

# Implementation research for the control of infectious diseases of poverty



Strengthening the evidence base for the  
access and delivery of new and improved  
tools, strategies and interventions

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**World Health  
Organization**



**For research on  
diseases of poverty**  
UNICEF • UNDP • World Bank • WHO



## Contents

Abbreviations .....	8
Acknowledgements .....	11
Aims of the report .....	12
Foreword .....	13
Executive summary .....	14
Roadmap .....	15
Report structure .....	16
<i>PART I: CONCEPTUAL DEFINITIONS AND CHALLENGES</i> .....	16
<i>PART II: PERSPECTIVES ON IMPLEMENTATION RESEARCH</i> .....	17
<i>PART III: ROADMAP OF IMPLEMENTATION RESEARCH FOR ACCESS     AND DELIVERY – CROSS-CUTTING THEMES</i> .....	18
 INTRODUCTION .....	 21
Chapter 1: Implementation research for the control of infectious diseases of poverty .....	21
A sense of urgency .....	21
Learning from past successes and failures .....	22
Implementation research: why now? .....	24
Challenges faced by implementation research .....	25
Pay-back from implementation research .....	26
References .....	27
 <b>PART I: CONCEPTUAL DEFINITIONS AND CHALLENGES</b> .....	 28
Chapter 2: Implementation research frameworks for disease control .....	31
Definitions: Implementation and implementation research .....	31
Conceptual frameworks for implementation research .....	32
Implementation research challenges for the control of infectious diseases of poverty .....	34
References .....	36
Chapter 3: Research studies for improving access to health technologies in poor countries .....	37
What do we mean by access? .....	40
Findings .....	43
Conclusions .....	52
Chapter acknowledgements .....	52
References .....	53
Chapter 4: Bridging health systems strengthening and innovations for disease control ..	55
Case studies .....	58
Challenges of implementation research for health systems strengthening .....	61
References .....	62

<b>PART II: PERSPECTIVES ON IMPLEMENTATION RESEARCH</b>	64
<b>Chapter 5: Implementation research and product development partnerships</b>	67
Upstream implementation research	70
Research for scaling up	73
Types of PDP implementation research	74
Methodological challenges	74
Capacity building and strengthening	77
Conclusions	78
Chapter acknowledgements	78
References	79
<b>Chapter 6: Global health funders and implementation research</b>	81
Methodology to assess the landscape of implementation research among global funders	82
The implementation research agenda	82
Investing in implementation research	85
Dissemination of implementation research	86
Capacity building and strengthening for implementation research	86
Funders and implementation research governance	88
Conclusions	90
References	91
<b>Chapter 7: Implementation research and patient safety</b>	92
Challenges to patient safety interventions	94
Scope of implementation research for patient safety	95
Implementation research for patient safety in the scale-up of disease control programmes	97
Patient safety perspective in implementation research	98
Ethical issues of implementation research for patient safety	99
Conclusions	100
References	101
<b>Chapter 8: Country actors and communities for participatory implementation research</b>	102
Community barriers to adoption and scaling-up	102
Implementation research to address community barriers to adoption and scaling-up	104
Conclusions	106
References	107

<b>PART III: ROADMAP OF IMPLEMENTATION RESEARCH FOR ACCESS AND DELIVERY – CROSS-CUTTING THEMES</b>	108
<b>Chapter 9: Current and foreseeable themes in implementation research for disease control</b>	111
Implementation research focus	112
Common methods in implementation research	113
Nature of study conclusions and recommendations	115
Gaps and opportunities for implementation research	116
Guidance for the implementation research agenda	118
Conclusions	119
References	120
<b>Chapter 10: Research capacity and governance for collaboration in implementation research</b>	121
Implementation research capacity	121
Experience and models available for implementation research collaboration	126
Governance for implementation research collaboration	128
Conclusions	129
References	130
<b>Chapter 11: Uptake and use of implementation research evidence for policy-making</b>	131
Benefits of knowledge translation for implementation research	131
Knowledge translation and implementation research synergies	132
Challenges and opportunities for translating implementation research evidence	133
Capacity strengthening	136
Conclusions	138
References	139
<b>Chapter 12: Lessons, challenges and a roadmap for action on implementation research</b>	141
A. Lessons	141
B. Challenges for implementation research on access and delivery	143
C. Roadmap for Action	144
References	147
<b>Annex</b>	147

## Abbreviations

<b>3ie</b>	International Initiative for Impact Evaluations
<b>ACHEST</b>	African Center for Global Health and Social Transformation
<b>ACT</b>	artemisinin combination therapy
<b>ACU</b>	Association of Commonwealth Universities
<b>AHPSR</b>	Alliance for Health Policy and Systems Research
<b>AMFm</b>	Affordable Medicines Facility - malaria
<b>ANDI</b>	African Network for Drugs and Diagnostics Innovation
<b>APOC</b>	African Programme for Onchocerciasis Control
<b>ART</b>	antiretroviral therapy
<b>ASAQ</b>	artesunate-amodiaquine
<b>ASMQ</b>	artesunate-mefloquine
<b>CAH</b>	Child and Adolescent Health and Behaviour Programme (WHO)
<b>CAPRISA</b>	Centre for the AIDS Programme of Research in South Africa
<b>CBDOT</b>	community-based directly observed therapy
<b>CDC</b>	Centers for Disease Control and Prevention (USA)
<b>CDC-DHAP</b>	Centers for Disease Control and Prevention (USA), Division of HIV/AIDS Prevention
<b>CDC-DPDM</b>	Centers for Disease Control and Prevention (USA), Division of Parasitic Diseases and Malaria
<b>CEmOC</b>	Comprehensive Emergency Obstetric Care
<b>CHSRF</b>	Canadian Health Services Research Foundation
<b>CIDA</b>	Canadian International Development Agency
<b>CIHR</b>	Canadian Institutes of Health Research
<b>CIRCB</b>	Centre International de Référence Chantal Biya
<b>COHRE</b>	Clinical Operational and Health Services Research
<b>ComDT</b>	community-directed treatment
<b>COSTECH</b>	Tanzania Commission for Science and Technology
<b>CTC</b>	care and treatment clinic
<b>DAH</b>	development assistance for health
<b>DALY</b>	disability-adjusted life year
<b>DFID</b>	Department for International Development (UK)
<b>DGHS</b>	Directorate General of Health Services
<b>DIME</b>	Development Impact Evaluation Initiative
<b>DNDi</b>	Drugs for Neglected Diseases Initiative
<b>DOTS</b>	directly observed treatment, short course
<b>EC</b>	European Commission
<b>EDCTP</b>	European and Developing Countries Clinical Trials Partnership
<b>EOC</b>	emergency obstetric care
<b>EPI</b>	Expanded Program on Immunization
<b>ESSENCE</b>	Enhancing Support for Strengthening the Effectiveness of National Capacity Efforts
<b>EU</b>	European Union
<b>EVIPNet</b>	Evidence-Informed Policy Network
<b>FDA/CDER</b>	FDA Center for Drug Evaluation and Research



<b>FDA</b>	Food and Drug Administration (USA)
<b>FELTP</b>	Field Epidemiology and Laboratory Training Program
<b>FIND</b>	Foundation for Innovative New Diagnostics
<b>GAVI</b>	Global Alliance for Vaccines and Immunisation
<b>GHI</b>	global health initiative
<b>GHRI</b>	Global Health Research Initiative (Canada)
<b>GMP</b>	Global Malaria Programme (WHO)
<b>GSK</b>	GlaxoSmithKline
<b>HaRP</b>	Health Research Program
<b>HAT</b>	human African trypanosomiasis
<b>HIC</b>	high-income country
<b>HPV</b>	human papillomavirus
<b>HRP</b>	Special Programme of Research, Development and Research Training in Human Reproduction
<b>HRSA</b>	Health Resources and Services Administration
<b>IAVI</b>	International AIDS Vaccine Initiative
<b>IBDOT</b>	institutional-based directly observed therapy
<b>IFPMA</b>	International Federation of Pharmaceutical Manufacturers & Associations
<b>IFRC</b>	International Federation of Red Cross and Red Crescent Societies
<b>IGWG</b>	Intergovernmental Working Group on Public Health, Innovation and Intellectual Property
<b>IM</b>	intramuscular
<b>IMCI</b>	integrated management of childhood illness
<b>INDEPTH</b>	International Network for the Demographic Evaluation of Populations and Their Health in Developing Countries
<b>INESS</b>	NDEPTH Effectiveness and Safety Studies
<b>iOWH</b>	Institute for OneWorld Health
<b>IP</b>	intellectual property
<b>IPM</b>	International Partnership for Microbicides
<b>IPPPH</b>	Initiative on Public-Private Partnerships for Health
<b>ISHReCA</b>	Initiative to Strengthen Health Research Capacity in Africa
<b>ITN</b>	insecticide-treated net
<b>IVR</b>	Initiative for Vaccine Research
<b>KEMRI</b>	Kenya Medical Research Institute
<b>LMIC</b>	low-income and middle-income countries
<b>M&amp;E</b>	monitoring and evaluation
<b>MDG</b>	Millennium Development Goal
<b>MEDA</b>	Economic Development Associates, United Republic of Tanzania
<b>MEPI</b>	Medical Education Partnership Initiative
<b>MeSH</b>	medical subject heading
<b>M-Health</b>	mobile health
<b>MIEP</b>	Malaria Impact Evaluation Program
<b>MIM</b>	Multilateral Initiative on Malaria
<b>MMV</b>	Medicines for Malaria Venture
<b>MNC</b>	multinational company
<b>MoHFW</b>	Ministry of Health and Family Welfare
<b>NECT</b>	nifurtimox-eflornithine combination therapy
<b>NGO</b>	nongovernmental organization

<b>NIH</b>	National Institutes of Health (USA)
<b>NORAD</b>	Norwegian Agency for Development Cooperation
<b>NPSA</b>	National Patient Safety Agency
<b>NTD</b>	Neglected Tropical Diseases department (WHO)
<b>ODI</b>	Overseas Development Institute
<b>ORS</b>	oral rehydration salts
<b>PAHO</b>	Pan American Health Organization
<b>PATH</b>	Program for Appropriate Technology in Health
<b>PDA</b>	personal digital assistant
<b>PDP</b>	product development partnership
<b>PEPFAR</b>	The United States President's Emergency Plan for AIDS Relief
<b>PMIM</b>	paromomycin intramuscular injection
<b>PMTCT</b>	preventing mother-to-child transmission
<b>PPP</b>	public-private partnership
<b>R&amp;D</b>	research and development
<b>RAPLOA</b>	rapid assessment for <i>Loa loa</i>
<b>RBM</b>	Roll Back Malaria Partnership
<b>RDT</b>	rapid diagnostic test
<b>RDTm</b>	rapid diagnostic test for malaria
<b>RED</b>	reaching every district (strategy)
<b>REMO</b>	rapid epidemiological mapping of onchocerciasis
<b>RPC</b>	Research Policy and Cooperation
<b>SATVI</b>	South African Tuberculosis Vaccine Initiative
<b>SCI</b>	Schistosomiasis Control Initiative
<b>SEARO</b>	WHO Regional Office for South-East Asia
<b>SP</b>	sulfadoxine-pyramethamine
<b>STB</b>	Stop TB Partnership
<b>STI</b>	sexually transmitted infection
<b>SUZY</b>	Scaling Up Zinc Treatment for Young Children with Diarrhoea
<b>SWAp</b>	sector wide approach
<b>TB-DOTS</b>	tuberculosis directly observed treatment, short course
<b>TDR</b>	Special Programme for Research and Training in Tropical Diseases
<b>TPP</b>	target product profile
<b>TRAction</b>	Translating Research into Action
<b>UNAIDS</b>	Joint United Nations Programme on HIV/AIDS
<b>UNDP</b>	United Nations Development Programme
<b>UNICEF</b>	United Nations Children's Fund
<b>USAID</b>	United States Agency for International Development
<b>VCT</b>	voluntary counselling and testing
<b>VL</b>	visceral leishmaniasis
<b>VVM</b>	vaccine vial monitor
<b>WHA</b>	World Health Assembly
<b>WHO</b>	World Health Organization
<b>WRAIR</b>	Walter Reed Army Institute of Research

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This report is the result of the commitment of more than 120 people from across the globe who came together to identify the value of implementation research and the gaps in this area, share their experiences and produce this compilation of case studies, recommendations and a roadmap for action.

It began with a concept and draft chapter outlines, developed at the Special Programme for Research and Training in Tropical Diseases (TDR) by Dr Jane Kengeya-Kayondo and Mr Ivane Bochorishvili, with technical support by Dr Shenglan Tang and Dr Soumya Swaminathan. This team provided critical input and overall leadership to the project while Dr Miguel A Gonzalez Block (Centre for Health Systems Research of Mexico's National Institute of Public Health) acted as technical coordinator for the report. Its development was supported by the TDR stewardship and strategic alliances units, an in-house World Health Organization (WHO) working group, and a steering committee comprising members external to TDR (see Annex).

The concept was brought to a meeting organized in conjunction with the Ministry of Health of Uganda in Kampala, 28-30 June 2010. More than 70 researchers,

implementers, scientists and representatives from product development partnerships (PDPs) attended and provided further input and analysis. An interactive web space was created on the TropIKA.net knowledge platform\* and managed by Edith Certain to continuously share knowledge and information (such as relevant literature) and debate issues after the meeting, as well as provide support to the report coordinators and authors throughout the report development process.

Many partner organisations provided valuable contributions. Gratitude is extended to the members of this report's steering committee, who played an oversight role to the initiative, the WHO in-house working group, the participants of the consultative meeting in Kampala and other partners engaged throughout the initiative (see Annex for the list of contributors).

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\* Tropical Diseases Research to Foster Innovation and Knowledge Application (TropIKA.net) homepage: <http://www.tropika.net/>, accessed 30 September 2011.

### **Aims of the report**

This report recognizes the sense of urgency, the opportunities and challenges that implementation research has in supporting the adoption and scale-up of new tools, strategies and interventions to tackle infectious diseases of poverty. It aims to:

- focus the attention of country and global stakeholders on the value, needs, opportunities and challenges that are peculiar to implementation research;
- reflect the perspectives, needs, priorities, commitment and buy-in of important stakeholders in this area of research;
- identify a core set of tools to support this type of research and help package these into a toolkit; recommend ways of generating research tools that are currently lacking;
- present a constituency-wide roadmap and plan of action (with short-, medium- and long-term perspectives);
- contribute to a more general focus on health systems research.

## FOREWORD



Too often, millions of dollars are spent on health innovations that fail to live up to their promise. New public health interventions are often brought to disease endemic countries but issues of delivery, access and scale-up are not solved.

Implementation research is a critical tool for providing the scientific evidence necessary for improving and scaling up public health programmes around the world. The challenges faced by people living in high disease burden countries include badly functioning health systems, lack of basic infrastructure, and a paucity of health care workers. In the face of this, bringing health innovations from development to the field requires the same level of scientific rigor – testing, evaluation, and revision – that was used to devise the innovation in the first place.

The report on *Implementation research for the control of infectious diseases of poverty* is the result of collaboration led by the Special Programme for Research and Training in Tropical Diseases (TDR) in the context of the WHO Implementation Research Platform. More than 60 participants of a three day meeting held in Kampala, Uganda, co-hosted by the Ugandan Ministry of Health, and representing diverse countries, international institutions, and research centres, contributed to the report, which represents the first-ever roadmap for navigating the numerous challenges to making implementation research a standard part of global health programmes.

The report's twelve chapters address crucial, but often neglected, aspects to global health programmes, including strengthening health systems, patient safety, community-based interventions, and public-private partnerships. The report's "roadmap for action" positions implementation research as an integral component to public health interventions, a tool that can be used in advancing health systems, infrastructure, and financial constraints, improving governance and oversight, and including stakeholders as fundamental partners.

I urge public health providers, funders, and local and international partners to make use of the powerful tool of implementation research as an integral part of global health programmes in order to maximize effectiveness and provide the foundation for successful implementation and scale-up of these crucial health services.

Dr Marie-Paule Kieny  
Assistant Director-General  
Innovation, Information, Evidence and Research  
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## EXECUTIVE SUMMARY

This report shows through reviews and numerous case studies how implementation research (IR) can improve access to treatments, diagnostics, vaccines, strategies and interventions in low and middle income countries. It explains how it can be used to strengthen health systems, improve patient safety, expand community-based interventions and local implementation capacity, and improve the outcomes of public-private partnerships and global health initiatives.

The 43 authors, who come from low, middle and high income countries, review cross-cutting methods, capacity strengthening and governance challenges. They find that communities of learning, political support and interdisciplinary frameworks are all still to be established, while implementation research-specific methods need to be mapped in relation to product development, adoption and scale-up. Attaining such strategic goals is critical if investment in implementation research is to be increased.

### **Main findings on lessons learned include:**

- Implementation research has much to offer if mainstreamed in the research and development (R&D) process
- Partnerships are critical
- Health systems can be strengthened with the support of implementation research
- Organization and effective communication of IR is needed
- Capacity can be greatly improved

### **Challenges identified are:**

- Conceptual boundaries should be clarified if further support is to be mobilized
- Setting the R&D agenda and priorities should have a broad, participative focus
- Political support is critical for implementation research

A “roadmap for action” on how to better use this research field completes the report.

# ROADMAP FOR ACTION

The following five goals are proposed as a roadmap for further discussions and action.

## **1. Advocate for the use of implementation research to:**

- a. address health system constraints that may thwart or delay the adoption and delivery of new tools, strategies and interventions for disease control;
- b. make new disease control tools affordable and increase investments through public–private collaborations;
- c. strengthen patient safety and other cross-cutting health system strategies so as to improve service quality and to facilitate the scaling-up of disease control interventions.

## **2. Involve stakeholders in implementation research to:**

- a. evaluate options for scaling-up innovative tools, strategies and interventions;
- b. participate in equitable collaboration in priority setting, decision-making and resource allocation;
- c. integrate implementation research into intervention programmes so that policies are based on evidence and programmes can withstand organizational and political change.

## **3. Ensure that governance and investments for implementation research:**

- a. develop the implementation research knowledge base;
- b. stimulate institutional capacity building;
- c. strengthen training and establish career paths for young researchers;
- d. provide incentives for innovation at global, national and local levels.

**4. Call on ethics committees** to provide guidance and support for implementation research.

**5. Develop leadership** for implementation research as part of efforts to strengthen health systems.

# REPORT STRUCTURE

## INTRODUCTION

### Chapter 1:

#### **Implementation research for the control of infectious diseases of poverty**

The aim of the report is outlined, along with current challenges, lessons and best practices from the past, highlighting the value of research and the sense of urgency to move forward.

## PART I: CONCEPTUAL DEFINITIONS AND CHALLENGES

Challenges and opportunities that new products and strategies face for access and delivery in the global health context are outlined, with an explanation of the role of implementation research in addressing these challenges.

### Chapter 2:

#### **Implementation research frameworks for disease control**

Implementation research seeks to understand programme effectiveness in specific contexts, taking into consideration the diversity within health systems and across social and economic situations. This chapter reviews a range of definitions for implementation research, with a deeper look at: “What is happening in the design, implementation, administration, operation, services and outcomes of social programmes?” and “In which ways can the social programme be made to work better?”

### Chapter 3:

#### **Research studies for promoting access to health technologies in poor countries**

Access to interventions is here understood to be the result of four simultaneous and converging sets of activities: availability, affordability, adoption and architecture. Several implementation research studies are identified that can help inform access plans so that obstacles to the implementation of innovative tools, strategies and interventions for diseases of poverty are surmounted.

### Chapter 4:

#### **Bridging health systems strengthening and innovations for disease control**

Many disease control programmes are implemented through separate, vertical mechanisms that eschew the complexity or weakness of the underlying health system. These may further complicate or weaken underlying health systems, unless the disease is rapidly brought under control or affects populations that are otherwise unreachable. Systems thinking is proposed to address the complexity of the relationship between health systems and disease control programmes.



## PART II: PERSPECTIVES ON IMPLEMENTATION RESEARCH

This section addresses the perspectives of the product development partnerships (PDPs), global donors, national actors and specific initiatives that use implementation research. Access and delivery needs, initiatives, concepts and methods are described from the perspective of actors working at different stages in the development of innovative products, strategies and interventions. The conceptualization of access and delivery, and the roles given to research priority setting, funding, production and the dissemination of research results, are discussed.

### Chapter 5:

#### **Implementation research and product development partnerships (PDPs)**

PDPs represent a promising new approach to mobilize health research funding and to channel it towards the rapid development of innovative tools and interventions. As PDPs begin to bring health technologies to market, a coordinated set of activities is needed to ensure that the products developed will ultimately have an equitable health impact. Implementation research can support R&D governance to face the difficult issues of establishing innovation goals, including the strengthening of R&D capacity at country level as a means of assuring innovation ownership and adoption.

### Chapter 6:

#### **Global health donors and implementation research**

Global health initiatives are bringing much needed financial support to disease control; however, new actors are also increasing health sector complexity. A rapid global donor survey confirms broad interest to support implementation research, but also uncovers a bewildering array of definitions, where this implementation research is often confused with economic and impact evaluation as well as with operational research. This lack of precision is leading some agencies to misclassify diverse forms of research investments, with the risk of erroneously concluding that there is no pressing need to increase investments for implementation research. Nonetheless, donors are considering a wide range of options to fund research and research capacity strengthening that will undoubtedly help make their health development investments more effective and sustainable.

### Chapter 7:

#### **Implementation research and patient safety**

A framework is provided for how the implementation research can help maintain the safety of interventions during scaling-up. It also looks at how such implementation research can help scale-up cross-cutting patient safety programmes. Pharmacovigilance – a research-based, continuous monitoring of the adverse effects of drugs under real programme conditions – is an important component of implementation research. In this way, health and social system factors that allow improper or illegal use, misuse and abuse of drugs and other tools can be brought within the realm of research.

**Chapter 8:****Country actors and communities in participatory implementation research**

Increasingly, local government and nongovernment actors are being placed in charge of addressing important barriers to implementation that are leading to inadequate programme targeting and dilution of benefits to the end-users that most need them. National policy-makers, health authorities in decentralized settings and providers in the public and private sectors can apply implementation research methods to understand how best to adopt and adapt existing and innovative tools, strategies and interventions. Programme managers, community leaders and front-line health workers are critical beneficiaries as well as participants of implementation research.

**PART III: ROADMAP OF IMPLEMENTATION RESEARCH FOR ACCESS  
AND DELIVERY – CROSS-CUTTING THEMES**

This section of the report reviews current progress in implementation research as well as patterns of collaboration. Capacity strengthening and governance recommendations are made, and efforts and models to support use of research evidence are also addressed. It promotes state-of-the-art implementation research on access and delivery across the innovation value chain to provide a real-life roadmap for research development.

**Chapter 9:****Current and foreseeable implementation research for access and delivery**

Implementation research literature is growing, with a total of 237 papers published since 2005 on the control of diseases of poverty in developing countries. Predominant health topics are maternal and child health, HIV/AIDS and malaria, with 63% of papers covering these subjects. A wide range of methods have been used for implementation research, although quantitative studies predominate. Clinical trials have in some cases included qualitative implementation studies. Although much of the literature is descriptive, reporting on studies that lack the scale and scope necessary to influence policy and orientation, a broad range of recommendations have been identified. There is a clear need to strengthen methods and to invest in more rigorous studies at a scale that is commensurate with programme implementation at a population level.

**Chapter 10:****Research capacity strengthening and governance for collaboration in implementation research**

Implementation research capacity is reviewed via participation and collaborations across institutions and countries in the published literature. Developing country institutions are in the minority in implementation research, with their authors responsible for only 31% of papers. Furthermore, concentration is high among rich countries, with 41% of papers authored by researchers in the United States of America (USA) or the United Kingdom of Great Britain and Northern Ireland (United Kingdom). While most of the literature is published by academic and research institutions, multilateral agencies and PDPs are becoming important players, attesting to the applied nature of implementation research. A slight majority of papers are coauthored across two or more institutions, yet over half of the papers include only authors from developed countries. There is clearly ample room to strengthen collaboration between developing countries and between developed and developing countries. Models to govern collaboration are also identified to support the transfer of responsibilities for (as well as the benefits of) implementation research to developing countries.

**Chapter 11:****Implementation research uptake and use for policy-making**

Several proven strategies to support the transfer of implementation research results into policy-making are provided to help meet the standards that are increasingly expected from other research fields and from medical practice.

**Chapter 12:****Implementation research uptake and use for policy-making**

This concluding chapter draws from earlier chapters to highlight lessons and identifies the main challenges faced by implementation research. The chapter ends with a proposed roadmap to rally support for implementation research.



# INTRODUCTION

## Chapter 1: Implementation research for the control of infectious diseases of poverty

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Jane Kengeya-Kayondo,  
David Molyneux and Samuel Okware

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*“Money plus technology is 5 percent of the solution; the other 95 percent is delivery and implementation.”<sup>1</sup>*

*“Too often, investments worth many millions of dollars are made in the absence of good data, and too often we fail to learn from and share our experience...”<sup>2</sup>*

### A sense of urgency

Many lives could be saved if tools, strategies and interventions *already available* for disease control in poor countries and settings were fully implemented and if barriers preventing adoption and scale-up were broken down.

In the meantime, new tools, strategies and interventions continue to be developed – but face those same barriers; seemingly insurmountable political, socioeconomic, technological and legal challenges loom in the horizon, and there is a constant threat of resource, environmental and process bottlenecks.

Political commitment for the control of diseases of poverty has now increased and substantial financial resources are now being invested in various disease control strategies – ranging from technological innovation to health systems strengthening and scaling-up of intervention use. In this context, evidence on how tools, strategies and interventions work in different settings is urgently needed, and there is also a pressing need to improve methods to obtain such knowledge.

Implementation research is increasingly being recognized as one of the most important interfaces between the availability of tools, strategies and interventions and their use within health systems and control programmes.

Implementation research provides evidence on the best ways to support the adoption of, and optimize use of innovations. It holds promise for scale-up and for greater commitment and investment. The ability to test diverse implementation pathways and to identify what works in real country and poor community settings, through different types and at different levels of health systems, is critical to disease control. This would improve both the quality and the equity impact of health services and disease control strategies, and so contribute to effective strengthening of health systems.

There are two main areas in the life-cycle of innovations where implementation research can play a role: adoption and scaling-up.

Global donors and channels of financial assistance, governments and health systems at country level have to adopt innovations through policy and regulatory decisions. *Implementation research can help this adoption process by identifying the best ways to obtain support as well as by producing evidence for policy-making.*

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1 William Easterly, 4 Ways To Spend \$60 Billion Wisely, Washington Post, 2 July 2006.

2 Michel Kazatchkine. Executive Director of the Global Fund to Fight AIDS, Tuberculosis and Malaria at the opening plenary of the XVII International AIDS Conference, Mexico City, August 2008.

However, it is at the scaling-up stage where implementation research has been most widely understood and accepted. At this stage, *implementation research is about solving problems when making these new tools, strategies and interventions available to national health systems in “real life” conditions.*

### **Learning from past successes and failures**

There have been notable successes and failures in the way that the global community and control programmes have used implementation research to introduce, and scale-up use of, new and improved tools, strategies and interventions. The cases of malaria and onchocerciasis control are illustrative of where implementation research has played a positive role (see Box 1.1 and Box 1.2).

#### **BOX 1.1.**

#### **Implementation research and malaria**

Malaria is rampant in many countries. Its control or regional elimination requires multiple and changing strategies – from strategies for vector control to strategies for early diagnosis and curative medical care (at both individual and population levels). The introduction of new tools to support specific strategies has to address costs and benefits in the broad context of control and elimination.



Following large-scale trials into the use of insecticide-treated nets (ITNs) in the early 1980s, a global momentum through the Roll Back Malaria Partnership (RBM) aimed to substantially increase bednet use – particularly by those most vulnerable to malaria: pregnant women and children in sub-Saharan Africa. Avenues had to be identified to scale-up ITN availability and use. Attention also had to be given to address the possibility of resistance to pyrethroid insecticides, which represented a real threat to the future effectiveness of ITNs.

The most recent achievement in malaria chemotherapy has been the universal adoption of artemisinin-combination therapy

(ACT) to replace chloroquine and sulfadoxine-pyramethamine (SP) treatment of falciparum malaria. Adoption of the new treatment has been accelerated through World Health Organization (WHO)-supported regulatory changes at country-level, while massive financing by The Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) has helped scale-up product availability at health centre level. The use of a combination therapy and its implementation through a well financed and regulated process (which ensures its universal adoption) represent in themselves innovative strategies to scale-up control while delaying the onset of resistance to antimalarials. Implementation research has provided the evidence for the introduction and scale-up of ACT use in falciparum malaria endemic countries.

The importance of early diagnosis of malaria is fundamental for effective therapy and case management. Rapid diagnostic tests (RDTs) can reduce misdiagnosis, improve appropriate prescribing, reduce costs to patients and limit the onset of resistance arising through the misuse of antimalarials. However, RDTs come at a substantial financial cost and require the health system to be reshaped in a way that may have consequences for other programmes and sectors. Developing a sustainable way of introducing, financing and rolling out RDTs to remote settings has thus become a core item on the implementation research agenda. The implementation research model used for RDT scale-up can also help determine how other tools can be deployed within constraints of production, supply chain issues, logistics, health worker training, and affordability.

### BOX 1.2. Implementation research and onchocerciasis



The control of onchocerciasis in West Africa began with the Onchocerciasis Control Programme in 1974. Initially, the strategy focused on vector control through applying ecologically

acceptable organophosphate pesticides on a weekly basis to the breeding sites of *Simulium* (black fly) larvae. However, some cytospecies of *Simulium* developed resistance to these pesticides, leading to intensive applied research for new ecologically acceptable products.

From 1988 the pesticide approach was combined with treatment of *Onchocerca volvulus* infections at the community level with ivermectin, made available through an innovative donation programme by Merck & Co., Inc. Today the African Programme for Onchocerciasis Control (APOC) aims for mass delivery of ivermectin through community-directed treatment (ComDT), an innovative disease control strategy to ensure that a treatment-based control programme can be sustainable. Implementation research has supported this programme in various ways, including:

- helping evaluate potential clinical side-effects of ivermectin when used under field conditions;
- supporting development of the ComDT approach for onchocerciasis as well as for other health interventions (Homeida et al., 2002);
- supporting the development of rapid epidemiological mapping of onchocerciasis (REMO) and rapid assessment for *Loa loa* (RAPLOA) to prevent adverse events from ivermectin treatment where both diseases are prevalent (Gardon et al., 1997).



## Implementation research: why now?

The timing for a specific focus on implementation research in general and particularly for the adoption of new and improved tools, strategies and interventions is right for several reasons.

First, there are rich and promising product pipelines for vaccines, drugs and diagnostics resulting from investments made by foundations, pharmaceutical companies and others over the past decade. Adoption and scale-up of innovative interventions from such rich product pipelines requires systematic and evidence-based policy formulation. This is especially important in disease endemic countries.

Second, resources for adoption and scale-up of tools, strategies and interventions are becoming available through various global health initiatives such as the Global Fund, the Global Alliance for Vaccines and Immunisation (GAVI), UNITAID and others. National governments are also investing significantly in service provision. Evidence on the effectiveness of these resources in achieving scale-up is now more important than ever.

Third, there is a heightened global focus on health systems research – with researchers, policy-makers, funders and other stakeholders working together to share evidence, identify knowledge gaps, and set a research agenda with priorities that reflect the common needs of low- and middle-income countries. With a focus on universal health coverage and a drive towards science to accelerate universal coverage, critical issues related to health systems research are being analysed – including challenges in the development and application of robust research methods. A global agenda for health systems research is evolving and implementation research fills a special niche in this research agenda.

Important recommendations have also been recently formulated to address the lack of methodical and evidence-based approaches

for adoption and scale-up. The following can be highlighted:

- The Global Ministerial Forum on Research for Health in Bamako, Mali in 2008 called for pragmatic and effective use of potential innovative tools (Global Ministerial Forum on Research for Health, 2008).
- The Intergovernmental Working Group on Public Health, Innovation and Intellectual Property (IGWG) formed in 2008 in order to: tackle the issue of improving access to health products by poor populations; recommend strategies to foster innovation, build capacity and improve access to health products in order to achieve better health outcomes in developing countries (World Health Assembly resolution WHA61.21 in 2008).
- The Bill & Melinda Gates Foundation, various PDPs, nongovernmental organizations (NGOs) and other donors have recently constituted an ad hoc Access Group to focus on access issues.
- The INDEPTH Effectiveness and Safety Studies (INESS)<sup>3</sup> of antimalarials in Africa has become a platform to assess the effectiveness and safety of new malaria treatments, determine the factors that influence effectiveness and safety and develop a comprehensive pharmacovigilance system in the context of African health systems.<sup>4</sup>
- The William A. Haseltine Foundation for Medical Sciences and the Arts and its partners have formed the ACCESS Health Initiative (based in India) to address issues of access to high quality affordable health in low-, middle- and high-income countries.

3 INESS: <http://www.indepth-network.org/iness/>, accessed 30 September 2011.

4 INESS projects: [http://www.indepth-network.org/iness/index.php?option=com\\_content&view=article&id=134&Itemid=143](http://www.indepth-network.org/iness/index.php?option=com_content&view=article&id=134&Itemid=143), accessed 30 September 2011.



## Challenges faced by implementation research

Implementation research for adoption and scale-up is potentially attractive for researchers, product development organizations, academic institutions, donors and implementers of health programmes. But, when compared to product development, implementation research faces a number of challenges.

Presentation of a well defined portfolio of products at different stages of the pre-clinical and clinical research process is straightforward in product development. Research methodologies and standards – such as for clinical trials – are well defined and have a common meaning for everyone engaged the development process. Decision points and criteria are well accepted, appropriate skills are clear, ethical standards are recognized and the criteria for research centres are well characterized. An international register of clinical trials also allows transparency and accountability. These important attributes are lacking in implementation research.

There are additional challenges for implementation research. It requires a broad, systemic (and therefore interdisciplinary) approach, it cuts across public and private sectors, and it needs researchers from biomedical, pharmaceutical, social science, public health and health economics sectors to all work together. These researchers must take into account the local context of the health system, advocate for political commitment and most importantly must be driven by the needs of health-care providers, control programme implementers and policy-makers. It is critical to identify these contextual conditions and build them into the research process. On top of this, implementation research has to address ever more complex innovation processes at national, regional and global levels.

Yet another challenge for implementation research is the need to establish learning communities or “communities of practice” to aid effective communication – so that all stakeholders in implementation research can share what is learnt on the ground, know what obstacles are being encountered, and learn about resources that are available and the way in which these resources are being innovatively applied. The importance of effective communication and knowledge management cannot be overemphasized; in countries and settings with enormous knowledge gaps but with opportunities for innovation these represent a particular challenge.

Political advocacy and commitment at all levels is also critical for implementation research. Many access and delivery issues that hinder adoption and scale-up are not viewed as problematic by policy-makers – for example, the special needs of indigenous and vulnerable groups are often not addressed. Without political commitment, support from opinion leaders, and the buy-in of practitioners and others on the ground, implementation research will remain inadequate and ineffectual.

The engagement of ministries of finance is also crucial. Furthermore, health policy-makers should learn from other disciplines and fields, for example from engineering, communications, and energy distribution – often the constraints to access and delivery are not specific to health interventions; other sectors have long standing experience in how to adapt new tools to the users. Advocacy for political and grassroots support needs to extend beyond the public health sector to include the engagement of the private sector of all types.

The capacity of health systems to provide the required support to disease control programmes and to ensure the introduction of new and improved tools, strategies and interventions is a critical challenge. Human resource failures that occur while introducing new disease control tools can lead to important set-backs in adoption and scale-up. Lack of flexibility to shift from one strategy to another – for example from malaria control to elimination – can also lead to lost opportunities to improve health. A lack of capacity to adopt and integrate innovations can lead to vertical implementation and unnecessary competition across programmes. Efforts to improve the capacity of health systems and particularly to ensure quality and flexibility at point-of-care are therefore a key challenge to implementation research. Evidence-based strategies to improve quality of health care can benefit from research on the best way to introduce and scale-up the delivery and use of innovations (e.g. through training, motivating and retaining health-care workers at all levels).

The context in which health systems are set represents important challenges and opportunities for the adoption and scale-up of disease control innovations. Public–private collaboration and the harnessing of market forces is a case in point. Even in poor settings, business approaches based on franchising and other models are being implemented and show promise in empowering women and providing access to services to otherwise marginalized groups. Community insurance schemes and subsidy mechanisms can play an important role in scaling-up disease control innovations, and implementation research can provide much needed information on their potential use.

## **Pay-back from implementation research**

There is strong justification for improved coordination across stakeholders, stronger partnerships with health systems, better oversight, improved definitions, standardized methodologies, and shared targets and indicators. There is also a need for increased opportunities for cross learning and transparency, and a need to recognize the importance at national level of dialogue between different sectors. Experience, particularly within the water and sanitation field, shows that greatest impact (e.g. for water purification) can be made using different systems from different sectors.

This report, although heavily oriented towards communicable diseases and the health systems of poor nations, has broader implications. The benefits of properly conducted implementation research for adoption and scale-up, its power to bridge the “know-do gap” (by minimizing the delay between the availability or formulation of new tools, strategies and interventions and their full utility) and its immediate relevance for meeting health targets and closing the inequity gap are all benefits that are relevant to both *communicable* and *noncommunicable* diseases and for all types of health systems.

The value of implementation research for improved health outcomes is increasingly apparent.



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# PART I

## CONCEPTUAL DEFINITIONS AND CHALLENGES





## Chapter 2: Implementation research frameworks for disease control

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Kate Ramsey and  
Lynn Freedman

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Limited uptake of research findings and innovations in real-world settings has led to mounting interest in implementation research for public health. Many of those concerned with the health of poor people – particularly in the field of infectious disease control in developing country settings – have voiced alarm that while new technologies are being sought to combat disease, several effective tools remain “on the shelf” or, at best, partially implemented. Furthermore, there is concern in many countries that even when policies, tools and strategies have been formally adopted, they are only partially implemented, or used ineffectively (Plsek & Greenhalgh, 2001; de Savigny & Adam, 2008). This has raised a call for more systematic and scientifically supported approaches to planning and conducting implementation of new disease control tools, strategies and interventions at scale.

Although implementation research in the field of public health is fairly recent, the concept has historical roots going back to mid-twentieth century political science. For instance, the challenge of ensuring effective implementation of policies underlying social programmes was identified by political scientists in the 1970s in the USA (Pressman and Wildavsky, 1973). Several other fields, such as management science and engineering, consider implementation factors that are fundamental to health and even have findings useful for public health.

The pathway to current thinking on implementation research for public health began some thirty years ago and builds on a variety of research disciplines, including

translational research and systems science (Greenhalgh et al., 2004). Subsequently, a plethora of terminologies and conceptual frameworks have evolved – particularly in the past 10 years.

This chapter aims to provide an introduction to implementation research terminology and conceptual frameworks and give preliminary guidance on how they might be used for implementation research on access and delivery of new tools, strategies and interventions to fight diseases of poverty.

### Definitions: Implementation and implementation research

**Implementation** involves evidence-supported, systematic and planned efforts within a system (or organization) to institutionalize an intervention and to ensure its intended effects and impacts; it has been defined as the “constellation of processes intended to get an intervention into use within an organization” (Rabin et al., 2008). A variety of terms are used to describe the aims of implementation processes, including: uptake, integration, embedding, adoption, routinization, institutionalization and assimilation.

**Implementation research**, most simply described, asks: “What is happening in the design, implementation, administration, operation, services and outcomes of social programmes? Is it what is expected or desired? And why is it happening as it is?” (Werner, 2005). In contrast to other types of health research, implementation research focuses on “how?” and “why?” rather than “what?” Implementation research does not isolate the effects from the context – rather it focuses precisely on the interaction between the intervention and the context, thus distinguishing itself from clinical trials and impact evaluations (Allotey et al., 2008). Implementation research is usually considered a subset of health systems research that looks at how various functions (such as financing or governance)

affect the scaling-up uptake of innovations. Although related to operations research, implementation research differs in that it aims to produce “generalizable knowledge that can be applied across settings and contexts” (Madon et al., 2007).

Other definitions of implementation research note that it should be interdisciplinary; study influence on individual and organizational behaviours (Eccles & Mittman, 2006); develop practicable solutions to implementation problems (TDR, 2008); and recognize the complexity of health systems (Sanders & Haines, 2006).

While traditional implementation research focused on the roll-out of policies after they were formulated by legislative or other levels of government, today there is great interest in using implementation research to influence the actual *formulation* of policies. This means that information from research based on implementation approaches used in other countries or settings could be used to formulate policies and, through modelling and systems-thinking, could be used to analyse potential policy implementation and impact.

The globalization of policy design and technology development, as well as the increased funding of specific disease control programmes, has led to greater complexity in policy formulation and programme implementation processes. Stakeholders at the global level involved in the design and advocacy of innovative disease control tools, strategies and interventions will perceive their adoption by national government and by nongovernment agencies as part of the implementation process. Policy analysis at national level (e.g. to forecast the potential demand for innovative tools) can therefore be perceived as part of the arsenal of implementation research methods to ensure adoption, rather than solely as a tool to support policy formulation. Analysis of the readiness of a system to adopt an innovation may need to precede the policy formulation – it is here that potential challenges to implementation can be identified and addressed.

The relationship between implementation research, monitoring and evaluation, and impact research is still under debate.<sup>1</sup>

Implementation research’s relationship to the traditional research chain from laboratory bench to bedside also remains an area of discussion, although implementation research has been associated with formative research (before implementation), prospective research (that accompanies implementation) and retrospective review or evaluation (after implementation).

There is still no consensus on the methods that define implementation research, although there is general agreement that implementation research should draw from multiple disciplines including public health, political science, sociology, epidemiology, and health economics.

### Conceptual frameworks for implementation research

Several conceptual frameworks have been proposed to generate theory-driven research questions. These are mainly directed to the key factors that affect the implementation of interventions – broadly asking why implementation succeeds or fails.

The frameworks emerge mainly from two traditions. The first focuses on adoption of *innovations* (i.e. new tools, strategies and interventions); the second focuses on improving effectiveness and quality of *existing* health programmes and services.

Nearly all of the proposed conceptual frameworks have been developed recently; most have been designed for and applied in North American and European settings. But conceptual frameworks also need validation for diverse developing country settings, as implementation research usually focuses on challenges associated with changing the

<sup>1</sup> See <http://www.tropika.net/svc/specials/bamako2008/session-reports/monitoring-evaluation>, accessed 30 September 2011.



practice of health professionals based there. Frameworks also need to be applicable to other types of interventions, such as health systems and community-based interventions.

Implementation fidelity is a fundamental concept that appears almost universally in frameworks related to implementation research. Fidelity denotes the consistency and quality of the intervention's implementation, i.e. whether the intervention was implemented as intended (Klein & Speer Sorra, 1996; Carroll et al., 2007). If an intervention is not implemented as intended, the effect of the intervention is likely to be reduced. Yet interventions must adapt to the health system in which they are introduced (while concomitantly the health system adjusts to the intervention). Implementation research therefore has parallel interests: (a) to look at the extent of fidelity in the

implementation of core elements of an intervention and (b) to look at which aspects need to be dispensable or flexible to allow for contextual adaptation (Greenhalgh et al., 2004; Damschroder et al., 2009).

Two published reviews have attempted to bring together the multitude of concepts into one framework. The first review, by Greenhalgh et al. (2004) draws not only from health literature, but also management, organizational and systems science literature.

Subsequently, Damschroder et al. (2009) reviewed additional frameworks – leading to a meta-theoretical framework called the “Consolidated Framework for Implementation Research.” This framework encompasses many underlying concepts classified by the authors into five major domains as follows:

1

**The intervention:** The characteristics of the intervention determine whether it will be adopted or “fit” in the health system. Here the term intervention includes the core components of the intervention plus what is described as the “adjustable periphery,” whereby the intervention can be adapted to local needs. The characteristics of core components, such as complexity, cost and evidence strength, will play a crucial role.

2

**Outer setting:** The outer setting includes the economic, political, and social context in which implementation occurs, but is external to the organization or the institution conducting the implementation. It is influenced by external policy and incentives, such as global funding streams, as well by peer pressure between organizations.

3

**Inner setting:** The inner setting refers to the context within the organization or institution that is implementing the intervention. It includes the structure of the organization, culture and networks in the organization, and the organization's climate and readiness for change.

4

**Individuals involved:** These individuals are those who have a role in the implementation process. They include health-care providers, but would also include managers in different parts of the organization, policy-makers and many other stakeholders and beneficiaries. In addition to the traditional concerns regarding their capacity to implement, their perception of the intervention plays an important role in their commitment to its implementation.

5

**Process for implementation:** The process includes all of the methods used in facilitating adoption of the intervention at all levels of the organization, such as the planning of strategies and activities. Processes include those both explicitly planned as well as those that emerge unpredictably during implementation.

The above are not discrete components of the implementation research framework, but interact in ways that are complex and not yet fully understood. For instance, the dynamic and mutual relationship between individual and organizational behaviour needs further research. In addition, the line between the inner and outer setting is not solid, as individuals in the organization often support external social and cultural values in ways that influence the inner, organizational setting. The boundaries of a national health system are also important. Traditionally, focus has been on the public sector (i.e. government-owned facilities and structures) but this focus increasingly incorporates the private sector and communities. Health system boundaries may therefore need to shift according to the intervention. For instance, one intervention's implementation might require engagement of private pharmacies, while another's might require engagement of the transport sector.

### Implementation research challenges for the control of infectious diseases of poverty

Implementation research in wealthy countries is largely devoted to analysing the reasons why implementation of a proven intervention succeeds or fails *within a stable health system*. Typically, this occurs once the intervention has been defined through a rigorous and transparent policy process; also, evidence (through approval and regulatory processes) usually plays an important role for its adoption (Feldstein & Glasgow, 2008).

The context in which implementation research for diseases of poverty is set makes such research more challenging. The control of diseases of poverty – particularly of neglected infectious diseases – in developing countries is often set in weak health systems which may lack the capacity (a) to clearly articulate or achieve consensus for the full range of coordinated policies and (b) to implement programmes and innovations through national

efforts within predictable time periods and for the attainment of specific goals. Disease control is frequently implemented in a context where evidence-informed policies are not fully explicit at the national level, where global actors exert undue influence and where, during implementation, no clear linkages exist between policy-makers, local health authorities, providers and communities on the ground. Often the formal health systems in these settings are bureaucratic and hierarchical, driven by guidelines rather than learning processes, with limited space for innovation and participation from actors at lower levels of the system. There may also be multiple (and rapidly changing) national and global actors influencing all stages of policy formulation and programme implementation, with poor coordination and collaboration among them. In such settings innovations and existing technologies may also be implemented in competition, with rival leadership and insufficient resources.

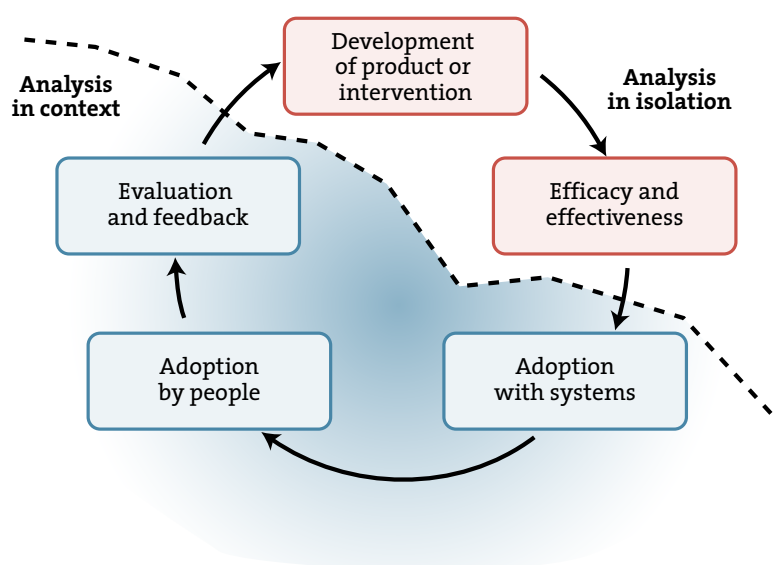
Such weaknesses in health systems and in the capacity to make use of research evidence make implementation research more complex, requiring both investment and coordination. The implementation research agenda therefore needs to be driven by those with a clear understanding of context and of the realities “on the ground” (Whitworth et al., 2010). Countries implementing disease control interventions are therefore the greatest source of expertise to drive this agenda. In such contexts, implementation research should widen countries' research focus to address the gap between the efficacy and effectiveness of innovations for disease control (as evidenced in the international literature) and implementation on the ground (Fig. 2.1). Within this scope, national policy formulation will come under the lens of implementation research, asking why governments have not taken advantage of proven interventions that have been successfully implemented in comparable settings. In this situation, implementation research may help to understand why existing or innovative tools, strategies and interventions are not implemented – is it because of failures

in the design of the intervention's core characteristics, or because of the context or actors that are influencing implementation?

Implementation research for innovative tools, strategies and interventions for diseases of poverty in developing countries and poor communities requires an assessment of how such innovations actually strengthen or weaken health systems (see chapters 4 and 8). Also, as there is a high degree of dependency between health systems and social and political actors, implementation research has to pay close attention to the effects of the outer setting. Given weaknesses in policy formulation and lack of a clear boundary between policy formulation and implementation, implementation research has to take a step back to ask: "What disease control options are selected?" "Why these are selected?" and "How are they adopted in different settings?" This may imply the need to analyse (a) the evidence base behind tools, strategies and intervention, (b) the characteristics of the boundary between policy and practice, and (c) how such characteristics influence implementation.

It has often been assumed that the level and rigour of available evidence is sufficient to drive implementation of innovations – but there is also a need to focus on the characteristics of the implementation methods and the context, as more fully elaborated in the above framework. Change must be planned not as a linear process, but through an analysis of complexity and the establishment of probabilistic scenarios of which those in charge of implementation should be aware (Kitson et al., 1998; de Savigny & Adam, 2008).

Given current levels of investment, it is critical to identify a strategy that can incrementally build implementation research capacity by focusing on critical aspects of research that can in turn yield immediate benefit to both implementation by health authorities and to research teams and institutions so as to improve health. This implies a continuous effort to identify the strengths and weaknesses of different implementation research approaches and to strengthen the implementation research community at national, regional and global levels.



**Fig. 2.1.** The cycle of applied and implementation research

Implementation research focuses on the interaction between the innovations and their social and health system contexts.

Source: Allotey et al., 2008.

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## Chapter 3: Research studies for improving access to health technologies in poor countries

Michael R Reich and Laura J Frost

Many people in developing countries lack access to health technologies, even basic ones. These technologies include life-saving medicines (such as antiretrovirals for HIV/AIDS) as well as medicines that are marketed mostly for their life-enhancing benefits (such as medications that help control arthritis and its associated symptoms). Limited access is also a problem in relation to many other health technologies, such as vaccines that can prevent debilitating diseases, preventive technologies such as insecticide-treated bednets, diagnostics for infectious and chronic diseases, and various kinds of contraceptives.

In 1999 the World Health Organization (WHO) estimated that since the mid-1980s around 1.7 billion people – approximately one third of the world's population at the time – did not have regular access to essential medicines and vaccines. The estimate from WHO was based on a questionnaire survey of national experts in pharmaceutical policy<sup>2</sup>. Ideally, more accurate population-level data should be used to identify access to medicines for specific groups within countries, yet such information is not readily available (WHO, 1988; WHO, 2004).

In recent years, the issue of access to medicines and other health technologies has risen on the global policy agenda. The most contentious debates about inadequate access

in poor countries have focused on drugs and vaccines, but similar problems exist for other health technologies. Access to diagnostics, for example, has been relatively unexplored in policy debates, while the focus on certain types of access barriers (especially pricing and patents) has tended to obscure the fact that there are also other important obstacles to access, such as problems with distribution, delivery, and adoption.

As the basis for creating a more comprehensive view of access to health innovations, we recently analysed the histories of six health technologies (see Box 3.1; Frost & Reich, 2008):

1. the drug praziquantel (used to treat schistosomiasis, a disease caused by parasitic worms)
2. the hepatitis B vaccine
3. a subdermal implant contraceptive
4. malaria rapid diagnostic tests (RDTs)
5. vaccine vial monitors (VVMs)
6. the female condom.

Four criteria guided our selection of case studies. We chose cases that together:

- cover different types of health technologies
- relate to a range of health problems
- span different phases of access, and
- have been successful as well as cases that have encountered obstacles and faltered.

Our approach in these case studies drew from anthropological research that traces the “life-cycles” or “biographies” of medicines from production to end-user (Van der Geest et al., 1996; Whyte et al., 2002; Whyte et al., 2004) and from public health case study research on barriers to technology access (Sevane et al., 2005).

For each case study, we analysed the social, economic, political, and cultural processes that shaped access to the health technology in developing countries. We followed the technology's flow through different phases

2 The WHO survey in 1999 asked national experts “to estimate the percentage of the population who have access to a minimum list of 20 essential medicines, which are continuously available and affordable at a health facility or medicines outlet, within one hour's walk from the patients' home.” For more information, see <http://www.who.int/medicinedocs/en/d/Js6160e/9.html>, accessed 30 September 2011.



### Box 3.1. Access case studies<sup>1</sup>

#### *Access to a medicine: praziquantel*



Praziquantel is the drug of choice for treatment of schistosomiasis, an infectious disease caused by parasitic worms (schistosomes) that live in the blood vessels of the human host.

Praziquantel became generally available on the international market in the 1980s but during the 1980s and 1990s access in most schistosomiasis-endemic countries was limited. The key access barrier was the drug's affordability. In 2002 the Schistosomiasis Control Initiative (SCI) was established with US\$ 27.8 million funding from the Bill & Melinda Gates Foundation to tackle the disease. SCI significantly increased access to praziquantel in Africa through a series of strategies related to procurement, collaboration, information, registration, local formulation, and donation. From 2003 to June 2008, SCI delivered a total of over 40 million treatments in six countries in Africa, to nearly 20 million individuals. However, although this accomplishment represents a significant success for SCI, the effort has reached only about 10% of the population estimated to be infected with schistosomiasis and needing praziquantel treatment. Future access to praziquantel will depend on many factors, including the evolving market for the product, the actions of key players, the availability of international aid funding, and the perceptions of national ministries of health regarding both the disease and its treatment.

#### *Access to a vaccine: hepatitis B vaccine*

Hepatitis B is a serious liver infection caused by the hepatitis B virus. The first hepatitis B vaccine became available in 1981, making it possible to prevent hepatitis B virus infection. Introduction in developing countries in the 1980s and 1990s was slow and limited due to problems in affordability (high product price) and product adoption (safety concerns about plasma vaccines and a limited understanding about the hepatitis B burden). By 1995, only 35 of 90 countries with prevalence rates greater than or equal to 8% had begun hepatitis B vaccination programmes. Key groups – including WHO, the International Task Force on Hepatitis B Immunization, and later the Global Alliance for Vaccines and Immunisation (GAVI) – then undertook a series of actions to overcome access barriers. Their strategies included fostering competition, showing companies that a market existed in developing countries, forecasting demand across countries, and financing the procurement of hepatitis B vaccine for developing countries. The combined efforts led to a change in the global architecture for hepatitis B vaccine access, resulting in dramatic increases in access to the vaccine in the 2000s. As of June 2004, 82% of GAVI Fund-eligible countries with adequate delivery systems had introduced the vaccine into their routine systems (61 countries). Current challenges include (a) addressing low coverage levels in many countries and (b) ensuring continued future access to the vaccine.

#### *Access to a diagnostic: malaria rapid diagnostic tests*

An estimated 40% of the world's population today is at risk of malaria infection. A major challenge for malaria treatment is the prompt and correct diagnosis of malaria infection. Rapid diagnostic tests for malaria (RDTs) – antigen-detecting tests based on immunochromatographic methods – offer a new diagnostic alternative for health professionals. The first RDTs for malaria became commercially available in the mid-1990s. In the early 2000s, the use of RDTs increased rapidly – fuelled by increased

<sup>1</sup> A full description of each case study can be found in Frost LJ, Reich MR. *Access: how do good health technologies get to poor people in poor countries?* Cambridge, MA, Harvard University Press, 2008.

funding through the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund). At the same time, the total number of products available for diagnostic use rose quickly. WHO estimates that procurement nearly doubled between 2000 and 2004. The number of countries adopting RDT use and budgeting for RDTs in malaria control activities rose from one country (in 2000) to 32 countries (in 2005). In this period of rapid uptake, three RDT-associated challenges emerged: (a) varying performance of RDT products in field use, (b) a confusing range of products on the market, and (c) limited acceptance of results by health workers and patients (e.g. so that they prescribe or take medicines in spite of a negative result due to a lack of trust in the new technology, or simply continuing with clinical habits). In early 2002, a “global focal point” for malaria RDTs was established at WHO in its Western Pacific Regional Office in Manila. This group used three strategies to address barriers to access for RDTs: policy development, information dissemination and quality assurance. Whether the use of RDTs leads to a decrease in malaria mortality and morbidity ultimately depends on what happens in the periphery of health systems in poor countries – whether end-users can obtain RDTs, how test results are used in patient management decisions, and on the availability and appropriate use of antimalarial medication.

#### ***Access to a subdermal impact contraceptive:***

The Norplant® system is a reversible subdermal implant contraceptive that can prevent pregnancy for up to five years with an efficacy rate of over 99.9%. The implant system consists of six capsules containing synthetic progestin levonorgestrel that are inserted into a woman’s upper arm and release the hormones on a continual basis. The NGO Population Council began developing Norplant® in the 1960s and negotiated patent and licensing arrangements to make a low-priced product available in developing countries in the early 1980s. Norplant® was repeatedly shown to have high

safety, efficacy, and effectiveness in clinical trials and post-marketing surveillance, but still encountered numerous access problems within developed and developing countries, including: (1) affordability, (2) adoption by end-users, and (3) removal services by providers. The relative importance of these barriers depended on the particular setting. Problems with provider removal services ultimately led to the product’s withdrawal in the USA in 2002. Nevertheless, millions of women around the world became Norplant® users. By the end of 1992, 24 countries had granted regulatory approval to Norplant®; by mid-1997, that number reached 58. As of 2002, an estimated 10.5 million units had been distributed worldwide.

#### ***Access to a device: vaccine vial monitors***

The vaccine vial monitor (VVM) is a miniaturized time–temperature technology that allows health workers to assess heat damage to vaccines, and thus helps to reduce vaccine wastage and assure coverage in hard-to-reach areas. WHO and the Programme for Appropriate Technologies in Health (PATH) began the search for a VVM in 1979 and provided critical assistance in product development and market entry to a small firm, Temptime Corporation (based in New Jersey). A suitable product was ready for introduction in 1991. Introduction of the vaccine vial monitor label on the oral polio vaccine began in 1996 (PATH, 2005) and, five years later, the use of the device was scaled-up so that it was used on all vaccines of the WHO Expanded Program on Immunization (EPI). Between 1996 and 2007, Temptime’s sales of VVMs for oral polio vaccine rose more than threefold to nearly 200 million vials per year; for other EPI vaccines, sales rose from nothing to over 100 million vials per year. By the end of 2005, close to 100% of WHO-prequalified vaccine producers used the technology. Successful access to VVMs depended crucially on assuring the availability of high-quality products designed for different

**continue >>**

kinds of vaccines and the adoption and use of VVMs by global vaccine producers. However, although VVM success has occurred for UNICEF-supplied vaccines this is not the case for two other important developing country vaccine markets – vaccines provided by the Pan American Health Organization (PAHO) and those sold by domestic manufacturers within developing countries.

***Access to a dual protection technology: female condoms***

In 2006, nearly 40 million adults were estimated to be living with HIV infection worldwide; almost half of these were women. As of mid-2006, the only female-initiated HIV prevention method on the market with proven efficacy in preventing both pregnancy and sexually transmitted infections has been the female condom. The female condom – designed and produced by the Female Health Company – was first introduced in 1992 and has been launched in almost 100 countries worldwide. While the technology generated high levels of initial enthusiasm, adoption by end-users, providers, and national governments has remained low. By 2004, approximately 12.2 million units were sold per year, representing only 0.1–0.2% of the number of male condoms sold worldwide. Access barriers include: (a) limited affordability due to high product price, (b) low end-user adoption due to technical characteristics and the politics of sexual relations, (c) lack of provider adoption due to limited training and support to promote the female condom and problems in availability, (d) insufficient global consensus about the need for the technology and its relationship to other family planning and HIV prevention technologies, and (e) inadequate architecture and access planning. In a renewed effort to increase access to female condoms, product advocates and donors are attempting to increase affordability through the development of new, cheaper products; expand adoption for the technology through training and promotion; and build a new global architecture including strategic planning for access.

of access, identified barriers, and looked for measures that enhanced access.

Our analysis of the case studies pointed to seven major findings. These have important implications for the global health initiatives currently engaged in developing innovative health products for control of the diseases of poverty, as well as for initiatives striving to improve access to existing interventions. The findings (discussed in more detail later) highlight the importance of using implementation research early in the development process of a product or intervention. By helping to anticipate implementation barriers, implementation research can support the design of an “access plan” that can help improve access to innovations for those who need it.

This chapter presents lessons about barriers to access and describes some of the strategies that both product developers and champions can use to overcome them. It also outlines 13 kinds of implementation research studies that can help with the development of access plans for the implementation of innovative tools, strategies and interventions for diseases of poverty, and discusses implications of each.

## **What do we mean by access?**

Stated simply, *access* refers to the ability of people to obtain and use tools, strategies or interventions; for this study we are concerned with access as the ability to obtain good quality health technologies and interventions when and where they are needed and in ways that contribute to positive health impact.

Access is not just a *technical issue* involving the logistics of transporting a technology from the manufacturer to the end-user, or of regulating, managing, and training health-care providers on how to apply an innovative health intervention. Access is also affected by *social values, economic interests, and political processes*. Access requires products, strategies



and services and will depend on how health systems perform in practice.

In this chapter we think of access to new technologies, strategies and interventions (which we call “health innovations”) not as a single event but as a continuous process involving a series of activities and actors over time.

#### **Access framework:**

The framework presented in this chapter provides a more complex understanding of access than the conventional model of a linear “value chain” based on, for example, the stages of discovery, development, and delivery (IBM Institute for Business Value, 2004). Our approach builds on previous research on barriers to access (Aday & Andersen, 1974; Hanson et al., 2003), and adapts the approach developed by the Global Alliance for TB Drug Development.<sup>3</sup>

In this chapter we have changed some terms and added some ideas to our original analysis (Frost & Reich, 2008) to improve both clarity and comprehensiveness. Our conception of *access* to innovative technologies and interventions is based on four “As”: **architecture**, **availability**, **affordability**, and **adoption** (see Fig. 3.1). These four As for access are activity streams that occur simultaneously.

**Architecture:** Our framework explicitly recognizes architecture – i.e. the organizational dimension influencing access to health innovations. This activity stream involves making decisions about organizational structure so that the other three activity streams are coordinated and access is achieved.

**Availability:** The second stream concerns the availability of health innovations. This includes the activities of manufacturing, forecasting, procurement, distribution, and

delivery to ensure a reliable and regular supply of the innovation, as well as the activities of regulation, management, and training to ensure effective delivery of innovations.

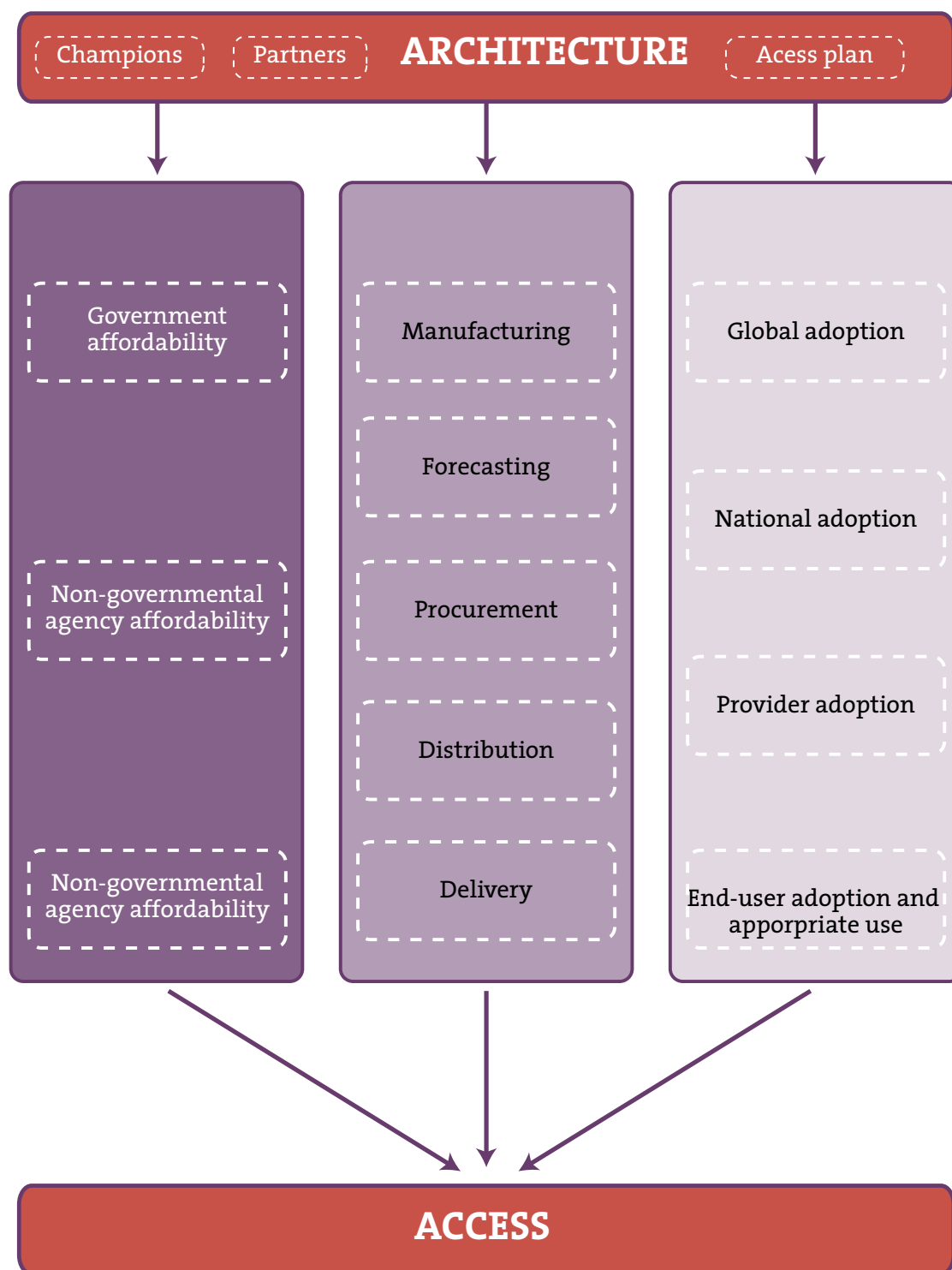
**Affordability:** The third stream concerns the affordability of innovations for developing-country governments, nongovernmental agencies, and individual end-users. This includes activities ensuring that health innovations and related services are not too costly for the people who need them.

**Adoption:** The final stream involves the adoption of health innovations. This involves activities at the global, national, district, and community levels to ensure acceptance of the health innovation, with a view to generating demand.

Our framework uses a comprehensive approach to access, mapping activities from the global level to the end-user. The framework breaks down the process of creating access into several activities, which are defined by specific events and which must occur if access is to result in health benefits.

In the framework, we view access as beginning in the development stage and concluding when end-users (including both health-care providers and patients) are using the innovation appropriately. Importantly, we have extended our view of access beyond simply physically *reaching* the end-user – we recognize that how people use the technology or intervention plays a major role in the ultimate health outcomes produced. Thus, our concept of access also includes ideas about both appropriate and inappropriate *use* of technologies and interventions.

3 See <http://www.tballiance.org/access/our-commitment.php>, accessed 30 September 2011.



**Fig. 3.1. The Access Framework**

The architecture of implementation underpins the affordability, availability and adoption of innovations to ensure widespread population access to them.

Source: Frost & Reich, 2008.

## Findings

Our research shows that getting the four activity streams right can result in successful access to health technologies. But doing so is not easy. Based on the case histories, we reached seven findings about creating access to health technologies. While our research was based on case histories of products, we believe that the findings can be extended to other health interventions and other “soft” technologies such as decision-making algorithms or health intervention packages. The findings point to 13 applied research studies that are needed to design a comprehensive access plan (these are discussed later and summarized in Box 3.2).

### **Finding 1: Developing access for a safe and effective technology requires an access plan based on both a problem statement analysis and a target product profile.**

Showing that a new technology is safe and efficacious in clinical trials represents an exciting and important result. Working through the regulatory process to license the new technology also constitutes significant progress. But these measures cannot be viewed as endpoints; they are only midway successes in the complicated process of creating access.

The case of the contraceptive implant Norplant® nicely illustrates this point, as shown in Box 3.1, where diverse avoidable problems led to the withdrawal of a highly effective contraceptive in the USA in 2002. This observation challenges the view held by some product developers that “if we make a good product that addresses an important health problem in developing countries, it will be used”. Products do not “fly off the shelf” by themselves – especially technologies aimed at improving health conditions in poor countries as these products do not fit a conventional market-

driven model. Many hurdles exist between the development of a new technology and its actual diffusion and appropriate use in developing countries (Juma et al., 2001).

It is clear that products need to be managed throughout the access process so that multiple hurdles along the pathway to the end-user can be overcome. But there are difficulties. On the one hand, some technology developers do not know or understand the markets in developing countries, do not have existing organizational bases in those markets, and do not know how to enter those markets. On the other hand, developing-country governments often lack the financial capacity to purchase new technologies; they also lack adequate purchasing mechanisms to push down prices and are unable to assure quality. For these and other reasons, creating access for good health technologies requires concerted efforts.

Two research-based analyses can help construct the foundation for access planning: the problem statement analysis and the target product profile (TPP).

An access plan begins with **problem statement research (Research Study 1)**. Problem statement research (which includes relevant epidemiological data) demonstrates a public health need for a product and provides an assessment of problems in developing effective products (both scientific and market problems). This research should include an assessment of potential access barriers posed by government, market, and NGO failures. It should also include an evaluation of whether the product has commercial market potential and if so, in which markets and under what conditions. General guidelines on how to conduct a problem statement analysis for policy-makers can be adapted for different health technologies and interventions (Lavis et al., 2009).

The access plan should also include an assessment of the basic characteristics of the product under development, the **TPP (Research Study 2)**. These characteristics can include potential health impact, target population, mechanism of action, indications and usage, route of administration, dosage schedule, efficacy, safety, clinical

pharmacology, price, product presentation, and storage. The TPP guides the product development process and, as a living document that is updated regularly, provides core data needed to plan access.

A good access plan allows champions to reshape their analysis and strategies when

### **Box 3.2.**

#### **Research studies for creating an access plan**

The following list of 13 research studies provide information and analysis needed for creating an access plan for a health technology. Although designed for health technologies the list can be adapted to studies that would help develop an access plan for “soft” technologies and health interventions.

#### **Architecture**

##### **1. Problem analysis**

This research study examines the public health need for a product (including epidemiological data) and assesses the scientific and market problems in developing an effective product. This includes an assessment of access barriers and an evaluation of whether a product has commercial market potential, and if so, in which markets and under what conditions.

##### **2. Target product profile**

This study describes the technical characteristics of the product under development. These characteristics include health impact, indications and usage, target population, mechanism, route of administration, dosage schedule, efficacy, safety, clinical pharmacology, price, product presentation and storage.

##### **3. Partnership analysis**

This study evaluates different potential partners and their roles. It also examines the structural and organizational challenges to coordinating partners. Managing the architecture often requires aligning the different interests and values of key stakeholders.

##### **4. Political analysis**

This study conducts stakeholder analysis and designs political strategies to manage partners and to create expert consensus and set the policy agenda in international technical agencies.

#### **Adoption:**

##### **5. Product acceptability study**

The information gathered in this study is particularly important in designing products that meet the needs and desires of the target population (including both end-users and providers).

##### **6. Communications and branding study**

This study is important for designing messages and brands targeted to end-users and providers.

unexpected circumstances arise and as the broader context evolves. The example of the female condom shows what can happen when there is no access plan. Although “next steps” for access were identified in global meetings between interested individuals and organizations promoting the female condom during the introduction

stage, these steps were not prioritized or written into a plan. As a result, they were never systematically implemented, meaning that advocates had no clear guide for advancing access efforts.

### **Affordability:**

#### **7. Cost analysis**

This study examines the different costs involved in manufacturing, distribution, social marketing, and other components of access.

#### **8. Willingness-to-pay analysis**

This study assesses the capacity and willingness of end-users to use their own money (out-of-pocket) to purchase the product.

#### **9. Financial sources analysis**

This study identifies and examines potential donors who could provide funding to assure access for the product and related services.

### **Availability:**

#### **10. Market forecasting**

This study estimates the potential market, as part of efforts to persuade manufacturers to produce the product.

#### **11. Regulatory analysis**

This study identifies national procedures and standards, as well as the requirements of international agencies, to assure registration and financial support, and to meet both national and international quality standards.

#### **12. Production analysis**

This study assesses quality and cost issues in manufacturing, and ways to improve the efficiency and safety of production processes.

### **Health systems:**

#### **13. Health system analysis**

This study identifies health system functions that are needed to assure that effective access is produced for specific health technologies. The diagnostic process in the book *Getting Health Reform Right*<sup>1</sup> provides one method for assessing health system barriers and designing interventions to assure access.

1 Roberts et al. (2004). *Getting Health Reform Right*. A guide to improving performance and equity. New York, NY, Oxford University Press.

## **Finding 2: Creating access depends on effective product advocacy by a product champion.**

Product champions in global health are people or organizations that believe in new technologies and are committed to helping develop products that will have wide access in poor countries and settings. The product champion's role can range from stimulating awareness of the technology among specific groups to more strategic activities that aim to overcome specific product development or access barriers.

Product champions also play a major role in constructing and managing the architecture of access, especially the relationships among different organizations. Product champions and their partners can use an access plan to frame their activities, map the position and power of diverse actors, identify obstacles and opportunities, and prepare concrete strategies to promote access.

Product champions are found in many types of organizations working in global health (including technical agencies, non-profit organizations, academic institutions, and manufacturers).

- For Norplant®, Population Council staff developed the product, introduced it, and acted as product champion.
- In the case of VVMs, staff from the Program for Appropriate Technology in Health (PATH) collaborated closely with WHO staff to ensure the introduction and scale-up of the technology on all Expanded Program on Immunization (EPI) vaccines.
- The main product champion for the female condom has been the manufacturer – the Female Health Company – and its foundation.

PATH proved to be an effective product champion in guiding the development of VVMs (miniature time–temperature indicators printed onto the label of a vaccine

vial that aim to reduce vaccine wastage) - see Box 3.1. Representatives from PATH visited the developer (Temptime Corporation) in 1989, at a critical point during product development when, after months of failing to achieve technical success, the corporation had decided to give up on the project. PATH staff explained the global significance of VVMs and convinced Temptime to continue its work – without additional funding but with PATH's assistance (PATH, 2005). For example, Temptime, needed help from PATH to enter the global health market (a market in which Temptime had no experience), to negotiate with international agencies, and to redesign its product for end-users. PATH staff members continued to guide the access process for VVMs (showing the value of collaboration) and provided crucial support to WHO staff (coordinating VVM access efforts) through mentoring, technical assistance, and project documentation. By the end of 2005, close to 100% of WHO-prequalified vaccine producers used VVM technology on their vaccine labels. However, major challenges still remain – e.g. in expanding VVM access in the Pan American Health Organization (PAHO) region and in vaccine markets in developing countries (Frost & Reich, 2008).

Product champions often work with actors that hold widely divergent views about new health technologies. In the case of VVMs, the technology was viewed by WHO staff and health workers as key to improving the cold chain (the process of keeping a vaccine at a safely cold temperature throughout production and transportation) and decreasing vaccine wastage. However, VVMs were a problem for the United Nations Children's Fund's (UNICEF's) supply division, as VVMs challenged UNICEF's policy on sole suppliers and created stress in already established relationships with vaccine producers. For vaccine producers, attaching VVMs to their vaccines sold to UNICEF meant several legal, logistical, and commercial challenges to their business. The VVM case demonstrates how advocating



VVMs required a concerted effort – and a significant amount of time – to bring these diverse groups together and address their different perspectives on the technology.

For effective product advocacy, product champions and their partners (sometimes with the assistance of external consultants) need to develop an access plan that frames the activities of champions and partners and takes into account the perspectives of different actors. This will allow an assessment of potential barriers and opportunities at the global and national levels and identify strategies to navigate and shape the complex terrain of access. It is also important to note that funding is key to the effectiveness of product champions.

Managing the access architecture often requires that product champions work to align the different interests and values of key stakeholders. One research tool that can help construct and manage the access architecture is **partnership analysis (Research Study 3)**. This type of analysis can address the problem of how to organize the diverse partners involved in creating access. Partnership analysis evaluates different potential partners and their roles, and evaluates potential structures to coordinate partners. **Political analysis (Research Study 4)**, which involves analysing political strategies, can also support development of the access plan. One effective tool for conducting such analysis and for managing partners is the free software program known as PolicyMaker (Reich & Cooper 2009).

**Finding 3: Product champions need to create expert consensus about their health technology in international technical agencies and global health policy communities.**

Our case studies highlight the importance of creating “expert consensus” on a new technology, within both the international

health technical agencies and the broader international public health community. The importance of expert consensus is also emphasized by other public health analysts (Levine et al., 2004).

As one of their first tasks, product champions need to design strategies for producing expert consensus. The key question for this is: “Whose agreement needs to be gained in constructing consensus at the global level?” The answer differs by technology – but for most technologies, approval by the relevant international technical agency and other bodies (e.g. by WHO expert groups) is required. Agencies signal their backing for adoption with official decisions about the technology and the related disease or health condition.

One good example of expert consensus is Resolution 54.16 adopted at the World Health Assembly in May 2001 on the treatment for schistosomiasis and soil-transmitted helminths (intestinal worms that include ascaris and hookworm). This recognized “...that repeated chemotherapy with safe, single-dose, affordable drugs at regular intervals ensures that levels of infection are kept below those associated with morbidity, and improves health and development, especially of children”. The Resolution thus helped promote new efforts to make praziquantel (the drug used to treat schistosomiasis) more widely available in Africa (World Health Assembly resolution WHA54.16 in 2001). Another example is the case of Norplant®, where WHO conducted a technical evaluation that stated that the contraceptive was “particularly advantageous to women who wish an extended period of contraceptive protection” (WHO meeting signatories, 1985).

These official announcements by an international agency, however, are not simply the result of technical consultations and decisions. They often depend on highly political negotiations among actors with different interests in the technology.

Product champions would be helped in these negotiations by identifying key stakeholders and designing explicit political strategies for managing them. The political analysis (Research Study 4) can also help to produce expert consensus in support of the technology (Reich, 2002). In addition, the results from the problem statement analysis (Research Study 1) and TPP (Research Study 2) can be used by product champions to identify strategies for mobilizing support from both international agencies and technical experts.

**Finding 4: End-user adoption of a technology is an essential but often overlooked component of the entire process of creating access.**

Adoption of a technology by the end-user is vital to ensuring access – whether the end-user is a patient, a consumer, or a provider. Adoption by end-users is influenced by the characteristics of the technology and the health problem it addresses, as well as by social, political, and historical contexts.

The female condom demonstrates how a technology's characteristics can make adoption difficult for end-users in some contexts. Developers of the first generation of female condoms did not adequately take into account the perspective of end-users. Some women, for example, considered the female condom to be extremely large and bulky, aesthetically unappealing, prone to slippage and twisting during sexual intercourse, and stiff in its internal rings (The AIDSCAP Women's Initiative, 1997). Such negative impressions can be addressed and the chances of long-term use can be increased through extended and supportive counselling by providers (Telles Dias et al., 2006). Some women, however, do not have access to counselling, while others are unwilling to endure a series of awkward "practice sessions" to get use of the female condom "right." Sales of the female condom have remained low since its introduction in the early 1990s. By 2004, approximately

12.2 million units were sold per year, representing only 0.1–0.2% of the number of male condoms sold worldwide (The Female Health Company, 2005). New female condom designs in development are seeking to address the adoption issues of end-users by changing these negative technology characteristics, making female condoms more user-friendly, and using less expensive material to make the technology more affordable.

Our case studies show that paying attention to adoption by end-users must begin early in the life of a new technology. This attention starts during product development, when technical characteristics of a new technology are first under consideration. It continues in field trials and pilot projects, when end-user views of a new technology can be assessed and addressed through technical changes. Attention to end-users is also important in later phases, when managing the perceptions of the technology is central to creating access. These efforts require an understanding of end-user preferences and concerns and of the context in which end-users interpret new technologies.

Research studies are essential in helping product developers understand problems from the perspective of end-users. Such research can include market surveys and focus groups, as part of **product acceptability studies (Research Study 5)**. The information gathered in these studies is particularly important if products are to be designed so that they meet the needs and wishes of the target population (including both end-users and providers).

**Communications and branding studies (Research Study 6)** are also important for tailoring messages and brands targeted to end-users and providers. These studies provide the basis for the development of social marketing campaigns to promote adoption of the technology. Branding studies can help develop the public image for innovative technologies – they ensure that communities and practitioners readily



identify such technologies as trustworthy and effective tools for meeting “felt” needs, even in the most difficult of circumstances.

**Finding 5: The cost of health technologies and related services is a key barrier to access; strategies to expand access must address affordability.**

The literature on access highlights cost to governments and individuals as a major obstacle to access and use of innovations; our findings support this.

Decreasing the cost of products for governments can involve a range of strategies. For instance, the Schistosomiasis Control Initiative (SCI) used a bulk purchasing approach to lower the price of praziquantel; it also expanded competition by assisting manufacturers with registration and stimulating local formulation in Africa. By increasing the number of registered suppliers in Burkina Faso, for example, SCI helped to create a more competitive bidding process for government purchases, reducing the price per praziquantel tablet from US\$ 0.14 to US\$ 0.09 (Frost & Reich, 2008). Other strategies to address government affordability are tiered pricing and threats of compulsory licensing (Reich & Bery, 2005).

Another measure used to address the issue of high cost is to obtain external funding for government procurement. For example, the Bill & Melinda Gates Foundation supports SCI to finance praziquantel purchases for the six African countries that SCI works with. The biggest problem with such an external financing approach concerns its sustainability over the medium- and long-term, as donors usually wish to limit the timeframe of their funding commitments.

Research on several topics is important to address affordability barriers. One topic is product cost. **Cost analysis (Research Study 7)** can be undertaken to study the

different costs involved in manufacture, distribution, social marketing, and other components of access.

A second topic is end-users’ willingness to pay for products. **Willingness-to-pay analysis (Research Study 8)** assesses the capacity and willingness of end-users to use their own money (out-of-pocket) to purchase the product. (It is worth noting, however, that what people say they are willing to pay does not always translate into reality, particularly for new products.)

A third topic that addresses affordability is financing. **Financial sources analysis (Research Study 9)** looks at the different potential donors who could provide funding to assure access to the product and related services.

Although affordability is essential, our case studies show that making a technology more affordable is rarely sufficient on its own to create access for the product. Availability constraints as well as factors related to adoption and architecture all also need to be considered and addressed.

**Finding 6: Supply-side strategies (that ensure availability) are needed to help expand access to health technologies in developing countries.**

Two supply-side strategies are of particular importance to assure availability. The first relates to information failures. Suppliers often lack good or complete information about product demand in developing countries. These information problems affect supply, since manufacturers may underestimate the potential market in a poor country or region and may not take the necessary steps to enter the market (such as registering the product with relevant governments). Strategies to address these problems include disseminating information to manufacturers about demand and assisting manufacturing

companies in product registration. The Global Health Forecasting Working Group, convened in 2006 by the Washington-based Center for Global Development, provides recommendations to the global health community for improving demand forecasting. The proposals include the establishment of an “infomediary” that would allow product demand to substantially increase and would allow coordinated sharing of information among manufacturers and global health partners (Center for Global Development Global Health Forecasting Working Group, 2007). Another information barrier is that government procurement agencies in poor countries often have incomplete information about the availability and quality of products and suppliers for a particular health technology. For example, although many government procurement agencies have financing from the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) to procure malaria RDTs, they confront a rapidly changing range of available products and suppliers, making the purchase of diagnostics extremely difficult. One simple strategy that WHO has used to address this problem is to give countries regularly updated information about rapid diagnostic products and suppliers on its web site<sup>4</sup> and in a “Sources and Prices” document for malaria products (WHO et al., 2004). Reducing information asymmetries, by regularly disseminating updated information both to producers and to potential purchasers, can contribute to increased availability.

A second important supply-side strategy relates to the difficulty of finding commercial partners willing to develop or manufacture a technology for use in poor countries. Such challenges are a major access barrier, particularly for lower-profit technologies (relative to, for instance, drugs and vaccines for sale in rich countries). Our study found that suitable private partners for low-profit technologies may be located among small to midsize companies that have existing

commercial products, are already generating revenues from these products, and have experience in working with regulatory authorities such as the Food and Drug Administration (USA) (FDA). This finding concurs with a 2005 study on neglected disease drug development that urged policy-makers to target research and development (R&D) commercial incentives to smaller companies that have a good chance of becoming engaged with neglected disease markets (Moran, 2005).

One example of a technology that was produced by a small to midsize company is that of a malaria RDT that was initially developed by the research arm of the Walter Reed Army Institute of Research (WRAIR). When looking for a commercial partner to manufacture the test, the institute needed a company that could take its product through the FDA regulatory process. However the institute encountered many barriers that significantly set back its timeline. It learned that most diagnostic companies are small “mom-and-pop” businesses that do not possess the resources, know-how, experience, or willingness to navigate the FDA process. It also discovered that large companies that did have these features were not interested in becoming a partner because the technologies were not profitable enough for them. After years of seeking a partner, WRAIR eventually found a midsize company – Binax, Inc. – to take on the task.

Product developers and champions therefore need to expand their search for manufacturing partners to small and midsize companies willing to take on niche products. They also need to consider high-quality manufacturing firms in emerging markets (such as China and India). However, although several groups have found good manufacturing partners in these countries (as shown by the success of the SCI in working with praziquantel producers in both China and India), the challenges of finding good partners in such markets should not be underestimated, especially given the difficult

4 Malaria - Rapid Diagnostics Tests: <http://www.wpro.who.int/sites/rdt>, accessed 30 September, 2011.

regulatory environments in those countries (for example, see article New York Times article by Yardley & Barboza, 2008)<sup>5</sup>.

Several research studies can provide the empirical basis for market forecasting and can help identify the most promising partners for manufacturing and market introduction.

**Market forecasting (Research Study 10)** is needed to estimate the potential market, as part of efforts to persuade manufacturers that a sufficiently large market exists to produce the product. **Regulatory analysis (Research Study 11)** identifies national procedures and standards, as well as the requirements of international agencies, to assure registration and to meet quality standards. **Production analysis (Research Study 12)** assesses quality and cost issues in manufacturing, and also assesses the efficiency and safety of production processes.

**Finding 7: Limited health infrastructure in many developing countries impedes technology access, making it important to invest in health system strengthening to ensure sustained access.**

The successful delivery of technologies to patients and consumers depends in large part on the capacity of the health sector's human resources, network of public and private providers, and availability of functioning equipment – in short, how the health system performs on a daily basis (Roberts et al., 2004). Different technologies, however, may depend on improvements in the performance of different aspects of the health system.

Health system strengthening is especially important for new technologies (which often require new systems and skills); it is

also necessary for products that will be used in areas with limited health infrastructure – such as in poor countries, and in disadvantaged areas (both urban and rural) in middle-income countries.

The Norplant® case study demonstrates how a failure to invest in health systems can lead to impeded access. Norplant® requires both insertion and removal by a trained health-care provider. In the rapid scale-up of Norplant® use in countries such as Indonesia and the USA, many health-care providers received detailed training on insertion, but not much instruction on removal. As a result, many women who accepted this contraceptive implant confronted problems when they asked for removal because health-care providers were not well trained on the technical or social aspects of removal.

Overall, our study shows that strategies for health system strengthening are product and context specific, but they all require sufficient funding, attention, and time if they are to adequately address health system barriers and if access is to be produced and sustained. Research studies on **health systems analysis (Research Study 13)** can help identify health system functions<sup>6</sup> that are needed to assure that effective access is produced for specific health technologies.

5 *Despite Warnings, China's Regulators Failed to Stop Tainted Milk*: <http://www.nytimes.com/2008/09/27/world/asia/27milk.html?ref=melamine>, accessed 30 September 2011.

6 The diagnostic process in the book *Getting Health Reform Right* (Roberts et al., 2004) provides one method for assessing health system barriers and designing interventions to assure access.

## Conclusions

Access to health technologies and interventions in poor countries is hindered by multiple obstacles. Inadequate access is rarely a single-failure problem; access problems typically result from a combination of failures, including market, government and NGO failures. These failures often affect all four dimensions of access – architecture, availability, affordability, and adoption – although the patterns differ by specific technology.

Addressing the multiple failures requires many steps directed at global-level, national-level and local-level actors and depends on various kinds of expertise. Creating access requires that individuals and organizations devote time, passion, and resources to the particular objectives and that they craft strategies for addressing the multiple barriers along the path to access.

Some developers and champions without prior field experience may not fully appreciate the kinds of research that are necessary to develop an access plan and how the plan must be updated throughout the stages of product development, launch, and scale-up. In this chapter we have identified 13 specific research

studies that provide the basis for planning for access and lay the foundation for an effective access plan. While our research cases focused on “hard technology,” the research framework can also be applied to “soft” technologies related to strengthening health programmes and systems.

Organizations with existing products and prior market experience may have the expertise and capacity to undertake these research studies, but even they are not always successful at assuring access to new products. Product development partnerships are now grappling with the complexity of developing a strong evidence base for creating access for the products they are developing.

These research studies can assist the process of designing an access plan and can thus help ensure that safe and effective health innovations reach the hands of people in poor countries who need them most. Other chapters in this report provide additional lessons on the types of strategies and policies that will promote widespread access for products and interventions in low- and middle-income countries.

## Chapter acknowledgements

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## Chapter 4: Bridging health systems strengthening and innovations for disease control

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Health systems in infectious disease endemic countries are notoriously weak. Today, due to the involvement of new players, increased financial resources, novel strategies and innovative technologies, there are unprecedented opportunities for implementation research to contribute to health systems strengthening. The main challenge, however, is how to take advantage of these opportunities so that they can help achieve the United Nations Millennium Development Goals (MDGs) and strengthen health systems.

Although worldwide health indicators are generally improving, weak health systems and uneven global financing and support may lead to fragmentation of policies and programmes, unnecessary complexity, and avoidable inefficiencies that slow down progress in tackling disease. The impact of health investments are certainly improving (though more slowly than expected), but health disparities are increasing (WHO Maximising Positive Synergies Collaborative Group et al., 2009). The challenge of managing health systems strengthening has never been greater for the stewards of health systems in developing countries.

In this chapter we highlight key issues in bridging the complementary efforts in health systems strengthening and in supporting access to innovative tools, strategies and interventions for disease control innovations in poor countries and settings. The key message is that health systems strengthening should create the environment in which disease control innovations can thrive.

Disease control innovations that are fostered by global initiatives and national governments (with the rich array of resources that accompany them) should also facilitate health systems strengthening. Through this reciprocal relationship new investments will be able to have a horizontal impact in strengthening the system-wide building blocks of financing, human resources, information systems, technology, health delivery and stewardship (WHO, 2007). This requires that health system stewards, policy-makers, research funders, researchers and industry have common avenues for dialogue and analysis, so leading to greater communication and trust.

This chapter suggests how implementation research that focuses on “hard” technologies (e.g. drugs, treatment regimens or diagnostics), strategies (e.g. integrated management of childhood illness, IMCI; or community-directed fever management), public health interventions (e.g. insecticide-treated nets, ITNs) and health system interventions (e.g. pay-for-performance schemes) can contribute to reciprocal understanding and trust between health systems stewards and disease control programmes. Health systems (and their subsystems) need to be adaptive and able to respond to inputs, not only in predictable (and desirable) ways but also in unpredictable ways (de Savigny & Adam, 2008). For example, the distribution of free ITNs to pregnant women through antenatal clinics in Kenya led to a predictable increase of use of regular services at antenatal clinics; in the United Republic of Tanzania, unpredictably, it also increased the uptake of ITNs in antenatal clinics in the *private* sector (Guyatt et al., 2002; personal communication, MEDA). This illustrates how introducing a new disease control innovation can affect the entire health system and its related subsystems.

The implementation of innovations in disease control efforts therefore requires a systems approach in intervention design,

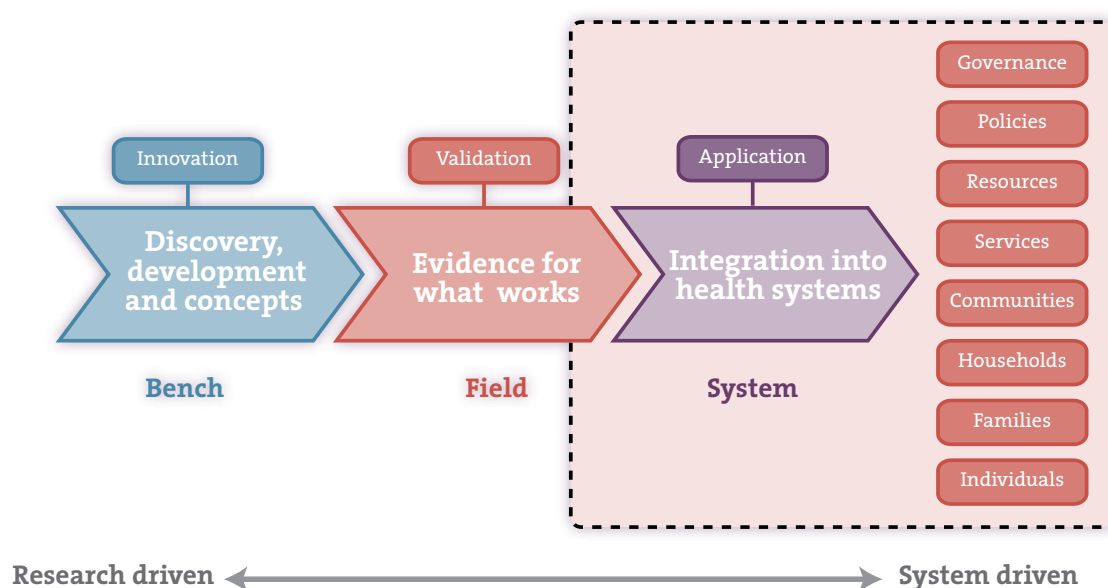


implementation planning and delivery, and continuous system-wide monitoring and quality assurance. System-level bottlenecks as well as programme-specific bottlenecks have to be identified to ensure foresight and careful consideration of potential implications (both positive and negative) across all health system building blocks and subsystems (see Box 4.1 for an illustration of this in relation to malaria control).

Complex interventions such as the scaling-up of antiretroviral (ART) for HIV/AIDS can be expected to have more profound effects on health system components such as financing and human resources than relatively simpler interventions such as adding an additional vaccine or ITN distribution to existing programmes (Noor et al., 2007) – particularly in weaker health systems. The relationship between an intervention and the health system highlights the importance of carefully analysing the health systems’

capacities and responses to change at all stages of the intervention’s R&D pathway through implementation research – from the early, researcher-driven innovation phase to the system-driven application phase of scaling-up, system integration and evaluation (Fig. 4.1).

This chapter reflects on the readiness of the health system to engage with infectious disease control innovations. Case illustrations are used to examine the interplay between, on the one hand, the capacity of health systems’ building blocks to support disease control innovations and, on the other, how the design of disease control innovations can be made system friendly and be supported by other specific building blocks (Collins et al., 2010). Case studies were selected to focus on both upstream and downstream parts of the health system, and at different stages of policy formulation and implementation.



**Fig. 4.1. R&D for system friendly intervention development**

While basic and applied research depend more on research institutions, the integration of findings into practice relies more on a complex network of health system actors.

**Box 4.1.****Addressing systems-wide and malaria-specific implementation bottlenecks**

A dispersible version of Coartem® (artemether lumefantrine), an artemisinin combination therapy (ACT) was co-launched by the Medicines for Malaria Venture (MMV) and Novartis in 2009 as the first targeted treatment for paediatric malaria. Over 33 million treatments of Coartem® Dispersible have been procured across 24 malaria-endemic countries since March 2009. Improving access to such quality treatment for children requires a coordinated approach to address critical bottlenecks both at the systems and the disease control programme level.

• *Health system bottlenecks that need to be addressed include those described below:*

**National stocks and a smooth supply chain** are critical to ensure ACT availability in primary health-care settings. Failure to deliver adequate quantities of treatment becomes increasingly problematic at the outer edge of public health systems (such as in rural areas). Consequently, paediatric deaths from malaria are often skewed towards such areas. In the United Republic of Tanzania, the innovative use of private mobile phones by health workers to report peripheral stock outs of ACTs has helped to improve a needs-based supply chain at national level and to forecast national supply needs.

**Predictability of financing and sound financial controls** can make financing flows for the routine procurement of essential medicines more stable, and so help avoid national level stock outs of ACTs. Transparency in procurement practices and financial accountability diminish the risk that international donors will suspend financing. This is crucial, as some countries have experienced grant suspensions to support ACT procurement by the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund). International donors also need to ensure that financial disbursements are harmonized with countries fiscal plans.

**Timely, contract-stipulated delivery timelines** can make manufacturers and drug suppliers fully accountable for their promises and contractual obligations to deliver purchased drugs on time to malaria endemic countries. Kenya's national malaria programme was crippled in much of 2008–2009 by rolling shortages due to manufacturer delays in the delivery of ACTs that met the country's required specifications.

• *Paediatric malaria-specific programme bottlenecks that need improvement include:*

**Strengthening international guidance** for paediatric malaria medicines is being addressed, but not sufficiently. Current WHO guidelines for the treatment of malaria (WHO, 2010) acknowledge but do not prioritize the importance of paediatric formulations.

**Revise international malaria policies to re-prioritize the needs of children.**

As new breakthroughs in terms of rapid diagnostic tests (RDTs) and paediatric-friendly treatments for malaria become available, countries must play "catch up" in revising national treatment recommendations in favour of these improved options for saving children's lives.

**Combat outdated, ill-informed beliefs about what constitutes acceptable care for children.** Historically, a range of substandard options for treating children with malaria has been used by health-care practitioners and supplied by drug sellers, despite warnings from WHO about the inadequacy and instability of these products (e.g. powders and syrups). Re-educating consumers and health-care professionals about WHO recommendations for treating paediatric malaria is essential.

## Case studies

### Rapid diagnostic tests for malaria (RDTm)

Early detection of malaria cases has been hampered by the lack of appropriate technology that can be used easily by front-line workers facing febrile cases (i.e. cases with fever) in contexts where traditional microscopy skills are low or absent, where human resources with an appropriate standard of training are in short supply and where infrastructure is not available to support the logistics of blood smear testing.

RDTms were designed in response to health system weaknesses at peripheral health facilities lacking both infrastructure and electricity. The aim was to produce a highly reliable, low cost tool that would be quick and easy for health assistants to use. Use of RDTms successfully improved case detection and contributed to better treatment and service delivery. Drugs were used more rationally, so the risk of building up drug resistance was also decreased.

RDTms have the potential to strengthen health systems by helping diagnosis and treatment integrate; they thus may increase the possibility of rapidly scaling-up malaria programmes and giving effective coverage (Hamer et al., 2007; WHO, 2010). However, use of RDTm technology has its own health system needs. The procurement and use of tests (and of an associated device for collecting specimens) requires transport, distribution, storage and waste disposal at point of use; it thus requires strengthened procurement and supply management. Systems analyses suggest that failed management of the RDTm supply chain may affect the supply of antimalarial drugs: in the absence of RDTms the consumption and over-prescription of antimalarials quickly returns to pre-RDTm levels, resulting in antimalarial drug stock-outs. Therefore, implementation research should be considered early on for the validation of strategies for scale-up and to address issues of procurement, packaging, shelf-life, storage,

re-use and safe disposal of such RDTms. The issue of strengthening and preserving existing microscopy services also needs to be addressed as these may be needed for other purposes beyond malaria diagnosis.

### Target product profiles (TPP)

Originating from industry, TPPs (also discussed in chapter 3) are used as a strategic tool to guide product development at the earliest discovery phase of research and development (R&D). Current TPP guidelines specify “go” or “no-go” criteria for product development in terms of the product’s desired benefits and basic health system requirements (e.g. patient safety, storage, handling and post-implementation monitoring of safety issues) (FDA/CDER, 2007). While such specifications are usually sufficient for preparing new drugs or medicines for introduction in well developed and functioning health systems of industrialized countries, they fall short of what is required in the weak health systems that have to address infectious diseases of poverty.

Early consideration of access and coverage requirements of poor populations in highly varied geographical contexts should also influence product R&D: the availability of the product in the store or health facility may be determined by the stability and shelf-life of the drug in non-refrigerated conditions and at different humidity levels, by requirements for a cold chain for transport, or by storage requirements. Also, adoption by end-users may depend on (a) the needs for diagnostic specimen collection, (b) available formulations, (c) schedules for treatment and dosage and (d) the training needs of health staff responsible for administering the product. The potential for coadministration with other drugs, vaccines or existing outreach strategies should also be considered during R&D. For example, RTS,S, a promising malaria vaccine candidate, was designed to be deployed together with other vaccines on the Expanded Program on Immunization (EPI) schedule (Abdulla et al., 2008). The TPP should therefore also consider affordability – as this will depend

not only on the unit price of the drug or test, but also on the cost of delivery and support. Some cheaper interventions may be more costly to deliver than others because systems for training, supervision, distribution, specimen collection, storage, quality control, etc. need to be put in place.

TPPs usually define a range for expected product efficacy. Product impact modelling should consider epidemiologic and economic consequences of deployment in different scenarios as coverage and efficacy are likely to differ. Estimations of the product utility should also include cost-effectiveness scenarios based on different coverage, efficacy and effectiveness decay-assumptions, all of which should be integrated into the TPP.

Consideration of a broad range of health systems criteria through comprehensive modelling approaches defines a research niche not yet fully considered within the implementation research agenda. Traditionally this niche has been a stronghold of academic institutions, but such research should be furthered by strengthening research systems (to ensure the right qualifications by academic partners) and reducing their divide with the private sector (see chapter 5). Partnerships need to be particularly well established for product development in the stages following the publication of a TPP: these will be best served if basic information is made available early during modelling and primary field research.

### **Insecticide-treated bednets (ITNs)**

Research establishing the efficacy of this now widespread technology was well funded and supported in the 1990s through the Special Programme for Research and Training in Tropical Diseases (TDR) and other partners. Research trials in Burkina Faso, the Gambia, Ghana and Kenya provided solid evidence for the efficacy and safety of ITNs in reducing morbidity and mortality: this research led to a WHO and Roll Back Malaria Partnership (RBM) recommendation for widespread use

of such bednets (Lengeler, 2004). However, this powerful research wave was not carried forward into the application phase with the same vigour and support from research funders or researchers. In fact, research on ITN delivery mechanisms and on scaling-up and integrating ITN use within country health systems has been rare. Ten years later, the evidence of “what works and under what circumstances” is being produced on the basis of monitoring and evaluation of large programmes, including the analysis of multiple ways of deployment (such as mass distribution of ITNs outside the health system) (Nyarango et al., 2006; Noor et al., 2007; O’Meara et al., 2008; Ceesay et al., 2008). These insights could have been obtained through appropriate modelling in the product design phase and could well have avoided the confusion among donors and countries over which programme delivery model to adopt.

### **Global health initiatives**

Development assistance for health quadrupled between 1990 and 2007, rising globally from US\$ 5.6 billion to US\$ 21.8 billion (Ravishankar et al., 2009). The massive rise was driven mainly by (a) donors increasing their attention to the health challenges presented by the Millennium development Goals (MDGs) as well as by (b) global mobilization – at the highest levels of power needed – to confront the HIV/AIDS pandemic.

While funding was mainly directed to specific disease areas, it also had considerable impact on national health systems. Prominent examples include the impact that investments directed to HIV/AIDS had on (a) health worker training in more general aspects of health care and treatment (and, more specifically, on maternal-child health care and on treatment of HIV and tuberculosis coinfection) and (b) detailed, donor-required reporting of disease surveillance. These both led to strengthened health information systems.

Although there is a lack of quantifiable information on how health systems have been strengthened by global health initiatives, it is well recognized that a strong health system is a key determinant for long-term effectiveness of disease-specific programmes. The Global Fund has been supporting health systems strengthening since its inception in 2002; since 2007, countries have been able to incorporate strategic health systems strengthening activities into their disease-specific funding applications, covering human resources, infrastructure, equipment, and monitoring and evaluation. Strategic actions are coordinated with in-country partners and with reference to national health plans. As of 2009, a total of US\$ 1.2 billion has been approved for cross-cutting interventions for health systems strengthening.

In 2008, the Global Fund, World Bank, GAVI, WHO and other partners launched a funding platform for health systems strengthening (the Taskforce on Innovative International Financing for Health Systems, 2009), components of which include a common funding policy for health systems strengthening, common country eligibility criteria, joint review mechanisms for proposals, joint programme oversight, harmonization of technical support and a common framework for measuring performance. The extent to which implementation research will feature in the platform's funding plans is not yet known.

### **Mobile health (m-Health or e-Health)**

Together with the informatics revolution, the wide scale availability of technologies such as mobile phones and personal digital assistants (PDA) have led to a "leapfrogging" of technology in developing countries with otherwise weak communications infrastructure. Relatively inexpensive and powerful for the user, mobile technologies and informatics are increasingly used for acquiring and distributing health information, supporting clinical decisions, enhancing disease surveillance, improving

wireless communication with community-based health staff, and managing drug supply and procurement or treatment prescriptions.

New opportunities presented by m-health are, however, at risk of falling into a technology and information harmonization trap. For example, software for diagnosis and treatment protocols or decision charts programmed for remote use (via inexpensive mobile phones) by frontline health workers in both clinical and community settings may differ for specific diseases (e.g. malaria, HIV/AIDS), disciplines (e.g. paediatrics, mental health) or purposes (e.g. for patient follow up). Also, software and devices (hardware) needed for quality control, supervision, drug prescription, dispensing, supply chain management, and communication may differ from that needed for drug procurement.

The diversity of systems, software, hardware and data formats and the related needs for training, management and maintenance present a challenge in the expansion of this promising new area. Current gains achieved through m-Health technologies in a few selected fields may soon lead to a call for harmonization of technical platforms (in dialogue with industry and providers) to make m-Health an integrated, interoperable and sustainable health system component for the future. In other words, we are soon reaching the stage where the promise of unconstrained innovation needs to take on a deliberate, open source development by design, to ensure that it strengthens rather than fragments and weakens health systems.

As a social and technical innovation, m-Health provides truly valuable options, but also raises challenges for the future that require cooperation and coordination at all possible levels. M-Health requires networking, planning, and readiness to learn from others (to avoid "re-inventing the wheel"). The main challenge is to ensure that available options are used optimally and in a coordinated manner so that improvements in primary health care are realized and



resources are not diverted away from basic needs and health worker priorities.

Although the promises, challenges and current experiences with m-Health have been documented, a concerted m-Health research agenda has not yet been defined (ITU-D Study Group 2, 2010). M-Health thrives on synergies among the building blocks of a health system. It also emerges in the downstream systems integration phase between health systems and telecommunications. There is a particular need to understand the current and potential impacts that m-Health can have on health systems while the needs of specific infectious disease control programmes are addressed.

### **Challenges of implementation research for health systems strengthening**

Specific disease control programmes can make valuable contributions to health systems; health systems strengthening can, in turn, support their development. Implementation research can greatly contribute to enhance such synergies – this requires improving the value chain of R&D through improved mutual understanding of the agendas and realities of key stakeholders. Listening to the voices of those that are grappling with the issues on the ground (i.e. local scientists, policy-makers, health workers and civil society) should be the starting point for increasing the capacity to carry out health research at the local level. Global initiatives developed in London, Geneva or Washington should follow what these groups are saying, and not vice versa. Meanwhile, research collaborations such as the Initiative to Strengthen Health Research Capacity in Africa (ISHReCA) can raise awareness of the interrelationship between implementation research, improved health systems and better disease control programmes.

Research funders should focus on downstream implementation research (when innovations are taken to scale), increasing investments after efficacy studies have proven concepts and innovations have been piloted. This will help identify opportunities for systems strengthening and integration, leading towards more effective and equitable scaling-up and assessing post-policy health system effects.

Implementation research and research systems can be advanced through a similar synergistic relationship. Specific investments for implementation research should not be divorced from efforts to strengthen national research capacity and its development into sustainable health research systems (Ijsselmuiden, 2007). Implementation research is particularly appropriate to integrate policy-makers to research efforts through appropriate mechanisms, while donors could be more willing to invest in strengthening career paths for national researchers creating, for example, specific funding sources for health systems research in this area. Implementation research activities should also be integrated into funding guidelines and used as specific tools for programme design, implementation and monitoring.

On their part, researchers should seize the opportunities that implementation and systems research offer as a promising vocation and career. Researchers should define research agendas in partnership with national programmes, prioritizing, developing, conducting and disseminating research as part of national health and health research systems and specifically of infectious disease programmes. Participation of researchers in the design of intervention roll-outs requires training in different skills, and also requires that researchers are stimulated through appropriate incentives.

System stewards, funders, product developers and researchers should demand, convene and participate in systems thinking with a

broad stakeholder base before designing and adopting new interventions. They should also use the full spectrum of implementation research to guide them.

Implementation research should be a part of system-wide evaluations and of impact evaluations. Implementation research designs can make use of quasi-experimental and multidisciplinary methods to test different processes for adoption and scaling-up, and so establish the need for investments before full scale-up. Ultimately, implementation research results should feed into, and become an integral part of, decision-making processes.

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# PART II

## PERSPECTIVES ON IMPLEMENTATION RESEARCH



## Chapter 5: Implementation research and product development partnerships

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The pharmaceutical industry has few financial incentives to invest in research and development (R&D) in diagnostics, drugs or vaccines for diseases endemic countries with resource-limited markets. Chirac & Torreele (2006) reported that of the 1556 new drugs registered between 1975 and 2004, only 21 (less than 2%) had indications for tropical diseases and tuberculosis – although such diseases comprised over 12% of the global burden of disease (Chirac & Torreele, 2006). Product development partnerships (PDPs) have emerged to fill this R&D gap and work within a broad definition of access to innovations. One group of PDPs recently defined access as “a coordinated set of activities needed to ensure that the products developed will ultimately have an equitable health impact” (Brooks et al., 2010). This implies a focus on knowledge sharing and capacity building to help improve both the acceptability of a product and the ability of disease endemic countries to engage in follow-on innovation.

PDPs approach to developing products for neglected diseases brings together a diverse range of public and private organizations. PDPs are characterized by their use of both public and private inputs to develop products and/or implement strategies for delivery. Over the past decade, PDPs have worked to fill R&D pipelines with potential products for neglected diseases. One study on PDPs described 63 neglected disease projects that had reached various stages of development at the end of 2004 (Moran et al., 2005). Nearly 75% of these (47/63) came under PDP stewardship; the remaining

25% (16/63) belonged to multinational companies (MNCs) alone. Moreover, half of the neglected disease drug projects in which MNCs participated were undertaken as part of a PDP, and PDPs manage nearly a quarter of the global neglected disease product investment today (Moran et al., 2008).

The proportion of public and private inputs varies from PDP to PDP. At one end, the Special Programme for Research and Training in Tropical Diseases (TDR) is mostly publicly-funded (TDR, 2011). The GlaxoSmithKline (GSK) Tres Cantos research facility in Spain relies on a mix of private and public sector resources. GSK provides the R&D, technology, manufacturing and distribution expertise while non-profit funders help share costs and risks by funding a percentage of the staffing, R&D and delivery costs.<sup>1</sup> At the other end, Merck developed ivermectin (brand name Mectizan®) to treat onchocerciasis and lymphatic filariasis and brought the drug to market with support for clinical trials from the World Health Organization (WHO). In the subsequent public–private partnership (PPP), Merck and the Task Force for Child Survival and Development – a nonprofit public health organization based in Atlanta, Georgia – started the Mectizan® Donation Program.<sup>2</sup> Support from the World Bank, the United Nations Children’s Fund (UNICEF), WHO and various nongovernmental organizations (NGOs) then allowed the drug to be distributed to communities in endemic regions (Collins, 2004).

Implementation research will become increasingly important as PDPs begin to bring health technologies to market. Of the 63 neglected disease projects in the PDP pipeline in 2004, 18 products were in clinical trials, with half in phase III clinical

1 Tres Cantos Medicines Development Campus: <http://www.gsk.com/collaborations/tres-cantos.htm>, accessed 30 September 2011.

2 Mectizan® Donation Program: <http://www.mectizan.org>, accessed 30 September 2011.

trials and two in registration (Moran, 2005). The same study accurately predicted that by 2010 between eight and 10 of these products would have been brought to market (by October 2010, eight products had reached the market). For example, in 2007, the Drugs for Neglected Diseases Initiative (DNDi) and Sanofi Aventis developed and introduced ASAQ, an antimalarial combination of artesunate and amodiaquine. Now registered in 25 African countries and in India, Sanofi Aventis distributed 25 million doses of ASAQ in 2009.<sup>3</sup>

Another antimalarial combination, artesunate and mefloquine (ASMQ), resulted from a partnership among DNDi (See Box 5.1 for more about DNDi's access strategy.), Cipla (an Indian public limited company), and Farmanguinhos (a Brazilian public drug manufacturer). This is now entering the market in Brazil and soon will be doing so in Asia. Furthermore, in 2009 the Medicines for Malaria Venture (MMV), together with Novartis, introduced Coartem® Dispersible, the first high-quality artemisinin combination formulated specifically for children.

PDPs primarily focus on R&D to accelerate the development and implementation of new products for neglected diseases. While implementation research typically

focuses on delivery processes, PDPs can use implementation research at all stages of the development process to inform both upstream factors (including PDP structure and policy) and downstream factors. Downstream product delivery typically takes place in complex country and field situations. Product design (incorporated in the target product profile) is important in this and requires implementation research at an early phase to ensure that actions taken in the design phase do not preclude maximizing later access (Fig. 5.1 and Box 5.2).

Some public–private partnerships, such as the Global Fund and the Global Alliance for Vaccines and Immunisation (GAVI), focus on the delivery of existing products. Their experience with implementation research offers a roadmap of what is in store for PDPs. The Global Fund, for instance, now encourages recipients of its funding to devote 5–10% of their budget to evaluation (which includes implementation research). Moreover, after observation of the ad hoc efforts of fund recipients in the field of implementation research, in 2008 the Global Fund/WHO/TDR published a framework (which also received endorsement from the United States Agency for International Development, USAID; the Joint United Nations Programme on HIV/AIDS, UNAIDS; and the World Bank) on standardizing operations and implementation research. The access framework within which PDPs

3 ASAQ: hope for malaria: <http://www.actwithasaq.org/en/updates.htm>, accessed 30 September 2011.

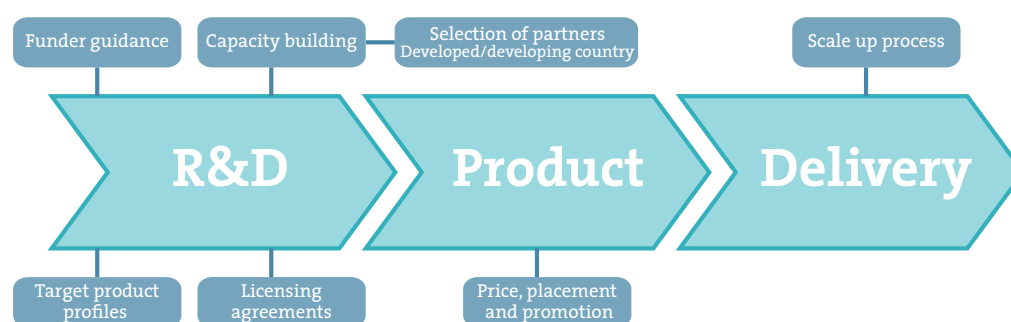


Fig. 5.1. Decision points informed by implementation research



**Box 5.1.****DNDi's access strategy**

DNDi's primary objective is to develop treatments for neglected tropical diseases (NTDs) identified by gathering input from endemic country stakeholders. DNDi aims to support the recommendation and implementation of those new treatments to facilitate equitable access.

DNDi's strategy is four-pronged:

**1. DNDi emphasizes a collaborative process with governments and endemic country stakeholders at early stages of every project:**

This collaboration involves the development of target product profiles (TPPs) with input from ministries of health, control programmes, and other local and international stakeholders to ensure the development of a treatment that responds to patients' needs and meets demand. Endemic country founding partners of DNDi are critical in defining such field needs and priorities. Regional disease platforms, set up to strengthen clinical capacity and the development of good clinical practice, naturally become strong partners for implementation.

**2. Strict business development principles guide access work:**

Selection of the manufacturing partner and management of the collaboration are essential for access. DNDi aims to facilitate global product access by ensuring mutual understanding and agreement with the manufacturing partner regarding the need for supply obligations to ensure national markets are fully satisfied with essential drugs in the context of external demand, that pricing is affordable and that intellectual property is protected. To ensure sustainability of production, DNDi strives to obtain agreements from manufacturers to work either on "no-profit, no-loss" pricing or on an "at cost plus a small margin" scheme – so long as the price remains affordable for patients.

DNDi works closely with the manufacturer to try to find options to lower costs.

Competition is usually not an option to bring down prices for NTD drugs as there are typically no paying markets and no alternative treatments (although this is not true for malaria). DNDi currently has three marketed treatments (the antimalarials ASAQ, ASMQ and the nifurtimox-eflornithine combination treatment for human African trypanosomiasis, NECT) which, to facilitate access for patients, are developed as public goods without patents. However, other potential treatments under development may entail the ownership of some intellectual property (IP) by DNDi partners. In such cases, DNDi always retains march-in rights to regain intellectual property in the event of the manufacturer's default.

**3. DNDi implements field trials and interventions strategically:**

This is done in collaboration with national programmes, NGOs and WHO, depending on partners' needs and/or ability to generate additional data that may be needed for policy change and adoption by governments. These partners are also sometimes selected based on their potential to help generate data that may be required for policy change and adoption at government level.

**4. Advocacy strongly supports access:**

For DNDi, advocacy involves working towards getting the most neglected diseases included on the global agenda, and increasing awareness about the most neglected diseases in both developed and disease endemic countries. Advocating for political leadership to ensure access is essential to sustaining financial support, defining priorities, creating a more favourable environment that will stimulate health R&D, and facilitating access to new health tools.



are now striving to work provides ample scope for upstream and downstream implementation research, although emphasis has been given to the downstream phase.

This chapter is intended for PDPs, funders, policy-makers and other stakeholders engaged in the R&D and delivery of health technologies for infectious diseases of poverty. The chapter seeks first to identify the diverse opportunities for implementation research. Such implementation research can ensure that upstream, PDP governance, PDP organization and PDP policies contribute to accelerated product adoption at country level, while downstream, implementation research can inform product scale-up, adoption and adaptation to local contexts. Types of implementation research are then characterized to demonstrate the broad range of studies now being undertaken, and methodological challenges for implementation research and capacity strengthening are addressed. Surmounting these challenges can improve information and have an impact on product design, implementation and access.

### Upstream implementation research

Implementation research can help identify how PDP governance structures and policy influence product affordability, adoption, and scale-up. For instance, PDP governance can shape the conditions under which a product is developed, the product TPP, and the degree to which other partners can be engaged in product development. An illustrative example is the Doris Duke Charitable Foundation's 2003 funding portfolio for the development of affordable point-of-care diagnostics for HIV/AIDS. Their grant agreements retain a non-exclusive, royalty-free license to any patents filed in developing countries (Doris Duke Charitable Foundation, 2004). Such a license allows the Foundation to sublicense rights to make and distribute the product if

the grantee fails to deliver on the charitable objective (So & Stewart, 2009).

Intended beneficiaries of PDP products may influence product development policy through the board of directors and scientific advisory committees of these organizations. However, some scientists involved with the South African AIDS Vaccine Initiative have questioned whether African representation in PDP governance is sufficient to redress longstanding power inequities in these partnerships, where developing country actors tend to be placed in a subordinate position. This group of scientists also urged the African research community to cultivate PDP leadership, to combat corruption in the handling of donor monies, and to invest in African-based initiatives (Tucker & Makgoba, 2008).

Implementation research can also play a role in the design of a PDP's product portfolio – by informing whether a vaccine, drug, diagnostic, or vector control intervention would result in the highest levels of uptake and impact. For example, a diagnostic or vaccine might decrease the pressure for natural selection to develop drug resistance. An effective vaccine might diminish the need for infrastructure for continued monitoring and treatment, but require a cold chain for delivery, limiting its usefulness. Combination drug treatment may be necessary to increase uptake.

Once the product portfolio has been defined, PDPs and their partners begin to define the strategic entry point in tackling a disease and formulating a TPP (which provides specifications for what the end product should be like). The TPP defines product characteristics (such as route of administration or transport requirements) and also takes into account the characteristics of the population that the product is intended to serve (such as age and income level). After disease and technology modality have been determined, there are also questions about delivery and access that

need to feed into the TPP. For instance, will the health product work in remote settings, or will it require access to tertiary referral laboratories for confirmatory diagnosis? How affordable will the end product be? At this stage, the parameters set in the TPP

already begin to constrain the likely findings of downstream implementation research.

Transparency is necessary if early implementation research is to provide effective input into the TPP as the parties carrying

### **Box 5.2. International Partnership for Microbicides (IPM): Anticipating barriers to adoption**

The introduction of microbicides to local markets and health systems as tools in the fight against infectious diseases must overcome significant cultural, ethical, and religious barriers. Implementation research can provide the necessary feedback to overcome these challenges.

IPM works to bring microbicide-based products to market to prevent the spread of HIV infection in developing countries. IPM engages in extensive research and planning efforts, working closely with its target population to ensure acceptance and adoption of controversial products. It also engages in several supporting activities to prepare for implementation and access, including early acquisition of intellectual property rights; identifying the needs and preferences of women living in developing countries; conducting clinical trials; identifying strategies to expedite regulatory approval; identifying manufacturing options; performing social and policy research to inform implementation; and partnering with key organizations.

IPM's implementation research runs the gamut of studies available to a PDP. IPM uses mathematical modelling of community introduction scenarios to prioritize techniques; performs qualitative and quantitative surveys and interviews to better understand gender and sexuality issues as well as to consider the vaginal practices of women; examines lessons from previous introductions of contraceptive technologies; and studies country profiles on infrastructure,

sociocultural patterns, and economic landscapes.<sup>1</sup>

One of IPM's phase I/II studies is an evaluation of the use of a vaginal ring that slowly releases microbicides over time to protect against HIV and other sexually transmitted infections (STIs). IPM is currently performing a controlled study in Kenya, South Africa, and the United Republic of Tanzania where to evaluate the safety and efficacy of the ring. At the end of the study subjects will be asked to participate in focus groups to assess the acceptability of vaginal rings (IPM, 2008). Such feedback will allow IPM to design products that address the concerns and needs of their users more effectively – so that designs tailored to end-users should ensure user acceptance.

These efforts are complementary to the recent CAPRISA 004 clinical trials undertaken by the Centre for the AIDS Programme of Research in South Africa (CAPRISA) that are the first to show that a microbicide gel can significantly reduce the risk of HIV transmission.<sup>2</sup> These types of successes from other, non-PDP led clinical trials can also inform IPM's future research.

1 International Partnership for Microbicides. Ensuring access to microbicides: <http://www.ipmglobal.org/access>, accessed 30 September 2011.

2 *African Studies Give Women Hope in H.I.V. Fight*. [http://www.nytimes.com/2010/07/20/world/africa/20safrica.html?\\_r=1](http://www.nytimes.com/2010/07/20/world/africa/20safrica.html?_r=1), accessed 30 September 2011.

out the implementation research must have access to the evolving plans of a PDP. TPP transparency can align priorities across a PDP and its partners so that they are striving to achieve the same, agreed upon goal.

Once the product has been developed, patents and licensing agreements (which can affect prices, place limits on local production, and shape how knowledge is transferred) are key to ensuring access. Licenses may give preferential treatment to developing countries through lower royalty

rates or lower product price – although defining which countries are “developing countries” (and so receive preferential pricing treatment) can create a huge difference in affordable access. For example, the burden of disease from NTDs such as Chagas disease and leishmaniasis falls largely on middle-income countries such as Brazil, which are outside the list of countries classified as “least developed”.

Negotiated royalty rates sometimes comprise a significant component of a product's

### Box 5.3. Scale-up of paromomycin delivery in South Asia

The Institute for OneWorld Health (iOWH) developed paromomycin intramuscular injection (PMIM) for the treatment of visceral leishmaniasis (VL). PMIM was registered in India for the treatment of VL in 2006, after completion of an iOWH-sponsored phase III clinical trial conducted in partnership with WHO/TDR and four VL research centres in Bihar State. PMIM is manufactured at “no profit, no loss” by the Indian company Gland Pharma Ltd.

After investigating possible routes for PMIM introduction in Bangladesh, India and Nepal, iOWH decided to focus its initial strategy on public sector adoption of PMIM for several reasons:

- 1) a regional VL elimination programme was underway in Bangladesh, India and Nepal;
- 2) the WHO/SEARO Regional Technical Advisory Group made a strong recommendation to the three governments to use the same drugs through their public health sectors for a coordinated regional strategy; and
- 3) lessons from prior VL drug launch experiences suggested to iOWH that oversight of VL treatments in the public sector would be better than that in the private sector. iOWH has placed

special emphasis on the improvement of pharmacovigilance reporting through the clinical studies it has sponsored. While the private sector is an important provider of VL treatment in India, proper usage is more difficult to ensure. Private sector introduction was thus a secondary strategy.

iOWH is now working with the governments of Bangladesh and Nepal to help ensure availability of PMIM, and is focused on obtaining regulatory approval of PMIM so that the injection can be included in the VL elimination programmes of these countries. Working with the respective governments and leading national research institutions, iOWH is sponsoring a clinical study in Bangladesh and an effectiveness study in Nepal. Recent developments in VL therapy are beginning to shift therapeutic focus to the development of combination therapies (to help prevent the development of potential drug resistance) and shorter treatment regimens – PMIM was a component of two combination therapies investigated in clinical studies conducted by DNDi in India, while a proposed study in Nepal will help assess the potential use of PMIM in government health facilities in combination with other VL therapies.

end price. For example, Merck pays 24% to 26% royalties on total sales of human papillomavirus (HPV) vaccines to GSK and other patent holders.<sup>4</sup> This indicates that up to a quarter of the sales revenue from the approximately US\$ 360 price tag for a full treatment goes to paying for royalties. Other licensors, by contrast, have issued royalty-free licenses. For example, the University of California offered a royalty-free license for the microbial synthesis of artemisinin to the for-profit Amyris Biotechnologies in exchange for a commitment to manufacture the drug for use in malaria-endemic developing countries on a no-profit basis (Coloma & Harris, 2005).

### Research for scaling up

Scaling up is one of the primary challenges that implementation research addresses (see Boxes 5.3 and 5.4). Following phase III clinical trials, much remains to prepare a product for dissemination. Pilots and demonstration projects can pave the way forward by engaging local stakeholders in the delivery system, mobilizing the evidence needed to recruit more funding, and providing needed assurances for country regulatory authorities. Monitoring and evaluation during this phase can be critical for the feedback loop that provides information for future iterations of the product and/or delivery mechanisms.

Some PDPs are involved in downstream delivery processes and must assess the best routes for supply and scaling up. This involves collaborating with national governments and choosing between private or public sector delivery schemes. (Choosing between public or private delivery approaches may affect other conditions, such as adherence to dosage, drug resistance, and correct use.)

#### Box 5.4.

#### **The Foundation for Innovative New Diagnostics improves uptake through collaboration**

Bringing diagnostics to developing countries involves production and distribution processes different from that for medicines. However, like other PDPs, the Foundation for Innovative New Diagnostics (FIND) relies on collaborating with networks and experts with experience in resource-limited settings for input into TPPs; it also relies on its partners for implementation expertise.

FIND notes that WHO endorsement of a new product or technology is important, but is not sufficient to ensure uptake. FIND secures local buy-in, both before undertaking clinical trials and before initiating implementation-related activities. For example, since countries like India require that evidence be gathered locally, FIND set up an office in India. In targeting its work, FIND considers the local burden of disease as well as the country's capacity to carry out the R&D collaboration.

The fixed cost of the diagnostic instrument and the variable costs of reagents to run tests are important considerations. Laboratory infrastructure, human resources, and other overhead expenses are also significant cost drivers. In introducing new tools, these factors have to be taken into account. Some countries require a cost-effectiveness trial. Brazil, for example, requires such trials before integrating a diagnostic into its public health system. Another mechanism for reducing overall cost (not just the cost of diagnostics) is the implementation of both diagnostics and drugs. FIND is currently in collaborations with other PDP partners; while these partners are developing medicines for malaria, FIND focuses on developing diagnostics for the disease. Such co-development should ensure more effective deployment of drugs and diagnostics.

4 See *Despite Merck's Leg Up, Glaxo Sees Cancer Vaccine Success*: <http://www.chartsbank.com/DrugPipelineNewDetail.aspx?NewsID=13>, accessed 30 September 2011.

Implementation research undertaken before product dissemination can shape implementation success. Well conducted studies on demand forecasting, branding, and stakeholder preferences can answer “why?” and “how?” a product is taken up and has impact, and can thus help project the level of manufacturing capacity needed for scale-up. Artemisia is a key component in artemisinin combination therapies (ACTs) used to treat malaria. When ACTs first appeared on the market in 2001, demand grew slowly until 2005 when the price of artemisia spiked to US\$ 1200 per kilogram. Expecting high rates of return, farmers and producers then entered the market in droves. Unfortunately, procurement agencies failed to purchase in the expected time, so that artemisinin flooded the market – resulting in a price drop to nearly US\$ 200/kg in 2007 (Van Noorden, 2010; also <https://www.ghdonline.org/malaria/discussion/artemisinin-market-instability>). Better demand forecasting may have alleviated the supply shocks (and the related price fluctuations), and demand forecasting that took into account the policies and plans of various procurement agencies and ministries of health could have mitigated these extreme price fluctuations.

The Global Health Forecasting Working Group under the Center for Global Development, a non-profit US organization, suggests that well executed demand forecasting can alleviate risks of supply shortages and high costs. They advocate for the creation of an infomediary – a neutral third party to collect and disseminate demand forecasting data. The group also proposes that purchasers should accept more risks from unforeseen demand shocks by taking on minimum quantity guarantee contracts with manufacturers (Center for Global Development Global Health Forecasting Working Group, 2007). Demand forecasting can help prevent these perturbations along the supply chain by creating stable prices for continued procurement. This, in turn, creates enabling environments for scale-up, reduced prices, and ultimately improves access.

## Types of PDP implementation research

In anticipation of scaling up, PDPs and academic researchers have commissioned or performed a variety of implementation research studies. Research methodologies range from mathematical modelling to surveys and market analyses. These studies enhance PDP decision-making and determine implementation strategy. They also help determine the adequacy of R&D pipelines; inform optimal treatment regimens; offer marketing insights; evaluate the use of innovative approaches to delivery; and eventually, through pilot and demonstration projects, provide evidence for uptake. MMV has performed market forecasting (MMV, 2008); IPM has carried out studies on cultural acceptability and preferences;<sup>5</sup> and the TB Alliance has looked at market environments, demand forecasts, health system readiness and stakeholder preferences (TB Alliance, 2007; Wells et al., 2010; TB Alliance, 2009). The International AIDS Vaccine Initiative (IAVI) has performed extensive research on product acceptability in forming a TPP (Chataway & Smith, 2006), and PATH and the iOWH are assessing delivery systems and strategies<sup>6</sup> (see Table 5.1).

## Methodological challenges

How PDPs define their implementation goals has consequences for the measurement of implementation success and the selection of research frameworks and indicators. Identifying the unit of analysis for PDP outcomes presents an important challenge. Possible outcomes include the success of the product, the portfolio of products, or disease eradication.

5 International Partnership for Microbicides. Ensuring Access to Microbicides: <http://www.ipmglobal.org/access>, accessed 30 September 2011.

6 Malaria Vaccine Initiative. Ensuring access to malaria vaccines, once they are available: <http://www.malariavaccine.org/preparing-access.php>, accessed 30 September 2011.



**Table 5.1. PDPs and types of implementation research**

Typology	Example	Downstream effects
Robustness of R&D pipeline	Glickman et al. (2006) report on a portfolio based, Monte-Carlo simulation to evaluate the likely number of products developed for tuberculosis, and the probable costs for all drugs in the pipeline – including both those successfully and unsuccessfully brought to market – and discussed these decisions from the point of view of a PDP.	These pipeline analyses can guide prioritization of funding, shed light on the need for compound acquisition at each stage to generate high likelihoods of creating a successful product, and highlight the need for increased funding and cost sharing.
Cost effectiveness and comparison of drug treatments	Coleman et al. (2004) used a threshold analysis applying Monte-Carlo simulations to determine the cost effectiveness of combination therapies for malaria under varying conditions. They found that ACTs proved to be a cost-effective solution in 95% of situations where antimalarials might be delivered.	Using combination therapies instead of monotherapies can impact clinical trials. Knowledge of the situations where ACTs would not be cost effective helps target locations and populations.
Prioritizing treatment vectors	Goodman et al. (1999) used cost-effectiveness models to calculate cost per DALY averted for various methods of malaria control, including nets, residual spraying, and medicines. They showed that insecticide-treated bednets were the lowest cost intervention (although they did not account for the costs of distribution and implementation).	Cost-effectiveness analyses can help set priorities and estimate the number of DALYs that can be averted with a given amount of funding.
Market analysis and demand forecasting	MMV has commissioned extensive market analysis studies on the malaria market in Uganda. In their supply chain study, they examine the types of antimalarial medicines available on the market, the availability of product by outlet type, the range of prices, affordability, supply-chain structure, and price mark-ups (MMV, 2008).  The TB Alliance commissioned a market analysis study, “the first comprehensive analysis of how today’s tuberculosis drugs reach patients on a global scale” which addressed “pricing, purchasing, procurement and distribution mechanisms for tuberculosis treatments in target countries” (TB Alliance, 2007).	Market analyses provide evidence of how to go about replacing traditional first-line therapies with high quality ACTs, without leaving a gap in supply and access. Sizing up markets provides partners with realistic expectations for revenue and provides feedback for pricing and delivery strategies.
Stakeholder acceptability analyses	iOWH worked extensively with governments in South Asia to assess what these governments would require in order to accept and distribute paromomycin through their public health sector. The TB Alliance commissioned a study, “What Countries Want” (TB Alliance, 2007) to determine how best to develop products that aligned with government and public sector needs.	Developing products and delivery systems in conjunction with government and stakeholder input helps to ensure that products will be acceptable and adopted.



For instance, for access to tuberculosis products, outcomes might be: access to tuberculosis drugs, access to tuberculosis diagnostics, or reductions in the prevalence of tuberculosis. Alternatively, outcomes could be measured in terms of success of the actors in delivering the intervention, or the health system's effectiveness in tackling the disease. If measuring the success of the actors, a study could measure the impact of a tuberculosis-focused PDP, success and capacity of other partners, or success of country-wide health systems.

Implementation research faces several obstacles to establishing robust methodological frameworks. Study controls may not be possible or ethical; the time lag between implementation and impact may require the use of indirect measures of success, and the mix of inputs into the development of the product make attribution of outcomes more difficult. For instance, the variety of funding inputs into disease eradication makes it difficult to attribute reductions in disease prevalence to a single PDP or a group of PDPs. While 41% of the global funding for diarrhoeal disease research goes to PDPs and intermediaries, only 9% of global funding for leprosy research goes to PDPs or intermediaries (Moran et al., 2008). Sources of R&D funding, licensing decisions, partnerships with manufacturers, promotion, delivery systems and other factors all have differing impacts on access.

The time from bench to bedside is measured in years, so efforts to ensure that the feedback from implementation research remain relevant and timely are critical. Early sharing among PDPs of their experiences, the use of closer-to-real-time and actionable data, and sentinel or surrogate markers (a measure of the effect of a certain treatment that may correlate with a real clinical endpoint but doesn't necessarily have a guaranteed relationship) flagged by advance studies can all help in this respect. Some PDPs engage in the difficult task of ensuring sustainability for follow-on innovation and

access through capacity building. FIND, for instance, works extensively on strengthening laboratory capacity for diagnostics in disease endemic countries,<sup>7</sup> and DNDi has created several innovation platforms that encourage innovation in these regions.<sup>8</sup> These actions represent both an attempt to ensure health systems strengthening and an effort to ensure sustainable access to medicines over time.

Continuity of support for PDP implementation research is important across the product lifecycle. R&D for health technologies can take at least a decade, and funder priorities and programme officers can change in that period. At the same time, the longer such funding commitments are maintained, the more entwined the funder–PDP relationship may become. Implementation research that is independently initiated and conducted provides assurances of objectivity and transparency. Global health partnerships, such as the Global Fund's Affordable Medicines Facility for Malaria (AMFm), have recognized the importance of this by planning independent evaluations of their programmes.

A difficult trade-off in defining access goals involves prioritizing numbers of people served as opposed to ensuring equitable reach. Does reaching those most in need count more than serving greater numbers through the existing health-care infrastructure? Early stakeholder research and discussions with governments can help set some of these priorities. PDPs may need to work alongside organizations that engage in creative delivery approaches to reach those who are most in need. Consideration of the needs of the end-users and the delivery mechanisms can influence product design.

7 Foundation for Innovative New Drugs. Overview: [http://www.finddiagnostics.org/programs/scaling\\_up/lab\\_preparedness](http://www.finddiagnostics.org/programs/scaling_up/lab_preparedness), accessed 30 September 2011.

8 Drugs for Neglected Diseases *initiative*. Overview products: <http://www.dndi.org/overview.html>, accessed 30 September 2011.

## Capacity building and strengthening

PDPs have been criticized for being predominantly located in or led from Europe or the USA (Tucker & Makgoba, 2008). If the lead comes from such countries it may make it more difficult to transfer technology and know-how to developing country partners. Efforts by PDPs to overcome this challenge by building and strengthening country-level capacity for implementation research can improve access in several ways (see Box 5.5). First, involving local expertise in product design and implementation can increase product uptake by providing valuable information on local contexts. Second, working with developing country scientists and pharmaceutical firms may increase the latter's capacity to pursue follow-on innovations that will address access at the country level. TDR's support of community-directed interventions tested the value of the local expertise model by comparing the uptake of various drugs and products in communities that recruited community members for distribution against uptake in communities that relied on traditional delivery systems. In almost all instances, community-directed interventions resulted in higher levels of uptake than the traditional delivery system. In an anecdotal example of one way in which locally-based delivery resulted in higher uptake, community distributors noted that they were more successful in monitoring and explaining the appropriate dosage for malaria, since they were often neighbours or friends with the patients (TDR, 2008).

The South African Tuberculosis Vaccine Initiative (SATVI) is one exception to the standard developed-country location for PDPs. Housed at the Institute of Infectious Disease and Molecular Medicine of the University of Cape Town, SATVI seeks to develop new and effective tuberculosis vaccines.<sup>9</sup> This PDP brings expertise together and

### Box 5.5.

#### Efforts at increasing uptake through capacity strengthening: DNDi and ANDI

DNDi has opted to engage in this type of capacity building by establishing a clinical research network for human African trypanosomiasis (HAT) in disease endemic countries. This network creates appropriate clinical trial methodologies for HAT; overcomes administrative and regulatory challenges; assists with infrastructure, resources and equipment; and shares information and communication among endemic countries. In this way, interventions for HAT can be evaluated more effectively within HAT-endemic countries, registered more quickly, and made more readily available to patients.<sup>1</sup>

The African Network for Drugs and Diagnostics Innovation (ANDI) provides an example of another platform, in this case focused on innovation through collaboration between developing countries.<sup>2</sup> Africa bears the greatest burden of disease in the world today, but has little control over the source or supply of medicines most needed by its citizens. ANDI seeks to foster collaboration and innovation among the universities and institutions of disease endemic countries to improve capacity and collaboration. Launched in 2008, the network emphasizes the value of local knowledge and priorities in developing health products while building a sustained research infrastructure (Nwaka et al., 2010). In 2010, ANDI launched its first call for applications for Centres of Excellence in Health Innovation in Africa. The ANDI network is also in the process of being emulated in Asia and Latin America to facilitate innovation in those regions.

1 Drugs for Neglected Diseases initiative. HAT platform: <http://www.dndi.org/hat-platform.html>, accessed 30 September 2011.

2 The African Network for Drugs and Diagnostics Innovation: <http://www.andi-africa.org>, accessed 30 September 2011.

9 South African Tuberculosis Vaccine Initiative: <http://www.satvi.uct.ac.za/>, accessed 30 September 2011.

reaches the underserved by building on local resources. It also takes local infrastructure requirements into consideration in order to ensure long-term access to tuberculosis vaccines. SATVI has developed capacity to conduct trials of novel tuberculosis vaccines for product registration in South Africa. SATVI focuses on surveillance, professional development, and data management as key aspects of capacity building at its field site, located in a poor rural area where tuberculosis is highly endemic.

In selecting partners for clinical development, trade-offs may need to be made between investing in those outside the country that already have capacity to conduct trials and investing in those who are local, but whose capacity to conduct trials must be built. The latter should result in higher levels of local expertise in adapting products for local distribution; this may subsequently translate into improved uptake. Increasing capacity in this way also improves the ability of partners to engage in follow-on innovation (where products specific to their populations are developed).

Capacity building as a factor to improve implementation can have various measures e.g. the number of scientists from disease endemic countries involved in pre-clinical or clinical research phases; publications coauthored by such scientists; clinical trials managed and conducted in these settings; representation on scientific advisory and PDP governance structures; location of manufacturing facilities; engagement of local distributors; and sustainable funding.

## Conclusions

PDPs differ in their approaches to implementation research and in their degree of involvement during the product delivery and implementation phase. However, there are some consistent implications for implementation research and PDPs. First and foremost, implementation research adds value across the spectrum of PDPs and across the timeline of product development. Performing implementation research further upstream at the policy formulation level can inform governance processes, TPP development, and decisions over the licensing of products or drugs. Demand forecasting, cost-effectiveness studies, market analyses, and stakeholder acceptability analyses (see also chapter 3) can help lay the groundwork for successful implementation with partners in target countries. Finally, engaging in implementation research further downstream, such as pilot projects and demonstration projects, can prepare the groundwork for scale-up. During these processes, capacity building can play a critical role in positioning developing country researchers and manufacturers to perform follow-on innovation and clinical trials.

More funding and support for independently conducted implementation research would better prepare PDPs and their partners to advance new health technologies to combat infectious diseases of poverty. The importance of focusing on portfolios and disease control efforts, rather than on the success of a specific product, needs to be communicated to and understood by all stakeholders to ensure sufficient funding and focused priorities.

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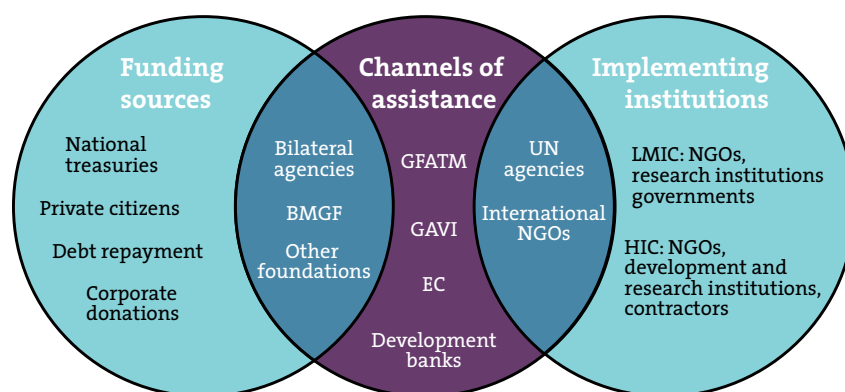
## Chapter 6: Global health funders and implementation research

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The global health architecture has undergone rapid and significant changes in the past decade, with the emergence of new public and private funders, of innovative channels of development assistance and of actors focusing on implementation, technical support, scaling-up and delivery of specific disease control interventions. Major new actors emerging with force during this period were the Bill & Melinda Gates Foundation (GFATM) (on the funding front) and the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) as well as the Global Alliance for Vaccines and Immunisation (GAVI) (with innovative roles as channels of development assistance). The emergence of global health initiatives (see chapter 5), global health programmes and global networks exemplify innovative ways of partnering research and development as well as of providing technical support and training (Fig. 6.1).

The enormity of the global health field today, as well as the challenges it faces to ensure its effectiveness, is reflected in the growth of development assistance for health (DAH), from US\$ 5.6 billion in 1990 to US\$ 21.8 billion in 2007 (Ravishankar et al., 2009). Based on this analysis a broad definition of global donors or funding organizations is used in this chapter, to include primary financiers, channels of assistance and implementation institutions. Primary financiers include private foundations (e.g. the Bill & Melinda Gates Foundation), bilateral agencies (e.g. the Department for International Development (UK), DFID) and multilateral agencies (e.g. the World Bank). Channels of assistance include agencies (e.g. the Global Fund) that receive funding from a variety of sources to identify and finance country beneficiaries. Implementing institutions include a range of stakeholders for whom research may be one of a number of important activities (e.g. TDR).

Complexity in the global health funding landscape can be inferred from the dual roles that many actors play. Funders often participate in the organization of channels of assistance. Increasing complexity is also apparent at country level, where global



**Fig. 6.1.** Relationships in development assistance for health (DAH) across global health

There is a significant overlap between institutions that provide funding for implementation research and channels that deliver such funding to where resources are required, and between these latter and the institutions undertaking research on the ground.

Source: Modified from Ravishankar et al., 2009.



health initiatives and national health systems interact (see chapter 4). All players are also becoming aware of the need for improved coordination between research and practice to ensure synergies towards the common goal of improving population health.

This chapter was developed with the support of information from an Internet survey with health research donors and channels of assistance (see below), conducted in July and August 2010, supplemented through phone interviews. In this chapter we discuss the important role of implementation research in helping global health funding organizations realize their goals. As stated in chapter 2, the need for consensus on a definition of implementation research is identified as a prerequisite (a) to increase funding for the field and (b) to obtain agreement on the agenda that will oversee implementation research's most effective growth and partnerships. Implementation research capacity strengthening needs are discussed in relation the capability of organizations and nations to conduct this type of research.

Given that implementation research is an emerging area of inquiry and practice, most of the organizations interviewed did not have specific or long-standing programmes focused solely on implementation research; rather, those interviewed referred to the inclusion of activities in this field within broader research categories. Furthermore, implementation research activities typically spanned several disease programmes or initiatives, which complicated efforts to aggregate programme and financial data. We found that while interviewees were highly relevant for implementation research within their institutions, they were often unaware of the entire spectrum of implementation research funding and activities.

## Methodology to assess the landscape of implementation research among global funders

Assessment of the implementation research funding landscape was undertaken in two stages. A preliminary identification of stakeholders was undertaken at the consultative meeting on implementation research (sponsored by TDR in Kampala, Uganda, 28–30 June 2010), complemented by an Internet search. At this stage 49 organizations were identified as global health funders. A comprehensive Internet search was then undertaken for each organization, retrieving information about implementation research funding from organizational publications, financial reports and press releases.

The second stage consisted of the validation and supplementation of data; at this stage organizational contacts (selected by consultative meeting participants and by the authors) were requested to take part in interviews through e-mail (Table 6.1). Definitions of implementation research as outlined in chapter 2 of this Report were provided to orient the interviews. A total of 41 organizations were identified as global health funders, of which, 22 were interviewed. There were 19 organizations that participated no further due to (a) lack of response (four organizations) or (b) lack of time to interview and process data (15 organizations).

## The implementation research agenda

Implementation research is being widely undertaken and supported by funders (as well as by networks and organizations channelling development assistance) to address a wide range of policies and programmes. Examples of areas of inquiry include:

- strategies to increase case detection, prevention, diagnosis and management of tuberculosis and evaluation of progress (Stop TB Partnership);
- identification of specific implementation bottlenecks that need to be addressed to achieve national and regional targets (RBM);
- quality of care, increasing access within the community, getting recommendations implemented and emphasizing research dissemination (HRP);
- access to and scale-up of proven interventions (TDR);
- follow-up of projects already being implemented to learn from them and scale them up if successful (Norwegian Forum for Global Health Research);
- comparative effectiveness and cost effectiveness of interventions (World Bank). (For more about the World Bank's support of implementation research see Box 6.1.)

#### Box 6.1.

#### **World Bank support to implementation research: the Development Impact Evaluation Initiative and the Malaria Impact Evaluation Program**

The Development Impact Evaluation Initiative (DIME)<sup>1</sup> is a World Bank programme to support government agencies in adopting a culture of real time, evidence-based policy-making. DIME works with 300 agencies in 72 countries worldwide to improve knowledge, quality of operations and country capacity for evidence-based policy-making. The objectives of the initiative include comparing the effectiveness and cost effectiveness of alternative interventions and the costs of doing nothing to address a problem in real implementation settings so as to help programmes learn how to improve their performance over time. DIME therefore focuses on impact evaluation while also supporting implementation research.

The Malaria Impact Evaluation Program (MIEP)<sup>2</sup> aims to improve understanding of how innovations in service delivery and subsidized prevention and treatment provision impact on health-seeking behaviour, health status, school performance, labour productivity and socioeconomic status. Via impact evaluation,

policy-makers and programme managers learn how to enhance the delivery of key disease control and treatment services, and strengthen health-care systems to maximize the benefits of interventions on health and welfare. Evaluation also helps to implement interventions more cost-effectively and equitably. MIEP is building and supporting a focus on evidence, and helping policy-makers and programme managers to:

- adopt a strong country-led approach to ensure ownership and relevance;
- create learning teams within ministries of health and build capacity through a “learning-by-doing” approach;
- support governments through all stages of design and implementation;
- create multi-country communities of practice for sharing experience and evidence;
- pursue system-wide approaches to help resolve health system bottlenecks – such as by developing public–private partnerships and community-based/performance-based approaches; alleviating human resource constraints; streamlining health management; and strengthening information systems.

1 For more information about DIME, see [http://siteresources.worldbank.org/INTDEVIMPEVAINI/Resources/DIME\\_project\\_document-rev.pdf](http://siteresources.worldbank.org/INTDEVIMPEVAINI/Resources/DIME_project_document-rev.pdf)

2 For more information about MIEP, see <http://go.worldbank.org/EIUK5P38M0>

These areas all fall within the scope of health systems research, although several could be deemed to be “at the border” or even outside the scope of implementation research as defined in chapter 2 of this report. Indeed, when queried about how funders in global health define implementation research, organizations proposed a wide range of conceptual and practical definitions. Out of all 22 organizations interviewed, only 14 made reference to a formal definition of implementation research of any kind. Of these, six referred to the exact or a slightly modified version of the definition

proposed by the open-access journal *Implementation Science*:

Implementation research is the scientific study of methods to promote the systematic uptake of clinical research findings and other evidence-based practices into routine practice, and hence to improve the quality and effectiveness of health care. It includes the study of influences on health-care professional and organizational behaviour.<sup>10</sup>

<sup>10</sup> *About Implementation Science*:  
<http://www.implementationscience.com/about>,  
accessed 30 September 2011.

**Table 6.1. Global funders with interest in implementation research included for interviews**

1. Global Alliance for Vaccines and Immunization (GAVI)
2. Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund)
3. Stop TB Partnership
4. Department for International Development (UK) (DFID)
5. World Bank
6. Norwegian Forum for Global Health Research
7. Special Programme for Research and Training in Tropical Diseases (TDR)
8. Special Programme of Research, Development and Research Training in Human Reproduction (HRP)
9. Roll Back Malaria Partnership (RBM)
10. Centers for Disease Control and Prevention (USA), Division of Parasitic Diseases and Malaria (CDC-DPDM)
11. Centers for Disease Control and Prevention (USA), Division of HIV/AIDS Prevention (CDC-DHAP)
12. Doris Duke Charitable Foundation
13. Rockefeller Foundation
14. Wellcome Trust
15. United States Agency for International Development (USAID)
16. International Initiative for Impact Evaluations (3ie)
17. European and Developing Countries Clinical Trials Partnership (EDCTP)
18. National Institutes of Health (USA) (NIH)
19. Canadian International Development Agency (CIDA)
20. Association of Commonwealth Universities (ACU)
21. Global Health Research Initiative (Canada) (GHRI)
22. Alliance for Health Policy and Systems Research (AHPSR)

The other eight organizations with a formal stance defined the field as consisting of actions to:

- Identify problems and develop and test practical solutions to those problems that are specific to particular health systems and environments.
- Undertake impact evaluation aimed at assessment of the contributions made by interventions of different programmes.
- Assess the improvement in practices and services as a result of the programmes' interventions.

Implementation research was also conceived as:

- Health services research aimed at bringing research into practice and policy.
- Methodology to establish the degree to which implementation strategy success can be generalized before scaling-up.

It can be seen from these definitions that implementation research is not clearly distinguished from impact evaluation which, as discussed in chapter 2 of this report, addresses the consequences rather than the processes of implementation.

Among those organizations that could not offer any formal definition for implementation research the field was understandably described as covering a wide range of subjects. Some of these have been identified at a higher level of generality, overlapping with or even outside implementation research. These include:

- operations research
- health and social care services research
- applied research
- health systems/services research
- optimization research
- translational research
- cost-effectiveness research.

Without an agreed-upon definition of the field it is practically impossible to collate studies, review progress and to make

decisions on how to move this field forward. Furthermore, lack of precision is leading some agencies to misclassify or conflate diverse forms of research investments, and therefore to conclude that there is no pressing need for them to help develop or invest in implementation research.

## Investing in implementation research

The majority of funders of global health programmes provide funding directly to low-income and middle-income countries (LMIC) so that these countries can achieve their implementation goal through country institutions and individual researchers (e.g. the Global Fund, TDR, Wellcome Trust, HRP, and 3ie). Funding is mostly provided through grants mechanisms (e.g. TDR, Wellcome Trust, EDCTP, NORAD, and DFID). However, a broad variety of approaches are used to integrate financial support through grants and other types of programmes. While the Global Fund and GAVI do not have separate funding for implementation research, they encourage applicants to include implementation research activities in the monitoring and evaluation (M&E) section of their application, as a means of addressing specific concerns in roll-out and scaling-up of massive disease control programmes. For instance, the Global Fund encourages fund recipients to devote 5–10% of their budget to monitoring & evaluation (which may include implementation research). Moreover, after much observation of the ad hoc efforts made by such fund recipients in the field of operations/implementation research, the Global Fund/WHO/TDR published a framework in 2008 on standardizing operations and implementation research, which also received endorsement from USAID, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Bank (TDR, 2008).

The more traditional research funding agencies (TDR; the Alliance for Health Policy and Systems Research, AHPSR; CDC-DHAP; NIH; HRP; and RBM), organize their implementation research support through dedicated resources for extramural research on the subject, and target implementation research through specific calls for proposals. Larger organizations such as the World Bank and CDC conduct in-house implementation research through the organization's professional staff and within specialized units for analysis and evaluation.

Implementation research is often funded to cover moderately long follow-up periods, with half of funders investing in three to six year projects. While such funding is commendable, the long scaling-up periods that characterize many disease control programmes calls for implementation research to accompany these programmes all the way from adoption to full-scale implementation so as to improve knowledge on equity and effectiveness.

Most funding agencies cannot as yet attest to the benefits that implementation research has had for global health, given that most funding in the area has only existed for a couple of years. However, some insight is already available – particularly for malaria prevention and treatment programmes where implementation research has been successful in orientating the best ways to scale up use of insecticide-treated nets (ITNs). The United Republic of Tanzania's National Voucher Scheme was mentioned as a programme that included a pioneer study on the benefits of financial innovations to ensure access to ITNs (Hanson et al., 2008).

### Dissemination of implementation research

Peer-review journals are the main way that results from projects funded by global funders are disseminated. Organizations such as the CDC, RBM, AHPSR and GHRI

also encourage traditional or innovative means of broadcasting their implementation research results, including word-of-mouth (CDC), direct distribution of products (CDC), the use of working groups (RBM) and an open access library for researchers (GHRI). Increased interest in the field is also leading to result dissemination at conferences and meetings such as the Global Forum for Health Research annual meetings and the Ministerial Summits on Health Research for Development, held every four years. Since 2007 the NIH has supported an annual Conference on the Science of Dissemination and Implementation, directed specifically to the subject. The majority of papers presented are by NIH supported USA-based researchers. This meeting has grown tremendously from 350 attendees in 2007 to over 900 in 2010. The 2011 Conference included, for the first time, a track on global health that recognizes implementation research for the support of health programme investments in LMICs.

Implementation research requires rapid and widespread dissemination of results, with policy-makers, analysts and the global health community being particular targets. It is therefore salutary that implementation research is now stimulating the rise of new journals while seeking open access through the Internet. These journals include: *Implementation Science*, *BMC Public Health* and *Health Research Policy and Systems*. Such journals assign full copyright to authors and make no money once the papers are published. Instead, they request authors to pay for publication up-front. Donor funding can easily be identified to support such efforts.

### Capacity building and strengthening for implementation research

Capacity building and strengthening for implementation research are essential if institutions and researchers from LMIC as well as from high-income countries (HIC)



are to contribute to this emerging field in a context where health systems research in general has a worldwide shortage of capacity (see chapter 10). It was therefore encouraging to find that nine of the 21 programmes reviewed support capacity strengthening for implementation research, and that some give a high degree of attention to this area, designating up to 40% of their budget towards capacity strengthening.

Nonetheless, a lack of capacity for implementation research constitutes a barrier for the scale-up of research projects in this field. This barrier is clearly perceived by funders. A foundation for building capacity in the field can be laid through competency-based curriculum development efforts as well as through identifying and instituting career paths that will encourage young researchers to consider implementation research for their professional development. Funders are already collaborating to lay such foundations, as evidenced in the joint USAID–TDR effort to harmonize curriculum development for implementation research. However, greater attention has to be given to implementation research, for example, across schools of public health and in development and public administration postgraduate courses. Demonstrating that implementation research can have value for global health policy-making and for people's health should act as incentive for this. Short-term training courses and workshops provide an immediate opportunity for building implementation research capacity. These can provide basic skills in how to use research tools and methods and can aim to raise awareness for the use of research results among decision-makers and analysts. Both the EDCTP and the CDC–DPDM fund training opportunities through their research grants. Global funders are already responding to training opportunities where implementation research is a topic within wider courses. CDC–DPDM for example funds both one-time workshops and longer-term training initiatives such as the Field Epidemiology and Laboratory Training Program (FELTP), which is designed to help countries develop

public health strategies and to strengthen health systems and infrastructure. Similarly, the EDCTP supports data manager training programmes so that individual capacity is maintained once projects are finished. Another example of capacity strengthening is presented in Box 6.2.

#### **Box 6.2.**

#### **USA government targets large-scale capacity strengthening. The Medical Education Partnership Initiative**

The Department of Health and Human Services (USA) is partnering with the United States President's Emergency Plan for AIDS Relief (PEPFAR) with a plan to invest US\$ 130 million over the next five years to transform African medical education and dramatically increase the number of health-care workers. Through the Medical Education Partnership Initiative (MEPI), grants are being awarded directly to African institutions in a dozen countries, working in partnership with medical schools and universities in the USA. The initiative will form a network including about 30 regional partners, country health and education ministries, and more than 20 collaborators from the USA.

The strategy of this initiative is to build human capacity for health in Africa by strengthening the medical education system in an environment that values and nurtures research and which will contribute to the sustainability and quality of the overall effort. These models will also contribute to the sustainability of PEPFAR investments by (1) the provision of excellence in clinical training and (2) improving the capacity of medical students and faculty to participate in and carry out multidisciplinary locally-driven research that responds to the health needs of their communities and improves health outcomes for men, women, and children. Support for strengthening medical education in African institutions is also being provided by 23 institutes and centres at the NIH, CDC, USAID and the Health Resources Services Administration.



Support through collaboration and networks (see chapter 10) is important for capacity strengthening. The EDCTP emphasizes networks both between developing countries and between developed and developing countries, the former for technology transfer and the latter for mentorship and capacity sharing. A pre-condition for grant application at the EDCTP is collaboration between at least two EU Member States. DFID sets similar conditions, funding groups of organizations within what it calls the South–South Consortiums. NORAD, on the other hand, supports partnerships between developed and developing countries through bilateral donations.

Funders consider country ownership and involvement of local policy-makers in project design and implementation as key aspects of their implementation research initiatives. The Global Fund described their grant process and implementation as entirely country-driven, while HRP support regional advisory panels and community-based interventions. The TB REACH programme developed by the Stop TB partnership is country implemented, and as such guarantees recipient ownership from the start. Other organizations such as GHRI and NIH encourage sustainability elements within programmes and capacity building of local researchers and institutions.

## Funders and implementation research governance

To assess and improve the impact and value of global health programmes, it is critical that global actors that are responsible for programme financing and for research funding work in partnership with national actors, thus supporting integration at all levels. Principles of harmonization agreed through the Paris Declaration (2005)<sup>11</sup> should apply to implementation research. This way, governance will support integrated programme and research platforms on the ground that can deliver on agreed priorities.

The most common form of partnership that has been established for implementation research is between organizations that fund and implement global health research (See Box 6.3). Partnerships have led to joint funding mechanisms across CDC-DPDM, CDC-DHAP and across the Stop TB partnership, HRP, NORAD, USAID, NIH and ACU. Meanwhile ESSENCE on Health Research (Enhancing Support for Strengthening the Effectiveness of National Capacity Efforts) serves as a collaborative framework for funding agencies to ensure synergies in addressing research capacity needs (including health systems research capacity).<sup>12</sup> An outstanding governance innovation that follows the ESSENCE recommendations is the Implementation Research Platform led by AHPSR in partnership with TDR, HRP, CAH and supported by a grant from the Government of Norway (See Box 6.4).

11 Paris Declaration on AID Effectiveness: [http://www.adb.org/media/articles/2005/7033\\_international\\_community\\_aid/paris\\_declaration.pdf](http://www.adb.org/media/articles/2005/7033_international_community_aid/paris_declaration.pdf), accessed 30 September 2011.

12 ESSENCE: “An initiative to increase effectiveness of research for health in Africa”, see: <http://www.who.int/tdr/svc/partnerships/initiatives/essence>, accessed 30 September 2011.

**Box 6.3.****The Affordable Medicines Facility - malaria: A model of collaboration**

The Affordable Medicines Facility - malaria (AMFm) is an innovative financing mechanism to improve access to affordable antimalarial artemisinin combination therapies (ACTs) through the public, private not-for-profit and private for-profit sectors. As well as lowering prices, the AMFm seeks to improve access and use of ACTs by increasing availability and by reducing the use of non-effective medicines for malaria. It is a “buyer subsidy” that, by enabling access to effective medicines for malaria, aims to save lives. The AMFm is hosted and managed by the Global Fund, with key financial support provided by UNITAID, the United Kingdom and the Bill & Melinda Gates Foundation and with technical support provided by members of RBM.

AMFm and its partners emphasize implementation research and “learning-by-doing” during implementation. This includes an emphasis on the “why?” and “how?” of implementation as well as improved understanding of reasons why things are – or are not – progressing as expected and how to improve them. Applicants for its phase I round of proposals were encouraged to undertake country-specific implementation research activities as part of their monitoring and evaluation grants. Activities to strengthen implementation research capacity have been included as part of proposal development workshops.

**Box 6.4.****The Implementation Research Platform leads the way towards integration**

The Implementation Research Platform recognizes for the first time the role of implementation research in the scale-up of effective interventions aligned to the Millennium Development Goals (MDGs). The Platform both fosters collaboration across global health research funders (with complementary roles for health systems and disease control) and encourages the integration of research to policy-making at country level (through the teaming-up of actors in both fields). The Platform also strengthens the science base by providing incentives to multi-country regional research projects. Research is encouraged across MDG-aligned interventions to address the issues of vertical programme integration within national health systems. Still at a very early stage, the Platform is in the process of funding up to US\$ 500 000 per project for teams in Africa, Asia and Latin America and the Caribbean – working in collaboration with partners from the developed world. This sets projects up with the right scale and scope to interact with massive disease control programmes.

## Conclusions

The foundation of implementation research is weakened without a standard definition. There is an urgent need for such a definition and for uniform implementation research nomenclature. Lack of a standard definition makes it difficult for funders to advocate and allocate resources for the field. Confusion about implementation research versus other types of research makes funding of this new area of research difficult, as many organizations feel they already conduct and support the field. Without a definition of implementation research, no structure can be built (e.g. methodology, curriculum, career path) and few investors can be convinced to invest. Improved definitions and standards will lead to the identification of specific implementation research protocols and methods that will serve as knowledge-generating interventions complementary to disease control interventions.

Implementation research will help global funders to help themselves as well as support country partners in achieving global health goals, so implementation research investments must be encouraged. Although implementation research is only beginning to be embraced in global health, it has already gained wide recognition as a set of tools to address the complexity that is inherent to massive investments in disease control programmes on the ground and the multifaceted nature of the global health architecture. As the global health community worldwide develops more efficacious and cost-effective interventions and better ways to scale them up, it is realizing the importance of investing in implementation research to help assess the effectiveness of scale-up in terms of access while maintaining efficacy and safety.

Implementation research capacity needs to be built and strengthened to ensure this field of study itself can be scaled-up worldwide. While the recognition of the importance of this endeavour to global

health programme success has grown, the human capacity to carry out the research has not kept pace. Some global health initiatives provide no funding for research capacity building, making their investment in research much less valuable. Often capacity building is left to the limited funding provided by bilateral and multilateral research organizations, United Nations partners and private foundations: capacity building efforts may be disconnected from the larger development programmes. To achieve global health goals, scaling up of implementation research capacity must be “front and centre” and linked to large global health programmes. Good practices of collaboration between developing countries and between developing/developed countries should be replicated at a larger level and implementation research capacity development should take place in LMIC research institutions.

Finally, partnerships are essential. No single entity can accomplish good global health on its own, especially given the diverse funding, resource channelling and implementing organizations working in the field of global health. Diversity is an asset as it allows actors to mobilize complementary values and sources of funding and to direct them to multiple opportunities and goals. However, innovative forms of governance are needed to ensure harmonization, particularly so that national actors can benefit. Various forums have been established to allow international funders and agencies for international development to coordinate and harmonize their efforts. Working together through such innovative models of partnership can lead to a global health architecture with a clear agenda and shared research priorities, methods and protocols. This way, the gap between “what we know” and “what we do” can be addressed systematically.



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## Chapter 7: Implementation research and patient safety

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Millennia ago, Hippocrates recognized the potential for injuries that arise from the well-intentioned actions of healers. Greek healers in the 4th Century B.C. drafted the Hippocratic Oath and pledged to “prescribe regimens for the good of my patients according to my ability and my judgment and never do harm to anyone.” Since then, the directive “first do no harm” has become a central tenet in contemporary medicine. However, recent evidence on the harm that health care can produce has led to patient safety being referred to as an endemic concern. It is important to remember that health care includes preventive interventions (e.g. vaccinations) or medical assistance given to healthy population (e.g. pregnancy and delivery, perinatal care, geriatric assistance, etc). This chapter aims to highlight the need for implementation research to address the harm caused by health-care interventions, and to advocate for patient safety as a means of ensuring effective implementation of disease control programmes.

Patient safety is defined as freedom from unnecessary harm or potential harm associated with health care. Patient safety is a health-care discipline that emphasizes the identification, harm mitigation, and prevention of health care failures that often lead to harm to patients or to users of health care. In this context, patient safety should be considered as a key element in the risk-benefit assessment of any medical intervention or assistance.

Available data suggest that harm from health care poses a substantial burden in terms of morbidity and mortality on people around the world. Much of the evidence base has

been created in the developed nations, although there is some epidemiological evidence of poor clinical outcomes due to unsafe medical care in developing countries and countries with economies in transition. According to recent studies poor health care is responsible for at least one adverse event occurring in about 10% of hospitalizations in middle- to high-income countries, causing thousands of deaths every year (Kohn et al., 2000; NPSA, 2004).

The situation is thought to be more acute in developing countries, although currently there is insufficient information to sustain that assumption. The risk of health-care-associated infection in some developing countries is as much as 20 times higher than in developed countries (World Alliance for Patient Safety, 2005; Zaidi et al., 2005). For instance, the proportion of injections given with syringes or needles reused without sterilization is as high as 70% in some countries, exposing millions of people to potential infections (Simonsen et al., 1999).

It is not the intent of the health professional to hurt patients. As Dr Lucian Leape stated when testifying to the (USA) President's Advisory Commission on Consumer Protection and Quality in the Health Care Industry, “Human beings make mistakes because the systems, tasks and processes they work in are poorly designed”. This is especially true in developing countries where health professionals are expected to carry out their job and deal with complicated situations with very limited resources. Often doctors and nurses have not received adequate training, are not adequately supervised, do not have protocols to follow, and do not have means to adequately record or communicate patients' information. Often they do not even have running water with which to wash their hands. Patient safety has to be addressed from a system perspective, examining the situation and putting in place the mechanisms to minimize the risk of harm. Blaming individuals for patient harm



can only lead to fear and occultism and cannot solve the underlying factors that lead to harm, which are often multiple.

Factors that contribute to unsafe care can be considered with reference to the health system dimensions of structure, process and outcome (Donabedian, 1966).

- **Structure:** comprises the resources and organizational arrangements that need to be in place to deliver care. Failures that occur in the infrastructure of health services, in the deployment of personnel, and in the availability of necessary goods and devices reflect poor structures and expose patients to harm.
- **Processes:** refer to the activities of health workers for delivering care, as well as other interactions in the operations of health care. For example, some of the most frequent underlying causes of patient safety problems, such as poor communication between clinicians, reflect poor processes.
- **Outcomes:** these are the results or consequences of clinical activities. Specific consequences, such as health-care-associated infections and adverse drug events, can be categorized as outcomes of unsafe care.

The importance of the problem is highlighted when looking at patient harm in relation to these dimensions from a developing country perspective. There are many recognizable health care safety concerns in such countries: scarce hygiene practices, unsafe maternal and newborn care, unsafe injection practices and blood transfusions, misdiagnosis and delays in diagnosis and referrals, unsafe surgical care, inappropriate disease and case management, insufficient patient adherence to treatment, poor management of health-care waste and other concerns, including those associated with the lack of access to effective medicines.

Safety concerns also abound in the use of drugs: overuse of injections when oral

formulations would be more appropriate, failure to prescribe in accordance with recommended guidelines, self-medication, and non-adherence to dosing regimes. Irrational drug prescribing and dispensing, and patients' failure to take medicines correctly, are the root causes of many safety problems. At its worst, fake or substandard drugs are estimated to account for up to 30% of the medicines consumed in developing countries (IMPACT, 2006; see Box 7.1.). The absence of pharmacovigilance systems to monitor and take action on adverse drug events (especially with the first large-scale introduction of a novel medicine such as an antimalarial to a developing country) and the improper disposal of unused or expired drugs together with their use beyond the expiry date further enhances the risk of poor therapeutic outcome and adverse events.

Patient harm can also arise less directly and can particularly affect diseases of poverty. Unsafe blood transfusion practices together with overuse of transfusions for complications of pregnancy, childhood anaemia and trauma increase the risk of transmission of many severe diseases such as HIV, hepatitis B and C, syphilis, malaria, Chagas disease and West Nile fever. Patient stigmatization can be a consequence of diagnosis or treatment for any of these diseases. Stigma can jeopardize not only the physical but also the emotional and social safety of individuals. At health care, individual, family and community level, stigma is an issue of concern that can jeopardize the outcome of interventions.

The ultimate beneficiaries of patient safety actions are patients, their families and communities. In addition, there are also direct benefits to health workers given their interest in safe working conditions and in quality care and to policy-makers given that patient safety can increase the effective adoption and scale-up of disease control programmes. Given the growing role of product development partnerships (PDPs) and global health initiatives (GHIs)



in addressing the generation and delivery of health tools, strategies and interventions, such partnership and initiatives should pay special attention to patient safety.

#### Box 7.1.

#### Patient safety threats from fake and substandard drugs

More and more products are being produced with an intention to cheat patients (e.g. mislabelled products, products with missing or insufficient quantities of active ingredients, or with incorrect active ingredients). These products account for more than 10% of the world's medicines market.<sup>1</sup> In addition, substandard drugs (produced by legitimate manufacturers) that do not meet quality specifications due to deficiencies in the manufacturing process are also reaching patients. Most fake medicines are sold as treatments for life-threatening conditions (such as malaria, tuberculosis and HIV/AIDS). However, expensive lifestyle drugs, such as hormones, steroids and antihistamines are also appearing in developing countries. Furthermore, many drugs that are banned in industrialized countries often continue to be manufactured and sold in developing countries. Unfortunately, the exact cost on human life associated with the circulation of these products is unknown. International concern has prompted a mandate to WHO to establish an Intergovernmental Working Group to address the problem (World Health Assembly Decision WHA63(10) in 2010).

<sup>1</sup> See: <http://www.who.int/mediacentre/factsheets/fs275/en/>, accessed 30 September 2011.

## Challenges to patient safety interventions

Many disease control programmes in poor settings are delivered in the context of community-based or community-directed interventions (e.g. vaccination campaigns and mass drug distributions). In these circumstances, health care is often poorly integrated and delivered through weak systems with suboptimal infrastructure, where it is difficult to apply universal standards and protocols. Measures as simple as hand hygiene (proven to be efficient in the reduction of hospital acquired infections) are often difficult for health-care professionals, patients or families to implement. Lack of clean running water, soap or alcohol-based hand rub impede compliance with this measure

The lack of a culture of patient safety and high levels of illiteracy impede recognition of many of the failures or problems with drugs, vaccines and devices. The frequency of use of informal and uncertified providers of care – such as vendors, community aids/facilitators, informal attendants and traditional healers – also has to be borne in mind. Most health systems in developing countries do not have the mechanisms to deal with the consequences of harm when it has occurred, and face great difficulties in deploying quality and patient-centred health care.

Patient safety is also challenged by a marked weakness of the legal and regulatory framework to address its social, political and economic implications at the various health system levels. In particular, there is a lack of appropriate frameworks to monitor the introduction of new drugs in the health-care system, impeding the reporting of adverse drug reactions and of adverse drug events. Fragmentation and a lack of integration of many disease control programmes in the health-care system may also hinder the coordinated consideration of patient safety issues. Many disease control programmes or health interventions address patient safety marginally or outside the context of health-care delivery organizations.

## Scope of implementation research for patient safety

Evidence about the magnitude of unsafe care, its root causes and contributing factors, as well as the most cost-effective solutions for the most frequent problems is very limited. In 2006, the WHO Patient Safety Programme set up an international expert working group to identify a global agenda for patient safety research. Its aim was to provide general guidance to research commissioners and funding institutions on the priority topic areas where new research will significantly contribute to improve patient safety. In mid-2007, after a rigorous literature review, assessment and consensus building efforts, the expert working group delivered a list of research priority areas (Table 7.1). The expert group stressed the importance of using global priorities as a guideline and to engage in priority setting to respond to local needs (World Alliance for Patient Safety, 2008; The Research Priority Setting Working Group, 2008).

The main emphasis in developing countries and countries with economies in transition focused precisely on the importance of promoting and fostering applied and evaluative research aimed at the identification and implementation of locally cost-effective solutions –that is, on what this report calls implementation research. It was recognized that only the knowledge that responds to the priority needs and circumstances of the different local contexts can provide the tools to facilitate the change and momentum necessary to bring safer care.

The knowledge currently available on patient safety interventions provides guidance on efficacious solutions only for some of the most relevant problems and for highly specific settings. For example the use of the surgical checklist developed by WHO has proven to decrease adverse events related to surgery in several sites where the checklist was piloted (including hospitals in developing countries) by

50%. Similarly, adequate hand hygiene has proven to diminish to a great extent hospital acquired infections (Pittet & Boyce, 2001). Such interventions may require specific environments, a locally trained workforce or a particular organizational culture. They may need to be integrated with other interventions and solutions, or perhaps be delivered under specific conditions. Their implementation may need to be overcome particular barriers, such as staff resistance or the perceived lack of relevance. Also, their implementation may be so costly that potential benefit may be hindered. To ensure the successful implementation of interventions, it is necessary to investigate and learn how to adapt existing patient safety solutions to different local contexts in a manner that retains effectiveness.

Many patient safety problems have no applicable solutions as yet. For example, the optimal strategies to ensure the correct prescription of antibiotics in community-based settings; or the most successful messages to increase compliance with hand hygiene practices by ancillary staff in developing countries remain unknown. Nevertheless, in many cases it is possible to develop practical approaches that facilitate local improvement. It is imperative to address local priorities and to do so, in many cases, practical solutions will need to be developed.

Patient safety implementation research requires a wide range of researchers. Health services and health systems researchers and epidemiologists should become familiar and, to an extent become specialized in studying the performance and quality of health services that are relevant to patient safety. Public health officers, clinicians and administrators can be trained and encouraged to support implementation research to introduce quality and safety interventions and strategies. To this end, such professionals require a broad understanding of the principles of research and epidemiology, and should be willing to investigate patient safety concerns. Specialists in human behaviour

**Table 7.1. Top five research priorities in developing countries and research questions emerging from the Patient Safety Expert Working Group**

TOPIC	RESEARCH QUESTION
1 <b>Counterfeit and substandard drugs</b>	<p>How effective are regulatory actions and interventions in addressing this issue?</p> <p>How much do counterfeit and substandard drugs contribute to the problems of patient safety?</p> <p>What are the factors that lead to the use of counterfeit and substandard drugs?</p>
2 <b>Inadequate competence training and skills</b>	<p>Are health-care professionals adequately trained in assessing and dealing with patients with reported adverse events or medical errors?</p> <p>Is patient safety a specific topic in the core curricula of physicians, nurses and health managers?</p> <p>What kind of continuing medical education programmes are most effective for ensuring that physicians and nurses retain competency in patient safety?</p>
3 <b>Maternal and newborn care</b>	<p>What are the main safety issues in maternal and newborn care?</p> <p>What is the burden of unsafe maternal and newborn care?</p> <p>What are the most cost-effective strategies for improving the safety of maternal and newborn care?</p> <p>What resources and systems are needed to implement recommended maternal and newborn care interventions effectively?</p>
4 <b>Health-care-associated infections</b>	<p>What are the epidemiology of and risk factors for health-care-associated infections in hospitals?</p> <p>What is the availability and cost of commercial hand-rub products and how does that affect hand hygiene promotion strategies?</p> <p>What strategies are effective in optimizing participation in infection control practices?</p> <p>Are there effective plans in place for the control of epidemic outbreaks of health-care-associated infections?</p> <p>Does use of new practices (e.g. silver-coated catheters) reduce the incidence of health care-associated infections?</p>
5 <b>Unsafe injection practices</b>	<p>How much awareness and information is there among health personnel about the risks of unsafe injection practices?</p> <p>How should the local production of inexpensive syringes be promoted?</p> <p>Are there adequate safe injection protocols in place?</p> <p>What are the main issues for lack of compliance with safe injection practices?</p>

and organizational psychology can make important contributions to patient safety given the difficulty in addressing behaviour change under adverse conditions. Finally, specialists in research and knowledge translation can play a critical role to help bridge the research and practice communities with specialized methods to tackle difficult patient safety issues.

Implementation research on patient safety must be considered from two complementary perspectives, that of health services and that of disease control programmes. Research at the health services level should include research on a full spectrum of preventive and curative interventions and should include the formal and informal sectors. Implementation research can significantly contribute to meet the following cross-cutting patient safety needs:

- Define the magnitude of the problem – by focusing on implementation of effective safety interventions.
- Raise awareness – by identifying critical implementation areas.
- Prioritize patient safety implementation at local level – using rigorous methodologies involving needs assessment.
- Identify and develop locally effective solutions – by highlighting implementation barriers.
- Evaluate the effectiveness of the implementation process in the roll-out and scaling-up of patient safety solutions.
- Identify existing policies that are effective in terms of their ability to improve access to health interventions by the most needy.
- Define how to engage health users to be active participants in patient safety and how to mobilize communities to work together to identify solutions to safety issues.
- Propose how to address patient safety concerns of users.

### Implementation research for patient safety in the scale-up of disease control programmes

It is unacceptable to put any person at risk when implementing a population targeted disease control programme or intervention. But interventions that have proven safe and efficient in some settings could pose a risk to patients in a different context. For instance, a certain surgical technique could be safe and efficient if performed by skilled professionals but could be risky if performed by personnel with inadequate training. A treatment that requires some level of patient involvement and compliance can pose a risk if patients do not adequately receive appropriate information. A vaccination campaign could be a disaster if an adequate supply of disposal syringes is unavailable.

Implementation research can play a critical role in reducing the risk to patients when rolling-out interventions at the individual or community levels, or during scaling-up. Research is needed to identify the different risks to patients under different disease control programmes. Implementation research can contribute to the following important patient safety requirements for disease control:

- Identification of the health workforce training needs on critical safety concerns in the context of scaling-up interventions.
- Evaluation of the essential hygiene conditions for when an intervention is administered.
- Availability to patient safety guidelines and protocols for the personnel delivering the intervention.
- Availability of the necessary equipment (e.g. an adequate supply of sterile syringes in a vaccination campaign).
- Availability of information for patients about the intervention, particularly on how to comply with treatments and about their efficacy and risks.

- Availability of an adequate infrastructure (such as a cold chain) to ensure and maintain the quality of intervention products.
- Compliance with ethical and quality standards to avoid moral harm (such as stigmatization) to patients.
- Mechanisms to strengthen the prescription practices of pharmacists, drug dispensers and community workers in the context of poverty and weak health systems.
- Prevention of treatment errors when running mass delivery strategies for disease control programmes.

**Box 7.2.****Pharmacovigilance framework**

Pharmacovigilance is the science of collecting, monitoring, researching, assessing and evaluating information from health-care providers and patients on the adverse effects of medicines or biological products (including herbal and traditional medicines) in order to:

- (a) identify hazards associated with use of particular medicines or biological products;
- (b) assess the risk-benefit ratio in order to maximize benefit to patients while minimizing harm.

Pharmacovigilance itself can be the subject of implementation research as it has to be developed and strengthened for specific disease control programmes and across the health system. Priority areas for research could include how to:

- optimize post-registration risk detection systems with patient participation;
- optimize the roles and responsibilities of stakeholders (e.g. patients, prescribers, drug sponsors, product development partnerships (PDPs), suppliers, providers, health authorities and global health initiatives) in actions that minimize risk;
- define realistic product risk-benefit ratios.

Implementation research should include the evaluation of drug safety in the health-care process after regulatory approval, particularly when interventions are scaled-up and operate under real programme conditions. Pharmacovigilance (see Box 7.2) can be viewed as an implementation research component during roll-out and scaling-up of new drugs. It is particularly important during scaling-up use of a drug in developing countries, where it is common to observe changes in product label and recommendations for use: sometimes a drug continues to be used even after marketing authorizations have been withdrawn. Given that increased numbers of new products are being adopted for specific developing countries diseases or needs, it is imperative to conduct research that will define the best approaches to achieve the objectives of pharmacovigilance, given local realities and capacities.

Furthermore, implementation research can be valuable in addressing the issue of fake or substandard products, as outlined in Table 7.1.

**Patient safety perspective in implementation research**

Many disease control programmes already conduct research to evaluate the effectiveness of specific interventions when adapted to different contexts (e.g. when trying specific local solutions or when rolling out mass control programmes). The research protocols often require small changes in the normal delivery of the health-care programmes (e.g. modified drug-packaging or dosage, a new combination of drugs, or the assignment of specific roles within closed communities). Research subjects often have to commit to certain behaviours or rules to be part of the study, and need to forgo other attitudes or practices. However, the effect of the research protocol on the well-being of the research subjects is often not investigated. Questions addressing this include:

“Have treatment needs been properly assessed and preserved when enrolling research subjects in the study?” and “Is the research at risk of stigmatizing participating or non-participating individuals?”

While such questions usually fall in the domain of research ethics, implementation researchers (and those designing and leading implementations research) need to consider such questions.

The individual and collective risks raised by a particular research protocol need to be anticipated and considered before performing any kind of implementation research. These include assessing if:

- the infrastructures used in the study are fit for purpose;
- staff involved in the study have the appropriate training as well as access to sufficient protocols or checklists (both for conducting the specific intervention and for problem solving and dealing with unexpected situations);
- any change in the treatment plan (such as a different dosage, combination or presentation of drugs) is adequately described and understood by all the study participants;
- any of the drugs may increase the risk of side-effects or complications;
- there are adequate plans to deal with possible adverse events, and if those responsible for implementation (a) have access to these plans during the intervention and (b) understand how to implement such plans.

The bottom line is that any change in the treatment plan, even if for the legitimate purposes of researching a more effective treatment, may result in additional risks for study participants. Such risks need to be anticipated and prevented or mitigated, and weighed up against the potential benefits of a study. Researchers and ethicists need to work together to identify such risks and set

up mechanisms to prevent research subjects from being harmed.

### Ethical issues of implementation research for patient safety

Many authors argue that health-care organizations have a moral obligation to work to continuously improve the quality and safety of care delivered to patients (Baily et al., 2006; Bellin & Dubler, 2001). Eran Bellin and Nancy Dubler suggest that patient safety research and implementation has to be conducted with appropriate ethical standards: “in an implicit social contract... the medical care community obligates itself to prevent failures, identify them when they occur, learn from them, and preclude their repetition.” Some difficulties in interpreting how to apply ethical principles to the conduct of patient safety research have arisen because of the complex characteristics of the subjects, the sensitivity of some of the data collected, and also the difficulty in differentiating the research study environment from regular daily practice. Issues include:

- when and how to seek informed consent
- how to protect privacy and confidentiality
- how to respond to an adverse event
- how to communicate adverse events to patients and health care personnel.

As yet there are no clear ways to address such concerns. The lack of well established guidance in this area creates uncertainty for both researchers and ethics reviewers. This leads to difficulties in how research projects are reviewed and conducted. In some instances this has led to researchers shying away from submitting proposals to ethics review committees or has led to reviewers failing to understand proposals. Guidance on how to apply the well established principles of ethics to patient safety research is imperative if patient safety is to be improved.



## Conclusions

Individuals receiving a health intervention expect to benefit from it; they do not expect it to cause harm to them, their families or their community. Patient safety is a fundamental condition for successful implementation of new products or strategies, and has to be considered in product design, implementation and scaling-up.

Health-care delivery is complex; there are many risks that need to be mitigated if the exposure of patients to avoidable harm is to be minimized. Global health initiatives targeting specific diseases of poverty should embrace patient safety when rolling out interventions; this should strengthen health systems. This is often not the case, especially in developing countries. Latent factors that may lead to avoidable harm are many and include the lack of critical support systems, strategies, guidelines, tools and patient safety standards.

Harmful incidents are often related to failures of commission (those that occur at the end of the delivery chain, such as the bedside or the operating theatre) or failures of omission (those that relate to the failure to act). Most are associated with underlying problems such as the lack of adequate capacity, training, regulations or tools. This limited awareness of the risks to patient safety in health care is also a very important constraint to implement patient safety programs.

Political pressure to overcome the high burden of disease in developing countries often emphasizes the implementation of specific control programmes to the detriment of other cross-cutting issues such as patient safety (both at the health system level and within specific disease control programmes). Implementation research can help strengthen patient safety at both levels by improving the understanding of how solutions can be adapted to local circumstances, how new safeguards can be designed and implemented in resource poor settings, and of what the conditions are for the safe roll-out of existing

and innovative interventions in large, complex and resource constrained settings.

Many potential causes of patient harm can be addressed even in the most resource limited settings. Recognizing the underlying conditions that lead to patient harm is essential if harm is to be reduced. Implementation research is needed to understand how patient safety solutions might best be adapted to specific disease control programmes, and how to safely extend the benefits of disease control programmes across the health system.

Strengthening patient safety activities, requires substantial political commitment while guidance on how to apply ethics principles to patient safety research is imperative to improve patient safety.

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## Chapter 8: Country actors and communities for participatory implementation research

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Walter Flores and  
David Zakus

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Implementation of innovations faces particular constraints in relation to creating and responding to demand, and in mobilizing health workers, local actors, intended beneficiaries and civil society as a whole (the latter are particularly important in promoting and facilitating adoption). To ensure that innovations are adopted and scaled-up within countries, particularly at the community level, innovations need to have features that will ensure their adaptability to the local health system (TDR, 2003). Such features will help ensure that barriers between innovations and their intended beneficiaries are surmounted.

The participating and decision-making role of country and community actors in relation to health-care delivery has rapidly changed in the past decade or so. In many developing countries a wave of state reforms has been implemented – including decentralization, privatization and public–private partnerships. These reforms have transformed the structure and organization of ministries, local governments and other public agencies that traditionally were in charge of overseeing, financing and delivering health and social services to the population. Actors involved in adoption and scaling-up of disease control programmes are therefore much more varied than they used to be. For instance, health sector decentralization has meant that provincial and municipal governments, local health authorities, subcontracted private providers and civil society organizations are now included among those responsible for health policies, disease control interventions and service delivery. Meanwhile, a surge in international financing for disease control has led to the greater presence at country level of

donors, international financial organizations and international foundations.

These different groups all have diverse interests and respond to different incentives, making the goal of reaching agreement on working arrangements challenging (Zakus, 1998).

Successful joint collaboration among all or most of the key country and community actors requires communication, engagement and trust. It also demands skills to work with strategic issues, negotiation and conflict resolution. All of the above can only occur within a participatory approach, a key component of primary health care (Flores, 2010; Zakus & Lysack, 1998).

This chapter outlines an approach that attempts to make the tasks of adoption and scaling-up of innovation more effective through implementation research, and to ensure the inclusion of an increasingly diverse range of actors at country and community levels in the development of innovative approaches for access and delivery of new tools, strategies and interventions. First, the most common barriers to scaling-up access are addressed; a framework to deal with existing barriers through implementation research is then outlined.

### Community barriers to adoption and scaling-up

Disease control programmes face barriers to adoption and scaling-up within the health-care system and in social/material environments of potential beneficiaries. Cultural diversity, natural disasters, civil conflict and economic downturn are just some of the many factors that affect the appearance of barriers or exacerbate barriers that are already present. Health authorities, managers and practitioners must therefore pay close attention to the specific barriers to implementation that may exist in a given country or context.

Barriers to equitable access probably exist in all health-care systems, but particularly so in developing countries. If new technologies are delivered through the existing networks of facilities and providers, there is a clear chance that better-off populations may gain access and those regularly facing access barriers, including financial barriers, will not. This effect, known as “the inverse equity hypothesis,” creates an exacerbation of inequity during a given period that only diminishes once better-off populations have had their needs relatively satisfied (Victora et al., 2000).

The first implementation step in delivering new or improved tools, strategies and interventions is to inform key local stakeholders about expected benefits and challenges. Such stakeholders include front-line health-care workers, local authorities and informal leaders, as well as the intended beneficiaries themselves. In reality, this information usually reaches only technical experts and authorities. This is an important barrier to implementation. There is already evidence that front-line health-care workers feel poorly informed and not taken into account whenever decisions on new health-care interventions are carried out (Walker & Gilson, 2004). Without adequate information, front-line workers might perceive a new tool or intervention only as adding a burden to their work. Therefore, much more attention needs to be paid to involving primary care workers and informal leaders in decision making.

Intended beneficiaries (including patients and their guardians) also need clear and easy-to-understand information about the benefits, costs and risks of innovations, particularly if the adoption of a particular innovation affects options for seeking health-care, or involves changes to their schedule of visits to health-care facilities or to their schedule of treatment. In an assessment of the barriers to collaborative planning between municipal health authorities and community-based

organizations in Guatemala, community leaders perceived that Ministry of Health authorities were always imposing their own priorities for service delivery and seldom asked what the communities’ priorities were. Such situations lead communities to remain passive and disinterested in innovations, suspecting that changes to health-care provision are done for government interests only (Flores & Gomez, 2010). Without appropriate information, potential beneficiaries will not be clear about what they will gain from the use of a new tool, strategy or intervention.

Often, the implementation of new tools, strategies and interventions need additional public or donor funding. To keep control of additional expenditures, authorities may request details of inputs and services rendered (often including the registration of direct beneficiaries). This may also impose a barrier to access – particularly if beneficiaries perceive themselves to be outside legal mandates or if they are afraid of government interventions. For example, immigrants may delay seeking health care if there are registration requirements. The variable levels of stigma associated with some illnesses may also preclude potential beneficiaries accessing an innovation (Long et al., 2008).

New or improved technologies may make the use of public resources more efficient. However, their implementation may require additional investment. In some cases, financial costs may be transferred to local authorities or to direct beneficiaries, thus imposing important affordability barriers. While the adoption of a new technology might reduce some costs for families (e.g. by reducing the illness period or by avoiding disability), but in other cases it may increase costs (e.g. costs associated with diagnosis and treatment). This very real cost barrier can perhaps be addressed by a detailed priority setting and planning between national authorities and international donors.

Some questions relating to uptake that might be asked at this stage are:

- Is the new technology a highly priced patent drug?
- Are families expected to contribute with out-of-pocket co-payments for the new technology or service?
- Will the uptake of the new technology need more visits to a health-care facility, thereby incurring transportation costs and time costs?

Although tools are available to forecast the financial cost of adopting and scaling-up new technologies for public budgets, much less is known about the additional burdens that new technologies may impose on families. Close monitoring of such costs through implementation research can help assess the extent to which barriers are erected or surmounted through specific programme actions.

### Implementation research to address community barriers to adoption and scaling-up

Barriers to adoption and scaling-up are often complex and may involve many context-specific factors. Implementation research can respond to this problem and point to solutions that speed-up implementation. A framework for such research that would include all possible situations that may exist in different countries and communities is difficult to propose. However, basic, logical steps that can guide actions and strategy development, implementation and evaluation are discussed below.

#### 1. Identifying stakeholders and other key actors.

Stakeholder mapping is a basic research tool that has to be deployed at all levels to identify all actors with the power to ensure successful implementation. Some stakeholders, such as health authorities, programme managers and intended beneficiaries, are relatively easy

to identify. However, depending on the innovation and the disease area, other relevant stakeholders may need to be identified (e.g. in non-health sectors such as education, agriculture, engineering, industry, security and social services). Mapping of stakeholders, as suggested in chapter 3, should be comprehensive at country level and more selective as the analysis is carried to community level.

Many other actors also play important roles for implementation in disease control without necessarily being stakeholders. For instance, health-care facility cleaning and administrative staff often have good rapport with intended beneficiaries. They can play a critical positive role (e.g. by helping to communicate the benefits of an innovation) or a negative role (e.g. by spreading false rumours that may reduce acceptance of an innovation). Mass media plays a similar role and should be identified and involved as a valuable resource via which to communicate with potential beneficiaries, health-care professionals and the general public can take place.

Rapid political mapping and other similar techniques can be used to identify stakeholders and key actors. Understanding the interests of stakeholders in a particular innovation and appreciating the magnitude of their power can help forge alliances that ensure support or minimize resistance for an innovation (Flores & Gomez, 2010; Brinkerhoff & Crosby, 2002; Holland, 2007). The mapping process can be participatory – including authorities, managers, providers and key staff from other sectors. NGO representatives working in health and civil society organizations can complement government and private-sector participants and help achieve a comprehensive mapping of stakeholders and key social actors.

**2. Understanding barriers to access.** The specific nature of implementation barriers has to be identified if access to an innovation



is to be improved. Rapid organizational and financial assessments can be carried-out, paying particular attention to human resources and local conditions (Flores et al., 2009; Green, 2000; Collins, 1995). General questions to guide such organizational assessment include:

- Does the new technology require new skills from health-care providers?
- Is there a need to supply new equipment to health-care facilities?
- Are health-care providers and facilities accessible to potential beneficiaries?
- How can changes in health policy be best implemented to have the highest impact?
- Such questions generate more specific questions e.g.
- What new skills are required?
- How will these skills be provided, and by whom?

Rapid ethnographic assessments can address barriers stemming from the social and material conditions of beneficiaries. Such assessments may be conducted in a number of ways, such as through group and individual interviews, surveys and participant observations. They can provide valuable knowledge and understanding of (a) the characteristics of barriers and (b) ways to overcome such barriers (Narayanasamy, 2009; Scrimshaw & Gleason, 1992).

**3. Implementing strategies to overcome barriers.** Once actors and barriers have been identified and analysed, implementation research can help identify the most appropriate implementation strategies and plans. For instance, if the barrier to acquisition of a new technology is a long procurement process, critical stakeholders might include administrative and managerial personnel who can help design a strategy that ensures success. If the barrier is a lack of information for potential beneficiaries and lack of trust,

then community-based organizations and community leaders (together with any appropriate health facility personnel or authority) should be involved in designing and implementing the strategy.

In some cases there may be several strategies to overcome certain barriers. Field-testing of potential strategies can ensure that they will work in practice as well as on paper. It also ensures that implementation is cost effective and socially acceptable. Implementation research can help ensure that front-line health-care workers are fully involved in the design and implementation of the strategies to lower implementation barriers. These workers have privileged information and experience that is crucial to assess the feasibility of proposed changes and then see them through to implementation.

**4. Monitoring adoption and scaling-up.** After field testing strategies to overcome barriers, innovations have to be fully implemented and scaled-up. Field testing is generally a rapid exercise carried out in a limited geographical area. Thus, even with excellent field test results, there is still a need to closely monitor actual roll-out. New barriers might emerge during the rolling-out process, or the strategy might work differently once it is scaled-up. Whether a comprehensive or selective (rapid) monitoring system is implemented will depend on the characteristics of the new technology and the potential beneficiaries. Regardless of the degree of monitoring during roll out, it should include not only a survey of the actions within the health-care system (the supply side) but also a survey of what is happening with the beneficiaries of the innovation (the demand side). Setting up a monitoring system that includes both supply and demand side information is challenging and requires close collaboration between national health authorities, nongovernmental agencies and community-based organizations.

Nongovernmental agencies and community-based organizations are vital actors in the identification and analysis of barriers



affecting potential beneficiaries, particularly those stemming from the demand side. Many organizations already carry-out local level assessments as part of their routine activities, including surveys, group interviews and ethnographic studies. These organizations should be encouraged to take an active role in identifying pre-existing or emergent barriers to innovations, and in the design of strategies to lower barriers – including an ongoing monitoring system for adoption and scaling-up.

In some countries, new technologies and strategies for disease control have been introduced by NGOs as part of their own strategic development. Yet, a lack of coordination between NGOs and health authorities may hinder the full potential of such innovations, or inhibit their scaling-up through public providers and other NGOs. There is ample opportunity for collaboration (through implementation research) to make innovations more widely available and more effective. This implies strengthening capacities of both NGOs and health authorities to undertake well coordinated implementation research. Improving communication, transparency and mutual accountability can also contribute to successful collaboration.

## Conclusions

Adoption and scaling-up of disease control technologies and innovations are not easy tasks; nor are they tasks that only concern health authorities. Complex processes of implementation involve addressing different kinds of barriers and working with multiple stakeholders and actors both inside and outside the health-care sector. There is a need to complement the core aspects of innovations with features that will ensure their appropriateness and adaptability to the health system, beneficiary communities and the local context.

Country actors involved in adoption and scaling-up of disease control programmes are much more varied than they used to be. Actors will have diverse interests and respond to different incentives. A successful joint collaboration for implementation research requires communication, engagement and trust. It also demands skills to work with strategic issues, negotiation and conflict resolution. All of the above can only occur within a participatory approach.

Barriers for adoption are often complex and there are likely to be many context-specific factors involved. Implementation research can respond to their specific and changing nature of barriers and point towards ways of speeding up implementation. Several logical steps can guide actions and strategy development, implementation and evaluation. These steps include (a) identifying stakeholders, (b) understanding barriers, (c) overcoming barriers, and (d) monitoring adoption and scaling-up. Having all stakeholders and other key social actors agreeing on an intervention and scaling-up plans is a major challenge. This is where implementation research can play a valuable role.

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# PART III

## ROADMAP OF IMPLEMENTATION RESEARCH FOR ACCESS AND DELIVERY – CROSS- CUTTING THEMES





## Chapter 9: Current and foreseeable themes in implementation research for disease control

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Research on the success of implementation and scaling-up of innovative strategies, tools and interventions for disease control in poor countries can be critical to strengthening the decision-making capacity of health policy-makers, stakeholders and service managers. The question thus arises of the extent to which the literature covers critical disease control areas, and of the range of methods

and disciplines involved. Recognizing this diversity can be useful to improve research capacity as well as to identify gaps and opportunities for further research.

This chapter identifies the range and characteristics of implementation research by referencing the implementation of disease control interventions, particularly in relation to infectious disease control in poor countries and settings.

Information for this chapter was sought through search and review of both published and unpublished literature. The systematic search identified 237 papers in PubMed or other regional literature databases relevant to implementation research of diseases of poverty since 2005 (see Table 9.1). Additional publications analysed for this chapter came

**Table 9.1. Review of implementation research according to intervention areas**

Number of articles retrieved	Topic or intervention area	Specific examples
95	Maternal and reproductive health	Maternal mortality reduction programmes, comprehensive emergency obstetric care (CEmOC), emergency obstetric care (EOC), infertility diagnosis, prevention of postpartum haemorrhage, maternal referrals and care, Caesarean delivery, skilled birth attendant strategy, contraception, safe motherhood and new born health, abortion care, obstetric fistula, pregnancy outcomes, deliveries.
30	HIV/AIDS	Voluntary counseling and testing (VCT), care and treatment clinics (CTCs), government response, prevention of mother-to-child transmission (PMTCT), contraception and HIV/AIDS, HIV/AIDS certified deaths, behavioural prevention.
25	Tuberculosis, malaria, and other communicable diseases	Tuberculosis directly observed treatment short course, (TB-DOTS), care seeking, antimalarial drugs, bednets and other malaria control interventions, community-directed treatment of lymphatic filariasis.
16	Health Sector reforms and health systems	Hospital reforms, health financing, service integration, health equity, health insurance, sector wide approaches (SWAp), user fees, cross-sectorial coordination, private practices, pay for performance, patient information leaflets, referral systems, incentives to reduce health worker absenteeism.
13	Other areas in relation to health	Orphans and vulnerable children, surgery, emergency services, poverty, migration, human rights, globalization, inequality, school-based health interventions.
9	Nutrition	Micronutrients supplementation, malnutrition, rickets, conditional cash transfers, diabetes and over-nutrition.
5	Child health	Integrated management of childhood illness (IMCI), reaching every district (RED), newborn survival, perinatal mortality, immunization rates.
5	Mental health	Mental health programmes, depression, post-trauma interventions, conflict situations.
2	Technology	Mobile phone communications and health, hospital audits.



from suggestions from researchers who have conducted implementation research and also through recommendations from WHO regional offices.

### Implementation research focus

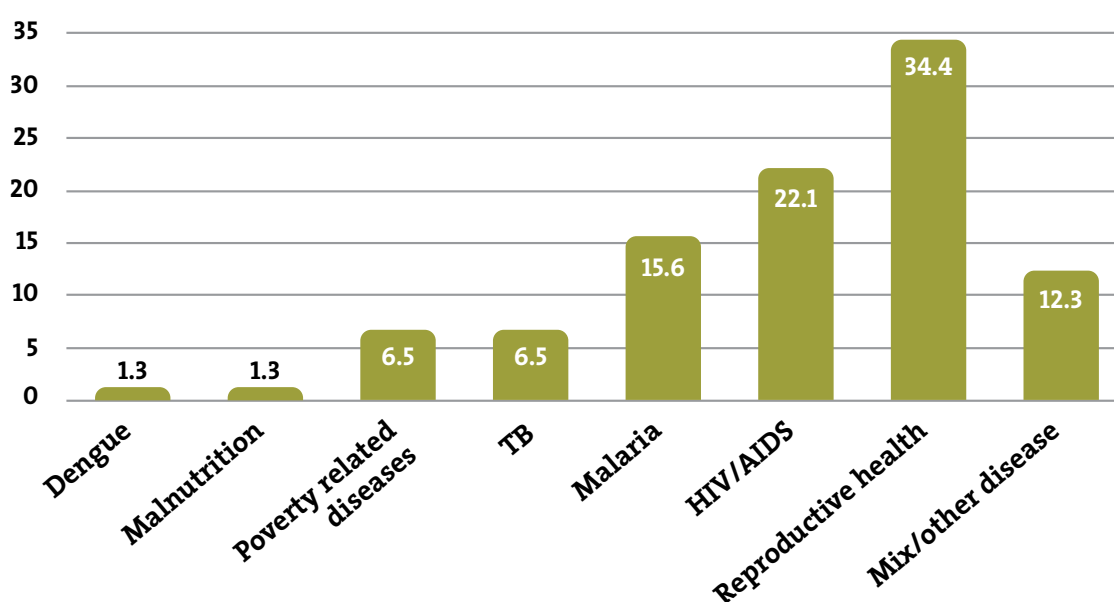
Implementation research literature can be classified in three ways – it may (a) focus on a specific intervention, disease or health problem (b) have wider focus – on a health programme or the health system, or (c) have dual focus.

It was found that 154 of the 237 implementation research papers (65%) had a specific disease or health problem focus while 209 (88%) had a wider programme or health system focus. Maternal and reproductive health and specific infectious diseases received most attention, while attention to many others diseases of poverty lagged far behind. Out of the 154 papers with a disease or health problem focus, 34.4% focused on maternal and reproductive

health, followed by 22.1% on HIV/AIDS and 15.6% on malaria (Fig. 9.1). Little attention has been given to the implementation of integrated disease control strategies.

Out of 209 papers with a health system focus, the prevailing themes, when classified by health system component (WHO, 2007), are governance (research concepts and findings on health system actors and strategic directions; 51.7%) and health service delivery (efficiency, efficacy, coverage and quality; 36.4%). Other components such as human resources and financing – key weaknesses in health systems received very low attention (e.g. human resources had only one paper; 0.5%) (Fig. 9.2).

Innovations reported in the literature have included the development of products (such as medicine formulations, vaccines and rapid diagnostics), tools and behaviour change strategies for disease prevention. Innovations have been followed by an increase in operations research to facilitate service delivery and



**Fig. 9.1.** Implementation research articles published according to disease or health problem focus, 2005–July 2010.  $n = 154$

Infectious disease implementation research in developing countries is concentrated in reproductive health, HIV-AIDS and Malaria.

by implementation research to inform implementation processes. As mentioned above, maternal and reproductive health and infectious disease research dominate the implementation research literature. Health sector reform has also had a generous share of the implementation research literature, following after implementation research for communicable diseases such as HIV/AIDS, tuberculosis and malaria. Other main areas of research include nutrition, child health, mental health and technology (see Table 9.1).

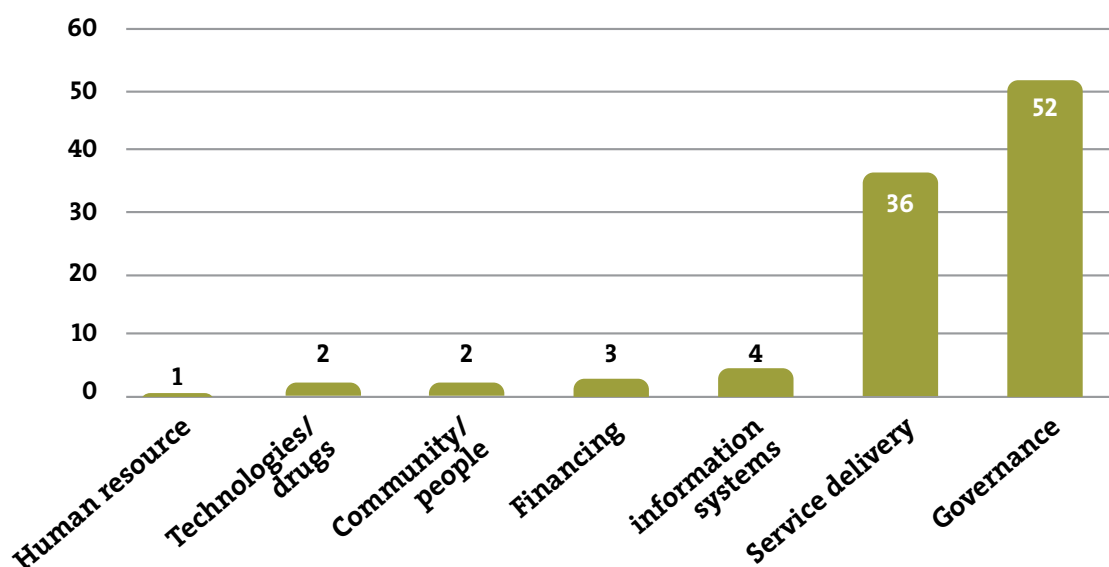
### Common methods in implementation research

Implementation research has mainly focused on increasing the efficiency of delivery of tools, strategies and interventions, assessing acceptance of new products, promoting accessibility (and targeting vulnerable groups), enhancing affordability (through variations in pricing), identifying barriers to implementation and determinants of technology adoption, assessing outcomes and

impacts of novel strategies for implementation, and estimating costs and comparative cost effectiveness. Effectiveness studies (also called impact evaluations, phase IV trials, or experimental evaluations) have claimed a role as the “gold standard” in the design and testing of improved implementation strategies. These trials commonly use mixed methods – both quantitative and qualitative techniques – to demonstrate both what works and why it works.

Traditional methods of qualitative and quantitative research have been used as means for undertaking implementation research. Although quantitative methods dominate the field it is common for studies to employ a mix of qualitative and quantitative methods, particularly where the study has multiple objectives.

Qualitative methods include cross-sectional surveys, longitudinal cohort studies, interrupted time series data, experimental and quasi-experimental evaluations, and retrospective reviews (meta-analyses) of



**Fig. 9.2.** Implementation research articles according to health system focus, January 2005–July 2010. n = 209

Implementation research articles concentrate on governance and service delivery processes.

**Box 9.1.****INDEPTH effectiveness and safety study (INESS) on antimalarials**

This implementation research project aims to develop and maintain a phase IV safety and effectiveness platform in Africa as well as to assess the effectiveness of new malaria treatments and the determinants of effectiveness in real life health systems and to evaluate the safety of new malarial treatments through comprehensive pharmacovigilance. Countries included in the study are Burkina Faso, Ghana, Mozambique and the United Republic of Tanzania.

The project includes seven modules for the application of both qualitative and quantitative methods to study the system effectiveness and safety of antimalarials in real life settings. The modules are: (1) access, (2) targeting accuracy and provider compliance, (3) patient

adherence, (4) community acceptance, (5) other contextual factors, (6) cost and policy analysis and (7) safety monitoring. Study methods include demographic and health household surveys, patient exit interviews, health facility surveys, health provider surveys, focus group discussions, in-depth interviews, illness narratives, stakeholder analysis, cohort event monitoring and data linkage using different databases. (Other less common methods that have been employed for implementation research are: ecological studies, exploratory multicentric descriptive studies, review of historical trends, policy analysis and mathematical modelling of intervention alternatives.)

**Box 9.2.****Community-based direct observed short-course treatment for the control of tuberculosis in Kilombero district, United Republic of Tanzania**

Scaling-up of directly observed tuberculosis treatment with short-course treatment (DOTS) could be achieved through community health workers in many contexts lacking professional health personnel. This project, in the United Republic of Tanzania, aimed to assess the efficiency, cost effectiveness and acceptability of community-based directly observed therapy (CBDOT) with a short treatment regimen, in comparison with the existing institutional-based (IBDOT) strategy. Study methods included an unmasked cluster-randomized controlled trial comparing CBDOT with that of IBDOT. The intervention involved training a community member to observe a patient daily during the first two intensive months of treatment (the “observer” living in the same village as

the patient). A fortnightly follow-up by the health worker from the health facility and a monthly visit by the district tuberculosis and leprosy coordinator was included. The visit involved monitoring of adherence by pill count and checking of treatment cards. During the intensive course, in the IBDOT arm of the study, patients were obliged to visit the health facility on a daily basis during the first 2 months of treatment to be observed swallowing their pills. The two interventions were compared, based on conversion rate (primary outcome) and cure rate (secondary outcome). (Lwilla et al., 2003).

published research. In some instances implementation research has involved qualitative methods such as in-depth interviews, focus group discussions, observations and ethnographic perspectives. Literature review of both published and unpublished data has also been used, some using systematic search strategies, while others using exploratory, scoping or horizon-scanning approaches.

Highly relevant and useful implementation research studies have been undertaken in poor countries such as the United Republic of Tanzania, demonstrating that well designed studies can become essential components of scaling-up of disease control programmes (see Boxes 9.1, 9.2 and 9.3).

### Nature of study conclusions and recommendations

Studies discussed in the implementation research literature can be characterized with respect to:

- a focus on descriptions of the status quo with existing programmes or more specific innovative tools, strategies and interventions;
- a focus on specific recommendations for innovations, or the application of known solutions;
- studies that propose broader policy innovations.

One useful example of descriptive research for a known intervention is the Caesarean Outcomes Study from the WHO Global Survey in Africa (Shah et al., 2009). According to African health facility surveys this study revealed limited Caesarean delivery and late emergency Caesareans; thus there is low impact on reduction of perinatal deaths. Other studies recommend specific interventions to ensure quality of care through improved processes of implementation. For example, a qualitative study on maternal referrals in rural United Republic of Tanzania

#### Box 9.3.

#### Assessment of a national voucher scheme to deliver insecticide-treated mosquito nets to pregnant women

The Tanzanian National Voucher Scheme is an innovative system that uses cash discounts as a means of targeting the delivery of insecticide-treated nets (ITNs) to pregnant women and infants. An analysis of the process was carried out to identify potential ways to equitably improve overall coverage of the scheme.

Study methods included a household survey where head of households and all women of childbearing age were interviewed. Additional modules were applied for women who had

had a live birth in the preceding 12 months, and for those pregnant at the time of survey. The socioeconomic status of each household was constructed using principal component analysis of household indicators, including asset ownership, housing conditions and education level of the head of household. A multistage cluster survey was undertaken of nationally representative households across 21 districts (Marchant et al., 2010).

describes the differences in health services delivery between hospitals and health centres, with the latter providing lower quality services (Pembe et al., 2008).

Studies have recommended continued monitoring and evaluation of disease control interventions, particularly as health programmes are dynamic and change with time and contexts. An example is an impact evaluation of India's Janani Suraksha Yojana (a conditional cash transfer programme to increase births in health facilities). This evaluation proposed continuous monitoring to measure the long-term effects of the programme (Lim et al., 2010). Such an approach is the health systems' equivalent of the post-approval surveillance of patient outcomes in drug trials, which often reveal unanticipated adverse events and other complications upon implementation.

More analytical studies attempt to determine the outcomes and impact of particular implementation strategies of interest. For example, an evaluation of mandatory HIV testing and uptake of antenatal services in Nigeria concluded that the intervention caused significant *decrease* in antenatal visits, leading to a recommendation to discourage the approach (Onah et al., 2008). A range of studies has been able to recommend policy innovation with specific options to address systematic or institutional failures in current implementation processes. In an attempt to develop standards for postpartum haemorrhage in Malawi, a study recommended involvement of stakeholders from multiple professions for a unified effort to promote ownership, sustainability and allocation of resources for implementation (Kongnyuy & van den Broek, 2009).

Studies focused on programme implementation have identified the barriers to the adoption of certain interventions. These types of implementation research characterize the temporal, geographical, and institutional dynamics involved in the delivery of an intervention, and seek to

understand how different factors that are responsible for implementation success interact. Others go further, outlining the consequences of implementation strategies and processes on the outcomes and impact of health programmes. An interesting study on the association between globalization and perinatal medicine concludes that poverty is related to maternal and childhood mortalities and morbidities and recommends that the world community prioritize and enact economic and social reforms to address the health needs of mothers and children (Martens et al., 2010).

Many implementation research studies recommend further research in the same area to allow for more data/better research designs to make generalization possible and to thus get greater support for recommendations aiming for policy change e.g. a study to evaluate the IMCI strategy in Zimbabwe found that there were few IMCI-trained health workers and that there was lack of essential drugs; in this case the authors recommended that a larger study be undertaken to design and test improved implementation strategies (Gombe et al., 2006). Given the need for research at multiple scales, in various contexts, and using a variety of methods, these publications refrain from making any definite conclusions.

### Gaps and opportunities for implementation research

While many studies address the implementation of proven health interventions, this has not necessarily translated into evidence that can influence policy. There is limited mention in the literature of how research results influence policy changes, or even future plans and strategies to promote evidence-based policy. The literature, to a large extent, misses the point that – unlike many other research fields – implementation research is a means to an end. This means that implementation research loses its uniqueness in being able to improve policies and processes.

Increased interest in implementation research provides an opportunity to standardize approaches and methods for specific research questions and objectives. It also provides a chance to clearly identify the capacity that different approaches and methods have for providing recommendations for policy-making, and so producing better evidenced-based policies.

Implementation research should look at the barriers to access that innovations impose on populations (see chapter 8). Results and recommendations from the research should provide knowledge and guidance on how to overcome these barriers as well as foster delivery of effective public health interventions to poor people. The key challenges to improve health conditions in low- and middle-income countries (LMICs) include unaffordable costs to households, limited availability of new products and health-care services, and inadequate design and organization of services.

Gaining access to health care is not only dependant on supply-side factors under the control of health providers. It also depends on demand by intended beneficiaries.

Whether a patient comes forward for medical treatment depends on many factors, including their ability to travel to health facilities and to pay for consultation fees and for drugs. It also depends on their perceptions of illness and knowledge of health services, as well as on gender and empowerment within their community.

Conceptual frameworks to identify the implementation research agenda should focus on both supply and demand factors in the implementation of existing and innovative tools, strategies and interventions. Such frameworks should allow for analysis and action to improve access issues in LMICs and for different diseases. The “four As” framework proposed by Reich and Frost in chapter 3 of this report outlines a framework to develop the research agenda, paying attention to both the demand and the supply side. The Novartis Foundation’s “five As” model, with its proposed focus on the barriers and facilitators to access in the course of the health-seeking process, is also worth outlining here (Obrist et al., 2007; see Table 9.2).

**Table 9.2. The five dimensions of access to health-care**

Dimension	Examples
<b>Availability.</b> Degree of fit between existing health services and clients’ needs	Therapies and necessary medical equipment for diseases; health personnel able to diagnose and treat diseases
<b>Accessibility.</b> Extent to which the geographical location of health service delivery coincides with the location of clients	Acceptable distances and transport to health services; health personnel offer services such as vaccination locally
<b>Affordability.</b> Degree of fit between service prices and clients’ ability to pay	Clients can pay fees of health services without selling critical assets, e.g. through health insurance coverage
<b>Adequacy.</b> Extent to which the organization of services meets clients’ expectations	Opening hours of services match daily schedules of clients (e.g. small-scale farmers) and are acceptable to health personnel (e.g. day/night shifts are established)
<b>Acceptability.</b> Degree of fit between characteristics of the provider and those of clients	The provider is able to communicate with the client during medical consultations; clients are satisfied with the welcome and quality of care

Source: Obrist et al., 2007.



Regardless of which framework is used, identification of the influence that each specific dimension has on access is essential for improvement of the implementation process.

In this framework, each dimension is associated with a specific actor or a set of actors who carry out the access activities. Actors involved at the international and regional levels include: international organizations, such as the World Health Organization (WHO); private-sector organizations at the global level, such as multinational pharmaceutical companies; and private and public sector donor organizations at the global level, such as the Bill & Melinda Gates Foundation. Within countries, the actors include national public sectors such as the health ministry, regional and community-based public sectors such as health-care providers and schools, private distributors, media outlets, and the end-users (including patients and consumers).

### Guidance for the implementation research agenda

Country needs assessments are required to orient the implementation research agenda. This should lead to the establishment of specific research priorities in close agreement across diverse actors and stakeholders. In some countries with no prior implementation research experience or capacity, the main focus could be on how to develop new projects through a relatively narrow partnership to inform broad health policy and programme implementation in the short-term. In other countries with ongoing implementation research projects and greater research capacity, diversification could ensue – with some projects still focusing on immediate programme implementation while others (developed through wider collaboration) focus on promoting more integrated and efficient health-care implementation.

Globally recommended and highly structured interventions such as DOTS are showing an increase in the diversity of implementation strategies at country level, whereby they are adapted according to the requirements of local health systems. While commendable, these efforts also require a diversity of implementation research approaches to ensure their success and rapid transfer for use in different contexts and countries. In most countries there is acceptance that a wide range of implementation research is needed to ensure compliance with globally agreed targets. There is also a strong desire to implement more effective implementation research projects with limited resources, and to demonstrate informative, relevant research results on a relatively shorter timescale (i.e. months rather than years).

Guidance is needed to help decide on the balance of different types of research required in each country. Several objectives can help develop guidance for the implementation research agenda. The first would be to ensure that the allocation of new health programme and research funding be related to the projects' potential impact on programme effectiveness. Second, to establish an external mandate based on research priorities that are clearly shared by policy-makers, programme managers and researchers. Third, to demonstrate accountability to stakeholders on whether community needs are being addressed through implementation research.

Several questions can be posed to ensure the development of country guidance, e.g.:

- What are the overall objectives of public health in this country?
- What tasks or actions should be implemented in order to achieve objectives?
- What are the barriers to achieving objectives?
- Is implementation research needed to improve health care quality, efficiency and effectiveness?

- What are the specific problems or gaps that implementation research can answer or resolve?
- Has implementation research been implemented (or is it being implemented) in this country?
- Does the existing implementation research respond to programme priorities?
- Is more implementation research needed to fulfil the overall objective of public health?
- What are the institutions and contexts that need to be targeted by further implementation research?

To help strengthen the impact of research on policy, the following questions should be answered:

- How will implementation research be used to inform policy and practice?
- Are existing knowledge translation mechanisms adequate?
- Are implementation research outcomes helping to solve problems?
- Is there a need for efforts to promote implementation research-based institutional learning and change within health institutions and programmes?

## Conclusions

Most of the implementation research literature focuses on a few health or disease control areas, chiefly reproductive health, HIV/AIDS, malaria and tuberculosis. Moreover, the health system is mainly analysed from the perspective of specific disease control programmes or overall health system design, with little attention being given to specific health system components such as information systems, financing, community participation, technologies or human resources. Little attention has been given to the implementation of integrated disease control strategies.

Implementation research has been undertaken using a wide range of methods, although quantitative studies predominate. The field has demonstrated its capacity to help make effective recommendations as part of monitoring and surveillance, in policy-making and as a tool for the scaling-up of programmes. The experience of the United Republic of Tanzania demonstrates that well-designed studies can be undertaken in poor countries through a modular approach that can be extended to study different disease control implementation challenges.

Implementation research is proven to contribute to effective and safe scale-up, so there is a need to advocate for more investment in the field and to strengthen research capacity across a wide range of health policies and programmes.

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## Chapter 10: Research capacity and governance for collaboration in implementation research

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To be effective, implementation research for access to innovations in disease control has to be closely engaged with health policy-makers and providers as well as with civil society organizations engaged in service delivery and representation. The research agenda needs to be identified through collaborative mechanisms to ensure research objectives and methods are appropriate to innovations and implementation processes, and that results are relevant and will be valued by stakeholders. Research itself requires adequate access to decision-makers, facilities and populations. Engagement with policy-makers, providers and civil society organizations requires, in turn, close relationships with actors at global, national and local levels to support the life-cycle of innovation development. Two key questions arise: (a) “What is the capacity to engage in implementation research, particularly from the perspective of poor countries and settings?” and (b) “What models and experiences are available to build and strengthen the type of capacity required for implementation research?”

This chapter addresses implementation research capacity by reviewing evidence on the characteristics of organizations undertaking implementation research, their country setting, their research focus and the inter-institutional collaboration. Evidence is based on past research as well as bibliometric analyses. Models available for collaboration are then addressed through a literature review. The chapter also reviews governance strategies for collaboration in implementation research that would more likely foster the field in the context of real-world innovations.

## Implementation research capacity

Units and institutions that can conduct high quality health systems research and more specifically implementation research are still scarce and weak in developing countries. In 2000, the Alliance for Health Policy and Systems Research was able to identify the existence of only 607 of them in the developing world, of which 176 were surveyed (González Block & Mills, 2003). These are mostly small units with an average portfolio of three projects then worth around US\$ 155 000, projected to US\$ 58 million overall or 0.007% of total health expenditure. International sources account for 69% of direct project funding, with national governments contributing 26% and private and other donors 5%. Actual research costs would be greater when considering infrastructure and salaries. The size of institutions is generally small, with only around 30% having more than 10 researchers and 24% having at least three researchers with a PhD (Fig. 10.1). (As a whole, only 19% of researchers had a PhD in 2000.) However, the interdisciplinary mix is important, with close to 80% having five or more disciplines. Most institutions report good engagement with policy-makers and programmes through diverse knowledge management strategies (Fig. 10.2).

Research capacity is now addressed by identifying and analysing the institutions worldwide that engage in implementation research through an analysis of publications to date (see Box 10.1 for details).

**Box 10.1.****Implementation research bibliometric methodology**

Two search strategies were used:

- (1) Exemplary publications from 2005 onwards were identified through a citations snow-ball strategy departing from exemplar publications focusing directly and mostly on implementation research (as defined by TDR in 2003) as well as on implementation research definitions now presented in chapter 2. The search was stopped after a reasonable sample of 112 publications was retrieved.
- (2). A systematic search in PubMed, African Index Medicus and BIREME to capture a wide range of research papers from 2005 onward. Medical subject headings (MeSH) were used as search terms (see below). A total of 125 publications were selected after reviewing abstracts. Results from both search strategies were merged for analysis for a total 237 publications.

MeSH search terms used to retrieve publications:

**Research terms**

- Translational research
- Operations research
- Community-based participatory research
- Process assessment (health care)

**Programme terms**

- Health plan implementation
- Government programmes
- National health programmes
- Organizational efficiency
- Patient acceptance of health care
- Health services accessibility
- Reproductive health services

**Diseases and health conditions**

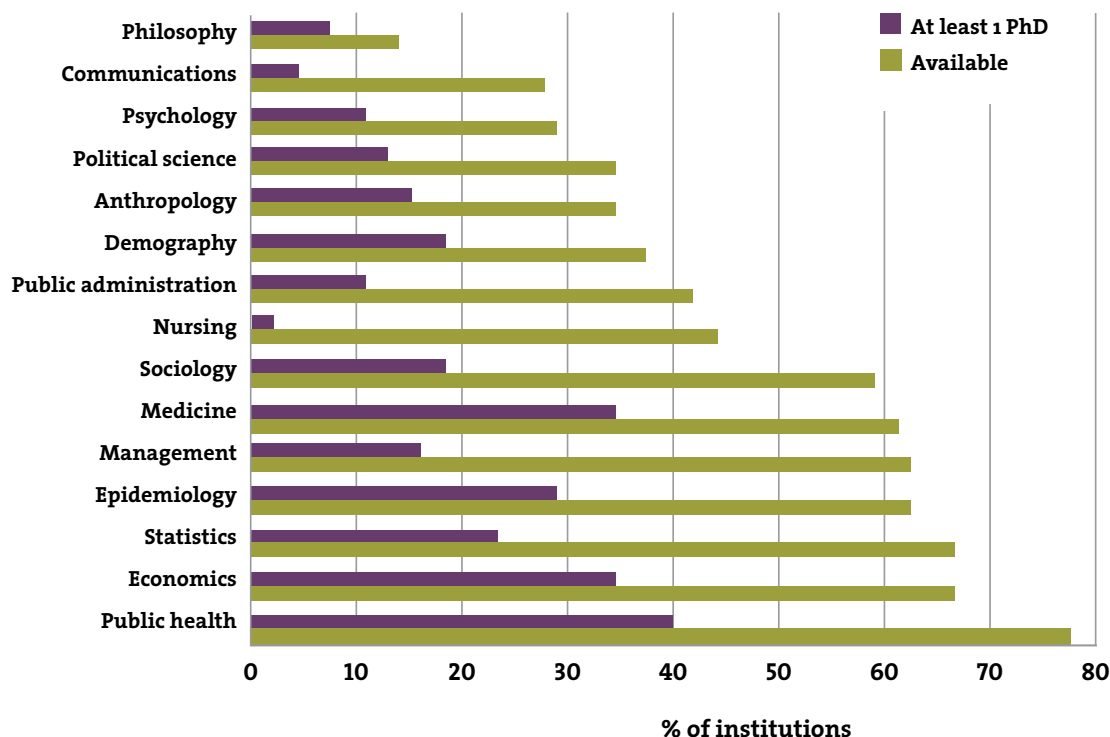
- Communicable diseases
- Malnutrition
- Maternal mortality

A marked increase in implementation research publications between 2005 and 2009 was noted; in 2005 only 6% of the total papers covered implementation research, while in 2009 this figure went up to 26% (Fig. 10.3).

In 78.0% of publications, the affiliation of first authors is to institutions with a national charter (including international nongovernmental organizations and NGOs) and to multilateral organizations for the remaining 22.0% (mostly the World Health Organization, WHO and the Pan American Health Organization, PAHO). Country affiliations of national institutions are 25.8% in the USA, followed by 15.2% in the United Kingdom. The developing country with greatest score of papers is South Africa with 4.2% (Table 10.1).

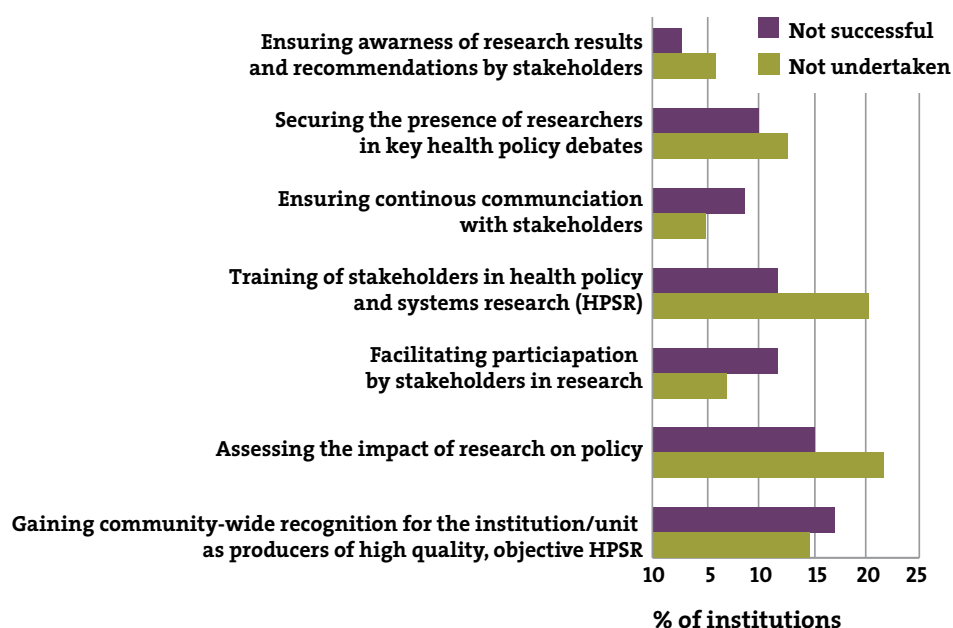
Considering all author institutions as units of analysis (426, when all unique author institutions are counted), 80% are national and the remaining 20% multilateral – mainly WHO. Considering national institutions, most are from high-income countries (69.0%), followed by those in low-income countries (16.5%) and then middle-income countries (14.5%). Top publishing institutions are from the USA with 31.2% of publications – far in front of the United Kingdom with 13%. Top developing country author institutions are from China (5%) and South Africa (3%). Universities and research institutions account for over half of institutions in the sample (66.2%) followed by multilateral institutions, mainly WHO and PAHO (12.2%). Health providers and health authorities account together for 16.0%, with industry and donors accounting for 5.7% (Fig. 10.4).

The frequency of papers coauthored by individuals from two or more institutions is high, (53.2% of publications in the sample). Of them, 53.0% include only national institutions whereas the remaining 47.0% correspond to collaborations across multilateral organizations. Considering the



**Fig. 10.1.** Disciplines available in institutions undertaking health policy and systems research in developing countries. 2000–2002

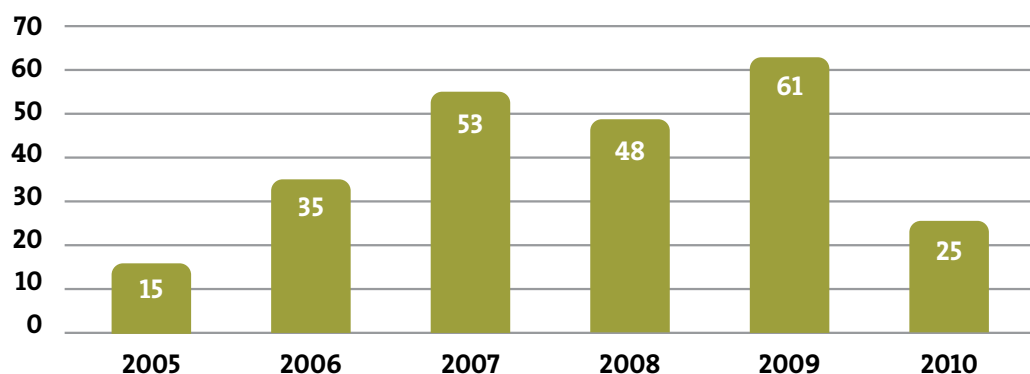
A wide array of disciplines is available for health systems research in developing countries, with public health and medicine being amongst the most available disciplines. *Source: González Block & Mills, 2003.*



**Fig. 10.2.** Engagement between researchers and stakeholders by institutions undertaking health policy and systems research in developing countries. 2000–2002

Assessing the impact of research on policy and training stakeholders in health policy and systems research are among the least undertaken liaison activities. *Source: González Block & Mills, 2003.*



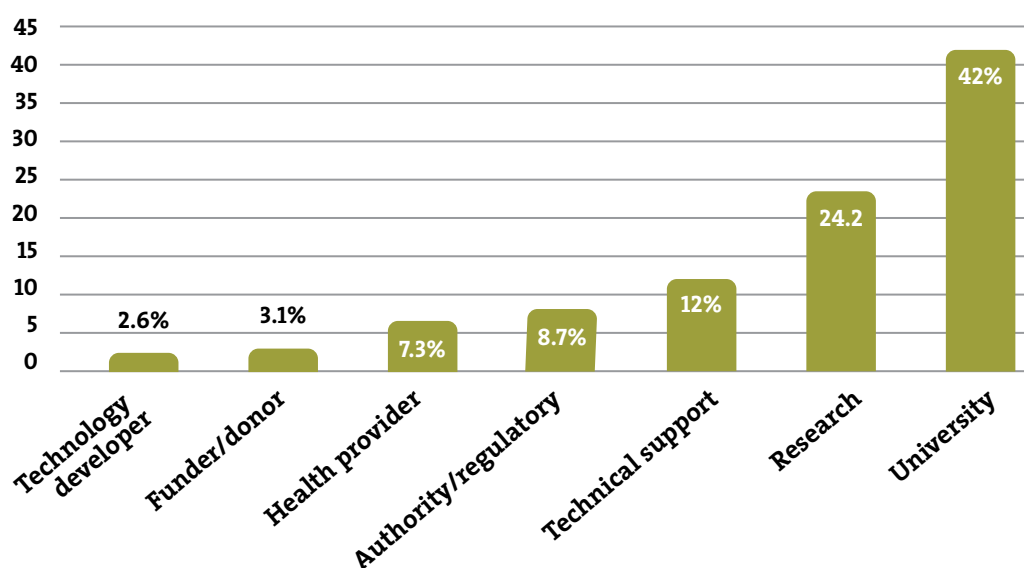


**Fig. 10.3.** Implementation research on diseases of poverty in developing countries. Number of papers published by year, 2005–July 2010.

Publications on implementation research of infectious diseases of poverty are increasing.

**Table 10.1.** Top five countries with most number of publications as first author

High-income			Low- and middle-income		
	n	%		n	%
<b>USA</b>	61	25.8%	<b>South Africa</b>	10	4.2%
<b>United Kingdom</b>	36	15.2%	<b>Brazil</b>	4	1.6%
<b>Canada</b>	19	8.0%	<b>Malawi</b>	4	1.6%
<b>Belgium</b>	15	6.3%	<b>China</b>	3	1.2%
<b>France</b>	14	6.0%	<b>India</b>	3	1.2%



**Fig. 10.4.** Type of institution publishing implementation research on diseases of poverty in developing countries, January 2005–July 2010. n = 426

Universities are the institutions that publish the most implementation research papers.



Institutions with the most connections to others – or nodes – in the network are the University of London (which comprises of a number of discrete colleges/research institutes), PAHO, WHO, University of California, Johns Hopkins University, the Program for Appropriate Technology in Health (PATH), and the Malaria Vaccine Initiative, in that order (Table 10.2). Makerere University in Uganda is the only developing country institution in the top 10 nodes. The percentage of links across coauthor institution out of all possible links – the network density – is 1.3%, suggesting that collaborations are scattered.

Health systems research capacity, particularly for implementation research, has increased in developing countries in the past five years, as the publication trends indicate. In middle-income countries disease control programme evaluations are becoming more current and even obligatory (Oxman et al., 2010). Even if funding for health systems research could now be estimated at 10 times the figure of 0.007% estimated for 2000, it would still be too low for a health sector that accounts for an increasing share of national health expenditure and of international aid.

### Experience and models available for implementation research collaboration

Institutions that want to focus on implementation research need to consider partnerships with policy-makers, health programme managers, local health authorities and complementary research institutions. Partnerships are equally critical between developing country research institutions and international organizations, global health initiatives, product development partnerships and expert academic institutions. They are also important between national academic and research institutions in middle-income countries and their local-level counterparts, particularly those working in poor regions and settings.

Partnerships can support all stakeholders to achieve higher levels of quality in decision-making, particularly related to policy formulation and implementation. In order to increase their opportunities and outputs, partnerships need to identify their common interests within a framework of solidarity that enables investment planning in the mid-to long-term (Rathgeber, 2009).

**Table 10.2. Degree of centrality measures**

	Degree*	NrmDegree
University of London	16	2.807
PAHO	16	2.807
WHO	15	2.632
University of California	8	1.404
Johns Hopkins University	8	1.404
PATH Malaria Vaccine Initiative	8	1.404
Global Fund	7	1.228
Harvard University	7	1.228
Clinton Foundation	6	1.053
Makerere University	5	0.877

\* NrmDegree corresponds to the coauthorships that an institution has on the total network.

Old models of research collaboration where data gathering by local researchers and interpretation and publication is undertaken by national or international researchers need to be abandoned. Even more collaborative models are being questioned where, in spite of greater local involvement throughout the project, the agenda is still donor-driven. New models should place building mutual trust and shared decision-making with clear national data ownership and development of research capacity across all stakeholders at the forefront (Costello & Zumla, 2000).

Several innovative partnerships are now breaking new ground. Partnerships between developed and developing countries include the Multilateral Initiative on Malaria (MIM) and the European and Developing Countries Clinical Trials Partnership (EDCTP). Partnerships between developing countries include the African health researcher platform ISHReCA (the Initiative to Strengthen Health Research Capacity in Africa), the African Network for Drugs and Diagnostics Innovation (ANDI) (Nwaka et al., 2010) and the Mesoamerican Public Health Institute. Product development partnerships and public–private partnerships are also a new type of collaboration (see chapter 5) – although they were shown to have important shortcomings: they tend to be localized in high-income countries, have weak representation from low-income countries on their governing boards, have poorly-defined research ownership and intellectual property and a “quick-results” orientation without a focus on national health priorities (ODI, 2007). Partnerships with NGOs are promising, given the latter’s understanding of the local contexts and their advocacy, priority-setting, capacity building and networking skills (Delisle et al., 2005). However, while large NGOs have taken on important implementation research tasks, the majority lack training, funding, time and motivation and have weak links with international research systems and universities (Rathgeber, 2009).

As implementation research aims to generalize knowledge as well as to inform decision-makers (see chapter 2), partnerships need to carefully balance scientific or primary research benefits from the problem solving and development of secondary benefits of research (Buxton et al., 2000; Ijsselmuiden, 2008). Primary benefits will be sought by national and international partners whose main interest is to make knowledge widely available, whether for theory development or for application by third parties. They will therefore choose means of dissemination such as peer-reviewed journals (that privilege scientific standards but that may take months or even years to be published). Secondary benefits will be sought by policy-makers and programme managers as well as by technology developers and applied researchers, who would rather assess their findings against more intuitive standards, informed by policy and market responses and opportunities.

Given the unique challenges of implementation research, research networks seem particularly appropriate to channel the right mix of incentives. The “strength of weak ties” that characterize networks – that is, relationships that depend on common interests rather than institutional hierarchies, can help build capacity within their own ranks – with stronger members mentoring weaker ones, as exemplified ANDI. Networks can empower developing country scientists and increase the chances of high quality research that can be both informative and be published scientifically. Thus there is an increase in local as well as more general impact for development.

Characteristics of successful research partnerships are difficult to pin down, but clear indicators are available. Science and development objectives should be clearly balanced in the agenda, with clear stages, products and beneficiaries. Implementation research programmes can be identified with greater emphasis on scientific objectives as an initial capacity strengthening

strategy, phasing towards a greater focus on development issues over time. Developing country scientists' capacities should be developed with explicit targets and procedures, and their research results disseminated and recognized internationally (Maselli, 2002). As implementation research partnerships increase, it will be important to evaluate them and to integrate results into capacity strengthening strategies. Ethical and strategic guidelines are already available to support partnerships.

Recent trends in global health initiatives to provide more support for research capacity strengthening in developing countries are noteworthy – e.g. the Medical Research Partnership Initiative supported by the United States President's Emergency Plan for AIDS relief (PEPFAR) through the National Institutes of Health, USA (NIH) and Health Resources and Services Administration (HRSA), and the USA's Global Health Initiative's promise to transfer more research resources to developing countries and to foster collaborations between such countries.

### **Governance for implementation research collaboration**

Innovation within organizations has been studied for many years and diverse models and approaches have been recognized.

Many useful innovations rise from the bottom-up, through unpredictable, emergent and adaptive processes whereby local actors respond to challenges posed by national programmes (Greenhalgh et al., 2004). Scarcity of resources at the local level in the face of national/international challenges has been shown to advance highly important innovations (Srinivas & Sutz, 2008); such was the case with elements of directly observed short course therapy for tuberculosis, developed during war time in Mozambique (González-Block, 2004).

On the other hand, innovations are promoted through more rational frameworks, following

a planned and managed approach. Such is the case for the implementation of new tools and diagnostics for disease control. Efforts range from market forecasting to widespread training and logistics. Intermediary innovation processes rely more on diverse forms of leadership, such as those that allow innovators to express their ideas and to find support for their undertakings. These are the real scenarios where implementation research has to take place, and for which appropriate governance mechanisms should be identified.

Innovation is favoured in mature, larger institutions with functional differentiation and a focus of professional knowledge in decentralized settings (Greenhalgh, 2004). Governance for implementation research has to be aware of these factors, encouraging implementation research wherever it will be most successful as a tool for innovation. Governance has to be aware of opportunities to engage in implementation research, such as situations characterized by tensions and uncertainty in contexts with on-the-ground capacity for research and evaluation.

Implementation research governance must encourage informal networks and dissemination strategies that will favour the utilization of results (see chapter 11). Developing countries and poor settings are good locations at which to focus on the interface between technological and social innovation, as innovations may be the only truly sustainable means of improving the effectiveness of their health systems (Gardner, 2007). Developing countries can develop innovative implementation strategies that can help deliver the still largely untapped potential of scientific research. This implies defining social and administrative innovations (such as community-directed interventions) with the same rigour as technological innovations, and applying implementation research to the capacity to adopt and scale up such innovations.

Implementation research faces the challenge of being adopted as an innovation in its own right, with scale-up to make it available and

able to compete for funding in an ever more competitive field. There is a need to position implementation research as a tool with which to manage the uncertainty surrounding access to innovations, and to apply the science of large-scale change in global health through a consensus on the “way forward” (McCannon et al., 2007). Best practice guidelines are already under development around the implementation and evaluation of “Access with Evidence Development” schemes (Stafinski et al., 2010). Governance for implementation research should ensure strengthening of the knowledge base, the stimulation of capacity building, the opening of spaces for local entrepreneurship and the provision of incentives for innovation.

## Conclusions

Capacity for implementation research is growing, as evidenced from the increasing number of publications and by the accelerated rate of publication in the field. However, most research capacity is concentrated in a few rich countries – a situation of concern given that implementation research typically benefits from a close understanding of the field and of country actors. Furthermore, collaboration across institutions is still low and dominated by institutions from developed countries.

A wide range of institutions are involved in implementation research. Universities and research institutions predominate, although there is an interesting participation by donors, providers, health authorities and by multilateral organizations. Models for collaboration between research, product and strategy development (that will address both informal and formal innovation processes) are being identified. The role of developing countries in building the interface between technology and social innovations is promissory, while ample opportunities exist for collaboration between developing countries.

There is an urgent need to invest in research capacity strengthening for implementation research, (with a particular focus on developing countries) and in building collaborations between developing countries and between developed/developing countries. Career paths for researchers need to be built with a strong implementation research focus.



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## Chapter 11: Uptake and use of implementation research evidence for policy-making

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The 2010 Millennium Development Goals Report reveals that without a major push forward, many of the Millennium Development Goal (MDG) targets are likely to be missed in most regions and concludes that improvements in the lives of the poor have been unacceptably slow.

Consider MDG 6 (Combat HIV/AIDS, malaria and other diseases), which explicitly outlines that people at risk of malaria (and especially children under the age of 5) should be sleeping under insecticide-treated bednets. The value of insecticide-treated bednets is supported by high quality systematic reviews which indicate that bednets are highly effective in reducing childhood mortality and morbidity from malaria (Lengeler, 2004). However, in 2001, only 2–15% of African children were sleeping under bednets (WHO, 2004). This is just one example among many where the availability of evidence on the effectiveness of an intervention does not guarantee its delivery and access.

Research on the effectiveness of interventions is necessary but not sufficient to produce better health outcomes; implementation research is needed to identify implementation barriers and find effective implementation strategies. However, emphasis must be placed not only on the production of implementation research, but also on its uptake and use. As such, implementation research must be integrated into the knowledge translation process to ensure its use by policy-makers and programme managers.

The main objective of this chapter is to explore the different ways in which implementation research can inform policy-making through knowledge translation processes as they are institutionalized in knowledge translation platforms. The chapter also discusses available tools and methods to improve the demand for, access to and delivery of implementation research for policy-making. To this end, the chapter discusses the relationships between knowledge translation and implementation research and identifies the role of implementation research in the design and implementation of evidence-informed policy.

### Benefits of knowledge translation for implementation research

The potential benefits of knowledge translation and implementation research can be far-reaching. It has been suggested that health-care transformations are social experiments that (as with clinical trials) require ethical and scientific review (Daniels, 2006) – and that therefore compulsory evaluations should be considered (Oxman et al., 2010). Furthermore, health policy and programme changes that yield null or negative health impacts represent a waste of financial resources, a consequence which is especially harmful in low- and middle-income countries where resources needed to meet basic needs are scarce.

This report places emphasis on ensuring delivery of and access to interventions. The integration of implementation research into the knowledge translation continuum can help minimize health and economic risks by ensuring that both policies and programmes are informed by sound evidence. Implementation research can play a role in informing stakeholders on progress, with the objective of advancing health equity through targeting the disadvantaged.

A new way of thinking is needed about the relationship between knowledge

translation and implementation research. Emphasis must be placed not only on the production of implementation research, but also on the uptake and use of its results. We also envision a broader definition of implementation research that encompasses tools that help policy-makers to identify problems in implementation, clarify solutions and map the diverse contexts in which innovations will be rolled-out. In essence, the knowledge translation process must use implementation research as much as implementation research must use knowledge translation.

The ultimate outcomes that can be expected from using implementation research in knowledge translation to address demand, delivery and access are:

- improving health equity and the health situation of populations
- avoiding causing harm through public health interventions
- strengthening all health systems functions
- improving the quality and the ethical basis of interventions
- rationalizing efficient use of resources, and
- meeting strategic national goals and global targets (such as the MDGs).

### **Knowledge translation and implementation research synergies**

Implementation research is both a source of health systems knowledge (see Chapter 2) and a methodology to bridge the research to policy gap. Thus Sanders and Haines (2006) propose that implementation research “focuses on how to promote the uptake and successful implementation of evidence-based interventions and policies that have...been identified through systematic reviews”. This definition makes implementation research as a component of knowledge translation which, as defined by the Canadian Institutes of Health Research

(CIHR), is “a dynamic and iterative process that includes synthesis, dissemination, exchange and ethically-sound application of knowledge, through sustainable partnerships to improve the health of citizens, provide more effective health services and products and strengthen the health-care system” (Graham et al., 2006). From this perspective, implementation research can be seen to be a part of implementation science, defined as “the use of strategies to adopt and integrate evidence-based health interventions and change practice patterns within specific settings” (Madon et al., 2007).

Understanding the synergy between implementation research and knowledge translation is vital to strengthen health systems. There has been a surge in health systems research in recent years and, along with it, a growing attention to the uptake of systems innovations through knowledge translation to increase the benefits and minimize the risks of public health interventions. It has been suggested that health systems research should be particularly influential in those poor countries and settings that have both the greatest needs and the greatest resource constraints. Implementation research should therefore also support innovation scaling-up through its role as a component of knowledge translation processes, particularly to address policy decision-making; in the end this will create both evidence-informed policy options and policy-informed research.

Decision-making for health policy is influenced by multiple sources of information and insight, including research evidence, tacit knowledge and negotiations. Furthermore, effective policy-making requires that research evidence be contextualized according to the “environment or setting in which the policy is being developed and implemented” (Bowen & Zwi, 2005). Additionally, research can provide input at many points along the knowledge translation continuum. For example, research evidence can be used to identify problems, to set country

priorities during the design stages of policy-making, to monitor and evaluate policies and programmes or ensure the successful implementation of policies once they have been devised. The synergy between implementation research and knowledge translation can thus address the political, historical, cultural, socioeconomic, health services and resource factors that affect policy-making.

Clearly, knowledge translation has to address the complexity of health systems through complementary processes and interventions. However, too often the knowledge translation process is viewed in an oversimplified and linear fashion, built upon a singular input of research on the effectiveness of a health intervention, and not addressing the policy process as a whole, nor the capacity that organizations have for policy implementation (Bowen & Zwi, 2005). To address this, knowledge translation has to involve policy-makers as active players in the systematization of evidence. While still rare (Lavis et al, 2005), the involvement of policy-makers in knowledge translation is now being promoted by global initiatives such as the Evidence-Informed Policy Network (EVIPNet) as well as regional and country initiatives (Hamid et al., 2005; González Block, 2008).

### Challenges and opportunities for translating implementation research evidence

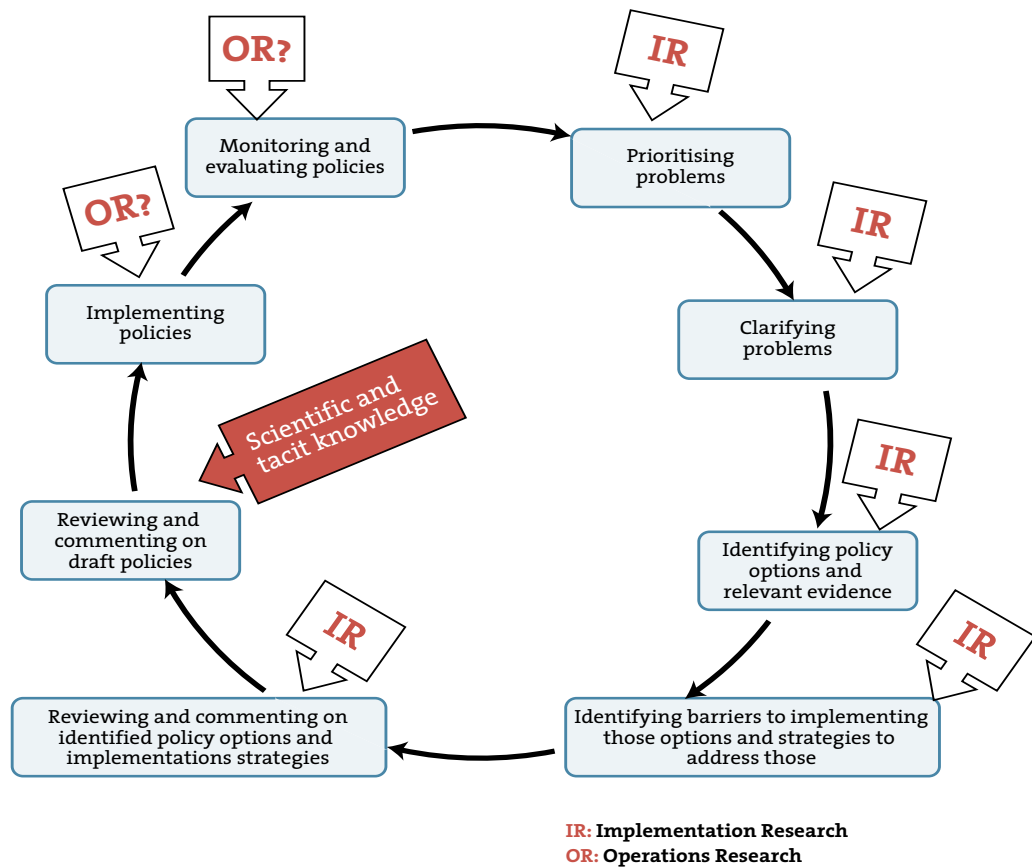
Implementation research faces special challenges in informing policy development, particularly if it addresses the implementation of innovative programmes and tools. Massive investments will have been made and stakeholders will be at greatest political risk. Typically, implementation has a large number of highly interested stakeholders favouring a policy (although they may not agree on expected benefits). Implementation also faces opposition at multiple decision points

– although how intense and focused this opposition is will depend on a number of circumstances. Research results on the implementation process will thus be interpreted in both technical and political contexts that will need to be managed in special ways (Hanney et al., 2003). To ensure the full support for implementation research, knowledge translation has to ensure that evidence is perceived as a way of reducing political risk, rather than as a threat to stakeholders (Oxman et al., 2010). Furthermore, knowledge translation has to frame research results in such a way that recommendations can be acted upon, thus avoiding (as much as possible) unwanted or unexpected effects on policy.

There are many ways to synergize knowledge translation with implementation research so that demand, delivery and access to interventions is improved (see Fig. 11.1). For example, at the start of the policy cycle, when problems are prioritized, implementation research can clarify policy-makers' understanding of problems and help identify those problems most worthy of attention. Likewise, in the latter half of the policy cycle, policy-makers can use evidence (such as results from opinion polls or stakeholders perceptions) when reviewing and commenting on draft policies and while monitoring and evaluating policy implementation. At this stage operational research can also be used to address the local contexts (Remme et al., 2010).

As discussed in chapter 5, knowledge translation can use implementation research evidence for the development of innovative tools and products at nearly every stage of the policy process, including the following:

- mapping the political and institutional context in which policies will be implemented;
- identifying barriers to implementation, and identifying the determinants which prevent effective access to interventions;



**Fig. 11.1.** Opportunities for the use of research evidence in the policy cycle

There are ample opportunities to use research evidence for policy making and program implementation.  
Source: Modified from Oxman et al., 2009.

- developing practical solutions and monitoring and evaluating new implementation strategies;
- identifying how to introduce implementation strategies into the health system;
- facilitating full scale implementation; and
- collaborating in policy evaluation and modification.
- deliberative dialogues on policy implementation processes, with involvement of researchers and policy-makers to elicit tacit knowledge and policy positions;
- priority setting exercises where a shared implementation research agenda is developed by policy-makers and researchers;

There are various tools and processes that can help integrate implementation research into policy in an effective way (see Box 11.1). They include<sup>1</sup>:

- clearing houses of easy-to-access and clearly relevant case studies, systematic reviews and other publications relevant for implementation of specific policies;
- training workshops for policy and decision-makers to find, appraise (both in terms of quality and relevance), and apply implementation research;

<sup>1</sup> Please also refer to the SUPPORT tools for evidence-informed policy-making: [http://bit.ly/SUPPORT\\_Tools](http://bit.ly/SUPPORT_Tools), accessed 30 September 2011.



**Box 11.1.****Knowledge translation for scaling up use of zinc for childhood diarrhoea**

Systematic reviews of the research literature plus a joint UNICEF/WHO recommendation have established that zinc provides a very effective treatment for diarrhoea among children under five years of age – it reduces the severity and duration of diarrhoea as well as the likelihood of future episodes of diarrhoea and the need for hospitalization (Lazzerini & Ronfani, 2008; Aggarwal et al, 2007; Bhutta et al, 1999; Rivera et al, 2003). In Bangladesh alone it has been estimated that zinc treatment could save the lives of 30 000 to 75 000 children per year.

Knowledge translation and participative implementation research were critical to scale-up zinc usage in Bangladesh through the Scaling Up Zinc Treatment for Young Children with Diarrhoea (SUZY) programme. As a first step, the Ministry of Health and Family Welfare (MoHFW), in collaboration with the SUZY team, developed two committees: (1) a National Advisory Committee, headed by the Health Secretary and (2) a Planning and Implementation Committee, headed by the Joint Secretary (Public Health & WHO) of the Ministry of Health & Family Welfare of Bangladesh. Based on the evidence, the National Advisory Committee approved the policy on using zinc in addition to oral rehydration salts (ORS) for children under five years with diarrhoea, and incorporated the use of zinc into a revised national diarrhoea treatment guideline. The following evidence-based policy changes were approved in relation to the national scale-up of zinc use in Bangladesh:

- the tablet formulation approved by the Bangladesh Drugs Administration
- branding the product as “Baby Zinc”
- allowing over-the-counter sales through a specific regulatory waiver
- promoting Baby Zinc use via the mass media

To increase the scaling up process, the committee suggested asking the Bangladesh Paediatric Association as well as the Directorate General of Health Services (DGHS) for their technical opinion.

Research also guided development and pricing of a dispersible zinc tablet. In an early attempt at scale-up, community health workers whose primary focus was family planning were used to deliver zinc – but a lack of success led to the commission of quantitative studies to identify who should be responsible for delivery. The studies discovered a cascade effect for adoption: even though the product was available over-the-counter and could be easily administered, physicians (especially paediatricians) were identified as key players in promoting and prescribing it. Based on this evidence, the project embarked on a training blitz of students at all medical colleges, of public health physicians (at the district and subdistrict level), and of 8000 village doctors; in turn they acted as trainers for the more than 200 000 informal health care providers. Repeat impact surveys were conducted every three months and then annually to monitor for intended and unintended consequences. Rapid increase in awareness about the benefits of zinc occurred – from near zero before the launch to nearly 90% of urban and over 70% of rural caregivers by year 3 of the launch. However, use of zinc lagged far behind awareness in all settings – the national average after launch being only 17% of caregivers. Among the rural poor and in urban slums, zinc coverage rates stagnated by the end of the first year of the campaign. Further research was undertaken to identify barriers to sale of zinc by medicine vendors.



- training of researchers to develop and translate research that targets current health systems needs;
- systematic reviews of relevant, wide-ranging and high quality implementation research literature focused on specific recommendations;
- research briefs and executive summaries on implementation research results focused to policy-makers;
- scientific publications with shared authorship between researchers and policy-makers.

The interactive knowledge translation processes at the top of this list can help policy-makers and researchers to identify mutual interests and to relate to research evidence with greater trust and interest. As a starting point to identify the research evidence needed to confirm (or critique) policymaker's positions, deliberative dialogues can be especially designed to elicit their tacit knowledge and negotiating positions (González Block et al., 2011).

Interactive processes can help develop a common value framework across researchers and stakeholders, thus promoting team building and distributed leadership for action. Care has to be taken to select stakeholders, as well as to propose – and comply with – house-rules on the diffusion of deliberations and on the confidentiality of participants. The aims of building trust and leadership should be carefully balanced with aims to relay technical information. Trust in individual researchers and in institutions publishing results and reviews can help validate the policy process while also helping policy-makers accept recommendations. However, trust in researchers and their institutions is not enough to guarantee evidence-informed policy-making. Research results must be thoroughly evaluated and graded to decide how much confidence to place in the evidence presented (Lewin et al., 2009).

The knowledge translation tools cited above, from the middle of the list downwards, can play important roles to improve scientific communication between researchers and policy-makers, although trust is still an important objective.

## Capacity strengthening

How can the use of knowledge translation and implementation research be encouraged at organizational and country level? This chapter has provided reasoning for the generation of implementation research and outlined its potential use in knowledge translation. However, preparing the policy environment to reap benefits from this can be difficult – sufficient capacity must exist at the organizational and country levels to acquire, analyse, adapt and apply implementation research (Kothari et al., 2009).

There are many strategies for strengthening capacity to encourage evidence informed decision-making (e.g. Lavis et al., 2005). One systematic review (Innvaer et al., 2002) looked at the barriers to and facilitators of evidence-informed decision-making in public health and, although focused in a high-income country, made the following recommendations that can be applied elsewhere:

- encourage strong relationships between policy-makers and researchers – interactions increase the likelihood of research use by policy-makers;
- manage any conflicts that may arise between policy-makers and researchers;
- promote interactions between stakeholders, researchers and policy-makers so that decisions will be informed in part by stakeholder input;
- encourage collaboration between health-care organizations and networks, particularly between new and more mature organizations;
- encourage capacity building for research use among policy-makers

One way to combine these strategies and create a fertile knowledge translation environment is to promote country mechanisms or knowledge translation platforms to systematically use evidence in policy-making in low- and middle-income countries. Building capacity is vital to the continuous engagement of various participants in the policy-making process. A successful example of a knowledge translation platform is EVIPNet, a WHO programme with characteristics of a global social network. Currently, EVIPnet encompasses 26 knowledge translation platforms (also known as country teams) worldwide. The paramount goal of each country team is to promote evidence informed decision-making in public health at both national and other jurisdictional levels. EVIPNet promotes the philosophy of “learning by doing together”, so as to better work together. Each country team consists of researchers, high level decision-makers and other stakeholders (e.g. patients, health-care workers, civil society representatives). Diversity of membership promotes sustainable partnerships between individuals and organizations and allows the sharing of best practices and feedback; capacity-building workshops are also enhanced when diverse participants are involved as policy-makers, researchers and stakeholders can learn with each other and from each other.

EVIPNet’s capacity-strengthening programmes place emphasis on producing tangible objects such as research briefs for policy-makers as well as the preparation of processes such as deliberative dialogues (see Box 11.2 for an example of this). While products can be used readily, plans and processes contribute to health systems strengthening. This approach enables policy-makers to develop skills in areas such as problem identification, framing a research problem, context mapping, or priority setting.

#### **Box 11.2.**

#### **Strengthening knowledge translation for scaling-up use of antimalarial interventions**

The EVIPNet team in Burkina Faso focused on strengthening the country’s capacity for knowledge translation and use of research through (a) a workshop aiming to produce a research brief for policy-makers and (b) by engaging in a deliberative dialogue. Both targeted access to artemisinin combination therapies (ACTs) for uncomplicated malaria.

The process aimed to reach consensus to:

- engage the private sector on adherence to national guidelines on subsidized drugs in all settings;
- motivate and retain community health workers involved in the home management of malaria;
- ban monotherapies, after ensuring that ACTs are fully deployed across the country and that pharmacies are informed about the policy.

The knowledge translation process helped participating stakeholders reach agreement on the proposal tendered to the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) in its 7th round of funding. Project implementation was therefore able to make an early start (with the implementation of the community health worker option through a pilot in three districts of the country). Full-scale implementation is aimed for the 8th round of the Global Fund. An implementation research protocol (mostly a rapid ethnographic assessment) applied to each participating district helps to monitor and evaluate the advantages, disadvantages, costs, barriers and facilitators in the execution of the policy option at the very specific district level.

**Box 11.3.****Strengthening capacity to close the know-do gap through TRAction**

The United States Agency for International Development (USAID) supports the Health Research Program (HaRP) as an approach to research and the translation of research into use. A key component of HaRP is the Translating Research into Action (TRAction) Project, a five-year research grants project focusing on maternal, newborn and child health and other related services. The project is directed by University Research Co., LLC in collaboration with partner Harvard University School of Public Health.

TRAction addresses the “know-do” gap or delay between the discovery of effective ways to combat the causes of mortality and morbidity and the application of these proven interventions on a wide scale. The project’s rationale is that rigorous research has demonstrated the effectiveness of numerous ways of reducing health disparities around the world. However, national level decision-makers, donors, and programme implementers in many settings often lack evidence about the best ways to introduce and implement such interventions on a national scale. These know-do gaps must be quickly closed if each country’s MDGs are to be met in the targeted timeframes.

**Conclusions**

Implementation research is an integral part of the knowledge translation continuum. Emphasis must be placed not only on the production of implementation research, but also on its quality, proper use and uptake in decision-making. To more effectively implement evidence-based policy, policy-makers and researchers should learn together and work in partnership to improve access and delivery. Steps should be taken to increase the demand for research use and knowledge translation through sustainable partnerships and mechanisms including knowledge translation platforms at the country level (national, provincial, district levels) that promote the early involvement of policy-makers, managers, health-care providers and patients and serve as the basis for capacity-strengthening activities.

There is a need also for control mechanisms through which civil society can hold policy-makers accountable (such as legislating for the use of knowledge translation for policy decisions). It is necessary to develop networks and linkages to support actors in health systems in making use of knowledge translation, and towards collaborating to generate and use knowledge. Clearing houses and repositories for synthesized, easy-to-use, relevant evidence are urgently needed (See Box 11.3).

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## Chapter 12:

# Lessons, challenges and a roadmap for action on implementation research

Pamela Ananda, Gerald Keusch and Miguel Á González Block

This report's chapters were contributed by teams of researchers and stakeholders in global health and national health systems who are vitally interested in the growth of implementation research. They want implementation research to reach its full potential to support access to innovative tools, strategies and interventions for the control of diseases of poverty. This concluding chapter draws from earlier chapters to highlight lessons and identifies the main challenges faced by implementation research. The chapter ends with a proposed roadmap to rally support for implementation research.

## A. Lessons

### Implementation research has much to offer if mainstreamed in the research and development (R&D) process

This is the most fundamental message of this report. Implementation research must be engaged at the beginning of the R&D process, and must feed into all stages/angles of developing new tools, strategies and interventions of R&D – i.e. innovation, product development, access, patient safety, communication, improving acceptance, capacity building, governance, and ultimately the delivery of health services. These often can be informed by evidence that only implementation research can provide. This is an almost heretical concept, as the implementation research community is typically excluded from the early formulation of research questions and methodologies. Efforts to understand diseases and develop

tools to combat them are often detached from efforts to implement and deliver interventions. This means that critical opportunities for science and for practice are missed.

The chance of developing products or strategies that populations will not accept can be minimized by connecting upstream and downstream activities early in the process of implementation research. This was a clear lesson learned from attempts to combat malaria, onchocerciasis and leishmaniasis in developing countries (Keusch et al., 2010). To properly understand implementation problems it is critical that implementation research creates active links between disease control and the design and development of an innovation. Two research-based strategies – the Problem Statement Analysis and the Target Product Profile – provide the foundation for initiating innovative product development and access planning.

Judicious use of funding can be instrumental in ensuring that connections are made between upstream and downstream innovations development and health systems strengthening efforts. The implementation research scientist must be brought together in a relationship with those working on technology R&D and on applied health systems research. This communication between researchers who do not necessarily occupy the same “academic space” will be difficult unless there is a strategy that is strong, clear and agreed upon. Thus, national, international and multinational organizations and other key actors need to develop such a common strategy.

### Partnerships are critical to undertake implementation research

End-users of innovation can play critical roles in promoting (or justifiably resisting) innovations for health, particularly for infectious diseases of poverty. Their active engagement (characterized as linking the demand and the supply sides) is thus critical for implementation. The implementation



research scientist is perhaps in the most strategic position to help to identify these linkages or pinpoint the barriers to effective cross communication. It should become a major responsibility of the implementation research scientist to make cross-communication happen. Product Development Partnerships (PDPs) are also interested in relating to end-users in such a way that development of new health technologies is accelerated with a view to an equitable health impact. Acceleration requires (a) considering implementation research to inform on appropriate innovation design and (b) investing in health system strengthening to meet the needs of, and ensure adoption by, end-users.

Stakeholder partnerships are clearly needed for the successful control of diseases that require multiple interventions and continuing R&D. This is also made evident by global initiatives (such as those aiming to ensure patient safety) that require legal and regulatory frameworks to be strengthened to address social, political and economic implications of possible adverse events at all levels of health systems. Connecting R&D to implementation can help eliminate the historical divide between academic research, industry development, and “real world” implementation (Keusch et al., 2010). Partnerships can support all stakeholders to achieve higher quality decision-making, particularly in relation to policy formulation and implementation. Creating learning communities or communities of practice so that all implementation research stakeholders can share lessons from the ground would help improve the functionality of partnerships with stakeholders.

Building effective implementation research partnerships is a governance responsibility which must begin with the communities being served. It needs to address the fact that the landscape is fragmented by various players who come from both the public and private sectors, from charitable foundations and from nongovernmental organizations (NGOs). Even

when addressing the same topic, these groups often either act in almost total isolation from the others or build boundaries around their particular interest/approach. In order to avoid unnecessary friction with the community (and possibly delaying or precluding the introduction of innovative ways to reduce the impact of infectious diseases of poverty) governance must be oriented towards the end-user, and not simply organized to serve the programmes’ leaders and their organizational goal.

### **Health systems can be strengthened with the support of implementation research**

A health system’s performance in terms of its financing of both public and private providers as well as in terms of the availability of human resources and functioning equipment is central to ensuring access to and sustained use of new products. For instance, a lack of supplies in government public hospitals discourages community members from seeking health-care services and getting access to health innovations.

Yet ensuring the adequate financing of health systems is not enough in and of itself. The strength of health systems lies not so much in their static resources, but in their capacity to relate to their contexts and to respond to opportunities. Implementation research can help identify implementation processes that will successfully enhance the capacity of health systems to scale-up use of innovations.

### **Organization and effective communication of implementation research is important**

Issues of data collection, data sharing, and collaborative data analysis are obviously important for diverse stakeholders. The best way to meet their information needs might be to bring stakeholders together and to coincide R&D agenda-setting with research proposal development to best define how

data needs to be organized and presented to each stakeholder group. Effective brokering between implementation researchers and other stakeholders is important. Implementation research should be directed to and demanded by champions of innovations, who are critical in ensuring access by end-users.

Implementation evidence helps experts reach a consensus on the need for/use of an innovation; this has been found to play a significant role in enhancing access and to overcome the barriers imposed by conflicting views on innovations. Effective communication and knowledge management are vital for this purpose – local stakeholders can increase the value of their collaboration if they are informed of the expected benefits and challenges resulting from access to innovation. Such information can be produced through participatory implementation research processes as a first step to delivering new or improved tools, strategies and interventions.

### **Capacity for implementation research can be greatly improved**

Extreme lack of capacity in the field of implementation research acts as a bottleneck to advancing this science. An important approach to building capacity is for donors (and other channels of development assistance) to invest in strengthening the knowledge and skills of individuals through training opportunities and workshops. It is also important to include greater collaboration both between developing countries and between developed and developing countries. Such collaboration would lead to scientific publications or proposals that could strengthen health systems or disease control.

## **B. Challenges for implementation research on access and delivery**

This report identifies several challenges that need to be addressed if the full potential of implementation research to support access to innovations is to be realized.

### **Conceptual boundaries should be clarified if further support is to be mobilized**

Implementation research focuses on national and even global processes for roll-out and scale-up of innovations; it aims to identify and explain how the broad context of innovations affects access by end-users and health system effectiveness under real conditions. Implementation research can be distinguished from health policy analysis (with its focus on innovation options), from operations research (with its focus on local adaptations) and from impact evaluation (which looks at the attainment of specific outcomes). However, all these efforts are clearly complementary and closely related in R&D. This report highlights existing confusion across these fields both by researchers and, perhaps most importantly, by those with a potential interest in funding and/or using implementation research – data from funders of implementation research showed that most had no formal definition of implementation research, while research papers and literature search engines also lack an ability to distinguish implementation research from the wider field of health systems research.

Another conceptual challenge facing implementation research is the lack of a framework for the definition of the goals of innovations. Should innovations and associated implementation strategies focus predominantly on saving the most lives possible in the short-term? Will investment in R&D only have short-term impact because of the time needed for translation to something ready for introduction in the field? What should be the balance between these

two perspectives? How can the R&D agenda and implementation research also consider specific objectives that aim to strengthen and develop effective, equitable and sustainable disease control programme through health systems strengthening?

It will remain difficult to mobilize financial and human resources to advance implementation research without an agreed definition of the field and a clear taxonomy by which the goals can be evaluated.

### **A broad, participative focus is needed to set the R&D agenda and priorities**

Implementation research can help evaluate how R&D is helping to strengthen health systems. The significance of this is that the value chain of R&D can be substantially improved by enabling stakeholders to understand each others agendas and realities. This is a critical challenge for implementation research and for research brokers supporting the mainstreaming of implementation research. The globalized environment calls for a globalized approach to partnership, in which each actor is given equal treatment in any new relationship that may develop (European Commission, 2009). It is particularly important that the agenda-setting process leads to increased acceptance and demand for the new technologies among patients, providers, programme managers and policy-makers.

Ethical issues can arise when implementing technologies destined for both industrialized and developing countries. For example, production of a vaccine protective against diarrhoea was ceased in the USA (where only 30–50 people die of dehydrating diarrhoea per year) because the risk of intussusceptions was assessed to be greater than life saving benefits. But this decision terminated any chance of using the same vaccine in developing countries where the risk-benefit ratio is many orders of magnitude lower.

### **Political commitment is critical to support implementation**

Political commitment and grassroots support is essential to tackle infectious diseases of poverty. Apart from developing appropriate policy and regulatory frameworks, stakeholders should be involved in the development of treatment protocols and in allocating funding for the use of new technologies. In some cases stakeholders should also be willing to take control of programme interventions associated with the new technology. In particular, political commitment is needed to strengthen and scale-up patient safety activities across health systems and to increase opportunities for effective implementation of specific infectious disease control innovations.

## **C. Roadmap for action**

Five actions are proposed to move forward on these lessons and help overcome the challenges faced by all actors interested in implementation.

### **1. Advocate for the use of implementation research**

#### **a) Address health system constraints that may thwart or delay the adoption and delivery of new tools, strategies and interventions for disease control.**

A successful collaboration among all or most of the key country and community actors requires communication, engagement and trust.

Implementation research should be used to identify the diverse decision points on the path to access. Implementation research can be used to widen the definition of accessibility – to identify all obstacles (from global to local levels) that hinder patient access. Rapid ethnographic assessments should be undertaken to address barriers stemming from the social and material conditions of beneficiaries.

Incentive programmes and social marketing might be used to change the behaviour of health care providers in relation to a new technology (e.g. through incentive programmes and social marketing). Patient perceptions also need to be considered and managed, particularly by taking social, economic and cultural factors into consideration. Participatory research that involves communities in decision-making has been important for the implementation of a number of programmes.

**b) Make new tools affordable without compromising incentives for private-sector investment.**

While public investment is vital, it should not be considered in isolation from private-sector investment, where incentives may differ. This calls for a proper recognition of intellectual property (IP) rights. Implementation research can help address the need for exceptions and innovations in IP management. Implementation research on demand forecasting, branding, and stakeholder preferences can delineate more clearly the “why?” and “how?” of increasing uptake and impact of a product, and can project the manufacturing capacity that is needed for scale-up.

**c) Strengthen patient safety and other cross-cutting health system strategies to improve service quality and facilitate the scaling-up of disease control interventions.**

Research should be conducted to identify the different risks to patients when accessing different disease control programmes. Implementation research should include the evaluation of drug safety in the health-care process (after regulatory approval), particularly when interventions are scaled-up and used in real conditions.

**2. Involve stakeholders in implementation research**

**a) Introduce and scale-up new tools, strategies and interventions.**

Innovative product and strategy champions, a coordinating architecture and an access plan should be included as critical components for access to innovative strategies and tools. Stakeholder mapping is a basic research tool that has to be deployed at all levels to identify the local actors with the power to ensure successful implementation. The four key groups to be involved are global experts, national policy-makers, providers and end-users.

The experience from malaria research and control should be applied across programmes given that it amply demonstrates where there have been shifts in the types of participating actors, in the roles they have assumed, and in the control of morbidity and mortality. The main attributes of the new modes of operation which have been established from this experience (Keusch et al., 2010) are:

- a more central role for endemic-country researchers in an increasingly globalized research system;
- direct funding to local researchers and institutions;
- the involvement of affected communities not only as targets of interventions but as co-producers of results;
- new actors taking on tasks formerly vested in WHO; and
- new public–private product development partnerships to drive research towards unmet needs and towards new product development.

**b) Promote participative and equitable models of collaboration in priority setting, decision-making and resource allocation;**

New models that build mutual trust and foster shared decision-making should be the norm rather than the exception.

**c) Integrate implementation research within intervention programmes in order to support evidence-based policies and to build robust programmes that withstand organizational and political change.**

Such a strategy can combat the lack of political commitment to health improvement. An effort should be made to ensure that implementation research is recognized as an integral part of disease control interventions and as a means of firmly integrating these interventions to the health system and the health culture of the disease endemic setting. Closely related to this is the challenge of agenda/priority setting. A broad-based participatory process (anchored by WHO's global political legitimacy) should be used as a model, as also suggested by other authors (Moon et al., 2010).

Country stakeholders should begin to determine implementation research priorities. These priorities can ultimately be decided based on policy-makers' and managers' individual interests, but other stakeholders can and must participate in the priority setting process. National governments should be challenged to increase investment in implementation research in terms of human capital, infrastructure and finances; they should also negotiate the earmarking of funds into implementation research with their partners.

**3. Ensure that governance and investments for implementation research:**

- a. develop the knowledge base
- b. stimulate institutional capacity building
- c. strengthen training and establish career paths for young researchers
- d. provide incentives for innovation at global, national and local levels.

Governance entails "directing or setting goals, selecting means, regulating their operation and verifying results" (Kjaer, 2004).

Establishment of a clear governance structure among global health partners is one of the factors associated with health partnership

success. As well as having a clear governance structure in place, it is vital that a clear set of rules are established to ensure that powerful and financially independent actors do not use their resources to influence the outcomes of multilateral initiatives or create bilateral ones (Szelezák et al., 2010). A process for setting an agenda for action within the health problem area (without the risk of actors developing a perception of loss of autonomy) is important as the problem attracts new actors and activities (Moon et al., 2010).

**4. Call on ethics committees to provide guidance and support for implementation research**

The ethical conduct of research is an essential component of research governance in any field. However, implementation research poses specific ethics challenges, given that it involves retrieving information from a wide range of subjects and in varying situations. Ethics committees should therefore become more adept at reviewing proposals and ensuring that all actors' perspectives are protected. Furthermore, implementation research ethics should be couched in the broader ethical frameworks that guide public accountability, yet confidentiality of sources should be ensured to enable actionable findings to be reported.

**5. Develop leadership for implementation research as part of efforts to strengthen health systems**

Country ownership and involvement of local policy-makers in project design and implementation are key aspects of implementation research initiatives. This issue therefore needs special attention. Elsewhere, the need to "nurture persons who can develop the strategic vision, technical knowledge, political skills, and ethical orientation to lead the complex processes of policy formulation and implementation" has correctly been identified as the most complex challenge in health systems (Frenk, 2010).

Finally, each of the roadmap initiatives proposed requires a champion who will invest time and effort in bringing the actors together, and who will do the hard work of engaging community leadership (both local community providers and the recipients of health care). Without such leadership the likelihood of drift or stagnation is too great.

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## Annex

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“ We urge public health providers, funders, and local and international partners to make use of the powerful tool of implementation research as an integral part of global health programmes in order to maximize effectiveness and provide the foundation for successful implementation and scale-up of these crucial health services.”

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