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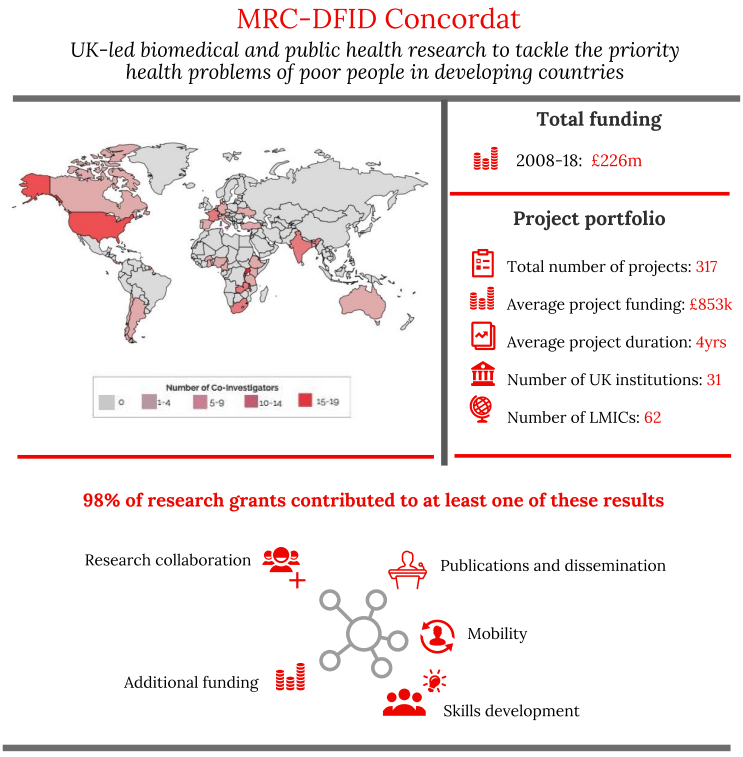
RAND EUROPE

20 July 2018

Review of the MRC-DFID Concordat

Final report



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Review of the MRC-DFID Concordat

technopolis |group| and RAND Europe July 2018

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List of abbreviations

ACT	Artemisinin-based combination therapy
ADH	Implementation research to improve adolescent health in low and middle-income countries
AIDS	Acquired Immune Deficiency Syndrome
ANRS	Agence Nationale de Recherche sur le Sida (French Agency for Research on AIDS and Viral Hepatitis)
ARL	African Research Leaders
ART	Antiretroviral therapy
BBC	The British Broadcasting Corporation
BEIS	Department of Business, Energy and Industrial Strategy
BMJ	British Medical Journal
CAPS	Cook Stoves and Pneumonia
CD4	Cluster of differentiation 4
CDA	Career Development Award
CDC	Centers for Disease Control and Prevention
CFS	Chronic Fatigue Syndrome
CGMR-C	Wellcome Trust Centre for Geographic Medical Research (Coast)
CNRS	French National Centre for Scientific Research
DAC	Development Assistance Committee
DART	Development of AntiRetroviral Therapy in Africa
DCS	Developmental Clinical Studies
DFID	Department for International Development
DP	Delivery Partner
DPFS	Developmental Pathway Funding Scheme
DPhil	Doctor of Philosophy
DSJI	Disposable syringe jet injectors
EDCTP	European and Developing Countries Clinical Trials Partnership
EM	Experimental Medicine
ENID	Early Nutrition and Immune Development
EPI	Expanded Programme on Immunization
EPSRC	Engineering and Physical Sciences Research Council
ESRC	Economic and Social Research Council
EU	European Union
FWCI	Field Weighted Citation Impact
GCP	Good Clinical Practice
GCRF	Global Challenges Research Fund
GH	Global Health
GHT	Global Health Trials
GLOBVAC	Global Health- and Vaccination Research programme

GSK	GlaxoSmithKline
HBV	Hepatitis B vaccine
Hib	Haemophilus influenzae type b
HIV	Human Immunodeficiency Virus
HPV	Human papillomavirus
HSPHRB	Health Services and Public Health Research Board
IIB	Infections and Immunity Board
Inserm	French public research institution solely focused on human health and medical research
IP	Intellectual Property
IPM	International Partnership for Microbicides
IPV	Intramuscular polio vaccine
IRD	French National Research Institute for Sustainable Development
JRF	Junior Research Fellow
KEMRI	Kenya Medical Research Institute
KPS	Karonga Prevention Study
LAIV	Live attenuated influenza vaccine
LMIC	Low- and Middle-Income Countries
LSHTM	London School of Hygiene & Tropical Medicine
MCMB	Molecular and Cellular Medicine Board
MD	Doctor of Medicine
ME	Myalgic encephalomyelitis
MLW	Malawi-Liverpool Wellcome Trust
MoU	Memorandum of Understanding
MRC	Medical Research Council
MRCG	MRC Unit in The Gambia's
MRP	Methodology Research Programme
MRTC	Malaria Research and Training Centre
NCD	Non-Communicable Disease
NCI	Normalised Citation Index
NGO	Non-governmental organisation
NIH	National Institutes of Health
NIHR	National Institute for Health Research
NMHB	Neurosciences and Mental Health Board
NORAD	Norwegian Development Agency
ODA	Official Development Assistance
OECD	Organisation for Economic Co-operation and Development
PCV	Pneumococcal conjugate vaccine
PENTA	Paediatric European Network for Treatment of AIDS

PhD	Doctor of Philosophy
PHIND	Public Health Intervention Development scheme
PI	Principal Investigator
PSMB	Population and Systems Medicine Board
R&D	Research and Development
RCN	Research Council of Norway
RCT	Randomised controlled trial
REA	Rapid Evidence Assessment
REF	Research Excellence Framework
SA	Severe Anaemia
SDGs	Sustainable Development Goals
SIDA	Swedish International Development Cooperation Agency
SMART	South Malaria Antigen Research Partnership
STIs	Sexually Transmitted Infections
STREAM	Standardised Treatment Regimen of Anti-TB Drugs for Patients with MDR-TB
TB	Tuberculosis
THET	Tropical Health Education Trust
UK	United Kingdom
UKAID	UK Aid Direct
UKRI	UK Research and Innovation
UNAIDS	Joint United Nations Programme on HIV/AIDS
US	United States (of America)
UVRI	Uganda Virus Research Institute
WHO	World Health Organization

Executive Summary

The UK Medical Research Council (MRC) and the Department for International Development (DFID) have had a Concordat agreement in place since 1993 to support a jointly funded portfolio of biomedical and public health research tackling the priority health problems of poor people in low and middle income countries.

This report presents the results of an independent Review of the MRC-DFID Concordat, undertaken by Technopolis Group and RAND Europe between March-June 2018 on behalf of the MRC and DFID. The aim of this study was to review the performance and added value of the Concordat that emerged between 2013 and 2018, covering the following aspects:

- The portfolio and quality of activities supported and their outcomes
- The relevance of the activities supported to the needs of developing countries
- The added value of the Concordat agreement to the MRC and DFID including the relevance, effectiveness, benefits and complementarity/synergy of the partnership
- The value for money combining the quality of financial management, cost of conducting research and quality of outputs
- The effectiveness of the operational, management and governance framework
- The relevance and benefit of the Concordat in the current ODA landscape
- The nature, range and timeliness of impacts (particularly in policy and/or practice) achieved from the activities funded under the Concordat including the time and route to impact, reach and significance of the impact and key facilitators of, or barriers to, achieving the impact

The study built on five main data collection and analytical research components: desk research, including a rapid evidence assessment, review of Concordat documentation, and analysis of Researchfish data; a multi-stakeholder interview programme; field visits; impact case studies and synthesis and reporting. The findings are divided into two sections: Part A - Review the Concordat's performance and value for money; and Part B - Review of the outputs, outcomes and impacts of the Concordat and the routes through which these occur. In this summary, we present the key findings for each of these areas, followed by overarching recommendations.

Part A: MRC-DFID Concordat performance and value for money

Awareness of the Concordat: The Concordat draws on the expertise of two organisations, both having strong identities and networks and complementary fields of expertise, in addition, to high reputation in their respective communities. Stakeholders are aware of the MRC and DFID funding for global health research but are not familiar with the Concordat or its full portfolio. However, individual programmes such as the African Research Leaders scheme, the MRC Units in Africa and MRC-DFID funding towards European and Developing Countries Clinical Trials Partnership are recognised on their own merits.

Relevance of the Concordat: The Concordat is responding to some of the most pressing health challenges worldwide by supporting health research and research capacity building in and concerning LMICs. The Concordat as it stands delivers many high quality outcomes and impacts but there is scope to review the coherence of the portfolio. Concordat projects are broadly relevant to global health research needs and have the potential to address key societal challenges in LMICs. Some structural and thematic gaps in the Concordat portfolio were identified by interviewees, but there was no consensus regarding them. Structural gaps concerned funders coordination, limited engagement with local stakeholders in LMICs, lack of South-South links and concentration of funding to a small number of high-performing Southern institutions. Thematic gaps were highlighted outside the infectious diseases area.

Quality of activities supported by the Concordat: The research supported by the Concordat is of the highest quality according to published reports and experts interviewed, and the MRC's robust project selection and management system is seen to be a contributor to this. Evidence collected during the review identified sustainable capacity building as a key achievement of the Concordat portfolio.

International reputation of the Concordat/funded research: The contributions of the MRC and DFID funding to global health research and research capacity building are recognised internationally for the quality of the resulting outputs and impacts. Concordat funding contributes to the UK's international reputation according to a majority of the stakeholders interviewed.

Capacity building in the Concordat portfolio: Capacity building is a key outcome of the Concordat portfolio which is not limited to the project teams but expands to wider researchers and practitioners engaged in their work. However, capacity building is not embedded centrally or considered across the entire portfolio. The small pool of in-country researchers and lack of structured career pathways makes it challenging for LMIC research partners to recruit and retain staff. The UK PIs retain a strong role within much of the research conducted. Consideration could be given to the best ways to ensure true partnerships in research and offer appropriate opportunities for leadership and development to non-UK researchers.

Management of the Concordat: The Concordat portfolio is solely administered by the MRC, and quarterly management reviews and the MRC's Global Health Group are the main platforms for interaction between the MRC and DFID personnel. The partnership between the MRC and DFID however also sets high expectations of the Concordat portfolio to address dual objectives, which have to be accomplished through creating a delicate balance between the mission of the two organisations. Given its centrality to the Concordat's aims, capacity building in projects could be better monitored and reported on.

Value for money: The Concordat presents good value for money through efficiencies gained from joint working, particularly regarding grant administration costs saved by DFID using MRC's existing management processes. The partnership also offers value for money by promoting synergy and complementarity through pooling of resources, creating critical mass, aligning work programmes, avoiding duplications leading to the high quality research outputs.

The Concordat in the Official Development Assistance (ODA) funding landscape: Global health research and development is increasingly being funded by public-private partnerships involving businesses, government funders and NGOs. The Concordat funding is part of the UK Government's committed spend (i.e. 0.7% of Gross National Income) on ODA along with the Global Challenges Research Fund and the Newton Fund. While DFID's funding to the Concordat will be reduced for the next five years, this does not represent a reduction of global health research funding, but a reallocation of funding channels used.

Part B: Research outcomes and impacts

The Concordat portfolio has produced a range of important outputs and benefits spanning high quality academic research outputs, local capacity building at LMIC partners, and wider benefits, notably on health policy and practice. Given the focus of the current review on research outcomes that have emerged in the past 5 years, it can be expected that these will develop to broader impacts over time. Key themes regarding the outputs and impacts achieved, the way they were captured, and the barriers and enablers of those impacts are as follows:

Relationships and networks: A core element underpinning the functioning of the Concordat portfolio is the diversity of networks and relationships which have been cultivated, particularly on the local level in LMICs, and which researchers draw upon to effectively conduct and communicate their research.

Role of units as hubs for research: The presence of a research hub, whether that is an MRC research unit, or a unit or centre run by another organisation (e.g. Wellcome Trust, CDC) is an important facilitator of research through sustaining relationships, research infrastructure and capacity building.

Researchfish and evaluation: Researchfish offers a comprehensive data set across the entire project portfolio that captures a wide range of output and outcome data in a consistent way. It is generally appreciated by researchers as an accessible platform to use, and it provides a longitudinal portfolio-wide data set that would be challenging to replicate ex-post otherwise. Despite these advantages, there are limitations to Researchfish in the specific context of the Concordat, particularly in relation to the way in which it addresses capacity building. It is currently not set up to capture capacity building outputs and partner country researchers could be more involved in the impact reporting process.

Translating research in challenging local contexts: In many LMICs, the resources available to health systems are limited and opportunities for training and skills development for practitioners are constrained. This restricts the ability of LMIC researchers to promote the uptake of research findings by policy makers and practitioners. In addition, political will is required to enable research translation into practice. In some cases, political instability has been a challenge not only in terms of building and maintaining the necessary stakeholder relationships, but on a practical level, conducting the actual research. There may be a role for funders to help address this barrier, by building on their existing networks to establish links across the research-policy divide and facilitate buy-in at the national level.

Considerations of impact channels: Applicants consider stakeholders required for translation of their research and potential pathways to impact already at the proposal stage. However, the scope and quality of these differs significantly over time and between funding streams. The MRC could provide applicants detailed guidance and examples of good practice of pathways to impact statements. Guidance could also be offered how to target capacity building as potential impact at the proposal stage.

Recommendations for the future development of the Concordat

1. The MRC and DFID through the Concordat should continue to fund high quality work selected on merit, that offers opportunities for creating new knowledge, capacity building and impacts on policy and practice. This should include continued support to the existing units as well as looking beyond and build further networks and relationships with other units and centres in LMICs, which could become key hubs for researchers to conduct research across different regions.
2. Capacity building should be a key consideration across the whole portfolio. Potential ways to support capacity building across different funding streams could include increased flexibility in funding awards, making funding available specifically for training, requiring specific plans on capacity building within applications, and strengthening partnership and leadership opportunities for partner country researchers.
3. Building on the theory of change, the MRC and DFID should establish a clearer strategy setting out the routes through which the Concordat invests and how they contribute to the ultimate goals of the programme. In addition, setting out a joint vision and key priorities would also help to clarify the identity and brand of the Concordat, and increase its visibility.
4. The Concordat has the potential to benefit more fully from input from both funding partners, especially DFID. Thinking through ways to integrate the Concordat into the wider work of the two organisations could help capitalise on shared knowledge, networks and expertise of the MRC and DFID. Increased integration into the work of the two organisations would also help to address some of the wider societal challenges which can be a barrier to translation of research findings.
5. The MRC and DFID could further the implementation of research results by building on and developing existing and new relationships with wider non-research organisations (e.g. government bodies, health providers) in partner countries.
6. Since capacity building is a core element of the programme, reporting should be expanded to capture information on capacity building more effectively and by engaging researchers across the project team.
7. More guidance should be provided on how to complete the pathways to impact statement in proposals. This could also help researchers to consider more thoroughly how they intend to achieve impact through their research.

1 Introduction

This is the final report of the Review of the MRC-DFID Concordat. The study has been undertaken by Technopolis Group and RAND Europe on behalf of the MRC and DFID.

The report describes the main findings of the study based on the data collected and analysis undertaken during the four months of the study (between March-June 2018) and puts forward recommendations for the consideration of the MRC and DFID.

This final report is structured as follows:

- The remaining part of this chapter presents the objectives and scale and scope of this study, and it also provides a brief description of the methodology applied
- **Chapter 2** provides includes an analysis of the Concordat project portfolio
- **Chapter 3** presents the key findings of this review in two parts:
  - **Part A** discusses the DFID-MRC Concordat performance and value for money, through exploring the relevance; the quality of activities supported; the international reputation of the Concordat/funded research; the management of the Concordat and the Concordat in the Official Development Assistance (ODA) funding landscape and international examples
  - **Part B** summarises the study findings with regards to research outcomes and impact of the funded activities, and analyses the impact pathways available in the Concordat funded portfolio
- **Chapter 4** provides the study team's recommendations and considerations for future Concordat working
- The **appendices** of the report provide more information on the methodology applied in the review, including the data collection tools developed (interview guidelines and impact case study templates), the list of interviewees consulted, a detailed description of the different schemes under the Concordat as well as the impact case studies

1.1 Objectives of the review

The MRC commissioned this study on behalf of both the MRC and DFID to review the performance and added value of the Concordat that emerged between 2013 and 2018. Building on the findings of the light touch review[1] that was carried out in 2012, the current review encompasses the following aspects:

- The portfolio and quality of activities supported and their outcomes
- The relevance of the activities supported to the needs of developing countries
- The nature, range and timeliness of impacts (particularly in policy and/or practice) achieved from the activities funded under the Concordat including the time and route to impact, reach and significance of the impact and key facilitators of, or barriers to, achieving the impact
- The added value of the Concordat agreement to the MRC and DFID including the relevance, effectiveness, benefits and complementarity/synergy of the partnership
- The value for money combining the quality of financial management, cost of doing research and quality of outputs
- The effectiveness of the operational, management and governance framework

[1] Wyss K et al. 2012 Interim (light touch) review of the DFID/MRC Concordat. Swiss Tropical and Public Health Institute. Quest number 3434805

- The relevance and benefit of the Concordat in the current ODA landscape. ODA is meant to promote economic development and welfare of developing countries and the UK has made available additional funding through the Newton Fund and Global Challenges Research Fund

1.2 Scale and scope of the review

Under the Concordat, £90m (£41m from DFID, £49m from the MRC) has been pledged from 2013 to 2018 for research and capacity building in developing countries. Projects are funded through one of two funding modes: responsive mode and strategic initiatives. The MRC also fund two Units in Sub-Saharan Africa (in The Gambia and Uganda) that contribute to the research programme under the Concordat.

The following range of activities are supported under the Concordat:[2]

- High quality biomedical and health research with a focus on translational and implementation research of relevance to developing countries which can include public health, health services and health systems research (approx. £35m) – basic research done in the UK with little direct relevance to DFID priorities is specifically excluded
- Clinical trials of relevance to developing country issues (approx. £24m)
- Match funding for European and Developing Countries Clinical Trials Partnership (EDCTP, approx. £15m for research and £5m for capacity strengthening)
- Capacity development activities to strengthen the scientific research base for both individuals and institutions, particularly in Sub-Saharan Africa (£5m from each The MRC and DFID), including the African Research Leaders (ARL) Scheme

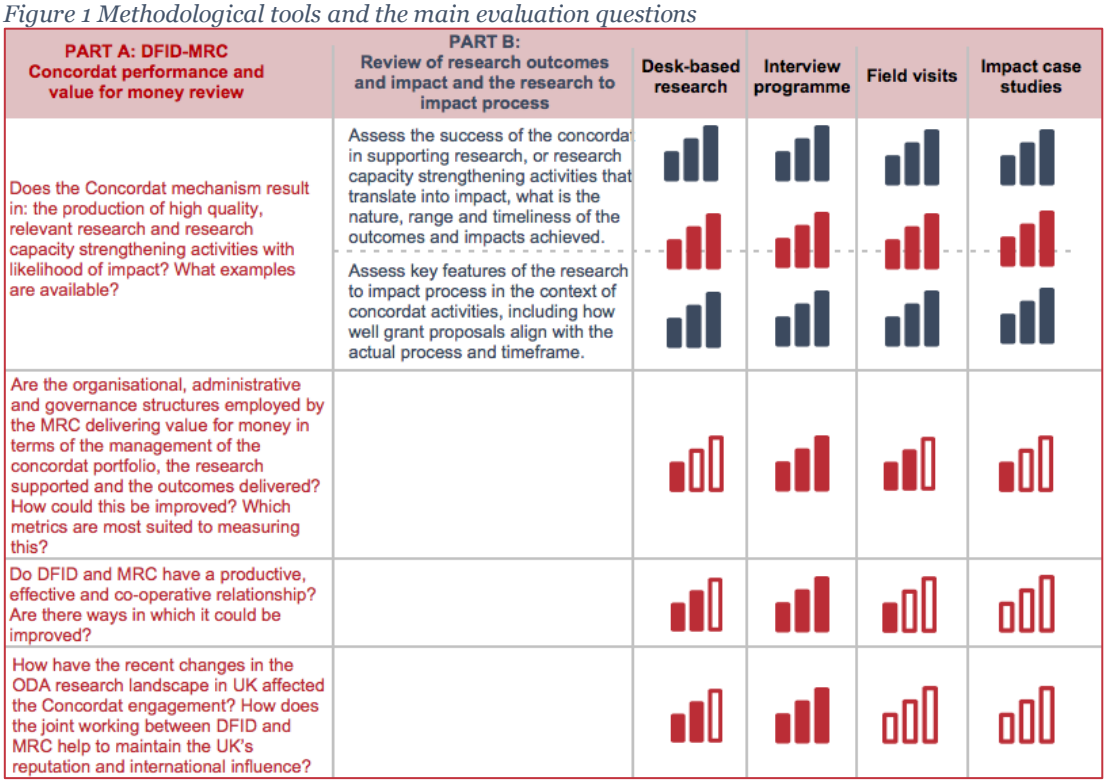
We provide a more detailed description of the different types of grants awarded under the Concordat portfolio in the appendix. This review also considers grants funded during the previous two cycles of the Concordat (2005-2013) to explore the longer-term impact pathways of the funded portfolio.

1.3 Overview of our methodology

The methodology applied in this review was designed to provide robust answers based on the collected evidence for the main evaluation questions posed by the MRC and DFID. The study built on five main data collection and analytical research components: desk research; a multi-stakeholder interview programme; field visits; impact case studies and synthesis and reporting. This section describes our approach to undertaking the assignment, and more details on the methodology are provided in the separate methodological annex.

[2] Business Case and Intervention Summary, http://iati.dfid.gov.uk/iati_documents/3952581.odt

Figure 1 Methodological tools and the main evaluation questions



Note: the red (Part A) and blue (Part B) bars represent which data collection tool addresses the given evaluation question to what extent (where 3 bars show the highest level)

1.3.1 Desk-based research

Desk-based research focused on three different sources of evidence, and entailed:

(1) Review of the documentation available on the DFID-MRC engagement activities and processes for working together, such as annual reports, the Memorandum of Understanding between the two institutions, DFID's approach to Value for Money and indicators used.[3] In addition, available documentation on the funded portfolio, such as programme level documentation, the quinquennial reviews of the MRC Units in the Gambia and Uganda, the ARL annual reports and other relevant studies, background documents were reviewed. This document review was complemented by a composition analysis of the funded portfolio that is presented in Chapter 2.2. This step also entailed reviewing and analysing the pathway to impact abstracts of the projects within the Concordat portfolio, to enable comparison with the reported impact analysis based on Researchfish (step 3 below)

(2) Rapid evidence assessment (REA) of literature and commentary on the Concordat to understand the existing evidence, views and perspectives on the performance of the Concordat and the related funding schemes that fall within its remit. The search focused on three databases to cover relevant literature sources: PubMed, Scopus and standard Google search. The scope and coverage of the review was restricted through search criteria, as agreed with the MRC and DFID during the inception phase of the study.

(3) Analysis of Researchfish data and comparison to other datasets. Researchfish is a system used to collect information on the outcomes and impacts of research funded by the MRC and over 60 other research funders.[4] It is a self-report online platform which is completed by the principal investigators

[3] Further information: https://devtracker.dfid.gov.uk/projects/GB-1-203085/documents

[4] https://www.ukri.org/funding/information-for-award-holders/research-outcomes1/

(PIs) for awards annually throughout the lifetime of the project and for at least five years subsequently. The aim of this task was to analyse the self-reported data submitted by the PIs about projects funded within the timeframe of the review for three main purposes:

1. To understand the range, nature and distribution of impacts as reported in Researchfish, across programmes, projects and geographies, and how these relate to the impact plans associated with a sample of projects
2. To investigate the time lags to impact across the portfolio
3. To support the selection of case studies and provide baseline information for those case studies

The Researchfish data was supplemented by additional portfolio data needed for this analysis which also allowed us to analyse the composition of the portfolio in terms of the range of characteristics of the awards it contains (i.e. which different funding streams are included, the size and duration of awards, and the partner countries involved).

1.3.2 Structured interview programme

Seeking the views of a broad range of stakeholders about the Concordat and the funded portfolio through an interview programme was a central element of the study. The interviewees were selected through a discussion with the MRC and DFID during the inception phase. We consulted the following stakeholder groups:

- **Group 1 -** MRC and DFID personnel, programme management, MRC board membership of the Concordat portfolio
- **Group 2 -** relevant national and international stakeholders, funding bodies and policy makers, with a special focus on those, who also provide co-funding to the Concordat funded schemes
- **Group 3 -** UK and international global health research community
- **Group 4 -** selected grant holders, including both UK Principal Investigators and developing country partners selected from across the portfolio of the different schemes

To provide additional input to Part A of the study and complement the results of the rapid evidence assessment on the Concordat, we also undertook interviews with international funders and/or programmes, where the relationships between a research funder and development agency could serve with insight and lessons learnt for the management of the Concordat. Based on the discussions with the MRC and DFID, the study team focused this element of the interview programme on consulting relevant stakeholders from the US, Canada, Norway, France and Sweden.

Figure 2 Breakdown of interviews conducted by group

Stakeholder group	Number of stakeholders identified	Interviews completed
Group 1 - MRC and DFID personnel	8	8
Group 2 – Research funders, aid agencies and policy makers	36	17
Group 3 - Global health research community	19	8
Group 4 - Grant holders	55	43
Total	**118**	**76**

In terms of the geographical distribution of the interviewees in Group 4 i.e. grant holders, the study team consulted PIs and co-investigators, further to members of the wider research team, including 9 persons in Kenya, 4 persons in Malawi, 15 persons in The Gambia and 8 persons in Uganda. All of the interviews were carried out in a semi-structured way, the majority face-to-face during the field visits and in the UK, with the others conducted over the telephone. The interview guidelines used are included in the methodological appendix. The study team consulted in total 76 people in total.

1.3.3 Field visits and impact case studies

The tasks of preparing case studies and undertaking field visits were strongly linked. The field visits were selected based on the results of a preliminary analysis of the Researchfish data and Concordat portfolio provided by the MRC. The selection criteria used, and the list of case studies put forward for the MRC and DFID to choose from are included in the methodological appendix. Based on the initial assessment of the impacts delivered across the portfolio, four countries were selected for field visits: The Gambia, Uganda, Kenya and Malawi. The field visits were undertaken in May 2018 by experienced researchers from the study team.

The purpose of the field visits was to gain insight into the impact of the Concordat-funded research at three levels:

- Individual researchers and research teams – both in the UK and in low- and middle-income countries (LMIC)
- LMIC partner institutions through capacity building
- Research partners, governmental organisations and other institutions in the LMIC ecosystem

The field visits entailed a series of consultations with stakeholders in the low- and middle-income countries including co-investigators of the Concordat-funded grants, policy makers, representatives of different international organisations, management and researchers of the two MRC Units in The Gambia and Uganda.

Ten case studies were selected in total from among the projects focusing on the four countries visited. The unit of analysis for each case study was a specific funding award (whether for a project grant or a fellowship). For each of Uganda and The Gambia, we selected the 'highest impact' fellowship award and two projects randomly selected from the top 10 most impactful project grant awards. From among the projects focusing on Kenya and Malawi, we selected two 'high impact' awards which were conducted within the same country and one additional project from each country to ensure that there is a suitable coverage across the different types of awards. The impact case studies were all prepared in a standard structure as presented in the methodological annex.

2 The MRC-DFID Concordat

2.1 Overview of the Concordat and its development over time

2.1.1 Overview of the past Concordat funding (2003-2013)

The interim (light-touch) review of the MRC/DFID Concordat carried out by the Swiss Tropical Institute[5] and published in 2012 outlined that the support provided under the Concordat was viewed as a success. Reasons given included high-quality scientific outputs (Global Health Trials), opportunities for career development and retention (African Research Leader scheme) and the matching of UK funds to broader initiatives (the European & Developing Countries Clinical Trials Partnership, EDCTP). Figure 3 provides an overview of the changes in the Concordat funding.

Figure 3 Concordat funding over time

Time period	Total Concordat	DFID contribution to Concordat	MRC contribution to Concordat	Comments
2003-08	£122m	£20m	£102m	DFID direct contribution to EDCTP and MRC direct contribution to global health trials
2008-13	£136	£45m	£91m	EDCTP and MRC Global Health trials were encompassed within the Concordat
2013-18	£90	£41m	£49m	EDCTP is encompassed within the Concordat

The 2012 review highlighted a shift towards more applied and implementation focused research from the primarily basic research projects initially, as well as an increased emphasis put on research to be carried out with/for the benefit of developing countries. Another take away from the 2012 review was the acknowledgement that the funding through the Concordat 'is in line with priority health issues in developing countries', although health systems research and health service delivery research are areas where progress has not been as fast as anticipated.[6]

The interim review also outlines a broad range of collaborations established by projects funded under the Concordat over the period. Between 2006 and 2010, Concordat funding resulted in a total of 1,457 scientific publications in journals. The geographical spread of the 230 registered co-investigators of funded activities: 15% were located in low income countries, 4% in lower-middle income countries and 76% in upper income countries.[7]

2.1.2 Theory of change of the MRC-DFID Concordat

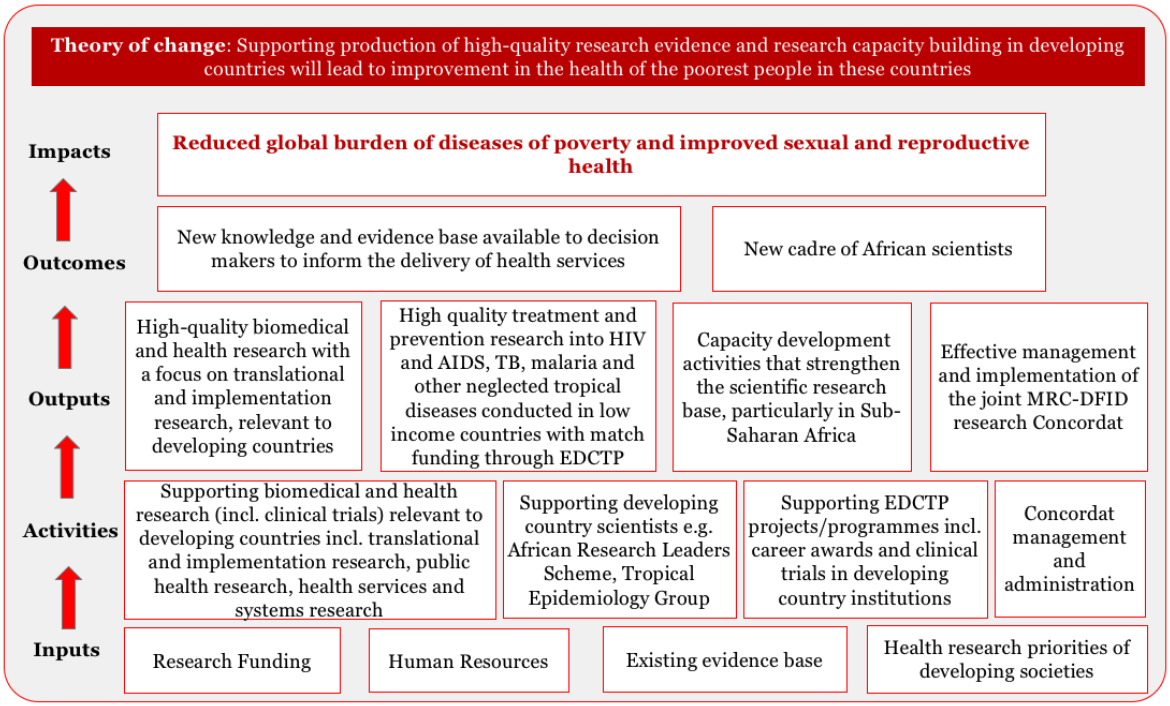
The study team developed a theory of change during the proposal phase, which still stands valid after concluding this Review (Figure 4). The theory of change has to be interpreted in the context of the MRC's Global Health Research activities which reach beyond the funding provision through the Concordat, as well as in the changing ODA landscape.

[5] Swiss TPH: Interim (light touch) Review of the MRC/DFID Concordat, 2012

[6] Ibidem

[7] Ibidem

Figure 4 Theory of change of the Concordat



The MRC funds research in two different modes: response mode and strategic schemes. Response mode funding is distributed through research boards and panels, which fund grants at multiple times during the year. Investigators have more freedom to determine their research agenda and approach. On the other hand, strategic schemes may run for just one, or a small number of, funding rounds per year and are more directive in nature. Usually, strategic calls are set up to address complex health-related issues such as antimicrobial resistance, adolescent health, or to stimulate research activity in strategic areas such as stratified medicine or methodological research. Consequently, the remit is narrower and specific criteria e.g. industrial involvement, LMIC partnerships etc. may have to be fulfilled. As part of the Concordat, the MRC Council provides funding through a variety of schemes and initiatives.

2.2 Activities funded under the Concordat

The MRC funded a large number of projects as part of the Concordat over time. We analysed the databases on the funded projects provided to the study team by the MRC to gain an understanding of the nature and composition of the Concordat portfolio. While the study team received access to the projects funded since 2005, due to the differences in database structure and content,[8] the 2005-07 portfolio was excluded from the current analysis. Additional notes on and limitations of the data, including the data cleaning steps undertaken are included in the methodological appendix of the report.

After processing the information received, the study team used a database of 317 unique research grants, 306 of which also had impact data from Researchfish. The analysis of the latter is presented in Chapter 3. The 317 projects were funded across the above described programmes and initiatives between 2008-2017, as presented in Figure 5.

[8] The 2005-2007 datasheet does not contain information on start or end date of research grants, nor does it link research grants to developing countries. Furthermore, the datasheet contains information on the type of funding associated with each research grant, but the categorisation of funding is different to data in subsequent years. More specifically, the dataset does not disaggregate between different types of intramural funding, and extramural funding is categorised using labels that do not match those in the later Concordat Portfolio files.

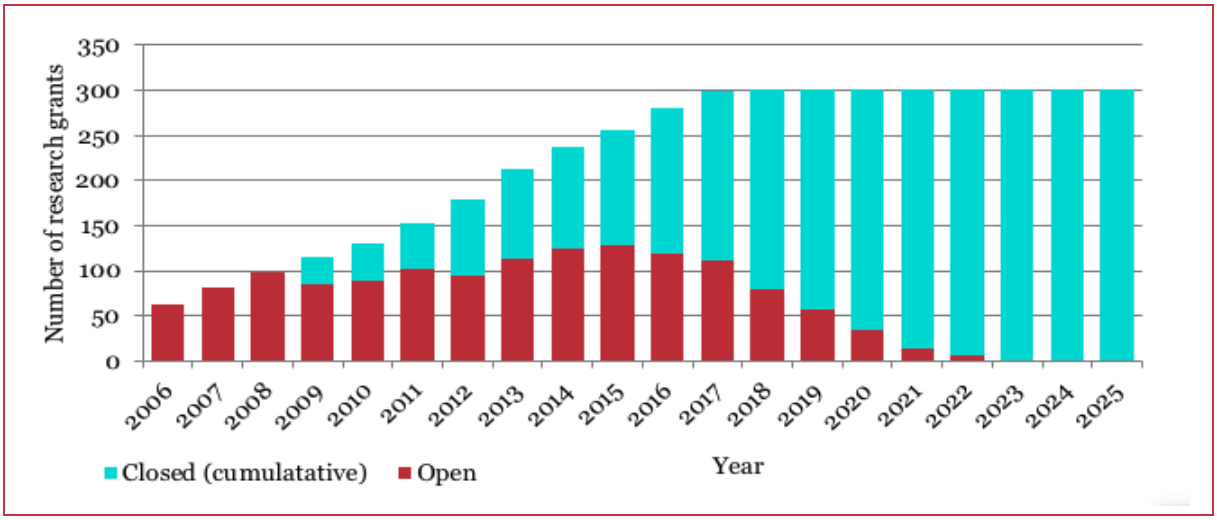
Figure 5 Number of grants per funding type in the Concordat portfolio

Broad category	Board/Panel/Scheme	Number of research awards
MRC Research Boards – response mode	Health Services and Public Health Research Board (HSPHRB)	1
	Infections & Immunity Board (IIB)	46
	Population and Systems Medicine Board (PSMB)	6
Unit programmes / Intramural MRC	Intramural Infections & Immunity Board (IIB)	111
	Intramural Molecular and Cellular Medicine Board (MCMB)	1
	Intramural Neurosciences and Mental Health Board (NMHB)	1
	Intramural Population and Systems Medicine Board (PSMB)	29
Concordat-specific funding	Implementation research to improve adolescent health in low and middle-income countries (ADH)	5
	European & Developing Countries Clinical Trials Partnership (EDCTP)	2*
	MRC Global Health (GH) trial	14
	African Research Leader (ARL) scheme	15
MRC awards with some Concordat funding	Developmental Pathway Funding scheme / Developmental Clinical Studies (DPFS/DCS)	12
	Experimental Medicine (EM)	1
	Fellowship	46
	Methodology Research Programme (MRP)	4
	Public Health Intervention Development (PHIND) scheme	16
Other MRC funding	AStar/MRC Infectious Disease scheme	1
	Biomarkers 2007 + 2008	2
	Other (Strategic funding, unknown)	4
Total		***317***

Note: * the EDCTP figures reflect the two contributions made by the UK to the EDCTP

To understand the status (closed vs ongoing) of the projects in the Concordat portfolio, the study team prepared an overview of the stock of projects that have been open and closed since 2006.

Figure 6 Number of open and closed (counted as cumulative figure) research grants in the Concordat portfolio since 2006



Source: study team analysis, based on the Concordat portfolio database

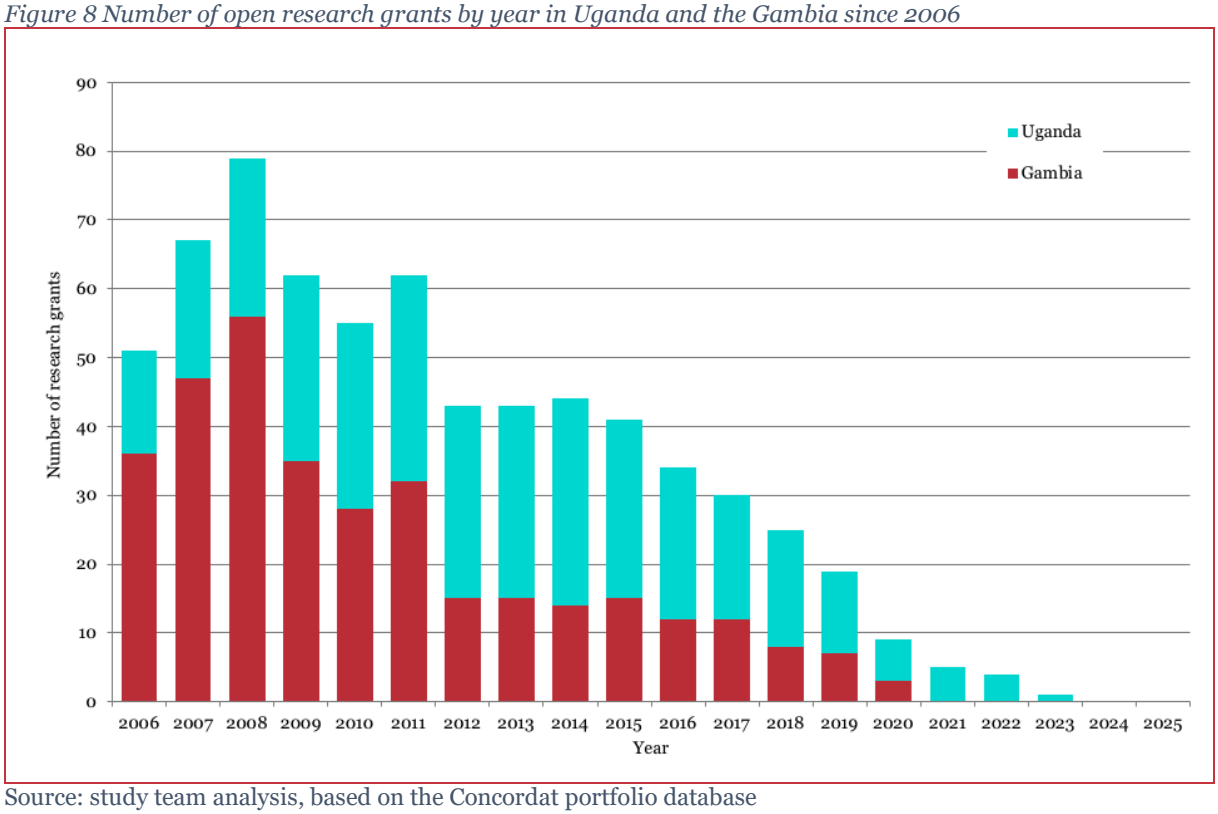
The average size of awards made through Concordat funding is £853,184, with some variation by funding type as set out in Figure 7, with Concordat specific funding in particular attracting larger awards reflecting the nature of the funding schemes within this category which include the EDCTP funding and the Global Health Trials scheme. In terms of award duration, the average length of an award within the portfolio is 4.4 years although this ranges from 0.5 years to 27 years.[9] However, this is skewed by the particularly long awards through intramural funding (where the typical award length is 5.7 years). The average duration of a funding award excluding the intramural schemes is 3.4 years. EDCTP research grants are on average the longest in the dataset, although as described elsewhere, this category includes only a small number of research grants (2).

Figure 7 Average size and duration of funding awards by award type in the Concordat (2008-2017).

Broad category	Number of research grants	Average award size	Average award duration
MRC Research Boards	53	£867,597	3.6 years
Unit programmes / Intramural MRC	142	£901,997	5.7 years
Concordat-specific funding	36	£1,506,520	4.1 years
MRC awards with some Concordat funding	79	£569,290	3.1 years
Other MRC funding	7	£697,157	3.3 years

The African MRC Units' programmes represent the largest share of the Concordat portfolio based on the number of projects granted; therefore, the Units' activities are set out in further details in the appendix.

Figure 8 Number of open research grants by year in Uganda and the Gambia since 2006

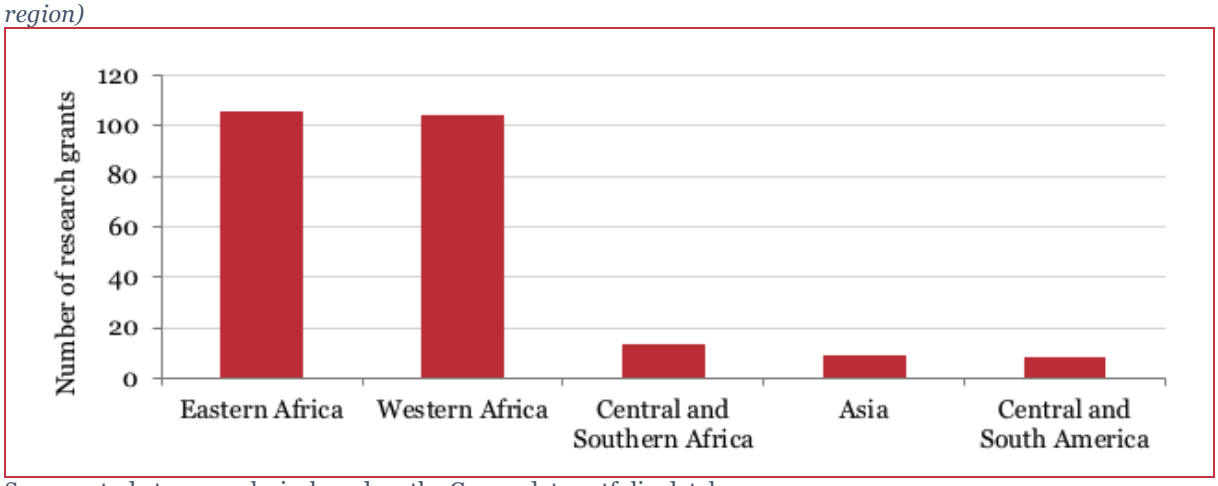


Source: study team analysis, based on the Concordat portfolio database

[9] This excludes research grants that had recorded end dates as either 2050 or 2100 in Researchfish

In total, 62 developing countries[10] were involved in the Concordat portfolio, with some research awards linked to multiple countries. The categorisation of the countries to different regions is presented in the methodological annex.

Figure 9 The majority of research awards are in Eastern and Western Africa (number of research awards by region)



Source: study team analysis, based on the Concordat portfolio database

We analysed the average grant size and project length across the regions as well to understand whether there are any differences across the portfolio. The analysis did not result in any notable differences, partially due to the small number of grants in Asia, Central and South America and Central and Southern Africa.

The projects engaged 31 different higher education and research institutions from the United Kingdom, with a large number of projects concentrated in a few of the institutions (Figure 10):

- Imperial College London – 21 projects
- Liverpool School of Tropical Medicine – 13 projects
- London School of Hygiene and Tropical Medicine – 47 projects
- University of Oxford – 25 projects
- University College London – 13 projects

These institutions ranked among the top 20 in the UK for the overall quality of their research activities (in terms of outputs, environment and impact) in the subject areas of clinical medicine, public health and biological sciences[11] in the Research Excellence Framework exercise in 2014.[12] Moreover, at least 30%, 39% and 46% respectively of the research submitted to this exercise by these institutions under the aforementioned subject areas was deemed to be 4* i.e. world-leading in terms of originality, significance and rigour.

[10] This refers to the definition of 'Developing Countries' as included in the DAC List of ODA Recipients, and does not include the countries of co-investigators linked to research grants.

[11] LSTM and LSHTM did not submit under this subject area

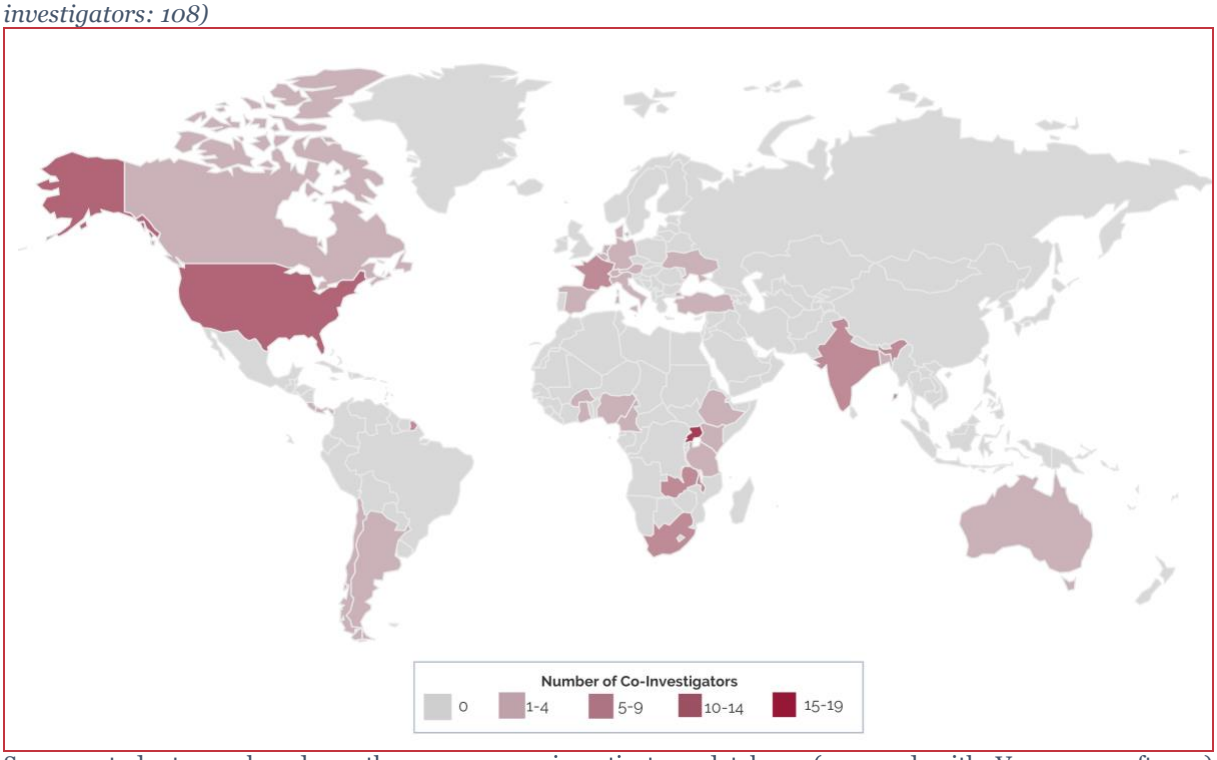
[12] Times Higher Education (2014) REF2014: results by subject.
https://www.timeshighereducation.com/sites/default/files/Attachments/2014/12/17/g/o/l/sub-14-01.pdf

Figure 10 Location of the UK institutions in the Concordat funded research projects

Source: study team, based on the Concordat portfolio database (prepared with Venngage software)

The study team also received access from the MRC to information about the co-investigators of the 2013-2017 funded projects and their country affiliation. The map in Figure 11 presents the geographical spread of the research teams, which was prepared by taking the country affiliations of the co-investigators.

Figure 11 Country affiliation of the co-investigators of the 2013-17 project portfolio (total number of co-investigators: 108)



Source: study team, based on the overseas co-investigators database (prepared with Venngage software)
Note: when a project had multiple co-investigators they were all included separately

3 Findings of the review

This chapter summarises the key findings of the review along the two main sets of study questions exploring first the Concordat performance and value for money (Part A), then the research outcomes and impacts delivered though the Concordat funded research (Part B). The findings below were formulated through analysis of all the information collected during the desk-based research, the interview programme as well as the field visits. The ten impact case studies that were prepared as part of the study with the aim to highlight the pathways to impact of the funded research are presented in the appendix in full, and they are also used as illustrative examples when describing the findings in the subsequent chapters.

3.1 Part A – MRC-DFID Concordat performance and value for money

This part of the review focused on assessing the relevance and quality of the activities funded by the Concordat, including the international reputation of the Concordat-funded research, as well as the management of the Concordat and its future role in the changing ODA landscape.

3.1.1 Awareness of the Concordat

- Stakeholders are aware of MRC and DFID funding for global health research, but are not very familiar with the Concordat or its full portfolio.
- Individual programmes such as the ARL scheme, the MRC Units in Africa and MRC-DFID funding towards EDCTP are recognised on their own merits.

From the results of the rapid evidence assessment and additional desk-based review, it is apparent that the Concordat and the partnership of the MRC and DFID has only had sporadic mentions in the literature in the past. Similarly, the interview programme highlighted that while the national and international stakeholders and funders as well as the members of the global health research community are familiar with and associate high reputation and importance to the MRC's global health research funding, and acknowledge DFID's role in aid provision, they are not very familiar with the Concordat or the specifics of its funding provisions. Over half of the national and international stakeholders and two-thirds of the global health research community members interviewed stated that they were unaware of the Concordat by name.

At the same time, most interviewees were aware of at least one programme that comprises the Concordat portfolio. The role and importance of the MRC Units in the Gambia and Uganda, MRC and DFID contributions to the EDCTP scheme, African Research Leaders awards, and the Joint Global Health Trials were recognised individually. Interviewees discussed the Joint Global Health Trials[13] as a good example of cooperation among funders.[14] However, this underlines the lack of identity associated with the Concordat among the international peer community, as the Joint Global Health Trials are not part of the Concordat portfolio. Only the MRC and DFID staff had more in-depth knowledge of the Concordat and its portfolio. Moreover, while academic members of the Global Health Group knew what the Concordat is, they were not confident about identifying programmes as Concordat-funded. One international stakeholder also raised concern about the visibility of the Concordat with the recent merging of the MRC into UKRI.

Grant holders' awareness of the Concordat is a little more even. The level of knowledge among these individuals varied from having heard the term but being unsure of the detail to full awareness of the rationale for the Concordat. Even so, many researchers reported that they were unaware of the Concordat, even when they knew about individual programmes. Field visit interviews revealed that the

[13] https://mrc.ukri.org/funding/browse/jght-8/joint-global-health-trials-scheme-call-8/

[14] Joint Global Health Trials are o-funded by the MRC, the Wellcome Trust, DFID and NIHR

requirements imposed on grant holders to acknowledge the Concordat funding, which were put in place based on the recommendations of the light touch review of the Concordat in 2012,[15] have resulted in an increased level of awareness among the grant holders of the joint MRC-DFID funding. At the same time, the term 'Concordat', its details, and the nature of collaboration between DFID and the MRC are not understood or well-known especially among the broader research team members.

3.1.2 Relevance of the Concordat

- The Concordat is responding to some of the most pressing health challenges worldwide by supporting health research and research capacity building in and concerning LMICs.
- National and international global health funders and organisations, global health experts and researchers concur that Concordat projects are broadly relevant to global health research needs and have the potential to address key societal challenges in LMICs.
- Structural and thematic gaps in the Concordat portfolio were identified by interviewees, although there was no consensus regarding them. Structural gaps concerned funder coordination, limited engagement with local stakeholders in LMICs, lack of South-South links and concentration of funding to a small number of high-performing Southern institutions. Thematic gaps were highlighted outside the infectious diseases area.

The aims and objectives of the Concordat have not changed significantly over time and remain to tackle selected priority health problems of people in developing countries as set out in the theory of change developed for the study (see Figure 4). The mode of implementation and selection of projects have, however, shown some variations, resulting in a diverse portfolio of programmes and initiatives, as described earlier in the report (see Figure 5).

Enhancing economic development in LMICs is a main goal of ODA. The Concordat contributes to fostering to this goal by providing research funding aimed at improving health and well-being, thereby aiding economic development. A consultation conducted by DFID on health research priorities in LMICs revealed non-communicable diseases as a priority for the long-term future and infectious diseases as a key area for funding reduction.[16] The importance of the early involvement of policymakers and other key stakeholders in research processes to improve research uptake as well as the need for research funding to be based on local needs were also emphasised in this consultation. Another study, focused on health research capacity development in LMIC,[17] identified three key narratives: the effect of power relations on capacity building; a demand for stronger links between research, policy and implementation; and the importance of a systems approach. It emphasised the importance of capacity outcomes to be valued as much as research outputs. The Concordat with its emphasis on capacity building and policy impact responds to these identified priorities.

The results of the desk-based research and the interview programme are highly concurrent with regards the relevance of the Concordat. The business case of the upcoming Concordat prepared by DFID[18] notes that MRC-funded research focuses on promoting excellent research to improve the health and wellbeing of society, while also supporting high-quality fundamental discovery science. The business case also notes that the latest delivery plan of the MRC set out priorities to support research into the most pressing

[15] Swiss Tropical Institute for Public Health: Interim (light touch) Review of the MRC/DFID Concordat, 2012

[16] David Mc Conalogue, Sue Kinn, Jo-Ann Mulligan, and Malcolm McNeil. 2017. "International Consultation on Long-Term Global Health Research Priorities, Research Capacity and Research Uptake in Developing Countries." Health Research Policy and Systems 15 (March 2015).

[17] Franzen, Samuel R. P., Clare Chandler, and Trudie Lang. 2017. "Health Research Capacity Development in Low and Middle Income Countries: Reality or Rhetoric? A Systematic Meta-Narrative Review of the Qualitative Literature." BMJ Open 7 (1): e012332.

[18] MRC-DFID Concordat – Business case for the 2018-2023 time period

health challenges worldwide, to explore new scientific principles and paradigms, and transform health research and innovation, such as embedding informatics and stratifying disease to tailor treatment. [19]

UK ODA is aimed at helping LMICs to progress towards the SDGs. To this end, the Concordat needs to address the priorities of the health-related SDGs which include reducing maternal mortality, ending preventable death of newborns and children under 5 years of age, reducing the communicable and non-communicable disease burden, promoting reproductive and mental health, reducing malnutrition and addressing issues such as substance abuse, and universal health coverage.[20] These are all areas that the Concordat is funding research in (See Section 2). The Concordat portfolio also encompasses some of the WHO work areas i.e. health systems, communicable and noncommunicable diseases and promoting health through the life-course.[21] One comparison of topics funded by the 10 largest funders of health research (NIH, EC, MRC, Inserm, US Department of Defence, Wellcome Trust, CIHR, NHMRC [Australia], Howard Hughes Medical Institute and DFG [Germany]) globally shows that most support research into communicable, maternal, neonatal, nutritional and noncommunicable disorders and diseases.[22]

In the neglected diseases space, overall $3.2billion were spent in 2016 with the NIH and Gates Foundations as the spenders contributing $1.3 and $0.5 billion respectively.[23] From the UK, the Wellcome Trust, DFID and MRC contributed $101 million, $56 million and $42 million respectively. SMEs and some smaller funders have been noticeably increasing their investment in this area too.[24] These include key global health initiatives (Unitaid, MSF and Gavi, the Vaccine Alliance), the Japanese government as well as governments in LMICs (particularly India, Brazil and South Africa). Notably, the LMIC countries invested more in TB, malaria, kinetoplastids, diarrhoeal diseases, dengue and leprosy than HIV/AIDS in 2016, unlike higher income countries where HIV/AIDS was prioritised more.[25]

Interviewees' opinion on relevance of Concordat activities to key societal issues in LMICs

Consistent with the desk research findings, the review found broad agreement among all types of stakeholders interviewed that the Concordat – as currently structured – is funding relevant research areas and activities. Interviewees in each group were asked whether the funding available through the Concordat addresses key societal issues in the countries targeted. Among the national and international stakeholders (Group 2) and global health experts (Group 3) interviewed, about half directly addressed this question, of which about three-fifths expressed a positive view on the relevance of the funding programmes under the Concordat in the context of key societal issues in LMICs and the SDGs. The remaining two-fifths did not wish to comment on the relevance owing to limited knowledge about the full thematic focus and range of projects included in the Concordat portfolio.

Among the comments on the relevance, it was stressed that the societal issues in LMICs are multifaceted, and this requires regular collaboration between countries and funders, and between researchers and customers. The continuity of the MRC funding calls was cited as a positive in this regard. The need to balance biomedical research with capacity building and 'non-traditional' research funding programmes was also raised as was the concern that funding may often be awarded to already well-funded institutions and activities, thus making the capacity building aspect less relevant. Another view was that the

[19] Ibidem

[20] WHO (2018) Progress towards the SDGs: A selection of data from World Health Statistics 2018. http://www.who.int/gho/publications/world_health_statistics/2018/EN_WHS2018_SDGhighlights.pdf?ua=1

[21] WHO (no date) What we do. http://www.who.int/about/what-we-do/en/

[22] Viergever, R. F., & Hendriks, T. C. (2016). The 10 largest public and philanthropic funders of health research in the world: what they fund and how they distribute their funds. *Health research policy and systems*, *14*(1), 12.

[23] Chapman, N., Doubell, A., Oversteegen, L., Chowdhary, V., Rugarabamu, G., Zanetti, R., Ong, M. & Borri, J. (2017) Neglected disease research and development: reflecting on a decade of global investment. G-FINDER 2017 Report by Policy Cures Research

[24] Ibidem

[25] Ibidem

relevance of the funding to LMIC societal priorities is guaranteed when local stakeholders in the target countries are involved in the decision-making process and hence one must be careful to consider who is 'pushing the agenda'. One global health expert suggested that the Concordat mechanism allows the MRC and DFID to mobilise resource quickly, making the funding continually reactive to emerging issues, while maintaining strong quality assurance.

Grant holders consulted on this question unanimously believe that the funds are addressing important issues in their local context, whether it is targeting awareness and treatments among specific subgroups in society, tackling particular diseases in countries or regions where they are endemic, or applying existing models to new contexts. A few examples cited in the interviews include the funding of key trials to explore childhood TB, and a 'critical lifeline' to healthcare services in a country with poor healthcare provision via the MRC Unit. Two of the researchers also expressed some caution about the degree of relevance of current activities to current needs. The points highlighted included a further need for capacity building activities and the fact that the local relevance of the activities is somewhat diminished by the lack of stronger involvement of the LMIC partner researchers in the design and development of the project proposals and research. This observation is illustrated by the example in the box below.

MR/L002515/1 Lung health and exposure to household air pollution in rural Malawi (CAPS)

This is a young investigator grant that provided protected time for the Principal Investigator, Dr Kevin Mortimer at the Liverpool School of Tropical Medicine, to dedicate his time to the larger MRC-Wellcome Trust Joint Global Health Trial project Cook stoves and Pneumonia (CAPS). The CAPS project aimed to address the lack of systematic evidence regarding the relationship between smoke and childhood pneumonia.

Pneumonia is recognised as a major burden of childhood disease in Malawi and similar developing countries.[26] However, it should be noted that some local study participants, as reported in a focus group with field officers, felt that the study did not address their health priorities (which were hernias and elephantiasis), nor was the local population consulted on the study design. The importance of clean cook stoves in Malawi is evidenced by the creation of a government appointed task force for the introduction of clean cook stoves and partners such as the Global Alliance for Clean Cook stoves who promotes the use of these cook stoves, not only for health reasons but also because of reduced fuel consumptions (helping to combat deforestation)

Interviewees' opinion on gaps in the current Concordat portfolio

Interviewees were also asked to comment on gaps (structural and thematic) in the current priorities of the Concordat portfolio.

Structural gaps were mainly identified by national and international stakeholders (Group 2) and global health experts (Group 3) in terms of funder coordination and programme features. The importance of funders' collaboration to collectively address the broad range of challenges in the global health field, in particular by discussing and agreeing priorities together was emphasised by several individuals. The partnership of a medical research funding council and an international development agency was considered a positive development in this regard. Individual suggestions included coordinating and dividing responsibilities among funding organisations globally by translating SDGs into specific programmes (though there was an acknowledgement that there is no mechanism to do this currently) and extending consultations beyond government departments in target countries, to include those who are more in the field, such as universities and NGOs.

In terms of programme-level gaps, one global health expert offered examples of an 'over-confluence' of health research-funding agendas among global actors that leaves some areas unaddressed. Among these were a lack of addressing the needs of the poor in wealthy countries (though this is not in the remit of the Concordat) and regional-scale diseases or health issues. The need for more south-south collaboration in research programmes was also raised, particularly the lack of connectivity between

[26] http://www.who.int/features/2013/malawi_pneumonia_diarrhoea/en/

centres of excellence across Africa. The focus on capacity building of individuals rather than institutions was seen as a drawback according to one comment, especially if these individuals move outside LMICs for their career. Moreover, according to one view much of the Concordat funding is allocated to already strong institutions such as the MRC Units, and the ARL grants are awarded to individuals who are in already-prominent institutions.

With regard to thematic gaps, several areas of research were identified as not being adequately funded at the moment. While there was no consensus as to these gaps/under-invested areas, they included the following areas:

- Implementation research
- Chronic non-communicable disease
- Health systems research
- Behavioural studies
- Translational science
- Broader population-based studies to examine exposure to health issues stemming from, for e.g., rapid urbanisation
- Mental health
- Maternal health
- Nutrition
- Qualitative social science
- Basic science (e.g. malaria resistance, immunology)

Using the keywords from the afore-mentioned areas (except for basic science), we investigated the NIH's WorldRePort data.[27] These searches showed that among the 728 MRC projects in the Global South (Asia, Africa, South America) in 2016, health systems and implementation research accounted for about half of the projects, while mental health, nutrition and behavioural studies combined accounted for about 19%. Chronic and non-communicable diseases as well as maternal health accounted for about 10% of projects each. It is important to note that not all these projects will be covered by the Concordat and that Concordat projects funded in the UK are excluded. There may also be some overlaps between the project categories. Nevertheless, these findings warrant further investigation of the Concordat portfolio in the context of health research priorities of LMICs.

Interviewees were also asked to comment on gaps (structural and thematic) in the current priorities of the Concordat portfolio.

3.1.3 Quality of activities supported of the Concordat/funded research

- The research supported by the Concordat is of the highest quality according to published reports and individuals interviewed.
- The MRC's robust project selection and management system is seen to be a contributor to the high quality of research funded.

The rapid evidence assessment carried out as part of the current review did not find any studies evaluating the performance of the MRC-DFID Concordat. However, the business case prepared by DFID for the upcoming Concordat period[28] highlights the research excellence arising from the MRC-funded research. This is evidenced by the high field-weighted citation impact factor for MRC-funded research overall (2.73) compared to the world average (1). Similarly, the Swiss light touch review concluded that

[27] https://worldreport.nih.gov/app/#!/

[28] MRC-DFID Concordat – Business case for the 2018-2023 time period

the portfolio procures high quality research, and put forward recommendations for some alignment in the portfolio funded to optimise its scale and scope.[29]

When asked to consider the quality of the science funded through the Concordat, the interviewees mostly gave positive views, characterising the quality of science as excellent, or very good on average, and of high quality internationally, both currently and historically. However, about one-third of those who answered this question felt unable to judge the quality of the activities supported without more knowledge of projects or their outputs.

The strong selection and peer review processes within MRC were cited as one of the reasons for the resulting high quality of outputs. In addition, the quality of and the ability of the MRC Units in Uganda and the Gambia to leverage research funding from other external funders was also mentioned as a contributing factor. One respondent acknowledged being impressed with the quality of proposals discussed during board meetings, noting in particular the presence of both LMIC representation and development expertise. Another respondent stated that historical quality is evidenced in the many "game-changing observations" from the MRC Units in Uganda and the Gambia that have improved the understanding of epidemiology.

Most respondents did not comment on the quality of capacity building activities. Among those that did (one-fifth of all interviewees), almost all were complementary about the ARL scheme. However, the Concordat's capacity building activities were seen as one among several similar activities funded by international funders in Africa, and hence it was suggested that there could be more coordination and synergy in these efforts. One international stakeholder was concerned that capacity building activities were targeting the same small number of already well-developed institutions while one global health research expert highlighted a need for further capacity building at the undergraduate, graduate and postdoctoral levels.

3.1.4 International reputation of the Concordat/funded research

- The contributions of MRC and DFID funding for global health research and research capacity building are recognised internationally for the quality of the resulting outputs and impacts.
- Concordat funding contributes to the UK's international reputation according to a majority of the stakeholders interviewed.

Individually, both the MRC and DFID, are recognised in their fields. DFID is regarded as one of the leading agencies focusing on extreme poverty around the world,[30] while the MRC is regarded as the leading UK-based funding source for biomedical research, especially in the field of infectious diseases.[31,32,33]

[29] Swiss TPH: Interim (light touch) Review of the MRC/DFID Concordat, 2012

[30] Ottersen T, Kamath A, Moon S, Martinsen L, Røttingen, JA (2017) Development assistance for health: What criteria do multi- and bilateral funders use? *Health Econ Policy Law* Apr; 12(2): 223-244

[31] Head MG, Brown RJ, Clarke SC (2018) Research investments for UK infectious disease research 1997-2013: A systematic analysis of awards to UK institutions alongside national burden of disease. *J Infect*. Jan; 76(1):11-19

[32] Head MG, Fitchett JR, Cassell JA, Atun R (2015) Investments in sexually transmitted infection research, 1997-2013: a systematic analysis of funding awarded to UK institutions. *J Glob Health*. Dec; 5(2): 020405

[33] Head MG, Fitchett JR, Cooke MK, Wurie FB, Hayward AC, Atun R (2013) UK investments in global infectious disease research 1997-2010: a case study. *Lancet Infect Dis*. Jan; 13(1):55-64

Studies show the positive impact of DFID partnerships in Sub-Saharan Africa,[34,35,36,37] mainly on capacity building through skills sharing, educational programmes, and informal health provision. The MRC is also recognised for its contributions to biomedical research beyond the UK, especially in Africa.[38]

The MRC Unit in The Gambia is a major UK investment in medical research in Africa and is currently considered one of the strongest research institutions in the continent, focusing on disease control and elimination, vaccines and immunity, and nutrition.[39] Similarly, the Uganda Unit is seen as being uniquely positioned to address health systems questions in Uganda and across the region with great potential for facilitating the delivery of interventions against HIV and NCDs, for example.[40]

The REA exercise revealed that in 2007, the MRC-DFID Concordat was referenced in the Science and Technology-Ninth Report.[41] In this document, the impact on vaccination programmes and the elimination of Hib –a form of meningitis- as a result of research done at the MRC Unit in The Gambia is used as an example of the value of partnerships between DFID and UK Research Councils. The MRC and DFID are also mentioned in the 2009 progress report on the implementation of the European Programme for Action to Confront HIV/AIDS, Malaria and Tuberculosis through External Action,[42] as the main UK link with the EDCTP, thus adding to their joint international reputation.

The MRC-DFID Concordat model was referenced in a report for Australian funding of global medical research[43] as an example of successful joint funding of global health research in terms of quality and quantity of research outputs, referring to their policy impacts and emphasis on collaborations with developing countries. This report also mentioned that 60 per cent of the awards supported by the MRC-DFID Concordat in 2013/2014 reported at least one policy impact, and 44 per cent of projects were led by a co-principal investigator from a developing country.

Interviewees were asked whether the Concordat contributed to the UK's international research reputation. All groups were positive in this regard. National and international funders offered further explanations that this is because i) researcher engagement reflects joint interests – i.e. good people looking to work with other good people – which is a significant; ii) that specific activities such as the ARL and MRC Units in Uganda and the Gambia are well known and well-regarded in Africa, and ii) the funding is 'aspirational' and highly sought after. Nonetheless, one LMIC stakeholder suggested that the activities are too ad hoc to have much reputational impact. Among global health experts, half of those who answered the question did not feel able to comment, but the other half agreed that the Concordat did indeed contribute to the UK's international research reputation. The vast majority of grant holders

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[34] Jack BA, Kirton JA, Downing J, Frame K (2015) The personal value of being part of a Tropical Health Education Trust (THET) links programme to develop a palliative care degree programme in Sub Saharan Africa: a descriptive study of the views of volunteer UK health care professionals. *Globalization and Health* **11**:47

[35] Kinnear JA, Bould MD, Ismailova F, Measures E (2013) A new partnership for anesthesia training in Zambia: reflections on the first year. *Can J Anesth/ J Can Anesth* **60**:484-491

[36] Sudhinaraset M, Ingram M, Lofthouse HK, Montagu D (2013) What is the role of informal healthcare providers in developing countries? A systematic review. *PLoS ONE* 8(2): e54978. doi:10.1371/journal.pone.0054978

[37] Campbell J, Jones I, Whyms D (2011) "More money for health - more health for the money": a human resources for health perspective. *Human Resources for Health* **9**:18

[38] Green A (2018) A new paradigm for the MRC Units in The Gambia and Uganda. *Lancet –World report* Vol 391.

[39] Green A (2018) A new paradigm for the MRC Units in The Gambia and Uganda. *Lancet –World report* Vol 391.

[40] MRC Global Health Group: Minutes of Meeting 29th September 2016

[41] House of Commons (2007) Science and Technology –Ninth Report. https://publications.parliament.uk/pa/cm200607/cmselect/cmsctech/472/472we19.htm

[42] European Scrutiny Committee (2009) Commission Staff Working Document: Progress report on the implementation of the European Programme for Action to Confront HIV/AIDS, Malaria and Tuberculosis through External Action (2007-2011) – The EU And HIV/AIDS, Malaria and Tuberculosis in Sub-Saharan Africa. https://publications.parliament.uk/pa/cm200809/cmselect/cmeuleg/19xxvii/1922.htm

[43] Burkot C and Howes S (2017) Australian funding of global medical research: how to scale up? Development Policy Centre. http://devpolicy.org/publications/reports/Australian-funding-global-medical-research.pdf

and researchers also agreed. They elaborated that i) the funding is life changing in low income countries, ii) the MRC is highly regarded, and the Units in Uganda and the Gambia well known, and iii) the quality of funded outputs and funded scientists is notably high.

3.1.5 The management of the Concordat and value for money

- The Concordat portfolio is solely administered by the MRC.
- Quarterly management reviews and the MRC's Global Health Group are the main platforms for interaction between the MRC and DFID personnel.
- Outputs, outcomes and impacts of the funded projects are tracked through self-reporting by researchers in the Researchfish database. However, capacity building impacts do not appear to be captured adequately.

As already mentioned, while both DFID and MRC provide funding under the Concordat, the MRC is the sole administrator for the portfolio of Concordat-funded activities. The MRC also represents DFID's interests externally, for instance, in EDCTP. The relationship has been quoted as being "strong and open", providing "a platform for both agencies to discuss and develop new ideas and to fill gaps in the research base".[44] The working relationship includes Quarterly Management Review meetings involving staff from both organisations and DFID representation on the MRC Global Health Group, which allows it to actively contribute to MRC's global health research strategy. [45]

According to interviews with MRC and DFID staff, it appears that the Concordat has enabled MRC to undertake a broader spectrum of activities, for instance, in areas like capacity building and applied research in LMICs including health systems research, clinical trials and implementation research. The relationship has been mutually beneficial in the eyes of the DFID and MRC staff interviewed. DFID can make use of the MRC's knowledge and expertise in global health and grant management while the MRC can benefit from DFID country offices and their knowledge of research priorities in LMICs. In addition, since it is a long standing relationship, there is mutual trust and engagement and working together is a comfortable experience according to one interviewee. Moreover, the Concordat has acted as a platform for further cooperation between the MRC, DFID and other funders such as the Joint Global Health Trials programme (with The Wellcome Trust and NIHR) and the Health Systems scheme (with ESRC).

The most common critique of the Concordat by the stakeholders consulted in this area is a lack of visibility of DFID in the partnership. The role of DFID is seen by them as a funder behind the scene, although they are involved in the discussions about prioritisation and the direction of funding allocations, their role is not visible to external stakeholders. This is not only true for the LMIC partners, but even the UK PIs reported no contact nor any information on the DFID involvement. At the same time, those consulted in interview with a view, found the relationship between the MRC and DFID as positive or potentially positive.

This opinion is echoed by the national and international stakeholders as well as global health research experts we interviewed. These interviewees reiterated that the Concordat offers DFID the ability to tap into the MRC's well-developed processes for funding and managing research, and that it also provides both the DFID and the MRC to influence each other's priorities. One global health research expert felt that DFID involvement has boosted the MRC's interest in global health and ensures the best use of taxpayers' money. National and international funders felt that greater coordination between research funders and development aid agencies is important, and that the MRC-DFID partnership is a very good example of how such organisations could work together. Indeed, Written Evidence ordered by the House of Commons for the Science and Technology-Thirteenth Report on DFID in 2004 referenced the Concordat and acknowledged the joint efforts to create a mechanism for the MRC and DFID to combine their research efforts in support of developing countries. The report used the MRC-DFID funded

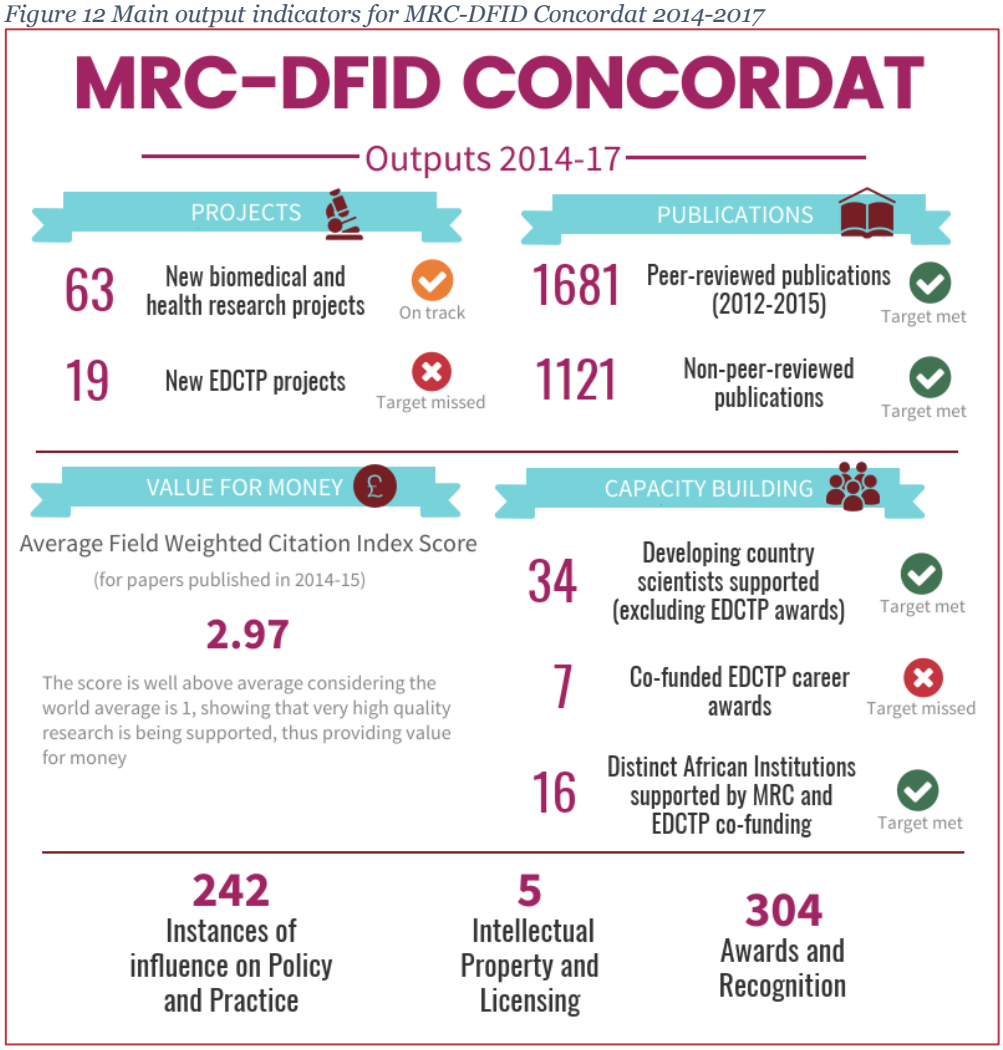
[44] Based on DFID-MRC Concordat Annual Report (2017)

[45] Ibidem

randomised trials of insecticide-treated bednets in 1982 that led to 30 per cent decrease in infant mortality as an example of successful cooperation.

In terms of monitoring the Concordat activities, the outcomes and outputs are reported annually (in Annual Reviews) against set indicators and evaluated against set targets (see Figure 12). Effective management and implementation of the Concordat is also seen as a major output and is monitored against indicators such as Quarterly Management Reviews between DFID and MRC and an external independent evaluation of the Concordat during the term of the Concordat.[46]

Figure 12 Main output indicators for MRC-DFID Concordat 2014-2017



Source: Technopolis, based on DFID-MRC Concordat Annual Reviews

In addition, grant holders are required to report outputs, outcomes and impacts through the Researchfish system. Among grant holders there were mixed feelings about Researchfish when discussing reporting and monitoring requirements. Two-thirds of the grant holders were happy with the system, citing it as "not too time consuming" and covering most types of outputs and areas of impact. However, one-third of those interviewed characterised Researchfish as not user friendly (e.g. when reporting for consortia where only a sub-set of partners receive Concordat funding) and limiting in terms of what can be reported (i.e. outputs rather than outcomes or impacts, and nowhere to include research communication activities like talks to academia).

[46] DFID-MRC Concordat Logical Framework (Published 07/2017) http://iati.dfid.gov.uk/iati_documents/8572672.xlsx

The flexible approach adopted for project management was appreciated by the grant holders interviewed as was the low administrative burden compared to other funders. Proposal selection is seen as robust, based on peer review of past performance - a strong motivation for high quality research by the UK PIs. In our view, the MRC could however also consider capturing the performance of the LMIC partners more effectively as well as the capacity building elements of the projects and the impact thereof. The current reporting system – except for the ARL scheme – leaves little room for early signs of progress and therefore the possibility for intervention or assistance, if needed.

Interviewees across all groups were subsequently asked to recommend suitable metrics to capture the broad array of impacts possible through Concordat funding. Many suggested standard quantitative indicators, such as citation impact, publications (which could also measure collaborations), applications for further funding, students/PhDs trained, etc. In addition to this, one global health research expert suggested the collection of more proximal indicators of impact, for example the number of policy makers influenced through the research activities, number of people sanitised, etc. There were strong views as well on the use of qualitative reporting, with the suggestion to introduce high-level narratives on the accomplishments of projects, similar to the UK REF case studies of impact on policy and practice. Interviewees suggested that this could better capture the impact of, for example, the MRC Units in the Gambia and Uganda, which were described as gamechangers in the fields of malaria and HIV/Aids, and also the impact of capacity building activities in terms of individuals' trajectories and development of regional capabilities. One interviewee also suggested the use of final reports to understand the research impacts and pathways to impact better.

3.1.6 Value for money

- The Concordat presents good value for money through the efficiencies emerging from joint working, particularly grant administration costs saved by DFID through using existing MRC management processes to deliver the Concordat.
- The partnership also offers value for money by promoting synergy and complementarity through pooling of resources, greater critical mass and avoidance of duplication and by facilitating the production of high quality research outputs.

As stated in the Business Case and Intervention Summary,[47] through the Concordat arrangement DFID wishes to take advantage of the MRC's expertise and reputation for funding the highest quality health-related research and its transparent, trusted and mature research management processes (including its peer review college), an expertise that it does not have in-house. Similarly, the MRC can make use of DFID's international networks and increase the breadth and volume of its activities in developing countries. As such, the view from the MRC and DFID is that the partnership allows complementarity and synergy resulting in greater critical mass, avoidance of duplication and better value for money than working individually.

This point was reiterated in the interviews. Apart from MRC and DFID staff, national and international partners and funders as well as members of the global research community remarked that such a relationship offers significant added value. For instance, DFID would have to invest considerable resources to develop the capacity to fund research projects in a responsive mode and run a peer review process. One DFID interviewee commented that MRC provides exceptional value for money for DFID in terms of the very small amount it has to spend on the administration of the Concordat. Interviewees also suggested that pooled funding allows for more flexibility, also adding that it is possible to support projects of greater scale than individual funders may be able to alone. One international stakeholder remarked that the relationship also allows projects to consist of both research and capacity building elements with limited constraints in terms of reporting and management of resources.

[47] http://iati.dfid.gov.uk/iati_documents/3952581.odt

In the DFID business case and the annual reviews, value for money assessment and the indicators-related use the method of the Independent Commission for Aid Impact (ICAI).[48] These focus on whether the objectives are realistic and appropriate; the programme has robust delivery arrangements in place to support the achievements of these objectives; whether the programme has transformational, positive and lasting impact on the lives of the intended beneficiaries and lastly whether the programme incorporates learning to undertake future improvements?[49] The main selected value for money indicators included in the annual reports are:

- The volume and quality of evidence produced
- Mean Normalised Citation Index (NCI) score50 (international score indicating quality of published research) remains above average

In 2017, the indicator was changed from the Mean Normalised Citation Index (NCI) which had been used in previous years to the Field Weighted Citation Impact (FWCI) score, a method used by Elsevier. The FWCI takes account of differences in size, disciplinary profile, age and publication type composition. An FWCI score of 1 means that the paper is being cited as frequently as the world average for its subject area. The FWCI score of Concordat Publications has ranged from 3.05 for 2008-9 to 2.52 for 2012-13, the latest figure being 2.97 for 2014-15. [51] This indicates that Concordat publications are cited well above the world average. The programme is hence seen as presenting very good value for money in terms of producing high quality research, which is one of the main aims of the Concordat funding.

3.1.7 The Concordat in the Official Development Assistance (ODA) funding landscape

- The Concordat funding is part of the UK Government's committed spend (0.7% of Gross National Income) on ODA along with the Global Challenges Research Fund and the Newton Fund.
- Global health research and development is increasingly being funded by public-private partnerships involving businesses, government funders and NGOs.
- Global health research funding is greatly focused on developing interventions against infections and infectious diseases.

The UK Government is committed to spend 0.7% of the UK's Gross National Income (GNI) on ODA. DFID monitors and reports on the ODA spend against the target set to the OECD Development Assistance Committee (DAC) on behalf of all Government Departments. DFID has been in charge of the largest share of UK ODA allocation in the past, however recently an increasing share is spent by other Departments, such as the Health and Social Care, the Foreign and Commonwealth Office as well as the Business, Energy and Industrial Strategy (BEIS).

An important new element of the ODA funding landscape was the establishment of the Global Challenges Research Fund (GCRF) in 2015, in addition to the already existing Newton Fund targeting bilateral activities. The GCRF provides funding to UK-led research in addressing global challenges in areas which have the largest impact on developing countries. The funded activities support research and innovation capacity building in developing countries, while representing the UK's national interest. Projects with the largest potential impact are to be funded across selected challenge areas. The GCRF is also creating strategic GCRF Challenge portfolios. The challenge portfolios reflect the UN Strategic Development Goals (SDGs), and of relevance to this review, Global Health is included among the initially

[48] https://icai.independent.gov.uk; ICAI's Approach to Effectiveness and Value for Money

[49] DFID: Business Case and Intervention Summary for the 2013-18 time period

[50] NCI is a score based on the number of publications citing the article and normalises the score using the relative number of publications citing other articles in the same journal or the same research category worldwide in the same year. An NCI score of 1 means that the article was cited the worldwide average number of times for its subject area. The NCI average for the UK is usually 1.3-1.4. A paper is considered highly cited if it has an NCI of 4 and around 5% of papers published in the UK achieve this.

[51] Based on DFID-MRC Concordat Annual Report (2017)

selected ones. The GCRF is administered through Delivery Partners (DPs) including UK Research and Innovation (UKRI), the four higher education academies, the UK Space Agency, and the four national higher education funding councils. Due to the creation of the GCRF and funding allocation to global health through this new channel, the funding from DFID through the Concordat will be reduced in the upcoming five-year period. From the previously allocated amount of ca. £9m per annum (total of £41m), the new Memorandum of Understanding between the two organisations foresees a total DFID contribution of £25m. The reduction of DFID funding has however to be considered in the broader funding landscape. Based on the consultations undertaken with the MRC and DFID personnel, the new funding landscape represents a reallocation of distribution channels rather than a reduction of total funding allocated to global health funding.

Global health funding in terms of health research and development has increasingly been led by public-private partnerships. The main funders in public-private partnerships to date have generally been foundations rather than governments, with 40 per cent of all health research in high-income countries funded through public and philanthropic organisations.[52] The focus of public-private partnerships in product development is "neglected diseases", managing a multi-candidate approach, with a public health objective rather than a commercial aim.[53] Non-governmental organisations (NGOs) also play an important role in global health research, contributing at all stages of the research cycle and playing a key role in promoting and advocating for research, resource mobilisation, capacity building, and knowledge generation and management.[54] The benefit of NGOs to research comes mainly through their knowledge of and presence in local communities, increasing the relevance of research to communities.

Funding agencies that support global health research for development have also seen a rise in number and scope of projects over the last 25 years. In 2005, the Global Health Research Initiative[55] was established in Canada consisting of a partnership between five governmental agencies (Canadian Institutes of Health Research, International Development Research Centre, Health Canada, Canadian Agency for International Development and Public Health Agency of Canada). This partnership has supported research, capacity building and knowledge transfer and exchange on a wide range of topics over 45 countries. An examination of 14 research teams supported by this partnership revealed six main themes in work funded through the partnership: excellence in research, long-term visions and time frames for research, focus on implementation, partnerships, ethical foundation, and skilled people.[56] This evaluation also found three priority areas that donors and institutions need to address to encourage strategic thinking and actions to achieve innovative and effective global health research: they should have a clear conception of what they support; they must invest in research on how to evaluate the short-term contributions and forecast long-term impacts; and they must be people-centric.

Looking at existing evidence with regards to the lessons about collaboration between international development organisations and health research funders, partnerships between biomedical research agencies and developmental agencies are expected to accelerate testing, distribution, and adoption of the new technology by assessing the economic landscape, coordinating R&D and business development, and supporting innovation.[57] One example is the multi-lateral partnership between the Clinton Health

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[52] Røttingen JA, Regmi S, Eide M, Young AJ, Viergever RF, Ardal C, Guzman J, Edwards D, Matlin SA, and Terry RF. 2013. "Mapping of Available Health Research and Development Data: What's There, What's Missing, and What Role Is There for a Global Observatory?" Lancet (London, England) 382 (9900): 1286–1307.

[53] World Health Organization (2012) Research and Development to Meet Health needs in Developing Countries: Strengthening Global Financing and Coordination. http://www.who.int/phi/implementation/CEWG_Report_5_April_2012.pdf?ua=1

[54] Delisle H, Roberts JH, Munro M, Jones L, and Gyorkos TW. 2005. "The Role of NGOs in Global Health Research for Development." Health Research Policy and Systems 3 (1): 3.

[55] IDRC (2017) Global Health Research Initiative. Available at: http://ghri.ca/

[56] Stephen C, and Daibes I. 2010. "Defining Features of the Practice of Global Health Research: An Examination of 14 Global Health Research Teams." Global Health Action 3 (1): 5188.

[57] Abbas JJ, Smith B, Poluta M, and Velazquez-Berumen A. 2017. "Improving Health-Care Delivery in Low-Resource Settings with Nanotechnology: Challenges in Multiple Dimensions." Nanobiomedicine 4 (January): 1849543517701158.

Access Initiative, Unitaid, DFID, Medicines for Malaria, and the governments of Uganda, Nigeria, Malawi, Kenya, Cameroon, and Zambia, aimed at addressing the barriers for injectable artesunate, a more effective treatment of severe malaria. Another example comes from the International Partnership for Microbicides (IPM) funded by the Belgian Development Cooperation, DFID, SIDA, and the Canadian International Development Agency among others. IPM has contributed with the development of multipurpose prevention technologies in the field of sexual and reproductive needs.[58] Another initiative funded by DFID, the French Development Agency, EDCTP, and others is the Visceral Leishmaniasis Global R&D & Access Initiative aimed at developing affordable drugs and strengthening cross-regional coordination.[23]

International outlook

- Partnerships between research funders and development aid agencies/ministries also exist in Norway and France.
- In both cases, the research funders select and manage the projects, but priorities and activities are driven by the development agency or ministry in question and their chosen priority countries.

As part of the current review, an international benchmark exercise was also undertaken to understand lessons learnt and key elements of the partnerships between medical research funders and development aid agencies from other countries. In particular, we studied the Norwegian and French examples of partnership programmes, since they were developed in different systems, and can serve as good practices and lessons learnt on transferability:

- The GLOBVAC programme of the Research Council of Norway (RCN) and the Norwegian development Agency (NORAD), and
- Agence Nationale de Recherche sur le Sida[59] (ANRS) and the French Ministry for Europe and Foreign Affairs
- NIH Institutes and Centres and USAID

The Research Council of Norway funds research across all disciplines in Norway. The GLOBVAC programme started in 2006. The primary objective of the programme is to support high-quality research with potential for high impact that can contribute to sustainable improvements in health and health equity in LMICs. The secondary objectives of the programme are to:

- Strengthen internationally competitive and sustainable research groups and institutions in Norway
- Strengthen national and international research collaboration and partnerships
- Strengthen capacity of research groups and institutions in LMICs by supporting collaborative research and training, and
- Increase awareness of the need for global health research among policymakers, researchers and the general public

The programme has a wide scope but gives the highest priority to projects in the following thematic areas: i) Prevention and treatment of, and diagnostics for, communicable diseases, particularly vaccine and vaccination research; ii) Family planning, reproductive, maternal, newborn, child and adolescent health; iii) Health systems and health policy research; iv) Innovation in technology and methods development.

GLOBVAC has a work programme which was agreed upon in 2012 (until 2020), and it is steered by an external programme group. The programme is run through open calls and applications or projects are

[58] UAEM. RE:ROUTE - A map of the alternative biomedical R&D landscape. http://www.altreroute.com/assets/download/UAEM_Reroute_Report.pdf

[59] National Agency for Research on AIDS and Hepatitis

reviewed by a process panel and judged upon their quality and their coherence with the GLOBVAC work programme.

In France, the Ministry for Research provides the bulk of the ANRS budget, but the Ministry of Health and the Ministry of Foreign Affairs also contribute. There is no specific agreement between the ANRS and the ministries, rather allocation letters for funding are issued. The ANRS is an autonomous body. The ANRS is quite a unique organisation in the French research landscape which was created in 1998. It focuses on HIV and viral hepatitis research in both high- and low– and middle-income countries. The ANRS has no laboratories of its own, it 'borrows' researchers from IRD, Institut Pasteur, CNRS, Inserm, and CNRS. The ANRS uses in general two annual calls for research proposals – although provides additional funding outside of these calls as well - and funds those that are selected by an international advisory committee. The relevance of prioritised subjects is validated yearly by an international scientific board and is reviewed in light of the progress of research programmes.

Both for the Research Council of Norway/GLOBVAC and ANRS, the projects funded incidentally reflect the aid priority countries of respectively NORAD and the Ministry of Foreign Affairs.

The USAID is funding national research thanks to special agreements and contracts with a myriad of research teams at NIH (27 Institutes and Centres) and other non-public teams like not-for profit organisations such as the Bill and Melinda Gates Foundation, or private research organisations such as the Howard Hughes Medical Institution and disease focused organisations such as the American Cancer Society. But all research projects are selected through a tendering process, and on the basis of project proposals. Financed topics include: i) Infectious diseases (Ebola, HIV/AIDS, Malaria, Tuberculosis, Zika), ii) maternal & child health (MCH), iii) mobile Health (mHealth). USAID would focus on new technologies, interventions and strategies including vaccines, medicines and diagnostics, and also on strengthening health systems and its core functions such as human resources, information, governance, finance, medical commodities and service delivery. Some funding is channelled through private Foundations such as the Bill and Melinda Gates Foundation is a private institution, which at times can also be co-funding projects. USAID's Bureau for Global Health would support health programs in partner countries, advance research and innovation in relevant areas, and transfer new technologies through its programmatic work.

The ANRS support is not only financial, the agency oversees projects from conception to completion through continuous dialogue with the research teams and by making available human and technical resources and assistance to logistics. These activities form an integral part of the Agency and are linked to the scientific priorities of the ANRS. They are designed to mobilise teams and researchers involved in the fields of HIV or viral hepatitis research and to help with the design, review and writing of research projects.

In the last years, the funding of ANRS from the Ministry of Foreign Affairs and Ministry of Health has drastically decreased, due to financial constraints and reorientations of international aid to multilateral bodies, notably the Global Fund to Fight Tuberculosis, Malaria and HIV/AIDS. Some funding has even been channelled through the 5% Initiative of Expertise France, which is funding operational research in LMICs since 2012, and to which ANRS has recently decided to apply for funding.

In Norway, ministries have sectorial responsibility for funding research in their fields (e.g. agriculture, health). They predominantly use two mechanisms. A direct one, that takes the form of national competitions on a predefined research topic, which is open to all research institutions, and is validated by external experts. Alternatively, they can provide funding through the Research Council of Norway (RCN). The RCN runs open calls without any predefined research topics and it handles the call procedures in its entirety from tendering to selection. While the RCN do not have specific contracts with ministries, it receives annual funding letters specifying the scope, budget, goals, and areas to be covered. Concerning the GLOBVAC programme, the RCN receives an allocation letter from the Ministry of Foreign Affairs (MoFA) through Norad which sits on the GLOBVAC board, including not only the scope, budget, goals and areas, but programme guidelines including specification for the funding as well. In

terms of selecting the funded portfolio, when the RCN identifies any gaps in the project portfolio, the decision for change is first agreed with Norad and MoFA to ensure that the changes suit their research agendas. The dialogue only focuses on strategic level, and operationalisation remains with the GLOBVAC programme management at the RCN.

To ensure that capacity building efforts are maximised, and the best quality research is funded, the GLOBVAC programme management and Norad have annual meetings where they discuss the reporting and general programme directions including the anticipated outputs, outcomes and impacts. The results are captured by and presented in the annual programme level reporting which are also made publicly available.

The GLOBVAC programme uses a set of indicators which were defined specifically for the programme in compliance with the RCN guidelines. Similarly, to DFID, there is no programme level indicator used to capture impacts. Instead, at the selection stage, the set of impacts sought were identified, and the projects are expected to provide self-reporting on early signs of impact. This information however does not form part of the statistics collected on the projects. The French example shows a similar approach, since very few indicators are reported, and those predominantly focus on the use of inputs, such as budget spending and human resources. The USAID does not require reporting from the research projects and is not requiring specific indicators on research conducted.

The indicators collected by RCN include: : i) data on gender balance, ii) number of programme board meetings; iii) number of active projects; iv) number of proposals approved; v) number of completed projects; vi) number of project managers (man/women) by geographies ; vii) number of postdoctoral fellows (man/women); viii) number of conferences and events; ix) scientific publications by type; x) dissemination activities by type; xi) innovation results by type; xii) type of research funded (basic, applied, development, demonstration); xiii) topic of research funded (medicine, social sciences, basic medical sciences, health sciences including clinical); xiv) type of project partners (in higher education, institute, industrial sector, from regional health authorities); xv) type of international cooperation (project collaboration, mobility grants, stimulation packages, hosting, collaboration on proposals).

Hence when comparing with other systems, the MRC-DFID Concordat appears very well tuned. One aspect which could be improved though are the reporting requirements, i.e. qualitative reporting and indicators. In Figure 13 we summarise the indicators used for monitoring of the MRC-DFID Concordat and the Research Council of Norway's GLOBVAC programme and comment on their suitability.

Figure 13 Comparison between MRC-DFID Concordat and RCN GLOBVAC indicators

Topic	MRC-DFID Concordat	GLOBVAC	Comments of the study team
Impact Indicators	Reduce child mortality, improve maternal health and combat HIV and AIDS, malaria and other diseases		The MRC-DFID indicator covers several impact areas and has no defined targets or monitoring scheme in place. If impact is to be measured against progress towards SDGs, then this should be made explicit. An indicator on number of policy makers influenced through the research initiative would help.
Outcome Indicators	Citation of Concordat funded research publications using Normalised Citation Index Score or Field Weighted Citation Impact Score		This is a useful indicator to compare the citation impact of the research funded against the world average.
	Percentage of projects currently funded through the Concordat with PI or co-PI from a developing country institution	Number of project managers (man/women) by geographies Type of project partners (e.g. higher education / research institute, business, regional health authority)	Monitoring gender balance as well as geographical balance of PIs and co-PIs could be something for MRC/DFID to consider. RCN indicators also allow a better understanding of the type of

Topic	MRC-DFID Concordat	GLOBVAC	Comments of the study team
		Type of international cooperation (project collaboration, mobility grants, stimulation packages, hosting, collaboration on proposals)	collaborations and partners supported
Output Indicators: Research	Number of new proposals/applications approved	Number of proposals approved Number of active projects Number of completed projects Type of research funded (basic, applied, development, demonstration) Topic of research funded (medicine, social sciences, basic medical sciences, health sciences including clinical)	MRC/DFID could again consider using RCN's indicators to get a better idea of ongoing and completed activity as well as the relative balance between the different activities undertaken. For example, MRC and DFID put an emphasis on translational research, but current indicators do not capture data on how the field is represented in the portfolio.
	Number of publications from Concordat funded projects	Number of scientific publications by type (high impact journal, local journal)	Journal impact factor is a flawed metric and hence number of publications in high impact journals is not a suitable indicator. However, type of journal e.g. subject area, language, local or international could provide an indication of likely audience and reach.
	Number of: Dissemination to non-academic audience Influence on policy & practice Research materials made available IP & licensing Awards & recognition	Number of conferences and events Dissemination activities by type Innovation results by type	The MRC-DFID indicators are more comprehensive in covering different pathways of impact.
	Number of EDCTP projects/programmes supported with UK funding		Indicator specific to MRC-DFID co-funding of EDCTP
	Overall number of UK co-funded EDCTP approved proposals with Southern Principal Investigator		Indicator specific to MRC-DFID co-funding of EDCTP
Output Indicators: Capacity Building	Overall number of developing country scientists supported (disaggregated by sex)	Number of postdoctoral fellows (man/women)	Additional disaggregation by career stage could provide information on how capacity building is supported across the career pathway
	Number of developing country scientists with support by UK co-funded EDCTP career awards (disaggregated by sex)		Indicator specific to MRC-DFID co-funding of EDCTP
	Number of distinct African Institutions supported by MRC and UK co-funded EDCTP career awards		This indicator can help monitor spread of capacity building and disaggregation of numbers by region could provide further information on this.
Output Indicators: Management	Quarterly management reviews with DFID and MRC officials	Number of programme board meetings	The milestones for this MRC-DFID indicator concern informing awardees of DFID funding and introduction of mandatory pathway to impact statements. It is not clear how these represent effective management.

Topic	MRC-DFID Concordat	GLOBVAC	Comments of the study team
	External independent evaluation of the Concordat		

3.2 Part B – Research outcomes and impact

The aim of this part of the review was twofold:

1. To assess the success of the concordat in delivering a range of research outcomes and impacts, and to characterise the nature, range and timeliness of these impacts.
2. To provide evidence on the research to impact process for concordat-funded research including how well grant proposals align with the practical processes of research translation and implementation.

Based on our rapid evidence assessment, there are no prior studies which provide an overall picture of the impact of the MRC-DFID Concordat overall, though several studies point to the impacts and outcomes of specific funded research. The evidence in this section also draws on the findings of the interview programme (including field visits in selected countries) which provided many useful insights into the results of the funded research, in particular the impact delivered. In addition, the assessment of all funded projects, through the analysis of Researchfish data, highlighted a range of outcomes and impacts delivered through the Concordat portfolio as a whole, as well as some information on the pathways to those impacts and the timelines over which they are realised. In addition, projects with notable impacts delivered across the funding types are captured in the ten impact case studies (see Appendix C).

In this section, we provide an overview of our analysis looking at four main elements:

- What is the range and nature of impacts resulting from the concordat portfolio, as reported in Researchfish and through the case studies?
- What are the time lags from funding to these impacts being realised, and how do the impacts and time lags vary depending on the characteristics of the funding awards?
- What are the pathways to impact for this research, and how closely do these align with those identified in applications?

3.2.1 What is the nature, range and timeliness of the outcomes and impacts resulting from the Concordat

The Concordat produces a wide range of outputs and impacts across the portfolio at levels that are broadly comparable to international benchmarks. Researchfish reporting indicates a diversity of outputs particularly in terms of the direct outputs of research such as collaborations and publications, but there is also a wide range of policy engagement reported, spanning around a third of the portfolio, and much of this reflects the esteem in which researchers are held internationally and their resulting roles within advisory committees on a national, and often international level. This is also reflected in the evidence from the two units which note a wide range of relationship building and engagement with local and international stakeholders particularly in the policy sphere. Notable from the case studies is the importance of awareness-raising as part of the outputs of the projects with examples of the awareness raised through research, rather than the outcomes of the research itself, leading to policy and practice change.

Capacity building is a key outcome of the Concordat portfolio which is emphasised in the unit reviews and illustrated through the case studies. This is not limited to the project team but expands to wider researchers and practitioners engaged in the work and there are several examples in the case studies where the work supported led to new fields or techniques being opened up within the country.

In terms of timeliness, we note many outputs being recorded in Researchfish very quickly, with time lags to first reported output across categories fairly short, with many categories seeing initial entries within a few years. However, it is worth bearing in mind that this is a relatively 'young' portfolio, and what we see here is likely to be the early emerging relationships, outputs and outcomes. The outputs and impacts of the portfolio will likely emerge and evolve over time and as such this measure of time lag is also likely to change and evolve. This is reflected in the case studies where policy engagement and interest in the work and plans for implementation and wider action are more widely reported than concrete changes in policy and practice at this stage, even though case studies were selected from the 2008-2013 portfolio. Wider literature tells us that the ultimate impacts of biomedical and health research on practice and health take a long time (typically on the order of 15-20 years) to be realised and this is likely to hold true for much of this work. However, we do observe evidence of the development of appropriate networks and relationships, and practical and needs oriented research (as described in Part A) which suggests that the research conducted is well placed to achieve intended impacts over the longer term.

The evidence collected on the outputs and impacts of the Concordat portfolio is described in more detail in the remainder of this section covering the following areas:

- Overview of the project outputs, outcomes and impacts reported across the Concordat portfolio
- Research outcomes and impacts of the MRC units in Africa
- Research outputs and impacts identified in the case studies
- Time lags between funding awards and reported outputs

3.2.1.1 Overview of project outputs, outcomes and impacts reported across the Concordat portfolio

- Outputs are observed across a broad range of areas, with nearly all projects reporting outputs in at least one category in Researchfish
- Most commonly recorded outcomes are in the skills, publications and secondments category
- Downstream outcomes and impacts are less commonly reported, however, more than a third report outputs in the policy category
- Policy outputs are most commonly related to participation in advisory committees, though training of practitioners is also relatively frequently reported, and more than half of outputs recorded are international in scope.

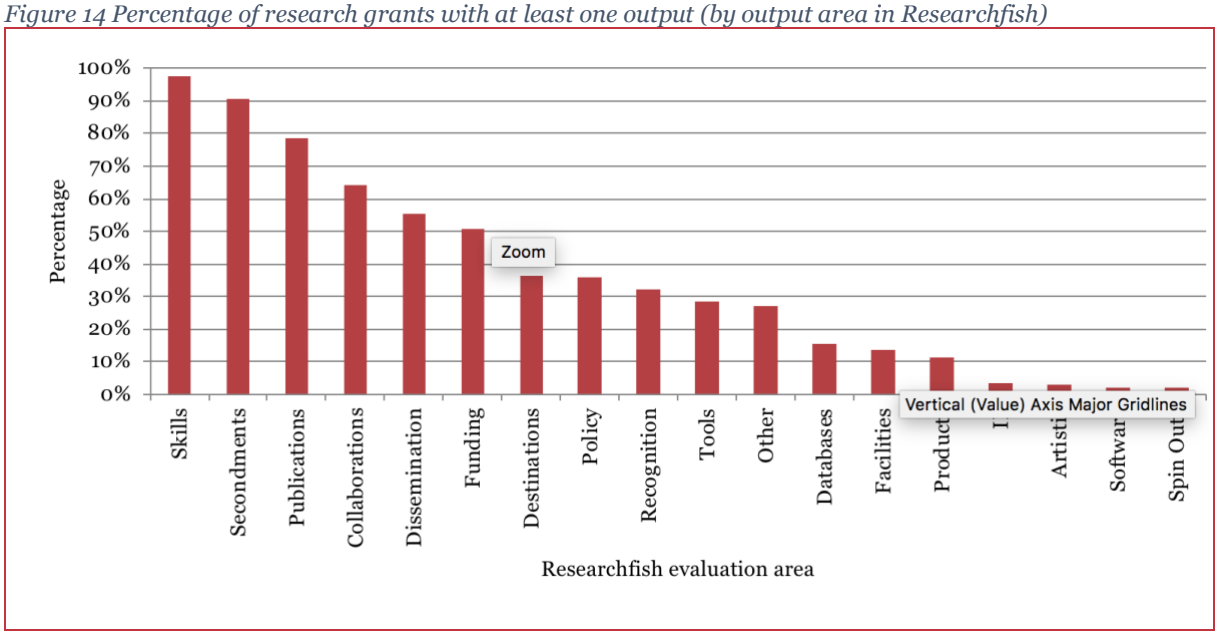
Analysis of the overall outputs across the portfolio of 317 projects where data is available across the datasets analysed[60] (see methodological appendix for details) suggests that the portfolio has had outputs in a broad range of areas, but these are more common in the upstream areas such as publications and skills development than downstream impacts such as those on policy or product development (Figure 14). The majority (98%)[61] of research grants record at least one output, although this varies considerably when broken down into different output areas used in Researchfish as defined in the table included in the methodological appendix. For example, the majority (98%) of research grants record at least one output in the Skills area, and similarly high proportions are also observed in Secondments (91%) and – to a lesser degree - Publications (79%). In other areas, only a small proportion of research grants record any outputs, with less than 4% of research grants registering outputs in the following areas: Artistic

[60] It should also be noted that Researchfish contains self-reported information by PIs and absence of impact in the database may be due to lack of reporting or knowledge on their project's impact. Equally, the presence of impacts attributed to their project in Researchfish is not validated by database managers or researchers in this review. These, and other caveats related to the Researchfish data, are set out in more detail in the methodological annex.

[61] Impact figures quoted as proportions only include research grants that are included in both the portfolio and Researchfish databases, and do not include grants that are in the portfolio database but not in Researchfish.

(3%), Intellectual Property (IP, 3%), Software (2%) and Spin Outs (2%). Lower levels of output reported in these areas are to be expected and indeed are not key focus areas for these research areas. However, a remarkable achievement in terms of the downstream impacts is the outputs in Policy, which is reported for more than a third of projects in the Concordat portfolio.

Figure 14 Percentage of research grants with at least one output (by output area in Researchfish)



We can also make some comparisons of the outputs observed between the Concordat and GLOBVAC as a useful international comparator. Figure 15 provides a summary of the outputs of GLOBVAC 1 to a similar period of operation of the Concordat. The Concordat funding is around 2.5 times that allocated through GLOBVAC and this is reflected in the number of publications reported and products brought to market, though not in the number of dissemination outputs (however this may partly relate to differences in definition between sources) or patents. Spin outs are noted for the Concordat portfolio but not for GLOBVAC over the time periods in question.

Figure 15 Concordat and GLOBVAC performance

	Concordat	**GLOBVAC**
Period	2008-2013	2006-2011
Funding invested	£90M	~£35M
Scientific publications	3592	1,098
Dissemination for users & general public (outputs)	906	1,890
Products brought to market or in active development	24	10
Patents registered	11	8
New companies established	9	0

Source: Concordat information, analysis of Researchfish data. Evidence on GLOBVAC from Technopolis, 2016.[62]

Given the particular emphasis on policy outputs within the sample, we conducted additional analysis of the range and nature of the policy outputs reported within the sample. Here we analysed by 'instances' of particular outputs since we were looking to understand the full detail of the outputs reported within

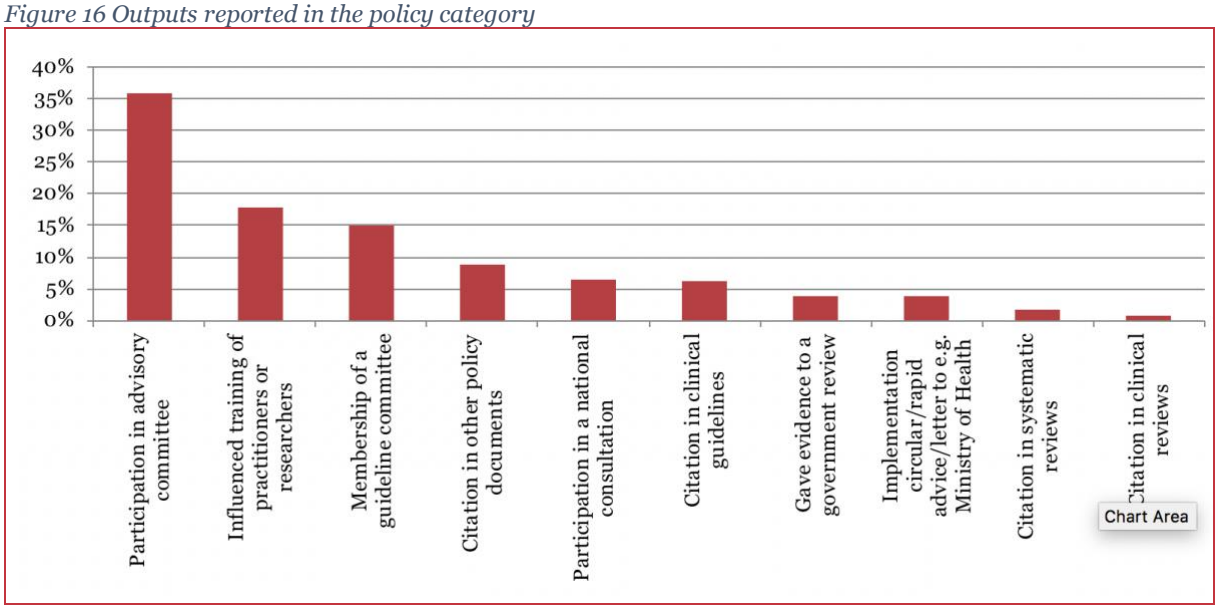
[62] Technopolis (2016) Mid-term evaluation of the second Programme for Global Health and Vaccination Research (GLOBVAC2)

the policy category. This means we looked at all the outputs reported individually, many of which will have come from the same project.

We find that the most common way in which policy outputs occur (as shown in Figure 16) is through participation in committees, particularly advisory committees which account for more than a third of all instances of policy output reported. Qualitative analysis suggests that researchers are considered experts in their field and are viewed as such by national and international policymakers We also see that influencing training of practitioners is quite commonplace, accounting for 18% of all reported outputs. This spans courses in academic curricula, training of healthcare workers in various areas, and outcomes of working groups of consultations aimed at training practitioners or researchers. Impacts in this area had a worldwide geographic reach and covered a variety of areas, including healthcare, education, agriculture, aerospace, defence and marine, food and drink. However, this is a more heterogeneous field with entries ranging from "improved public understanding…" to "trained medical professionals in quantitative methods".

Citation in guidelines or policy documents is understandably less common, though we see fairly significant numbers of instances of this being reported (104) – though it should be noted that some of these may be duplicated across projects. 17 project report being cited in or influencing WHO guidelines. Guidelines fell into 4 different areas of healthcare: infection, musculoskeletal, respiratory, and others. For those providing information on the area of healthcare the guideline impacts, the majority belonged to infection (70 per cent) followed by respiratory (21 per cent). However, there is overlap between both areas, since some of the impacts attributed to respiratory refer to TB which would also fall into the infection category.

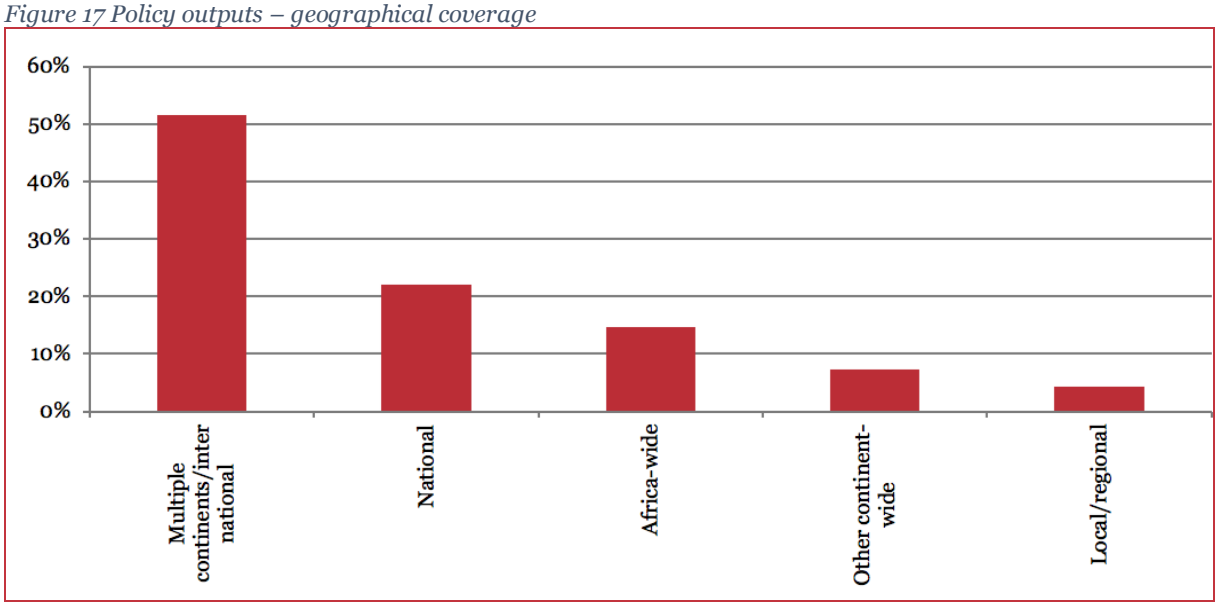
Figure 16 Outputs reported in the policy category



We also note that most policy outputs reported are international, with this accounting for more than half of the outputs reported where a geographical reach is identified (this is not provided for all outputs). This is reflected in the qualitative review (see section 3.2.8) and in the case studies where we note significant engagement with international bodies such as the WHO. Overall, 110 projects reported impacts through the WHO, mostly in the form of citations in WHO guidelines, policy reports or other documents, and participation in technical advisory committees. Of these, 83 reported to have an impact internationally in multiple continents, 25 per cent reported impact in Africa and 2 reported impact in Asia. This is not surprising given that WHO guidelines are the reference point for health policy worldwide, and an impact on WHO guidelines is likely to translate into worldwide impact. There were 32 projects that reported national impacts, 24 of which are related to national programmes against

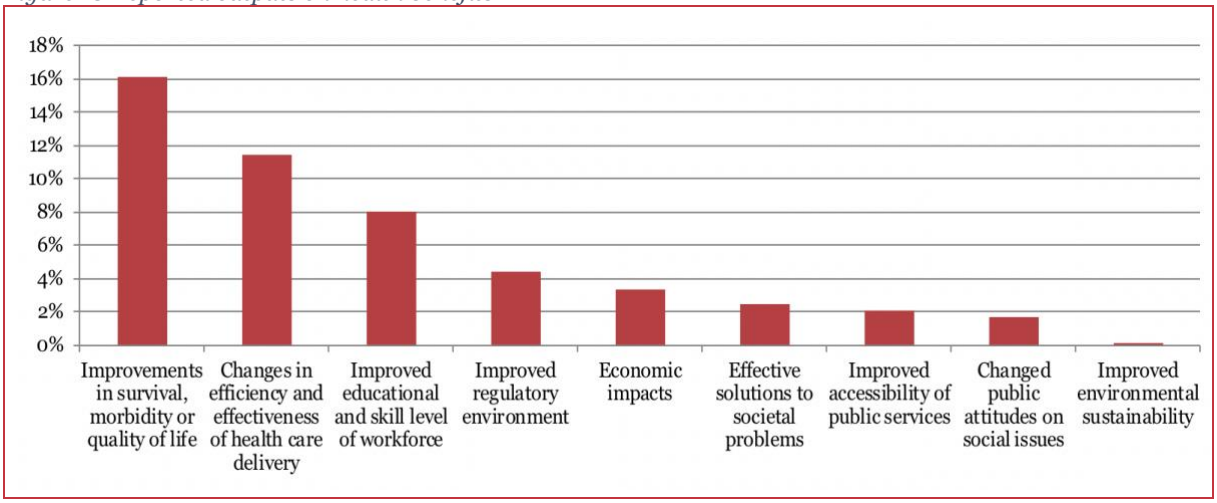
infectious diseases. The geographic distribution of national impacts is: 11 in Africa, 3 in Asia, 2 in the US, 10 in the UK, and 6 unspecified. The national impacts reflect the national priorities. The impacts in Africa are mostly related to treatment of infectious diseases and antimicrobial resistance, whereas in the UK they refer mostly to sexual and reproductive health.

Figure 17 Policy outputs – geographical coverage



Only around half of the outputs reported provide information on the nature of the benefit to health. However, of those that do, more than a third indicate potential improvements in survival, morbidity or quality of life. Also, relatively commonly reported are changes in efficiency and effectiveness of health care delivery (23%) and Improved educational and skill level of workforce (16%), reflecting the capacity building element of the portfolio, which extends beyond the research sphere. The type of influence corresponds with the area of impact in in some cases. For example, out of the 60 projects reporting impact on improving the educational and skill level of the workforce, 40 reported to have influenced the training of practitioners or researchers. Likewise, 22 projects leading to improvements in survival, morbidity and mortality reported impacts through engagement with the WHO, the agency that sets the health guidelines worldwide, through participation in advisory committees and citations in clinical guidelines as well as other policy documents. Improvements in survival, morbidity and mortality were also related to geographic needs: most projects reporting impact in Africa in this area referred to infectious diseases, whereas in the UK most referred to pregnancy and child health.

Figure 18 Reported outputs on health benefits



3.2.1.2 Research outputs and impacts of the MRC Units in Africa

- Units play a key role in the portfolio and both provide examples of important impacts on policy, practice and health
- The five year reporting provides examples of impact as well as a range of data on the outputs and outcomes of the units
- Both units can point to a significant range and number of individuals trained and wide ranging engagement with in-country and wider stakeholders.

As described already, the MRC Units have a unique position in the Concordat portfolio, therefore their outcomes and impacts are described first, before describing the impact analysis of the entire portfolio. The Units are evaluated in Quinquennial Reviews, the latest of which happened in 2015 in The Gambia and in 2016 in Uganda.[63,64]

The MRC/UVRI Research Unit in Uganda has achieved significant results from its research programmes. In consultation with global health experts, it was suggested that the Unit has contributed significantly to the understanding and control of the HIV epidemic in Uganda[65] and globally. This is mirrored in the last five-year review of Unit.[66]

Major public health outcomes and significant policy implications are assigned to a number of recent trials and observational studies in the unit review. Impacts range from indications of health and care conditions in subsets of the general population that will enable policy responses, to potential breakthroughs in prevention or treatment of disease, such as low-cost and lay-led modes of delivery. A number of examples include:

[63] MRC Global Health Group: Minutes of Meeting 7th-8th December 2015

[64] MRC Global Health Group: Draft Minutes and Matters Arising of 13th Meeting 11th-12th June 2015

[65] New infections among adults aged 15-49 have declined by 63%, from 140,000 in 1990 to 52,000 in 2016. Source: UNAIDS; http://www.unaids.org/en/regionscountries/countries/uganda

[66] MRC/UVRI Uganda Research Unit on AIDS, Quinquennial Review Research Proposals, 2011.

- The DART trial[67] showed that first line antiretroviral therapy (ART) can be safely provided without routine laboratory/clinical monitoring for toxicity, and that monitoring of CD4 cell count provides only limited benefit from the second year of ART to guide the switch to second line ART if required
- The Jinja ART delivery trial[68] (conducted under real life primary health care conditions) demonstrated that home-based provision of ART through trained and supervised lay health workers is as effective as the standard of care at health facilities through doctors and nurses
- The Cryptococcus prophylaxis trial[69] established that systemic cryptococcal disease can be prevented reliably and cost-effectively through oral prophylactic medication with fluconazole three times per week
- An observational study within HIV-positive cohorts[70] demonstrated that Cotrimoxazole prophylaxis leads to marked reductions in HIV-related morbidity and mortality
- Observational studies of the direct and indirect impact of the HIV epidemic on older people[71] have shown that increasing numbers of people over 50 are HIV-positive, and that nearly all older people suffer multiple health problems for which they receive inadequate care and lack social support
- Other studies still have contributed to the understanding of disease progression (including clinical, viral and immunological) and HIV prevention, with a focus on the treatment of sexually transmitted infections (STIs)

The Unit aims to build on its experience and increasingly take the lead in the coordination of policy defining clinical trials.

The MRC Unit in The Gambia's (MRCG) research has informed the implementation of public health interventions that have had significant impact on childhood mortality and morbidity in both the Gambia and elsewhere in sub-Saharan Africa. The latest five-year review[72] of the Unit sets out specific impacts of the three research themes. Two of these – Disease Control & Elimination and Vaccines & Immunity – appear to have provided major impacts in the last reporting period.

The report suggests that research conducted under the Disease Control & Elimination theme has had a visible and direct impact on public health in the Gambia and beyond. These impacts range from the elimination of trachoma, a substantial decrease in malaria transmission, the introduction of immunisation of Hib, HBV, PCV and rotavirus vaccines into the routine vaccination program[73]. The Unit's work has also estimated TB prevalence, which will result in the review of the national TB strategic plan. Other policy impacts from this theme include informing policy makers on the potential long-term impact of relevant vaccines in the sub-region on PCV and Hib transmission.

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[67] DART Trial Team. (2010). Routine versus clinically driven laboratory monitoring of HIV antiretroviral therapy in Africa (DART): a randomised non-inferiority trial. The Lancet, 375(9709), 123-131.

[68] Jaffar, S., Amuron, B., Foster, S., Birungi, J., Levin, J., Namara, G., ... & Bunnell, R. (2009). Rates of virological failure in patients treated in a home-based versus a facility-based HIV-care model in Jinja, southeast Uganda: a cluster-randomised equivalence trial. The Lancet, 374(9707), 2080-2089.

[69] Parkes-Ratanshi, R., Wakeham, K., Levin, J., Namusoke, D., Whitworth, J., Coutinho, A., ... & Cryptococcal Trial Team. (2011). Primary prophylaxis of cryptococcal disease with fluconazole in HIV-positive Ugandan adults: a double-blind, randomised, placebo-controlled trial. The Lancet infectious diseases, 11(12), 933-941.

[70] Walker, A. S., Ford, D., Gilks, C. F., Munderi, P., Ssali, F., Reid, A., ... & Darbyshire, J. H. (2010). Daily co-trimoxazole prophylaxis in severely immunosuppressed HIV-infected adults in Africa started on combination antiretroviral therapy: an observational analysis of the DART cohort. The Lancet, 375(9722), 1278-1286.

[71] Mugisha, J. O., Schatz, E. J., Randell, M., Kuteesa, M., Kowal, P., Negin, J., & Seeley, J. (2016). Chronic disease, risk factors and disability in adults aged 50 and above living with and without HIV: findings from the Wellbeing of Older People Study in Uganda. Global health action, 9(1), 31098.

[72] The Medical Research Council Unit, The Gambia. Quinquennial Review Version 2 (June 2015). Progress report: 2010-2015 And Future activities: 2016-2021

[73] Ibidem

The research output of the Vaccines & Immunity theme has impacted on both vaccine and TB-related public health policies, with vaccine studies conducted by the MRCG informing policy makers' vaccine deployment strategies. The Unit's 2011 study on the MenAfriVac® vaccine confirmed the safety and immunogenicity of the vaccine,[74] after which it was introduced into the vaccine schedule by the Gambian government in late 2013.[75] Further, a large trial on the 13-valent conjugated pneumococcal vaccine[76] has led to licensing of a new formulation. A trial studying the potential interference of intramuscular polio vaccine (IPV) with EPI vaccines has provided information on polio endgame decisions.[77] The Unit's childhood TB research program has resulted in increased notifications of childhood TB by the NLTP[78] and the Unit's TB researchers are directly contributing to shaping the next application to the Global Fund and National TB program in collaboration with the National Leprosy/TB Control Programme (NLTP).[79] The evaluation of TB diagnostics at the Unit has contributed to the WHO guidelines for use of these assays in resource-poor settings. The main impacts and future plans for the Units as described in their submissions to the Quinquennial Review as summarised in Figure 19.

Figure 19 Performance of the MRC Units in Africa

	MRC Unit, The Gambia (2010-2015)	MRC Unit, Uganda (2012-2016)
Capacity Building	• 30 BSc students • 50 MSc students • 26 PhD students • 35 Foundation degree students • 52 Other trainees undergoing external training	• 40 MSc students • 24 PhD students • 100 interns per year • 1 African Research Leader Fellowship
Engagement and outreach	• Unit Newsletter, Tama • Community Open Days • Scientific meetings • With external stakeholders: Gambian Government, Schools, WHO, media, international science community and funders	• Quarterly newsletter • 3 graphic novels about young people with HIV • Participation in networks: International AIDS Vaccine Initiative, International Partnership on Microbicides, African Partnership in Chronic Diseases Research, etc. • With external stakeholders: Ugandan Ministry of Health, the AIDS Control Programme, Uganda AIDS Commission, WHO and UNAIDS, university and research institutions, district health services, hospitals, HIV/AIDS support organisations, media
Wider impacts to which the unit's research has contributed	• Virtual elimination of trachoma in the Gambia • Decrease of malaria transmission in the Gambia • Introduction of routine immunisation with Hib, HBV, PCV and rotavirus vaccines in the Gambia • Commissioning of a review of the national TB strategic plan in the Gambia	• Social Gerontology Manual of Uganda's Ministry of Gender, Labour and Social Development • UNAIDS supplement to the Global Report 2013 focussing on HIV and ageing • WHO HIV treatment guidelines for adolescents • Paediatric European Network for Treatment of AIDS (PENTA) dissemination guidelines for trial results

[74] Sow, S. O., Okoko, B. J., Diallo, A., Viviani, S., Borrow, R., Carlone, G., ... & Elie, C. (2011). Immunogenicity and safety of a meningococcal A conjugate vaccine in Africans. New England Journal of Medicine, 364(24), 2293-2304.

[75] The Medical Research Council Unit, The Gambia. Quinquennial Review Version 2 (June 2015). Progress report: 2010-2015 And Future activities: 2016-2021

[76] This trial was endorsed by the Global Alliance for Vaccines and Immunisation and sponsored by Pfizer

[77] The vaccine was given to over 1,500 nine-month-old Gambian infants via routine and alternative delivery devices, and the results were reported to the SAGE committee

[78] Increase from 4.3% to 6.8% nationally

[79] The Medical Research Council Unit, The Gambia. Quinquennial Review Version 2 (June 2015). Progress report: 2010-2015 And Future activities: 2016-2021

	MRC Unit, The Gambia (2010-2015)	MRC Unit, Uganda (2012-2016)
	• Introduction of MenAfrivac into the Gambian vaccine schedule • WHO guidelines for use of TB diagnostic assays in resource-poor settings	• Guidelines on optimal Dry Blood Spot collection, storage, and shipping conditions for HIV drug resistance surveillance in resource-limited settings • Guidelines on Hepatitis C treatment in Uganda • Change in Uganda's National HIV testing algorithm
Future aims	• Control/elimination of infectious diseases of public health importance in West Africa and sub-Saharan Africa • Address high maternal and neonatal mortality • Design and implement next generation interventions against nutrition-related diseases • Strengthen research on NCD associated with infections	• Deliver excellent science aimed at controlling infectious and non-communicable diseases • Strengthen partnerships and collaborations • Build human and infrastructural capacity • Attract external funding • Translate knowledge into policy and practice

Source: (1) MRC/UVRI Uganda Research Unit (2016) Quinquennial Review – Progress Report 2012-2016 and Proposed Work 2017-2022; (2) The MRC Unit, The Gambia, Professor Umberto D'Alessandro and the Leadership Board (2015) Quinquennial Review (Version 2) – Progress Report: 2010-2015 and Future activities: 2016-2021

The role of the Concordat in public health beyond the work of the two MRC Units is illustrated through the development of the BREATHE Partnership - aimed at bringing African researchers together with international experts in key areas of household air pollution in order to quantify and reduce the health effects of air pollution.[80] Partners of the BREATHE Partnership include the Global Alliance for Clean Cookstoves, the American Thoracic Society, the Pan African Thoracic Society, the University of Malawi, and the Liverpool School of Tropical Medicine. The impact on public health extends to the outcomes of clinical trials such as those relating to treatment of multi-drug resistant TB (STREAM)[81] and nutritional supplementation on infant immune development (ENID).[82]

3.2.1.3 Research outputs and impacts identified in the case studies

- Case studies demonstrate a wide range of impacts
- Capacity building is a key outcome and extends beyond the project team
- Awareness raising is also an important outcome from the case studies and can support changes in policy and practice

As illustrated in Figure 20, we observe a range of impacts from the case studies spanning areas of knowledge creation, capacity building, policy and practice. A clear observation across all the case studies is the importance of capacity building as a key outcome of the projects, particularly noting that in many cases this extends beyond the project team to support wider researchers engaged in the project as well as practitioners and others locally. There are examples where studies facilitated future work by building the skills base to make this feasible in the region, notably in terms of building capacity to conduct trials in SSA and to conduct modelling at UVRI. Also notable is the importance of awareness raising as an outcome of this work. For example, one of the studies increased awareness of mental health issues in relation to HIV/AIDS which is now informing policy development, and another raised the profile and skills base around TB monitoring which has informed practice at the national level. The extent to which

[80] BREATHE (2018) http://www.breatheafrica.org/

[81] Stop TB Partnership (2015) STREAM clinical trial reaches recruitment target. Available at: http://www.tbonline.info/posts/2015/6/28/stream-clinical-trial-reaches-recruitment-target/

[82] Moore SE, Fulford AJ, Darboe MK, Jobarteh ML, Jarjou LM, and Prentice PM. 2012. "A Randomized Trial to Investigate the Effects of Pre-Natal and Infant Nutritional Supplementation on Infant Immune Development in Rural Gambia: The ENID Trial: Early Nutrition and Immune Development." BMC Pregnancy and Childbirth 12: 107.

the case studies have had an impact on policy and practice varies, reflecting in part the applied or basic nature of the research. We note some engagement in policy or practice change for 6 of these 10 case studies. This is higher than the proportion reporting these impacts in Researchfish which we might expect given these were selected to cover research with a diversity of impacts reported.

Figure 20 Range of impact identified in the case studies

Project title	Brief description	Key outcomes and impacts
Developing methods to assess the impact of malaria interventions upon transmission and the progress towards elimination	Career development fellowship awarded to Dr. Patrick Walker from 2014 to 2018. Aim: building and calibrating models of malaria transmission that account for local ecology and epidemiology in western Kenya and integrate various interventions aimed at curbing malaria transmission.	• Directly informed future interventional research. • Contribution to recipient's career development through publications, networks and further funding.
Defining the merozoite targets of protective immunity against Plasmodium falciparum malaria through multi-centre cohort studies	African Research Leader Award granted to Prof. Faith Osier from 2013 to 2018. Aim: identifying the immune response in children infected with malaria, to aid in designing better malaria vaccines. The ARL award has also enabled the recipient Prof. Faith Osier to advance in her career	• Knowledge generation towards future malaria vaccines • Kenyan and regional research capacity building • Helped a mid-career African researcher transition to a higher stage in her career.
Studies to understand the response of the infant's immune system to infectious diseases and vaccines	Intramural Infections and Immunity Board grant managed by PI Dr. Ed Clarke from 2013 to 2018. Aim: understanding the immune response generated in infants through vaccination of pregnant women and infants, in order to understand age-dependent immune development in the context of vaccination, infection and important epidemiological and pathogen-derived factors.	• Important contributions to vaccine development and implementation
Plasmodium falciparum anti-malaria drug resistance in The Gambia: Identification of potential genetic markers by retrospective whole genome approaches	Career development fellowship awarded to Dr. Alfred Ngwa from 2013 to 2018. Aim: to identify and determine the distribution of malaria drug resistant markers in The Gambia, following five years of implementation of artemisinin-based combination therapies in this country.	• Important scientific contributions on resistance to malaria medication • Supported recipient and other researchers in career development • Foundation for developing MRC Gambia Unit into regional hub in African genomic research.
Childhood tuberculosis: Integrating tools for improved diagnosis and vaccines	Infections and Immunity Board award to Prof. Beate Kampmann (2013 to 2018). Aim: developing and evaluating new and existing tools for TB diagnosis based on both the immune response to the bacteria and the microbiological features of the bacilli.	• Contributing to scientific knowledge • Improved national Gambian TB programme in monitoring and reporting • Training of national practitioners and researchers (many now recognised experts in the field of childhood TB).
Transfusion and Treatment of severe Anaemia in African Children: a randomised controlled trial (TRACT)	MRC Global Health Trial (£3,046,319) led by Dr. Kathryn Maitland, Imperial College London. Aim: to investigate directly the factors contributing to severe anaemia and provide evidence on the effectiveness of blood transfusions in paediatric SA cases.	• Research and practitioner learning and wider capacity building. • Training of practitioners beyond those directly engaged in the study. • Initial engagement with WHO. It is expected the work may influence policy.
Lung health and exposure to household air pollution in rural Malawi (CAPS)	Young investigator grant (£484,680) to Dr Kevin Mortimer allowing him to dedicate his time to the larger MRC-Wellcome Trust Joint Global Health Trial project Cook stoves and *Pneumonia* (CAPS). Aim: to address the lack of systematic evidence regarding the relationship between smoke and childhood pneumonia.	• Results of the study were integrated into the WHO Guideline for Indoor Air Quality. • Coverage in major press outlets. • Sparked and informed academic and wider debate. • Likely helped avoid unnecessary investment in changes in cooking practices.
MRC/UVRI Uganda Research Unit on AIDS - Mental health	African Research Leadership award (£706,133) to Prof Kinyanda to support research on mental	• Informed and contributed to future research through scientific publications.

Project title	Brief description	Key outcomes and impacts
among HIV infected CHildren and Adolescents in KAmpala, Uganda (CHAKA)	health among HIV infected children and adolescents in Kampala, Uganda (CHAKA).	• Raised the profile of mental health research at the MRC/UVRI research unit on AIDS. • Contributed to the child mental health policy that is being used in the country. • Plan to develop an intervention and implement in the Uganda Health system in the future.
Prevention Programme - Microbicides	Intramural Population and Systems Medicine Board funding (£7,874,932) to Prof Sheena McCormack at UCL, 1998-2013. Aim: to develop and implement a microbiocide-based intervention to prevent or reduce the risk of acquiring HIV in South Africa, Tanzania, Uganda and Zambia.	• Results demonstrated microbicide ineffective targeting research and interventions. • Increased awareness of HIV issues and screening • Empowering female community of participants • Capacity building to conduct trials in SSA.
Calibration and analysis of complex models: methodological development and application to explore the impact of HAART in Africa	Methodology Research Programme funding (£515,607) awarded to Prof. Richard White at LSHTM 2012-2016. Aim: explore the costs and effects of different ART scale-up options in Uganda.	• Introduced new capacity to do modelling to MRC/UVRI. • Policy brief prepared and shared with ministry and presentations given to policymakers.

3.2.1.4 Time lags between funding awards and reported outputs

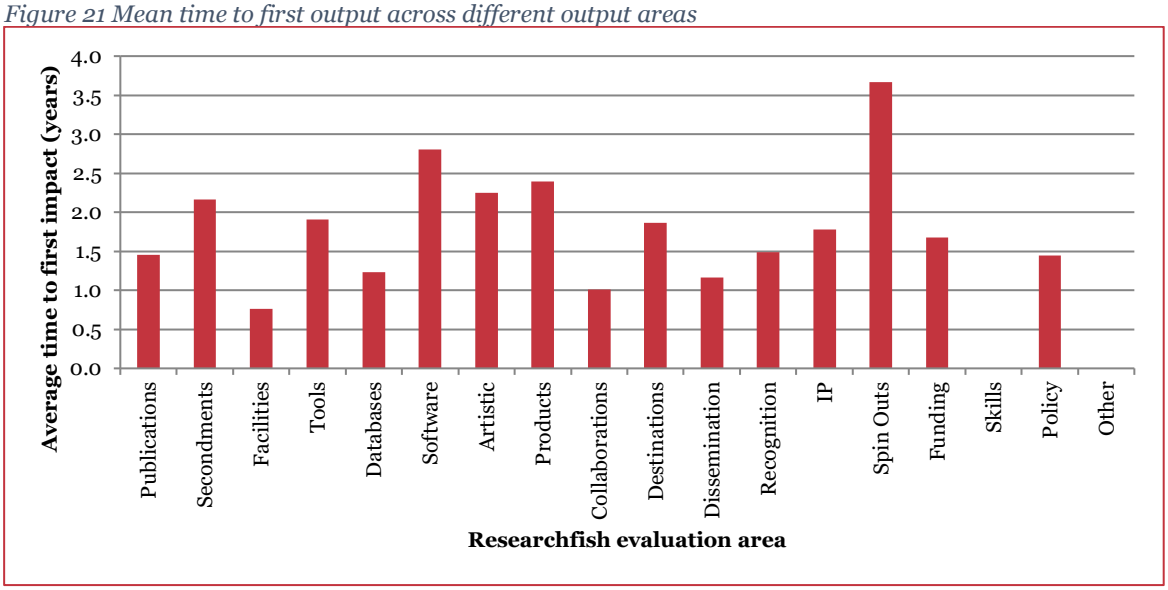
- On average, awards report first outputs within a year and the time to first output in a particular area ranges from less than a year for facilities and collaborations, to five years for spin outs.
- This reflects time to first engagement or activity within that area, rather than the ultimate outcome or impact
- We may also be seeing the earlier impacts given the age of the awards in the analysed sample, and we might expect the time lags (but also the number and range of impacts realised) to grow over time.
- Time lags do not differ by characteristics of the funding such as award size, funding stream or partner country.

The average time between the start of a research grant and the first recorded output across any area is less than 1 year (approximately 7 months), although this ranges from 0 to up to 5 years. Some research grants record their first output before the start date of the grant itself (i.e. negative time to first output), although these were not included in this part of the analysis as it was assumed that these outputs were linked to prior related work but did not result from the grant itself.

Figure 21 breaks down average time to first output according to each output area. More specifically, it illustrates the average time to first output across every project that records an output in a particular area. For example, a value of 2.8 years for software means that, across all grants that record at least one software output, the average time to the first recorded output in that category is 3.5 years. This illustrates that – when present - most output areas are recorded in the first one or two years after a research grant is awarded, with facilities a little earlier (just over 9 months on average), and secondments (2.2 years), artistic (2.3 years), products (2.4 years), software (2.8 years) and spin outs (3.7 years) each taking longer than 2 years on average. These latter five areas are somewhat expected results, as a greater level of maturity would be expected in a research project before outcomes such as product development or spin outs are possible. This contrasts with areas such as facilities or collaborations, each of which can be

achieved when the research itself is relatively nascent. It is also important to note that these time lags are significantly shorter than typically reported in wider studies on time lags in research translation.[83]

Figure 21 Mean time to first output across different output areas



To interpret this, it is important to note that these values do not represent the ultimate impacts of the research. Rather, they provide an indication of first active engagement with stakeholders and activities relevant to that type of output. For example, the first reported policy output may well be a meeting with a policy maker. This therefore does not represent the ultimate desired impact on policy from the research, rather the first step in engagement with relevant stakeholder on the pathway to impact in that field.

Given the variation in the time to first output across different output areas, it was important to test whether or not this was linked to the characteristics of different research grants such as funding type or region. To investigate the relationship, we used another statistical approach to identify if there is a difference between the underlying distributions of a set of non-normally distributed samples. The results show that there was no significant difference identified between the distributions of time to output for the different funding characteristics. In other words, the type of funding, region and funding amounts do not appear to influence the time to the first recorded output of a particular research grant. This suggests that the pathways to impact are not significantly influenced by these characteristics of funding and instead may be more strongly linked to other factors which are not easily characterised for this type of analysis such as the research fields, relationships of the individuals involved, or characteristics of the research team.

It is also worth reflecting on the overall age of the portfolio. Most of the awards are relatively recent (e.g. within the last 5 years). Therefore, it is likely that the outputs and impacts that we are observing in Researchfish at this stage are those which are emerging early. Over time, the nature and range of the outputs reported will change and grow. We would expect the average time lags to increase as the portfolio matures – but equally we would also expect the range and significance of the impacts reported to also expand.

[83] E.g. Morris, Z. S., Wooding, S., & Grant, J. (2011). The answer is 17 years, what is the question: understanding time lags in translational research. Journal of the Royal Society of Medicine, 104(12), 510-520.

3.2.2 What does the research to impact process look like for the Concordat portfolio?

The evidence collected also allows us to analyse the factors that can support the effective conduct and translation of research into outputs and impacts across the portfolio. A key enabler of impact for the portfolio is effective development and nurturing of relationships with in-country stakeholders, including politicians but also other local actors, such as health care practitioners and community leaders. The units, both MRC and others, are a key facilitator of this both in terms of providing a consistent presence and through demonstrating an ongoing commitment to develop capacity within the country.

Units also play an important role in terms of providing underpinning infrastructure, helping to address another challenge identified in relation to access to the equipment and materials needed to conduct research.

An ongoing challenge is recruitment and retention of high-quality staff reflecting the typically small pool of researchers in LMIC and the greater opportunities that may be available for the best of these in other countries. Providing more structured pathways for careers in-country might help to address this, alongside working to develop the wider research system in-country through better government engagement and potentially co-funding where possible. This could also promote more engagement at the government level and help build the political will needed to support uptake of research findings.

Evidence from the analysis of Researchfish data suggests that mode of funding is less important, and that awards are equally likely to have impact regardless of the partner country, funding stream or award size. The latter is particularly interesting and may merit further investigation to see if there could be better returns on smaller awards, something that has been observed in a previous study[84].

Flexibility of funding is also noted as important in allowing networking and the pursuit of promising research, and the mentorship relationships, both between and within countries are noted as supporting capacity building. Finally, it is worth highlighting resource challenges in implementing research outcomes in to practical changes in policy and practice. Relationships with policymakers and their engagement from the outset can help support this, and the MRC, and particularly DFID, may be able to draw more effectively on their in-country networks and resources, where available, to support research translation and implementation.

These different pathways and, particularly, the stakeholders needed for effective research translation, are typically reasonably well considered in pathways to impact statements at the application stage. However, the scope and quality of these differs significantly over time and between funding streams. There could be scope for MRC to offer better guidance and examples of good practice in terms of how to present information in pathways to impact statements to make them more useful both in terms of planning and for subsequent analysis. It is also worth highlighting that one of the key outcomes envisaged for the programme and highlighted in many of the pathways to impact statements is capacity building and this is not effectively captured across the portfolio through current reporting mechanisms (i.e. primarily Researchfish). Evidence is collected through other formats for some award types (e.g. in the quinquennial unit reviews and the annual ARL reporting), but a simple but useful way to capture this across the portfolio could offer benefits both analytically and in terms of ensuring these contributions are adequately valued and recognised.

The evidence collected on the research to impact pathway for the Concordat portfolio is described in more detail in the remainder of this section covering the following areas:

- Relationship between different types of output and between outputs and characteristics of funding
- Evidence on barriers and enablers from the interviews

[84] Wooding, Steven, Stephen Hanney, Martin Buxton, and Jonathan Grant, The Returns from Arthritis Research Volume 1: Approach, Analysis and Recommendations. Santa Monica, CA: RAND Corporation, 2004. https://www.rand.org/pubs/monographs/MG251.html

- Evidence on barriers and enablers from the case studies
- Review of pathways to impact statements

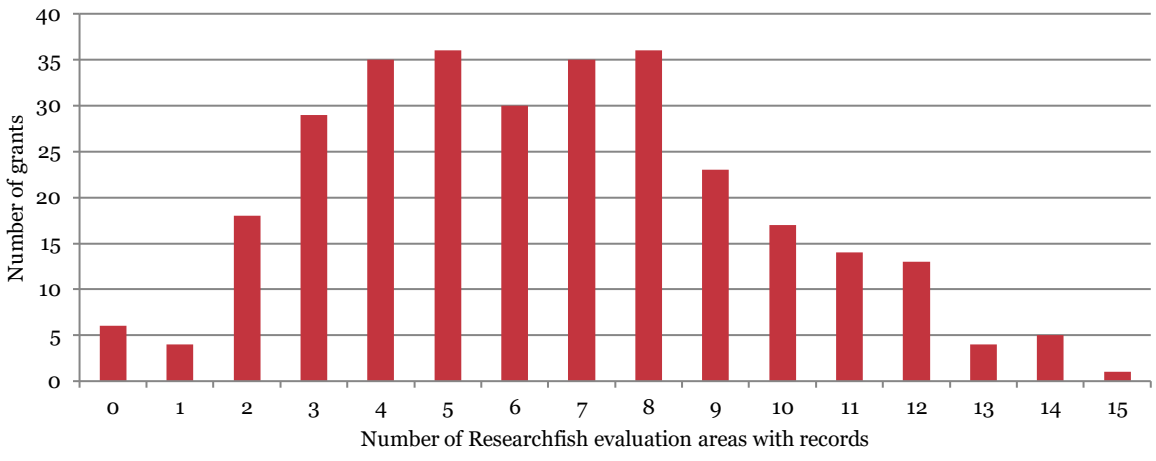
3.2.2.1 Relationship between different types of output and between outputs and characteristics of funding

- Most awards report outputs across multiple categories in Researchfish, and we find a positive correlation between reporting outputs in all categories.
- This suggests that all outputs are made more likely by underlying factors such as the age of the award, or the propensity of the researcher(s) involved to provide details in Researchfish.
- There is no correlation between funding amount, type and region and outputs reported in Researchfish

The majority of research grants record outputs across multiple areas. For each research grant, the average number of different categories in which awards have reported at least one output is 6.5, although this ranges from 0 to a maximum of 15. Very few projects record just one output (4) or no output (6).

Although Figure 22 illustrates that research grants typically record more than one type of output, it does not indicate whether these outputs are correlated. For example, if a research grant has an output in publications, is it more likely to record outputs elsewhere, such as policy or recognition? Similarly, if a research grant records an output in collaborations, is it more likely to record outputs elsewhere, such as dissemination or destinations? This is potentially interesting since it could show whether earlier stage outcomes might form part of the pathway to, or be early indicators of, more downstream impact.

Figure 22 Number of different output areas recorded for each grant



In order to test whether there was a relationship between reporting one type of output and reporting another type of output, pairwise statistical tests were carried out between each combination of output area. The results indicate that there is a statistically significant (but not necessarily causal) relationship between nearly all types of reporting, and where there is not a statistically significant result, this is likely due to there being less data available for these categories. This makes the results challenging to interpret, suggesting that having an output in one area is correlated with having an output in another area. This however might well result from some underlying characteristics which are strong predictors of all areas of output – such as the length of time elapsed since funding, or the extent to which the individuals involved take the time to provide complete Researchfish responses rather than specific correlations between output types. A more detailed and subtle classification of outputs (beyond the broad Researchfish categories) would likely be needed to better investigate these relationships and pathways

in detail. For example, it might be interesting to look at the different types of policy outputs reported, how they relate, and how they emerge over time. However, the number of awards in this sample makes this type of analysis challenging. We find that for most combinations of sub-groups of policy output there are insufficient numbers to draw conclusions, and where there is sufficient volume of awards, we find similar findings, with outputs in categories correlated.

The influence of various funding characteristics on the output of research grants was also investigated using statistical significance tests to identify whether differences in these characteristics corresponds to certain outputs. More specifically, we tested whether higher funding amounts, different funding types and different regions correspond to a higher proportion of research grants with at least one output recorded in each of the output areas. The results show that none of these funding characteristics has a statistically significant influence on output in any of the areas (see methodological details in appendix). This is an interesting observation which suggest that the differences in outputs from different research awards are due to other factors, which may include the characteristics of the researchers involved, or the nature of the research results.

The lack of any relationship between award type and likelihood of outputs and impacts being obtained is also very interesting as it suggests that larger awards are no more likely to achieve particular outputs than much smaller ones. It may be that the scale and nature of the outputs between different categories differ by award size however. To investigate this, we took a sample of eight small awards (less than £150,000) within the portfolio and eight large awards (more than £2.5M) and analysed their Researchfish data in detail. We observe that in both cases three of the eight awards report very little in Researchfish beyond a small number of publications and typically one or two entries in other categories (skills, collaborations). We assume these awards either were unsuccessful, or, more likely, that the response to Researchfish is incomplete in these cases.

Amongst the other five awards in each sample, we see a similar range of categories covered, with 4 of the small projects reporting development of tools, two of databases compared to two of each amongst the larger projects. For both the large and small projects, 2 from the 8 report outputs in the policy category and 3 report dissemination outputs. The number of outputs reported differs between the two groups. The total number of publications reported across all 8 small projects is 37, compared to 710 for the larger projects (though this is dominated by one project which reports 607 publications). Amongst the large projects we see one award which reports very high numbers of outputs across many categories, whereas the others are not significantly higher than the outputs reported in the group of small projects. Reviewing the qualitative material in detail we see that there are significant impacts on policy and practice from both groups though this is particularly the case for one large award where many outputs are captured. However, one small award demonstrates the development of WHO approved tools and practice manuals related to the Zika virus, for example, and another award points to important impacts on national guidelines. This suggests that although large awards can produce larger volumes of activity, interaction and outputs, this is not universally the case and that important outcomes can result from smaller awards in the portfolio which may offer good value for money. It also suggests that completeness of reporting by individuals may also be influencing some of the relationships observed, as suggested based on the quantitative analysis.

3.2.2.2 Evidence on barriers and enablers from the interviews

- Enablers focus on relationships and interactions between researchers and research funders and local stakeholders.
  - Incentives for and wider challenges facing these stakeholders should be considered, and better engagement and sustainability could be facilitated through commitment on both sides.
- Barriers to impact identified fall into two main areas:
  - Lack of long term perspective resulting from challenges in retaining staff and in consistency of funding
  - Social and political context, including capacity to take up findings, and changing personnel in senior positions within government and other organisations

There were a number of observations from the interviews that shed some light on the pathways to impact for research within the portfolio and what the key enablers of impact could be. These are summarised in Figure 23. Overall, the key message emerging across the stakeholder groups consulted is the need for the development and maintenance of relationships with key groups within the local country context, and thinking about their wider needs, incentives and challenges to understand the ways in which they are able to and would like to engage and how that can best be supported. There is a suggestion that commitment on both sides – both from MRC and DFID as funders in terms of showing genuine commitment to developing capacity within the country, and from the LMIC government in terms of early engagement and cofounding of work – can help ensure active engagement and sustainability.

Figure 23 Enablers of impact reported by the interviewees

Group 1 MRC and DFID personnel	Group 2 - national and international stakeholders	Group 3 - Members of the global health research community	Group 4 - Grant holders
• Early engagement of key stakeholders, particularly policymakers	• Holistic perspective needed considering local challenges in implementation • Diversification and integration of research networks building on key hubs (such as the MRC units) • Incentives for engagement and development of national research systems, e.g. cofounding • Political will and financial contribution facilitate buy-in and sustainability	• Demonstrating genuine commitment to develop capacity in LMIC	• Access to international networks • Core funding of underpinning resources and capacity – e.g. clinical trial network • Good local research partners to support local level engagement and share back data and results quickly and effectively

The interviews also provided some insights on the barriers to impact. When assessing the barriers to achieving the desired impact of Concordat-funded activities reported by interviewees, differences among the various stakeholder groups can be observed. For example, national and international stakeholders described generic, 'macro' barriers to consider when working in these research areas, members of the global health research community suggested more longitudinal views, while grant holders understandably tend to cite their own project-related experiences. The information in Figure 24 summarises the reported barriers to impact.

Figure 24 Barriers to impact reported by the interviewees

Group 2 - national and international stakeholders	Group 3 - Members of the global health research community	Group 4 - Grant holders
• Lack of sustainability plans when building capacity • Brain drain hinders the sustainability of projects. If the individuals leave the local system, then this also undermines capacity building efforts • Selection processes mean that well-performing institutions and countries may be successful at the cost of other, less-developed counterparts • Networks are underutilised • Gender barriers • No co-investment and low priority on research in the country. • Limited local research capacity creates imbalance in partnership • Local conditions can be barriers to impact - for example where there is a lack of security. Political instability, adverse economic conditions	• Lack of continuity of funding limits long term thinking (and limited other funding sources) • Timelines and policy cycles can vary and be unclear and when administrations change this can cause challenges in engaging with the right people and in creating consistent action in response to evidence. This strengthens the case for strong and continuous engagement with local policy makers and national government. • Lack of political will and resource • Advocacy for non-political scientific or medical appointments may also be considered to shield scientific work from these adverse changes • Language barriers and perception of focus on Anglophone countries • Translating research to policy and practice is always a challenge, this is exacerbated where target countries lack capacity to engage with evidence, or lack funding/skills/infrastructure or other elements necessary to adopt new innovations.	• Lack of understanding of impact among laypeople and media (including health impacts), including a lack of willingness to accept medicine for ailments that do not exhibit obvious symptoms • Lack of trust for some of the work due to scepticism, superstition and fear among public. This is tackled via meetings, open days and other advocacy work, but is time intensive • Dependence on external resources (including ministries) • Lack of equipment and technical skills • No structured fellowships for different career stages. • Language barriers

The lack of continuity of funding was also highlighted as an important consideration in one of the case studies as described below.

MC_UP_A900_1115 - Studies to understand the response of the infant's immune system to infectious diseases and vaccines

The aim of the research project was to provide insight into the development of natural and vaccine-stimulated immunity to guide future rational vaccine development and maximise the protection of infants. The grant served to build a core team and fund the activities of the Vaccines and Immunity Theme at the MRC Unit in The Gambia.

A key element for success of the research pathway has been the availability of clinical researchers - generally paediatricians or obstetricians who understand the clinical field and epidemiological traits as well as the core research processes. These researchers are generally West Africans – often Nigerians and increasingly Gambians.

The Unit's good reputation was another key element facilitating impact and was credited with enabling the recruitment of mothers and their children into clinical trials. Field coordinators also play an instrumental role in ensuring good relationships with the community by explaining the trials' procedures and obtaining permissions from the heads of communities to approach different populations in view of recruitment.

Another key element across the impact pathway has been the availability of skilled staff that understand processes in the lab including receiving, handling, storing, labelling and shipping of samples.

The experiences shared in relation to this case study suggest one main barrier which pertains to the continuity of funding for core staff. The interviewees highlighted that the main enabler for continuing to do this type of research pertains to the existence of the core team and therefore a perceived barrier was an eventual shrinkage of the team due to a loss of funding, which could affect the existing capacities.

3.2.2.3 Evidence on barriers and enablers from the case studies

- Key enablers identified through the case studies include ongoing engagement with policymakers, flexibility of funding awards, resources and relationships of the units in the region (both MRC and others), and mentorship support across and within countries.
- Key barriers identified include the retention and recruitment of staff, costs and willingness to implement findings in country, recruiting research participants, and logistical challenges around access to and funding for equipment and resources.

Figure 25 provides an overview of key observations from each of the case studies regarding the barriers and enablers identified in terms of delivery of the research projects and their translation into wider outcomes and impacts.

A number of enablers can be identified across the case studies. An important enabler is engagement and relationships with policymakers, including through the conduct of research. Also noted is the flexibility of funding allowing researchers to pursue different research avenues and take opportunities for network and collaboration as they emerge. Also noted is the support and underpinning resources and relationships offered by working with and through the units in the region, both MRC and others (e.g. Wellcome Trust, CDC). These units have a long-term presence and relationships in the countries which facilitate research, alongside a base of core resources and equipment to help support research to start quickly and proceed effectively. Also noted in several case studies are the importance and value of mentorship arrangements, both between project team members in-country and UK PIs, but also amongst and between in-country research teams.

A key barrier mentioned in many case studies was the challenge in retention and recruitment of high quality staff. The case studies note that there is a small pool of in-country researchers and that often good quality staff may be offered better opportunities overseas, particularly when there are gaps in funding in country. Attracting researchers from overseas can be challenging and may often be higher cost and not affordable within some project budgets. Also challenging is recruiting research participants – often a challenge in any country but exacerbated in some cases by the nature of the work, stigma, and a lack of understanding of research and science. This is often addressed through the close local relationships developed and by good quality engagement and information provision. The case studies also highlight logistical challenges in terms of access to equipment and resources, and funding for those resources. Finally, in terms of translation of research into changes in policy and practice, several of the case studies highlight challenges related to both the costs of implementation and low health system resources, and political will and the stability required to enable change in policy.

Figure 25 Key enablers and barriers identified

Project title	Enablers	Barriers
Developing methods to assess the impact of malaria interventions upon transmission and the progress towards elimination	• Flexibility and duration of the fellowship enabled flexible approach to research, supported networking and dissemination (e.g. with US CDC, WHO and PATH, national malaria control programs in Kenya, Zambia, El Salvador, the Gambia and Senegal) • Support from KEMRI/CDC Research Centre provided data to build the models • Collaboration with Professor ter Kuile and the Malaria in Pregnancy Consortium	• No major barriers in undertaking the research. • For implementation, barriers related to costs of implementation and willingness to implement.
Defining the merozoite targets of protective immunity against Plasmodium falciparum malaria through multi-centre cohort studies	• Mentorship relationship between ARL recipient and UK PI • Mentorship relationship between ARL and members of her research group who were empowered to conduct research, engage in dissemination activities, pursue independent	• Challenges obtaining ethical clearances and logistics around sample transport were time consuming. • Challenges in wider capacity building in the African context, particularly: limited career structure and

Project title	Enablers	Barriers
	funding and engage in mentorship activities of their own • Establishing the SMART network which facilitated greater South-South knowledge exchange between African researchers and has enabled young researchers to continue research and pursue PhDs • Ability of ARL to attract other prestigious awards and funding • Access to international networks based in the UK (Oxford) or Germany (Heidelberg) which further allowed knowledge transfer and leverage of cutting-edge technology	mentorship opportunities, few centres that provide the physical and intellectual environment needed to compete internationally; limited networking opportunities.
Studies to understand the response of the infant's immune system to infectious diseases and vaccines	• Availability of core funding which enabled continuity of staff needed for clinical research and community engagement • Nurturing a good relationship with communities through appropriate communications, open days • Engaging the government through meetings with the Unit's team and involving them in discussions on ongoing research data.	• Funding continuity for core staff
Plasmodium falciparum anti-malaria drug resistance in The Gambia: Identification of potential genetic markers by retrospective whole genome approaches	• Flexibility of the fellowship, enabled PI to design own research, support other researchers, engage in networking collaboration and increase visibility. • MRC Unit's platform and governance arrangements facilitated further in-house interactions with other researchers, access to necessary equipment and networking with local decision makers. • Publishing in open source journals increased visibility of research findings.	• Timely access to equipment and consumables (despite Unit efforts) • Accessing and retaining skills: small pool of researchers, ECRs often relocate overseas.
Childhood tuberculosis: Integrating tools for improved diagnosis and vaccines	• Gambia MRC Unit's good reputation and careful community sensitisation allowed good recruitment which could have been challenging given population (prophylaxis in children) • Unit's existing expertise and track record in TB and pool of paediatricians able to conduct high-quality research. • Publications and dissemination activities supported policy impact and development of research staff's careers -especially PhD level, who gained further funding for national capacity building activities or further projects for the Unit. • Engagement with national policy makers enabled national level impacts (new ways of reporting data, training of practitioners and enhanced government expertise in the area of TB).	• Reticence of parents to engage in prophylaxis research for their children. • Retention of staff, particularly postdocs specialised in immunology, molecular biology, and bioinformatics – small pool locally, and international candidates too expensive and difficult to attract. • Access to equipment incl. issues with yearly competitive bidding system. • Expectation from national stakeholders that the Unit would contribute more to building national capacity to deliver health services, which is currently not in the remit of the Unit.
Transfusion and Treatment of severe Anaemia in African Children: a randomised controlled trial (TRACT)	• The scientific relevance of the project was repeatedly cited as an important success factor as it was relatively easy to mobilise support internally at the clinic sites and with crucial partners such as laboratories and blood banks. • Professional management/organisation of the study: all resources came in on time -money, medicines, blood, lab results, etc. Good communication and on boarding staff from the start.	• Development of local research capacity. Limited involvement in research design and subsequent capacity to carry out similar studies independently. • Change in the PI in Malawi, leading to lack of ownership over the study design and implementation which resulted in a large budget overrun.

Project title	Enablers	Barriers
Lung health and exposure to household air pollution in rural Malawi (CAPS)	• Very strong local research support capabilities of MLW and KPS, with a strong presence of field offices and good relationships with local populations. • Highly developed science communication strategy ensured effective implementation of and a positive outlook of the local participants towards science. • Attitude of the MRC-DFID Concordat fund management, allowing scientists to focus on their research due to the low administrative burdens.	• Ensuring use of cook stoves by trial population – can be impractical, and spare parts not available if they break. • Field officers noted difficulties mobilising women to use the cook stoves without compensation. • Lack of initial engagement with the MLW due to the limited local senior presence of the study in Malawi.
MRC/UVRI Uganda Research Unit on AIDS - Mental health among HIV infected CHildren and Adolescents in KAmpala, Uganda (CHAKA) - African Research Leader Award	• The African Leadership award allowed the awardee dedicated time to undertake research. • Having an encouraging mentor, Prof. Patel from LSHTM and a well written proposal were positive elements that helped guide the study. • Working within the research environment of MRC/URVI was regarded as conducive as it already had certain structures in place such as financial, accounting, procurement, storage services that could be used.	• Limited time: two years' funding is not enough, especially when considering the duration for PhD studies. However, this was decided by the ARL and the research team, in spite of the MRC/DFID allowing for a period of up to five years. • Funds specifically for capacity building were not included in the proposal by the ARL.
Prevention Programme - Microbicides	• Trial co-ordinators received training beyond the operational aspects of trial implementation. For example, after attending scientific writing workshops, they went on publishing papers.	• Lack of direct health benefits of MDP was seen negatively in Zambia. Limited male engagement in trial and insufficient senior capacity locally to communicate findings. • Participant recruitment and retention. • Health and safety conditions for staff
Calibration and analysis of complex models: methodological development and application to explore the impact of HAART in Africa	• Enabled cross fertilization of ideas and better awareness of modelling and its uses. • Experience from interfacing with the Ministry of Health and sharing the results of the study with them.	• Results relied heavily on what the needs of the Ministry of Health but there was no funding set aside for any implementation. • Most communication virtual, some face to face meetings/trainings would have further strengthened collaboration and networking

3.2.2.4 Review of pathways to impact statements

- Pathways to impact statements provide a diverse range of information on the intended impacts and approaches to impact across the portfolio
- They differ significantly between funding schemes, making comparison difficult, and the specificity and utility of the information provided varies significantly
- Making comparisons to Researchfish data is challenging, however where this can be done we find discrepancies between planned and achieved outputs, including in the specific details (e.g. collaboration partners) of the plans.

Pathways to impact from ARL scheme

The study team has reviewed the pathways to impact statements[85] for the activities funded through the African Research Leaders (ARL) scheme, drawing on UKRI guidance[86] to assess the ways in which these

[85] These descriptions are part of the proposals submitted by the researchers setting out the way how they wish to achieve impact through their research.

[86] See: https://www.ukri.org/innovation/excellence-with-impact/pathways-to-impact/

are constructed. All documents set out clear pathways to impact, i.e. the project-specific steps taken to ensure that these impacts occur.

It is clear that each of the ARL activities are well-considered in terms of their potential impacts, and all proposals clearly articulate an in-depth understanding of context and user needs. Most are holistic, and take consideration in addressing the full range of impacts that are identifiable in the UKRI guidance:

- Economic: products and procedures, increase productivity/reduction of costs of treating disease
- People: skills, people pipeline (increasing capacity of research)
- Knowledge: scientific advances, techniques, increased knowledge of specific diseases and mechanisms, inputs to/spurs for further studies
- Society: quality of life, health improvement, access to treatments, reduction of anxiety/stigma, policy impacts (evidence bases, intervention revision or design)

The language used when describing these impacts is often rather cautious but addresses the expected long lead-in time to many of the substantive impacts being realised.

Societal and knowledge impacts are most-commonly addressed in the ARL documentation. Least commonly addressed among these potential impacts is capacity-building. However, where this is acknowledged, it is addressed in one of three ways: i) the presence of a senior scientist in the field of study that can drive the development of the field at their institution and draw in research funding; ii) training of the next cohort of scientists through specific Master's and PhD courses established by the host School and taught by the senior scientist and co-investigators iii) regional knowledge exchange among other research centres and universities.

Each ARL identifies a range of appropriate activities to enable impacts to emerge. These include identifying a full and holistic range of stakeholders and beneficiares, including users/patients, researchers/drug developers, policymakers, other regional bodies (institutes, centres, and pan-continental organisations), and global bodies (large medical charities, and the WHO).

The documents also detail specific engagement or dissemination activities and discuss existing engagements where applicable. Some examples of the engagement activities include:

- Ensuring access to the findings for other local, regional and global researchers to use via presentation in scientific conferences, publication in open-access peer reviewed journals and open public domain platforms
- Series of workshops to disseminate findings and discuss approaches for implementation
- Enabling links between resultant data sets and results generated by other work to compare results from different settings
- Active partnerships among other named regional institutes and/or laboratories to collaborate on research problems or foster knowledge exchange (including existing long-standing strategic partnerships between participating universities and large private pharmaceutical companies)

The role of south-south collaboration is also discussed as an important avenue for facilitating and sustaining impact. An example of such network developed is showcased though the case study prepared on the ARL awarded to Prof. Faith Osier in 2013.

MR/L00450X/1 - Defining the merozoite targets of protective immunity against Plasmodium falciparum malaria through multi-centre cohort studies

This is an African Research Leader award to Prof Faith Osier, a researcher from Kenya working on malaria paediatric immunology.

Throughout her ARL award, Prof. Osier was able to use the resources available at KEMRI CGMR-C – both researchers and infrastructure and build a network that would allow knowledge sharing with other African scientists and attract additional funding from entities such as Wellcome Trust and EDCTP.

Using the ARL award, Prof. Osier built the South-South Malaria Antigen Research Partnership (SMART)[87] in 2013, a virtual South-South network which brings together African scientists to share resources and expertise towards producing malaria vaccines and increasing research capacity in Africa. The network shares serum samples and epidemiological data on malaria gathered through prospective cohort studies. Initially envisaged as a network with 3 partner countries – Burkina Faso, Tanzania and Kenya, SMART has grown to 7 countries expanding to Ghana, Senegal, Uganda and Mali.[88] The network took the SMART name under an EDCTP Senior Fellowship which Prof. Osier won in 2016.[89]

The rapid evidence assessment reinforced the above findings, by highlighting that the role of the Concordat in career development is illustrated through the African Research Leader (ARL) Award[90] and the Career Development Award Fellowship[91], with particular note made of the development of Faith Osier's career. She also received the prestigious Royal Society Pfizer prize. Professor Osier has been quoted saying "this award helps put African science and scientists firmly on the map. We can bring positive and meaningful change to African communities through effective research, innovation and leadership".[92] A second recipient of the African Research Leader Award, Iruka Okeke received the Microbiology Society's International Development Fund to develop a discovery-based laboratory course in Nigeria where students with little microbiology skills can develop practical skills in the field.[93] Only one example of career development associated with MRC-DFID Concordat funding different from the African Research Leader Award was found using the search terms for the review. Professor Andrew Prentice has received continuous core funding from the MRC-DFID for 40 years, is currently Professor of International Nutrition at the London School of Hygiene and Tropical Medicine and has been a part of expert panels for numerous national and international organisations.[94]

Pathways to impact for other funding awards

The pathways to impact for the 80 non-ARL projects funded through the MRC-DFID Concordat demonstrate a high level of consideration to the expected impacts of the funded work. Similarly, most applicants made concerted effort to identify the beneficiaries of the work. Across all documents, eight target beneficiary groups were identified (1) General public, (2) Users / beneficiaries, (3) Academics / research community, (4) Public sector / policy makers, (5) Private sector / industry, (6) Practitioners, (7) International community, and (8) Internal staff.

Projects most commonly consider pathways to impact in the academic / research community, followed by the public sector / policy makers, practitioners, and the general public. Pathways to impact in the international community are often cast as advocacy for the project results, or as a route to scaling the results of the project (such as the drafting of international guidelines).

There is little difference in identified pathways to impact between projects funded through the various mechanisms under the Concordat, though the focus of the work itself may differ. The majority of projects propose similar pathways to impact, largely based around one-to-many communication approaches, such as publishing in peer-reviewed journals or non-academic medical journals. Presentation of results

[87] SMART (2018) Science. Africa. Solutions Once Experiment at a Time: https://www.smartpartnership.net/

[88] SMART includes the following centres: Malaria Research and Training Centre (MRTC), Bamako, Mali, Kintampo Health Research Centre, Kintampo, Ghana, Institut Pasteur Dakar, Dakar, Senegal, Centre Nationale de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso, KEMRI-CGMRC in Kenya,

[89] SMART Homepage: https://www.smartpartnership.net/

[90] Medical Research Council (2018) African Research Leader scheme. https://mrc.ukri.org/funding/science-areas/international-and-global-health-research/funding-partnerships/arl/

[91] Medical Research Council (2018). Career Development Award (CDA): Transition to independence. https://mrc.ukri.org/skills-careers/fellowships/non-clinical-fellowships/career-development-award-cda-transition-to-independence/

[92] Faith Osier (2014) Faith and hope: leading malaria research in Africa. https://www.insight.mrc.ac.uk/2014/08/06/faith-and-hope-leading-malaria-research-in-africa/

[93] Microbiology Society (2016) Developing Microbiology Around the World. https://microbiologysociety.org/publication/past-issues/future-tech/article/developing-microbiology-around-the-world.html

[94] Global fNIRS (2018) Andrew Prentice. http://www.globalfnirs.org/45-andrew-prentice

at national and international meetings or conferences is also almost always proposed. Other common approaches include project websites, information leaflets, newsletters, press releases and briefings, policy briefings, and use of video or audio media to reach broader audiences. A small number of projects have suggested the use of mass media awareness-raising campaigns, though only one suggested an additional mass media campaign at the end of the project to publicise results. Serious consideration is often given to access to results, with a number of projects proposing to also publish in open access journals, and to make the analysis of project data available via open repositories. One project specifically intends to make their analytical code available in an open source format.

Most projects have a focus on active two-way communication as well. For example, many will engage stakeholders in advisory roles via the formation of steering groups or advisory boards. These are often made up of academics, policy makers, practitioners and representatives of relevant international bodies. Two projects suggest intensive working meetings with senior ministry staff to substantively engage with the national government. Projects funded through the ADH programme commonly suggest the formation of Community Advisory Forums or Community Advisory Boards, which will include, in addition, members of target populations and their families. The necessity of patient dialogue means that projects funded via the MRC Global Health Trials also each establish similar mechanisms – namely, community meetings and patient/carer groups.

There are examples of more novel approaches in some projects. For example: Sessions at annual science festivals to target younger members of the public, outreach through schools, use of existing broad discussion forums such as Café Scientifique, and the use of learned societies in the UK as a base for specialist engagement.

Capacity building is a major feature of many projects. While this is often limited to training internal staff and students, others focus on training practitioners or other regional stakeholders, and or making cost-effective resources and materials available to them. For example, one ADH-funded project will embed intervention trainers within selected schools and health centres to enable capacity building. Another, funded through the same scheme suggests working sessions and follow-up with local managers to explain the study, clarify implementation procedures, and refine the process based on feedback. One project planned to train counsellors and health workers to be trainers themselves to facilitate cascade capacity building.

Industry-facing pathways are often vaguely described. Many projects suggest having (or forming) active partnerships with named large manufacturers. While these seem appropriate, there is little detail included of how and when this will be undertaken, or what the result of the partnership would be. This is most concrete among projects that suggest the use of existing institutional links and platforms to engage with industry.

Use of institutions' existing functions or platforms is suggested by a number of projects to reach broader audiences, and these often include professional communications functions or other existing groups. This is particularly seen within the fellowships and those projects funded through the MRC Units in Africa.

These factors instead are investigated qualitatively in the case studies. However, to investigate whether there are other data sources which can provide information on the routes to impact on an aggregate level, we also reviewed the useful information available in the prospective pathways to impacts statements[95] for a sample of projects, as follows, comparing this to the impacts subsequently reported in Researchfish. It is important to note that whereas Researchfish responses are large based on a defined set of 'dropdown' menu options, a pathway to impact statement is free text and as such more varied and potentially nuanced though also more difficult to compare and/or aggregate.

[95] Pathways to impact statements are completed by applicants for funding setting out their plans for achieving wider impact from their research and as such detail the planned impact of the research before work starts.

Comparison between pathways to impact statements and Researchfish data

Figure 26 provides a comparative overview of different reporting as envisaged in the pathways to impact statements produced at the proposal stage and those subsequently reported in Researchfish for a sample of 25 projects across five funding routes. More detail on sampling is provided in the methodological appendix.

Figure 26 Description of the impacts for the different funding schemes predicted in the pathway to impacts and the achieved impacts entered in Researchfish

	ADH		ARL		GHTs		Fellowships and IIB	
	Pathway to impact	Research fish	Pathway to impact	Research fish	Pathway to impact	Research fish	Pathway to impact	Research fish
Publications	1	0	2	3	3	2	10	9
Collaborations	3	1	4	4	3	2	12	10
Funding	0	1	1	3	0	2	4	8
Capacity building	2	N/A	3	N/A	1	N/A	6	N/A
Dissemination	2	2	3	2	3	2	11	7
Policy	1	1	2	2	3	0	8	5
Tools	0	0	1	1	0	0	6	5
Databases	0	0	1	0	1	1	1	6

Note direct evidence on capacity building is not available in Researchfish (hence N/A).

Pathways to impact statements typically focus on a more limited range of areas than those covered in Researchfish. For those areas, we identify some differences between the information in the pathways to impact statements and Researchfish data:

- **Collaborations:** All pathways to impact reviewed mentioned collaborations, partnerships, or engagement events as an outcome of the research. Collaborations were reported in Researchfish for 88 per cent of the pathways reviewed, but for the majority of these the collaboration listed is not the collaboration expected. It is worth noting that not all pathways provide the same degree of details on what collaborations they wish to establish. For example, one pathway mentions "partnerships with Western Cape Town Education Department and Cape Town City Health Department" while others refer only to "engaging with local communities". Reporting in Researchfish on collaborations is consistent throughout with entries providing the name of the institution, location, and sector (academic, public, private, hospital, learned society, charity/not-for-profit, multiple) with which collaboration was actually established
- **Publications:** Peer-reviewed publications are mentioned in 52 per cent of pathways to impact and reported to Researchfish in 70 per cent of these. Most pathways to impact mention publications in peer-reviewed journals, usually high-impact journals, but provide no information on number or journal. However, there was one exception that mentioned "8 PLoS-type publications" in their application and has to date produced 13 publications of which 3 are in PLoS One. It is worth noting that it is not necessary for researchers to specify a journal at the proposal stage, or a number of publications – rather it is important that key findings of the work are openly published.
- **Capacity building:** Capacity building is also mentioned in nearly half of the applications (48 per cent). However, it is not consistently captured in Researchfish, as there is no dedicated field for this category. The skills section of Researchfish refers mainly to issues encountered regarding a potential

lack of skills during their project, rather than efforts to develop skills. For example, one Researchfish entry mentions "study doctor position- post difficult to fill due to security risks of working in the study area". Details such as the number of researchers that were supported or trained through the funding (research assistants, post-graduate students, and post-docs) are not evidently available in Researchfish, there are however details provided in the case studies as exemplified below

MR/JO12483/1 - Transfusion and Treatment of severe Anaemia in African Children: a randomised controlled trial (TRACT)

This award was an MRC Global Health Trial, comprising a multicentre randomised controlled trial in Uganda and Malawi of 3,700 children who suffered from severe anaemia (SA). The aim of the study is to investigate directly the factors contributing to severe anaemia and provide evidence on the effectiveness of blood transfusions in paediatric SA cases.

Regarding research capacity, there were a number of different outcomes and achievements. The interviewed co-investigators were in agreement about the added value of the study for their own career development. They identified different pathways of impact for personal capacity building. The first one was through interaction with the PI throughout the implementation of the project, including the discussions on the study design, responding to impromptu challenges and in the general running the trial. A second pathway was through collaboration with the PI on (upcoming) scientific peer-reviewed publications and presentations at conferences. One of the five co-investigators was made full professor on the basis of the published works related to the research project.

Research capacity development is also apparent for support staff. Nurses in Malawi and Uganda were trained to improve their skills set, including medical training as well as training on documenting project results and research management. As a result, they were asked to participate in other (RCT) studies at the clinics and hospitals where they were working. In Malawi, medical students were trained in the hospital where the trial took place, so there is a potential for further knowledge transfer to a new generation of physicians once the results of the study are made available.

- **Additional funding:** Obtaining additional funding is only mentioned in 20 per cent of pathways to impact, yet reported in 72 per cent of the assessed Researchfish entries. This suggests that although not necessarily noted in pathways to impact, a majority managed to secure further funding. This perhaps reflects the fact that this is not a key focus of the pathways to impact statements. As highlighted by the example taken from the case study on 'Childhood tuberculosis: Integrating tools for improved diagnosis and vaccines' the funding attracted include both private and public sources

MC_EX_MR/K02440X/1- Childhood tuberculosis: Integrating tools for improved diagnosis and vaccines

The grant represents a Concordat career fellowship award, the first to be awarded to an African scientist – Dr Alfred Ngwa – to support his research between 2013 and 2018 on projects conducted at the MRC Unit in The Gambia. The projects conducted under his leadership aimed to identify and determine the distribution of malaria drug resistance markers in The Gambia, following five years of implementation of ACT in the country.

Building on the track record and platform established through the grant, the PI was able to attract further research funding from the Global Challenges Research Fund, the EU's Innovative Medicines Initiative, the Program for Appropriate Technology in Health, and a number of pharmaceutical companies.[96]

Collaborations were established with institutions from both the academic and the public sector in the U.S., Canada, U.K., Nigeria, Tanzania, South Africa, Senegal, Denmark and Germany. Research into a TB biosignature of childhood TB has also resulted in a patent filing for this new technology.[97]

We also see differences in the pathways to impact statements between funding schemes, possibly reflecting the different funding schemes' aims and priorities:

- **ADH:** Pathways to impact for applications to the ADH funding scheme focus on collaborations and dissemination as the main outcomes of the funding. There is no mention of peer-review publications but rather social media, newsletter and bulletin communications. Impact on dissemination is

[96] INT Gambia_20A_Researcher

[97] Research Fish Data for the Concordat from 2003 until 2017

reflected in the information provided to Researchfish, where dissemination of the work through magazine, newsletters or online publication is mentioned in the pathways to impact. However, only 1 of the 3 projects reviewed reported on collaborations. Overall, recipients of the ADH award did not provide detailed reports on their impacts, filling on average two fields of impact

- **ARL:** Applications for the ARL Award focus mainly on capacity building, strengthening networks, and policy impacts. However, only half of the ARL Award recipients included in the sample provided descriptive information to Researchfish on these. The ones that provided information to Researchfish referenced collaborations established, additional funding secured, and routes for dissemination of the work as well as policy impacts
- **Global Health Trial scheme:** Applicants for the Global Health Trial scheme focus their pathway to impact on health policy guidelines and engaging communities and national groups. For this sample, these are not reflected in Researchfish, where the main impacts reported refer to publications, collaborations with academic institutions, and additional funding obtained
- **Fellowships and IIB:** The pathway to impact documents focus mainly on peer-reviewed publications, collaborations established, tool development, dissemination, and policy impacts. Because the content of the pathways to impact statements were similar for these two funding routes, they were analysed together. Peer-reviewed publications are envisaged in 75 per cent of pathways to impact statements for both schemes and over 83 per cent envisage collaborations. Policy impact, mainly in the form of participation in advisory committees and influencing WHO guidelines in their field are reported in Researchfish for 41 per cent of recipients of the Fellowships and Infection and Immunity Board scheme reported policy impacts. Tool development in the form of new diagnostics or novel techniques were mentioned in 50 per cent of the pathways to impact and reported by 42 per cent on Researchfish. Dissemination activities, mainly attendance at conferences and international meetings to communicate results of the research were mentioned in 92 per cent of the pathways to impact for both. Dissemination activities, including filming, press release, and conferences were reported by 58 per cent of recipients for both of the schemes in Researchfish. Overall compared with other funding streams, the pathway to impact statements as well as the Researchfish reporting were more comprehensive at least for the sample reviewed

Overall, recipients of all funding streams reported on publications, collaborations, dissemination, and additional funding on Researchfish, regardless of the main focus of impact indicated in their pathway to impact documents. In any case, we might not expect that the outcomes of the project directly align with the pathways to impact statement. The statement is intended to show thinking about engagement mechanisms and key stakeholders for the work. The way in which this is then characterised in Researchfish (e.g. though policy, dissemination or collaboration) may vary and as such making direct comparisons on a numerical basis is challenging.

4 Conclusions and recommendations, future considerations

This review was aimed at providing the MRC and DFID with answers about the performance and added value of the Concordat that emerged between 2013 and 2018 by looking at the collaboration between the two organisations as well as the portfolio of funded projects. The methodology applied made use of all existing and accessible evidence, and the design of the review ensured that the finding of the different data collections tools and analytical technics can be triangulated. The methodological considerations further to the limitations of the data used during the study and therefore the analysis undertaken are described in the appendix of the report. The findings based on the evidence collected were presented in the previous chapter, next we set out our conclusions and put forward recommendations for further considerations.

4.1 Part A: MRC-DFID Concordat performance and value for money

Awareness of the Concordat and its international reputation

The two organisations, the MRC and DFID, are well known and widely respected, the Concordat brand is still not well recognised in the scientific community, although there have been some improvements since 2012. Stakeholders are aware of MRC and DFID funding for global health research but are not very familiar with the Concordat or its full portfolio. The work delivered through the Concordat funding is, however, well regarded both nationally and internationally. In particular, the African MRC Units have a strong reputation and the ARL scheme is highly regarded.

The Concordat portfolio represents a pool of money which the funders use to address (1) new and upcoming topics and challenges through high quality research funding, in combination with (2) long-term strategic funding initiatives e.g. the African MRC Units. The contributions of MRC and DFID funding for global health research and research capacity building are recognised internationally for the quality of the resulting outputs and impacts. The Concordat as it stands delivers many good outcomes and impacts, but there is scope to review the coherence of the portfolio. The Concordat does not have an agreed theory of change nor a clear strategy around how objectives are achieved through the different funding streams used. A theory of change (as presented in Figure 4) has been developed for the Concordat in this review, that clearly sets out the inputs, activities, outputs, outcomes and impacts to be achieved – this could provide a starting point for more strategic thinking about the composition of the portfolio, and a structure for analysing whether the portfolio achieves its aims.

Overall, the extent to which the Concordat needs to have a clearer external brand is a matter for the MRC and DFID to determine. In any case, based on our review, the funded project portfolio contributes to the delivery of the expected outcomes and impacts through the various schemes and initiatives and Concordat funding contributes to the UK's international reputation according to a majority of the stakeholders interviewed.

Relevance of the Concordat

The Concordat is responding to some of the most pressing health challenges worldwide by supporting health research and research capacity building in and concerning LMICs. The Concordat documentation states that capacity building is intended to be a key outcome of the funding. Evidence collected during the review identified sustainable capacity building as a key achievement of the Concordat portfolio. Some award schemes are particularly focused on supporting research capacity building – notably the ARL scheme, which has been effectively replicated by the Wellcome Trust, an indicator of good practice. The capacity building is not limited to research capacity building, but also extends to health systems and practitioners within the countries and settings the research is taking place.

National and international global health funders and organisations, global health experts and researchers concur that Concordat projects are broadly relevant to global health research needs and have

the potential to address key societal challenges in LMICs. There are some structural and thematic gaps in the Concordat portfolio that were identified by interviewees, although there was no consensus regarding them. Structural gaps concerned the need for further coordination among the research funders, limited engagement with local stakeholders in LMICs, lack of South-South links and concentration of funding to a small number of high-performing Southern institutions. Interviewees formulated thematic gaps outside the infectious diseases area.

Capacity building in the Concordat funding

Capacity building is a key outcome of the Concordat portfolio which is emphasised in the unit reviews and illustrated through the case studies. This is not limited to the project teams but expands to wider researchers and practitioners engaged in the work. There are several examples where the work supported led to new fields or techniques being opened up within the country, such as the case studies highlight. Some award schemes are particularly focused on supporting research capacity building – notably the ARL scheme, which has been effectively replicated by the Wellcome Trust, an indicator of good practice.

However, it is not clear that capacity building is built in as centrally and as carefully considered across the portfolio as a whole. For example, we noted cases where it had been challenging to access funds for training opportunities for junior staff, or to advance staff into PhDs. This may be because this had not been anticipated or could not be costed at the outset in a given funding stream. This links to one of the key challenges noted which is recruiting and retaining quality staff in-country. This is because in many LMIC there is only a small pool of researchers available, and many of these will seek opportunities overseas. Attracting overseas researchers to replace them can be challenging and is typically costly. Linked to this is the lack of a structured career development pathway and scope to build a research career and win independent funding.

Linked to this, we also note that UK PIs still retain a very strong role within much of the research conducted. While this is not necessarily an issue per se, it might be beneficial to think through at a programme level the extent to which leadership and direction for research should come from UK-based and in-country researchers. Consideration could be given to the best ways to ensure that this is a true partnership in research and that appropriate opportunities for leadership and development are offered to non-UK researchers.

In addition, interviewees from the global health research community suggested that a number of smaller grants could be made available to allow younger or earlier-career researchers to engage with the funding. This should be underpinned by a clear capacity building plan already at the proposal stage including how funds will be allocated. Such funding would be especially important in Sub-Saharan Africa where there is little, if any, training available for early stage career researchers who represent the future leaders of research groups in their respective countries. Overall, the Concordat could consider more strategically how the portfolio actively supports capacity building, perhaps working more collaboratively with in-country funders (or potential funders).

Management of the Concordat

The management of the Concordat draws on the expertise of two organisations with high reputation among their respective fields. Combining the expertise of a research funder and an aid agency created a unique partnership. The MRC and DFID both have strong identities and networks and complementary field of expertise. The Concordat portfolio is solely administered by the MRC, but DFID adds value through the country specific knowledge and drive for implementation.

The partnership however also sets high demands and expects the Concordat portfolio to address dual objectives, which have to be accomplished through creating a delicate balance between the mission of the two organisations. The long-term relationship between the two organisations and the management arrangements set to overview the progress of the Concordat portfolio have established well-functioning working processes that create a win-win situation for both organisations and delivers mutual benefits. Important platforms for cooperation are the quarterly management reviews between DFID and the MRC as well as the MRC's Global Health Group meetings. While the former includes discussions on more

administrative and operative aspects and concentrates predominantly on the Concordat portfolio, the Global Health Group meetings provide the broader perspective of MRC's Global Health Funding and engage external expert opinions as well.

While DFID personnel are participants at these meetings, the role of DFID within the Concordat, beyond its funding contribution, is not clear to most stakeholders externally. Indeed, their active engagement seems to be primarily focused on input at the priority setting stage. There may be opportunities to draw more fully on DFID's expertise and networks and to create a more joined up approach between the work of the Concordat and their wider activities and resources especially in the fields of health support and wider capacity building in the health sector. Similarly, the MRC could foster further synergies with their wider global health research funding and relationships internationally. This links to the potential for more strategic planning as set out above. Therefore, the Concordat may wish to consider setting out a joint vision and key priorities to capitalise on the shared knowledge and expertise across the organisations.

An important aspect of the management of the Concordat is about capturing the outputs, outcomes and impacts of the funded projects. This topic is discussed in detail in the next chapter. The outputs, outcomes and impacts of the funded projects are tracked through self-reporting by researchers in the Researchfish database predominantly, although different schemes such the ARL or the Unit programmes have additional complementary monitoring procedures in place as well. An underlying issue that needs consideration for the future is, that capacity building impacts do not appear to be captured adequately. Given its centrality to the Concordat's aims, capacity building could be better addressed by project reporting. This encompasses two elements: the ability to capture capacity building evidence within existing reporting mechanisms, and engagement of partner country researchers in the impact reporting process. A more holistic reporting approach might be useful to help ensure this important element of the work of the portfolio is adequately acknowledged, captured and recognised.

Measures of capacity building could include number or proportion of local staff taking on different (including leadership) roles within projects, and markers of subsequent career success for members of the project team - for example, securing independent funding (some information on this is captured in next destination information, but it is limited in scope). Taking a slightly different perspective, it is also important to note that Researchfish is typically completed only by awards' PIs, who are usually UK researchers. Engaging the co-investigators and developing country partners more in the reporting of the outcomes and impacts of research could be beneficial in terms of capacity building since it would build an increased understanding of research processes, reporting, and the expected outputs of research. This may equip those individuals with the capabilities to seek additional funding and engage effectively with research funding organisations.

Value for money

The Concordat presents good value for money through the efficiencies emerging from joint working, particularly grant administration costs saved by DFID through using existing MRC management processes to deliver the Concordat. In addition, the partnership also offers value for money by promoting synergy and complementarity through pooling of resources, greater critical mass and avoidance of duplication and by facilitating the production of high quality research outputs.

The evidence collected as part of this review on and main findings-related to the quality of research outputs and the impacts delivered are summarised in the Part B of this study. However, it is important to highlight with regards the value of money the Concordat that the portfolio is seen as presenting very good value for money in terms of producing high quality research.

The Concordat in the Official Development Assistance (ODA) funding landscape

There have been a number of significant changes in the UK ODA funding landscape in the recent years. The Concordat funding is part of the UK Government's committed spend (0.7% of Gross National Income) on ODA along with the Global Challenges Research Fund and the Newton Fund. While it is already decided that DFID's funding to the Concordat will be reduced for the next five years, this does not represent a reduction of global health funding, but a reallocation of funding channels used. A key

priority objective of the ODA funding remains that projects with the largest potential impact across challenge areas to be selected. Considering funding allocations, it also has to be taken into account, that global health research and development is increasingly being funded by public-private partnerships involving businesses, government funders and NGOs. The latter are highly important as they have presence in local communities, thereby their knowledge helps increase the relevance of research to communities.

International outlook

Reviewing the work and relationship of aid agencies and research funders in other countries highlights, that the MRC-DFID relationship has a lot of similar features with it counterparts. Looking at examples from France, Norway and the US, experiences highlight that the combination of formal and informal arrangements result in efficient joint implementation and high-quality results. There is a need for well-established working processes, regular meetings between the partners that are supported by external expertise such as by advisory boards and committees that input to the development of strategic directions of funding. These arrangements can take different shapes and forms, and the collaborations can be governed by multiannual work programmes or letters of funding allocation for example. The selection of priority countries and funding themes and topics represent areas of mutual interest.

4.2 Part B: Research outcomes and impacts

Evidence suggests that the Concordat portfolio produces a range of useful outputs and benefits spanning high quality academic outputs, local capacity building at the LMIC partners, and wider benefits, notably on policy and practice, in line with at least one international comparator. Given the relatively young age of the portfolio this can be expected to develop and broaden over time. The impact case studies developed as part of the review provide insight into the different impacts achieved as part of the funding provision. They also highlight a broad range of benefits delivered not only to the project participants, but more broadly in terms of scientific knowledge, results concerning research capacity building as well as impacts on policy in LIMC. Reporting through Researchfish provides a collection of scientific publications, collaborations, skills development and examples of policy impacts. Interviews emphasised the high esteem in which the research conducted by the portfolio is held.

Figure 27 Suggestions and recommendations from case studies

Project title	Recommendations
Developing methods to assess the impact of malaria interventions upon transmission and the progress towards elimination	• Maintain flexibility in use of funding • To support translation, DFID could become more engaged (e.g. organise workshops for programme managers from various institutions to discuss use of evidence in policy) • Specify funding limit for Joint Global Health Trials • Allowing financing of PhD students in projects through this funding scheme to support capacity building
Defining the merozoite targets of protective immunity against Plasmodium falciparum malaria through multi-centre cohort studies	• ARL award is extremely helpful and interviewees suggested expanding number of available awards throughout Africa • Consider articulating a structured fellowship scheme that could allow African researchers to move from the early to the late stages in their careers
Studies to understand the response of the infant's immune system to infectious diseases and vaccines	• Maintain core funding for the Unit and an open dialogue on potential adjustments that may be needed to support an increasing body of work in the area of vaccines and immunology • Create opportunities for the Unit to disseminate their research funding for projects that are not solely funded by the Concordat • Communicate to researchers the use of Researchfish data and the type of analysis the Unit could potentially undertake in house in order to produce materials that may be used to showcase their achievements

Project title	Recommendations
Plasmodium falciparum anti-malaria drug resistance in The Gambia: Identification of potential genetic markers by retrospective whole genome approaches	• Maintain the current degree of flexibility in use of funding • Emphasise the importance of career development for both recipients and wider researchers – including metrics to recognise this • Development partners (e.g. DFID) could invest more in capacity to supply and deliver equipment • Consider developing additional funding streams for national or regional early career researchers (potentially including bridging funding to support retention)
Childhood tuberculosis: Integrating tools for improved diagnosis and vaccines	• Support more capacity building elements by ring-fencing some grant finances for PhD studies • Access to equipment could be facilitated by organising specific calls for special overseas units • Considerations by both the Unit and the Concordat of incentives for postdocs, considering the challenges with attracting and retaining qualified staff • Improved incentives for collaboration between different units operating in Africa including between MRC units and Wellcome Trust units • Collaborations with industry were described as rudimentary, partially because industry has a very set scientific agenda. Knowledge sharing on how to best engage with industry and establish agreements that have provisions for capacity building could be considered
Transfusion and Treatment of severe Anaemia in African Children: a randomised controlled trial (TRACT)	• Need to involve local investigators[98] as PIs from the start of projects to ensure sustainable local capacity building and execution of the projects • More attention should be paid to policy follow-up by both the research team and the funder • Part of the grant should be allocated towards sharing the results and ensuring engagement with policymakers
Lung health and exposure to household air pollution in rural Malawi (CAPS)	• Increasing the local research involvement at a more senior level for large trial studies could ensure smoother engagement and increased capacity building • More intensive training of participating government health staff in terms of Good Clinical Practise could have been helpful to ensure lower drop-out rates and higher consistency of care during the trial • More attention could be paid by the research designers to the sustainability of the local health interventions
Mental health among HIV infected CHildren and Adolescents in KAmpala, Uganda (CHAKA)	• The provision of a wider range of schemes that would address early career and intermediate level researchers to develop their research capacity would be very helpful to have
Prevention Programme - Microbicides	• Ensure that an investment is in place for a strong PI's role in local host centres, to represent and lead as issues arise • The community of women participating in HIV research should be sustained beyond the end of the trial, because this community could continue to benefit from a privileged access to outpatient services at the host centres and may constitute a cohort of participants for the next trial[99] • A specific need to capture the delivery and the adherence of HIV drug treatment to communities was voiced. In order to achieve this through indicators, it is necessary to involve the national government so as to access people's national identity numbers[99]

[98] By 'local' interviewees meant researchers who worked and lived for a long period of time in the host-country. As a rule of thumb one could consider a criterion of paying taxes in the host-country to be qualified as a 'local' researcher.

[99] Face-to-face interview held on May 22nd 2018.

Project title	Recommendations
Calibration and analysis of complex models: methodological development and application to explore the impact of HAART in Africa	• Build the capacity of policy makers with regards to modelling and what it can be used for, to make them understand and believe in its results • Training more local researchers in modelling to strengthen this field and build critical mass so that these methods can be used in other areas of importance like non-communicable diseases • Setting aside some funds to follow up the results of the modelling study over time to see if what was predicted actually happens • Finally, for successful implementation the health system itself would need to be strengthened via the Ministry of Health. Some thoughts for how this can be achieved, warrants some consideration in future studies

Challenges faced by researchers working on the awards within the portfolio, in terms of both conducting the research and translating it into practice, have been varied and there have also been a range of enabling factors. Figure 27 summarises the key recommendations at a case study level, and some of the key themes emerging in relation to impact and research to impact pathways are summarised below.

Relationships and networks

A core element underpinning the functioning of the portfolio are the diversity of networks and relationships which have been cultivated and which researchers draw upon to effectively conduct and communicate their research. Good relationships particularly on a local level, with participants, community leaders and policy stakeholders emerge as key facilitators of research and its translation, and international profile and networks (e.g. with the WHO) have also been core to the international impacts noted on policy. A strand of this which emerges from the case studies in particular is the importance of awareness raising and community mobilisation as part of the outcomes of the projects examined, with not the research outcomes specifically, but rather the wider awareness raised and community support gathered around issues such as mental health that have led to policy change and engagement.

Role of units as hubs for research

The presence of a research hub, whether that is an MRC research unit, or a unit or centre run by another organisation (e.g. Wellcome Trust, CDC) is an important facilitator of research and translation. Part of this links to their ability to build and maintain these crucial relationships on a local level over the long-term, which is further strengthened through clear evidence of a long-term commitment to capacity building and health improvement in the country. They are also important in offering core research infrastructure and equipment which can be challenging to source in some regions for both logistical and financial reasons. Moreover, they offer the potential to develop and nurture core human capacity over time, which is an important challenge noted across the analysis.

Researchfish and evaluation

Researchfish offers a comprehensive data set across the entire portfolio that captures a wide range of useful output and outcome data in a consistent way. It is generally appreciated by researchers as being relatively quick and easy to complete, and from an evaluation perspective it is important for a number of reasons. Firstly, to collect a comprehensive cross-portfolio data set similar to Researchfish retrospectively would be at a minimum costly, and likely unfeasible. Response rates to surveys of researchers for evaluation purposes vary but typically levels of around 50% can be expected. Furthermore, many researchers from older projects would be difficult if not impossible to contact and recall on the outputs of projects historically can be limited. It is also comparable to other funders and is unique in providing a broad, longitudinal dataset on the outputs of research across not just the Concordat portfolio, but all MRCs (and many other funders') research.

Despite these advantages, there are a number of limitations to Researchfish in the specific context of the Concordat, particularly in relation to the way in which it addresses capacity building. This encompasses

two elements – the ability to capture capacity building evidence within existing reporting mechanisms, and engagement of partner country researchers in the impact reporting process.

At present, the impacts of the research on capacity building are not fully captured by the key reporting mechanism for the portfolio, Researchfish. This is because the fields within Researchfish are intended for a wide range of research reporting and as such impacts on wider capacity building (rather than just specific awards and honours to members of the team, for example) are not fully addressed. A more holistic reporting approach might be useful to help ensure this important element of the work of the portfolio is adequately acknowledged, captured and recognised. Some of this is captured in the five-year Unit reviews but this does not span the entirety of the portfolio. Measures of capacity building could include number or proportion of local staff taking on different (including leadership) roles within projects, and markers of subsequent career success for members of the project team - for example, securing independent funding (some information on this is capture in next destination information, but it is limited in scope).

Taking a slightly different perspective, it is also important to note that Researchfish is typically completed only by awards' PIs, who are usually UK researchers. Engaging the co-investigators and developing country partners more in the reporting of the outcomes and impacts of research could be beneficial in terms of capacity building since it would build an increased understanding of research processes, reporting, and the expected outputs of research. This may equip those individuals with the capabilities to seek additional funding and engage effectively with research funding organisations.

Translating research in challenging local contexts

A key challenge identified in the translation of research into practice is the local context in which researchers and other stakeholders are operating. In many LMIC, the resources available within the health system are limited and opportunities for training and skills development for practitioners may be limited also which can make the uptake of findings into practice challenging. Many concordat-funded researchers invest significant effort into practitioner training and capacity building as noted above, however it is more challenging for them to address resource limitations within the system. Alongside this, political will is needed to uptake new findings into practice, and in some cases beyond this political instability has been a challenge not just in terms of building and maintaining the necessary stakeholder relationships, but on a practical level in terms of conducting the research. There may be a role for the funders, particularly DFID, to play, to help mobilise and draw on their networks and resources, where feasible, to help address some of these challenges by providing researchers with links to key stakeholders, and perhaps where appropriate and feasible, linking other activities that may be ongoing around education and health to the research work being conducted. Better integration might support the more effective delivery of work across the DFID portfolio. MRC could also have a role to play in terms of mobilising research networks and looking to build collaborative co-oproduction relationships with some national governments to facilitate better buy-in and sustainability for the research and its applications. This links to the potential for more strategic planning as set out above. Therefore, the Concordat may wish to consider setting out a joint vision and key priorities to capitalise on the shared knowledge and expertise across the organisations.

Considerations of impact channels

These different pathways and, particularly, the stakeholders needed for effective research translation, are typically reasonably well considered in pathways to impact statements at the application stage. However, the scope and quality of these differs significantly over time and between funding streams. There could be scope for MRC to offer better guidance and examples of good practice in terms of how to present information in pathways to impact statements to make them more useful both in terms of planning and for subsequent analysis. More consistency would also be valuable in terms of understanding the real differences between plans. As noted above, guidance could also be offered regarding capacity building and how this should be captured at the proposal stage since at present this is unclear for some programmes. Having clear capacity building plans across the portfolio, including

how funds will be allocated, may help ensure this is adequately considered and costed for more consistently across awards.

4.3 Recommendations for the future development of the Concordat

1. The MRC and DFID through the Concordat should continue to fund high quality work selected on merit, that offers opportunities for creating new knowledge, capacity building and impacts on policy and practice. This should include continued support to the existing units as well as looking beyond and build further networks and relationships with other units and centres in LMICs, which could become key hubs for researchers to conduct research across different regions.
2. Capacity building should be a key consideration across the whole portfolio. Potential ways to support capacity building across different funding streams could include increased flexibility in funding awards, making funding available specifically for training, requiring specific plans on capacity building within applications, and strengthening partnership and leadership opportunities for partner country researchers.
3. Building on the theory of change, the MRC and DFID should establish a clearer strategy setting out the routes through which the Concordat invests and how they contribute to the ultimate goals of the programme. In addition, setting out a joint vision and key priorities would also help to clarify the identity and brand of the Concordat, and increase its visibility.
4. The Concordat has the potential to benefit more fully from input from both funding partners, especially DFID. Thinking through ways to integrate the Concordat into the wider work of the two organisations could help capitalise on shared knowledge, networks and expertise of the MRC and DFID. Increased integration into the work of the two organisations would also help to address some of the wider societal challenges which can be a barrier to translation of research findings.
5. The MRC and DFID could further the implementation of research results by building on and developing existing and new relationships with wider non-research organisations (e.g. government bodies, health providers) in partner countries.
6. Since capacity building is a core element of the programme, reporting should be expanded to capture information on capacity building more effectively and by engaging researchers across the project team.
7. More guidance should be provided on how to complete the pathways to impact statement in proposals. This could also help researchers to consider more thoroughly how they intend to achieve impact through their research.

Appendix A Schemes and initiative in the Concordat portfolio

A.1 Schemes and initiatives funded through the Concordat

We provide a brief description of the different schemes and initiatives that provide funding as part of the Concordat portfolio:

1) **MRC Research Boards** - There are currently four permanent research boards viz. the Infections and Immunity Board (IIB), the Neurosciences and Mental Health Board (NMHB), the Molecular and Cellular Medicine Board (MCMB) and the Population and Systems Medicine Board (PSMB). The boards have broad remits[100] (see appendix), hold their own research budgets and review and manage scientific activity within their specialist areas.

2) **Unit Programmes (Intramural)** - Concordat-related research is carried out in the two MRC Units based in Uganda and the Gambia. The MRC acted as the main employer of staff until February 2018, when the Units transferred to the London School of Hygiene & Tropical Medicine (LSHTM). The Units remain Africa-based academic research institutions with scientific independence within the LSHTM. In general, units are set up to meet specific needs, for example, to provide scientific leadership in key research fields, or to tackle important research questions where the need cannot easily be addressed through response mode grant funding only

3) **Concordat-specific funding**

- **African Research Leader (ARL) scheme:** The ARL scheme is a prestigious award available to researchers based in sub-Saharan Africa. The scheme aims to strengthen research leadership in the region by attracting and retaining exceptionally talented individuals who will undertake high-quality programmes of research on key global health issues of relevance to the region. [101] A total of 14 African Research Leader awards have been awarded between 2011 and 2017 through the Concordat, with an average grant size of £0.9m
- **European & Developing Countries Clinical Trials Partnership (EDCTP)** - The MRC funds clinical trials under the Concordat as part of the UK contribution to the EDCTP programme of the EU.[102] Under EDCTP2, Member states and the European Commission together with partner states in sub-Saharan Africa have developed a 10-year programme focused on late phase (phase 3) intervention studies on products against HIV, TB and malaria, and also extending into neglected tropical diseases and post-efficacy studies (phase 4) including health systems optimisation
- **Implementation research to improve adolescent health in low and middle-income countries (ADH) -** A total of £3m research funding was available under this strategic call, which was open from May 2015 to January 2016. Applications were accepted from principal investigators based at organisations either in the UK or in low, lower-middle and upper-middle income countries. As the underlying aim of this call was to provide the research evidence needed to affect real and practical changes to improve adolescent health in LMIC, the main focus was on conducting implementation research. After the pilot call, £10m call with joint funding from DFID, NIHR and MRC was subsequently launched for 2017/18. [103, 104]

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100 Further information on the remits of the Research Boards can be found at: https://mrc.ukri.org/about/our-structure/research-boards-panels/

101 https://mrc.ukri.org/funding/browse/arl-2018/mrc-dfid-african-research-leader-scheme-2018/

102 Further information http://ec.europa.eu/research/evaluations/pdf/edctp2_evaluation_experts_report_2017.pdf

103 MRC Global Health Group: Minutes of Meeting 11th-12th April 2017

104 Further details on the call https://mrc.ukri.org/funding/browse/mrc-dfid-nihr-adolescent-health-lmic/mrc-dfid-nihr-call-for-research-to-improve-adolescent-health-in-an-lmic-setting/

4) MRC awards with some Concordat funding

- **Developmental Pathway Funding scheme / Developmental Clinical Studies** (DPFS/DCS) – the scheme[105] is a key part of the MRC's Translational Research Strategy106 and supports the translation of fundamental discoveries toward benefits to human health. It funds the pre-clinical development and early clinical testing of novel therapeutics, devices and diagnostics, including "repurposing" of existing therapies. In other words, projects that concern improving prevention, diagnosis, prognosis, or treatment of significant health needs, or that focus on developing research tools that increase the efficiency of developing interventions are within scope
- **Experimental Medicine (EM)** – the scheme is a core element of the MRC's overarching translational research strategy. Under this research area, the MRC funds investigations in humans to identify mechanisms of pathophysiology or disease, or to demonstrate proof-of-concept evidence of the validity and importance of new discoveries or treatments
- **Fellowship schemes** - At any one time, the MRC supports around 1,900 PhD students (including pre-doctoral fellows) and 200 post-doctoral fellows. Some of these are under the Concordat based on the decisions made by the MRC on a case-by-case basis
- **Methodology Research Programme (MRP)** – jointly funded by the MRC and NIHR[107] is overseen by an expert panel that considers response-mode grant applications in selected research method-related fields. Priority methodological challenges are signposted to applicants in highlight notices. An MRP Advisory Group advises the MRP Panel on the strategic priorities.
- **Public Health Intervention Development scheme (PHIND) -** supports the early stages of development of new innovative interventions that address an important UK or global public health issue and complements funding schemes from NIHR and MRC (Global Health schemes) that also support public health intervention development and evaluation.

4.3.1 MRC Research Boards

There are currently four permanent research boards viz. the Infections and Immunity Board (IIB), the Neurosciences and Mental Health Board (NMHB), the Molecular and Cellular Medicine Board (MCMB) and the Population and Systems Medicine Board (PSMB). The boards have broad remits[108] and hold their own research budgets, review and manage scientific activity within their specialist areas (Figure 28).

Figure 28 The MRC Research Boards and the Concordat

Research Board	Remit and Scope	Current priority areas	Strategic relationships
Infections and Immunity Board (IIB)	• Infections • Immunology in health and disease • Global infections	Antimicrobial resistance, vaccines, systems immunology, neglected tropical diseases, ageing	• Responsibility for MRC research units in Africa (Uganda, the Gambia)

[105] https://mrc.ukri.org/funding/browse/biomedical-catalyst-dpfs/biomedical-catalyst-developmental-pathway-funding-scheme-dpfs-mar-2017/

[106] https://mrc.ukri.org/funding/science-areas/translation/

[107] https://mrc.ukri.org/funding/browse/mrp/methodology-research-programme-nov-2018/

[108] Further information on the remits of the Research Boards can be found at: https://mrc.ukri.org/about/our-structure/research-boards-panels/

Research Board	Remit and Scope	Current priority areas	Strategic relationships
		immune system, fungal disease	
Molecular and Cellular Medicine Board (MCMB)	• Structural biology and biophysics • Molecular and functional genetics, epigenetics, genomics • Developmental and stem cell biology, and regenerative medicine • Molecular haematology • Chemical biology • Medical bioinformatics • Cancer • Toxicology, and environment and health • Pharmacology • New technologies	Repair and replacement, molecular datasets and disease, environment and health, and capacity and skills	• MRC institutes, units and centres in areas relevant to the remit and scope of Board • Generic infrastructures that underpin many other areas of basic and translational medical research e.g. UK Stem Cell Bank, UK Biobank, European Bioinformatics Centre, Diamond Light Source
Neurosciences and Mental Health Board (NMHB)	• Neurodegeneration • Clinical neurology and neuroinflammation • Mental health • Addictions and Substance Misuse • Behavioural and learning disorders • Cognitive and behavioural neuroscience and cognitive systems • Sensory neuroscience, vision and hearing • Neurobiology and neurophysiology • Underpinning support such as neuroimaging technology, brain banking and neuroinformatics • Chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME)	Addiction, autism, neurodegenerative diseases and dementia, mental health, PET imaging	• Partnerships with organisations such as other research councils, biomedical research charities, international funders or industrial partners (e.g. ESRC, EPSRC, Alcohol Research UK, EU Joint Programme – Neurodegenerative Disease and Centres of Excellence Network)
Population and Systems Medicine Board (PSMB)	• Cardiovascular disease • Neurovascular Ageing • Respiratory medicine • Musculoskeletal research • Gastroenterology • Renal medicine and liver function • Endocrinology and reproductive health • Maternal health and the early origins of health and disease • Nutrition, metabolic regulation, diabetes and obesity • Trauma, acute medicine and surgery • Medical sociology • Population health	Experimental medicine, prevention research, stratified medicine, lifelong health and ageing, informatics, systems medicine, methodology research (e.g. in relation to clinical trials methodology)	• Three centres jointly funded with Arthritis Research UK and Asthma Research UK • British Heart Foundation • MRC institutes, units and centres in areas relevant to remit and scope of board

Apart from grants funded through the research boards, the following response-mode and strategic programmes and schemes also contribute to delivering the objectives of the Concordat.

4.3.2 Unit Programmes (Intramural)

Concordat-related research is carried out in the two MRC Units based in Uganda and the Gambia. The MRC acted as the main employer of staff until February 2018, when the Units transferred to the London School of Hygiene & Tropical Medicine (LSHTM). The Units remain Africa-based academic research institutions with scientific independence within the LSHTM.

In general, units are set up to meet specific needs, for example, to provide scientific leadership in key research fields, or to tackle important research questions where the need cannot easily be addressed through response mode grant funding only. They have no set time limit or end date of the funding foreseen by the MRC. Moreover, in addition to generating relevant scientific knowledge, the units have contributed to developing capacity of future research leaders in their specialist areas. For example, the Gambia Unit ran a West African Fellowship Scheme in partnership with the London School of Hygiene and Tropical Medicine to fill the gap in postdoctoral-level capacity in Africa and to encourage young UK-based researchers to engage in global health research.[109] The scheme was purposefully aimed at researchers at an earlier stage in their career than those applying to the African Research Leadership scheme to ensure that it was clearly differentiated from other capacity building schemes.

The MRC/UVRI & LSHTM Uganda Research Unit

The MRC/UVRI & LSHTM Uganda Research Unit is an internationally-recognised centre of excellence for research on HIV infection and related diseases, based at the Uganda Virus Research Institute (UVRI) in Entebbe.[110] The Unit has over 30 years of experience and has developed significant expertise in conducting studies to the highest international scientific and ethical standards. It is equipped with state-of-the-art infrastructure at its Entebbe base and at field stations in neighbouring districts.

As of 2017, the Unit employed over 360 scientific and support staff (13 of the core positions, such as the director of the Unit and the head of sections, are funded by the MRC Head Office[111]), and has received research funding from multiple organisations in the UK, the US and the Netherlands, as well as large international organisations.[112] The Unit has undertaken collaborations with other research groups in Uganda[113] and regional bodies such as the Africa Centres for Disease Control and Prevention, and is continuing to establish local and international collaborations across each of its research programmes.[114]

A consultative and desk-based review of the Uganda unit in 2014 identified a range of issues facing Uganda and East Africa including the changing demographic of Uganda, growing population, magnitude of issue of infection, growing issue of NCDs, maternal, infant and child health, urban living and health systems research.[115] On this basis, it was recommended that the scope of the Unit should be broadened with some internal restructuring to accommodate this shift. There was also a desire to forge stronger partnerships in the region to further develop the Unit, for example, with Makerere University.

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[109] MRC Global Health Group: Minutes of 9th meeting, 2 May 2013, obtained from the MRC

[110] https://www.mrcuganda.org

[111] List of key positions funded by the MRC Head Office can be found in the MRC/UVRI Uganda Research Unit on AIDS, Quinquennial Review, May 2016

[112] Including: The UK Department for International Development, the UK Economic and Social Research Council, the Wellcome Trust, the US National Institutes of Health, the International AIDS Vaccine Initiative, the European Union, the European and Developing Countries Clinical Trials Partnership, the Food and Agriculture Organisation of the United Nations, Cordaid, the World Health Organisation

[113] Including: The Joint Clinical Research Centre, the Infectious Disease Institute, and Makerere University

[114] For example: Pfizer, the International Partnership for Microbicides, the University of Minnesota, the INSIGHT Network, the University of York, Dignitas International Malawi, the Uganda Ministry of Health Mental Health Division, Makerere University Department of Psychiatry, the University of California San Francisco, the Child Health Development Centre in Kampala, the London School of Hygiene and Tropical Medicine, the Sanger Institute, the Leiden University Medical Centre

[115] MRC Global Health Group: Draft Minutes and Matters Arising of 12th Meeting 8th-9th January 2015

Due to the diverse characteristics of HIV infection, the Unit takes a multi-disciplinary approach. The Unit ran several research programmes between 2012 and 2017, [116] comprising around 40 projects. Basic science studies and work in HIV prevention and epidemiology each represented almost one third of the Unit's budget over the period, while work on HIV care and Social sciences studies each represented just over one sixth. The Unit's budget for the period was over £16m from Concordat funding, with an additional almost £13m attracted in grant funding. A further almost £5m was expected at the time of reporting. The Unit also undertakes broader work, in priority areas for the Uganda Ministry of Health, for which it receives external funding.[117]

The MRC Unit in The Gambia at the London School of Hygiene and Tropical Medicine (LSHTM)

The MRC Unit in The Gambia at London School of Hygiene and Tropical Medicine (LSHTSM) aims to accelerate progress in international health research.[118] The Unit comprises laboratory facilities and enables access to the field with well-defined and highly supportive populations. The Unit is based in the city of Banjul and represents almost 70-year presence of the MRC in the Gambia. The Unit operates field stations in Basse, Walikunda, and Keneba.[119] In the period 2010-2015, the Unit's total budget was over £88m, including estates capital and equipment and asset renewal, and inclusive of core and additional funding.

The Unit delivers research, clinical services, and GCP-compliant clinical trials. The Unit's large research portfolio includes both basic research and the evaluation of interventions for the control of diseases of public health importance in sub-Saharan Africa. The Unit's research is organised in three major themes:[120]

- Disease Control & Elimination focuses on investigating the interactions between hosts, pathogens and vectors, and evaluating interventions aimed at interrupting transmission and/or reducing the disease burden. Its research portfolio includes malaria, bacterial diseases, hepatitis B and other diseases of public health importance in West Africa
- Nutrition aims to understand the pathophysiology of diet-disease interactions in order to accelerate the development of more effective next-generation community and clinical interventions, for example, the relation of iron regulation with infectious diseases such as malaria and bacterial infections
- Vaccines & Immunity aims to i) understand the ontogeny of immunity to inform the design of vaccines and maximise their impact, and ii) to contribute to the evidence-based development and deployment of vaccines. Research is conducted through laboratory science and clinical trials, as well as a series of translational and more fundamental immunological studies. Part of this latter aspect is, for example, aiming to understand the development of the immune system in infancy in the context of bacterial colonisation and infectious diseases, and research in TB which focuses on the identification of correlates of protection in adults and children in order to ultimately inform TB vaccine design

Research services are divided into two clusters. The Research governance and support services cluster was created to better coordinate activities including clinical trial support, data management and statistics, research development and project management. The Laboratory services cluster provides

[116] HIV Care, HIV Prevention & Epidemiology, Social Sciences, Basic Science, and Co-infection Studies (plus Observational Studies and STI Research)

[117] Further information on the Unit's performance and key figures: MRC/UVRI Uganda Research Unit on AIDS, Quinquennial Review, May 2016;

[118] This is in line with strategic aim 3 of the MRC 10-year strategic plan, 'going global'

[119] http://www.mrc.gm/research-sites/

[120] http://www.mrc.gm/research-themes/

support to investigators to carry out clinical research to the highest possible standards and includes all laboratory activities carried out at the Unit, plus the biobank and biomedical engineering. The Unit's Malaria Diagnostic, Entomology, and Epidemiology work, and the clinical lab, serology and TB labs have also been fully integrated into the laboratory services cluster.

An overview of the key activities, research themes addressed, and funding attracted by the two Units are summarised in Figure 29.

Figure 29 Overview of the main features of the two MRC Units

	MRC Unit, The Gambia (2010-2015)	MRC Unit, Uganda (2012-2016)
Research themes	• Disease Control and Elimination • Vaccines and Immunity • Nutrition	• HIV/AIDS – epidemiology, prevention, care, social sciences, basic sciences • Endemic, neglected, emerging and re-emerging infections • Non-communicable diseases (NCDs) especially coinfection studies
Research platforms and facilities	• Health and Demographic Surveillance Systems • West Africa Collaboration (with other West African institutions) • Clinical Research Platform • Tuberculosis Case Contact Platform • Laboratory platform (key diagnostics for malaria, bacterial and viral diseases) • Research governance (clinical trial support, statistics, bioinformatics, data management) • Biobank	• Population platform: General Population Cohort, Fisherfolk cohort • Clinical services platform • Data management platform • Clinical diagnostics laboratory services • Statistics and modelling • Bioinformatics • Grants support office
Total core funding	£46.8m for the five-year period	On average £3.5-4m per annum, 50% of the budget
Competitive funding secured	on average £6million/year from funders including Bill and Melinda Gates Foundation, MRC, EDCTP, Wellcome Trust, GSK and Pfizer	on average £4million/year from funders including MRC, USAID, Wellcome Trust, NIH, CDC, EDCTP, GSK and Johnson & Johnson
Publications*	259 (from 2013 to 2015)	263
Interventions worked on	• Insecticide-treated bed nets • Vaccines against *Haemophilus influenzae* type b (Hib), hepatitis B (HBV) • Prenatal dietary supplementation • Pneumococcal conjugate vaccines (PCV) • Azithromycin mass administration against trachoma • Seasonal malaria chemoprevention	• Monthly vaginal ring to prevent HIV-1 infection in women • Cotrimoxazole prophylaxis among HIV positive adults • Anti-retroviral therapy • Vaccines: HIV, Ebola • Counselling intervention to link HIV-infected patients to HIV care

Source: Technopolis, based on MRC/UVRI Uganda Research Unit on AIDS, Quinquennial Review, May 2016; The Medical Research Council Unit, The Gambia, Quinquennial Review, June 2015

Note: based on available data reported by the Units

Concordat-specific funding

4.3.3 African Research Leader (ARL) scheme

The ARL scheme is a prestigious award available to researchers based in sub-Saharan Africa. The scheme aims to strengthen research leadership in the region by attracting and retaining exceptionally talented individuals who will undertake high-quality programmes of research on key global health issues of relevance to the region.[121]

Applications are considered on the basis of the candidate's profile, a high-quality science programme proposal, a research-conducive academic environment at the candidate's host institution and partnership with a UK institution. An investigator at the UK-based institution is designated the Principal Investigator of the grant. This individual is meant to mentor the ARL, and in partnership with the ARL, is expected to further institutional collaboration between the UK and African host institutions.

A total of 14 African Research Leader awards have been awarded between 2011 and 2017 through the Concordat. The 14 awards amount to over £12m, with the investment spread over nine countries across the continent and five broad fields of research (Figure 30). The average grant size is £0.9m, though awards range between £0.4m and £1.9m. The majority of ARL awards (10 of 14) are over a 60-month period, with one funded over 36 months and the remaining three over 48 months.

Figure 30 Field/focus of ARL awards

Field/focus	No. of awards
Infectious diseases, HIV (i - co-infection with Mycobacterium tuberculosis; ii - broader outcomes of HIV-positive adolescents, iii – impact of psychiatric disorders on HIV progression)	3
Infectious diseases, Malaria (i - control of mosquito populations by targeting male reproductive behaviour; ii - deciphering the targets of, and mechanisms underlying naturally acquired immunity; iii - determining cellular correlates of immunity; iv - new knowledge with regard to the potential for a new vaccine antigen; v - pool of human malaria infection and transmission to mosquitoes)	5
Other infectious diseases (i - Buruli ulcer, investigating markers for patients with early infection; ii - Childhood bacterial illness, epidemiology of enteric pathogens; iii - Lymphatic filariasis, addressing the challenges of a national programme through operational research)	3
Nutrition (metabolic disease risk)	1
Mental health and brain disorders (i - detection of depression with a view to scaling mental health care in low income countries, ii - epilepsy Nodding Syndrome in children)	2

Source: Technopolis, based on MRC-DFID Concordat portfolio

As part of broader engagement activities, 7 ARLs presented their work to the MRC's Global Health Group at an ARL conference in December 2013. The Global Health Group members were impressed by the variety of projects and the implementation of the scheme.[122] The ARL awards relate to high-burden

[121] https://mrc.ukri.org/funding/browse/arl-2018/mrc-dfid-african-research-leader-scheme-2018/

[122] MRC Global Health Group: Draft Minutes and Matters Arising of 11th Meeting 29th-30th May 2014

infectious diseases (HIV, TB and Malaria, with one focusing on co-infection), as well as other infectious diseases (pathogens), but also cover nutrition and mental health and brain disorders.

Continuity of funding for the ARL scheme has allowed African researchers to plan for future applications to the scheme.[123] However, gender balance remains a concern. Consequently, steps were taken to ensure that the call actively targets both men and women. This effort resulted in similar proportions of applications submitted from men and women in the 2016 round.[124] Nonetheless, a gender imbalance in the shortlisted applications remains.[125]

4.3.4 European & Developing Countries Clinical Trials Partnership (EDCTP)

The MRC funds clinical trials under the Concordat as part of the UK contribution to the EDCTP programme of the EU.[126] The first phase of the programme ran from 2003 to 2015. A second phase was launched in 2014 as part of Horizon 2020, the EU Framework Programme for Research and Innovation. Under EDCTP2, Member states and the European Commission together with partner states in sub-Saharan Africa have developed a 10-year programme focused on late phase (phase 3) intervention studies on products against HIV, TB and malaria, and also extending into neglected tropical diseases and post-efficacy studies (phase 4) including health systems optimisation.

Three different types of grants are funded:[127]

- Research and innovation actions – primarily consisting of clinical research activities and clinical trials in partnership with sub-Saharan Africa, but also nested sub-studies, epidemiological studies and supporting activities such as fostering networking (within Africa and within Europe, as well as between Africa and Europe) or capacity development of researchers, institutions and sites in sub-Saharan Africa to conduct clinical trials and related research, including observational studies
- Coordination and support actions – primarily consisting of measures, such as activities to develop, strengthen and extend clinical research capacities in sub-Saharan Africa; activities to promote networking and collaboration between European and African researchers as well as among African researchers, clinical research institutions and sites; and activities to foster coordination and cooperation between public and private funders
- Training and mobility actions – primarily consisting of activities fostering career development of individual junior and senior fellows from sub-Saharan Africa, supporting training and mentorship of researchers, and promoting mobility of individual researchers and research staff

It has been noted that the changed legal framework in EDCTP2 to allow African countries to become members has been very successful, allowing for greater engagement and participation with many countries initiating activity to generate wider in-country science funding engagement.[128] In addition, expansion of the EDCTP remit has led to broad call specifications and extremely high demand and competition for funding.[129]

4.3.5 Implementation research to improve adolescent health in low and middle-income countries (ADH)

A total of £3m research funding was available under this strategic call, which was open from May 2015 to January 2016. Applications were accepted from principal investigators based at organisations either in the UK or in low, lower-middle and upper-middle income countries. As the underlying aim of this call

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[123] MRC Global Health Group: Minutes of Meeting 29th September 2016

[124] Ibidem

[125] MRC Global Health Group: Minutes of Meeting 11th-12th April 2017

[126] Further information http://ec.europa.eu/research/evaluations/pdf/edctp2_evaluation_experts_report_2017.pdf

[127] Further information http://www.edctp.org/funding-opportunities/grant-types/

[128] MRC Global Health Group: Draft Minutes and Matters Arising of 13th Meeting 11th-12th June 2015

[129] MRC Global Health Group: Minutes of Meeting 29th September 2016

was to provide the research evidence needed to affect real and practical changes to improve adolescent health in LMIC, the main focus was on conducting implementation research. As such, applications were expected to concentrate on the following topics:[130]

- Understanding which interventions of known effectiveness are most appropriate for whom, in which contexts and why
- How those interventions might best be implemented and scaled up in health (and/or other e.g. education) systems to achieve improved population level health outcomes
- Basic, aetiological, epidemiological research and early development of interventions were out of scope. However, research in the following areas was within scope:
  - Implementation of public health, behavioural, nutritional, contraception, safe abortion care and biomedical interventions
  - Community health and health systems approaches that are responsive to specific needs of adolescents, addressing, for instance, mental health care and substance abuse interventions
  - Implementation and scale up of known perinatal stage interventions to improve the health and survival of adolescent mothers and newborns, and to prevent stillbirths
  - Implementation of intervention strategies which can form part of a life-course approach, e.g. scale-up of nutrition interventions
  - Prevention of sexually transmitted infections in adolescents and implementing care for HIV-positive adolescents
  - Population health research on wider determinants of adolescent health including interpersonal, community and environmental factors, lifestyle and socioeconomic impacts on health, and inequalities of health, and interventions to address them

The pilot phase for this scheme conducted in 2015/16 (as described above) demonstrated high demand for research funding in this area combined with an excellent quality of applications as noted by the funding panel.[131] This led the Global Health Group[132] – the strategic advisory body of MRC addressing the Council on topics of global health issues - to recommend that the funding for the subsequent round be given flexibility to be increased if all high quality proposals could not be funded within the initially allocated amount.[133] A £10m call with joint funding from DFID, NIHR and MRC was subsequently launched for 2017/18.[134, 135]

Generic MRC-funded research with some Concordat funding

4.3.6 Developmental Pathway Funding scheme / Developmental Clinical Studies (DPFS/DCS)

The DPFS scheme[136] is a key part of the MRC's Translational Research Strategy[137] and supports the translation of fundamental discoveries toward benefits to human health. It funds the pre-clinical development and early clinical testing of novel therapeutics, devices and diagnostics, including

[130] Further information on the call and its objectives, results https://mrc.ukri.org/funding/browse/adolescent-health-in-low-and-middle-income-countries/implementation-research-for-improved-adolescent-health-in-low-and-middle-income-countries/

[131] MRC Global Health Group: Minutes of Meeting 20th-21st June 2016

[132] Global Health Group members and mandate - https://mrc.ukri.org/about/our-structure/strategy-board-overview-groups/global-health-group/

[133] MRC Global Health Group: Minutes of Meeting 20th-21st June 2016

[134] MRC Global Health Group: Minutes of Meeting 11th-12th April 2017

[135] Further details on the call https://mrc.ukri.org/funding/browse/mrc-dfid-nihr-adolescent-health-lmic/mrc-dfid-nihr-call-for-research-to-improve-adolescent-health-in-an-lmic-setting/

[136] https://mrc.ukri.org/funding/browse/biomedical-catalyst-dpfs/biomedical-catalyst-developmental-pathway-funding-scheme-dpfs-mar-2017/

[137] https://mrc.ukri.org/funding/science-areas/translation/

"repurposing" of existing therapies. In other words, projects that concern improving prevention, diagnosis, prognosis, or treatment of significant health needs, or that focus on developing research tools that increase the efficiency of developing interventions are within scope.

Outline submissions are accepted every four months under this scheme. Individual projects can start and finish at any point along the translational pathway but would not typically cover initial development through to phase 2 clinical testing in a single grant. However, sequential applications to cover the various steps are encouraged. All disease areas (including those relevant to global health) and modalities of intervention are eligible for support from the scheme, including small molecules, peptides, antibodies, vaccines, cell and gene therapy, devices, surgical techniques and psychological approaches. Late-phase trials and clinical studies aimed at investigating a disease mechanism are not covered under this scheme; however, they are covered through the research boards or other clinical trial funding schemes.

4.3.7 Experimental Medicine (EM)

The MRC is the lead public sector organisation for Experimental Medicine[138] in the UK and co-ordinates activities on behalf of UK Clinical Research Collaboration partners. EM is a core element of the MRC's overarching translational research strategy. Under this research area, the MRC funds investigations in humans to identify mechanisms of pathophysiology or disease, or to demonstrate proof-of-concept evidence of the validity and importance of new discoveries or treatments.

Response-mode applications are accepted in this area with strategic calls for proposals at regular intervals, for example, on biomarkers, animal models of disease, creation of patient research cohorts or stem cell research.[139]

4.3.8 Fellowship schemes

At any one time, the MRC supports around 1,900 PhD students (including pre-doctoral fellows) and 200 post-doctoral fellows. The aim is to:

- Train and develop the next generation of research leaders
- Support excellent individuals at critical points of their careers
- Help address national strategic research skills needs identified with partners

The MRC currently has five fellowship schemes that are available to conduct research in the UK.[140] Some of these are under the Concordat based on the decisions made by the MRC on a case-by-case basis:

- Clinical Research Training Fellowship – for clinicians in specialty training who want to embark on a dual academic-clinical career by undertaking a PhD
- Career Development Award – for PhD/DPhil holders who want to transition to independence
- Clinician Scientist Fellowship – for clinicians who have gained a PhD/DPhil/MD and are looking to transition to independence
- Senior Clinical Fellowship – for clinicians who have gained a PhD/DPhil/MD and are looking to become research leaders
- Senior Non-Clinical Fellowship – for independent researchers with a PhD/DPhil and a proven track record of research excellence in their field who are looking to become research leaders

[138] https://mrc.ukri.org/research/initiatives/experimental-medicine/

[139] Example of an open call - https://mrc.ukri.org/funding/browse/experimental-medicine-challenge-grants/experimental-medicine-challenge-grants-discovery-science-in-humans/

[140] https://mrc.ukri.org/skills-careers/fellowships/

4.3.9 Methodology Research Programme (MRP)

The MRP is jointly funded by the MRC and NIHR and covers[141]

- Research methods in disciplines underpinning health research including: biomedical, behavioural and social science, experimental and stratified medicine, randomised trials, cohorts and other research designs investigating health, healthcare, health services and health policy
- Methods for effective regulation (including indices for decision making), approval, adaptation and reporting of new interventions (including behavioural and digital)
- Research methods for valid measures of health, e.g. health outcomes, exposure and risk (including behaviour, cognition and emotion) and wellbeing

The programme is overseen by an expert panel that considers response-mode grant applications. Priority methodological challenges are signposted to applicants in highlight notices. An MRP Advisory Group advises the MRP Panel on the strategic priorities.

4.3.10 Public Health Intervention Development scheme (PHIND)

PHIND[142] supports the early stages of development of new innovative interventions that address an important UK or global public health issue and complements funding schemes from NIHR and MRC (Global Health schemes) that also support public health intervention development and evaluation.

A novel, high-risk approach to intervention development is encouraged including population-level interventions focusing on non-health care settings. Alignment of proposals with the NIHR Public Health Research Programme and MRC Global Health schemes and inclusion of user participation is particularly desired according to the call for proposals. Applicants have to demonstrate a pathway to further development and evaluation of the proposed intervention and specify criteria for progression to the next stage of development.

The scheme was launched in September 2013 and was well received, with a lot of interest. 47 applications were received before the October 2013 deadline of which around 25% fell within the Global Health remit.[143]

[141] https://mrc.ukri.org/funding/browse/mrp/methodology-research-programme-nov-2018/

[142] https://mrc.ukri.org/funding/browse/public-health-intervention-development-scheme/public-health-intervention-development-scheme-phind-july-2018/

[143] MRC Global Health Group: Minutes of 10th meeting, 2 December 2013

Appendix B Methodological annex[144]

This annex provides additional methodological detail to supplement that provided in the main report, section: Overview of our methodology. The annex consists of the following sections:

- Additional information on the rapid evidence assessment: This provides more information on the exact search strings used and the results returned
- Methodological note to the analysis of the Concordat portfolio and the Researchfish data: This provides more detail on the data sources used, the analysis performed and the caveats and limitations of the approach
- Interview protocol: This section provides the detailed interview protocol used for the interview programme
- Case study details: This section provides additional detail on the case studies conducted, particularly we set out the way in which the case studies were selected, and we provide the template used to structure the case studies

B.1 Additional information on the rapid evidence assessment

We conducted a rapid evidence assessment (REA) of literature and commentary on the MRC-DFID Concordat in order to understand the existing evidence, views and perspectives on the scheme. The search covered academic literature, grey literature (i.e. policy reports and studies), and commentary and editorials referring to the performance of the MRC-DFID Concordat. The search focused on three databases to cover all literature sources: PubMed, Scopus and normal Google search. The following search terms were used:

8. ("Medical research council" OR MRC) AND ("Department for international development" OR DFID) OR (UKAID)
9. ("Medical research council" OR MRC) OR ("Department for international development" OR DFID) AND "Concordat"
10. ("Medical research council" OR MRC) OR ("Department for international development" OR DFID) AND ("global health" OR "LMIC" OR "low and middle income countr*" OR "developing countr*" OR ODA OR "official development assistance")
11. ("Medical research council" OR MRC) OR ("Department for international development" OR DFID) OR "Concordat" AND (EDCTP OR "European and developing countries clinical trials partnership")
12. ("Medical research council" OR MRC) OR ("Department for international development" OR DFID) AND ("African research leader" OR ARLS
13. ("Medical research council" OR MRC) OR ("Department for international development" OR DFID) AND Uganda OR UVRI OR Gambia
14. ("Medical research council" OR MRC) AND ("global health" OR "LMIC" OR "low and middle income countr*" OR "developing countr*" OR ODA OR "official development assistance")
15. Biomed* AND ("international development" OR "global health") AND (funding OR research)

The search was conducted on May 2018. Publications were initially screened on title and abstract (where available). For searches 1-7, only studies referencing the performance of the MRC, DFID, partnerships including either the MRC or DFID, or the Concordat dated 2008-2018 were considered for the purposes of this literature review. Articles referring to scientific studies acknowledging funding received from the MRC or DFID, or calls for funding were excluded. For search 8, studies referencing partnerships

[144] Technopolis Group was leading on the interview programme, case study development and field visits to Malawi and Uganda and Rand Europe was leading on the desk-based research, and case studies conducted related to the field visits to The Gambia and Kenya

between international development agencies and medical research funders, as well as trends in global health research funding were included. Calls for funding were excluded.

The search on PubMed and Scopus of searches 1-7 produced 249 results, of which only 14 met the criteria to be included in this literature review. Search sequence 3 produced the highest number of relevant results using PubMed and Scopus, with 13 publications meeting the inclusion criteria described above. Google search for searches 1-7 produced 386 results, of which 47 referenced impacts of the MRC, DFID or the Concordat. Search sequences 1 and 2 produced the highest number of relevant results in Google search, with 44 results meeting the inclusion criteria described above. For search 8, only Google search was used producing 199 results, of which only 21 met the inclusion criteria described above.

B.2 Methodological note to the analysis of the Concordat portfolio and the Researchfish data

Data sources

The data used in this analysis combines both Concordat portfolio data[145] and Researchfish data provided by the MRC and DFID. This includes:

- Concordat Portfolio 2008-2013
- Concordat Portfolio 2013-2018
- Researchfish 2005-2007
- Researchfish 2008-2013
- Researchfish 2013-2018

The Concordat Portfolio data contains administrative information including grant reference, principal investigator, research organisation, funding board/panel/scheme, funding amount, project duration (including start and end dates), title, technical summary, and developing county(ies) attached to the research. The majority of this information is also contained in the Researchfish data, except for the funding board/panel/scheme and the list of developing countries linked to each funding grant.

The Researchfish data also contains impact reported by grant holders for each of the grants broken down into 19 areas: publications, collaborations, funding, destinations, skills, secondments, dissemination, policy, tools, databases, software, artistic, intellectual property (IP), products, spin outs, recognition, facilities, and other. The definitions of impact areas are provided in Figure 31. The data associated with each impact area is primarily qualitative in nature, and includes information such as the author, journal and date of each publication linked to a particular research grant, or the type, date and geographic reach of any recorded policy impact.

Figure 31 Definitions of Researchfish output areas

Output Area	Definition
Publications	Publications that have resulted from the grant
Collaborations	Collaborations that have been formed with the grant funding or as a result of the grant
Funding	Further funding obtained as a result of the grant
Destinations	The destination of staff members (such as PhD students) as a result of the grant
Skills	Skills obtained by team members as a result of the grant
Secondments	Secondments carried out by team members as a result of the grant
Dissemination	Dissemination of the work carried out during the grant

[145] Project level information is available on the Gateway to Research website, available at: http://gtr.ukri.org

Output Area	Definition
Policy	Impacts on policy as a result of the grant
Tools	Tools developed as a result of the grant
Databases	Databases created as a result of the grant
Software	Software created and developed as a result of the grant
Artistic	Artistic outputs, such as videos, that have resulted from the grant
IP	Intellectual property applied for or gained as a result of the grant
Products	Products produced as a result of the grant
Spin Outs	Spin out companies set up, or being set up, as a result of the grant
Recognition	Awards obtained as a result of the grant
Facilities	Facilities used as a result of the grant
Other	Other impacts

We also received Concordat Portfolio data from 2005-2007, although this was excluded from the quantitative analysis due to differences in the quantity and type of information included in this dataset. In particular, the 2005-2007 datasheet does not contain information on start or end date of research grants, nor does it link research grants to developing countries. Whilst the datasheet does contain information on the type of funding associated with each research grant, the categorisation of funding is different to data in subsequent years. More specifically, the dataset does not disaggregate between different types of intramural funding, and extramural funding is categorised using labels that do not match those in the later Concordat Portfolio files.

A database of overseas co-investigators linked to individual research grants was also made available, although it was not included in the quantitative part of this study. This database contains information on co-investigators, their location and their organisational affiliation, but these areas were not used as variables within the quantitative analysis as it was not considered an important disaggregation between research grants. The overseas co-investigator database does not include any further administrative information such as funding amount, duration, or type of funding. The co-investigator database was used in other areas of this study, including in the identification of interviewees for case study analysis.

Limitations of the data

This analysis is subject to a number of caveats and limitations, many of which stem from the nature and completeness of the underlying data.

Within the Concordat Portfolio a considerable number of data points were missing from the datasets: 50% of the research grants do not specify funding amount; 42% of the research grants do not have sufficient information to calculate the duration of a funding grant; and 23% of research grants do not include any association with a developing country. We supplemented this missing information with data from Researchfish where possible, and any data points with missing entries were labelled with the text "Unknown" in order to differentiate easily from values of "0". Key definitions within the Concordat Portfolio dataset are provided in Figure 32.

Additionally, a number of the research grants in the Portfolio datasets are not included in the Researchfish data (11 out of 317, or just under 3.5%). It is unclear whether these grants are not included in Researchfish because they have had no impact, or they are missing for another reason, such as the failure of the grant holder to input the data into Researchfish. Research grants that lack Researchfish data entries were therefore excluded from any analysis that included a measure of impact.

Finally, the Researchfish data itself is self-reported and is therefore subject to issues around completion rates, accuracy of self-reported data, and bias in sampling. The latter of these is somewhat mitigated since completing Researchfish, at least for a number of years, is mandatory as a requirement of the funding award. Despite this, there may be differences across awards in the quality and completeness of the available data, and we are aware from previous work that Researchfish data typically underreports impacts from research. We are also aware that there are likely differences in the approaches taken by individuals to completing Researchfish – for example, some individuals might be scrupulous in which impacts are attributed to which particular funding awards, whilst others might take a broader view of the contribution of different funding awards and link particular outcomes and impacts to many different funders and grants.

Figure 32 Key definitions in the Concordat Portfolio data

Term	Definition
Grant Reference	A unique reference code assigned to each research grant
Funding Board/Panel/Scheme	The specific process through which the grant funding was awarded to the recipient
Funding Amount	The total amount of funding that was provided through the grant
Developing Countries	The countries linked to a research grant, typically where the research itself is applicable
Funding Type	Groupings of funding boards/panels/schemes assigned by the research team

Data processing

Combining data sources

The data sources were combined into a single dataset, with the Portfolio data forming the primary dataset, supplemented by the impact information contained in the Researchfish data. When grant information was not included in the Portfolio database but was included in Researchfish, such as start and end date of a grant, the Researchfish data was added. When grant information differed between the Portfolio and Researchfish data, data from the Portfolio database was used. For example, if both Researchfish and the Portfolio data described different funding amounts for the same research grant, then the funding amount from the Portfolio data was selected. Research grants that were included in Researchfish but not in the Portfolio data were not included in the final combined dataset.

Data cleaning

Some research grants are included in both Concordat Portfolio data files and more than one of the Researchfish data files listed above. These grants are typically those that were on-going across the periods covered by the respective data files, such as a grant between 2010 and 2015 that would be included in both the 2008-2013 and 2013-2018 Portfolio datasets. When compiling the initial combined data set, research grants such as this would appear as duplicate entries. These were removed by comparing the unique reference number that is attached to each research grant, with the most recent data prioritised based on the assumption that this information would be the most up-to-date.

A similar approach was taken when combining the different Researchfish databases, each of which not only contained duplicate research grants, but also duplicate entries in research impact. Returning to the above example, a grant between 2010 and 2015 may record the same research impact (such as a publication or collaboration) in both the 2008-2013 and 2013-2018 Researchfish databases, and so would appear initially as a duplicate entry in the combined dataset. Similar to the research grants themselves, each impact has a unique identifying number, meaning duplicate entries could be easily removed, again prioritising more recent information.

In spite of these measures to remove duplications, it is nonetheless possible that some duplicate entries still exist in the combined dataset if, for example, these unique identifying reference numbers were to have been modified for the same research grant across different datasets from different years. It is also worth acknowledging that some of the impact entries recorded in Researchfish may appear to be duplicate entries, but refer to different research grants and hence remain in the data. For example, a single publication may be associated with two separate research grants, in which case it would appear twice in the data (once for each of the two research grants).

Finally, a small amount of spurious data was also removed from the combined dataset, such as end dates for research grants in 2050 or 2100. Projects that began before 2006 were marked in the data set to enable temporary removal from analysis when required, as Researchfish only systematically recorded information from 2006 onwards, although some earlier information is included.[146]

The final combined dataset contained 317 unique research grants, 306 of which also had impact data from Researchfish data.

Data clustering

Two additional categories were added to the data in order to group similar types of research grants into larger clusters: 'Funding Type', which grouped together similar boards, panels and funding schemes; and 'Region', which grouped developing countries based on geographical proximity. Clustering by funding type and by region are outlined in more detail in the following two subsections.

Grouping by funding type

In total, 19 different Board/Panel/Schemes were identified in the data. In order to investigate the importance of different types of funding, these funding boards/panels/schemes were clustered into groups based on similar characteristics. This clustering was undertaken in order to increase the number of research grants (and hence data points) included in each category. A total of 5 clusters were used, which are outlined in Figure 33.

Figure 33 Categorisation of funding streams

Broad category	Board/Panel/Scheme	Number of research grants
MRC Boards/ Response-mode	Health Services and Public Health Research Board (HSPHRB)	1
	Infections & Immunity Board (IIB)	46
	Population and Systems Medicine Board (PSMB)	6
Unit programmes / Intramural MRC	Intramural Infections & Immunity Board (IIB)	111
	Intramural Molecular and Cellular Medicine Board (MCMB)	1
	Intramural Neurosciences and Mental Health Board (NMHB)	1
	Intramural Population and Systems Medicine Board (PSMB)	29
Concordat-specific funding	ADH	5
	European & Developing Countries Clinical Trials Partnership (EDCTP)	2
	MRC Global Health (GH) trial	14
	African Research Leader (ARL) scheme	15
MRC awards with some Concordat funding	Developmental Pathway Funding scheme / Developmental Clinical Studies (DPFS/DCS)	12
	Experimental Medicine (EM)	1

[146] Some data fields - such as "Total Funding Amount" - explicitly refer to 2006-onwards only, whereas other areas - such as "Publications" – do not explicitly define a timeline, and also include data from pre-2006. When timelines are used in the analysis, research grants that began before 2006 are excluded in order to remove this ambiguity.

	Fellowship	46
	Methodology Research Programme (MRP)	4
	Public Health Intervention Development (PHIND) scheme	16
Other MRC funding	AStar/MRC Infectious Disease scheme	1
	Biomarkers 2007 + 2008	2
	Other (Strategic funding, unknown)	4
Total		***317***

Grouping by region

In total, 62 developing countries[147] were included in the dataset, with some research grants linked to multiple different countries. These countries were initially clustered into regional areas according to the UN Statistics Division M49 classification, [148] but due to the small number of data points in some of these regions, further grouping was then applied in order to create the categories outlined in Figure 34. Regions were then assigned to research grants according to the developing country linked to the project, and for research grants with more than one developing county listed across different regions, the region with the highest number of countries was selected. If more than one region had an equally high number of countries for a particular research grant, then no region was assigned in order to maintain a mutually-exclusive categorisation.

Figure 34 Regional groupings of countries for the 62 countries in the dataset

Eastern Africa	**Western Africa**	**Central and Southern Africa**	**Europe**	**Asia**	**Central and South America**
Burundi	Benin	Botswana	Estonia	Afghanistan	Argentina
Ethiopia	Burkina Faso	Cameroon	Lithuania	Bangladesh	Brazil
Kenya	Gambia	Central African Republic	Ukraine	Cambodia	Chile
Madagascar	Ghana	Chad		China	Colombia
Malawi	Guinea	Congo		India	Costa Rica
Mozambique	Guinea-Bissau	Equatorial Guinea		Indonesia	Mexico
Rwanda	Mali	Gabon		Laos	Panama
Sudan[149]	Mauritania	Lesotho		Malaysia	Peru
Tanzania	Morocco[150]	Namibia		Myanmar	Uruguay
Uganda	Niger	South Africa		Pakistan	

[147] This refers to the definition of 'Developing Countries', and does not include the countries of co-investigators linked to research grants.

[148] https://unstats.un.org/unsd/methodology/m49/

[149] Sudan is categorised as 'Northern Africa' according to the UN Statistics Division m49 classification, but is moved here into the 'Eastern Africa' category due to the small amount of data associated with 'Northern Africa'.

[150] Morocco is categorised as 'Northern Africa' according to the UN Statistics Division m49 classification, but is moved here into the 'Western Africa' category due to the small amount of data associated with 'Northern Africa'.

Eastern Africa	Western Africa	Central and Southern Africa	Europe	Asia	Central and South America
Zambia	Nigeria			Philippines	
Zimbabwe	Senegal			Thailand	
	Sierra Leone			Vietnam	
	Cote D'Ivoire				

Data analysis

The above data was stored in Excel spreadsheets, and data analysis was carried out using a combination of Excel and R. R is an open source programming language that supports statistical analysis of large datasets.

The data analysis comprised of a combination of descriptive statistics and statistical significance tests, including Chi-squared, and Kruskal-Wallis tests. Descriptive statistics were used in order to identify and understand different characteristics of the dataset, such as the distribution of funding amounts across different funding types or the distribution of research grants across different regions. Statistical significance tests were then applied in order to determine whether some of the differences and trends in the data were significant, and thus provide more concrete answers to the questions outlined at the start of this chapter. For all sets of tests, we have performed false discovery rate multiple testing correction to reduce the number of false discoveries due to running a large number of statistical tests. Tests could only be carried out when there were sufficient observed data points in a category to meet the requirements for the test). For this reason, no tests were carried out for the following impact categories: Skills, Secondments, Software, Artistic, IP, Products, Spin Out, and Facilities.

It is important to note that, throughout the analysis, we have taken a binary approach to measuring impact rather than summing the total number of impacts within each category. For example, if a research grant were to record 10 impacts within the 'policy' category, this would be record as *an* impact on policy (denoted by a '1'), and would carry the same weight as a grant that has had either 100 or 1 recorded impacts. In other words, we are comparing whether a project has any impact on policy, rather than the number of impacts on policy. Similarly, when looking at time lags, we have assumed the time lag to impact in a particular category is the time between the funding award and the first impact being recorded in that category. An alternative approach could, for example, use the average time to all impacts as the measure of time lag, but suffers from the same type of summation error in that it attributes each impact with equal weighting.

This binary approach was taken because of the varying types, levels of significance and reach of impacts recoded within each category, which means it is difficult to interpret and attribute meaning to any summation of impact. A binary approach removes this uncertainty, although in doing so it also removes any measure of the degree of impact in a particular area. For example, a single small impact attributed to one research grant in one area would be weighted the same as multiple large impacts attributed to another research grant in the same area, meaning this difference in impact would be lost.

Comparing data reported in Researchfish with pathway to impact statements submitted by applicants for grants

In addition to the data analysis, we also examined whether the impact that grants have reflect what grant holders predicted when they applied for the funding. A total of 25 pathways to impact were semi-randomly selected to include representatives from all schemes and different countries. This implied first a random selection from each scheme followed by further selection within the schemes to avoid

examples from the same country. Pathways were selected for the funding period between 2013-2017, covered approximately 15 countries (some examples were multi-country projects), and included representatives from all schemes: 3 ADH, 4 African Research Leader Awards (ARL), 3 fellowships, 3 Global Health Trials, 9 Infections and Immunity Board, 1 Methodology Research Programme, and 2 Population and Systems Medicine Board. The analysis was carried out qualitatively. Each document was screened for descriptions of the following impacts that can be submitted to Researchfish: publications, collaborations, funding, skills, dissemination, policy, tools, and databases. Data obtained through the screen was then compared to data provided through Researchfish to assess whether the pathways had been achieved.

B.3 Interview guidelines

Figure 35 below provides the overall structure and questions used across interviews. Each individual protocol is then broken out in the following sections.

Figure 35 Overall question structure for interviews

Question	Group 1 – MRC/DFID personnel	Group 2 – national /international stakeholders	Group 3 – GHRC	Group 4 – grant holders
Introduction				
Please say a little bit about your position and/or research/role				
Are you aware of the MRC/DFID Concordat? [if not interviewer to explain the Concordat portfolio] – How do you asses the level of visibility of the MRC/DFID Concordat?				
How/why did you or your organisation get involved in the funded project?				
Does your organisation receive funding from other donors? For what purposes and from which ones?				
Relevance of the MRC-DFID Concordat				
What are your expectations from the Concordat?				
How does the Concordat agreement add value to the MRC/DFID agendas? – Is the Concordat complementary to the agendas of MRC/DFID?				
Do you believe that any adjustments to funding priorities are needed? – In terms of funding research that contributes to the health of developing societies				
Has there been a shift in the nature (scope and quality) of proposals received over the years? – What do you think has driven this?				
How does the Concordat address the key issues for your/the LMIC partner organisations? (e.g. equity, access, gender balance, maternal and child health, marginalised communities, SDGs, etc. both of researchers and beneficiaries of research) – Are any changes required to the Concordat to improve its relevance?				

Question	Group 1 – MRC/DFID personnel	Group 2 – national /international stakeholders	Group 3 – GHRC	Group 4 – grant holders
Quality of activities supported through the MRC-DFID Concordat portfolio				
How would you judge the quality of the science funded/produced through the Concordat-funded activities?				
How do you judge the ability of the funding to support research capacity building?				
To what extent does the Concordat contribute to the UK's reputation regarding research of relevance to developing societies? Are you aware of specific examples? – Has this changed over the past years?				
Outcomes and impacts of supported activities through the MRC-DFID Concordat				
What are the main results and outcomes from the Concordat-funded research activities?				
Have you observed outcomes or impacts from Concordat-funded capacity building activities? – What mechanisms are in place to ensure the results of capacity building are maximised?				
Has the Concordat resulted in any 'spin off' activities/projects in your organisation?				
How were the results and outcomes taken forward (impact pathways)? – What is the nature, range and timeliness of these impacts? – How did the MRC/DFID support this? – In your experience, what are the pathways and enablers to ensuring impact is realised? Can you explain the timeframe needed? – What are the barriers to realising impact?				
In your opinion, do the outcomes and impacts delivered through the Concordat provide value for money? – How could this be improved?				
What changes would you recommend the MRC/DFID make to improve support for realising impact from funded activities?				
The MRC-DFID relationship				
What are the main areas of interaction between the MRC and DFID? (e.g. specific contributions to the developing/delivering the Concordat)				
What institutional support does the Concordat get from your organisation to administer and manage the portfolio?				
How do the MRC/DFID discuss and agree priorities? – What is the split of representation in these decisions? – What mechanisms exist to support this?				
Do you view the MRC-DFID relationship to be productive / effective?				

Question	Group 1 – MRC/DFID personnel	Group 2 – national /international stakeholders	Group 3 – GHRC	Group 4 – grant holders
– What aspects of the collaboration between MRC/ DFID went particularly well? – Where can/should the collaboration improve in the future? – Are there other ways in which you think the MRC-DFID relationship could be improved?				
Effectiveness of operational management of the MRC-DFID Concordat				
How does a combination of development/capacity building and medical research deliver better value in LMICs?				
Overall, do you believe that the MRC delivers value for money in terms of the quality of its operational (e.g. financial) management of the Concordat portfolio? – Are there ways in which this could be improved? – What metrics would you suggest for measuring these aspects				
Co-design and co-funding: – What is the role and involvement of co-developers from Southern countries in the portfolio? – What role do national funders take in supporting activities (e.g. co-funding?) – Is there scope for other bodies to become involved?				
How would you judge the relevance of the Concordat in the current Official Development Assistance (ODA) landscape (e.g. the promotion of economic development/welfare)? – In your view, have recent changes in the ODA research landscape in the UK affected engagement with the Concordat? – How might future funding arrangements/ landscape impact on the Concordat?				
Other comments, recommendations				

Note: the highlighted cells show which question is relevant for which stakeholder group

Group 1 - MRC and DFID personnel

	Introduction
1	Please say a little bit about your position and/or your research/role
	Relevance of the MRC-DFID Concordat
2	What are your expectations from the Concordat?
3	What role does the Concordat play in the wider MRC/DFID funding portfolio? • How does the Concordat support your wider strategic goals?
4	Do you believe the funding available through [name of specific Concordat funding] addresses the key issues for societal needs in [LMICs/specific country]? E.g. equity, access, gender balance, maternal and child health, marginalised communities, vulnerable groups, SDGs, etc. both of researchers and beneficiaries of research

5	Can you identify any specific gaps in the current priorities? [Interviewer may prompt a specific country or challenge]
6	Has there been a shift in the scope of proposals that you have received/selected for [name of specific Concordat funding] funding over the years? • What do you think has driven this?
7	How would you judge the relevance of the Concordat portfolio [prompt specific Concordat funding if needed] in the current Official Development Assistance (ODA) landscape (e.g. the promotion of economic development/welfare)? • In your view, have recent changes in the ODA research landscape in the UK affected engagement with the Concordat? • How might future funding arrangements/ landscape impact on the Concordat?
8	What is the role and involvement of co-developers from Southern/Northern countries in the portfolio?
9	Are you aware of other funders that support complementary or similar activities? • Is there scope for these other bodies to become involved in the Concordat?
	Quality of activities supported through the MRC-DFID Concordat portfolio
10	In your view, does the [Concordat/programme] contribute to the UK's international research reputation? • Can you name any specific examples? • Has this changed over the past years?
11	What are your expectations of the Concordat-funded activities in terms of quality of science/research (e.g. new knowledge and evidence base)? • How do your expectations compare with results? • Are there particular good examples?
12	What are your expectations of the Concordat-funded activities in terms of capacity-building (e.g. new cadre of African scientists)? • How do your expectations compare with results? • Are there particular good examples?
	Outcomes and impacts of supported activities through the MRC-DFID Concordat
13	What do you view as the main results and outcomes from the Concordat-funded [prompt specific Concordat funding if needed] research activities? • [If required, e.g. uncertainty from respondent about the meaning of the question, interviewer to prompt array of impacts, including whether the activity was/is expected to impact on LMIC health policies and practices] • Can you provide examples of major impacts? • Anything outside of funding period?
14	Have you had/observed any follow-up activities to extend/build on the [name of specific Concordat funding] results? If required, e.g. uncertainty from respondent about the meaning of the question, interviewer to prompt, e.g. leveraging other funding, activities outside the funding period]
15	What mechanisms are there in [name of specific Concordat funding} or in other similar schemes to ensure the results of capacity building are maximised? [e.g. to strengthen the scientific research base] • Do you have any recommendations to improve achieving such impact?
16	What are the enablers to ensuring that the desired impact [prompt if needed based on previous answer to the results/impact questions] is realised? • How does the MRC/DFID support the impact being achieved (e.g. through events organised, using their national and LMIC networks, etc?)? • What more could they do to support this?
17	What are/were the barriers to achieving the desired impact [prompt if needed based on previous answer to the results/impact questions]? • [Not for the MRC/DFID] Are there any barriers that MRC/DFID could help you address?

18	Do you have any recommendations for suitable metrics to capture the array of impacts?
	The MRC-DFID relationship
19	What are the main areas of interaction between the MRC and DFID? (e.g. specific contributions to the developing/delivering the Concordat)
20	How do the MRC/DFID discuss and agree priorities? • What is the split of representation in these decisions? • What mechanisms exist to support this? • Could you provide examples? (e.g. frequency of meetings, minutes circulated, etc.)?
21	Do you view the relationship between the Medical Research Council (MRC) and the UK international development Agency (DFID) to be productive / effective? • What aspects of the collaboration do you think went particularly well? • Where can/should the collaboration improve in the future? • Are there other ways in which you think the relationship could be improved?
	Effectiveness of operational management of the MRC-DFID Concordat (2)
22	[Interviewer to define 'Value for Money' to the interviewer before asking this question] Overall, do you believe that the MRC delivers value for money in terms of the quality of its operational (e.g. financial) management of the [Concordat portfolio / programme]? • Are there ways in which this could be improved?
23	How do you regard the administrative requirements of the Concordat, including the scientific and financial reporting of the grant holders? [Prompts not for the MRC] • Do you have a specified contact point? • What support do the MRC provide (if any)? • Are they effective and efficient in their administrative processes and the support that they provide (if any)? • What could they do better?
	Other comments, recommendations
24	Are there any other recommendations that you would make to MRC/DFID that could improve the quality of funded activities, or more broadly improve processes and enable impact?
25	Any other recommendations/suggestions

Group 2 – National and international stakeholders

	Introduction
1	Please say a little bit about your position and/or your research/role
2	Are you aware of MRC's global health funding? • Could you tell me a little about what you know?
3	Are you aware of the MRC/DFID Concordat? [if not interviewer to explain the Concordat portfolio] • How well known is the MRC/DFID Concordat among your peers / policymakers / funding agencies / international aid agencies / researchers?
	Relevance of the MRC-DFID Concordat
4	What are your expectations from the Concordat?

5	Are you aware of any other agreements between medical research funders and international development agencies? • What do you think these offers over and above separate funding from the separate agencies? • Are you aware of any interesting examples?
6	Do you believe the funding available through [name of specific Concordat funding] addresses the key issues for societal needs in [LMICs/specific country]? E.g. equity, access, gender balance, maternal and child health, marginalised communities, vulnerable groups, SDGs, etc. both of researchers and beneficiaries of research
7	Can you identify any specific gaps in the current priorities? [Interviewer may prompt a specific country or challenge]
8	How would you judge the relevance of the Concordat portfolio [prompt specific Concordat funding if needed] in the current Official Development Assistance (ODA) landscape (e.g. the promotion of economic development/welfare)? • In your view, have recent changes in the ODA research landscape in the UK affected engagement with the Concordat? • How might future funding arrangements/ landscape impact on the Concordat?
9	What is the role and involvement of co-developers from Southern/Northern countries in the portfolio?
10	Are you aware of other funders that support complementary or similar activities? • Is there scope for these other bodies to become involved in the Concordat?
	Quality of activities supported through the MRC-DFID Concordat portfolio
11	In your view, does the [Concordat/programme] contribute to the UK's international research reputation? • Can you name any specific examples? • Has this changed over the past years?
12	How would you judge the quality of the science funded by the [name of specific Concordat funding] compared to other, similar schemes? • How do your expectations compare with results? • Are there particular good examples?
13	How do you judge the ability of the [programme/scheme] to support research capacity building, compared to other similar schemes? • How do your expectations compare with results? • Are there particular good examples?
	Outcomes and impacts of supported activities through the MRC-DFID Concordat
14	What do you view as the main results and outcomes from the Concordat-funded [prompt specific Concordat funding if needed] research activities? • [If required, e.g. uncertainty from respondent about the meaning of the question, interviewer to prompt array of impacts, including whether the activity was/is expected to impact on LMIC health policies and practices] • Can you provide examples of major impacts? • Anything outside of funding period?
15	What mechanisms are there in [name of specific Concordat funding} or in other similar schemes to ensure the results of capacity building are maximised? [e.g. to strengthen the scientific research base] • Do you have any recommendations to improve achieving such impact?
16	What are the enablers to ensuring that the desired impact [prompt if needed based on previous answer to the results/impact questions] is realised? • How does the MRC/DFID support the impact being achieved (e.g. through events organised, using their national and LMIC networks, etc?)? • What more could they do to support this?
17	What are/were the barriers to achieving the desired impact [prompt if needed based on previous answer to the results/impact questions]? • [Not for the MRC/DFID] Are there any barriers that MRC/DFID could help you address?

18	Do you have any recommendations for suitable metrics to capture the array of impacts?
	The MRC-DFID relationship
19	Do you view the relationship between the Medical Research Council (MRC) and the UK international development Agency (DFID) to be productive / effective? • What aspects of the collaboration do you think went particularly well? • Where can/should the collaboration improve in the future? • Are there other ways in which you think the relationship could be improved?
	Other comments, recommendations
20	Are there any other recommendations that you would make to MRC/DFID that could improve the quality of funded activities, or more broadly improve processes and enable impact?
21	Any other recommendations/suggestions

Group 3 – Global health research community

	Introduction
1	Please say a little bit about your position and/or your research/role
2	Are you aware of MRC's global health funding? • Could you tell me a little about what you know?
3	Are you aware of the MRC/DFID Concordat? [if not interviewer to explain the Concordat portfolio] • How well known is the MRC/DFID Concordat among your peers / policymakers / funding agencies / international aid agencies / researchers?
	Relevance of the MRC-DFID Concordat
4	Are you aware of any other agreements between medical research funders and international development agencies? • What do you think these offers over and above separate funding from the separate agencies? • Are you aware of any interesting examples?
5	Do you believe the funding available through [name of specific Concordat funding] addresses the key issues for societal needs in [LMICs/specific country]? E.g. equity, access, gender balance, maternal and child health, marginalised communities, vulnerable groups, SDGs, etc. both of researchers and beneficiaries of research
6	Can you identify any specific gaps in the current priorities? [Interviewer may prompt a specific country or challenge]
7	[Only for those on MRC committees] Has there been a shift in the scope of proposals that you have selected for [name of specific Concordat funding] funding over the years? • What do you think has driven this?
8	How would you judge the relevance of the Concordat portfolio [prompt specific Concordat funding if needed] in the current Official Development Assistance (ODA) landscape (e.g. the promotion of economic development/welfare)? • In your view, have recent changes in the ODA research landscape in the UK affected engagement with the Concordat? • How might future funding arrangements/ landscape impact on the Concordat?
9	What is the role and involvement of co-developers from Southern/Northern countries in the portfolio?
10	Are you aware of other funders that support complementary or similar activities? • Is there scope for these other bodies to become involved in the Concordat?
	Quality of activities supported through the MRC-DFID Concordat portfolio

11	In your view, does the [Concordat/programme] contribute to the UK's international research reputation? • Can you name any specific examples? • Has this changed over the past years?
12	How would you judge the quality of the science funded by the [name of specific Concordat funding] compared to other, similar schemes? • How do your expectations compare with results? • Are there particular good examples?
13	How do you judge the ability of the [programme/scheme] to support research capacity building, compared to other similar schemes? • How do your expectations compare with results? • Are there particular good examples?
	Outcomes and impacts of supported activities through the MRC-DFID Concordat
14	What do you view as the main results and outcomes from the Concordat-funded [prompt specific Concordat funding if needed] research activities? • [If required, e.g. uncertainty from respondent about the meaning of the question, interviewer to prompt array of impacts, including whether the activity was/is expected to impact on LMIC health policies and practices] • Can you provide examples of major impacts? • Anything outside of funding period?
15	What mechanisms are there in [name of specific Concordat funding} or in other similar schemes to ensure the results of capacity building are maximised? [e.g. to strengthen the scientific research base] • Do you have any recommendations to improve achieving such impact?
16	What are the enablers to ensuring that the desired impact [prompt if needed based on previous answer to the results/impact questions] is realised? • How does the MRC/DFID support the impact being achieved (e.g. through events organised, using their national and LMIC networks, etc?)? • What more could they do to support this?
17	What are/were the barriers to achieving the desired impact [prompt if needed based on previous answer to the results/impact questions]? • [Not for the MRC/DFID] Are there any barriers that MRC/DFID could help you address?
18	Do you have any recommendations for suitable metrics to capture the array of impacts?
	Other comments, recommendations
19	Are there any other recommendations that you would make to MRC/DFID that could improve the quality of funded activities, or more broadly improve processes and enable impact?
20	Any other recommendations/suggestions

Group 4 – Grant holders

	Introduction
1	Please say a little bit about your position and/or your research/role
2	How did you learn about MRC's global health funding?
3	Are you aware of the MRC/DFID Concordat? [if not interviewer to explain the Concordat portfolio] • How well known is the MRC/DFID Concordat among your peers / policymakers / funding agencies / international aid agencies / researchers?

4	Does your organisation receive other funding from the MRC? • How do you use the MRC funding compared to other funding sources?
5	Why did you apply for MRC funding for [specify project]?
	Relevance of the MRC-DFID Concordat
6	Are you aware of any other agreements between medical research funders and international development agencies? • What do you think these offers over and above separate funding from the separate agencies? • Are you aware of any interesting examples?
7	Do you believe the funding you received through [name of specific Concordat funding] addresses key societal issues for your country? E.g. equity, access, gender balance, maternal and child health, marginalised communities, vulnerable groups, SDGs, etc. both of researchers and beneficiaries of research)
8	Can you identify any specific gaps in the current priorities? [Interviewer may prompt a specific country or challenge]
9	What is the role and involvement of co-developers from Southern/Northern countries in the portfolio?
	Quality of activities supported through the MRC-DFID Concordat portfolio
10	In your view, does the [Concordat/programme] contribute to the UK's international research reputation? • Can you name any specific examples? • Has this changed over the past years?
11	How do you judge the ability of the [programme/scheme] to support research capacity building, compared to other similar schemes? • How do your expectations compare with results? • Are there particular good examples?
	Outcomes and impacts of supported activities through the MRC-DFID Concordat
12	What do you view as the main results and outcomes from your [project]? • Most important/major impact? [If required, e.g. uncertainty from respondent about the meaning of the question, interviewer to prompt on array of impacts, e.g. improved health outcomes] • Reflecting on the pathways to impact note that you prepared, how have your results compared to your expectations? [Interviewer could also prompt on main learning points from this process in terms of understanding/achieving impact]
13	Have you had/observed any follow-up activities to extend/build on the [name of specific Concordat funding] results? If required, e.g. uncertainty from respondent about the meaning of the question, interviewer to prompt, e.g. leveraging other funding, activities outside the funding period]
14	Has the funding had any effect on your or your colleagues' career development? • In what way?
15	What mechanisms are in place in your organisation to ensure the results of capacity building are maximised? • What support do you receive from the MRC/DFID concordat? • Do you have any recommendations to improve achieving such impact?
16	What are the enablers to ensuring that the desired impact [prompt if needed based on previous answer to the results/impact questions] is realised? • How does the MRC/DFID support the impact being achieved (e.g. through events organised, using their national and LMIC networks, etc?)? • What more could they do to support this?
17	What are/were the barriers to achieving the desired impact [prompt if needed based on previous answer to the results/impact questions]? • [Not for the MRC/DFID] Are there any barriers that MRC/DFID could help you address?
18	Do you have any recommendations for suitable metrics to capture the array of impacts?

	The MRC-DFID relationship
19	Do you view the relationship between the Medical Research Council (MRC) and the UK international development Agency (DFID) to be productive / effective? • What aspects of the collaboration do you think went particularly well? • Where can/should the collaboration improve in the future? • Are there other ways in which you think the relationship could be improved?
	Effectiveness of operational management of the MRC-DFID Concordat (2)
20	How do you regard the administrative requirements of the Concordat, including the scientific and financial reporting of the grant holders? [Prompts not for the MRC] • Do you have a specified contact point? • What support do the MRC provide (if any)? • Are they effective and efficient in their administrative processes and the support that they provide (if any)? • What could they do better?
	Other comments, recommendations
21	Are there any other recommendations that you would make to MRC/DFID that could improve the quality of funded activities, or more broadly improve processes and enable impact?
22	Any other recommendations/suggestions

B.4 List of interviewees

Stakeholder group*	Name	Institution
1-MRC/DFID	Dr Carolyn Sunners	DFID
1-MRC/DFID	Dr Sue Kinn	DFID
1-MRC/DFID	Jo Mulligan	DFID
1-MRC/DFID	Dr Mark Palmer	MRC
1-MRC/DFID	Dr Morven Roberts	MRC
1-MRC/DFID	Prof Pontiano Kaleebu	MRC
1-MRC/DFID	Prof Peter Piot	MRC
1-MRC/DFID	Rebecca Nsubuga	MRC
2-National/international stakeholders/funders	Dr Michael Kilpatrick	African Academy of Sciences
2-National/international stakeholders/funders	S. Wardle	British High Commissioner
2-National/international stakeholders/funders	Prof Gagandeep Kang	CEPI, Coalition for Epidemic Preparedness Innovation
2-National/international stakeholders/funders	Dr Michael Makanga	EDCTP
2-National/international stakeholders/funders	Dr Ole Olesen	EDCTP

Stakeholder group*	Name	Institution
2-National/international stakeholders/funders	Dr Thomas Nyirenda	EDCTP
2-National/international stakeholders/funders	Dr Julie Jacobson	Gates Foundation
2-National/international stakeholders/funders	Chifundo	Malawi Liverpool Welcome Trust
2-National/international stakeholders/funders	Stephen Gordon	Malawi Liverpool Welcome Trust
2-National/international stakeholders/funders	Dr Val Snewin	NIHR/Department of Health
2-National/international stakeholders/funders	Prof John-Arne Røttingen	Research Council of Norway
2-National/international stakeholders/funders	Glaudina Loots	South African Department of Science and Technology
2-National/international stakeholders/funders	Dr John Nkengasong	The Africa Centres for Disease Control and Prevention
2-National/international stakeholders/funders	Dr Mary De Silva	Wellcome Trust
2-National/international stakeholders/funders	Simon Kay	Wellcome Trust
2-National/international stakeholders/funders	Dr Kabir Sheikh	WHO, Alliance for Health Policy and Systems Research
2-National/international stakeholders/funders	Anonymous	WHO, The Gambia
3-Global health experts	Prof Peter Hotez	Baylor College of Medicine
3-Global health experts	Prof Charlotte Watts	LSHTM
3-Global health experts	Rebecca Grais	Médecins Sans Frontières
3-Global health experts	Professor Paul Moss	University of Birmingham
3-Global health experts	Kevin Marsh	University of Oxford
3-Global health experts	Philip Bejon	University of Oxford
3-Global health experts	Prof Philippe Guérin	University of Oxford
3-Global health experts	Prof Sabu S Padmadas	University of Southampton
3-Global health experts	Anonymous	Ethics Committee, external assessor The Gambia
4 -Grant holders	Prof Sarah Kiguli	Dept. of Paediatrics Mulago Medical School, Kampala
4 -Grant holders	Richard Idro	Dept. of Paediatrics, University of Makerere Kampala Uganda
4 -Grant holders	Beate Kampmann	Imperial College London
4 -Grant holders	James Seddon	Imperial College London

Stakeholder group*	Name	Institution
4 -Grant holders	Lucy Okell	Imperial College London
4 -Grant holders	Patrick Walker	Imperial College London
4 -Grant holders	Dr Andrew Kambugu	Infectious Diseases Institute, Uganda
4 -Grant holders	Amina Abubakar	KEMRI
4 -Grant holders	Faith Osier	KEMRI
4 -Grant holders	J. Tuju	KEMRI
4 -Grant holders	K. Niare	KEMRI
4 -Grant holders	Simon Kariuki	KEMRI
4 -Grant holders	Feiko ter Kuile	Liverpool School of Tropical Medicine
4 -Grant holders	Jenny Hill	Liverpool School of Tropical Medicine
4 -Grant holders	Kevin Mortimer	Liverpool School of Tropical Medicine
4 -Grant holders	Prof Anne Mills	LSHTM
4 -Grant holders	Prof Helen Weiss	LSHTM
4 -Grant holders	Prof Richard Hayes	LSHTM
4 -Grant holders	Eugene Kinyanda	MRC Unit, Uganda
4 -Grant holders	Richard Mbango	MRC Unit, Uganda
4 -Grant holders	A. Bojang	MRC Unit, The Gambia
4 -Grant holders	A. Jaye	MRC Unit, The Gambia
4 -Grant holders	A. Ngwa	MRC Unit, The Gambia
4 -Grant holders	A. Roca	MRC Unit, The Gambia
4 -Grant holders	E. Clarke	MRC Unit, The Gambia
4 -Grant holders	H. Mbye	MRC Unit, The Gambia
4 -Grant holders	J. Lexow	MRC Unit, The Gambia
4 -Grant holders	J. Tomas	MRC Unit, The Gambia
4 -Grant holders	M. Antonio	MRC Unit, The Gambia
4 -Grant holders	M. Jaiteh	MRC Unit, The Gambia
4 -Grant holders	M. Okoye	MRC Unit, The Gambia
4 -Grant holders	U. Egere	MRC Unit, The Gambia

Stakeholder group*	Name	Institution
4 -Grant holders	U. Okomo	MRC Unit, The Gambia
4 -Grant holders	Andrew Abasa	MRC Uganda Virus Research Institute Uganda
4 -Grant holders	Zacchaeus Anywaine	MRC Uganda Virus Research Institute Uganda
4 -Grant holders	Prof Umberto D'Alessandro	MRC Unit, The Gambia
4 -Grant holders	Katherine Nakingudde	Psychologist Department of Psychiatry College of Health Sciences Makerere University
4 -Grant holders	Felistas Mwakiseghile	Queen Elizabeth Children's Hospital, Blantyre
4 -Grant holders	George Chagaluka	Queen Elizabeth Children's Hospital, Blantyre
4 -Grant holders	Prof Sheena McCormack	University College London
4 -Grant holders	Professor Catherine Law	University College London
4 -Grant holders	Yamikani Dickson	University of Malawi

Note: * some of the stakeholders represent multiple stakeholder groups, but are allocated only to one above

B.5 Impact case study details

Case study selection

Case study selection was based on an analysis of the portfolio and Researchfish data and discussion with MRC at the inception meeting. The unit of analysis for each case study is a specific funding award (whether for a project grant or a fellowship). We selected case studies across four LMIC where field visits were conducted. A significant proportion of the Concordat's investment has been in the two countries where there is an MRC unit – Uganda and The Gambia. Because of the MRC's wider presence in these countries, the diversity and scope of funding awarded to projects focusing on these countries, and the presence of African Research Leaders in those countries, we decided that focusing case studies on research benefiting these countries would likely be productive, because the key stakeholders in these two countries should have an awareness of the work conducted and we may be able to see some collective as well as individual project impacts. Therefore, we conducted three case studies in each of these two countries. This approach was agreed during the inception meeting with MRC.

Of the remaining funding, 51% of awards have been to nine countries: Tanzania, South Africa, Kenya, Malawi, Zimbabwe, India, Zambia, and Ghana. We therefore decided to select two further countries from this set of countries, and conduct two case studies focusing on each of these countries.

As well as a mix of countries, we also wished to cover a mix of funding mechanisms. In particular, we wanted to identify impact and impact pathways for both research project awards and fellowship and capacity building awards. With this in mind, we chose to start from the principle that, where possible, we would select 1 fellowship award (from either the African Research Leader Scheme or awards marked as 'fellowship') and 2 project grant awards for each country: The Gambia and Uganda. For the remaining two countries we selected across the available awards since the number of projects per country is be more limited.

Our final selection criterion was to select a sample of case studies that we anticipated to have had a range of impacts beyond the academic sphere. There are pros and cons for selecting case studies in this way. It is certainly a purposive sampling, but with a sample of only 10 case studies it is not in any case likely

to be completely representative of the portfolio as a whole. Our experience is that case studies which have had downstream impact are generally more informative about the mechanisms for impact and both the drivers of and barriers to that wider impact than a random sample. There are many ways that a piece of research can fail to achieve impact and many of them are not of interest and do not provide useful lessons learnt. For example, research may not work out as planned, or just not be ground-breaking. Researchers might move on to new topics or positions, or they may just still be pursuing the research at this stage. Although this might be of limited interest, research that has gone on to have a real impact often provides much more interesting insight into the processes through which this can happen – and typically these cases will have also faced barriers, dead ends and challenges (as well as solutions) along the pathway to that impact as well. With this small sample, case studies selected as likely to have an impact can be expected to provide a richer dataset, and while still likely comprising a mix of levels and types of impact as well as pathways and mechanisms by which those impacts have come about.

With this in mind, we chose to select case studies based on those projects which show impact across the widest range of downstream impact categories (excluding impacts within academia such as publications). This is still imperfect as a metric – one or two deep and meaningful impacts in a limited range of areas might be more significant than a very wide range of impacts – but it is the best heuristic we had available based on the existing data. Our case study selection protocol therefore was as follows:

- For each of Uganda and the Gambia select the following:
  - The 'highest impact' fellowship award
  - Two projects randomly selected from the top 10 most impactful project grant awards
- From among the remaining most widely funded countries (Tanzania, South Africa (non-DFID priority country), Kenya, Malawi, Zimbabwe, India, Zambia, Ghana):
  - Select two 'high impact' awards which are conducted within the same country
  - Consider the coverage across types of award holistically

There are several other criteria which may be of interest which we have not used as selection criteria, such as the size of award. However, by selecting across different types of award, we anticipate producing a diverse set of case studies by award size. We would also have been interested in case studies which are diverse in terms of discipline and 'appliedness'. However, we did not have HRCS codes or other categorisation based on discipline or stages along the health innovation pathway to enable us to select on this basis in the current data set.

Finally, given the typical time lags between research and impact, but the need to balance this with availability of informants for interviews and their likely recall of the work, we chose to limit our selection of case studies to awards that reported to Researchfish in 2017 but for which the award was made in early 2014 at the latest.

Based on these criteria and the selection approach set out above, we proposed a longlist of options for our selection of case studies as shown in Figure 36. These options were reviewed by MRC, and combined with our input a final selection was reached. The final selection of case studies was focused on research conducted in The Gambia, Uganda, Kenya and Malawi, corresponding to the projects listed in the first 10 rows of the table in Figure 36.

Figure 36 Proposed projects for impact case studies – final selection highlighted.

Project reference	Project title	PI	Country	Co-Investigator	Funding stream	Award size	Award start date	Award end date	Key areas of impact
MC_EX_MR/K02440X/1	Plasmodium Falciparum anti-malaria drug resistance in The Gambia: Identification of potential genetic markers by retrospective whole genome approaches	Alfred Ngwa	The Gambia	Unknown	Fellowship	Not available	01/06/2013	28/02/2018	Tools, Databases, Dissemination, Career development
MC_EX_MR/K011944/1	Childhood tuberculosis: Integrating tools for improved diagnosis and vaccines	Beate Kampmann	The Gambia	Philip Campbell Hill	IIB	Not available	01/01/2013	31/08/2018	Policy, tools, recognition and IP
MC_UP_A900_1115	Studies to understand the response of the infant's immune system to infectious diseases and vaccines	Ed Clarke	The Gambia	Unknown	Intramural IIB	Not available	01/04/2011	31/12/2100	Policy and products
MR/L004623/1	E Kinyanda, MRC/UVRI Uganda Research Unit on AIDS - Mental health among HIV infected CHildren and Adolescents in KAmpala, Uganda (CHAKA)	Vikram Patel	Uganda	Paul Bangirana	ARL	£706,133	01/01/2014	30/09/2017	Recognition, Dissemination and policy
MC_U122861322	Prevention Programme - Microbicides	Sheena McCormack	Uganda	Unknown	Intramural Population and Systems Medicine Board	Not available	01/12/1998	31/07/2013	Dissemination, Policy, Artistic, Recognition
MR/J005088/1	Calibration and analysis of complex models: methodological development and application to explore the impact of HAART in Africa	Richard White	Uganda	Pontiano Kaleebu	Methodology Research Programme	£515,607	01/10/2012	30/06/2016	Policy, Recognition, Dissemination, Software
MR/J012483/1	Transfusion and Treatment of severe Anaemia in African Children: a randomised controlled trial (TRACT)	Kathryn Maitland	Malawi, Uganda, Kenya	Michael Boele van Hensbroek	MRC Global Health trial	£3,046,319	31/03/2013	30/09/2019	Dissemination, tools and recognition
MR/L002515/1	Lung health and exposure to household air pollution in rural Malawi	Kevin Mortimer	Malawi	Unknown	Population and Systems Medicine Board	£484,860	02/01/2014	31/12/2017	Dissemination, policy and recognition
MR/L012189/1	Developing methods to assess the impact of malaria interventions upon transmission and the progress towards elimination	Patrick Walker	Kenya	Unknown	Fellowship	£299,834	01/04/2014	31/03/2017	Dissemination and policy
MR/L00450X/1	Defining the merozoite targets of protective immunity against Plasmodium falciparum malaria through multi-centre cohort studies	Kevin Marsh	Kenya	Unknown	African Research Leader scheme	£738,228	10/10/2013	31/12/2018	Recognition
MC_U122886353	Paediatric programme - HIV and other diseases of poverty NB. Also renewed under another award number 2013 onwards (see below)	Diana Gibb	Zimbabwe, Uganda, Zambia	Unknown	Intramural Population and Systems Medicine Board	Not available	01/04/2006	31/07/2013	Dissemination, products, policy, recognition and career progression

MC_U122888469	Tuberculosis Treatment Trials	Andrew Nunn	Malawi, South Africa, Zambia	Unknown	Intramural Population and Systems Medicine Board	Not available	01/04/2007	31/07/2013	Policy, dissemination and tools
MC_UP_A620_1016	Nutrition, Development and Lifelong Health: Studies in Developing and Transitioning Populations	Caroline Fall	India	Unknown	Intramural Population and Systems Medicine Board (PSMB)	£920,938.58	01/04/2010	30/04/2013	Dissemination, Policy, Tools, Databases, Artistic, Products, Recognition, Facilities, Other
MC_U130031238	Sexual Health and Families Programme	Lisa McDaid	Tanzania	Unknown	Intramural Population and Systems Medicine Board (PSMB)	£3,963,385.91	01/01/1987	31/05/2013	Dissemination, Policy, Tools, Databases, Recognition, Other
MR/K012126/1	Epidemiological and statistical research on health problems of developing countries: MRC Tropical Epidemiology Group	Richard John Hayes	Malawi, Ethiopia, Burkina Faso, Gambia, Senegal, Colombia, India, Guinea, Zimbabwe, Uganda, Kenya, South Africa, Guinea-Bissau, Zambia, Ghana, Tanzania, United Republic Of	Unknown	Infections & Immunity Board (IIB)	£2,723,902.66	01/11/2013	31/10/2018	Dissemination, Policy, Tools, Databases, Recognition, Other
MC_U105960371	Nutrition and Bone Health Research: Diet, bone health and osteoporosis and rickets (NBH)	Ann Prentice	Malawi, Gambia, India, Uganda, South Africa, China, Bangladesh	Unknown	Intramural Population and Systems Medicine Board (PSMB)	£10,954,772.81	14/06/1999	31/12/2020	Dissemination, Policy, Artistic, Recognition, Facilities, Other
MR/N028481/1	Improving uptake of delivery care services in rural Tanzania through demand creation, ambulance transport and quality of care: a feasibility study	Christian Hansen	Tanzania	Unknown	Public Health Intervention Development (PHIND) scheme	£117,586.14	01/05/2016	31/10/2017	Dissemination, Policy, Tools, Databases, Other
MR/P020526/1	H Mwandumba, CoM, Characterisation of the breakdown in immune competence of the lung that favours development of tuberculosis in HIV-infected adults	Stephen Squire	Malawi	Unknown	MRC/DFID African Research Leader (ARL) scheme	Unknown	01/09/2017	31/08/2021	Dissemination, Tools, Databases, Recognition, Other

MR/M01231X/1	Randomised trial of HPV vaccination for the control of HPV-related diseases in HIV-positive African populations: Preparatory phase (PH01/14-39)	Philipp Mayaud	South Africa	Unknown	Public Health Intervention Development (PHIND) scheme	£112,520.19	01/08/2014	31/07/2015	Dissemination, Policy, Tools, Databases, Recognition
MR/N015975/1	Development of a hand hygiene intervention to reduce bacterial infections among newborns & mothers delivered in maternity units in Tanzania	Wendy Graham	Tanzania	Said Mohammed Ali	Public Health Intervention Development (PHIND) scheme	£121,094.32	01/12/2015	30/04/2017	Dissemination, Policy, Products, Other
MR/J01477X/1	R Phillips, KNUST Ghana. Pathogenesis and management of M. ulcerans disease, Buruli ulcer	Mark Wansbrough-Jones	Ghana	Richard Phillips	MRC/DFID African Research Leader (ARL) scheme	£397,998.49	02/01/2013	01/01/2018	Dissemination, Policy, Tools, Recognition
MR/M011941/1	Peri-domestic behaviour of African malaria vectors and the impact of insecticides	Philip John McCall	Tanzania	David Towers	Infections & Immunity Board (IIB)	£530,886.48	01/07/2015	30/06/2018	Dissemination, Policy, IP
MR/M008940/1	Urban Drinking Water and Health Outcomes - Early Phase Study for a Randomized Controlled Trial in Accra, Ghana	James Wright	Ghana	Unknown	Public Health Intervention Development (PHIND) scheme	£125,632.67	01/07/2014	31/12/2015	Dissemination, Databases, Other
MR/M026639/1	Trial of vitamin D supplementation to prevent acquisition of latent tuberculosis infection in schoolchildren	Adrian Martineau	South Africa	Geeta Trilok-Kumar	MRC Global Health (GH) trial	£1,059,287.96	01/09/2015	31/08/2020	Databases, Products, Recognition
MC_UU_12023/17	Paediatric Programme - HIV and other Diseases of Poverty.	Diana Gibb	Zimbabwe, Uganda, Zambia	Unknown	Intramural Population and Systems Medicine Board (PSMB)	£2,201,000.00	01/08/2013	31/12/2100	Dissemination, Policy, Products
MR/P002404/1	Determining the importance of different locations to Mycobacterium tuberculosis transmission in high tuberculosis burden settings	Richard White	South Africa	Robin Wood	Infections & Immunity Board (IIB)	£26,022.00	01/02/2017	31/01/2020	Dissemination, Policy, Recognition
MR/K021222/1	Study of disease mechanisms in enteric fever to characterise innate & adaptive immunity in mucosa & blood in controlled human infection model	Vincenzo Cerundolo	Malawi	Branch Moody	Experimental Medicine (EM)	£2,769,902.39	01/09/2013	31/08/2018	Dissemination, Recognition, Facilities
MC_PC_13086	HPV - HIV association	Deborah Watson-Jones	Tanzania, Uganda, South Africa	Unknown	Public Health Intervention Development (PHIND) scheme	£143,663.00	01/02/2014	31/10/2014	Dissemination, Other
MR/N027442/1	Optimizing low-technology metofluthrin emanators to extend active ingredient release while maximizing protection against malaria transmission	Gerry Killeen	Kenya	Sheila Barasa	Public Health Intervention Development (PHIND) scheme	£49,505.67	01/07/2016	31/12/2017	Products, Other
MR/M025454/1	Abubakar;Pwani;Adolescent Executive Functioning Association with Scholastic Outcomes, Risk Taking Behavior and Medical Adherence in the Context of HIV	Charles Richard James Carruthers Newton	Kenya	Unknown	MRC/DFID African Research Leader (ARL) scheme	£157,770.60	01/08/2016	31/07/2021	Dissemination, Recognition
MR/P012485/1	The Friendship Bench for adolescents: evaluating strategies for scaling interventions to treat common mental disorders among adolescents in Zimbabwe	Frances Cowan	Zimbabwe	Dickson Chibanda	ADH	£69,795.82	01/02/2017	31/01/2019	Dissemination, Policy

MR/P011454/1	Improving adolescent access to contraception and safe abortion in sub-Saharan Africa: health system pathways	Ernestina Coast	Malawi, Ethiopia, Zambia	Eliya Zulu	ADH	Unknown	01/04/2017	31/03/2020	Dissemination, Other
MR/K012711/1	The role of enteropathy in the pathogenesis of severe acute malnutrition in HIV-infected African children	Andrew Prendergast	Zimbabwe, Zambia,	Beatrice Amadi	Infections & Immunity Board (IIB)	£724,831.14	02/01/2014	01/07/2018	Databases
MR/N023129/1	Shifts in the metabolic and virulence profiles of Streptococcus pneumoniae following the introduction of conjugate-polysaccharide vaccine in Malawi	Robert Heyderman	Malawi	Unknown	Infections & Immunity Board (IIB)	£43,092.46	01/12/2016	30/11/2019	Dissemination
MR/P01691X/1	Durable, practical, effective and affordable formats for insecticide-treated eave baffles that protect households and suppress malaria transmission	Gerry Killeen	Tanzania	Unknown	Public Health Intervention Development (PHIND) scheme	Unknown	01/03/2017	31/08/2018	Products

Note that additional narrative information from Researchfish was extracted to support case study selection

Figure 37 Case study template

Description of the scheme/project/initiative

- Brief description, incl. funding scheme, problems addressed, objectives, number and geographical coverage of participants, budget, key scientific disciplines covered
- Relevance of the activities to the local context - complementarity / overlaps with other local or regional activities (or stand-alone initiative)

Mode of implementation

- Key characteristics of the projects – length, type of research undertaken
- The level of support available – types of activities – networking, capacity building, knowledge sharing, how it is used and additional/complementary funding attracted
- Elements of international collaboration, academia-industry collaboration
- The main reasons for this mode of implementation and the advantages/disadvantages of it

Main achievements, results of the project (so far) and expected impact

- Description of the key elements of the impact pathway
- Results, achievements of the project (expected and delivered)
- Key benefits delivered to the different types of participants in terms of networking, capacity building, skills improvement, knowledge generation, knowledge transfer – level of individuals / institutions
- Impacts e.g. on setting research agendas, wider economy, health systems, society, policy and practice

Lessons learnt, changes over time

- Key success and enabling factors in the approach identified
- Main barriers overcome, possible solutions
- Monitoring and evaluation practices and key indicators used
- Sustainability of the results

Transferability of the scheme

- Assessment of the transferability of the approach
- Suggestions, recommendations

Appendix C Case studies

C.1 MR/JO12483/1 - Transfusion and Treatment of severe Anaemia in African Children: a randomised controlled trial (TRACT)

C.1.1 Description of the scheme/project/initiative

The project Transfusion and Treatment of severe Anaemia in African Children: a randomised controlled trial (TRACT), was funded by the Concordat grant MR/JO12483/1. It was an MRC Global Health Trial and the total awarded amount was £3,046,319. The study dealt with 3,700 children who suffered from severe anaemia (SA) in a multicentre randomised controlled trial in Uganda and Malawi and the Principal Investigator (PI) was Dr. Kathryn Maitland from Imperial College London.

According to the 2010 Malawi Demographic and Health Survey, Malawi alone has a 63% prevalence of childhood anaemia. [151] In Uganda it is estimated that 50% of children under five years have anaemia.[152] Anaemia is a condition in which the body cannot produce enough healthy red blood cells to carry oxygen to tissues and organs. Consequences of childhood anaemia are poor cognitive development for mild and moderate anaemia and death for severe anaemia.[153] Blood transfusions can be used to rapidly replace the missing blood cells and deter or reduce the consequences of anaemia.

The trial was set up to respond to these poor outcomes of SA, including high rates of in-hospital mortality, 6-month case fatality and chronic morbidity.[154] Factors associated with these outcomes include potentially treatable co-morbidities such as recurrent infection and multiple vitamin deficiencies, which were not addressed in current guidelines.[155] Moreover, existing policies guiding clinical management are in general fragmented, based on weak evidence and often impractical.[156] TRACT is designed to probe each of these contributing factors directly and add to the slim evidence base for blood transfusions in paediatric SA cases.[157]

C.1.2 Mode of implementation

The project started in the first quarter of 2013 and is currently still ongoing, until 2019. For a period of two years, 3,700 African children, aged two months to twelve years, were enrolled at admission in the hospitals and followed for six months after. In order to ensure proper ethical conduct, the researchers created a verbal consent process that was two-staged. Verbal assent was sought from parents or guardians on admittance to the hospital whereas full consent was sought once the child's clinical condition was stabilized.

All involved medical staff was trained on the practicalities of conducting randomised controlled trials and medical doctors were trained on triage. Knowledge sharing took place over the course of the project execution through formal and informal exchanges between the different project members.

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[151] Kazembe, Lawrence and A Ngwira. "Analysis of severity of childhood anaemia in Malwi: A Bayesian ordered categories model." *Journal of Open Acces Medical Statistics*. (2016).

[152] Kuziga, Fiona, Yeka Adoke, and Rhoda K. Wanyenze. "Prevalence and Factors Associated with Anaemia among Children Aged 6 to 59 Months in Namutumba District, Uganda: A Cross- Sectional Study." *BMC Pediatrics* 17 (2017): 25. *PMC*. Web. 5 June 2018.

[153] Kazembe, Lawrence and A Ngwira. "Analysis of severity of childhood anaemia in Malwi: A Bayesian ordered categories model." *Journal of Open Acces Medical Statistics*. (2016).

[154] Calis, Job CJ, et al. "Severe anemia in Malawian children." *New England Journal of Medicine* 358.9 (2008): 888-899.

[155] Ibidem

[156] Mpoya, Ayub, et al. "Transfusion and Treatment of severe anaemia in African children: a study protocol for a randomised controlled trial." *Trials* 16.1 (2015): 593.

[157] Ibidem

Since the results of the research were still under embargo at the time of writing this case study, there are no presentations or publications available on the final results as yet.

In Malawi, there was intensive collaboration between the different actors involved on the ground, such as the researchers from the Malawi Liverpool Wellcome Trust laboratories[158], Malawi blood transfusion services, other medical units outside the paediatric unit at the Queen Elisabeth Hospital, and the scientific team. This type of inter-organisational collaboration focused on Malawi only, while international collaboration engaged the different members of the project team in Malawi, Uganda, the UK and the Netherlands.

C.1.3 Main achievements, results of the project (so far) and expected impact

To appraise the achievements and expected impacts of the TRACT project it is necessary to distinguish between the different objectives of the project.

Scientific results

Although the results are not yet known, whatever the final results will be, they will be able to inform policies and guidelines by attending conferences and getting in touch with the WHO on how to use blood transfusion in treating children suffering from SA. Namely, if the intervention shows that following current WHO guidelines yields the best results for patients, it would imply that they have to keep blood for the very sick only but stick to the current conservative transfusion guidelines. If, the intervention approach of administrating blood transfusion in a more liberal manner and with follow-up multi-vitamin and mineral treatment will prove more successful, policy and guidelines should be changed, and more blood should be collected. This would in the long run improve the treatment of patients. In either case, this project significantly broadens the scientific evidence base on how to treat SA and what the effects are of blood transfusions in children. The high relevance of the project was one of the features that was reiterated throughout interviews with co-investigators and local staff as rendering the project a scientific success.

Results for participants

On the patient-level, participants received good care, better than other patients outside of study would receive, due to the additional resources availability. Some of the co-investigators indicated that there were children who received blood that would otherwise not have been made available to them. As such, participating children had a much better chance of survival. The emphasis on a well-informed consent and the study having as few exclusion criteria as possible, made the study inclusive to many children with SA.

Results concerning research capacity

On a very practical level, the skills and procedures pertaining to the labelling of blood and subsequent transfusion were also improved both in the participating clinics and hospitals in Uganda and Malawi. In Uganda blood was initially not or poorly labelled. According to the PI , this procedure was improved after a presentation for the Ugandan Medical Conference, also beyond the participating clinics and hospitals.

Regarding research capacity, there were a number of different outcomes and achievements. The interviewed co-investigators were in agreement about the added value of the study for their own career development. They identified different pathways of impact for personal capacity building. The first one was through interaction with the PI throughout the implementation of the project, including the discussions on the study design, responding to impromptu challenges and in the general running the trial. A second pathway was through collaboration with the PI on (upcoming) scientific peer-reviewed

[158] The MLW Trust is an affiliate of the Malawian College of Medicine. It has a Memorandum of Understanding with the University of Liverpool and the Liverpool School of Tropical Medicine.

publications and presentations at conferences. One of the five co-investigators was made full professor on the basis of the published works related to the research project.

Research capacity development is also apparent for support staff. Nurses in Malawi and Uganda were trained to improve their skills set, including medical training as well as training on documenting project results and research management. As a result, they were asked to participate in other (RCT) studies at the clinics and hospitals where they were working. In Malawi, medical students were trained in the hospital where the trial took place, so there is a potential for further knowledge transfer to a new generation of physicians once the results of the study are made available.

Results concerning policies, follow-up studies

Once the results are finalised there is a possibility that they will be included in new guidelines and standards. Dissemination of the results is already under preparation through session organised on how best to communicate the findings, engage with the WHO and attend large paediatrics conferences.

The co-investigators are also in the process of identifying follow-up studies from the TRACT project. However, this has only recently been set into motion as the project is still ongoing.

C.1.4 Lessons learnt

Co-investigators were in overall agreement that the project had run smoothly and collaboration between the members of the project team had gone well. The scientific relevance of the project was repeatedly cited as an important success factor as it was relatively easy to mobilise support internally at the clinic sites and with crucial partners such as laboratories and blood banks. Another enabling factor was that the management/organisation of the study was done professionally; all resources came in on time: money, medicines, blood, lab results, etc. Good communication and onboarding staff from the start were considered factors that benefited the project.

At the same time interviewees identified a few points of improvement, especially concerning the sustainability of the achievements. These concerns pertained most namely to the development of local research capacity. Although co-investigators did gain new skills and knowledge, the level of involvement in research design and subsequent capacity to carry out similar studies (more) independently remained limited. An unforeseen change in the PI in Malawi also meant that at a certain point there was a lack of ownership over the study design and implementation which, despite not compromising the project scientifically, did result in a large budget overrun in Malawi.[159]

C.1.5 Transferability of the scheme

The trial was unique in the way it dealt with a difficult issue with a relatively small existing evidence base and used a complex approach of a multi-centre randomised controlled trial. This elevates both the relevance of the study as well as the robustness of the findings, and thus serves as an example for future studies. Moreover, the development of a well-informed consent process is also notable as the study included children and posed an alternative treatment to an otherwise standard and regular treatment. As such, the consent process had to be of high standards in order to avoid ethical missteps.

Two key recommendations surfaced from the interviews with the different stakeholders. First of all, that there is a need to involve local investigators[160] as PIs from the start of projects to ensure sustainable local capacity building and execution of the projects. Secondly, more attention should be paid to policy follow-up by both the research team and the funder. Part of the grant should be allocated towards

[159] This had less impact on the research process in Uganda.

[160] By 'local' interviewees meant researchers who worked and lived for a long period of time in the host-country. As a rule of thumb one could consider a criterion of paying taxes in the host-country to be qualified as a 'local' researcher.

sharing the results and ensuring engagement with policymakers. Although this engagement has been set in motion in the project, this could be more heavily embedded in the requirements of the grant

C.2 MR/L002515/1 Lung health and exposure to household air pollution in rural Malawi (CAPS)

C.2.1 Description and relevance of the scheme/project/initiative

The MRC-DFID Concordat Grant MRL25151 on Lung Health in Malawi (484,680 GBP) was a young investigator grant that provided protected time for the Principal Investigator, Dr Kevin Mortimer at the Liverpool School of Tropical Medicine, to dedicate his time to the larger MRC-Wellcome Trust Joint Global Health Trial project Cook stoves and Pneumonia (CAPS). Since these were essentially twin grants, and have resulted in a single big research project, we will describe here the overall impact of the project, henceforth referred to as CAPS, drawing out specific impact of the support grant where relevant. The CAPS project aimed to address the lack of systematic evidence regarding the relationship between smoke and childhood pneumonia. Childhood pneumonia is among the major causes of childhood morbidity in developing countries[161], and exposure to household air pollution, mainly from cooking, was often assumed to be a major driver. This assumption was one of the main reasons behind the global investment in 'clean cook stoves', which reduce smoke and hazardous gasses. The CAPS study aimed to investigate this assumption through a randomised control trial in Malawi, building on insights from respiration science as well as more sociological studies.

In terms of local relevance of these activities, it is clear that pneumonia is recognised as a major burden of childhood disease in Malawi and similar developing countries[162]. However, it should be noted that some local study participants, as reported in a focus group with field officers, felt that the study did not address their health priorities (which were hernias and elephantiasis), nor was the local population consulted on the study design. The importance of clean cook stoves in Malawi is evidenced by the creation of a government appointed task force for the introduction of clean cook stoves and partners such as the Global Alliance for Clean Cook stoves who promotes the use of these cook stoves, not only for health reasons but also because of reduced fuel consumptions (helping to combat deforestation)

C.2.2 Mode of implementation

The project was implemented as an exposure-incidence study by randomly distributing clean cook stoves in rural Malawi. The main study group focused on children up to five year of age, across 52 villages in the Chikwawa and Karonga districts in rural Malawi. The goal was to determine whether the reduced exposure to open fire thanks to the cleaner cook stoves would result in lower incidence and mortality due to pneumonia. The project used modern electronic data collection tools. The project worked closely with the government health services in these districts to ensure the follow-up of patients. The main trial data collection took two years (2014-2016), with regular follow-up by field officers every three months, to prevent the common reversion to traditional cooking methods seen with clean cook stove projects. The project team existed of the PI (remote, based in Kenya), a research manager (in Malawi) and a team of field research officers and support staff. The project appointed an advisory board that included representatives from the Ministry of Health, and local healthcare research partners (Malawi-Liverpool Wellcome (MLW) Trust in particular) and the KPS (Karonga Prevention Study), which were all collaborators on the study. The main study was complemented by a cross-sectional support study among adults to determine the prevalence of obstructive lung disease in adults in the same grant.

A particularly noteworthy aspect of the project was its strong focus on community engagement and science communication, supported through the local science communication team of MLW. All villages

[161] http://www.who.int/features/2013/malawi_pneumonia_diarrhoea/en/

[162] Ibidem

appointed a local advisory group, and the field officers ensured proper consent of village and household heads before engaging the women in the studies.

C.2.3 Main achievements, results of the project (so far) and expected impact

The main impact pathway of the project was to contribute to more effective policy making and reduced childhood mortality through improved scientific insight into the relationship between smoke and pneumonia. Secondary benefits were sought in the area of capacity building, and direct benefits to the study population.

In terms of scientific and policy impact, the study had the unexpected result that no link was found between household smoke and pneumonia. These significant results were published in the Lancet peer reviewed journal, and have strongly boosted Dr Mortimer's career, who now leads a small team at LSTM and has won several subsequent grants (MRC JRF, NHI Global Health) to engage in new, larger studies in the field of lung health. He was also invited into the editorial board for several leading journals. The findings benefitted from attention from major media outlets (BBC[163], The Economist[164]), and have caused a renewed debate into the value of global investment in cook stoves as evidenced by the discussions in these articles. Academically, the new debate is moving towards a more holistic investigation of smoke and air pollution and the relationship with lung health, moving away from cooking only[165]. In terms of policy, the results of the study were integrated into the WHO Guideline for Indoor Air Quality. Currently, the policy direction of the MoH and the Global Clean Cook Stove alliance has not changed in a major way, as they are repositioning the benefit claims towards reduced fuel consumption. However, it is likely that this project has contributed to preventing a potentially large opportunity cost of misdirected public investment.

In terms of capacity building, the project had a significant impact on the team members involved in Malawi. A number of field officers (at least two out of 20) followed a Bachelor course, funded through the programme, while the others received other types of training. All medical staff involved in the project were also trained to improve their lung function evaluation skills. Senior members of the local team saw their career take off with international and national opportunities in research management. Training was also provided to local community members, and local field officers indicate that the local population in the target districts have become more supportive of research in general, possibly benefitting future studies. However, capacity building was less developed in terms of local research capacity. No local researchers were involved in the design, implementation and analysis of the study which were carried out at LSTM, and as such the project had only indirect effect on the Malawian health research capacity, i.e. exclusively on research support functions.

In terms of direct health benefits, the target population benefitted from improved access to medication during the trials, which is otherwise often problematic in Malawi. Furthermore, participating villages benefitted from the access to the cook stoves (the control group was also given a unit at the end of the study), which has other benefits such as fuel savings and reduced burns. However, since no local suppliers exist for cook stoves nor their parts, the sustainability of the latter benefit is minimal.

C.2.4 Lessons learnt, changes over time

Key success factors for this project included the very strong local research support capabilities of MLW and KPS, with a strong presence of field offices and good relationships with local populations. Furthermore, a highly developed science communication strategy ensured high-quality implementation of the project and a positive outlook of the local participants towards science. The science communication team of MLW is currently organising screenings of a movie that showcases the results

[163] https://www.bbc.co.uk/news/magazine-38160671

[164] https://www.economist.com/international/2018/04/05/household-smoke-may-be-the-worlds-deadliest-environmental-hazard

[165] http://www.environment-health.ac.uk/news/professor-majid-ezzati-editorial-lancet-do-smoke-free-stoves-really-save-lives

of the trials in each of the 52 villages. Another key success factor was the attitude of the MRC-DFID Concordat fund management, which was relatively light touch, allowing the scientists to focus on their research due to the low administrative burdens.

Key barriers during the trial included ensuring the continued use of the cook stoves by the trial population, as women sometimes find them unpractical, or they might break down and no spare parts are available. This challenge was addressed through improved training of the local population. Field officers noted the difficulties in mobilising women to use the cook stoves without compensation, and the solution which was found (giving T-shirts) was in hindsight not considered an appropriate gift by the target population (they do not need these). Finally, a key barrier was the lack of initial engagement with the MLW due to the limited local senior presence of the study in Malawi.

Sustainability of the project is likely to be high in terms of the academic follow-up, with major studies already underway. Policy-wise, the follow-up is less certain as there is no systematic engagement from the study team with policy makers post-project. The extent of local health benefits due to the cook stoves, training and medicine received, is likely to be very limited. In terms of capacity building, the local research support staff all managed to find relevant further positions, showing good sustainability for these results.

C.2.5 Transferability of the scheme

The transferability of the study approach is high in terms of the way the project dealt with community engagement and science communication. Working with an established centre like MLW, using good research support facilities, are other positive lessons.

C.2.6 Suggestions, recommendations

Increasing the local research involvement at a more senior level for large trial studies could ensure smoother engagement and increased capacity building. More intensive training of participating government health staff in terms of Good Clinical Practise could have been also helpful to ensure lower drop-out rates and higher consistency of care during the trial. Furthermore, more attention could be paid by the research designers to the sustainability of the local health interventions (e.g. better to use locally produced/available cook stoves, as was initially proposed in the proposal).

C.3 MR/L004623/1- MRC/UVRI Uganda Research Unit on AIDS - Mental health among HIV infected CHildren and Adolescents in KAmpala, Uganda (CHAKA) - African Research Leader Award

C.3.1 Description of the scheme/project/initiative

This case study describes the impact achieved by projects supported by the Concordat grant MR/L004623/1- MRC/UVRI to the Uganda Research Unit on AIDS. The grant (£706,133), an African Research Leadership award was given to Prof Kinyanda to support research done on mental health among HIV infected children and adolescents in Kampala, Uganda (CHAKA). The research built on the result generated by predecessor MRC funded projects in Uganda. The study was carried out with a lead PI, Prof Patel from the London School of Hygiene & Tropical Medicine, between 2014 to 2017. The project sought to investigate the impact of Psychiatric Disorders (PD) on HIV infected children and adolescents in Uganda and the implications for service provision. Studies have shown that PD is an issue with children and adolescents infected with HIV,[166] however, few of such Psychiatric studies have been conducted in Africa.[167] The CHAKA study was one of the first of its kind, dealing with children and

[166] Mellins CA, Malee KM. Understanding the mental health of youth living with perinatal HIV infection: lessons learned and current challenges. J Int AIDS Soc. 2013;16:18593. doi: 10.7448/IAS.16.1.18593.

[167] Erica Breuer, Landon Myer, Helen Struthers & John A Joska (2011) HIV/AIDS and mental health research in sub-Saharan Africa: a systematic review, African Journal of AIDS Research, 10:2, 101-122, DOI: 10.2989/16085906.2011.593373

adolescents, HIV and mental health in Uganda. The study addressed gaps in terms of knowledge deficiency and provided funding for areas where there was a need for certain expertise such as psychiatric epidemiology, psychiatric genetics as well as knowledge of qualitative research methodology in mental health. It comprised of epidemiologic, genetic and qualitative components with the objectives to:

- Determine the prevalence, 12-month incidence and predictors of PD (including neurocognitive impairment) among HIV infected children and adolescents
- Investigate the relationship between differences in the serotonin transporter gene and depressive disorder
- Examine the impact of PD on HIV disease progression
- Examine the impact of PD on social and academic functioning and risky behaviours (i.e. treatment adherence, alcohol use, sexual behaviour and suicidal behaviour)
- Investigate help-seeking behaviour and identify service delivery gaps in Ugandan HIV services.[168]

C.3.2 Mode of implementation

The project was one of the first longitudinal studies that have been conducted in Uganda and Sub-Saharan Africa, on the impact of Psychiatric Disorders on HIV disease progression in 1339 HIV infected children and their caregivers. During the three years of the study, data was collected at baseline, six and 12-months. The study collaborated with local institutions, Mbarara University and Kyambogo University in Uganda. It also benefitted from international collaborations through the involvement of Prof Kenneth D. Gadow from Stony Brook University, USA, who is a renowned researcher in the study field and provided the child and adolescent symptom Inventory-5 (CASI-5) to assess psychiatric disorders. The inventory was adapted for use in Uganda for the study. Furthermore, the ARL through the study collaborated with research partners from Norway, India, Ghana and South Africa.

C.3.3 Main achievements, results of the project (so far) and expected impact

Scientific results

The main impacts of this grant so far have been in the academic sector, informing and contributing to future research through scientific publications. The members of the international study team are writing articles169 to publish, and the study has also served as a basis for further studies of its kind. Four publications in peer reviewed journals have resulted from the study. The ARL has gone ahead to publish nine papers, out of which eight are under review, and one is submitted to date.

Another member of the study team has submitted a publication to BMC psychology as first author, got trained in behaviour activation programme as a result of working on the CHAKA study and is now using this in the management of depression in adults.

There was also a significant progression from presenting at conferences locally, to regionally and internationally over the years, including a presentation at the 28th World Congress of the International Association of Suicide prevention in Montreal Canada, June 2015; 8th Annual Pan-African PCAF Psychotrauma Conference, Nairobi, July 2015; the Africa- Norwegian Mental Health Research Group workshop at Ghana university, November 2015; 6th Annual Malawi Mental Health Research and Practice Development Conference, College of Medicine, University of Malawi, March 2016.

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[168] UK research and innovation- http://gtr.ukri.org/projects?ref=MR%2FL004623%2F1

[169] For example: Kinyanda E, Nakasujja N, Levin J, Birabwa H, Mpango R, Grosskurth H, Seedat S, Patel V. Major depressive disorder and suicidality in early HIV infection and its association with risk factors and negative outcomes as seen in semi-urban and rural Uganda. J Affect Disord. 2017 Apr 1;212:117-127

Results for participants

The research was regarded as beneficial and would for the first time lead the way for a comprehensive psychosocial management of emotional and behavioural problems in children affected by or infected with HIV in Uganda. The qualitative research revealed that care givers with HIV and their infected children could support each other and this was suggested as a possible form of social support that could be built on and explored further.

Results concerning research capacity

The profile of mental health research at the MRC/UVRI research unit on AIDS has been raised as a result of this funding. The MRC/UVRI has for the first time included funding for mental health in its next quinquennial review period (2017-2022) to the established mental health research group. This includes salary support for five years for the ARL and research funding for two pilot studies that are expected to lead to future clinical trials applications. The ARL grant enabled the provision of support to two PhD students and to one Master's student as well as the supervision of eight research assistants under the CHAKA study. One of the PhDs and the Master's degree student have finished their studies and both are engaged in different research work. The ARL, Prof Kinyanda has been promoted to Senior Scientist and is now on the research leader track with the MRC.

Results concerning policies, follow-up studies

The CHAKA study has contributed to the child mental health policy that is already being used in the country. The Ministry of Health of Uganda launched the Child and Adolescent Mental Health Policy Guidelines at the 2nd Annual Ugandan Conference of Child and Adolescent Mental Health that was held in March 2017. Furthermore, there is now a plan to develop an intervention as a result of the study with plans to implement and integrate it into the Uganda Health system in the future. This formative work for intervention is using the same contacts and networks and collaborators to go to next level. The research team from the study are now working on another study and their capacity to deliver results has improved from the experience of working on CHAKA.

The ARL successfully applied for a Senior Fellowship in Public Health and Tropical Medicine from the Wellcome Trust to undertake a study entitled, 'Integrating the management of depression into routine HIV care in Uganda (the HIV+D trial)' worth 2.02 million pounds for 5 years and is the first Ugandan to get such an award. In this new ongoing study, the research team is working to make sure that interventions are in line with polices and programme from the Ministry of Health.

C.3.4 Lessons learnt, changes over time

The African Leadership award is considered a prestigious scheme, which provides sufficient funding for the research that was envisaged. It allowed the awardee dedicated time to undertake research. Having an encouraging mentor, Prof Patel from LSHTM and a well written proposal were positive elements that helped guide the study. Working within the research environment of MRC/URVI was regarded as conducive as it already had certain structures in place such as financial, accounting, procurement, storage services that could be used.

One of the main challenges cited was the fact that the funding lasted for two years only, which was a bit rushed especially when taking into consideration the duration for PhD studies and the much-needed funding for their projects. Another challenge was that funds specifically for capacity building were not included in the proposal by the ARL. The timetable of two years for the study was set by the ARL and the research team in spite of the MRC/DFID allowing for a period of up to five years for the grant. It is however a lesson learned and more study time and stronger inclusion of capacity building elements would be included in any future grant applications.

C.3.5 Suggestions, recommendations

Overall the study was a pioneer study on mental health among adolescents and children. This African Research Leader award demonstrated that in addition to supporting the ARL a broad range of impacts can be delivered. The project contributed to the body of knowledge in mental health in children, established strong international networks, built the capacity of other African scientists and served as the basis for other studies in future. As a future suggestion, the provision of a wider range of schemes that would address early career and intermediate level researchers to develop their research capacity would be very helpful to have.

C.4 Developing methods to assess the impact of malaria interventions upon transmission and the progress towards elimination

C.4.1 Description of the scheme/project/initiative

Malaria is a major cause of morbidity and mortality in Kenya with over 70 per cent of the population at risk of infection.[170] Areas in Western Kenya around Lake Victoria and the coast present the highest risk, and children less than 5 years of age and pregnant women are most susceptible to infection. A study using data from 2012 to 2013 in Kisumu County found the prevalence of malaria in adults to be 28 per cent, with women being 50 per cent more likely to have malaria than men.[171] Since 2012, the WHO has recommended the use of insecticide-treated nets and intermittent preventive treatment in pregnancy.[172] Measuring progress towards elimination requires an estimate of the reduction in transmission that has occurred over time. Mathematical modelling in infectious diseases provides a framework for understanding the dynamics of disease transmission.[173] With the advent of new treatment options and control strategies, and concerns of climate change, mathematical models are necessary to better understand the impact of these factors on malaria epidemiology and transmission.

This case study[174] describes the impact achieved by projects supported by the Concordat fellowship MR/L012189/1 (£299,834) - *Developing methods to assess the impact of malaria interventions upon transmission and the progress towards elimination*, awarded in 2013, to Dr Patrick Walker, an infectious disease epidemiologist whose work is focused on conducting mathematical modelling of malaria in view of informing control and prevention strategies in various settings.

Using available data gathered by the Kenya Medical Research Institute (KEMRI) and the U.S. Centers for Disease Control and Prevention (CDC)'s Research Centre in Kisumu, Dr Walker was able to build and calibrate models of malaria transmission accounting for local ecology and epidemiology in Western Kenya and integrate interventions aimed at curbing malaria transmission. The models capture the progress being made by various control strategies as well as informing on optimal combinations of interventions in the region.

C.4.2 Mode of implementation

The mathematical modelling studies undertaken by Dr Walker allowed estimation of the control strategies required to achieve elimination in an area of intense transmission with high long-lasting

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[170] Republic of Kenya Ministry of Health.2016. *Kenya. Malaria Indicator Survey 2015. National Malaria Control Programme*.. Nairobi: Ministry of Health. accessed June 6, 2018. https://dhsprogram.com/pubs/pdf/MIS22/MIS22.pdf.

[171] Jenkins, Rachel, Raymond Omollo, Michael Ongecha, Peter Sifuna, Caleb Othieno, Linnet Ongeri, James Kingora, and Bernhards Ogutu. 2015. "Prevalence of Malaria Parasites in Adults and Its Determinants in Malaria Endemic Area of Kisumu County, Kenya." *Malaria Journal* 14: 263. https://doi.org/10.1186/s12936-015-0781-5.

[172] World Health Organization Global Malaria Programme. 2012. *Intermittent preventive treatment of malaria in pregnancy using sulfadoxine-pyrimethamine (IPTp-SP): updated WHO Policy recommendation*. 2012. Accessed June 6, 2018. http://www.who.int/malaria/iptp_sp_updated_policy_recommendation_en_102012.pdf?ua=1.

[173] Antao, Tiago, and Ian M. Hastings. 2011. "ogaraK: A Population Genetics Simulator for Malaria". *Bioinformatics* 27, no. 9: 1335–36. https://doi.org/10.1093/bioinformatics/btr139.

[174] The case study relies on experiences shared by six researchers who are familiar with the projects supported by the Concordat grant MR/L012189/1 and is supported by additional desk research. For purposes of respecting informed consent, individuals and their organisations are not named.

insecticidal nets coverage. It provided insights into the effects of insecticide-treated nets and estimated the impact of different control strategies involving mass administration of artemisinin combination therapy on transmission.

Dr Walker continues to develop his model in collaboration with the KEMRI/CDC Research Centre which houses researchers from KEMRI, CDC, and the Liverpool School of Tropical Medicine (LSTM). In particular, Dr Walker is working closely with Professor Feiko ter Kuile head of the Malaria in Pregnancy Consortium based in Kisumu.

The MRC-DFID Concordat offers a three-year fellowship with the benefit of flexibility allowed in managing the research. This administering enables grant holders to engage in dissemination and networking activities, which were highlighted as important enablers to both personal development and achieving research impact. This flexibility allowed Dr Walker to respond to the Ebola crisis, studying the effects of the outbreak on health systems and how this affected malaria prevalence, and evaluating the effect of mitigation strategies developed by the WHO Global Malaria Programme in response to the Ebola outbreak.[175]

The fellowship provided opportunities for Dr Walker to engage with important actors in malaria research and policy. Dissemination activities allowed interactions with the U.S. CDC, the WHO and the Program for Appropriate Technology in Health (PATH) as well as representatives from the national malaria control programmes from Kenya, Zambia, El Salvador, Gambia and Senegal.

C.4.3 Main achievements, results of the project (so far) and expected impact

Scientific results

Dr Walker's research used a combination of data analysis and mathematical modelling to evaluate the impact of a variety of strategies on the prevalence, incidence, and elimination of malaria. Studies focused on the sensitivity of available diagnostic tests at detecting malaria infection and how by increasing sensitivity, these could contribute to improving the prospect of malaria elimination through test-and-treat strategies.[176,177] A separate study explored data obtained from six cohort studies in West Africa and an individual-based malaria transmission model to evaluate seasonality, transmission intensity, and the interval between malaria episodes as factors influencing the success of post-treatment prophylaxis.[178] Results suggested seasonality and the overall intensity of transmission should be considered when deciding between artemisinin-based combination therapies. Further work focused on estimating the efficiency of malaria interventions at reducing malaria burden and transmission, and found that an initial intervention consisting of long-lasting insecticide-treated nets, followed by seasonal malaria chemoprevention or indoor residual spraying, was generally the most cost-effective intervention. [179]

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[175] Walker, Patrick G. T., Michael T. White, Jamie T. Griffin, Alison Reynolds, Neil M. Ferguson, and Azra C. Ghani. 2015. "Malaria Morbidity and Mortality in Ebola-Affected Countries Caused by Decreased Health-Care Capacity, and the Potential Effect of Mitigation Strategies: A Modelling Analysis." *The Lancet. Infectious Diseases* 15, no. 7: 825–32. https://doi.org/10.1016/S1473-3099(15)70124-6.

[176] Slater, Hannah C., Amanda Ross, André Lin Ouédraogo, Lisa J. White, Chea Nguon, Patrick G. T. Walker, Pengby Ngor, et al. 2015. "Assessing the Impact of Next-Generation Rapid Diagnostic Tests on Plasmodium Falciparum Malaria Elimination Strategies". *Nature* 528, no. 7580: S94–101. https://doi.org/10.1038/nature16040.

[177] Wu, Lindsey, Lotus L. van den Hoogen, Hannah Slater, Patrick G. T. Walker, Azra C. Ghani, Chris J. Drakeley, and Lucy C. Okell. 2015. "Comparison of Diagnostics for the Detection of Asymptomatic Plasmodium Falciparum Infections to Inform Control and Elimination Strategies". *Nature* 528, no. 7580: S86–93. https://doi.org/10.1038/nature16039.

[178] Cairns, Matthew E., Patrick G. T. Walker, Lucy C. Okell, Jamie T. Griffin, Tini Garske, Kwaku Poku Asante, Seth Owusu-Agyei, et al. 2015. "Seasonality in Malaria Transmission: Implications for Case-Management with Long-Acting Artemisinin Combination Therapy in Sub-Saharan Africa". *Malaria Journal* 14: 321. https://doi.org/10.1186/s12936-015-0839-4.

[179] Walker, Patrick G. T., Jamie T. Griffin, Neil M. Ferguson, and Azra C. Ghani. 2016. "Estimating the Most Efficient Allocation of Interventions to Achieve Reductions in Plasmodium Falciparum Malaria Burden and Transmission in Africa: A Modelling Study." *The Lancet. Global Health* 4, no. 7: e474–484. https://doi.org/10.1016/S2214-109X(16)30073-0.

Research also focused on modelling malaria in pregnancy.[180,181] This work combined maps of the current risk of malaria in pregnancy with maps of the level of drug resistance across Africa to estimate the impact of scaling up intermittent preventive treatment of malaria in pregnancy, and found evidence supporting preventive treatment in pregnancy. The cost-effectiveness of introducing the RTS,S[182] malaria vaccine in sub-Saharan Africa in addition to existing interventions was also investigated.[183] Results showed that implementing the RTS,S malaria vaccine was only optimal once very high coverage of the existing interventions had been achieved.

In the duration of this fellowship, the Ebola crisis in West Africa occurred, which overwhelmed healthcare systems in the affected countries from 2014. During this time, Dr Walker focused his work temporarily on the impact of decreased healthcare capacity and mitigation strategies on malaria as a result of the Ebola outbreak.[184,185] Dr. Walker estimated the number of cases and deaths due to malaria, and estimated additional deaths caused by reduced healthcare capacity as a result of the Ebola outbreak. Results showed that reduced healthcare capacity led to a higher number of untreated cases of malaria, which likely contributed to morbidity during the Ebola crisis. This burden could have been mitigated by mass drug administration, reducing the number of non-Ebola fever cases within healthcare systems.

Overall, the fellowship allowed Dr Walker to contribute to 12 publications with the majority of them being published in high impact journals such as the Lancet Global Health, Nature, the Lancet Infectious Diseases and PLoS Medicine.[186]

Results concerning research capacity

The research undertaken by Dr Walker has brought about benefits to the malaria research field and in particular to the West Kenyan setting, and has helped researchers at the KEMRI/CDC Research Centre by informing their thinking around the type and combination of interventions that would be most promising to curb transmission. This allowed these researchers to formulate successful proposals for further funding into malaria transmission, including the Joint Global Health Trial Scheme and the European and Developing Countries Clinical Trials Partnership (EDCTP) for work on large-scale trials expected to have important policy impacts.

Dr Walker was able to attract further funding from PATH's Innovation Fund to investigate changes in transmission of malaria in pregnant women attending antenatal services and the effect of various interventions aimed at limiting transmission in this population.

Dr Walker was also asked to deliver a short course to PATH on the basics of malaria modelling and was able to obtain funding for one of his collaborators in Western Kenya to attend a course on mathematical modelling at Imperial College London. Dr Walker's presence at the Research Centre in Kisumu facilitated other junior African researchers to become better acquainted with modelling, which is important as there are few Kenyan statisticians or mathematicians engaged in research.

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[180] Walker, Patrick G. T., Jessica Floyd, Feiko Ter Kuile, and Matt Cairns. 2017. "Estimated Impact on Birth Weight of Scaling up Intermittent Preventive Treatment of Malaria in Pregnancy given Sulphadoxine-Pyrimethamine Resistance in Africa: A Mathematical Model". *PLoS Medicine* 14, no. 2: e1002243. https://doi.org/10.1371/journal.pmed.1002243.

[181] Walker, Patrick G. T., and Matt Cairns. 2015. "Value of Additional Chemotherapy for Malaria in Pregnancy". *The Lancet. Global Health* 3, no 3: e116-117. https://doi.org/10.1016/S2214-109X(15)70081-1.

[182] RTS,S is a scientific name and represents the vaccine's composition, http://www.malariavaccine.org/files/MVI-GSK-FAQ-FINAL-web.pdf

[183] Winskill, Peter, Patrick Gt Walker, Jamie T. Griffin, and Azra C. Ghani. 2017. "Modelling the Cost-Effectiveness of Introducing the RTS,S Malaria Vaccine Relative to Scaling up Other Malaria Interventions in Sub-Saharan Africa". *BMJ Global Health* 2, no. 1: e000090. http://dx.doi.org/10.1136/bmjgh-2016-000090.

[184] Walker, Patrick G. T., Michael T. White, Jamie T. Griffin, Alison Reynolds, Neil M. Ferguson, and Azra C. Ghani. 2015. "Malaria Morbidity and Mortality in Ebola-Affected Countries Caused by Decreased Health-Care Capacity, and the Potential Effect of Mitigation Strategies: A Modelling Analysis". *The Lancet. Infectious Diseases* 15, no. 7: 825–32. https://doi.org/10.1016/S1473-3099(15)70124-6.

[185] Ghani, Azra C., and Patrick G. Walker. 2016. "Provision of Malaria Treatment for Ebola Case Contacts". *The Lancet. Infectious Diseases* 16, no. 4: 391–92. https://doi.org/10.1016/S1473-3099(15)00481-8

[186] Researchfish Data for the Concordat from 2003 until 2017

Results concerning policies, follow-up studies

Dr Walker has been able to engage with policy actors at national, regional and global levels. While direct policy impact is yet to be achieved, it has helped inform policy discussions and contributed to the wider evidence base. Participation in events such as the WHO Evidence Review Committee has been highlighted as important as in many countries national malaria policies are adapted from WHO recommendations.

C.4.4 Lessons learnt, changes over time

The data available through the KEMRI/CDC Research Centre allowed Dr Walker to rapidly build and calibrate the model. The close engagement with key scientific leaders in the field facilitated dynamic exchanges which helped researchers in Kisumu avoid research into interventions that would not have the desired benefits. The engagement with the KEMRI/CDC Research Centre also enabled interactions with the representatives of the Kenyan Malaria Control Programme. The collaboration with Prof ter Kuile and the Malaria in Pregnancy Consortium led to attending WHO Evidence Review Committee meetings on the updating of WHO's "Malaria in Pregnancy Guidelines" and delivering a presentation to CDC staff.

Due to the nature of the work, there were no major barriers highlighted in undertaking the research. In view of implementing the combination of suggested interventions predicted to have greatest impact some barriers to implementation could be related to the associated costs and the willingness from policymakers to implement.

Both the grant application process and the Researchfish reporting were perceived as valuable and positive experiences. In particular it was appreciated that Researchfish captures a range of activities including the ones pertaining to dissemination.

The results have already informed additional interventional research projects led by Prof ter Kuile and allowed Dr Walker to undertake follow-on research on transmission of malaria in pregnant women attending antenatal services. Engaging with the WHO, the U.S. CDC, the Malaria in Pregnancy Consortium and various representatives of malaria national programmes in a range of African countries represent meaningful milestones towards policy change.

C.4.5 Transferability of the scheme

Mathematical modelling is a highly specialised and relatively new field when compared to traditional epidemiology. The models that have been developed can be transformed and adapted to the ecology and epidemiology of different settings; however, this research endeavour is dependent on a skilled modeller.

C.4.6 Suggestions, recommendations

This case study describes how a Concordat fellowship led to research findings which directly informed interventional research avenues, while contributing to the recipient's career development.

Analysis of the case study suggests the following recommendations:

- Maintain the flexibility in administering the fellowship funds by the recipient.
- In view of helping with translating research findings and engaging with policymakers there could be an opportunity for DFID to become more engaged and potentially help organise workshops for program managers from various institutions to discuss use of evidence in policy.
- With regards to the Joint Global Health Trials, there were suggestions to specify if there is a funding limit for the applications. Reflections were offered on the potential to further contribute to capacity building in developing countries by allowing financing of PhD students as part of projects undertaken through this funding scheme.

C.5 Defining the merozoite targets of protective immunity against *Plasmodium falciparum* malaria through multi-centre cohort studies

C.5.1 Description of the scheme/project/initiative

The development of an effective malaria vaccine remains an important research priority as the global malaria control agenda moves from reductions in morbidity and mortality towards elimination. Whilst our understanding of the molecular complexity of *Plasmodium falciparum* has grown tremendously in the last decade, this has not been paralleled with equivalent strides in deciphering the underlying mechanisms and the targets of naturally acquired immunity.

This case study[187] describes the impact achieved by projects supported by the Concordat African Research Leader (ARL) award MR/L00450X/1 (£738,228)- *Defining the merozoite*[188] *targets of protective immunity against* Plasmodium falciparum *malaria through multi-centre cohort studies*, awarded in 2013, to Prof Faith Osier, a researcher from Kenya working on malaria paediatric immunology. All ARLs have a mentor within a UK University, who is officially the PI on the grant. The PI for Prof Osier's grant is Prof Kevin Marsh from the University of Oxford. Prof Osier is currently a visiting Professor of Malaria Immunology at the University of Oxford (since 2013), and a Group Leader at Heidelberg University Hospital, Germany and at the Kenya Medical Research Institute (KEMRI) Wellcome Trust Centre for Geographic Medical Research (Coast) (CGMR-C) in Kilifi, Kenya.

The projects supported by the ARL award aimed at identifying the immune response in children infected with malaria, to aid in designing better malaria vaccines. To achieve this, Prof Osier used four approaches: i) systematically analyse antibody responses to a number of parasite proteins; ii) conduct a cohort study, using previously collected serum samples and epidemiological data from established cohorts in Africa, to analyse the vast repertoire of responses; iii) standardise the protocols used for antigen testing; and iv) assess antibody-dependent mechanisms of action to specific antigens.

C.5.2 Mode of implementation

The first study funded through this award was conducted in Burkina Faso and Senegal, looking at the immune response in children in two settings with different intensity of malaria transmission.[189] Antibody levels to parasite proteins were measured and compared with the protective thresholds established in Kenyan children. The antibodies measured were not found to provide protection against severe malaria in young infants.

As a continuation of this work, with the aim of identifying protective antibody responses, the researchers made use of data from an ongoing cohort study known as the Kilifi Birth Cohort which is part of the Kilifi Health and Demographic Surveillance System, a well-established community surveillance framework that covers an area of 900 km^2 around Kilifi Country Hospital. One study used data collected between 2001 and 2010 and provided evidence that protective immunity is a result of multiple antibody-dependent mechanisms with distinct targets.[190] A second study used data from the same cohort collected

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[187] The case study relies on experiences shared by 6 researchers who are familiar with the projects supported by the Concordat grant MR/L00450X/1 and is supported by additional desk research. RAND Europe has also taken into account contextual knowledge gathered through the set of 12 interviews that were conducted in relation to Concordat supported projects undertaken in Kenya for the purposes of the wider Concordat evaluation project. For purposes of respecting informed consent, individuals and their organisations are not named.

[188] The merozoite is a form in the parasite's life cycle once this enters the human (host) organism, following its asexual division (schizogony). The next form the parasite takes after being a merozoite is the gametocytes which is the only form in which the parasite can infect the mosquito.

[189] Kangoye, David Tiga, Victorine Atanase Mensah, Linda Muthoni Murungi, Irene Nkumama, Issa Nebie, Kevin Marsh, Badara Cisse, et al. 2016. "Dynamics and Role of Antibodies to Plasmodium Falciparum Merozoite Antigens in Children Living in Two Settings with Differing Malaria Transmission Intensity". *Vaccine* 34, no. 1: 160–66. https://doi.org/10.1016/j.vaccine.2015.10.058.

[190] Murungi, Linda M., Klara Sondén, David Llewellyn, Josea Rono, Fatuma Guleid, Andrew R. Williams, Edna Ogada, et al. 2016. "Targets and Mechanisms Associated with Protection from Severe Plasmodium Falciparum Malaria in Kenyan Children". *Infection and Immunity* 84, no. 4: 950–63. https://doi.org/10.1128/IAI.01120-15.

from 2002 to 2010 and evaluated the role of special antibodies (cord blood IgG) in protection against severe malaria during the first year of life.[191] Results showed that antibody activity reduced the probability of developing severe malaria in the first 6 months of life, and identified targets of antibodies which could contribute to the development of vaccine candidates against severe malaria in infants.

Throughout her ARL award, Prof Osier was able to use the resources available at KEMRI CGMR-C – both researchers and infrastructure – and build a network that would allow knowledge sharing with other African scientists and attract additional funding from entities such as the Wellcome Trust and the European and Developing Countries Clinical Trials Partnership (EDCTP.)

Using the ARL award, Prof Osier built the South-South Malaria Antigen Research Partnership (SMART) in 2013, a virtual South-South network which brings together African scientists to share resources and expertise towards producing malaria vaccines and increasing research capacity in Africa. The network shares serum samples and epidemiological data on malaria gathered through prospective cohort studies. Initially envisaged as a network with three partner countries – Burkina Faso, Tanzania and Kenya, SMART has grown to seven countries expanding to Ghana, Senegal, Uganda and Mali.[192] The network took the SMART name under an EDCTP Senior Fellowship which Prof Osier won in 2016.[193]

C.5.3 Main achievements, results of the project (so far) and expected impact

Scientific results

Using the ARL award, Prof Osier designed a protein microarray to measure a variety of malaria proteins. The platform enables antigen discovery by mapping new proteins that can be further investigated in terms of immunity and vaccine development. Prof Osier's group has used it to run a multi-centre and multi-country study with over 10,000 data points from the seven SMART countries. The development of this platform has attracted a small grant from the Cambridge/Alborada Research Fund which fostered technology transfer of the protein expression array from the Wellcome Trust Sanger Institute in Cambridge, UK to KEMRI CGMR-C laboratories,[194] as well as funding from the Wellcome Trust, EDCTP, and the Humboldt Award.[195]

In regard to publications supported by the ARL award, Prof Osier has published five articles in journals such as Infection and Immunity, Vaccine, International Journal for Parasitology, and Trends in Parasitology.

Results concerning research capacity

The ARL award has brought about new scientific knowledge in the field of paediatric protective immunity against the malaria parasite and has contributed to the professional development of the ARL as well as that of members of her research group which in 2017 consisted of three Post Docs, seven PhD students, one statistician, three assistant research officers and two research interns all from various African countries.[196]

By building the SMART network, the award has led to greater South-South knowledge exchange between African researchers and has enabled early career researchers to continue engaging in research and pursuing PhD degrees by securing funding for research activities.

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[191] Murungi, Linda M., Klara Sondén, Dennis Odera, Loureen B. Oduor, Fatuma Guleid, Irene N. Nkumama, Mark Otiende, et al. 2017. "Cord Blood IgG and the Risk of Severe Plasmodium Falciparum Malaria in the First Year of Life". *International Journal for Parasitology* 47, no. 2–3: 153–62. https://doi.org/10.1016/j.ijpara.2016.09.005.

[192] SMART includes the following centres: Malaria Research and Training Centre (MRTC), Bamako, Mali, Kintampo Health Research Centre, Kintampo, Ghana, Institut Pasteur Dakar, Dakar, Senegal, Centre Nationale de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso and KEMRI-CGMRC in Kenya.

[193] SMART. n.d. [Homepage]. Accessed June 6, 2018. https://www.smartpartnership.net/.

[194] MRC/DFID African Research Leadership Awards Annual Progress Report Year 1 – F. Osier dated 9th May 2015

[195] SMART. n.d. [Homepage]. Accessed June 6, 2018. https://www.smartpartnership.net/.

[196] MRC/DFID African Research Leadership Awards Annual Progress Report Year 3 – F. Osier dated 22 May 2017

For the ARL, the award has been the catalyst of rapid professional development allowing her to pursue her own research ideas, obtain prestigious awards and a professorship as well as mentor other researchers.

Dr Osier was able to build on the Concordat award and go on to attract other prestigious awards such as receiving the 1st EVIMalaR African Scientist Award from the European Virtual Institute of Malaria Research in 2014, obtaining the 5th Merle A. Sande Health Leadership Award from the Accordia Foundation, USA in 2014, receiving the Royal Society Pfizer Award from the Royal Society, UK in 2014, being the Sofja Kovalevskaja Award Winner from the Alexander von Humboldt Foundation, Germany in 2016, and lately being appointed a TED Fellow by Technology, Entertainment, Design (TED), USA in 2018. Currently she holds the following funding: a Sofja Kovalevskaja Award, a Wellcome Trust Strategic Award for Controlled Human Malaria Challenge Infections, a Wellcome Trust DELTAS award for capacity building, an MRC/DFID African Research Leader Award, an EDCTP Senior Fellowship, and a Tackling Infections to Benefit Africa (TIBA) Award.[197] She routinely gives presentations at conferences throughout Africa and Europe[198].

For her peers and junior staff, Prof Osier is seen as an inspirational trailblazer with another ARL recipient commenting that interacting with Prof Osier gave her more confidence to apply for this award.

For the KEMRI CGMR-C, ARL awards including that of Prof Osier have expanded the work pursued in the centre and contributed to developing research capacity building by inspiring African researchers and building links with other groups such as the one at Heidelberg University, which facilitates access to German facilities and knowledge transfer between groups. The ARL award has also led to technology transfer to Kenya, with the KEMRI CGMR-C now being the one centre in Africa with the skills and technology to express proteins and protein microarray facilities.

Results concerning policies, follow-up studies

The work of Prof Osier and her team is contributing to regional research capacity development. This is particularly important due to the small number of existing African-based scientists compared to the size of continent -there are only 79 scientists per million Africans, compared to 4,500 per million in the US.[199]

It is also making important strides towards a malaria vaccine; however, the full effects of such basic research are expected to materialise in a wider timeframe.

C.5.4 Lessons learnt, changes over time

Several interviewees highlighted mentorship as a key facilitator to undertaking the research and building research capacity. The relationship between the PI and the ARL was seen as beneficial for providing advice on the strategic direction of the research and helping with networking and identifying additional opportunities. However, it was noted by both recipients of ARL and PIs on ARL grants that the PI terminology does not accurately represent their role, as the African researcher decides the funding allocation and leads the projects. It was suggested "mentor" would be a more appropriate title.

Prof Osier is a leader and mentor to members of her group who feel encouraged and empowered to conduct research, engage in dissemination activities such as presentations at conferences (e.g. the April 2018 Multilateral Initiative on Malaria in Senegal), pursue independent funding (e.g. one PhD student was able to attract a small grant from the EDCTP) as well as engage in mentorship activities of their own with Post Docs supervising master students and interns at KEMRI CGMR-C. She also has established a

[197] Osier, Faith. n.d. "Prof. Faith Osier CV". Accessed June 6, 2018. https://docs.wixstatic.com/ugd/ad1f32_1efc4f466aef416c84ed1a88f2ebb7d4.pdf.

[198] MRC/DFID African Research Leadership Awards Annual Progress Report Years 1,2 and 3 – F. Osier

[199] Kariuki, Tom. 2015. "Africa produced just 1.1% of global scientific knowledge – but change is coming". *The Guardian*, October 26, 2015. Accessed June 6, 2018. https://www.theguardian.com/global-development-professionals-network/2015/oct/26/africa-produces-just-11-of-global-scientific-knowledge

close collaboration between the two groups she is currently heading in Kilifi and Heidelberg, organising virtual group seminars.

The experiences shared by interviewees highlighted barriers pertaining to obtaining ethical clearances and handling the logistics around international sample transport which were noted as particularly time consuming.

In general, when it comes to wider capacity building in the African context, the interviewees mentioned the following barriers: limited career structure and mentorship opportunities, few centres that provide the physical and intellectual environment needed to compete internationally, and limited networking opportunities. However, it was also stated that the ARL award does address several of these challenges to a certain degree.

The current monitoring and reporting system used by MRC has been appraised as beneficial. In particular, the limited bureaucracy and its annual periodicity were appreciated (as opposed to reporting every six months or filling in timesheets). Researchfish was also considered effective at capturing a range of outputs and impacts and communication with the project officers was seen as straightforward and helpful.

A key element of the sustainability of results is the SMART network which provides samples from various settings leading to more generalisable results. As the work conducted is dependent on the latest technologies, it is important to secure further sources of funding in view of maintaining a steady research stream and developing SMART further. The ARL award has been particularly instrumental. However, as it is a one-time award, funders could also consider the possibility of establishing a structured fellowship scheme that could allow African researchers to move from the early to the late stages in their careers.

C.5.5 Transferability of the scheme

The ARL was seen to provide enough flexibility that would allow researchers from various settings to apply. However, it is dependent on the willingness of the UK-based PI to accompany the African researcher in the process. The grant administration is also done by the UK institution, although the way the money is used is decided by the ARL award recipient. There were mixed views on the potential to change this way of administration as there were views that while some African institutions have the capacities to administer the award, others may not. Some interviewees did feel that there are existing capacities to allow for African institutions to begin to solely manage the award.

C.5.6 Suggestions, recommendations

This case study highlighting Prof Osier's and her team's activities resulting from the ARL award provide an example of how such an award can contribute to knowledge generation towards developing future malaria vaccines, to Kenyan and regional research capacity building, and how it can help a mid-career African researcher transition to a further stage in her career.

The case study would suggest the following recommendations:

- The ARL award is seen as an extremely helpful award and from the interviewees perspective it would be beneficial to increase the number of available awards throughout Africa.
- Consider articulating a structured fellowship scheme that could allow African researchers to move from the early to the late stages in their careers.

C.6 Studies to understand the response of the infant's immune system to infectious diseases and vaccines (long version)

C.6.1 Description of the scheme/project/initiative

Despite world efforts to reduce child mortality under the age of 5 years as part of the Millennium Development Goals, in 2016 4.2 million deaths still occurred within the 5 years of life, meaning 30.5

deaths per 1,000 live births.[200] In the African region, the risk of a child dying before 1 year of age was 52 per 1,000 live births.[201] In The Gambia, the infant mortality rate was 60.2 deaths per 1,000 live births in 2017.[202] Although there are various causes of newborn mortality, over 25 per cent of deaths in this period occur as a result of infections.[203] Understanding the way in which infants develop their immune system in response to vaccines and infections is therefore a global health priority. Research into infant immunology could ultimately inform the development of novel interventions to protect newborns and infants.

The projects funded through grant MC_UP_A900_1115 (from 2013 to 2018) characterised key elements of the immune response to given pathogens, described the immune response generated as a result of vaccination, and established the optimum regimes for the use of current vaccines. This aimed to provide insight into the development of natural and vaccine-stimulated immunity, facilitating the development of novel protective strategies in order to guide future rational vaccine development and maximise the protection of infants. The grant served as core funding for the activities of the Vaccines and Immunity Theme, including building a core team by covering their overheads. Projects under this grant made use of core facilities at the MRC Unit in The Gambia (hereafter referred to as the Unit) rather than receive direct funding for specific projects. Therefore, we found it relevant to highlight cases where additional funding was obtained.

C.6.2 Mode of implementation

The projects funded through this grant investigated the immune response generated in infants through vaccination of pregnant women and infants in order to understand age-dependent immune development in the context of vaccination, infection, and important epidemiological and pathogen-derived factors. In addition to clinical trials, the projects made use of observational cohorts of mother/infant pairs as platforms to investigate host responses in different age groups and determine the interactions between host and pathogen under vaccine or infection pressures.

In explaining the rationale for choosing areas of research, one of the main researchers explained that the research questions driving these projects are aligned with global health priorities, including those identified through the WHO SAGE Committee, and are relevant for the needs of West African populations. The guiding principle of whether a certain type of research is justified in the West African context is used by the Unit to decide whether or not to undertake private sector sponsored research. The MRC/DFID/Wellcome Trust Global Health Trial Scheme has been found to be a particularly rapid and responsive mechanism in view of conducting research on urgent needs.

Conducting these types of projects relies on the Unit's established research platform, meaning the availability of core staff with particular expertise in conducting immunological studies in children as well as laboratory skills.

Over the last 10 years there has been a change in the funding model of the Unit, from core funding to more project-specific funding. This has attracted several projects to the Vaccine and Immunity Theme team, primarily financed through the Global Health Trial Scheme but also through donors such as the MRC, Wellcome Trust, Bill and Melinda Gates Foundation and industry (e.g. Merck, Novartis).

The projects have led to collaborations with pharmaceutical companies involved in vaccine development. These include: research on the meningococcal vaccine ACWY in collaboration with

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[200] World Bank. Mortality rate, infant (per 1,000 live births). https://data.worldbank.org/indicator/SP.DYN.IMRT.IN

[201] World Health Organization. Global Health Observatory (GHO) data –infant mortality. http://www.who.int/gho/child_health/mortality/neonatal_infant_text/en/

[202] Central Intelligence Agency. The World Factbook-infant mortality rate. (2017). https://www.cia.gov/library/publications/the-world-factbook/fields/2091.html

[203] The Republic of The Gambia, Department of State for Health & Social Welfare. The Gambian road map to accelerate the reduction of maternal & newborn morbidity & mortality (2005). http://www.nationalplanningcycles.org/sites/default/files/planning_cycle_repository/gambia/gambia_mnh_road_map_2005-2015.pdf

Novartis;[204] funding from Pfizer Vaccine Research for studies on pneumococcal PCV-13 in children;[205] and assistance in protocol preparation from GSK for work on Group B *Streptococcus*.[206] Collaboration with industrial partner PharmaJet facilitated research into vaccine delivery using needleless devices.[207,208]

C.6.3 Main achievements, results of the project (so far) and expected impact

Scientific results

The Unit is building a diverse portfolio in the field of infant immunology. One major stream of research focuses on vaccination during pregnancy. This has led to vaccines for influenza, tetanus and pertussis being recommended for use during pregnancy, and new vaccines being developed to prevent important neonatal infections in the future, including Group B *Streptococcus*[209] and pneumococcal vaccine PCV-13.[210]

Another major study used Concordat core support to evaluate the use of needleless devices to deliver vaccines. The system was set up to deliver inactivated poliovirus vaccine using disposable syringe jet injectors (DSJI) provided by PharmaJet.[211] The efficacy of DJSI was evaluated for intradermal vaccination rather than intramuscular vaccination in a nested clinical trial funded by the Bill & Melinda Gates Foundation and the MRC. DSJI were then used to deliver inactivated poliovirus vaccine in combination with measles-rubella and yellow fever in a study funded by the Bill & Melinda Gates Foundation from 2013-2014.[212] Results from these studies revealed the importance of training vaccinators for campaign and routine intradermal vaccination, as well as providing evidence to support the co-administration of inactivated poliovirus, measles-rubella, and yellow fever vaccines within the Expanded Programme on Immunisation (EPI) schedule at 9 months. Moreover, DSJI are being tested for delivery of other vaccines. Another study focusing on needleless vaccination is ongoing, funded by the Wellcome Trust, evaluating intranasal live attenuated influenza vaccine (LAIV). The Gambia does

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[204] Clarke, E. T., N. A. Williams, P. M. Dull, J. Findlow, R. Borrow, A. Finn, and R. S. Heyderman. 2013. "Polysaccharide-Protein Conjugate Vaccination Induces Antibody Production but Not Sustained B-Cell Memory in the Human Nasopharyngeal Mucosa." Mucosal Immunology 6 (2): 288–96. https://doi.org/10.1038/mi.2012.70.

[205] Trück, Johannes, Amber Thompson, Begonia Morales-Aza, Elizabeth A. Clutterbuck, Merryn Voysey, Ed Clarke, Matthew D. Snape, Dominic F. Kelly, Adam Finn, and Andrew J. Pollard. 2017. "Memory B Cell Response to a PCV-13 Booster in 3.5year Old Children Primed with Either PCV-7 or PCV-13." Vaccine 35 (20): 2701–8.

[206] Le Doare, Kirsty, Amadou Faal, Mustapha Jaiteh, Francess Sarfo, Stephen Taylor, Fiona Warburton, Holly Humphries, et al. 2017. "Association between Functional Antibody against Group B Streptococcus and Maternal and Infant Colonization in a Gambian Cohort." Vaccine 35 (22): 2970–78.

[207] Clarke, Ed, Yauba Saidu, Jane U. Adetifa, Ikechukwu Adigweme, Mariama Badjie Hydara, Adedapo O. Bashorun, Ngozi Moneke-Anyanwoke, et al. 2016. "Safety and Immunogenicity of Inactivated Poliovirus Vaccine When given with Measles-Rubella Combined Vaccine and Yellow Fever Vaccine and When given via Different Administration Routes: A Phase 4, Randomised, Non-Inferiority Trial in The Gambia." The Lancet. Global Health 4 (8): e534-547.

[208] Bibby, Jack, Yauba Saidu, Ama Umesi, Ngozi Moneke-Anyanwoke, Adedapo O. Bashorun, Mariama Badjie Hydara, Ikechukwu Adigweme, et al. 2017. "The Immunogenicity of Fractional Intradermal Doses of the Inactivated Poliovirus Vaccine Is Associated With the Size of the Intradermal Fluid Bleb." Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America 65 (5): 851–54.

[209] Le Doare, Kirsty, Amadou Faal, Mustapha Jaiteh, Francess Sarfo, Stephen Taylor, Fiona Warburton, Holly Humphries, et al. 2017. "Association between Functional Antibody against Group B Streptococcus and Maternal and Infant Colonization in a Gambian Cohort." Vaccine 35 (22): 2970–78.

[210] Trück, Johannes, Amber Thompson, Begonia Morales-Aza, Elizabeth A. Clutterbuck, Merryn Voysey, Ed Clarke, Matthew D. Snape, Dominic F. Kelly, Adam Finn, and Andrew J. Pollard. 2017. "Memory B Cell Response to a PCV-13 Booster in 3.5year Old Children Primed with Either PCV-7 or PCV-13." Vaccine 35 (20): 2701–8

[211] Bibby, Jack, Yauba Saidu, Ama Umesi, Ngozi Moneke-Anyanwoke, Adedapo O. Bashorun, Mariama Badjie Hydara, Ikechukwu Adigweme, et al. 2017. "The Immunogenicity of Fractional Intradermal Doses of the Inactivated Poliovirus Vaccine Is Associated With the Size of the Intradermal Fluid Bleb." Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America 65 (5): 851–54.

[212] Clarke, Ed, Yauba Saidu, Jane U. Adetifa, Ikechukwu Adigweme, Mariama Badjie Hydara, Adedapo O. Bashorun, Ngozi Moneke-Anyanwoke, et al. 2016. "Safety and Immunogenicity of Inactivated Poliovirus Vaccine When given with Measles-Rubella Combined Vaccine and Yellow Fever Vaccine and When given via Different Administration Routes: A Phase 4, Randomised, Non-Inferiority Trial in The Gambia." The Lancet. Global Health 4 (8): e534-547.

not have an influenza vaccination policy despite WHO recommendations for influenza vaccination to be considered in high-risk populations, including pregnant women and children under the age of five.[213]

A project funded by the MRC-DFID Concordat looked at the acceptance of intranasal LAIV in The Gambia using a cross-sectional survey in Gambian women whose children had or had not received the vaccine.[214] Results revealed that the acceptance of intranasal LAIV was higher in women whose children had already received the vaccine, but overall intent to vaccinate was very high, suggesting that it is feasible to include seasonal vaccination in the childhood vaccination schedule.

Other ongoing research at the Unit is investigating the immunogenicity of several doses of human papillomavirus (HPV) vaccine and the possibility of administering it to a younger age group, with the aim of understanding whether fewer doses could provide the necessary protection. Another ongoing research project focuses on the effectiveness of the rotavirus vaccine and understanding why it is less effective in African populations compared to European populations.

Academic impact has been achieved through 28 publications in scientific journals on topics ranging from natural immunity to challenges and opportunities for childhood immunisation in The Gambia.[215]

Results for participants

The studies provide important information in view of enabling decision makers to make evidence-informed decisions. For example, research into PCV vaccines, conducted from 2008 to 2010 found the Gambian PCV programme reduced the incidence of invasive pneumococcal disease in children by approximately 55 per cent.[216] Further research from the Unit on PCV-13 conducted from 2013 to 2014 generated data for the licensing and WHO pre-qualification of the vaccine.[217] Previously mentioned research on the effectiveness of the rotavirus vaccine in African populations compared to European populations could potentially inform the development of vaccines that are better suited for this population.

Studies on finding better ways of administering vaccines (e.g. the DSJI studies or the HPV studies) or on the acceptance on certain vaccines by the population (e.g. LAIV) could lead to greater efficiencies within vaccination campaigns as well as better vaccination experience for the population.

Results concerning research capacity

In addition to producing high impact publications, the research brought about professional development opportunities for researchers. The opportunity to work at the Unit in this field has enabled several researchers to develop critical skills needed to conduct high quality clinical research. In addition to engaging in project work, staff members were also encouraged to pursue distance learning courses and gain research-specific qualifications. For example, one researcher, in addition to getting on-the-job training, was able to diversify his expertise from clinical diagnostics to immunology, attend relevant conferences, and pursue independent research (on cellular components of breast milk).

The PI, Dr Ed Clarke, has become a leader in the field of immunology, and is frequently involved with the WHO SAGE Committee.

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[213] Meeting of the Strategic Advisory Group of Experts on immunization, April 2012 – conclusions and recommendations. Wkly Epidemiol Rec 2012;87:201–16.

[214] Armitage, Edwin P., Janko Camara, Sulayman Bah, Alice S. Forster, Ed Clarke, Beate Kampmann, and Thushan I. de Silva. 2018. "Acceptability of Intranasal Live Attenuated Influenza Vaccine, Influenza Knowledge and Vaccine Intent in The Gambia." Vaccine 36 (13): 1772–80.

[215] Research Fish Data for the Concordat from 2003 until 2017

[216] Mackenzie, Grant A., Philip C. Hill, David J. Jeffries, Ilias Hossain, Uchendu Uchendu, David Ameh, Malick Ndiaye, et al. 2016. "Effect of the Introduction of Pneumococcal Conjugate Vaccination on Invasive Pneumococcal Disease in The Gambia: A Population-Based Surveillance Study." The Lancet Infectious Diseases 16 (6): 703–11. https://doi.org/10.1016/S1473-3099(16)00054-2.

[217] Medical Research Council. WHO Prequalification of pneumococcal vaccine based on MRC Unit The Gambia study. http://www.mrc.gm/prequalification-pneumococcal-vaccine-based-mrc-unit-gambia-study /

In addition to MRC-DFID Concordat funding, this project attracted funding from other sources including the Bill & Melinda Gates Foundation, MRC, Wellcome Trust and National Institute for Health Research, UK.

The core team at the Unit has also focused on building relationships with colleagues from the government in The Gambia. As described by one interviewee, the government delivers antenatal care for some of the maternal vaccination trials and the Unit was able to deliver several training courses to government staff in relation to this research (e.g. emergency obstetric care, best practice for record keeping for delivery, midwifery training).

Results concerning policies, follow-up studies

This research has had an impact on policy, academic research, and in the public and private sectors. Data from the Unit showing that rotavirus made a significant contribution to morbidity and mortality in children in The Gambia, led to the introduction of a new rotavirus vaccine in The Gambia's EPI.[218,219]

Research from the Unit has been highlighted in the report *Maternal Immunization Safety Monitoring in Low- and Middle-Income Countries: A Roadmap for Program Development*.[220] This includes work done on maternal immunisation with *Haemophilus influenzae* type b (Hib) polysaccharide-tetanus protein conjugate vaccine in The Gambia,[221] work on Group B *Streptococcus* colonisation and disease,[222] and two ongoing trials to study the impact of conjugated pneumococcal vaccination on pneumococcal carriage and prevention of neonatal pertussis.

C.6.4 Lessons learnt, changes over time

A key element for success of the research pathway has been the availability of clinician researchers – generally paediatricians or obstetricians who understand the clinical field and epidemiological traits as well as the core research processes. These researchers are generally West Africans – often Nigerians and increasingly Gambians.

The Unit's good reputation was another key element facilitating impact, and was credited with enabling the recruitment of mothers and their children into clinical trials. Field coordinators also play an instrumental role in ensuring good relationships with the community by explaining the trials' procedures and obtaining permissions from the heads of communities to approach different populations in view of recruitment.

Another key element across the impact pathway has been the availability of skilled staff that understand processes in the lab including receiving, handling, storing, labelling and shipping of samples.

The experiences shared in relation to this case study suggest one main barrier which pertains to the continuity of funding for core staff. The interviewees highlighted that the main enabler for continuing to do this type of research pertains to the existence of the core team and therefore a perceived barrier was an eventual shrinkage of the team due to a loss of funding, which could affect the existing capacities.

The current reporting system using Researchfish was seen as positive. It was suggested that it would be beneficial for the MRC to provide feedback to the researchers on the information that is reported in order to better understand how the reporting of outcomes is being considered.

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[218] Medical Research Council. Outputs, outcomes and impact of MRC research: 2013/2014 report. https://mrc.ukri.org/publications/browse/outputs-outcomes-and-impact-of-mrc-research-2013-14/

[219] Researchfish Data for the Concordat from 2003 until 2017

[220] Bill & Melinda Gates Foundation and the Global Alliance to Prevent Prematurity and Stillbirth. Maternal Immunization Safety Monitoring in Low- and Middle-Income Countries: A Roadmap for Program Development. 2017. Available at: http://apps.who.int/medicinedocs/documents/s23275en/s23275en.pdf

[221] Mulholland, K., R. O. Suara, G. Siber, D. Roberton, S. Jaffar, J. N'Jie, L. Baden, et al. 1996. "Maternal Immunization with Haemophilus Influenzae Type b Polysaccharide-Tetanus Protein Conjugate Vaccine in The Gambia." JAMA 275 (15): 1182–88.

[222] Le Doare, K., S. Jarju, S. Darboe, F. Warburton, A. Gorringe, P. T. Heath, and B. Kampmann. 2016. "Risk Factors for Group B Streptococcus Colonisation and Disease in Gambian Women and Their Infants." The Journal of Infection 72 (3): 283–94. https://doi.org/10.1016/j.jinf.2015.12.014.

C.6.5 Transferability of the scheme

Conducting this type of research is highly dependent on the existence of the Unit's staff and lab capacity as well as community readiness and willingness to participate in this type of research. This can be in part attributed to the Unit's efforts of conducting research in The Gambia for the past 70 years.

C.6.6 Suggestions, recommendations

The projects conducted under the Intramural Infections and Immunity Board grant provide an example of how research can contribute to the generation of vaccines, which are one of the world's most important global public goods.

The case study suggests the following recommendations:

- Maintain core funding for the Unit and an open dialogue on potential adjustments that may be needed to support an increasing body of work in the area of vaccines and immunology.
- Create opportunities for the Unit to disseminate their research funding for projects that are not solely funded by the Concordat.
- Communicate to researchers about the use of Researchfish data and the type of analysis the Unit could potentially undertake in-house in order to produce materials that may be used to showcase their achievements. This in turn could attract additional research which would be in line with the current funding model that relies to a lesser extent on Concordat core funding.

C.7 Studies to understand the response of the infant's immune system to infectious diseases and vaccines (short version)

Despite world efforts to reduce child mortality under the age of five years, in 2016 4.2 million deaths still occurred, meaning 30.5 deaths per 1,000 live births.[223] In the African region, the rate of a child dying before one year of age was 52 per 1,000 live births.[224] Although there are various causes of newborn mortality, over 25 per cent of deaths in this period occurred as a result of infections.[225]

Vaccination is a key tool in early prevention of childhood infections. It is however vital to understand to whom to give the vaccine (either pregnant mother or the baby), when (at what age) and how frequently to give each vaccine such that it generates good, long lasting, protective immune response.

Through the Concordat, the MRC and DFID funded projects undertaken in the MRC Unit in The Gambia between 2013-18 to investigate the immune response generated in infants through vaccination of pregnant women and infants. The research helped understand age-dependent immune development in the context of vaccination, infection, and important epidemiological and pathogen-derived factors. The research questions (including the choice of infection/vaccine studied) were aligned the work of the WHO Strategic Advisory Group of Experts (SAGE) on Immunisation, while providing high levels of local relevance to West African countries. The projects made use of core facilities and research teams at the MRC Unit in The Gambia and involved cohorts of mother/infant pairs recruited through strong community engagement.

The projects have led to collaborations with pharmaceutical companies involved in vaccine development and resulted in 28 publications published in scientific journals on topics ranging from (biomedical knowledge of) natural immunity to more implementation related challenges and opportunities for childhood immunisation in The Gambia.[226] Research from the Unit has been highlighted in the report Maternal Immunization Safety Monitoring in Low- and Middle-Income Countries: A Roadmap for

[223] World Bank. Mortality rate, infant (per 1,000 live births). https://data.worldbank.org/indicator/SP.DYN.IMRT.IN

[224] World Health Organization. Global Health Observatory (GHO) data –infant mortality.

[225] The Republic of The Gambia, Department of State for Health & Social Welfare. The Gambian road map to accelerate the reduction of maternal & newborn morbidity & mortality (2005)

[226] Research Fish Data for the Concordat from 2003 until 2017

Program Development.[227] This includes work done on maternal immunisation with Haemophilus influenzae type b (Hib) polysaccharide-tetanus protein conjugate vaccine in The Gambia,[228] work on Group B Streptococcus colonisation and disease,[229] and two ongoing trials to study the impact of conjugated pneumococcal vaccination on pneumococcal carriage and prevention of neonatal pertussis.

The research also brought professional development opportunities for the researchers involved. The opportunity to work at the MRC Gambia Unit in this field has enabled several researchers to develop critical skills needed to conduct high quality clinical research through online learning and training provisions. The PI, Dr Ed Clarke, has become a leader in the field of immunology, and is frequently involved with the WHO SAGE Committee.

Government health care workers delivered antenatal care for some of the maternal vaccination trials and the Unit was able to provide these staff with several specific training courses (e.g. emergency obstetric care, best practice for record keeping for delivery, midwifery training). This not only improved the skills and capabilities of individual staff but reinforced the beneficial relationship with The Gambia Ministry of Health centrally.

A key policy impact is that based on evidence from the Unit showing that rotavirus made a significant contribution to reduction in morbidity and mortality in children in The Gambia, has led to the introduction of a new rotavirus vaccine in The Gambia's national Expanded Programme of Immunisation EPI.[230,231]

A key element for success of the research has been the availability of clinician researchers – generally paediatricians or obstetricians who understand the clinical field and epidemiological traits as well as the core research processes in the lab including receiving, handling, storing, labelling and shipping of samples. Field coordinators played an instrumental role in ensuring good relationships with the community by explaining the trials' procedures and obtaining permissions from the heads of communities to approach different populations. The MRC Unit's good reputation was credited with enabling the recruitment of mothers and their children into clinical trials.

The MRC Unit's good reputation and close working relationship with Ministry of Health, National immunization programmes both centrally and individually with staff was a key element facilitating impact.

Summary project information

PI: Dr Ed Clarke, MRC Unit, the Gambia

LMIC partners: MRC Unit, the Gambia

Project funding: £3,437,905

Project implementation: 2013-2018

Project ID: MC_UP_A900_1115

[227] Bill & Melinda Gates Foundation and the Global Alliance to Prevent Prematurity and Stillbirth. Maternal Immunization Safety Monitoring in Low- and Middle-Income Countries: A Roadmap for Program Development. 2017. f

[228] Mulholland, K., R. O. Suara, G. Siber, D. Roberton, S. Jaffar, J. N'Jie, L. Baden, et al. 1996. "Maternal Immunization with Haemophilus Influenzae Type b Polysaccharide-Tetanus Protein Conjugate Vaccine in The Gambia." JAMA 275 (15): 1182–88.

[229] Le Doare, K., S. Jarju, S. Darboe, F. Warburton, A. Gorringe, P. T. Heath, and B. Kampmann. 2016. "Risk Factors for Group B Streptococcus Colonisation and Disease in Gambian Women and Their Infants." The Journal of Infection 72 (3): 283–94.

[230] Medical Research Council. Outputs, outcomes and impact of MRC research: 2013/2014 report.

[231] Research Fish Data for the Concordat from 2003 until 2017

C.8 *Plasmodium falciparum* anti-malaria drug resistance in The Gambia: Identification of potential genetic markers by retrospective whole genome approaches

C.8.1 Description of the scheme/project/initiative

Globally, malaria is one of the main public health problems in terms of morbidity and mortality, with over 200 million cases and an estimated 500,000 deaths each year.[232] In The Gambia, the most represented species of the malaria parasite is *Plasmodium falciparum*, with an incidence of 85 per cent.[233] Artemisinin-based combination therapies (ACTs)[234] are the WHO-recommended first- and second-line treatment for uncomplicated *P. falciparum* malaria and chloroquine-resistant *Plasmodium vivax* malaria.[235] Resistance to ACTs has been documented worldwide in both *P. falciparum* and *P. vivax*, and *P. falciparum* has developed resistance to nearly all antimalarials in current use. In The Gambia, artemether-lumefantrine treatment failure rates exceed 10 per cent.

This case study[236] describes the impact achieved by projects supported by the Concordat grant MC_EX_MR/K02440X/1- *Plasmodium falciparum anti-malaria drug resistance in The Gambia: Identification of potential genetic markers by retrospective whole genome approaches*, awarded in 2013. The grant represents a Concordat career fellowship award, the first to be awarded to an African scientist – Dr Alfred Ngwa – to support his research between 2013 and 2018 on projects conducted at the MRC Unit in The Gambia. The projects conducted under his leadership aimed to identify and determine the distribution of malaria drug resistance markers in The Gambia, following five years of implementation of ACT in the country.

Research conducted under this fellowship focused on genetic changes in malaria infection following ACT implementation in The Gambia. Specifically, it aimed to look at characterising microsatellite variations and single nucleotide polymorphisms (SNPs), determining the prevalence of resistance markers in endemic communities, and defining the association of these polymorphisms with treatment failure and reduced drug sensitivity.[237]

C.8.2 Mode of implementation

To achieve its objectives, the projects employed hybrid select and Illumina sequencing[238] of retrospective isolates in collaboration with the Broad Institute in the U.S., flow cytometry techniques to assess the effects of artemisinin derivatives on early developmental stages of field isolates, and genotyping of isolates from *ex vivo* and *in vivo* studies in collaboration with the Wellcome Trust Sanger Institute in the UK.

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[232] World Health Organization. 2017. *World Malaria Report 2017*. Geneva: World Health Organization. Accessed June 5, 2018. http://www.who.int/malaria/publications/world-malaria-report-2017/en/.

[233] International Association for Medical Assistance to Travellers. n.d. "Country Health Advice Gambia. General Health Risks: Malaria". Accessed June 5, 2018. https://www.iamat.org/country/gambia/risk/malaria.

[234] The most commonly used ACTs are: mefloquine + artesunate, sulfadoxine/pyrimethamine (SP) + artesunate, and lumefantrine + artemether. In The Gambia, the first-line ACT is artemether-lumefantrine (AL), with artemether being the artemisin-derivative and lumefantrine the partner drug active against the erythrocytic stages of *P. falciparum*.

[235] Ceesay, Serign J., Climent Casals-Pascual, Jamie Erskine, Samuel E. Anya, Nancy O. Duah, Anthony J. C. Fulford, Sanie S. S. Sesay, Ismaela Abubakar, Samuel Dunyo, Omar Sey, Ayo Palmer, Malang Fofana, Tumani Corrah, Kalifa A. Bojang, Hilton C. Whittle, Brian M. Greenwood, and David J Conway. 2008. "Changes in malaria indices between 1999 and 2007 in The Gambia: a retrospective analysis". *Lancet* 372, no. 9649: 1545–54.

[236] The case study relies on experiences shared by two researchers working in the MRC Unit who are familiar with the projects supported by the Concordat grant MC_EX_MR/K02440X/1 and is supported by additional desk research. However RAND Europe has taken into account contextual knowledge gathered through all the 21 interviews that were conducted in relation to Concordat supported projects undertaken in The Gambia for the purposes of the wider Concordat evaluation project. For purposes of respecting informed consent, individuals or their organisations are not named.

[237] Researchfish Data for the Concordat from 2003 until 2017

[238] Illumina sequencing is a type of next-generation sequencing that allows low-cost high throughput whole-genome sequencing. Illumina sequencing can be used to study bacteria, bacterial populations and their evolution, and bacterial virulence.

The main researcher on the project was Dr Ngwa, who also provided support to two PhD candidates through the fellowship by involving them in particular work streams of the projects and offering mentorship towards their development as researchers. A Cameroonian national, Dr Ngwa joined the MRC in 2006 where he worked for five years before the fellowship award. Through building a research portfolio of publications in his time at the MRC and acquiring skills in articulating research questions, developing research plans, and grant applications, he decided to apply for the career development fellowship in 2013. He viewed the opportunity given by the Concordat particularly valuable as it offered a degree of personal visibility in the scientific community by being able to attend various meetings and flexibility in the overall research projects that was less common in other types of funding streams, manifested through the opportunities of employing researchers and tap into resources that permitted following up on the emerging results.

The fellowship provided many opportunities for collaborations in Senegal and Nigeria,[239] which facilitated access to sample banks and sample collection opportunities. It also enabled collaborations with UK-based institutions such as the Wellcome Trust Sanger Institute which provided support to generate data and support analysis, and the London School of Hygiene & Tropical Medicine (LSHTM) which facilitated access to training in evolutionary biology.

C.8.3 Main achievements, results of the project (so far) and expected impact

Scientific results

The main impacts of this grant so far have been in the academic sector, informing and contributing to future research through scientific publications, collaborations, the generation of genomic data and the development of a new tool for genotyping. Fifteen publications in scientific journals have resulted from the work, including in high impact journals such as Nature Genetics.[240] Collaborations have been established within UK research institutes and with other international institutions in Ghana, Nigeria, and Senegal.[241] This work has generated a pipeline for genotyping microsatellites from next generation sequencing data of wild isolates, contributing to research into structural variations in the genome of the parasite, and facilitating the evaluation of population structures as infection prevalence decreases across Africa. The researchers have also provided consensus sequences from whole genome sequencing analysis to PlasmoDB –a repository for *Plasmodium* research- and proteome antibody hybridisation data from The Gambia on selected asymptomatic and clinically infected cases.[242]

This work has also contributed to the development of a new technology with potential commercial applications. The tool consists of new fragment analysis assays for 35 microsatellite loci targeting signatures of selection from drugs and interventions that reduce transmission. These are now being applied to study parasite populations across the African continent.[243]

Results concerning research capacity

One key benefit resulting from the fellowship was developing research capabilities. In this respect, the collaboration with University of Lagos in Nigeria brought about the opportunity to supervise two PhD students which were embedded in the MRC Unit's platforms and gained skills in the methods proposed by Dr Ngwa's research plan, while working with their own samples. One of the students was awarded the title of Best Student in 2015 from the University of Lagos and is currently being hosted at The Gambia

[239] Nigerian Institute of Medical Research and the University of Lagos in Nigeria, Cheikh Anta Diop University in Senegal

[240] Researchfish Data for the Concordat from 2003 until 2017

[241] The institutions are the following: University of Ghana in Ghana, Nigerian Institute of Medical Research and the University of Lagos in Nigeria, Cheikh Anta Diop University in Senegal

[242] Researchfish Data for the Concordat from 2003 until 2017

[243] Ibidem

Unit for a Post-Doctoral fellowship. Following graduation, the second PhD researcher went on to support the Nigerian government by conducting research in Abuja.

Within the Unit, the fellowship facilitated training and involvement of junior staff members, including interns. It particularly supported researchers coming from a physical sciences background who gained skills in cell biology and genomics of malaria. These researchers went on to pursue MSc studies (one of them to Harvard University) or PhD studies, with one researcher gaining a Wellcome Trust Delta PhD position at the University of Ghana (there are no PhD programmes offered by the University of The Gambia) and conducting research housed at the MRC Unit in The Gambia. One PhD student credited the mentorship of Dr Ngwa in gaining skills that allowed her to articulate the research plan which won her the Delta scholarship. Furthermore, she stated she became much more confident in public speaking, networking, and reaching out to researchers outside The Gambia as a result of the coaching she received from Dr Ngwa.

Dr Ngwa is currently supervising three PhD students, two Post Docs, and a new PhD and two more Post Doc positions have recently become available as a result of Dr Ngwa's research projects. In his view, none of these opportunities would have been possible without the fellowship grant. Furthermore, the MRC career development award allowed him to develop rapidly at a critical time in his career and establish himself as a leader in his field.

With respect to capacity development, Dr Ngwa was able to attract funding that allowed acquisition of high performing equipment, which is now housed at the Unit. Throughout his fellowship, he was able to contribute to the Developing Excellence and Leadership Training in Genomics for the Elimination of Malaria (DELGIM) where he is now co-investigator on a project partially funded by the MRC. This allowed for the acquisition of a high-performance computer unit including a high-power server which is linked to research units in Mali and Kenya. As a result, students now have the opportunity to gain theoretical skills in bioinformatics and genomics, and then apply them directly in analysis at The Gambia Unit. Dr Ngwa's research efforts also facilitated acquiring the first next generation sequencing equipment available in The Gambia, and to his knowledge in all of West Africa, a machine which is also used to analyse samples from Nigeria, therefore contributing to wider regional capacity.

The DELGIM collaboration led to Dr Ngwa becoming part of another grant for the Human, Heredity and Health Collaboration in Africa (H3) amounting to a total of £3.6m awarded by NIH and Wellcome Trust across seven sites in Africa. This will allow Dr Ngwa to build further connections, expand the type of genetic research he is doing, and in his opinion propel the Unit towards becoming a widely recognised hub for genetics and genomics research in Africa.

Results concerning policies, follow-up studies

The clinical and societal applications of the research supported by the fellowship have not yet had time to deliver broader impact. However, it is anticipated that emergent research findings could inform decision makers on appropriate drug combinations which could help avoid development of resistance to malaria medications.

C.8.4 Lessons learnt, changes over time

Several key elements have been highlighted as important towards achieving the desired impact of this research. They pertain to the MRC Unit's existing platforms and governance arrangements.

Firstly, the flexibility of the fellowship allowed the PI to design his own research, support other researchers, engage in networking activities which opened doors for further collaboration, and increase his visibility as a researcher in the field of genomics.

An important facilitator to developing Dr Ngwa's career, which is one of the aims of the career development fellowships, was the opportunity to publish a significant number of articles and build a profile as a valuable researcher in the field. Dr Ngwa highlighted the importance of the MRC's policy to recommend publication in open source journals, which led to greater visibility of the research findings. The fact that the Unit attracts high quality researchers and invites high profile research leaders to deliver lectures offered in-house networking opportunities. Through the Unit's efforts, Dr Ngwa also stated that

he was able to establish good relationships with local communities and decision makers from the National Malaria Control Programme which allows him to attend regular meetings with the authorities on this topic and disseminate his findings.

The case study identified two main barriers that pertain to conducting research in The Gambia. First, the dynamic nature of research relies on having timely access to equipment and consumables which could be a challenge in this region. While the Unit has invested heavily in becoming self-sufficient which is reflected in the high number of projects they are able to conduct, purchasing remains a challenge, in particular when it comes to high-quality expensive equipment.

The second challenge is linked to researcher mobility as early career researchers can choose to relocate in pursuit of alternative opportunities overseas. This challenge is exacerbated by the small pool of Gambian researchers due to a fairly new university programme (the University was established in 2000 with the first undergraduate cohort graduating in 2006) and the absence of a PhD programme. This challenge is expected to decrease as the Unit has established a career development pathway for researchers, which is meant to lead to better retention of graduates. It was highlighted that support in the form of a bridging fund, would be beneficial to ensure funding for early Post Doc positions which in the Unit's funding model rely heavily on funding obtained from new projects, which may lead to potential employment gaps for these early career researchers.

The current system of using Researchfish as a means of reporting was seen as positive. However, potential refinement of the tool was suggested in order to ensure capturing career development activities (not only research development) such as supervising PhD students and demonstrating leadership.

Embedding the research into the Unit's research platform and a desire to establish the Unit as a regional hub in this field would suggest that this type of research has the potential to grow and inform policy decisions, and ultimately impact population health. The fellowship has already contributed to establishing a cadre of researchers, networks, and acquisition of high-quality and cutting-edge expensive equipment.

C.8.5 Transferability of the scheme

The capabilities and capacities of the MRC Unit in The Gambia have been instrumental in making the most of the fellowship funding. Therefore, fellowship plans should be mindful of regional context and leadership which would facilitate tapping into national, regional and global networks.

C.8.6 Suggestions, recommendations

Overall the study provides an example of how a fellowship grant was able to make important scientific contributions in the field of resistance to malaria medication, support both the recipient and other researchers in career development as well as lay the foundation for developing the MRC Unit in The Gambia into a regional hub in African genomic research.

The case study identified the following recommendations:

- Maintain the current degree of flexibility in administering the grant – meaning freedom to allocate the funds and pursue different research questions and engage in disseminating and networking activities.
- Emphasise the importance of career development for both recipients of the fellowship as well as researchers attracted by fellowship-related research and communicate metrics which could be used to capture this beyond academic impact with a particular focus on training and leadership development.
- Suggest the development of partners to invest more in developing country capacities that relate to medical supply and equipment delivery.
- Consider developing additional funding streams for national or regional early career researchers (considering the current Unit funding model which has decreased core capacity funding and relies predominantly on project funds to attract and retain early career researchers).

C.9 Predictive modelling to explore the policy impacts of antiretroviral therapy interventions in Africa (short version)

Since the beginning of the HIV/AIDS epidemic in the 1980s, more than 70 million people have been infected with the HIV virus and about 35 million people have died of HIV.[244] One of the highest prevalence and burden of the disease is in low- and middle- income countries, with an estimated 25 million living in sub-Saharan Africa. The management of HIV/AIDS normally includes the use of several antiretroviral drugs in combination in an attempt to control infection. One successful approach is to use multiple drugs that act on different viral targets relevant at different stages of the HIV life-cycle. This therapy is called highly active antiretroviral therapy or HAART. With ambitious new international targets to end HIV/AIDS by 2030, there is increased interest in designing strategies that help to scale-up antiretroviral therapy (ART).

Through the Concordat, the MRC and DFID funded a project under its Methodology Research Programme between 2012-2016, which explored the effects of different ART scale-up options in Uganda, using a bespoke mathematical model. Complex stochastic models are increasingly used in science and medicine to predict HIV transmission and facilitate public health decision making. The robustness of such models and thus the accuracy of predictions however rely on careful calibration with empirical data from local community settings. The project applied new methods to calibrate a model with detailed HIV/AIDS data from the community where the results were to be applied.

The Principal Investigator of the study was Richard White, currently Professor of Infectious Disease Modelling in the Centre for the Mathematical Modelling of Infectious Diseases and the TB Centre at the London School of Hygiene and Tropical Medicine and Director of the TB Modelling and Analysis Consortium. The study was conducted by a multi-disciplinary team involving UK researchers from Durham University, Universities of Cambridge, Exeter and Sheffield and the MRC/UVRI Research Unit in Uganda.

One specific application[245] of the project was to predict HIV/AIDS trends in Uganda before and after the introduction of HAART. Key data was made available from the MRC/UVRI General Population Cohort (GPC) of all residents of 25 villages in rural South West Uganda. Using the data, a detailed calibrated model was developed that was used to predict the future impact of a range of HAART strategies on HIV prevalence, incidence and mortality. The model was capable of simulating strategies that aimed at achieving the current WHO treatment recommendations and strategies of earlier treatment. In a recent report[246], the project used the model to simulate 22 ART scale-up strategies between 2016 to 2030, comprising different combinations of single interventions. Importantly, going beyond scientific modelling, the study involved the calculation of net monetary benefit (NMB) of each intervention, for a range of scenarios (e.g. different willingness/ability to pay (WTP) per DALY averted), bringing the scientific results to the real-world context of policy makers. The study was able to support the recent WHO guidelines in the Ugandan context and, dependent on resources available, recommended interventions to achieve the greatest reductions in HIV incidence.

This modelling tool can be applied in other contexts, after careful calibration, for TB/HIV control projections and costings. It can thus be used by country-level policy makers for decision making on control strategies and associated funding. The tool has now been used in workshops at global level by UNAIDS, the Global Fund and WHO, and at country level in South Africa, Vietnam, Ghana and Nigeria.

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[244] http://www.who.int/gho/hiv/en/

[245] http://cmmid.lshtm.ac.uk/mrccalib/

[246] McCreesh, N., Andrianakis, I., Nsubuga, R. N., Strong, M., Vernon, I., McKinley, T. J., ... White, R. G. (2017). Universal test, treat, and keep: improving ART retention is key in cost-effective HIV control in Uganda. *BMC Infectious Diseases*, 17, 322. http://doi.org/10.1186/s12879-017-2420-y

A new user-friendly modelling tool is now accessible through Avenir Health[247] (previously Futures Institute) a global health organization that works to enhance social and economic development by technical assistance in policy, planning, resource allocation and evaluation.

While the majority of the joint work was conducted at distance, the UK was successful in transferring knowledge and expertise on mathematical modelling to its LMIC partner. The study contributed to crucial capacity building in complex model calibration at the MRC/UVRI Research Unit in Uganda, which is now capable of conducting modelling work independently. It was reported that working with colleagues from the UK helped in gaining skills on how to run complex models as well as how to apply them. Thanks to the joint research project, one of the investigators from Uganda is now spearheading the modelling work at the MRC/UVRI Unit and was able to propose three further modelling projects in the Unit's current five-year plan. In addition, the project also contributed to training medical professionals in quantitative methods in Uganda who now use these skills in their decision making at country and global level.

Regarding national policy engagement, the research team met with Ministry of Health Officials in Uganda, and subsequently provided them with policy recommendations in the form of a policy brief entitled "Costs and effects of different ART scale-up options in Uganda". These scientific recommendations on adopting universal access to ART for all people living with HIV were underpinned by economic calculations showing that the new intervention would be highly cost effective, allowing savings on resources at the national level. Subsequent to this, the Ministry of Health revised its ART guidelines to recommend that ART be provided to all people living with HIV. This improved control and prevention of HIV should in time lead to improved survival, morbidity and quality of life, and the efficiency of health care delivery in Uganda.

One of the key challenges of successful implementation of the study results goes beyond any research project. It requires framework conditions to be in place such as a strong national health system with dedicated resources set aside for piloting, scale up and implementation of research findings. Nevertheless, the research project demonstrated that a mathematical model informed by local empirical data can provide accurate prediction of different strategies, enabling informed policy choices on the most cost-effective ways to reduce HIV infection.

Therefore, more effort should be invested in policy dialogues between researchers and decision makers, so that local and international policy makers gain sufficient trust in modelling and improved understanding to interpret results. Training more local researchers in modelling (and accurate calibration of complex models) would also strengthen the scientific field and build a critical mass so that predictive approaches can be used in other high-burden areas, including non-communicable diseases in low- and middle- income countries.

Summary project information

PI: Richard White, London School of Hygiene and Tropical Medicine

LMIC partner: MRC/UVRI and LSHTM Research Unit Uganda

Project funding: £515,607

Project implementation: 2012-2016

Project ID: MR/J005088/1

[247] http://www.avenirhealth.org/software-spectrum

C.10 Evaluating microbicides for HIV Prevention (short version)

In the early 1990s, new HIV infections increased rapidly, reaching an estimated 4.7 million new HIV infections by 1995: 2.5 million in southeast Asia and 1.9 million in sub-Saharan Africa. In order to target HIV transmission, a new range of experimental products, vaginal microbiocides were developed to potentially reduce the risk of HIV (or other sexually transmitted) infection in women. This specific target population was proposed as women are often unable to ensure the safe use of condom with their sexual partners.

Through the Concordat, the MRC and DFID initiated in 1998 the funding of the largest phase III clinical trial to test the effectiveness of microbicides in women. To help the preparations of the study, a new African-European not-for-profit partnership was established, the Microbicides Development Programme (MDP), co-ordinated jointly by the MRC Clinical Trials Unit and Imperial College London. The Principal Investigator for the study was Sheena McCormack, currently Professor of Clinical Epidemiology at the MRC Clinical Trials Unit at UCL.

The goals of the project and the MDP were multi-fold: (i) conduct social science research into the acceptability and barriers to the uptake of microbiocides; (ii) prepare clinical trial sites for a large, multi-national, randomised controlled trial; (iii) undertake early clinical studies of new microbicide products in African populations; and (iv) complete a major phase III effectiveness trial (MDP 301) of a safe, gel-based microbicide PRO2000. The MDP was funded over a 15-year period and brought together 16 research institutions or sites in Europe, South Africa, Tanzania, Uganda, Zambia and Mozambique, five not-for-profit organisations and industry to provide microbiocide gels.

While ultimately no evidence was found in the phase III clinical trial that the vaginal microbicide PRO2000 reduces the risk of HIV infection in women, it provided an important result as the trial was large enough to conclusively show the evidence for the lack of efficacy, ending scientific speculation about its clinical importance. The study however provided critical insight into social attitudes and helped create awareness about the vulnerability of women in Africa.

It was recognised early that the potential success of a vaginal product in reducing HIV transmission depends not only on clinical efficacy of the product used but also on the consistent and correct use of the product. Therefore, social science played an essential role in providing methodologies for identifying the many socio-economic and cultural factors influencing people's preferences and practices and in investigating the acceptability and the likelihood of use of such vaginal products in clinical trials and beyond.

A key success of the study that it managed to screen over 16,000 women at six research centres in four African countries to enrol over 9,000 women who were HIV negative with sexual partners who were HIV positive (i.e. sero-discordant couples). The management of the trial was led from the UK MRC Clinical Trial Unit which coordinated on the development of the trial protocol, established the central trial database, provided monitoring, analyses and oversight. This well-established infrastructure and governance model were rolled out and training about working practices and tools was given to trial co-ordinators at local trial centres. The DFID, on the other hand, contributed with its network in sub-Saharan Africa, providing a key point of entry in the communities, essential for prevention trials.

There were, however, a number of indirect benefits of conducting the MDP 301 trial:

Results for trial participants

- Awareness was raised with regards to issues related to sero-discordant couples. Many women participants reported to have been able to talk to their partners about HIV thanks to what they had learnt by participating in the trial
- An increase in the use of condoms was reported since the trial began, and the use of contraception grew in some areas. (Note that condoms were made available to trial participants.)

- The screening, which took place prior to the trial, disclosed a large number of HIV positive women. Lifelong treatment was offered to those who put themselves forward for the screening.
  - The association between screening and care was understood and created a growing demand for HIV care at local hospitals. This has an important impact on society, since earlier people did not want to know about their sero-positivity status, as they feared to be stigmatised.
  - Women participants were able to accompany their HIV positive partners to seek care.
  - Women participants who were HIV positive received a higher standard of care than they would if they had not been enrolled in the trial.
- Women who participated in the trial created a strong female community, which empowered them:
  - Trial co-ordinators reported that 1st trial participants sought permission from their partners before enrolling, whereas the same women enrolled in the 2nd trial without seeking permission.
  - Trial participation made the women 'research experienced' and more willing to read medical information.
  - There was an emerging awareness of women's rights over their bodies and there were reports of male partners being proud of their female partners, signalling the beginning of a change in local attitudes.
- Reimbursement of costs for the participants enabled some to buy essential products such as bicycles and telephones.

Results concerning research capacity

The MDP has contributed to build research capacity in its host centres in sub-Saharan Africa and established sustainable international research networks.

- Local trial co-ordinators received training beyond the operational aspects of trial implementation. For example, after attending scientific writing workshops, they went on publishing papers.
  - They were able to supervise post-graduate research using MDP data. This was described as a rare opportunity in SSA, only made possible by the link to the MRC.
  - They obtained transferable skills about governance and management of clinical trials.
  - They were subsequently recruited because their professional skills became visible.
- The Ebola vaccine trials, USAID trials and all other important research and data collection that followed the MDP trial have benefited from the enhanced expertise resulting from conducting trials on microbicides in the same region. The local capacity and the Community Advisory Board created by the MDP trial is still being used for vaccine efficacy study.
- Some research infrastructure in the trial centres remained available for subsequent studies.

Results concerning policies

A continuous provision of HIV data coming from SSA, through the MRC, is fed to the UK Department of Health, informing their policy-making. According to interviews, results from the MDP provided evidence to argue for home testing of HIV to become legal in the UK (April 2014).

The MDP 301 trial is ultimately considered a success because it left behind a legacy in a number of areas, including skills created and social attitudes changed. It proved essential to have the buy-in of local communities and the presence of local PIs in local trial centres. The local and empowered women continue to benefit from the experience during the trial and they effectively constitute a readily available cohort of participants for clinical trials. Nevertheless, in the absence of an ex-post evaluation of such a large and pioneering clinical trial, the present case study approach has its own limitations to triangulate findings.

The recent encouraging trend regarding the decline of annual numbers of new HIV infections in southern Africa (29% decline) and western and central Africa (9% decline) may indicate that awareness and social behaviour change may play an important role in preventing the transmission of the virus and achieving public health targets. In the words of a South African trial participant: "Even though the gel proved not to be effective, we played a role in the fight against HIV. We learnt a lot about caring for ourselves, such as using condoms. We also learnt to encourage others to test for HIV and we gained confidence in helping those who were already infected."

Summary project information

PI: Sheena McCormack, MRC Clinical Trials Unit

LMIC partner: multiple

Project funding: £43 million

Project implementation: 1998-2013

Project ID: MC_U122861322

C.11 Childhood tuberculosis: Integrating tools for improved diagnosis and vaccines

C.11.1 Description of the scheme/project/initiative

Tuberculosis (TB) is one of the top 10 causes of death worldwide, and causes significant morbidity and mortality in children worldwide. In 2016, an estimated 1 million children became infected with TB and 250,000 died because of it.[248] In low- and middle-income countries, diagnosis of TB relies on microscopy for identification of the bacteria and/or clinical diagnosis of TB.[249] Using these diagnostic techniques in children can be a challenge as they have fewer bacteria in their lungs that can be recovered in a clinical sputum sample.[250] Currently, there is a lack of suitable alternative diagnostic methods for childhood TB. This represents a major obstacle to progress in identifying paediatric patients in need of treatment.

This case study[251] describes the impact achieved by projects supported by the Concordat grant MC_EX_MR/K02440X/1- *Childhood tuberculosis: Integrating tools for improved diagnosis and vaccines* awarded in 2013. This is an Infections and Immunity Board Grant awarded to the project's Principal Investigator Prof Beate Kampmann. Prof Kampmann joined the MRC Unit in the Gambia (hereafter referred to as the Unit) in 2012 when she took up the position of Vaccines and Immunity Theme Leader, while maintaining her role as Professor of Paediatric Infection, Immunity and International Child Health at Imperial College London.

[248] World Health Organization. 2018. "Tuberculosis. Key facts." Accessed June 5, 2018. http://www.who.int/en/news-room/fact-sheets/detail/tuberculosis.

[249] Tuberculosis Coalition for Technical Assistance. 2006. *International Standards for Tuberculosis Care*. The Hague: Tuberculosis Coalition for Technical Assistance. Accessed June 5, 2018. http://www.who.int/tb/publications/2006/istc_report.pdf.

[250] World Health Organization. 2014. *Guidance for national tuberculosis programmes on the management of tuberculosis in children*. 2nd ed. Geneva: World Health Organization.

[251] The case study relies on experiences shared by three researchers working in the MRC Unit who are familiar with the projects supported by the Concordat grant MC_EX_MR/K02440X/1 and is supported by additional desk research. The study team has also taken into account contextual knowledge gathered through the set of 21 interviews that were conducted in relation to Concordat supported projects undertaken in The Gambia for the purposes of the wider Concordat evaluation project. For purposes of respecting informed consent, individuals and their organisations are not named.

The projects funded through this work stream aimed at developing and evaluating new and existing tools for TB diagnosis based on both the immune response to the bacteria and the microbiological features of the bacteria.

C.11.2 Mode of implementation

The main study involved primary data collection to assess the immunological differences in three categories of children: those infected with TB, children with TB disease, and uninfected children who have been exposed to TB. The researchers tested samples from TB-affected children (infected, diseased or exposed) obtained from household cohorts in order to characterise host responses associated with protection against infection in TB-exposed children who remain uninfected. The data obtained from household cohorts were used to expand existing epidemiological databases to include the epidemiological and microbiological context of household transmission and its impact on host responses. Additionally, the researchers developed a novel statistical approach to design prediction algorithms for the diagnosis of childhood TB.

The projects built on existing expertise and infrastructure available at the Unit. Implementation also made use of the relationships built in the Gambia between MRC researchers and Gambian decision makers.

C.11.3 Main achievements, results of the project (so far) and expected impact

Scientific results

The research has resulted in 66 publications in scientific journals, including high profile journals such as The Lancet.[252] One of the main research streams supported by this grant established household cohorts to evaluate contact tracing and assess the potential of preventive therapy in childhood contacts. A total of 4,000 child contacts aged below 15 years living in the same household[253] and compound[254] with adults showing a positive microscopy test for TB were recruited for this study.[255] Research found over half of TB disease in childhood contacts was missed when contact tracing was limited to symptom screening and immediate household contacts only, emphasising the importance of expanded contact tracing. Using the same recruiting process with an age limit of 5 years, a second project evaluated the potential of isoniazid preventive treatment among childhood contacts of adults who tested positive for TB.[256] Research showed home-delivered isoniazid preventive treatment had high uptake and adherence rates, illustrating the potential of isoniazid in TB prevention.

The household cohort also enabled the researchers to conduct an evaluation of diverse diagnostic methods in TB doing a side-by-side comparison of bacterial detection assays on sputum samples of patients presenting TB symptoms, and assessing their potential as screening tests. A biosignature consisting of immune molecules showed potential as a diagnostic tool for pulmonary TB disease.[257,258]

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[252] Research Fish Data for the Concordat from 2003 until 2017

[253] A household was defined as a group of individuals living in the same building and eating from the same pot.

[254] A compound was defined as a cluster of homes or buildings often owned by the members of the same family.

[255] Egere, Uzochukwu, Toyin Togun, Abdou Sillah, Francis Mendy, Jacob Otu, Mark Hoelscher, Norbert Heinrich, Philip C. Hill, and Beate Kampmann. 2017. "Identifying Children with Tuberculosis among Household Contacts in The Gambia." *The International Journal of Tuberculosis and Lung Disease: The Official Journal of the International Union Against Tuberculosis and Lung Disease* 21, no. 1: 46–52. https://doi.org/10.5588/ijtld.16.0289

[256] Egere, Uzochukwu, Abdou Sillah, Toyin Togun, S. Kandeh, F. Cole, Adama Jallow, A. Able-Thomas, et al. 2016. "Isoniazid Preventive Treatment among Child Contacts of Adults with Smear-Positive Tuberculosis in The Gambia." *Public Health Action* 6, no. 4: 226–31. https://dx.doi.org/10.5588%2Fpha.16.0073

[257] Awoniyi, Dolapo O., Andrea Teuchert, Jayne S. Sutherland, Harriet Mayanja-Kizza, Rawleigh Howe, Adane Mihret, Andre G. Loxton, et al. 2016. "Evaluation of Cytokine Responses against Novel Mtb Antigens as Diagnostic Markers for TB Disease." *The Journal of Infection* 73, no. 3: 219–30. https://doi.org/10.1016/j.jinf.2016.04.036

[258] Chegou, Novel N., Jayne S. Sutherland, Stephanus Malherbe, Amelia C. Crampin, Paul L. A. M. Corstjens, Annemieke Geluk, Harriet Mayanja-Kizza, et al. 2016. "Diagnostic Performance of a Seven-Marker Serum Protein Biosignature for the Diagnosis of Active TB Disease in African Primary Healthcare Clinic Attendees with Signs and Symptoms Suggestive of TB." *Thorax* 71, no. 9: 785–94. http://dx.doi.org/10.1136/thoraxjnl-2015-207999

Results for participants

Research into childhood TB funded through this programme has influenced training of practitioners and researchers, facilitating national age-disaggregated notifications of the condition to the WHO and increasing reporting of childhood TB in The Gambia by 60 per cent due to better awareness and identification of childhood TB cases. It is expected that all these efforts will enable more children with TB to be identified and treated, ultimately reducing the number of lives lost to the disease.

Results concerning research capacity

Overall, the projects conducted under this grant involved approximately 30 individuals with four of these (3 African scientists and 1 UK national) obtaining their PhD as a result of the research facilitated by the grant. All of them have continued their careers in research through positions at either the Unit, or the Universities of Edinburgh and Oxford.[259]

One of the African PhD scientists attracted additional funding from the WHO's Special Programme for Research and Training in Tropical Diseases (TDR) for rolling out the contact tracing platform. In recognition of his expertise on childhood TB, which was acquired mostly through the grant cycle as he had previously worked mostly on pneumonia, he was invited by the WHO to contribute to the development of Liberia's National TB Programme.

Building on the track record and platform established through the grant, the PI was able to attract further research funding from the Global Challenges Research Fund, the EU's Innovative Medicines Initiative, the Program for Appropriate Technology in Health, and from a number of pharmaceutical companies.

Collaborations were established with institutions from both the academic and the public sector in the U.S., Canada, UK, Nigeria, Tanzania, South Africa, Senegal, Denmark and Germany. Research into a TB biosignature of childhood TB has also resulted in a patent filing for this new technology.[260]

Results concerning policies, follow-up studies

This project impacted policy by informing childhood TB guidelines and influencing healthcare and education services. Prof Kampmann was part of an external review group on WHO guidance for national tuberculosis programmes on the management of childhood TB.[4] The work raised the profile of paediatric TB in international organisations such as ECDC and WHO, leading to the inclusion of recommendations specifically for children in the TB guidelines and to the work receiving citations in clinical guidelines, policy documents and systematic reviews.[261] The researchers provided assistance to the National Leprosy and TB Programme of The Gambia in preparation for a successful application to the Global Fund, which includes additional provision of services for children.[262]

C.11.4 Lessons learnt, changes over time

The Unit's prestigious reputation has been highlighted as an important factor in being able to recruit participants to the studies. The Unit already had expertise and a track record in TB research. This was combined with expertise on paediatrics developed through the vaccine and immunology trials run by the Unit, to focus on paediatric TB. The Unit employs the greatest number of paediatricians in the country, most of them international physicians attracted to The Gambia by the Unit.

Publications and dissemination activities which helped in attaining policy impacts contributed to the career development of research staff – especially at PhD level - who were also able to attract further funding for national capacity building activities and additional projects for the Unit.

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[259] Ibidem

[260] Researchfish Data for the Concordat from 2003 until 2017

[261] Sandgren, Andreas, Luis E. Cuevas, Masoud Dara, Robert P. Gie, Malgorzata Grzemska, Anthony Hawkridge, Anneke C. Hesseling, et al. 2012. "Childhood Tuberculosis: Progress Requires an Advocacy Strategy Now." *The European Respiratory Journal* 40, no. 2: 294–97. https://dx.doi.org/10.1183%2F09031936.00187711

[262] Researchfish Data for the Concordat from 2003 until 2017

The project team ensured that community sensitisation activities were undertaken prior to commencing recruitment. These consisted of open days and communications with community leaders during which the study was explained and permissions to approach members of the community were sought. Government representatives, members of the National TB Programme, were also invited and took part in some of these activities (e.g. communications during World TB Day). Engagement with national policy makers enabled national level impacts by introducing new ways of reporting data and training of practitioners, and enhanced government expertise in the field of TB.

Interviewees stressed several barriers encountered throughout the course of the research. One pertains to the reticence of parents to engage in prophylaxis research for their healthy children (for the isoniazid prophylaxis study). This was overcome by ensuring appropriate communication and explaining to parents what the trial consists of and the evidence base and rationale for conducting the research.

Another challenge pertained to retention of staff, particularly postdocs specialised in immunology, molecular biology, and bioinformatics. The pool of qualified people is smaller for these positions, and international staff are more expensive and more difficult to attract, as these positions are not usually covered by the programme funding.

More widely, limited access to equipment was highlighted as problematic at times. The Unit engages in a yearly competitive bidding system with other UK institutions. The call is once per year which is not necessarily when the need arises. At the same time, it is difficult to justify the need to update equipment and acquire it in a competitive process, considering equipment cannot be added to project budgets as they would skew the financial proposal. As overseas units strive to be more than sample collection sites, researchers find that it is important to have some of the latest technology on site.

In view of ensuring sustainability of results, a challenge towards achieving the desired impact is represented by limited national capacity. There is an expectation from national stakeholders that the Unit would contribute more to building national capacity to deliver health services, which is currently not in the remit of the Unit.

The current reporting system was seen as positive. In particular the responsiveness of the designated programme manager was highlighted as beneficial to the overall conduct of the projects.

C.11.5 Transferability of the scheme

Several of the projects' enablers pertain to the Unit's track record and capacities, which may limit transferability in a similar setting that does not benefit from such a research institution. Lessons pertaining to community engagement and dissemination are transferable and can be taken on board by researchers operating in other settings.

C.11.6 Suggestions, recommendations

The childhood TB programme grant provides an example of how research can contribute to expanding scientific knowledge in this field, help a national TB programme improve their monitoring and reporting approach, contribute to the training of practitioners and researchers, and help develop African researchers into recognised experts in the field of childhood TB.

The case study analysis draws the following recommendations:

- The Concordat could support more capacity building elements by ring-fencing some grant finances to finance PhD studies.
- Access to equipment could be facilitated by organising specific calls for overseas units.
- Considerations by both the Unit and the Concordat should be given to incentives for postdocs, considering the challenges in attracting and retaining qualified staff.
- One interviewee suggested there could be more incentives for collaboration between different units operating in Africa including between MRC units and Wellcome Trust units.

- Collaborations with industry were described as rudimentary, partially because industry has a very set scientific agenda. Knowledge sharing on how to best engage with industry and establish agreements with provisions for capacity building could be considered.