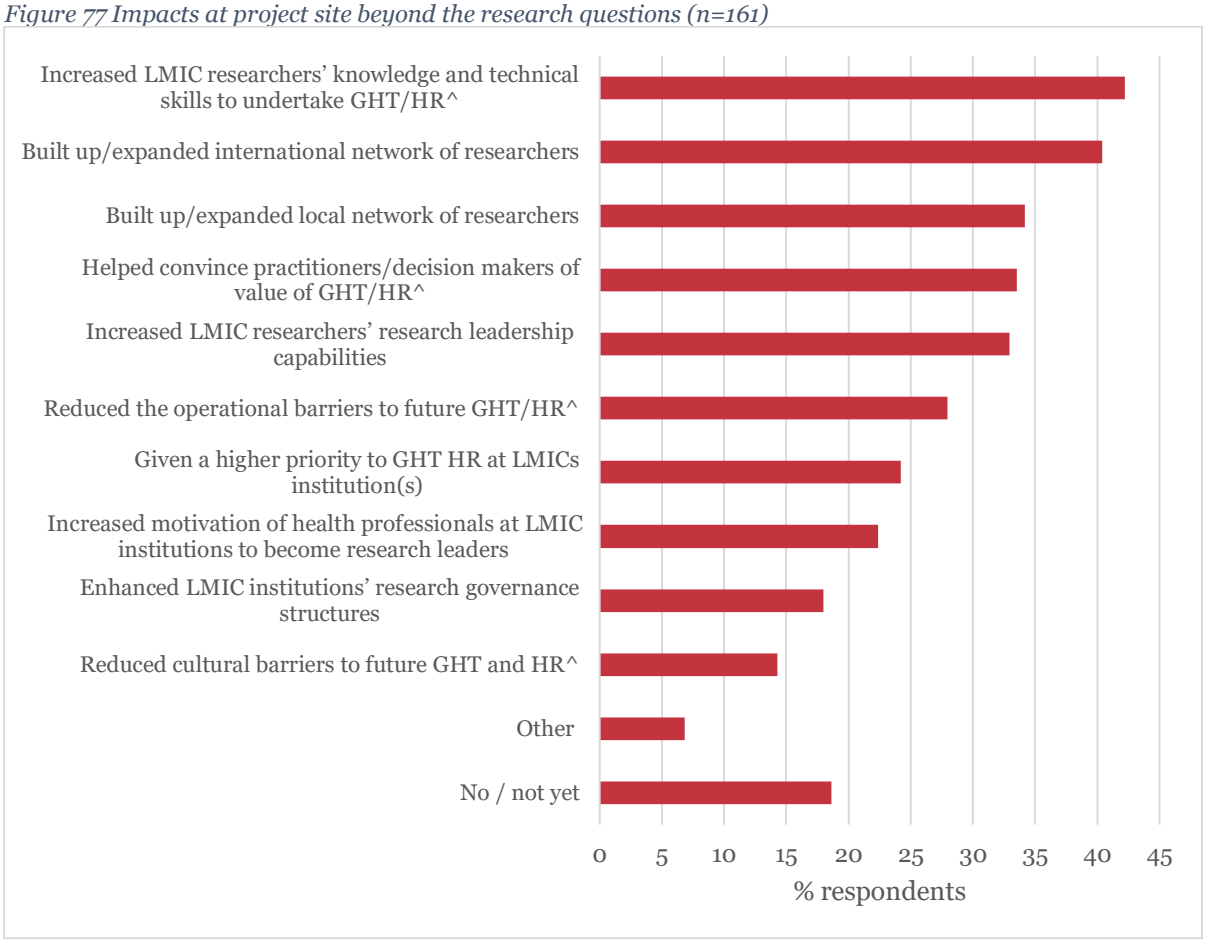
E.2.5. Impact at project site

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)

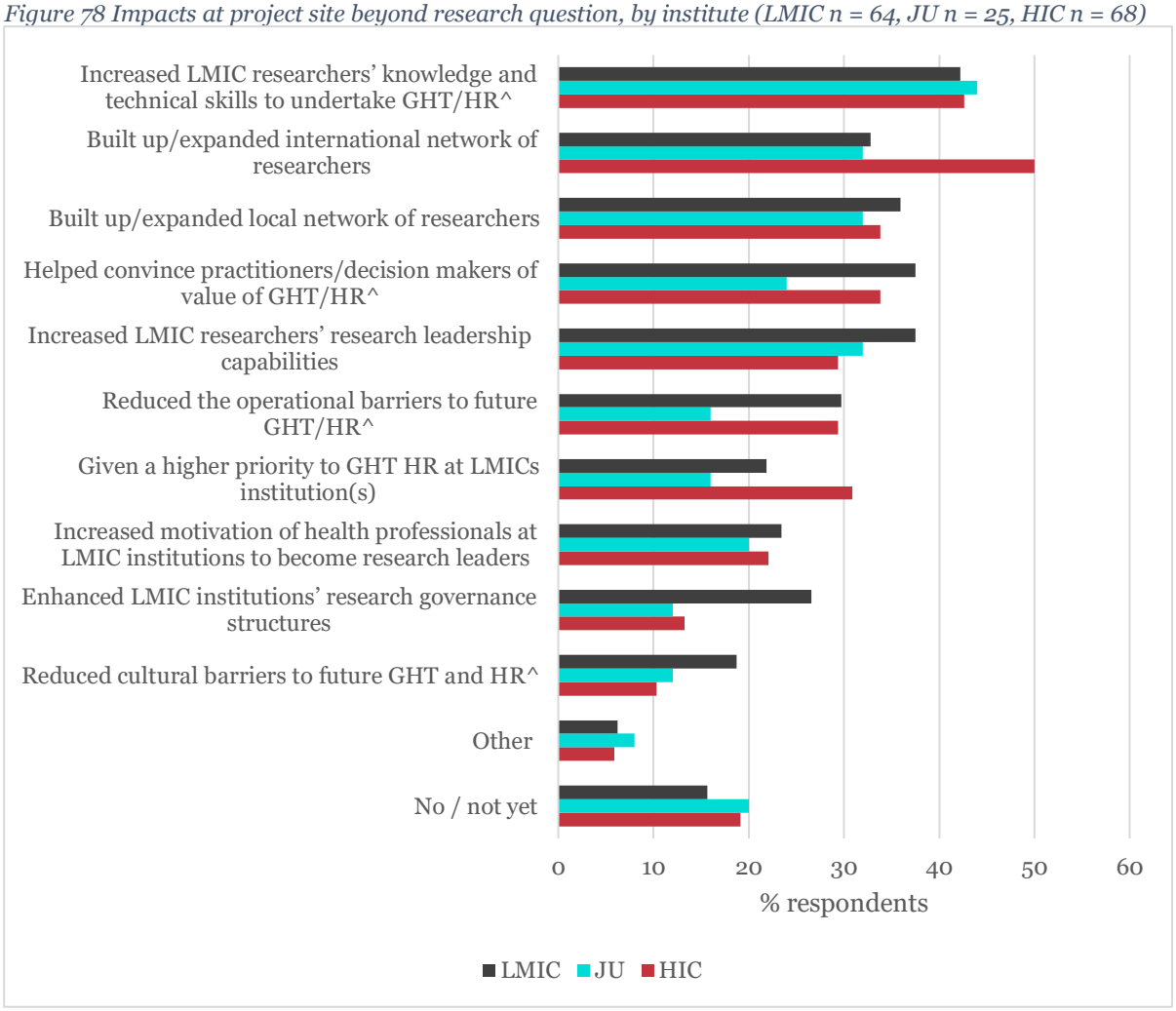


^GHT and HR = global health research and health trials.

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)



E.2.6. 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.

Funder		***n = 116***
UK	Wellcome Trust	28 (24%)
	MRC	11 (9%)
	NIHR	9 (8%)
	Global Challenges Research Fund	4 (3%)
	Global Alliance for Chronic Diseases	4 (3%)
	Newton Fund	1 (1%)
US	Bill & Melinda Gates Foundation	43 (37%)
	NIH^	37 (32%)
	USAID	2 (2%)
EU	EDCTP	39 (34%)
	EU	1 (1%)
	IMI	1 (1%)
Other	National Health Medical Research Council (Australia)	4 (3%)
	Grand Challenges Canada	4 (3%)
	UNITAID	4 (3%)
	Pharmaceutical companies/in kind	4 (3%)
	WHO	2 (2%)
	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	11 (9%)

^ 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

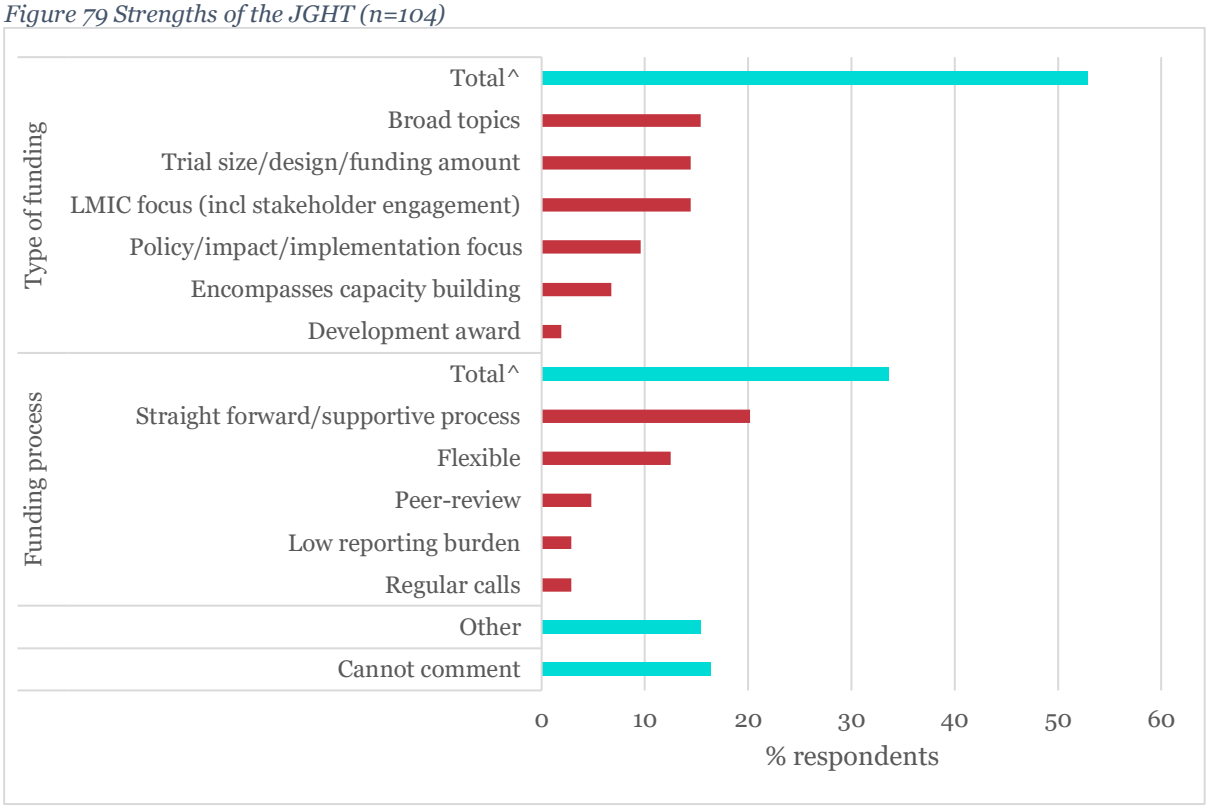
2) the administrative processes, including application and post award interactions with the funders

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).

Figure 79 Strengths of the JGHT (n=104)

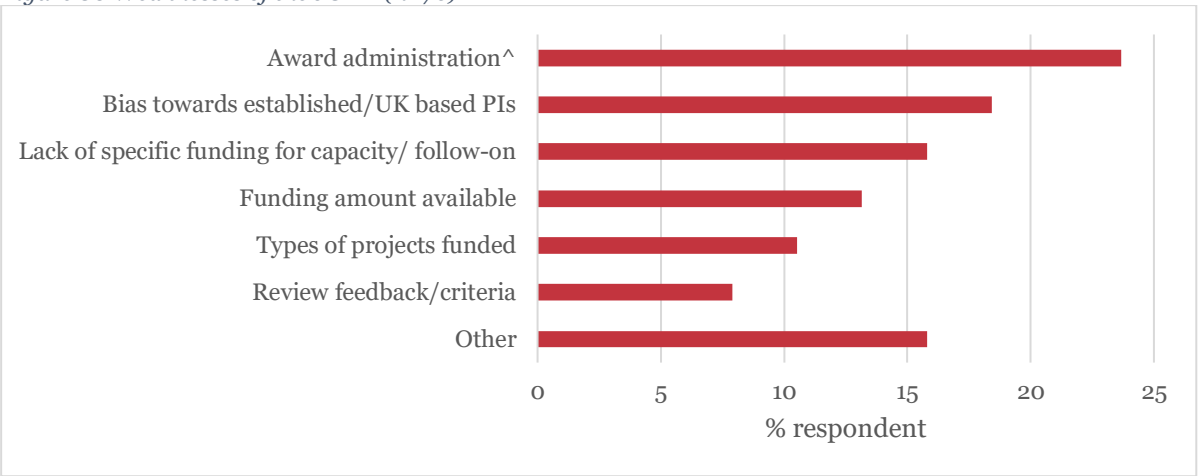


^ Total is the percentage of respondents who selected one or more of the options within each group.

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).

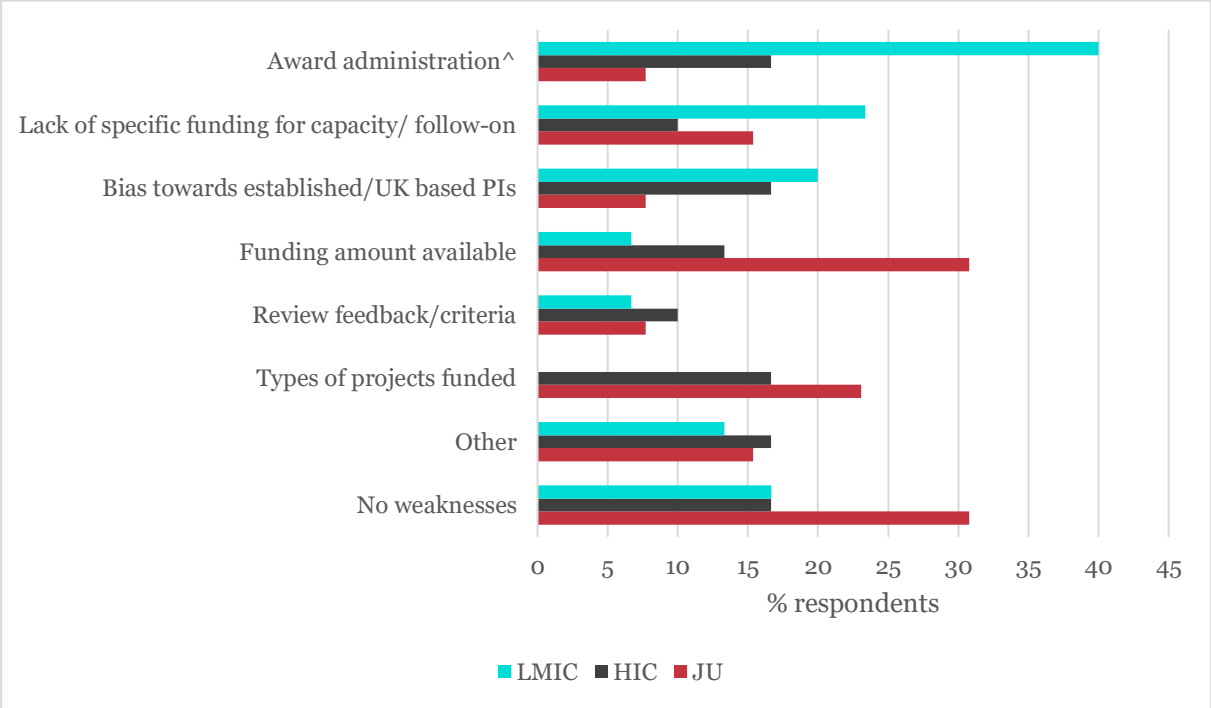
PIs from LMIC institutes most commonly reported funding processes as a weakness of the JGHT (40%, 12 of 30) (Figure 81). By comparison, views of PIs from HIC institutes were relatively evenly split between a range of weaknesses (between 10-17%, 3-5 of 30). It is of note that no PI from a LMIC institute 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.

Figure 80 Weaknesses of the JGHT (n=76)



^Funding processes include lengthy application time and lack of communication with the funders.

Figure 81 Weakness of JGHT by PI institute (LMIC n = 30, JU n = 13, HIC n = 30)



^Funding processes include lengthy application time and lack of communication with the funders.

- 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'.]

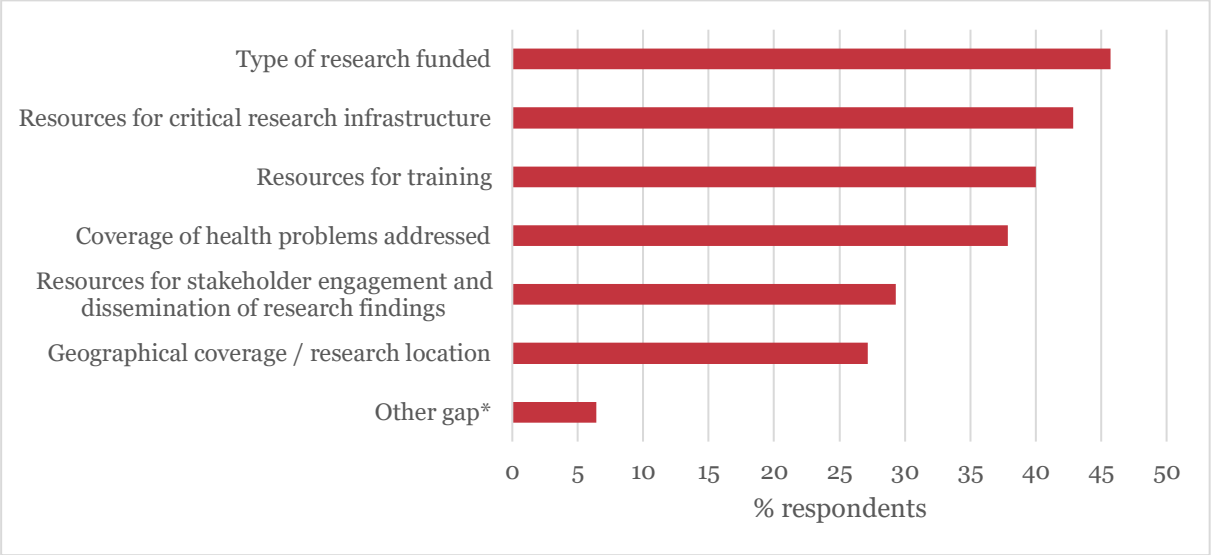
The most common gap identified was the type of research funded (46%, 64 of 140), followed by resources for critical research infrastructure (43%, 60) and resources for training (40%, 56) (Figure 82).

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)



* 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.

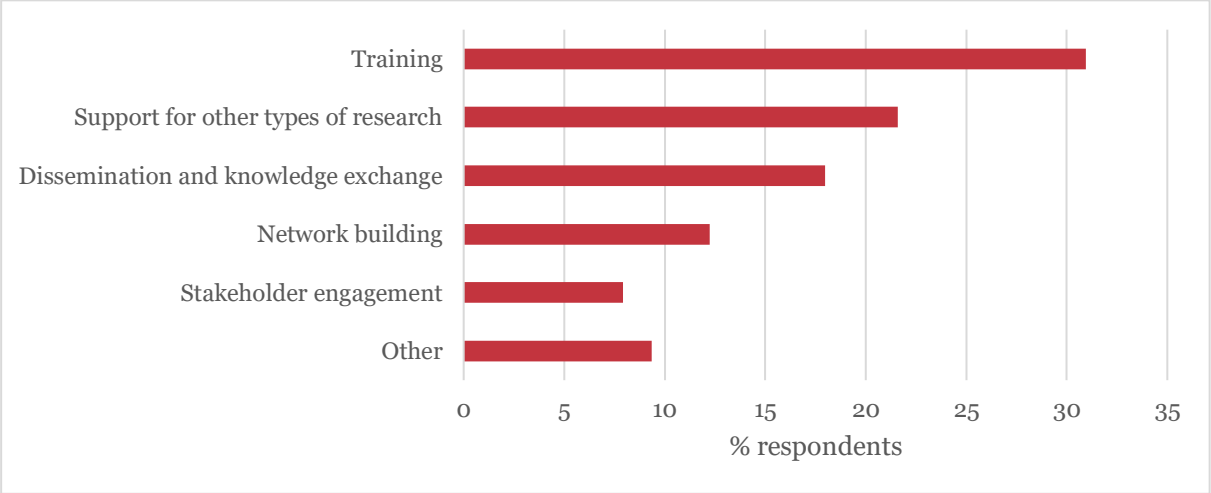
The majority (73%, 110 of 149) of co-investigators reported that the calls for proposals and other information on the JGHT are communicated through the right channels and reach the relevant research communities. The major comments for the improvements to the promotion of the scheme were reaching out 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).

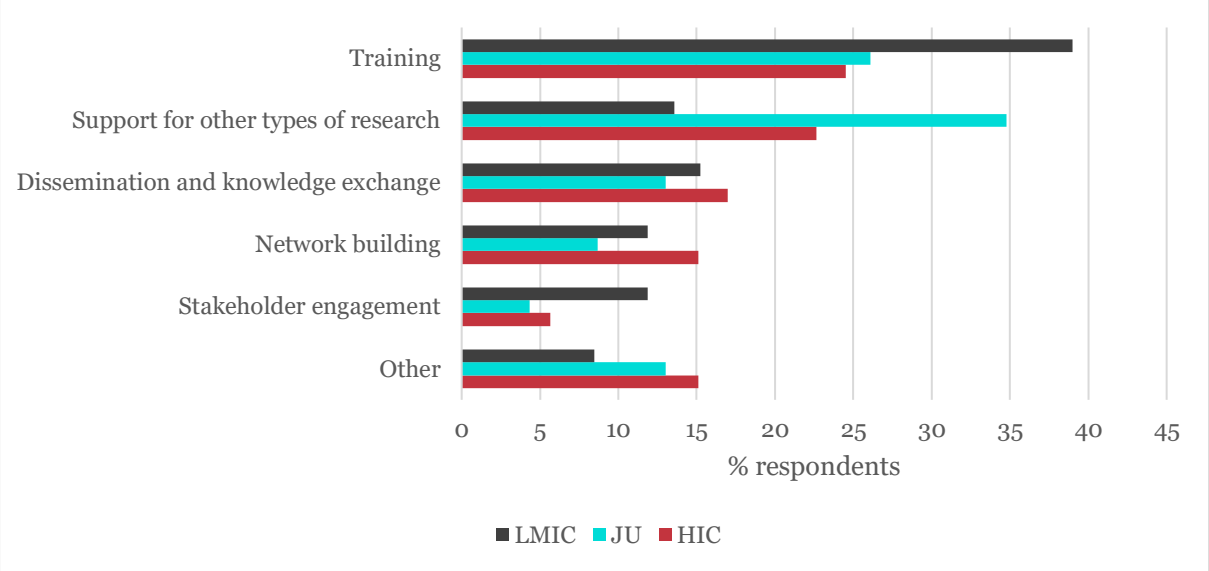
Figure 83 Additional activities the JGHT could support to increase the potential impact from its research (n=139)



Training was more commonly reported by LMIC respondents (39%, 23 of 59) than by respondents from HIC and JU (HIC 25%, 13 of 53; 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 84 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.

Grant Reference	Grant Holder	RO	Grant status	Call	Trial results paper
G1100654	Feiko ter Kuile	LSTM	Closed	Call 1	Ahmed R et al (2019) Efficacy and safety of intermittent preventive treatment and intermittent screening and treatment versus single screening and treatment with dihydroartemisinin–piperaquine for the control of malaria in pregnancy in Indonesia: a cluster-randomised, open-label, superiority trial. Lancet Infect Dis. S1473-3099(19)30156-2
G1100677	Penelope Anne Phillips-Howard	LSMT	Closed	Call 1	Phillips-Howard P et al (2016) Menstrual cups and sanitary pads to reduce school attrition, and sexually transmitted and reproductive tract infections: a cluster randomised controlled feasibility study in rural Western Kenya. BMJ Open 6:e013229
G1100682	Thuy Le	U Oxford	Closed	Call 1	Le T et al (2017) A Trial of Itraconazole or Amphotericin B for HIV-Associated Talaromycosis. N Engl J Med 376:2329-2340
G1100684	Jeremy Day	U Oxford	Closed	Call 1	Beardsley J et al (2016) Adjunctive Dexamethasone in HIV-Associated Cryptococcal Meningitis, N Engl J Med 374: 542-554.
G1100686	Andrew Weeks	U Liverpool	Closed	Call 1	Mundle S et al (2017) Foley catheterisation versus oral misoprostol for induction of labour in hypertensive women in India (INFORM): a multicentre, open-label, randomised controlled trial. The Lancet 390: P669-680
G1100693	Diana Gibb	MRC/ UCL	Closed	Call 1	Kityo C et al (2018) Raltegravir-intensified initial antiretroviral therapy in advanced HIV disease in Africa: A randomised controlled trial. PLoS Med 15: e1002706
G1100693	Diana Gibb	MRC/ UCL	Closed	Call 1	Hakim J et al (2017) Enhanced Prophylaxis plus Antiretroviral Therapy for Advanced HIV Infection in Africa. N Engl J Med 377:233-245
G1100693	Diana Gibb	MRC/ UCL	Closed	Call 1	Mallewa J et al (2018) Effect of ready-to-use supplementary food on mortality in severely immunocompromised HIV-infected individuals in Africa initiating antiretroviral therapy (REALITY): an open-label, parallel-group, randomised controlled trial. The Lancet HIV 5: PE231-E240
G1100699	Somphou Sayasone	Swiss Trop& PH Institute	Closed	Call 1	Sayasone S et al (2016) Efficacy and safety of tribendimidine against Opisthorchis viverrini: two randomised, parallel-group, single-blind, dose-ranging, phase 2 trials. Lancet Infect Dis. 16:1145-1153
MR/K006533/1	Stephen Gordon	LSTM	Closed	Call 2	Mortimer K et al (2017) A cleaner burning biomass-fuelled cookstove intervention to prevent pneumonia in children under 5 years old in rural Malawi (the Cooking and Pneumonia Study): a cluster randomised controlled trial. *The Lancet 389*: 167-175.
MR/K007203/1	Umberto D'Alessandro	MRC Unit, The Gambia	Closed	Call 2	Okebe J et al (2016) The gametocytocidal efficacy of different single doses of primaquine with dihydroartemisinin-piperaquine in asymptomatic parasite carriers in the Gambia: a randomized controlled trial. EBioMedicine 13: 348-355

MR/K007211/1	Gail Davey	U Sussex	Closed	Call 2	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:e795–e803
MR/K007270/1	Audrey Prost	UCL	Closed	Call 2	Nair N et al (2017) Effect of participatory women's groups and counselling through home visits on children's linear growth in rural eastern India (CARING trial): a cluster-randomised controlled trial. *The Lancet Global Health 5:* e1004-e1016
MR/K007319/1	Brian Greenwood	LSHTM	Closed	Call 2	Chandramohan D et al (2019) Effect of Adding Azithromycin to Seasonal Malaria Chemoprevention. N Engl J Med 380:2197-2206
MR/K007351/1	Dejan Zurovac	U Oxford	Closed	Call 2	Talisuna AO et al (2017) Efficacy of text-message reminders on paediatric malaria treatment adherence and their post-treatment return to health facilities in Kenya: a randomized controlled trial. Malaria J 16: 46
MR/K00736X/1	Sarah Staedke	LSHTM	Closed	Call 2	Staedke SG et al (2018) Assessment of community-level effects of intermittent preventive treatment for malaria in schoolchildren in Jinja, Uganda (START-IPT trial): a cluster-randomised trial. Lancet Glob Health 6: e668-e679
MR/K007408/1	Arri Coomarasamy	U Birm-ingham	Closed	Call 2	Lissauer D et al (2019) A Randomized Trial of Prophylactic Antibiotics for Miscarriage Surgery. N Engl J Med 380:1012-1021.
MR/K007424/1	Richard Price	U Oxford	Closed	Call 2	Taylor WRJ et al (2019) Short-course primaquine for the radical cure of Plasmodium vivax malaria: a multicentre, randomised, placebo-controlled non-inferiority trial. The Lancet 394: 929-938
MR/K00753X/1	Oyewusi Gureje	U Idaban	Closed	Call 2	Gureje, O et al (2019) Effect of a stepped-care intervention delivered by lay health workers on major depressive disorder among primary care patients in Nigeria (STEPCARE): a cluster-randomised controlled trial. *The Lancet Global Health 7*: e951-e960.
MR/L004321/1	Karen Devries	LSHTM	Closed	Call 3	Devries K et al (2015) The Good School Toolkit for reducing physical violence from school staff to primary school students: a cluster-randomised controlled trial in Uganda. The Lancet Global Health 3: PE378-E386
MR/M007375/1	Katherine Fielding	LSHTM	Closed	Call 4	Gupta-Wright A et al (2018) 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 392: P292-301
MR/N00597X/1	Rachel Pullan	LSTHM	Closed	Call 5	Pullan RL et al (2019) Effects, equity, and cost of school-based and community-wide treatment strategies for soil-transmitted helminths in Kenya: a cluster-randomised controlled trial. The Lancet 393: 2039–50
G1100570	Mark Hatherill	U Cape Town	Active	Call 1	Nemes E et al (2018) Safety and Immunogenicity of Newborn MVA85A Vaccination and Selective, Delayed Bacille Calmette-Guerin for Infants of Human Immunodeficiency Virus-Infected Mothers: A Phase 2 Randomized, Controlled Trial. Clin Infect Dis 66: 554-563
MR/L004437/1	Mark Rowland	LSHTM	Active	Call 3	Protopopoff et al (2018) 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 391: P1577-1588
MR/M007413/1	David Meya	Makerere University	Active	Call 4	Rhein J et al (2019) Adjunctive sertraline for HIV-associated cryptococcal meningitis: a randomised, placebo-controlled, double-blind phase 3 trial. Lancet Infectious Dis 19: P843-851
MR/M009211/1	Ian Roberts	LSHTM	Active	Call 4	The CRASH-3 collaborators (2019) Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial. The Lancet 394: P1713-1723

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[24].

The next programme phase, EDCTP2 was approved by the European Parliament and European Council in 2014[25], 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[26].

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[27]. 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

[24] EDCTP. Get to know us. http://www.edctp.org/get-know-us/ Accessed 20 Oct 2019

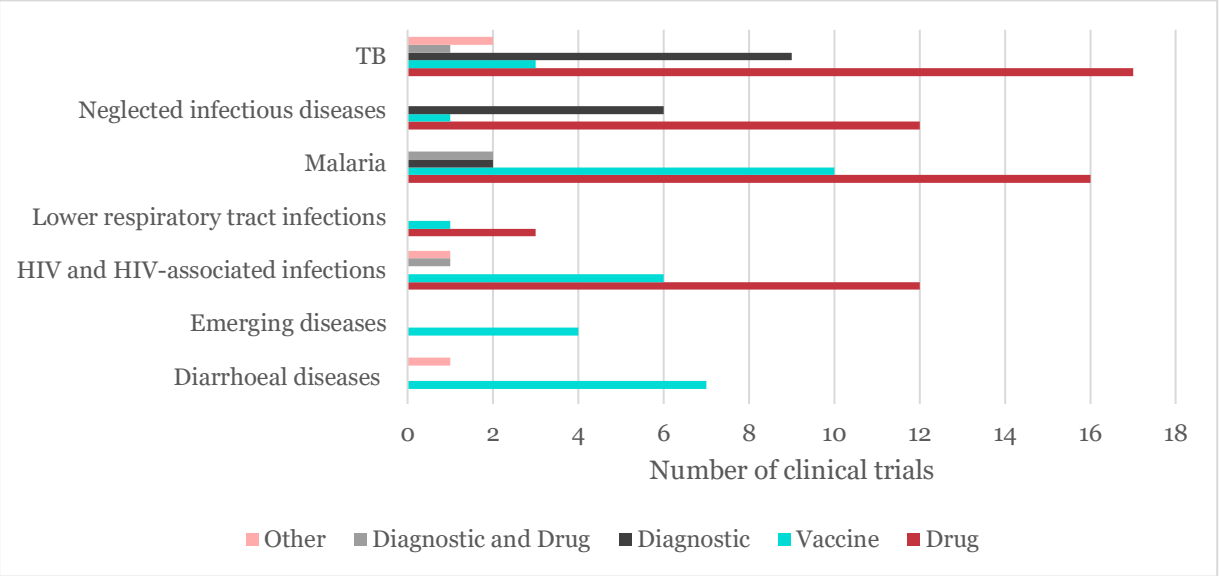
[25] European Union (2014). Decision of the European Parliament and of the Council on the participation of the Union in a second European and Developing Countries Clinical Trials Partnership Programme (EDCTP2) jointly undertaken by several Member States. PE-CONS 54/14.

[26] EDCTP. Strategy and work plans. Available at: http://www.edctp.org/see-work/strategy/ Accessed 20 Oct 2019

[27] EDCTP. Tackling infectious disease in sub- Saharan Africa. http://www.edctp.org/web/app/uploads/2018/09/Tackling-infectious-disease-in-sub-Saharan-Africa_EDCTP-funded-clinical-studies-for-medical-interventions-2003-2018-4.pdf Accessed 20 Oct 2019

a funding of €447m[28]. This includes €396m, for supporting large-scale trials. The average funding per clinical or operational research grant is €5.2m[29]. 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) []



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[30]. 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[31]. 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

[28] EDCTP. EDCTP Annual Report 2018. https://data.maglr.com/1883/issues/14737/222856/downloads/edctp_annual_report_2018_-_summary-v4.pdf Accessed 20 Oct 2019]

[29] Among interventional trials funded by EDCTP2. Data provided by EDCTP.

[30] BMGF. How we work. https://www.gatesfoundation.org/How-We-Work Accessed 20 Oct 2019

[31] BMGF. Our Global Health Division. https://www.gatesfoundation.org/what-we-do Accessed 20 Oct 2019

partnership with the NIH, Canadian Institutes of Health Research (CIHR) and Wellcome Trust. In 2014, the programme was relaunched as Grand Challenges[32]. 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[33]. 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[34]. Overall, Grand Challenges in Global Health awarded 44 grants with a total value of USD450m involving scientists and researchers from 33 countries[35].

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[36].

NIAID funds clinical research in one of two ways[37]. 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 consortiums 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

[32] BMGF. Grand Challenges. https://gcgh.grandchallenges.org/history Accessed 20 Oct 2019

[33] BMGF. Grand Challenges. https://grandchallenges.org/initiatives Accessed 20 Oct 2019

[34] BMGF. Grand Challenges. https://gcgh.grandchallenges.org/challenges?f%5B0%5D=field_initiative%3A37072 Accessed 20 October 2019

[35] BMGF. Grand Challenges. https://gcgh.grandchallenges.org/about Accessed 20 Oct 2019

[36] Fogarty International Center. Programs. https://www.fic.nih.gov/Programs/Pages/global-ncds-research.aspx Accessed 20 Oct 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[38].

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[39].

NIAID funds most of its clinical trials through networks and collaborations where NIAID determines the research topic and project scope i.e. NIAID-requested research[40]. 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[41]. 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[42].

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[43]. 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[44]. 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

[38] NIAID. Types of Funding Opportunities. https://www.niaid.nih.gov/grants-contracts/types-funding-opportunities Accessed 20 Oct 2019

[39] Personal Communication, Dr Clifford Lane (8 October 2019)

[40] NIAID. Clinical Trial Research. https://www.niaid.nih.gov/grants-contracts/clinical-trial-research. Accessed 20 Oct 2019

[41] Personal Communication, Dr Clifford Lane (8 October 2019)

[42] Personal communication, Joyelle Dominique (12 October 2019)

[43] https://www.theglobalfund.org/en/ Accessed 20 Oct 2019

[44] https://www.theglobalfund.org/media/7741/corporate_2018resultsreport_report_en.pdf Accessed 20 Oct 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[45] 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[45].

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[46].
- 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[47]. 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[48]. 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[49]. This programme is currently funding 19 Implementation Research Teams (IRTs) composed of African and Canadian researchers and African health policymakers to develop practical,

[45] Policy Cures Research (2019) G-Finder 2018 report

[46] FIND. https://www.finddx.org/ Accessed 20 Oct 2019

[47] EVI. http://www.euvaccine.eu Accessed 20 Oct 2019

[48] https://www.idrc.ca/en/what-we-do/programs Accessed 20 Oct 2019

[49] IDRC https://www.idrc.ca/en/initiative/innovating-maternal-and-child-health-africa Accessed 20 Oct 2019

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[50]. 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)[51] is an independent, not-for-profit organisation funded by the Canadian government and other partners[52] (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[53]. 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[54].

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[55].

[50] IDRC. https://www.idrc.ca/sites/default/files/sp/Documents%20EN/Maternal-Online-ENG.pdf Accessed 20 Oct 2019

[51] IDRC. https://www.idrc.ca/en/project/development-innovation-fund-global-health-research Accessed 20 Oct 2019

[52] Grand Challenges Canada. https://www.grandchallenges.ca/wp-content/uploads/2018/10/Annual_Report_2017-2018_FINAL.pdf Accessed 20 Oct 2019

[53] Ibid.

[54] Gouglas D & Plahte J (2015) Report to the Norwegian Agency for Development Cooperation (Norad): A review of MFA/Norad's support to global health product development. Norwegian Institute of Public Health, Oslo

[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[56].

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.

[56] https://www.forskningsradet.no/prognett-globvac/About_the_programme/1224697869303

Table 33 Comparison of global health funders' global health trials funding activity

Funder	Programme/s (if relevant)	Funding modality	Level of funding	Priority disease areas	Types of activities funded	Eligible locations	
						For PI	For trial
JGHT	NA	Open calls for proposals	£139m (2011-18)	None	Late stage intervention trials	UK and LMICs	LMICs
EDCTP	NA	Open calls for proposals	EDCTP1: €208m EDCTP2: €447m	Infectious diseases	Phase I to IV trials; capacity development; health services optimisation	Europe; Sub-Saharan Africa	Sub-Saharan Africa
BMGF	Grand Challenges (GC) Grand Challenge Explorations (GCE)	Commissioned research Open/restricted calls for proposals	GC: USD450m GCE: USD100m (2007-2012)	Infectious diseases Maternal, newborn and child health	Vaccine development; Surveillance; Discovery and Translational Sciences; Innovative Technological Solutions	Worldwide	Worldwide
NIH (including Fogarty International Centre and NIAID)	Programmes within individual institutes and centres	Extramural grants for solicited and unsolicited research through calls for proposals Intramural funding	NIAID: USD 443m in 2018 for clinical research in LMICs	Depends on call	Early to late stage trials; capacity development; trial networks	Depends on call – in principle worldwide	Depends on call – in principle worldwide
PDPs	E.g. International AIDS Vaccine Initiative (IAVI), Medicines for Malaria Venture (MMV) and PATH	Calls for proposals In-house research and manufacturing	USD508m in 2017	HIV/AIDS, tuberculosis, malaria and neglected tropical diseases	product development across all stages; vaccines, drugs, diagnostics	Worldwide	Worldwide
The Global Fund	Country level programmes	Funding requests made by national committees that include medical experts, government and civil society	Nearly USD4b a year	HIV/AIDS, TB and malaria	Predominantly implementation, but also discovery of better drugs, vaccines and tools	LMICs	LMICs
Global Challenges Canada	Stars in Global Health Transition to Scale Global Mental Health Saving Lives at Birth Saving Brains	Open call for proposals	CAD269m over 9 years	Maternal, newborn and child health, Mental Health, Hypertension	Innovation to address specified challenges, scale-up	Worldwide	LMICs

IDRC	Food, Environment and Health Maternal and Child Health Innovating for Maternal and Child Health in Africa	Open call for proposals	CAD 36m for Innovating for Maternal and Child Health in Africa (2014-20)	non-communicable and infectious diseases, maternal and child health	Prevention, implementation research, new technologies, community- and facility-based interventions, health systems research, capacity building	Canada and LMICs	Canada and LMICs
RCN/Norad	GLOBVAC	Open call for proposals	NOK121.8m annually	infectious diseases; maternal, newborn, child and adolescent health	Prevention, treatment, diagnostics, particularly vaccine research; technological innovation; methods development; health systems and health policy research	Norway and LMICs	Norway and LMICs

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 mid-way 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[57]. 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[58]. 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[59]. 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[60]. Outputs and outcomes associated with awards are tracked using ResearchFish and awardees have to include a narrative account within the final report[61].

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)

[58] Evaluation of the Second European and Developing Countries Clinical Trials Partnership Programme (2014-2016). Experts Group Report. 2017

[59] BMGF. https://www.gatesfoundation.org/how-we-work/general-information/evaluation-policy

[60] https://gcgh.grandchallenges.org/sites/default/files/additional-materials/GCE_Rules_and_Guidelines_Round18.pdf

[61] https://gcgh.grandchallenges.org/grand-challenges-explorations-tracking-outcomes-and-outputs-using-researchfish#FunFacts

signing[62]. 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[63] 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[64]. 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[65, 66, 67], 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[68]. While programmes are evaluated externally, the IDRC has also developed a practical tool called Research Quality Plus (RQ+)[69] 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[70]. The tool recognises that scientific merit is necessary, but not sufficient[71]. 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[72]. The views of consortium staff, applicants and grantees, other stakeholders and external

62 https://www.theglobalfund.org/en/monitoring-evaluation/framework/#modular-framework-handbook

63 Ibid.

64 FSG Social Impact Advisors (2007) Toward a New Approach to Product Development Partnership Performance Measurement

65 Boulton et al (2015) Evaluation of the Product Development Partnerships (PDP) funding activities

66 Ramchandani & Bulc (2017) Final evaluation of Australia's investment in Product Development Partnerships (2013-2018): Evaluation findings and options for future DFAT investment. Specialist Health Service

67 Technopolis (2014) Review of the Product Development Partnerships Fund 2011-2014. Final report to the Dutch Ministry of Foreign Affairs

68 https://www.idrc.ca/en/about-idrc/accountability/evaluation

69 IDRC (2016) Research Quality Plus - A Holistic Approach to Evaluating Research

70 McLean R & Sen K (2018) Making a Difference in the Real World? A Meta-Analysis of Research for Development. IDRC

71 Lebel, J. and McLean, R. (2018) A better measure of research from the global south. Nature 559: 23-26

72 Oxford Policy Management (2015) Development Innovation Fund – Health. Summative Evaluation Report.

experts were gathered. A framework analysis[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[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)[74] which classifies all health research along two dimensions: Research Activity and Health Category. The programme also actively incorporates the Health&Care21 monitor[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[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 34 Evaluation and monitoring approach and Key Performance Indicators (KPIs) used by different global health funders

Funder/ Programme	Type of evaluation / monitoring (year, if applicable)	Indicator types	Examples of KPIs
EDCTP	2007 and 2009 independent review 2009 internal assessment 2013 internal impact assessment 2014 independent performance and impact evaluation 2017 independent interim evaluation	Output Outcome Impact	Number of funded projects Number of publications Number of new interventions Proportion of clinical trials with African leadership Improved policies and guidelines
BMGF	Evaluation of clinical trials typically not undertaken Monitoring through self-reporting by grantees e.g. through technical and financial reports, ResearchFish	Output Outcome	Defined by project

[73] NatCen Learning (2012) The framework approach to qualitative data analysis. http://betterevaluation.org/resources/guides/natcen_framework_approach_QDA

[74] http://www.hrcsonline.net/

[75] https://www.helseomsorg21monitor.no/

[76] Fogarty International Center Evaluation https://www.fic.nih.gov/About/Staff/Policy-Planning-Evaluation/Pages/evaluation-framework.aspx Accessed 20 Oct 2019

[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].

[78] World Malaria Report 2018. Geneva: World Health Organization; 2018.

[79] Ibid.

[80] Action and Investment to defeat Malaria 2016-2030. For a Malaria-Free World.World Health Organization. 2015

[81] Head MG (2017) Global funding trends for malaria research in sub-Saharan Africa: a systematic analysis. The Lancet Global Health 5(8): e772-e781

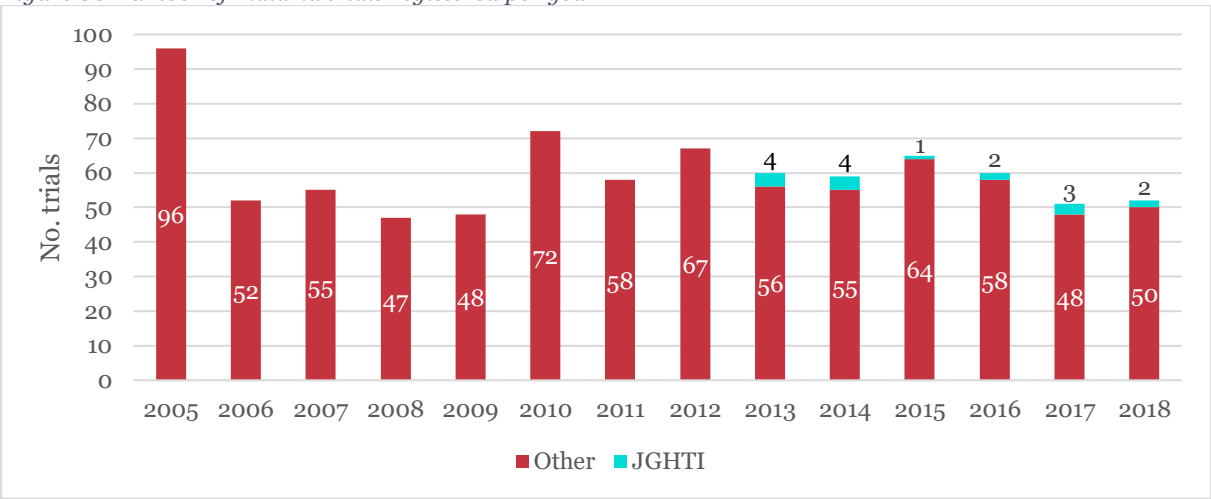
[82] Rabinovich RN et al (2017) malERA: an updated research agenda for malaria elimination and eradication. PLoS Medicine 14(11): e1002456.

[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.

[84] World Malaria Report 2018. Geneva: World Health Organization

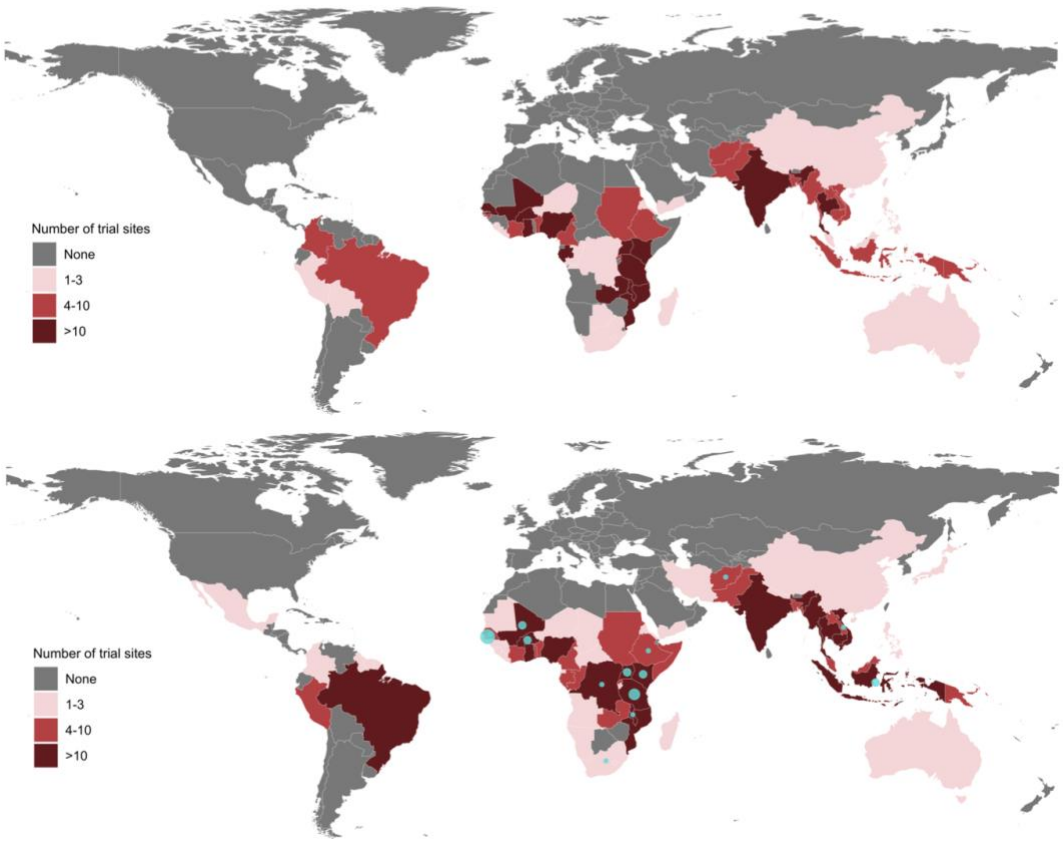
[85] The pre-JGHT period is 6 years and the post-JGHT period is 8. The increase in the number of trials should therefore be interpreted with caution.

Figure 86 Number of malaria trials registered per year



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.

Figure 87 Locations of clinical trials. (A) between 2005 – 2010, (B) between 2011 -2018

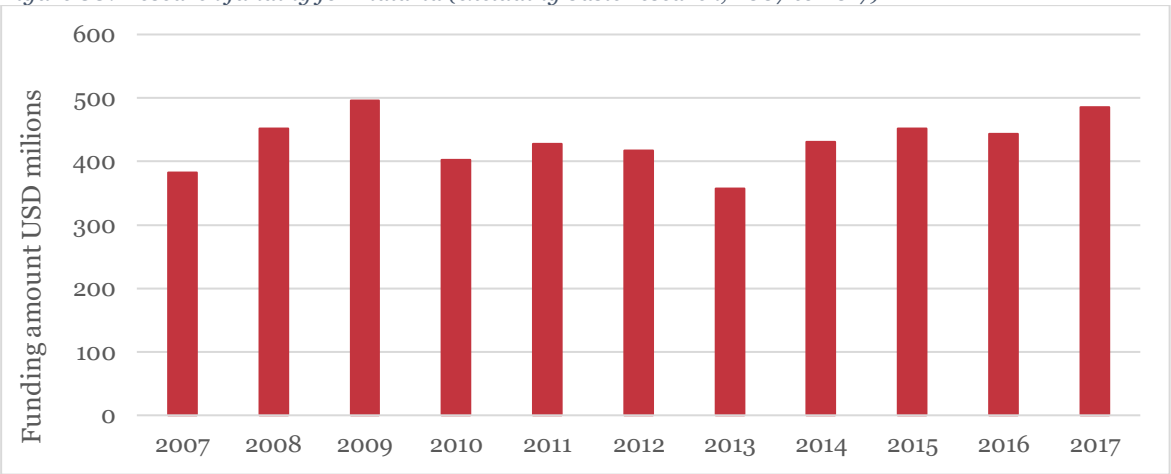


Source: Technopolis analysis of WHO ICTRP data. Locations of the JGHT trials are indicated in blue

- Funding landscape

Excluding funding for basic research, the level of funding for malaria research has remained relatively stable between 2007 and 2017 (Figure 88).[86] 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

Type of funder	Amount (1 million USD)
Philanthropic	1,232
Private sector	941
Public sector - Governments	809
Public sector - Multilaterals	31
Unspecified	0.05
Grand total	3,013

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[87]

Funders	Amount of funding, million USD (G-Finder, 2011-2017)	Number of malaria clinical trials other than JGHT (ICTRP, 2011-2018)	Number of malaria clinical trials (JGHT, 2011-2018)
Bill & Melinda Gates Foundation	872	11	0
US National Institutes of Health (NIH)	533	2	0
US Department of Defence (DOD)	156	0	0
UK Department for International Development (DFID)	129	5	16
US Agency for International Development (USAID)	63	1	0
The Wellcome Trust	53	2	16
European Commission (EC)	52	19	0
Indian Council of Medical Research (ICMR)	52	2	0
French National Institute of Health and Medical Research (Inserm)	36	0	0
German Federal Ministry of Education and Research (BMBF)	31	0	0
UK Medical Research Council (MRC)*	28	3	16
UK Department of Health and Social Care (including NHS and NIHR)*	10	0	5

*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.

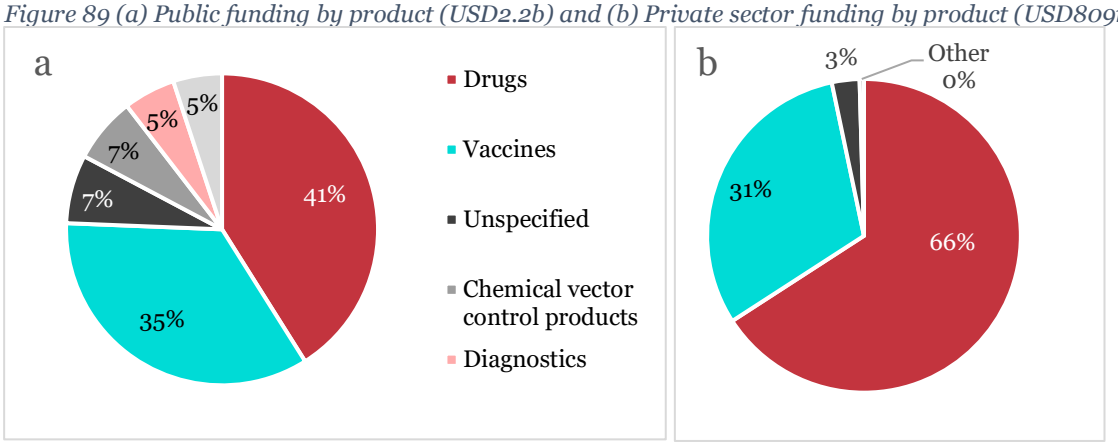
Of the 16 JGHT projects, half (8/50%) were investigating drug interventions, three (19%) were investigating chemical vector control and one was investigating a vaccine.

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

[87] 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.

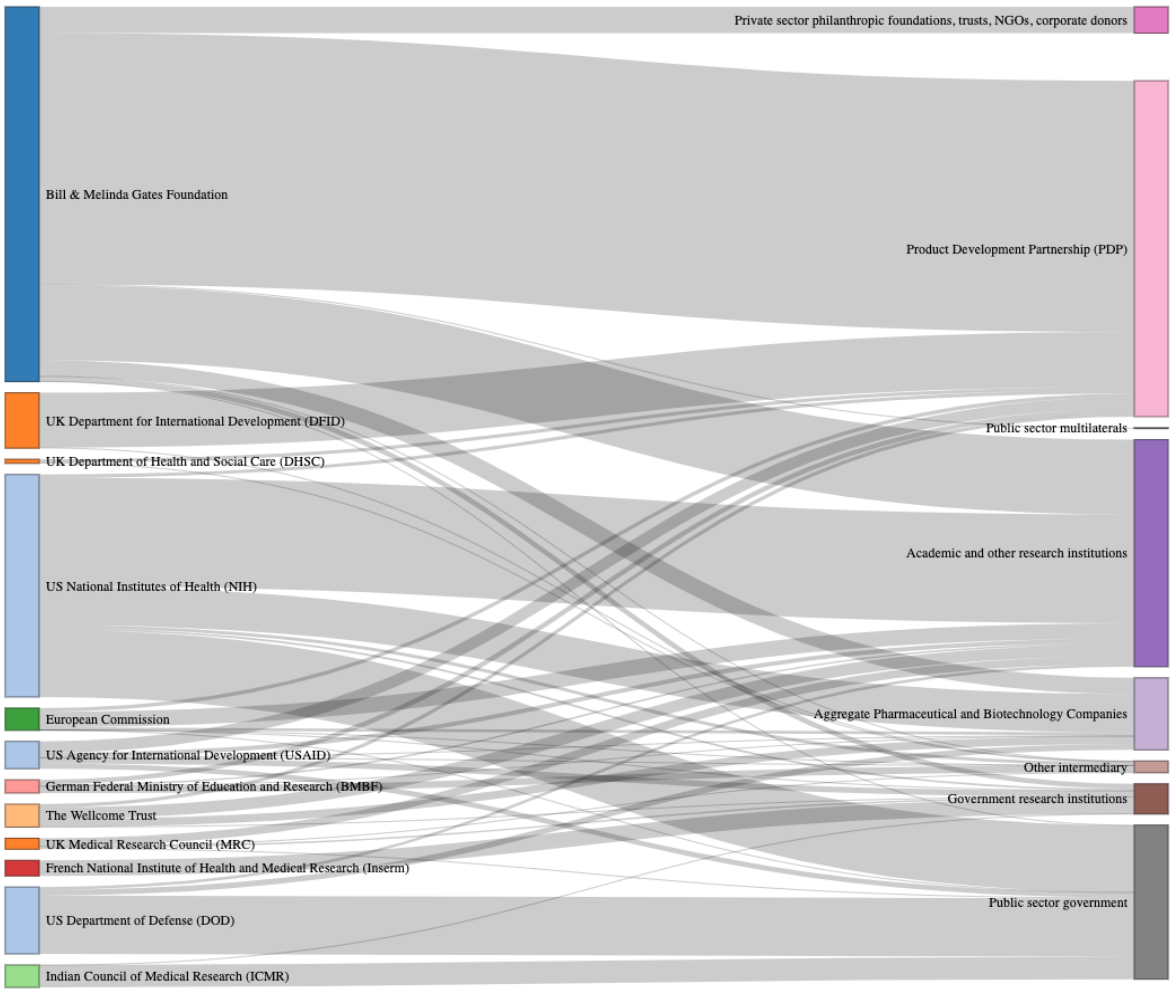
BMGF and DFID, respectively. Research at academic institutions is predominantly funded by the NIH (USD253m), followed by the Bill & Melinda Gates Foundation (USD174m), and the European Commission (USD36m). Half of the Wellcome Trust funding (50% or USD27m) and almost three-fourths of the MRC funding (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[94] 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[95].

G.3.2. Tuberculosis (TB)

- Current state of play

[88] https://www.theglobalfund.org/media/8752/corporate_2019resultsreport_report_en.pdf Accessed 11 Oct 2019

[89] https://data.theglobalfund.org/investments/grants Accessed 11 Oct 2019

[90] https://www.mmv.org/about-us Accessed 11 Oct 2019

[91] https://www.mmv.org/sites/default/files/uploads/docs/publications/MMV_at_a_glance_EN_2019.pdf Accessed 11 Oct 2019

[92] https://www.pmi.gov/about Accessed 11 Oct 2019

[93] https://www.pmi.gov/docs/default-source/default-document-library/pmi-reports/2019-pmi-thirteenth-annual-report.pdf Accessed 11 Oct 2019

[94] https://www.pmi.gov/docs/default-source/default-document-library/tools-curricula/pmiorstrategicguidance.pdf?sfvrsn=14 Accessed 11 Oct 2019

[95] https://www.pmi.gov/how-we-work/cross-cutting-technical-areas/operational-research-reports?select=research#filterPjts Accessed 11 Oct 2019

The massive disease burden of TB along with the emergence and rapid spread of drug-resistant TB[96] 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[97]) that will need clinical evaluation in combination with each other and with standard drugs to identify the best possible regimen[98].

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[99]. Moreover, current regimens are highly efficient and hence non-inferiority, pragmatic/adaptive trials seem to be the need of the hour[100]. 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)[101,102]. 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[103].

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[104]. 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[105]. The JGHT is also contributing in this regard, having funded the SURE[106], SHINE[107], TRUNCATE-TB[108] and RIFASHORT[109] 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[110] and JGHT-funded TB-CHAMP[111] 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

96 WHO (2018) Global tuberculosis report 2018. Geneva: World Health Organization.

97 Working Group on New TB Drugs, STOP TB Partnership. Accelerating discovery. www.newtbdrugs.org/pipeline.php Accessed 11 Oct 2019

98 Davies G et al (2019) Accelerating the transition of new tuberculosis drug combinations from Phase II to Phase III trials: New technologies and innovative designs. PLoS Medicine 16(7): e1002851.

99 Phillips P et al (2012) Innovative trial designs are practical solutions for improving the treatment of tuberculosis. Journal of infectious diseases, 205(suppl_2): S250-S257

100 Ibid.

101 Boeree MJ et al (2017) High-dose rifampicin, moxifloxacin, and SQ109 for treating tuberculosis: a multi-arm, multi-stage randomised controlled trial. The Lancet infectious diseases, 17(1): 39-49.

102 Papineni P et al (2016) TRUNCATE-TB: an innovative trial design for drug-sensitive tuberculosis. International Journal of Infectious Diseases 45: 404

103 Davies G et al (2019) Accelerating the transition of new tuberculosis drug combinations from Phase II to Phase III trials: New technologies and innovative designs. PLoS Medicine, 16(7): e1002851

104 Tiberi S et al (2018) Tuberculosis: progress and advances in development of new drugs, treatment regimens, and host-directed therapies. The Lancet Infectious Diseases 18(7): e183-e198.

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

108 Papineni P et al (2016) TRUNCATE-TB: an innovative trial design for drug-sensitive tuberculosis. Int J of Inf Dis 45: 404.

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

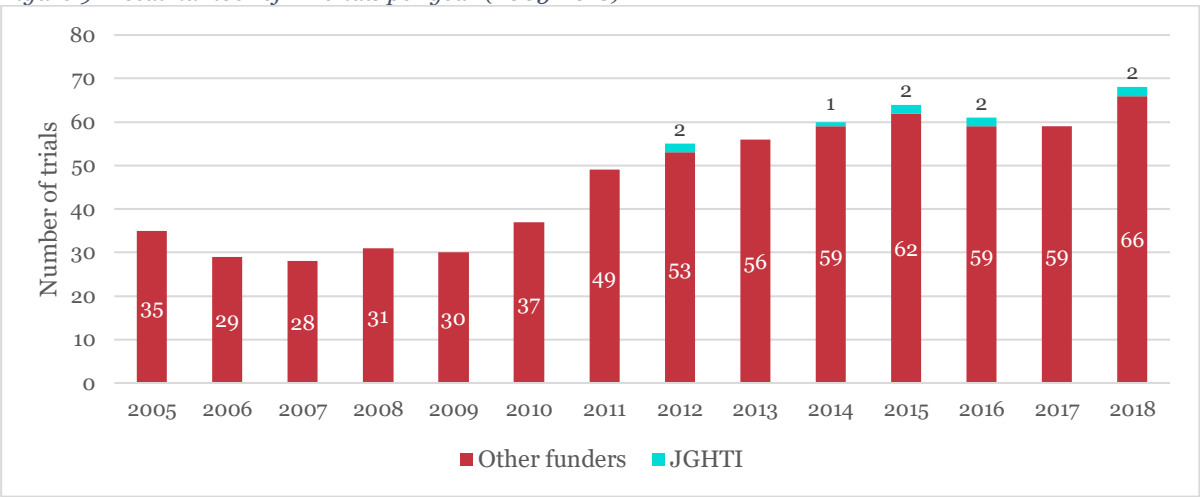
111 ISRCTN registry: Tuberculosis child multidrug-resistant preventive therapy: TB CHAMP trial. ISRCTN92634082

transcriptome as well as positron emission tomography–computed tomography (PET-CT) based assays[112]. Point-of-care assays such as the mycobacterial lipoarabinomannan (LAM) test using urine samples are also being evaluated clinically and improved upon[113]. The JGHT-funded STAMP[114] and TB Fast Track[115] 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[116]. 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

[112] Davies G et al (2019) Accelerating the transition of new tuberculosis drug combinations from Phase II to Phase III trials: New technologies and innovative designs. PLoS Medicine, 16(7): e1002851

[113] FIND. Point-of-care TB LAM tests. https://www.finddx.org/tb/poc-tb-hiv/ Accessed 11 Oct 2019

[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

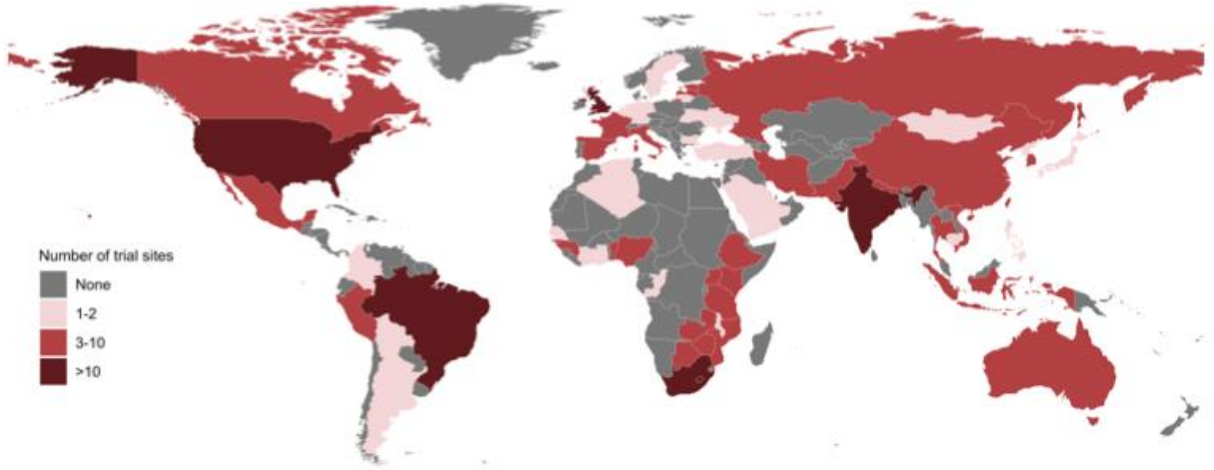
[116] TB trial entries were downloaded from the WHO International Clinical Trials Registry Platform (ICTRP). Duplicates were removed. Trials were excluded if they were deemed not relevant (phase 0, 1 and 2 trials, and observational studies) and if they were registered prior to 2005 or after 2018.

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.

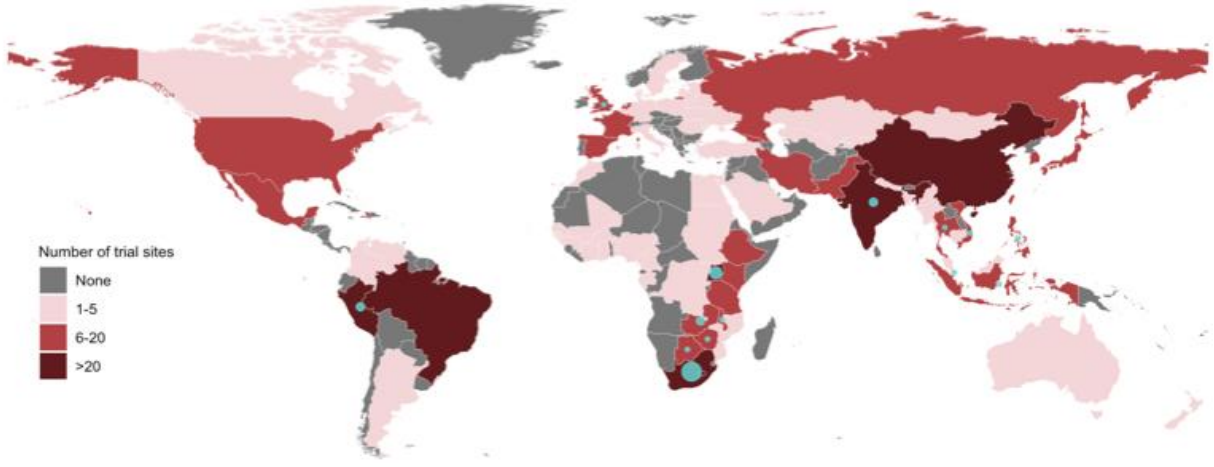
The JGHT TB trials cover 14 different countries. The majority of these (seven out of nine, 78%) have at least one site in sub-Saharan Africa, with five of the nine trials (56%) being conducted entirely or partly in South Africa (see Figure 92). Overall, five (56%) of the JGHT trials are multi-country, 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)

a)



b)



Source: Technopolis analysis of WHO ICTRP data

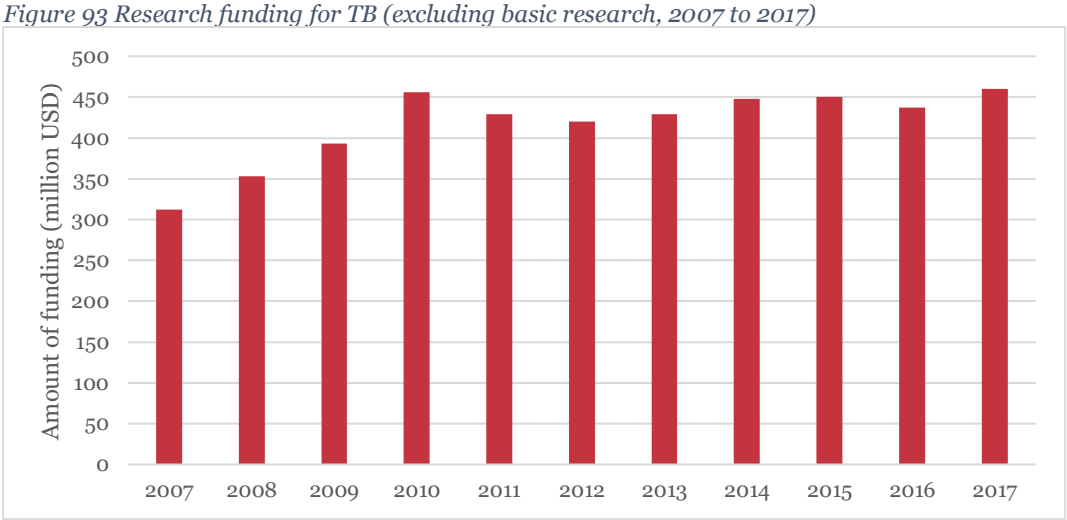
[117] Treatment Action Group and Stop TB Partnership. (2018). Tuberculosis research funding trends 2005-2017.

[118] Creswell J et al (2014) Tuberculosis in BRICS: challenges and opportunities for leadership within the post-2015 agenda. Bull World Health Organ 92(6): 459–460

- Funding landscape

Excluding basic research, research funding for TB amounted to around USD4.6b between 2007 and 2017[119]. 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

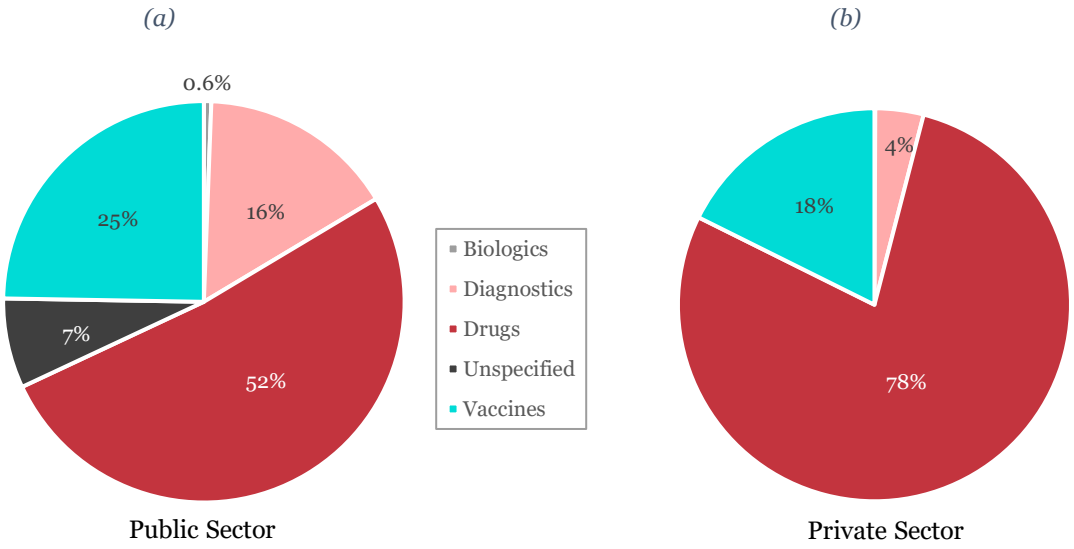
Table 37 Research funding for TB (excluding basic research, 2011 to 2017) by type of funder

Type of funder	Amount (million USD)
Public sector - Governments	1,380
Private sector	821
Philanthropic	810
Public sector - Multilaterals	59
Unspecified	3
Grand Total	**3,073**

Source: Technopolis analysis of G-Finder data

[119] Based on G-Finder data

Figure 94 Investment in different product types (2011-2017) by the public/philanthropic (a) and private (b) sectors



Source: Technopolis analysis of 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.

Table 38 Major public and philanthropic funders and number of TB clinical trials funded[120]

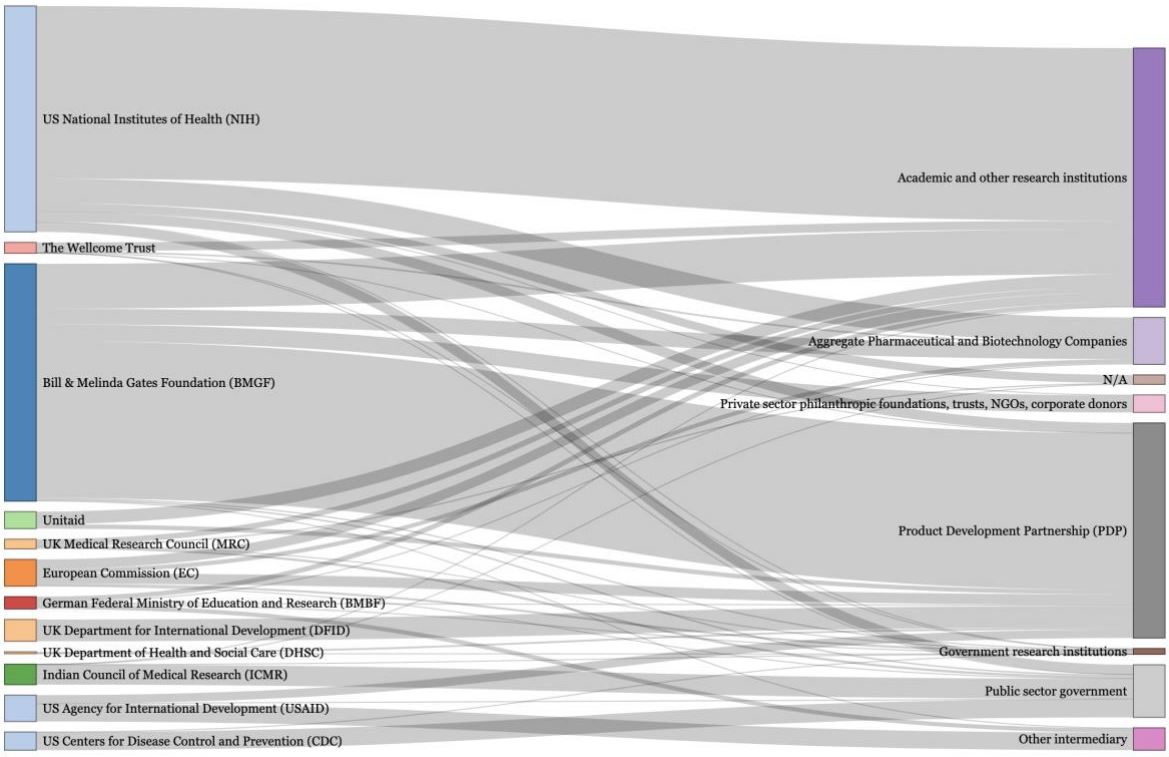
Funder	Amount of funding, million USD (G-Finder, 2011-2017)	Number of TB clinical trials other than JGHT (ICTRP, 2011-2018)	Number of TB clinical trials (JGHT, 2011-2018)
Bill & Melinda Gates Foundation (BMGF)	759	10	0
US National Institutes of Health (NIH)	722	20	0
European Commission (EC) including EDCTP	85	15	0
US Agency for International Development (USAID)	84	6	0
UK Department for International Development (DFID)	70	1	9
Indian Council of Medical Research (ICMR)	65	2	0
US Centers for Disease Control and Prevention (CDC)	58	10	0
Unitaid	54	0	0
German Federal Ministry of Education and Research (BMBF)	39	1	0
The Wellcome Trust	35	8	9
UK Medical Research Council (MRC)	31	4	9
UK Department of Health and Social Care (including NHS and NIHR)	6	8	2

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%).

[120] 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.

Figure 95 Flow of TB research funding (excluding basic research, in million USD) from selected funders by recipient type (2011-2017)



Source: Technopolis analysis of G-Finder data

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[121]. 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[122]. 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[123]. 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[124]. 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[125] in addition to capacity building, health system strengthening and operational research in countries affected by TB[126].

[121] The Global Fund. https://www.theglobalfund.org/en/ Accessed 15 Oct 2019

[122] The Global Fund. *Tuberculosis*. https://www.theglobalfund.org/en/tuberculosis/ Accessed 15 Oct 2019

[123] The Global Fund. *Results report 2018* https://www.theglobalfund.org/media/7741/corporate_2018resultsreport_report_en.pdf Accessed 15 Oct 2019

[124] Ibid.

[125] WHO ICTRP database

[126] The Global Fund. *Tuberculosis*. https://www.theglobalfund.org/en/tuberculosis/ Accessed 15 Oct 2019

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[127]. 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[128]. 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[129].

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[130]. 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[131]. 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)[132].

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)[133]. 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[134]. 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[135]. FIND has considerably advanced the field of TB diagnostics and provides diagnostics developers with access to its large TB specimen bank[136]. 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[137]. Current priority

[127] Stop TB Partnership. *About us*. http://www.stoptb.org/about/ Accessed 15 Oct 2019

[128] Stop TB Partnership. *TB Reach*. http://www.stoptb.org/global/awards/tbreach/about.asp Accessed 15 Oct 2019

[129] Stop TB Partnership. *TB Reach*. http://www.stoptb.org/global/awards/tbreach/interactive/pages/interventions00.html Accessed 15 Oct 2019

[130] TB Alliance. *Donors*. https://www.tballiance.org/about/donors Accessed 15 Oct 2019

[131] TB Alliance. *Clinical development and marketed products*. https://www.tballiance.org/portfolio/ Accessed 15 Oct 2019

[132] TB Alliance. *Developing new treatments*. https://www.tballiance.org/annualreport2018/developing-new-treatments Accessed 15 Oct 2019

[133] TB Vaccine initiative. https://www.tbvi.eu Accessed 15 Oct 2019

[134] Ibid.

[135] FIND. *Partners & Donors*. https://www.finddx.org/partners-donors/ Accessed 15 Oct 2019

[136] Boulton I et al (2015). *Evaluation of the PDP funding activities of DFID and BMBF*. https://assets.publishing.service.gov.uk/media/57a0897140f0b6497400000b0/Evaluation_of_the_Product_Development_Partnerships_funding_activities.pdf Accessed 15 Oct 2019

[137] FIND. *Diagnostic tools developed*. https://www.finddx.org/dx-developed/ Accessed 15 October 2019

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[138]. FIND has its own Clinical Trials Unit and a clinical trials network comprising 19 LMICs[139]. This has allowed FIND to train over 6,000 healthcare workers and strengthen 3,000 laboratories and trial sites.

G.3.3. Cryptococcal meningitis

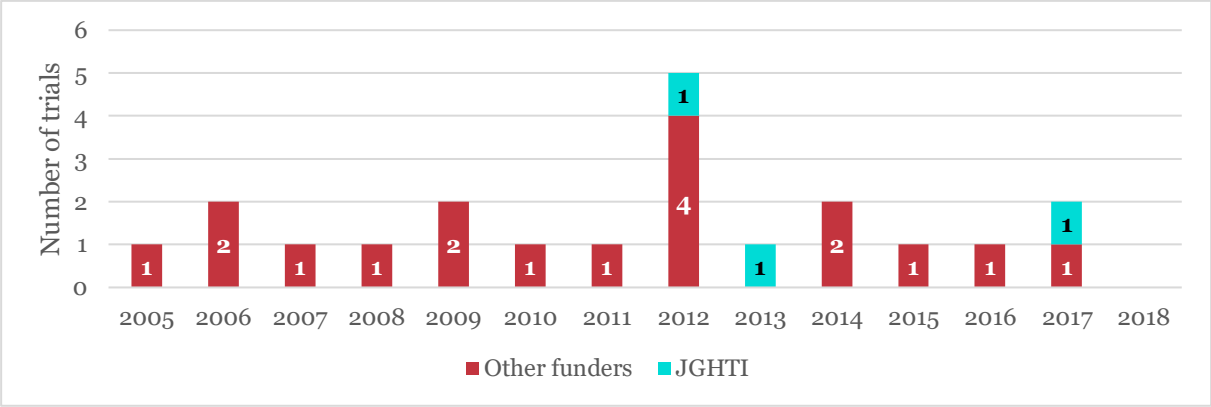
- Current state of play

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[140], causing more than 600,000 deaths each year[141]. 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[142]. 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)



Source: Technopolis analysis of WHO ICTRP data

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.

[138] FIND. *Tuberculosis*. https://www.finddx.org/tb/ Accessed 15 Oct 2019

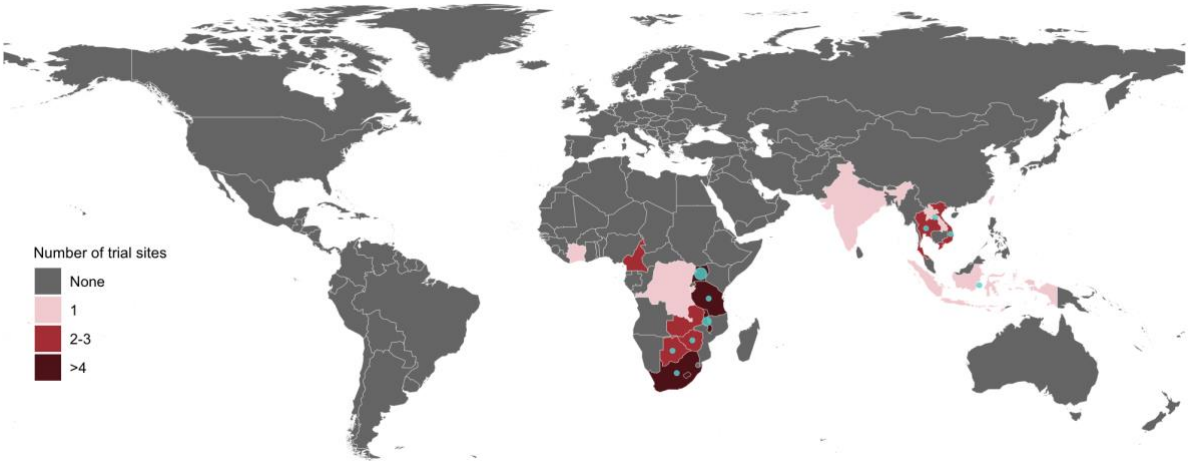
[139] FIND. *Clinical trials*. https://www.finddx.org/clinical-trials/ Accessed 15 Oct 2019

[140] WHO (2016) Guidelines for the diagnosis, prevention and management of cryptococcal disease in HIV-infected adults, adolescents and children

[141] Park BJ et al (2009) Estimation of the current global burden of cryptococcal meningitis among persons living with HIV/AIDS. AIDS 23:525-530

[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

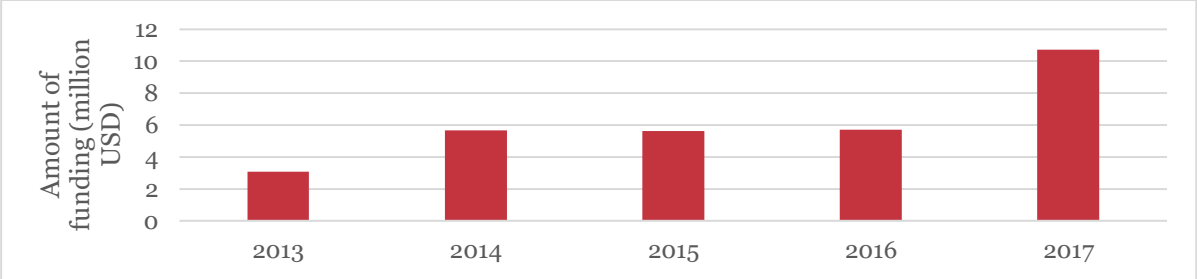


Table 39 Research funding for cryptococcal meningitis by type of funder (2013-17)

Type of funder	Amount (million USD)
Public sector - Governments	30
Philanthropic sector	1
Grand Total	**31**

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.

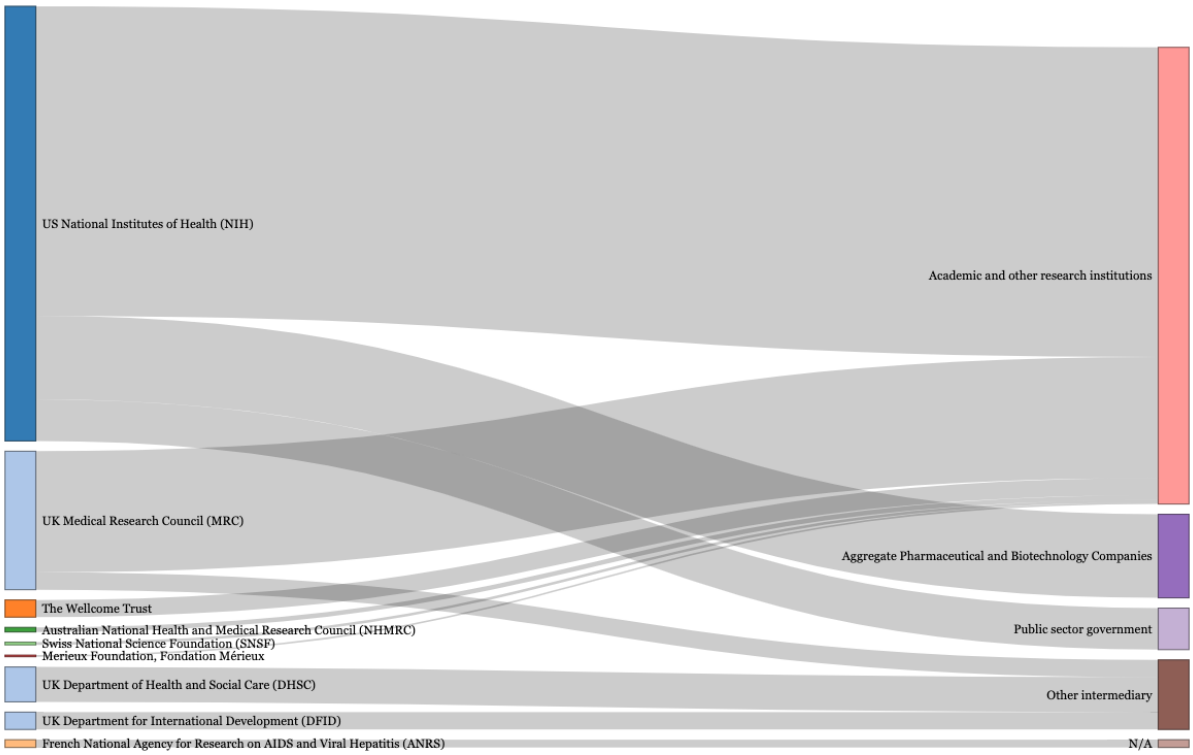
Table 40 Major public and philanthropic funders and number of cryptococcal meningitis clinical trials funded[143]

Type of funder	Amount, x 1000 USD (G-Finder, 2013-2017)	Number of clinical trials other than JGHT (ICTRP, 2011-2018)	Number of clinical trials (JGHT, 2011-2018)
US National Institutes of Health (NIH)	20,316	0	0
UK Medical Research Council (MRC)	6,473	1	3
UK Department of Health and Social Care (DHSC)	1,629	0	1
UK Department for International Development (DFID)	811	0	3
The Wellcome Trust	801	0	3
French National Agency for Research on AIDS and Viral Hepatitis (ANRS)	362	3	0
Australian National Health and Medical Research Council (NHMRC)	214	0	0
Swiss National Science Foundation (SNSF)	122	0	0
Merieux Foundation, Fondation Mérieux	75	0	0
Grand Total	**30,805**		

The proportions of funding for different types of recipients from the major pubic 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.

Figure 99 Flow of cryptococcal meningitis research funding (excluding basic research, in million USD) from selected funders by recipient type (2011-2017)



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

[144] Davey G et al (2007) Podoconiosis: a tropical model for gene-environment interactions?. Trans R Soc Trop Med Hyg 101: 91–6; Tekola AF et al (2012) HLA class II locus and susceptibility to podoconiosis. N Engl J Med 366: 1200–8

[145] Deribe K et al (2018) Global epidemiology of podoconiosis: A systematic review. PLoS Negl Trop Dis 12: e0006324 and references within

[146] Deribe K et al (2015) Epidemiology and individual, household and geographical risk factors of podoconiosis in Ethiopia: results from the first nationwide mapping. Am J Trop Med Hyg. 92: 148–589

[147] Deribe K et al (2015) Mapping and modelling the geographical distribution and environmental limits of podoconiosis in Ethiopia. PLoS Negl Trop Dis 9:e0003946; Deribe K et al (2017) Estimating the number of cases of podoconiosis in Ethiopia using geostatistical methods. Wellcome Open Res 2

grouped alongside lymphatic filariasis (LF) programmes, the 'better-known' elephantiasis caused by parasitic worms[148]. However, recent mapping efforts have shown that these diseases are frequently found in different regions of countries, or different countries altogether[149]. 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)[150] 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)[151]. Footwork was launched by Prof Gail Davey, University of Sussex, in 2012 to work towards the elimination of podoconiosis[152].

[148] Marks M & Mitja O (2019) Prevalence surveys for podoconiosis and other neglected skin diseases: time for an integrated approach. The Lancet Global Health 7: PE554-E555

[149] Deribe K et al (2017) Mapping the geographical distribution of podoconiosis in Cameroon using parasitological, serological, and clinical evidence to exclude other causes of lymphedema. Plos Negl Trop Dis. 12: e0006126; Deribe K et al (2019) Geographical distribution and prevalence of podoconiosis in Rwanda: a cross-sectional country-wide survey. Lancet Glob Health 7: e671–e680

[150] Brooks J et al (2017) A randomized controlled trial to evaluate the effect of a new skincare regimen on skin barrier function in those with podoconiosis in Ethiopia. Br J Dermatol. 177:1422-1431

[151] G-finder does not provide information on podoconiosis.

[152] Davey G et al (2012) Launch of the International Podoconiosis Initiative. The Lancet 379: P1004

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