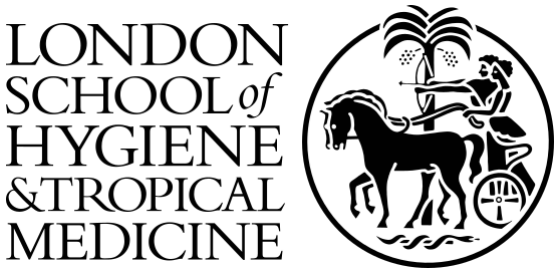

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Accounting for complexity: An examination of methodologies for complex intervention research in global health

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Thesis submitted in accordance with the requirements for the degree of

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of the University of London

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Declaration

I, Deborah D. DiLiberto, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Deborah D. DiLiberto

October 10, 2016

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Abstract

Accounting for complexity is now a feature of health interventions research, but it is unclear how this might best be accomplished. As the number of methodologies to account for complexity expands, developing a coherent approach to intervention research has become more urgent and yet more difficult. This thesis aimed to address this challenge by examining methodologies used to design and evaluate complex interventions in global health.

Four areas considered central to complex interventions research were explored – intervention design, evaluation of outcomes, assessment of causal mechanisms, and evaluation of context. In each of these areas, a different mixed method, statistical, or qualitative methodological approach was employed following available guidance. Data were drawn from the design and evaluation of the PRIME intervention, a complex health service intervention to improve care for malaria at health centres in rural Uganda.

Conceptual and methodological challenges were encountered in each area of investigation. Opportunities for improving each methodological application are suggested alongside an overall recommendation for greater reflection on, and reporting of, the processes and investments necessary for conducting complex interventions research. Additionally, the evidence produced in each area of investigation revealed different, partial and incommensurable accounts of the intervention and its effects. This draws attention to the challenges that can arise when seeking to combine evidence of 'what works' with evidence from methodologies that employ different approaches to understanding how interventions are taken up and produce effects.

Approaches to accounting for complexity in intervention research need to evolve from focusing on the narrow question of 'what works' towards emphasising a more dynamic and multi-perspective question of 'what happens'. Such an approach may be particularly useful for understanding the multiple and varied effects of complex interventions and their role in improving health and wellbeing.

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Abbreviations

ACT	Artemisinin combination therapy
AL	Artemether-Lumefantrine
CI	Confidence interval
cRCT	Cluster randomised control trial
FCM	Fever Case Management
HCM	Health Centre Management
ITN	Insecticide treated net
MRC	Medical research council
mRDT	Malaria rapid diagnostic test
OR	Odds ratio
PCS	Patient Centred Services
RCT	Randomised control trial
RR	Risk ratio
SD	Standard deviation
SEM	Structural equation modelling

CHAPTER 1. Introduction

1.1. Background

Complexity is a term now ubiquitous in health interventions research. Its use is broad; it is used to describe both the world that an intervention attempts to change as well as interventions themselves. Its use represents acknowledgement that changing situations in order to improve health is often not simple. Such situations include attempts to change social or behavioural processes related to health and health care (Hawe 2015a). This recognition of complexity has reshaped the approaches seen as appropriate for the design and evaluation of interventions (Craig et al. 2008; Moore et al. 2015). As the number of methodological approaches proposed for getting a handle on this complexity proliferates, efforts to bring together a coherent set of methods that can account for complexity become more urgent and yet more difficult. It is this task that this thesis aims to address.

Since the turn towards evidenced-based health care and policy, the randomised control trial (RCT) has been considered the gold standard study design for demonstrating the effect of an intervention (Sackett et al. 1996). The RCT is praised for the simplicity of its design. Through randomisation, RCTs minimise selection bias and control confounding in order to eliminate the role of chance, and to produce robust measures of an intervention's effect (ibid). However, some have argued that the RCT may be inappropriate to guide the design and evaluation of complex health interventions (Cohn et al. 2013; Hawe, Shiell, and Riley 2004; Ranson et al. 2006; Victora, Habicht, and Bryce 2004). These arguments emphasise both epistemological and practical limitations and suggest that RCTs may not be responsive to the complexities of the social world producing results which neither represent nor can be generalised to the everyday realities of improving health and wellbeing.

In response to these challenges, researchers have been integrating a range of methodological approaches to account more fully for complexity in intervention design and evaluation. Many of these approaches are drawn from disciplines outside of health and employ different considerations when accounting for the social world in evaluations of intervention effect. Several of these approaches have been consolidated into a series of highly influential guidance documents published by the UK Medical Research Council (MRC)

which outline a comprehensive framework for the design and evaluation of complex interventions in health (Campbell et al. 2000; Craig et al. 2008; Moore et al. 2015). The MRC guidance suggests that rigorous outcome evaluations should be complemented by a process evaluation. Process evaluations aim to open the 'block box' of how interventions function by examining the design of the intervention, assessing the fidelity and quality of implementation, clarifying mechanisms of impact, and identifying contextual factors associated with variation in outcomes (Craig et al. 2008; Moore et al. 2015). Together outcome and process evaluations are intended to provide a comprehensive package of evidence describing not only if an intervention works, but how, for whom, and under what circumstances (ibid).

In practice, however, there remains much uncertainty about which methodological approaches are best suited for designing and evaluating the different components of outcome and process evaluations. The increasing rhetoric on conducting these so-called comprehensive evaluations has not been met with sufficient empirical examples and practical guidance on how to employ certain recommended methodologies. Likewise, outcome and process evaluations remain largely unintegrated – they are usually conducted by different evaluation teams and findings are usually published in different journals. Some attempts at integrating findings have been successful (Christie et al. 2014; Oakley et al. 2006; Strange et al. 2006), while other attempts have been met with both epistemological and practical challenges (Moffatt et al. 2006; Munro and Bloor 2010; Riley, Hawe, and Shiell 2005).

The enthusiasm with which the complex intervention concept has been taken up in the last 15 or so years combined with the challenges encountered in practice is indicative of a more general observation of the field: accounting for complexity is now a feature of health interventions research, but it is unclear how this might best be accomplished. The current uncertainty in complex interventions research may be partly due to the lack of systematic appraisal of and reporting on evaluation concepts and their associated methodologies. As a result, it has been difficult to identify the points of connection across the recommended methodological approaches, as well as points where particular practices or interpretations may be contested. Further development of methodologies for analysing and evaluating complexity is needed in order to realise the potential of complex interventions to improve

health and strengthen health systems (Datta and Petticrew 2013; Smith and Petticrew 2010).

This aim of this thesis is to examine methodological approaches used in complex interventions research. The motivating case for this thesis is the PRIME intervention, a complex intervention to improve care for malaria at public health centres in Uganda. Improving the design and evaluation of interventions targeting health and access to care is important in low resource contexts where severe inequalities in health and wellbeing remain a pressing global challenge (United Nations 2015b). The PRIME malaria intervention forms a useful case for examining the wider implications of complex intervention research in global health. Recent efforts to improve malaria control and move towards elimination have been focused on developing, improving access to, and sustaining uptake of effective life-saving technologies (Bastiaens, Bousema, and Leslie 2014; Whitty et al. 2008). These efforts, some consider, serve as an 'entry point' for improving other health systems strengthening and disease surveillance initiatives more generally (World Health Organization 2015a). As such, gains made in malaria intervention research are believed to translate into wider global health solutions. Examining the experiences of designing and evaluating a complex malaria intervention may provide insights into improving the design and evaluation of interventions in a wider global health context.

In this thesis, I begin with a review of the literature to examine how 'complexity' and the complex intervention concept have been framed, and the discourses on the evaluation methodologies employed as a result, including in relation to global health research. Next, drawing on the PRIME intervention example, I examine methodological approaches to four areas of investigation considered central to complex intervention research drawn from the MRC guidelines: intervention design, evaluation of primary outcomes, assessment of causal mechanisms, and evaluation of context. I explore these areas through a series of methodological exercises which are intended as a way of engaging deliberately with each area's theoretical and methodological underpinnings, as well as with the process of implementing and interpreting findings. In so doing, I produce a detailed empirical example of each methodology in practice and examine the processes through which these methodological approaches attempt to account for complexity. I discuss how findings from the process of implementing each methodology might inform their future application. I also compare the commonalities and differences between the different methodological

approaches and their interpretations. I draw together these the findings to discuss the potential for different evaluation frameworks to advance complex interventions research in global health.

This thesis is comprised of eight chapters. Chapters 1-3 present the research focus and thesis framework: In Chapter 1, I review the literature contributing to the current efforts in complex intervention design and also outline the rationale, aims and objectives of the thesis. In Chapter 2, I describe the motivating case for this thesis – the PRIME intervention. In Chapter 3, I outline the overall methodological approach of the thesis. Chapters 4-7 present the methodological exercises in each area considered central to complex interventions research: In Chapter 4, I examine the process of designing the PRIME intervention. In Chapter 5, I analyse the primary outcomes of the PRIME cluster RCT (cRCT) including methods that extend the standard statistical approach to trial analysis. In Chapter 6, I assess the hypothesised causal mechanisms of the PRIME intervention using statistical mediation analysis. In Chapter 7, I evaluate the context influencing the PRIME intervention using a qualitative case study approach. Finally, In Chapter 8, I discuss the findings from across the methodological exercises and consider implications for complex interventions research in global health.

1.2. Literature review

1.2.1. Introduction

In this section, I present a review of the literature on the complex intervention concept as applied in health interventions research and examine the discourses around different approaches to intervention design and evaluation that have been employed as a result. Before presenting the findings of the review, I begin by describing my initial experiences with reviewing the complex interventions literature which prompted the review approach presented in this chapter.

The literature on designing and evaluating complex interventions has been expanding rapidly in the past ten or so years. As I began reviewing this literature for this study, it became clear that there were multiple pockets of literature to examine as a result. I began by focusing on the evaluation literature from disciplines outside of health and health care interventions, but which are being increasingly referenced in evaluations of health-related interventions. These included approaches such as realist (Pawson 2013; Pawson and Tilley 2004), theory of change (Blamey and Mackenzie 2007; Connell et al. 1995) and theory-driven evaluation (Chen 1990, 2005). These approaches were initially developed and applied to evaluations in education, criminology, political science, social policy, and health promotion. I was interested in drawing out methodological examples from theoretical proposals and empirical examples of these approaches. I reviewed numerous theoretical, methodological and empirical studies and reviews relating to these different evaluation approaches. However, I came to realise, like others (Coryn et al. 2011; Datta and Petticrew 2013; Marchal et al. 2012), that the application of each evaluation approach has been too inconsistently and poorly reported to usefully draw out methodological examples.

During this review process, it became clear that as these approaches were being integrated into the complex health interventions literature, the result appeared as a cacophony of theoretical commentaries, empirical studies, and new methodologies and tools. Also during this time, a group of researchers published a report of their efforts to draw together a similar literature into a new MRC guidance for process evaluations of complex interventions (Moore et al. 2013). This represented the next step in the progression of the highly influential MRC guidance documents for the design and evaluation of complex interventions which had been published in 2000 (Campbell et al. 2000) and updated in 2008

(Craig et al. 2008). Yet, these guidance documents were being contested by researchers drawing on expertise from different disciplinary perspectives (Anderson 2008; Cohn et al. 2013; Hawe, Shiell, and Riley 2009). It appeared that there was a growing body of diverse and contrasting literature focusing around the complex interventions concept in different, but intersecting ways.

To make sense of this heterogeneous literature, I realised that a static account of methodologies would be insufficient to describe the diversity and dynamics of emerging proposals and debates. Drawing on Foucault's idea of genealogy as 'a history of the present' which follows the rise of particular discourses (Foucault 1981), I chose to trace a genealogy of the complex interventions concept. This involved exploring the commonalities and tensions across and between the different perspectives contributing to current rhetoric in complex interventions research. In tracing a genealogy, or narrative, of this literature, I took the perspective that the ideas, practices and methodologies in complex interventions research have undergone a process of evolution and development. They are not inherent or immutable. Rather, they are shaped by events, institutions, people and politics which operate overtly or implicitly to influence how problems and solutions are proposed and resolved.

The set of literature for this review initiated from seminal papers and books related to the evaluation of complex interventions in health and allied fields (linked to the MRC Guidance documents and similar publications, for example by the Evaluation, Trials and Studies programme of the National Institutes for Health Research), and related to the evaluation of social programmes outside of health care (linked to theory-based evaluation, health promotion, complexity science). From here, references were identified by hand searching reference lists and key journals, electronic citation tracking of the MRC guidance documents and several key papers, and searching of electronic databases. To synthesise the literature, I mapped the key conceptual, theoretical, methodological contributions within each of the different perspectives including influential actors and events, and also identified points of intersection between the different perspectives. At the points of intersection, I examined the influence and role of different perspectives in shaping how ideas, concepts and methodologies have been taken up and applied to the complex interventions concept.

The genealogy presented traces the complex intervention concept and examines the roles of significant actors and movements in shaping research, evidence and practice. I examine how the concept of the 'complex intervention' has arisen in response to the perceived failures and limitations of previous policy and development programmes. With its origins in the evidenced-based medicine movement, I show that the concept of the complex intervention has been made to align with the desire for evidence to be gained through use of the RCT as the gold standard study design. I suggest that researchers in disciplines outside of health have used this dominant framework as a counterpoint against which to promote different research agendas. These contestations have been taken up into the dominant frame as research has moved towards defining and implementing a comprehensive approach to intervention design and evaluation that seeks to enhance the RCT framework. Despite the appearance of a consolidated framework represented in the MRC guidance documents accounting for a range of perspectives and methodologies, I argue that there is much uncertainty both in the conceptualisation and use of evidence to inform interpretations of complex interventions.

1.2.2. The rise of the complex health intervention

The desire to intervene in the world to improve health and wellbeing is not new. Hawe (2015a) describes that since John Snow's intervention at the Broad Street pump to halt the spread of cholera, interventions have always been based on particular views about why things are the way they are, and how they might be changed. Research on health, Hawe notes, has moved through phases including a rebound of science post World War II, through the mostly government-sponsored large-scale public and population health initiatives in the 1970s and 1980s, to the experience of poorly performing RCTs of social and community-based interventions in the 1990s (ibid). This is around the time when interventions began to incorporate ideas of complexity in design and evaluation, such as being described as comprehensive and multilevel. From this time, the concept of complex interventions has been shaped by contributions from the MRC (Campbell et al. 2000; Craig et al. 2008; Moore et al. 2015), the evaluation of social programmes in disciplines outside of health (Chen 1990; Pawson and Tilley 2004; Weiss 1998), and more recently the emerging ideas from fields such as complexity and improvement science (Kernick 2006; Rickles, Hawe, and Shiell 2007). This history demonstrates the manifold iterations and contributions that serve as the background to the "…vigorous and occasionally strident

contest of ideas (that) is now taking place" in complex health interventions research (Hawe, Riley, et al. 2015:308).

1.2.3. Approaches to accommodating complexity in health interventions research

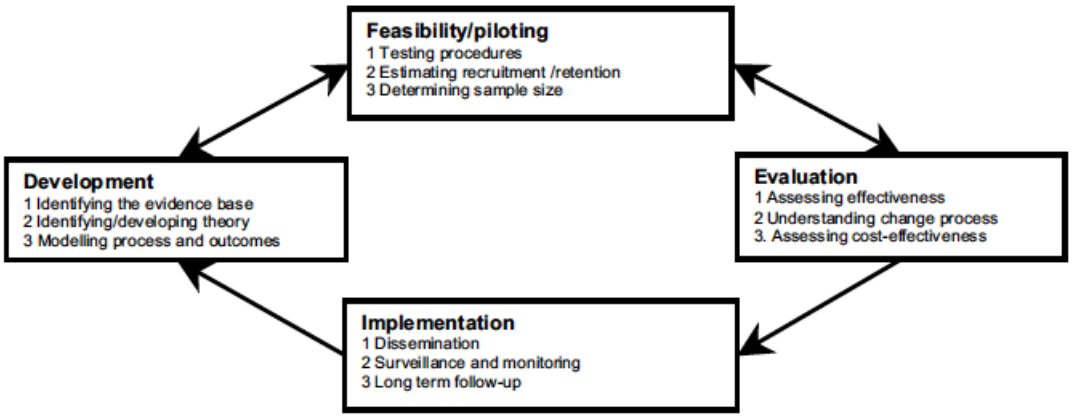
The concept of the complex intervention can be seen to have emerged as a counterpoint not to simplicity, but to the murkiness that accompanied attempts to understand the social world and why previous policy and development programmes were not functioning as expected (Hawe 2015a; Susser 1995). Different disciplines have placed emphasis on different modes of explaining these failures. Such differences are mirrored in the debates over conceptualisations of complex interventions and approaches to their design and evaluation.

The MRC has played a central role in framing health-related social and policy programmes as 'complex interventions' since its efforts from the late 1990s when they brought together scientists to define and propose models for evaluating interventions that were not as simple to define and assign as interventions that focus solely on biological processes of human health (i.e. development and testing of pharmacological products). Their *Framework for the Development and Evaluation of RCTs for Complex Interventions to Improve Health* (Medical Research Council 2000) released in 2000 was influential in providing an architecture on which researchers could hang questions derived from a biomedical research perspective onto non-biomedical arenas such as social, economic and political health-related experiences. The framework proposed RCTs as the gold standard study design for evaluating complex interventions and outlined a linear design and evaluation framework based on models applied in pharmaceutical research and development. Crucial here, rather than proposing the social world as too complex for this approach, researchers were compelled to deconstruct and define the notion of complex, rendering it somehow delineated and predictable and enabling it to be incorporated into the RCT framework. This has been referenced as the 'turn to the complex' in health interventions research (Cohn et al. 2013).

In response to critiques that the 2000 Guidance proposed an overly linear process of intervention design and evaluation, an expanded working group proposed that designs should consider the complex characteristics of designing multifaceted health-related social interventions (Craig et al. 2008). The revised guidance released in 2008, *Guidance on*

designing and evaluating complex interventions (Medical Research Council 2008), replaced the linear development process of interventions with a cyclical figure with four interacting phases: development, feasibility and piloting, evaluation and implementation, Figure 1.1. The 2008 Guidance still suggested the RCT as the ideal design, where feasible, but acknowledged the importance of incorporating 'process evaluations' to examine the many ways in which interventions may produce effects, or not. These process evaluations were intended to examine how interventions are designed, implemented and interact with context to produce anticipated, as well as unanticipated, outcomes.

Figure 1.1: MRC key elements for intervention design and evaluation



Source: Medical Research Council (2008:8)

The 2008 Guidance was helpful for summarising some of the messages emerging from debates in the complex interventions literature, but provided little in terms of practical guidance, empirical examples, or consolidation of best practices and lessons learned. For example, the 2008 Guidance simply states that "process evaluations should be conducted to the same high methodological standards and reported just as thoroughly as evaluation of outcomes" (Medical Research Council 2008:12). The lack of discussion of how this work should be done was picked up on by those attempting to follow the principles in practice, who proposed the need for methodological and practical examples (Moore et al. 2013). This same group was mobilised to set out a third guidance document in 2014, *Process Evaluations of Complex Interventions: Medical Research Council Guidance*, which expanded significantly the ideas of the 'evaluation' phase, providing more theoretical, practical and methodological guidance (MRC Population Health Service Research Network 2014). An additional contribution of this 2014 Guidance was to mobilise the term 'process evaluation' to represent specifically the evaluation elements of intervention implementation, causal

mechanisms and context, and the need to integrate these as part of the comprehensive design and evaluation of complex interventions.

Across these different iterations of the MRC Guidance, the approach to defining the complex intervention takes the drug trial as a frame of reference. As a medical research organisation familiar with the success of drug trials for identifying solutions to improve health outcomes, this appears salient. As it is played out in defining interventions fit for evaluation, the complex intervention is proposed as a composition of 'active ingredients' that, much like the chemical compounds of drugs, make an intervention work. The objective when evaluating complex interventions is to identify these 'active ingredients' for further study and replication. This notion of the active ingredient was informed by work in health psychology seeking to identify psychological techniques for changing individual health-related behaviours (Michie and Abraham 2004; Michie and Johnston 2012). This way of delineating social processes into constituent parts extends to the characterisation of people and places with which interventions interact – complex interventions are defined as having several interacting intervention components, target behaviours and groups, anticipated outcomes, and implementation options, Figure 1.2.

Figure 1.2: MRC definition of a complex intervention

Some dimensions of complexity:

- Number of and interactions between components within the experimental and control interventions,
- Number and difficulty of behaviours required by those delivering or receiving the intervention
- Number of groups or organisational levels targeted by the intervention
- Number and variability of outcomes
- Degree of flexibility or tailoring of the intervention permitted

Source: Craig et al (2008:7)

The MRC Guidance documents are now highly influential and have been taken up as the dominant approach in health interventions research (Craig and Petticrew 2013). In addition to this role in framing the current discourse, the MRC definition has performed a role as a point of departure for different actors in the health interventions arena to stake out their terrain and influence how complex health interventions are conceptualised.

As a counterpoint to the MRC framework, complexity science has been taken-up as way of explaining the social world as a dynamical system (Kernick 2006). Based on computer-based simulations of networks, the mathematical basis of complexity science offers a set of principles and formulae to explain the emergence of a particular patterns of occurrences from seemingly chaotic functions of a system (Paley 2010). Systems are said to exhibit the same properties such that the effects of implementing an intervention into the system can be explained using mathematical formula or more simply, using metaphors to represent social complexity such as the predictable patterns of "crowds behaving like the atoms in a magnet" (Rickles et al. 2007:935). Researchers have used these ideas to define interventions not in component parts, but as whole events that are implemented into systems where they either produce a range of effects, or not, depending on their interaction with the properties of the system (Hawe et al. 2009; Shiell, Hawe, and Gold 2008). While it has been argued that complexity science has been misappropriated into health interventions research (Paley 2010), what it has offered researchers is a set of ideas, definitions and methodologies for counteracting what they perceive as the limitations of the MRC guidance (Hawe, Shiell, and Riley 2004).

More recently, concepts from social theory have also emerged as a counterpoint to the MRC framework and have proposed a positioning of the social world as an ecological system. Researchers in this frame draw on concepts from evolutionary biology which proposes that environmental ecologies operate by sensing and evolving in reaction to constantly shifting elements. They contend that when interventions are introduced, they become entangled in the environment in multiple and unpredictable ways. Researchers propose that interventions are neither multicomponent (Craig et al. 2008) nor predictable events (Hawe et al. 2009), but rather "dynamic and constantly emerging sets of processes and objects that not only interact with each other, but come to be defined by those interactions" (Cohn et al. 2013:42). This framing is being advanced by anthropologists and sociologists drawing on social theory to examine and explain the agency of human, material and immaterial actors as they interact with each other in particular and unpredictable ways (Bilodeau and Potvin 2016; Rod et al. 2014).

Looking across these different conceptualisations of the complex intervention, two interconnected observations become salient. The first recites what has been acknowledged elsewhere: complexity is a construct. That is, the degree to which an

intervention is complex or simple is determined by a researcher's perceptions of the world and their engagements with the varying modes available for defining, evaluating and reporting interventions and their effects (Petticrew 2011; Rogers 2009). The second suggests that this constructed nature of the concept is its utility. 'Complex interventions' have become a thing around which to focus arguments about what constitutes meaningful and legitimate forms of knowledge production. The concept is taken up differently depending on who is using it and for what purpose. Some purposes, for example, have been to promote research agendas, such as those described above. Others have been to advocate for methodological advancement, such as the inclusion of more qualitative research within RCTs (Glenton, Lewin, and Scheel 2011; Lewin, Glenton, and Oxman 2009; O'Cathain et al. 2013), the application of novel statistical modelling techniques (Emsley, Dunn, and White 2010; Hawe, Shiell, Riley, et al. 2004; Rickles 2009; Watson and Lilford 2016), or the integration of new evaluation frameworks (Bonell et al. 2012; Fletcher et al. 2016; Jamal et al. 2015).

While the RCT framework as proposed by the MRC guidance remains dominant, these shifting uses of the complex intervention concept have become increasingly intertwined and influential. As these debates have expanded, it remains unclear how and what different epistemological and methodological approaches are intended to contribute to knowledge production. This raises questions as to what constitutes best practice for the design and evaluation of complex interventions in health and how these might be used to improve the production and use of evidence (Anderson 2008; Moore et al. 2013).

In the next section, I examine how the RCT framework has evolved in response to different perspectives of the complex interventions concept and the epistemological and methodological challenges that remain for complex interventions research.

1.2.4. The evolving RCT framework for complex interventions research

The features of the evidence-based medicine movement have played an important role in promoting the MRC guidance as the dominant approach for health interventions research. I use the term 'movement' deliberately to acknowledge that social and political processes are involved in establishing the evidence-based movement as a dominant paradigm (Pope 2003) and continually shaping it over time (Behague et al. 2009). Gaining strength since its inception in the early 1990s, the evidence-based movement argues that health practices

and policies should be based on rigorously derived evidence as opposed to unsystematically derived human opinion, experience or intuition (Sackett et al. 1996). The movement promoted the RCT as the gold standard study design for producing this evidence which is then synthesised in systematic reviews in order to determine which interventions work and which do not. Together, these technologies provided an empirical motivation for changing clinicians' behaviour to align with specific standards and expectations of practice (Lambert 2006; Timmermans and Berg 2003). The use of systematised evidence to standardise practice has been argued to have been particularly aligned to a climate of increasing demands for transparency and accountability across all public domains (Mykhalovskiy and Weir 2004) enabling the movement to be taken-up in non-clinical fields such as public health, health promotion and social policy (Behague et al. 2009; Gough and Elbourne 2002). There is now increasing emphasis on the inclusion of interpretive qualitative and experiential data which consider the social processes of evidence production and use shifting the focus of the movement to 'evidence-informed' (Gough and Elbourne 2002; Nevo and Slonim-Nevo 2011).

As the use of RCTs started to expand beyond biomedical interventions, researchers found that both the internal and external validity of trials were being threatened by the realities of implementing interventions beyond the confines of well-defined and controlled experimental practices of biomedical and pharmaceutical trials. Features that formed the cornerstone of the evidence-based agenda including blinding, control, outcome measurement, and causal interpretations had to be reconsidered (Bryce et al. 2004; Kirkwood et al. 1997; Ranson et al. 2006; Victora et al. 2004). The response was to refine experimental study designs and advance methodologies in an attempt to 'account for' social processes and context using quantitative measurements and statistics. Methodological advancements accommodated social processes considered to influence the effect of the intervention by identifying, enumerating and modelling specific behavioural, biological and environmental determinants in predictive and explanatory models of intervention effects (Eldridge et al. 2005; Hardeman et al. 2005; Victora et al. 2005). This response to complexity has been described as bracketing-out, or flattening, of the social world in order to maintain the evidence-based agenda of developing generalisable research recommendations based on a scientifically replicable method (Adams 2013).

In disciplines outside of biomedicine, the RCT has had a different trajectory which has since influenced the dominant discourses around the complex interventions concept in health interventions research. During the 1960's 'golden age of evaluation', significant advancements were made in the design and analysis of randomised controlled experiments for the evaluation of social reform and public policy programmes in areas such as health promotion, education, criminology and community services (Alkin 2012; Oakley 1998). In these disciplines, experimentation was marked by a different impetuous than in clinical medicine. Rather than using RCTs to generate systematised evidence to standardise clinical practice, evaluators were interested in using the methodology to test rival hypotheses and explain why social programmes were not working as expected (Oakley 1998). The complexity of intervening in the social world became a feature of, rather than a threat to, experimentation. For example, by 1991, a seminal evaluation textbook had already outlined important considerations for the evaluation of social programmes including: the internal structure and functioning of programmes being evaluated; the constraints that shape design and delivery; and the societal factors that influence development of programmes, how programmes themselves change over time, and how programmes contribute to social change (Shadish, Cook, and Leviton 1991).

To understand these processes, evaluators of social programmes have focused on advancing methodologies for defining and testing 'theories of change' and similar narratives explaining the social processes that produce intervention effects in dynamic settings (Connell et al. 1995; Pawson and Tilley 2004; Rogers and Weiss 2007; Weiss 1995). To do so, a range of different qualitative and quantitative data in addition to trial outcomes are seen as integral components of evaluation (Chelimsky and Shadish 1997; Chen and Rossi 1989; Ellard and Parsons 2010; Judge and Bauld 2001). These narratives provide an explanation of intervention effects that are more socially nuanced than the statistical explanations derived exclusively from statistical measurements of confounders, interactions, clustering, and sub-group effects, for example. Hawe (2015b) provides a useful description of how this approach to evaluation differs with her suggestion that the social world that produces challenges for trialists in the evidence-based movement is often simply 'business-as-usual' contexts for evaluators of social programmes.

These two different approaches to RCTs, the biomedical and the social, appeared to be in largely separate literatures until a cross-pollination of ideas apparent around the mid-2000s

when we start to see the rise of the complex intervention. Two notable papers were published in the influential biomedical journal, *The BMJ* – Hawe and colleagues (2004) and Oakley and colleagues (2006). These papers highlighted important considerations for complex interventions research drawing on experiences from the evaluation of health promotion and social programmes (Hawe, Degeling, and Hall 1990; Rootman et al. 2001; Rossi, Lipsey, and Freeman 2004; Wight and Obasi 2003). Hawe and colleagues' (2004) contribution challenged readers to reconsider the notion that standardised interventions were a group of components replicated in the same form at each implementation site. Instead, they introduced the idea of theorising and replicating the intervention's function, or hypothesised change mechanism, which could be introduced in different forms in each site depending on the participants and context. Oakley and colleagues' (2006) contribution introduced the need to look beyond outcomes and examine the processes involved in producing change such as participant experiences and features of the context into which interventions are implemented.

These papers, together with other similar contributions – see for example, Wight and colleagues (2003); Power and colleagues (2004); Audrey and colleagues (2006); Strange and colleagues (2006); and Hawe, Shiell, Riley and Gold (2004) – highlighted the challenges that arise when the RCT is considered in light of the social world of people, places, and processes that produce interventions and their outcomes. Importantly, these contributions served to bridge the clinician-evaluator audience to new opportunities for conceptualising and negotiating the complex interventions concept within the RCT framework. Since this initial work, the health interventions literature has expanded with contributions from a wide range of disciplinary perspectives. The result has raised a number of epistemological and methodological challenges to using the RCT framework for the design and evaluation of complex health interventions which I explore in the next section.

1.2.5. Challenges to evaluating complexity using the RCT framework

Epistemological critiques concerning the use of the RCT framework to evaluate complex interventions focus on the ways in which different approaches to evaluation perceive reality – as objective and measurable, or as subjective and relational, for example – and therefore, what research questions are asked and how data are generated and analysed to understand the effect of interventions in the real world (Robson 2011). For the RCT, critiques generally focus on the limitations of the positivist epistemology which suggests

that the causal effect of an intervention can be inferred from the comparison of objectively measured outcomes between intervention and control arms (ibid). Critics who instead perceive reality as subjective and relational argue that the RCT is an oversimplified model of reality and is inappropriate for evaluating the complexities of everyday life that comprise interventions and social change (Cohn et al. 2013; Pawson and Tilley 2004; Picciotto 2012). Researchers engaged in 'realist evaluation' have become increasingly vocal in this contestation (Van Belle et al. 2016; Marchal et al. 2013; Pawson 2013). They suggest that a realist epistemology, which proposes that reality is independent from what we can observe and measure, can be more productive in examining how interventions ignite mechanisms that interact with their surrounding contexts to produce change (Pawson and Tilley 2004). The introduction of realist evaluation in health interventions research has brought a heightened focus to the concepts of contexts, mechanisms and outcomes as key components of understanding how interventions produce change, and in what circumstances. Yet, the commensurability between the RCT and more relational ways of perceiving reality remains contested (Bonell et al. 2012, 2013; Marchal et al. 2013).

Methodological critiques concerning the use of the RCT framework to evaluate complex interventions focus on the challenges of implementing RCTs as well as implementing the interventions themselves. Features of the RCT, such as identifying feasible control arms and minimizing the crossover of intervention components between study arms, become challenging with increasing complexity of the intervention or the settings into which they are implemented (Hawe, Riley, et al. 2015; Okwaro et al. 2015; Ranson et al. 2006). Such settings have also been shown to introduce challenges when attempting to disentangle intervention effects from the different ways in which groups of people interact with the intervention and evaluation activities (Audrey et al. 2006; Bird, Arthur, and Cox 2011; Petticrew et al. 2012). Complexity of the setting and the intervention introduce challenges with theorising, measuring and reporting variations in intervention implementation across trial sites which has been shown to threaten the internal validity of the RCT (Lindsay 2004; Michie et al. 2009; Shepperd et al. 2009). Others suggest that the control and standardisation of the RCT framework conceals the synergistic interactions inherent in how interventions produce change (Hawe et al. 2009; Mackenzie et al. 2010). Researchers have also described that the complexities underlying the practices enacted in the process of 'doing' a trial influence interpretation of trial outcomes, but are rarely acknowledged or reflected in reports of intervention content and outcomes (Reynolds et al. 2014; Wells et al.

2012). While this is not an exhaustive examination, it demonstrates the range of critiques that have been wagered against the RCT.

Yet, instead of these contestations being seen to weaken the RCT position, it appears that they have been absorbed into the wider narrative emphasising the need for a comprehensive approach to intervention design and evaluation as promoted by the MRC guidance documents. Lambert (2006) has argued that this type of 'assimilationist property' wherein contestations become absorbed into new parameters is characteristic of the evidenced-based movement. Because the movement can be interpreted as a collection of processes built around a single idea – the RCT – these processes can also shift in response to different discourses. This characteristic, Lambert argues, has enabled the RCT to attain and maintain a dominant position amongst approaches to knowledge production in health research (ibid). The evolution of the MRC guidance documents appears the latest manifestation of this assimilation process. The 2008 and 2014 guidance have consolidated and repackaged a range of ideas and contestations under the rubric of complex intervention research which consists of outcome evaluations supplemented by process evaluations. In the next section, I examine the contributions of these guidance documents and discuss some of the conceptual and methodological challenges that remain for complex interventions research.

1.2.6. Accounting for complexity using outcome and process evaluations

Together, the MRC 2008 and 2014 guidance documents suggest that evaluations of complex interventions should consist of a rigorous outcome evaluation complemented by a process evaluation. Outcome evaluations determine if the intervention works, or not. Process evaluations determine how an intervention works, or not, by examining the fidelity and quality of implementation, clarifying mechanisms of impact, and identifying contextual factors associated with variation in outcomes (Craig et al. 2008; Moore et al. 2015). The guidance documents also suggest that these evaluations should be based on a detailed description of the intervention including its content and hypothesised theory of change linking the intervention inputs to intended outcomes (Craig et al. 2008; Moore et al. 2015). See Figure 1.3 for a description of these areas of investigation considered central to complex intervention research. By assessing and reporting detailed intervention characteristics and how, for whom, and under what circumstances interventions work, such comprehensive evaluations are suggested as a means to overcome the challenges of the

RCT by providing further evidence to explain the effect and functioning of the intervention. In so doing, comprehensive evaluations intend to improve the generalisability and transferability of evidence to guide health practice and policy (Hoffmann et al. 2014; ICEBeRG and Francis 2006; Michie et al. 2009).

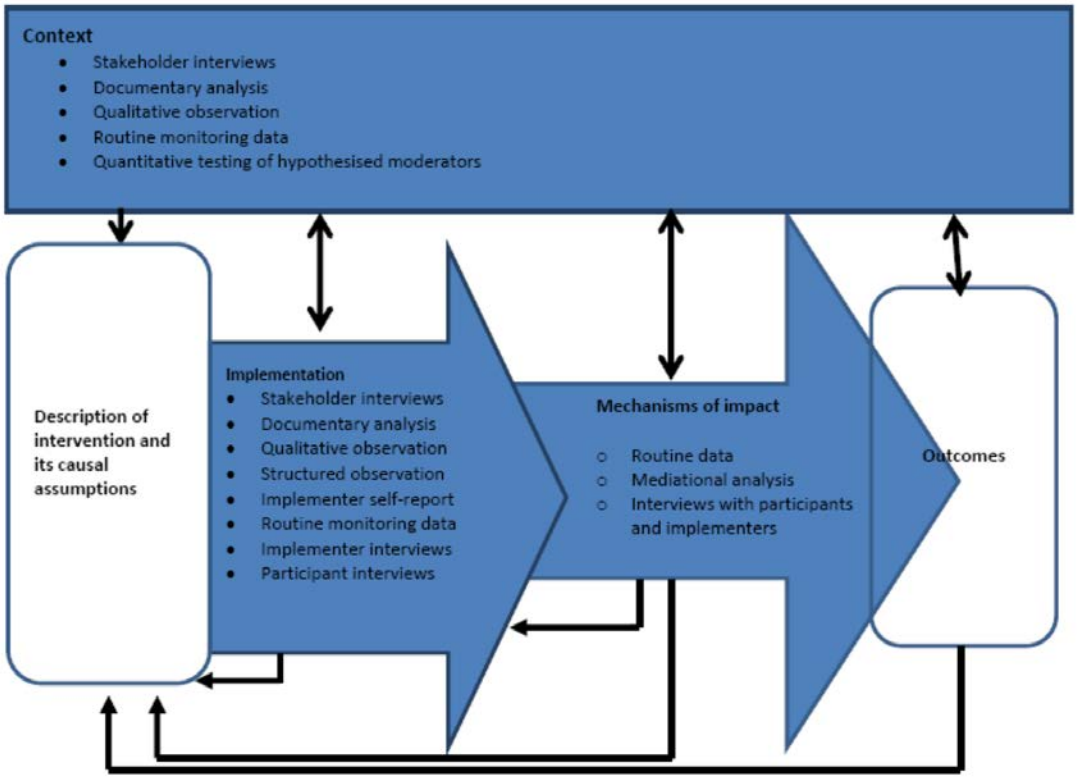
Figure 1.3: Areas of investigation considered central to complex intervention research

- Intervention content and theory – interventions should be evidence-based and theoretically informed, supported by a logic model and/or theory of change describing how the intervention inputs are hypothesised to produce outcomes
- Outcomes – the measure of the effectiveness of the intervention
- Implementation – the structures, resources and processes through which delivery is achieved, and the quantity and quality of what is delivered
- Causal mechanisms (mechanisms of impact) – the intermediate mechanisms through which intervention activities produce intended (or unintended) effects
- Context – the factors external to the intervention which may influence its implementation, or whether its mechanisms of impact act as intended.

Source: Moore et al (2014), Medical Research Council (2008)

The guidance also suggests that a combination of methodologies should be used to evaluate the different areas of investigation. This inclusion of multiple different methodological approaches in the guidance is an important step forward for evidence-based health interventions research. It affirms what has been noted elsewhere – that a diversity of evidence is needed to better understand how interventions function to produce effects (Lambert 2013). The 2014 guidance, specifically, suggests which types of quantitative and qualitative methods might be well suited to the objectives of the different areas of investigation. These are summarised in a schema which provides a useful visual representation of how the different areas of investigation are intended to fit together, Figure 1.4. As represented in the schema, each area of investigation is intended to provide a different piece of evidence describing a function of the intervention – how the intervention is intended to work, how the intervention was implemented, the effect of the intervention, the mechanisms that cause the observed effects, the contextual factors that influence the intervention and its effects, and so on. The assumption is that, when added together, these pieces of evidence will provide a comprehensive picture of the intervention and its effects.

Figure 1.4: Schema of perspectives integrated into the MRC process evaluation guidance



Source: Moore et al (2014:49)

Yet, despite the MRC guidance appearing rather prescriptive regarding the conceptualisation, methods and purpose of each area of investigation and how they are intended to fit together in a comprehensive evaluation, there are noted challenges when translating these into practice. In the paragraphs that follow, I provide a brief examination of the challenges in each of the areas of investigation to highlight the implications of these challenges in practice. Each of these areas are then explored in more detail in subsequent chapters of this thesis.

Outcome measures have become increasingly challenging to identify and define under conditions of increasing complexity of interventions and their settings (Datta and Petticrew 2013). These challenges may manifest when attempting to assess the effectiveness of interventions which may have effects across a range of domains (Lilford et al. 2010), or which may be implemented at the community level and intend to produce effects on individual level health or behavioural outcomes (Feldman 1997; Lilford et al. 2010). For example, a study assessing the effect of a nursing intervention for post stoke rehabilitation found that measuring intervention effect with an aggregate outcome comprising measures

from a validated health profile was not sensitive to the range of physical, emotional, psychological, and participation outcomes the intervention was targeting. Instead, the study authors found that re-analysing the study by expanding the aggregate measures into eight different outcomes provided a more nuanced assessment of intervention effect (Mayo and Scott 2011). Alternatively, in a study looking to assess the impact of a community health worker intervention on health seeking practices, a composite outcome was created to measure the uptake of three different community health interventions with the hypothesis that this could capture a more comprehensive assessment of intervention effect (Watt et al. 2015). Despite the acknowledgement that complexity introduces challenges for the appropriate selection of outcome measures, there are relatively few empirical examples specifically addressing this challenge and the influence on interpretations of intervention effect.

The concept of causal mechanisms has also presented challenges for researchers. For example, a review of studies employing realist evaluation techniques found that interpretation of the mechanisms concept ranged from being equated to a theory of how the interventions will work, to representing groups of actors participating in the intervention, to describing barriers and facilitators of intervention activities (Marchal et al. 2012). Recent work to define the concept suggests that mechanisms are often misunderstood in the evaluation literature and can be challenging to codify, but remain a useful concept for revealing intervention processes that would otherwise be obscured by focusing on outcomes alone (Astbury and Leeuw 2010; Dalkin et al. 2015). In the theory-based evaluation approaches, the mechanism is conceived as the response triggered in stakeholders that results in different outcomes (Weiss 1997b), or as any mediator that intervenes in the relationship between two other components of an intervention (Chen 2005). Studies employing statistical approaches to assessing mechanisms also employ this notion of mechanism as mediator of intervention effects (Emsley et al. 2010). Although there is much rhetoric on the mechanisms concept, there are relatively few empirical examples from which researchers can make informed decisions on how, and with what effect, data on mechanisms can be identified and incorporated with other areas of complex interventions research.

Context, likewise, has been a challenging concept to translate into practice. For example, a critical examination of conceptualisations of context in complex interventions revealed

variation in how the concept was applied: context ranged from descriptions of the setting where interventions were implemented, to lists of contextual 'barriers' and 'facilitators', to more dynamic processes of social interaction between people and their surroundings (Shoveller et al. 2015). These findings were echoed in another review to establish a state-of-the-art description of the context concept which found that definitions employed by researchers were varied and unspecific (Pfadenhauer et al. 2015). The concept, the authors argued, is only partially mature (ibid). While context is considered crucial to understanding the circumstances under which an intervention works, and might work elsewhere (Belaid and Ridde 2014; Edwards and Di Ruggiero 2011; Victora et al. 2005), its operationalisation for inclusion on evaluations remains uncertain (Bate et al. 2014).

The observation of this heterogeneity among these different areas of investigation has two implications. First, it suggests that these areas of investigation, like the concept of complexity itself, are not fixed ideas but are constructions used to represent how we perceive the social world and how we hypothesise change processes to happen. As such, these concepts are subjective and malleable, and therefore can be contested and taken up in different forms. A subjective understanding of these concepts invites uncertainty about what methods are best suited for their evaluation, and therefore, what we can expect these different areas of investigation to reveal about the intervention and how it functions.

Second, uncertainty around the conceptualisation of each area of investigation and the types of evidence produced suggests there will inevitably be uncertainty about how the different areas might fit together to produce a comprehensive picture of the intervention. The guidance suggests that a multidisciplinary team should be assembled to ensure sufficient expertise for conducting the different methodologies being employed and there is a recognition in the literature that special attention should be paid to how these teams will manage their contributions to such multidisciplinary work (Cathain et al. 2008). In practice, however, there have been noted challenges with this approach.

First, while there is advice on how to integrate qualitative data in RCTs (Moffatt et al. 2006; O'Cathain et al. 2010), these methods tend to disproportionally represent one methodological approach rather than present a balanced combination of evidence from the range of methods employed (O'Cathain, Murphy, and Nicholl 2008). When attempts have been made to bring studies together, researchers report that findings may not directly align

(Moffatt et al. 2006; Protheroe, Bower, and Chew-Graham 2007) and tensions arise when trying to negotiate these discrepancies within multidisciplinary teams (Audrey et al. 2006; Clarke et al. 2012; Riley et al. 2005). Second, process and outcome evaluations appear to have been mostly conducted by separate teams, usually divided into trialists and qualitative social science teams (Clarke et al. 2012; Reynolds et al. 2014). Some argue that this separation is necessary to ensure that results from one study do not interfere with the interpretation of the other, and therefore, maintain integrity and validity of each study's findings (Strange et al. 2006). However, there remain only a few examples where different areas of investigation are assembled into a single manuscript (Christie et al. 2014; Hind et al. 2014). Outcome and process evaluations are generally reported in separate papers and in different journals. As a result, evidence remains fragmented making it challenging for the reader to develop a comprehensive account of the intervention and its effects.

Given the current uncertainty in the literature regarding the conceptualisation and application of these areas of investigation in complex interventions research, it appears we could learn from examining each of these areas of investigation in detail looking for points of connection across the concepts and methods used accommodate complexity, as well as points where particular practices or interpretations might contradict each other. Such systematic comparison may advance methodological thinking both within and across these different areas considered central to complex interventions research.

1.2.7. Complex interventions and the global health context

In this penultimate section, I examine how the complex interventions concept has been taken up within the global health context. The MRC guidance documents, and the complex health interventions literature more broadly, have been conspicuously quiet regarding the potential implications for designing and evaluating complex interventions specifically related to the global health context. This may be partially explained by the high income setting focus of many of the authors of the MRC guidance documents. Indeed, there was only one case study in each of the 2008 and 2014 guidelines that were in a low income setting and neither of these provided any critical reflection on the opportunities or challenges for complex interventions research in a global health context. There appears to be an assumption within the guidance that the complex interventions concept and approaches for intervention research apply universally. To consider why this might be the case, I examined recent discourses shaping contemporary conceptualisations of global

health and the methodological implications for complex interventions research emerging as a result.

While the concept of global health has become increasingly popular over the last two decades, its definition is not straightforward nor universally agreed. Indeed, it has been suggested that global health is more a bunch of problems than a coherent discipline (Kleinman 2010). There have been, however, attempts at carving out an agreed definition around which the range of institutional efforts including funding, education, research and innovation might coalesce to address the 'bunch of problems' (Beaglehole and Bonita 2010; Benatar and Upshur 2011; Koplan et al. 2009). The highly cited definition of global health published in *The Lancet* is one such example:

> *"Global health is an area for study, research, and practice that places a priority on improving health and achieving equity in health for all people worldwide. Global health emphasises transnational health issues, determinants, and solutions; involves many disciplines within and beyond the health sciences and promotes inter-disciplinary collaboration; and is a synthesis of population- based prevention with individual-level clinical care" (Koplan et al. 2009:1995)*

It has been suggested, however, that this definition inadequately represents the multiple contrasting and conflicting agendas, policies and projects which shape the field and in so doing may serve to exclude and de-legitimise the perspectives of those who might not have the power and privilege to express their views in influential spaces such as *The Lancet* (Herrick and Reubi 2016). Despite this, the definition brings attention to the complexity and array of ideas and interest that contribute to contemporary conceptualisations of global health.

Contemporary conceptualisations of global health are, of course, the product of a storied history. Packard (2016) presents a narrative of global health over the course of the twenty-first century suggesting how the field has been shaped by medical discovery and technologically-based, impact-driven solutions for health and development. He suggests that "under pressure from donor organizations for measureable-impact programs, from neoliberal economic strategies that encourage the commodification of health, and from the changing landscape of public-health training, with its growing reliance on funding tied to scientific discovery, global health has become centered on developing, deploying, and measuring the impact of technologies" (Packard 2016:327). While this presents a history of

the dominant voices and powers, Packard acknowledges that there are other approaches to how global health has been, and is, conceptualised (ibid).

Discussions emerging at the turn of the century, for example, demonstrated the role of different geographic, financial and philosophical ideologies in shaping conceptualisations of global health. Views on how global health should be governed through transnational policies and institutions, such as the WHO, ranged from 'traditionalist' to 'interventionist' perspectives. The former emphasising the role of WHO as facilitating the creation and application of health knowledge aligned to a biomedical, evidence-based paradigm, and the later emphasizing WHO as the world's 'health conscience' with responsibilities for the mobilisation and reallocation of health-sector aid, expertise, and policies towards under-resourced and vulnerable groups (Lee 1998). Yet there remained little agreement on how these views could be reconciled (ibid). Some suggest that the more 'traditionalist' perspective has prevailed with the WHO's historical emphasis on biomedicine prioritising innovation and access to medical treatments and technologies over strengthening health systems and associated infrastructure, human resource, and information requirements (Benatar and Upshur 2011). Yet, in recent years the role of 'the social' in understanding health and access to care has come into greater relief. This has included ideas and ideologies drawn from disciplines of 'the social' such as anthropology, sociology, history and political science. Herrick and Reubi (2016) suggest that two disciplines, medical anthropology and international relations, have been at the forefront of such social scientific approaches to global health. The former of these disciplines, they argue, has been instrumental in drawing attention to factors such as the influence of globalisation, trade and macroeconomics on the relationships between politics, policies and disease. The latter discipline has focused on interdisciplinary pursuits to elaborate and put into practice principles of health equity and social justice.

Today, these different conceptualisations of global health are often presented as a counterpoint to the dominant paradigm either by highlighting what is missing in the dominant approach or presenting alternative paradigms. The work of influential physician-anthropologists such as Paul Farmer, Vinh-Kim Nguyen and Salmaan Keshavajee (Herrick and Reubi 2016), for example, has presented arguments against the 'medicalised' view of global health. Rather than focusing on attaining biomedically-defined measures of program effectiveness, their work has focused on ameliorating the conditions that underlie ill health

and access to care. The WHO Commission on the Social Determinants of Health has interpreted these conditions as specific determinants of health operating at different levels of social organisation (Solar and Irwin 2010). These levels are operationalised into different configurations to aid interpretation depending on the policy, practice or issue being framed (Neudorf et al. 2015; Parkhurst 2013). More generally, the levels of influence might be considered along the lines of macro, meso and micro structures. The macro level, for example, focuses on determinants that affect entire nations or regions such as economic and social policies. The meso level focuses on determinants operating within formal or informal regional or more localised groups such as ethnicity or cultural beliefs. The micro level focuses on determinants operating within families or affecting individuals such as material circumstances, economic or social vulnerability (Parkhurst 2013). These types of multi-level frameworks are proposed as a tool for evaluating which determinants are the most important to address, clarifying their mechanisms of action, and for mapping specific levels of intervention and policy entry points for action on the determinants (Neudorf et al. 2015; Parkhurst 2013; Solar and Irwin 2010).

Addressing health from a socially-informed lens aims to promote policies, programmes and interventions which emphasise the mobilisation and reallocation of aid and resources such that vulnerable and disempowered groups can gain access to sustainable, good quality healthcare. In so doing, efforts are directed towards groups of people that have been marginalised and for whom concerted efforts are required to achieve equity. As a counterpoint to biomedical approaches aiming to improve health through 'silver bullet' interventions and evaluation regimes, such socially-informed approaches are rooted in principles of human rights, equity and social justice which promote sustainable collective action by state and citizens, particularly marginalised groups, to redress the determinants that shape ill health (Anderson et al. 2009; Braveman and Gruskin 2003; Solar and Irwin 2010). In recent years, there has been a move towards restorative social justice practices which promote approaches that transform the condition and position of marginalised groups by engaging different actors, usually those in positions of power over marginalised groups, as partners for change (Harris, Eyles, and Goudge 2016).

With an increasing recognition of global health as heterogeneous concept, there is now more crossover in concepts and methodologies between these different conceptualisations. There is growing recognition of health inequalities as the manifestation

societal inequities and a push towards a social justice approach to health requiring action at global, national and local levels in *The Lancet* (Marmot et al. 2012), an influential biomedical journal (Shiffman 2014). More specifically, for example, the acknowledgement of gender as a socially-constructed determinant resulting in population-wide health disparities requiring deliberate approaches in order to achieve improved health outcomes for both men and women is now being increasingly acknowledged in the wider global health agenda. This is evidenced by the publication of persuasive arguments for gender-based approaches and the promotion of guidelines for publishing sex and gender-based analyses in influential biomedical journals (Heidari et al. 2016; Schiebinger, Leopold, and Miller 2016) and the implementation of gender-based development funding and programming by national governments , international philanthropic organisations and NGOs (Bill & Melinda Gates Foundation 2016; Sridharan et al. 2016; UN Women 2016).

It appears, however, that wider considerations of how equity, justice and participation as principles for delivering sustainable and inclusive change might factor into methodologies for intervention research are not visibly reflected in the MRC guidance. Incorporating these ideas into the dominant paradigm, some argue, may require a rethinking of the priorities that underpin different research paradigms in global health science and how these shape the production and use of evidence to address pressing disease and health care problems (Adams 2013; Farmer et al. 2013). But with increasing scrutiny of development aid driving the need to demonstrate impact, accountability to funders and value for money, more socially-informed intervention research will require significant efforts to be achieved in practice (João Biehl and Petryna 2013; Panter-Brick, Eggerman, and Tomlinson 2014).

The current emphasis on simpler, more technocratic approaches to intervention research has not always been the case in global health. Contemporary global health research has been influenced by the evidence-based movement and understanding 'what works' to improve health and wellbeing (Birbeck et al. 2013; Buekens et al. 2004). Two important trajectories in global health appear to have made important contributions to this discourse – an increasing emphasis on science as promoted by the evidence-based movement and an increasing emphasis on investments in global health research.

The emphasis on science as promoted by the evidence-based movement has gained traction over the last 25 years or so. Global events such as the identification and

agreement of the Millennium Development Goals in 2000 served to orient a multitude of actors around achieving specific, measureable targets to improve health and combat infectious diseases. Much of this early work in global health, conducted by universities and pharmaceutical companies, was focused on the development of and access to biomedical interventions, such as testing and treatment for specific diseases including AIDS, tuberculosis and malaria (Adams 2013; Crane 2013). It has been argued that this interventionist approach to achieving targets enabled the uptake of the evidence-based movement into global health as both public- and private-sector actors' priorities aligned with the emphasis on epidemiology and experimentation as a means of identifying problems, developing solutions, and measuring outcomes (Joao Biehl and Petryna 2013). At the same time, universities and research organisations from the global north became more embedded in health research initiatives in the global south, 'global health science' emerged as a particular set of ideas and practices built around the evidence-based movement (Crane 2013). The evidence-based global health paradigm is argued to now extend beyond its biomedical and pharmaceutical origins to encompass all aspects of health policy, programmes and services research (Behague et al. 2009).

The past two decades have also seen changes in how global health is financed. During the 1970s and 1980s, the neoliberalisation of health services paved the way for increasing participation of the private sector including civil society organisations (Janes and Corbett 2009). This was echoed by impressive increases in financial investments in global health from actors including, for example, the Bill and Melinda Gates Foundation, the Global Fund for a AIDS, TB and Malaria, and various national and non-governmental agencies in Europe and the US (Ravishankar et al. 2009). Operating under the principles of the capitalist market, these private sector organisations imported their emphasis on economic value-for-money and return-on-investment as important metrics of health programme success (Picciotto 2012). As the same time, increasing globalisation made the activities of both public and private sector organisations more visible, and therefore, subject to increasing scrutiny by taxpayers, shareholders, and governing bodies (Levine and Blumer 2007; Sridhar and Batniji 2008). The result has been an increasing emphasis on financial accountability and the need for funding recipients to attribute investments to intervention 'impacts' – or to demonstrate changes in selected outcomes attributable to specific interventions and investments (Savedoff, Levine, and Birdsall 2006; White 2009a). Increasingly, funders are turning to evidence-based practices, and RCTs in particular, as ideal evaluation schemes for

providing reliable, robust and quantifiable outcomes for attributing their investments to 'what works' (Joao Biehl and Petryna 2013; Picciotto 2012; White 2009a).

Together, these two trajectories have supported the prioritisation of research oriented around the question of 'what works' which advantageously satisfies the goal of attributing both interventions and investments to gains in health and wellbeing. Furthermore, the moral imperative of 'saving lives' – or indeed 'saving humanity' (Frenk and Hoffman 2015) – imbued in global health research appears to further intensify the need to produce objective and actionable evidence of effective solutions in the face of longstanding and emerging crises (Joao Biehl and Petryna 2013). This position is buoyed by the impressive gains in health and wellbeing that have been achieved under these efforts (United Nations 2015a). This focus on 'what works' in global health research has made it possible for the complex interventions concept and current methodological recommendations promoted by the MRC to be considered relevant and applicable in low resource settings.

There is, however, a noted difference in the political, social and economic characteristics of low income settings that influence how trials are conducted (Lang et al. 2010) and how evidence is produced and used (Adams 2013). Researchers have described how functional characteristics of low income settings have influenced intervention design and evaluation practice. Reflecting on the implementation of an evaluation a complex health service intervention, English and colleagues (2011) suggest that there is limited technical and financial capacity to undertake comprehensive evaluations in low income settings and that few groups have expressed an expertise on how to undertake these evaluations. Batura and colleagues (2014) described similar experiences with conducting economic evaluations of complex interventions in low income settings. Work by Reynolds and colleagues (2014) focused more on the evaluation practices themselves suggesting that certain features of low income settings such as limited research capacity, 'command and control' hierarchies that permeate organisational culture, and poorly functioning health systems influence how evaluation practices for complex interventions are enacted. These experiences, they argue, may influence the meaningful interpretation of trial results and how research problems are understood in these settings.

Alternatively, Okwaro and colleagues' (2015) work examines how different conceptualisations of complexity influence how RCT evaluation activities are conceived and

evidence interpreted. They examine the contrast between the conceptualisations of complexity described earlier in this chapter – complexity as conceived through the MRC framing and complexity as conceived from a holistic, ecological perspective. They contend that the crowded terrain common in low income settings characterised by a range of providers has created a dynamic context challenging the ability to define and maintain intervention and control groups. In such a setting, they argue, the logic of approaches to examining causal pathways as a linear relation between intervention input and outcome as currently proposed by the MRC guidance are challenged. Their findings suggest that there are important differences in how evidence is produced and interpreted between these two framings which has implications on making meaningful progress towards improving health and healthcare.- These types of critical reflections, however, are uncommon in the complex interventions literature, despite being thoughtfully considered elsewhere, for example in anthropology (Janes and Corbett 2009) of global health (João Biehl and Petryna 2013). There appears a need to engage in more critical perspectives which scrutinise different methodological approached applied to complex interventions research in global health and how these shape the production and use of evidence to address pressing health concerns in low resource context..

1.2.8. Current and future priority of complex intervention research

The activity contributing to the rise of the complex intervention and the influence of the MRC guidance has, according to Craig and Petticrew (2013:586), "encroached quite rapidly on the way researchers tackle evaluation problems". These authors note that the MRC guidance has been highly influential as evidenced by its inclusion as advice to grant applicants and use in education materials, being widely cited in grant applications, and being translated into guidance for other types of evaluations (ibid). Likewise, the comprehensive approach using a phased, mixed-methods design and evaluation practice set out in the MRC guidance has been widely promoted (Evans, Scourfield, and Murphy 2015; Richards and Borglin 2011). In response, researchers are working at all levels to translate the rhetoric into best practices as evidenced by the production of intervention design and evaluation tools and frameworks – a small snapshot: (Angeles et al. 2013; Bergström et al. 2014; Grant et al. 2013; Hargreaves et al. 2016), the investment in conferences (Craig et al. 2016; Institute of Medicine 2014) and the consolidation of knowledge in new textbooks (Richards and Hallberg 2015). It is clear that accounting for

complexity has become, and will likely remain, a top priority in health interventions research.

1.2.9. Summary

In this review of the literature, I have sought to demonstrate that the concept of the complex intervention is growing rapidly in the health interventions literature, but approaches to its definition and evaluation remain uncertain. I have argued that the concept is a construct employed differently by different actors and research movements to promote different forms of knowledge production. The efforts of researchers working under the auspices of the MRC to produce guidance for designing and evaluating complex interventions has been particularly influential for promoting the RCT, based on the principles of the evidence-based medicine movement, as the gold standard study design for evaluating complex interventions. As researchers from different perspectives have galvanised around the concept of the complex intervention, challenges and opportunities to using the RCT as an evaluative framework have arisen. Yet, the RCT has maintained its status as the gold standard study design by assimilating and transforming contestations of its applicability into new areas of investigation to augment the RCT framework. The comprehensive approach for the design and evaluation complex interventions as promoted in the MRC guidance is now considered to comprise a systematically designed intervention underpinned by a theory of change whose effect is assessed using a rigorous outcome evaluation complemented with a process evaluation examining intervention implementation, casual mechanisms and contextual factors. Researchers are now drawing on a range of perspectives and disciplines to account for complexity in intervention design and evaluation. As these perspectives proliferate, the conceptualisations and methodologies to assess the different components of outcome and process evaluations become more uncertain making it challenging to know how these might be usefully applied and contribute to comprehensive interpretations of intervention effects. Amongst this activity, there has been relatively little consideration of how current frameworks might relate to complex interventions research in a global health context.

1.3. Thesis rationale

Accounting for complexity is now a feature of health interventions research, but it is unclear how this might best be accomplished. Comprehensive evaluation frameworks, such as the one proposed in the MRC guidance documents, provide a way of organising the world into different areas of focus such that complexity can be assessed in a systematic fashion. These areas include: describing the intervention content and theory, assessing intervention implementation, evaluating outcomes, assessing causal mechanisms, and evaluating context. The suggestion here is that conducting research in these areas will produce a package of evidence that can be used to more comprehensively describe why an intervention was effective, or not. Researchers are now drawing on a range of disciplines and perspectives to account for complexity by conducting comprehensive evaluations that integrate methodologies to assess intervention outcomes and processes. This widening scope of approaches and methodologies presents two challenges. First, as more methodological approaches are sought to account for complexity, the literature becomes less specific and more dispersed. This makes it challenging to develop a repository of empirical examples and lessons learned from which to inform and improve future interventions and their evaluations. As a result, it is difficult to determine which methodologies might be suited to different areas of investigation, how they go about accounting for complexity, and how they can be usefully applied in a comprehensive evaluation. Second, the use of different methodologies to evaluate different areas of investigation suggests an approach where each area is defined and assessed from a different perspective, but is intended to contribute to an overall evaluation framework. Yet, the points of connection across the concepts and methods applied in each area, as well as the points where particular practices or interpretations may be contested remains unexplored. This makes it challenging to understand if these areas of investigation, and the evidence they produce, can be meaningfully related to each other to explain the effects and functioning of the intervention.

Given the lack of methodological guidance within and bridging between these areas of investigation, it seemed that an exercise where an investigation of each area was undertaken by the same individual could be fruitful in elucidating the processes, points of connection and departure, and consequences for interpretation that these different areas encompass. I therefore decided to undertake what might be termed a series of methodological exercises in four areas of investigation considered central to complex

interventions research. Drawing on current recommendations, I 1) examined the process of designing a complex health services intervention; 2) evaluated the primary outcomes using standard and extended statistical methods for cluster RCTs; 3) assessed causal mechanisms using statistical mediation analysis; and 4) evaluated context using a qualitative case study approach. Throughout the implementation of each methodological exercise, I engaged deliberately with the theoretical and methodological underpinnings, as well as with the processes of implementing each methodology and interpreting emerging findings. This provided the opportunity to reflect on the processes of implementing each methodology. I also examined the points of connection across the concepts and methods applied in each area of investigation, as well as the points where particular practices or interpretations were contested.

The motivating case for undertaking this work was the PRIME intervention, a complex intervention to improve care for malaria at public health centres in Uganda. The framework for the design and evaluation of the PRIME intervention was informed by MRC guidance for the design and evaluation of complex interventions (Medical Research Council 2008). The impact of the PRIME intervention on population-level health indicators was evaluated in a cRCT (Staedke et al. 2013). A parallel mixed methods study examined the implementation of the PRIME intervention activities, as well as the mechanisms of change, contextual influences and wider impact within and outside of the intended consequences of the intervention (Chandler, DiLiberto, et al. 2013). The design and evaluation of the PRIME intervention following the MRC guidance provides data specific to examining the four areas considered central to complex interventions research explored in this thesis.

This thesis presents two overall contributions to the literature on the design and evaluation of complex interventions. First, for each methodological exercise undertaken, I produce a detailed empirical example of the methodology in practice followed by a critique of the processes through which different methodologies attempt to account for complexity. In so doing, I contribute recommendations to improve the use of the specific evaluation concepts and methodologies in future studies. Second, I compare the commonalities and differences between the different methodological approaches and their interpretations. In drawing together the findings from the methodological exercises, I examine how using different approaches to evaluating the areas central to complex interventions research might enable better intervention design and evaluation. By using the PRIME intervention

as a motivating case for this thesis, I explore the implication of my findings within the current climate of interventions research in global health.

1.4. Aims and Objectives

The overall aim of this thesis is to examine methodological approaches used in complex interventions research.

Four areas of investigation considered central to complex interventions research are examined: intervention design, evaluation of primary outcomes, assessment of causal mechanisms, and evaluation of context.

In each of these areas of investigation, I engage in a methodological exercise drawing on the example of the PRIME intervention with the following objectives:

1. To apply methodological recommendations for the design and evaluation of complex interventions in practice, and
2. To examine the processes through which different methodologies attempt to account for complexity.

Furthermore, I draw together findings from across these methodological exercises with the following objectives:

3. To examine the commonalities and differences between the methodological approaches applied and the evidence they produce, and
4. To discuss how different methodological approaches might enable better intervention design and evaluation.

1.4.1. Thesis framework

The thesis framework, Figure 1.5, brings these objectives together and outlines how each methodological exercise relates to the PRIME intervention, what methodological practice is examined in each exercise, and the interpretation of findings from across the methodological exercises.

Figure 1.5: Framework for examining methodological approaches used in complex interventions research

Area of investigation	Methodological recommendation	Examination of methodologies applied	Interpretation across methodological exercises
Intervention design (Chapter 4)	Intervention is evidence-based, grounded in theory, appropriate for the study setting, and could be evaluated within a RCT	Examine the processes and methodologies used to design a complex intervention	**Discussion** (Chapter 8) Examine what interpretations of evaluating the PRIME intervention, and complex interventions more generally, can brought about from across the commonalities and contested findings of the different methodological exercises, and how this might enable better intervention design and evaluation
Evaluation of primary outcomes (Chapter 5)	Evaluate the effect of the PRIME intervention on prevalence of anaemia and parasitaemia in children under five years	Examine the process of using clinical outcomes to assess the effect of a complex health services intervention	
Assessment of causal mechanisms (Chapter 6)	Assess the causal mechanisms hypothesised in the PRIME intervention's theory of change	Examine the process of using mediation analysis to evaluate the causal mechanisms of a complex intervention	
Evaluation of context (Chapter 7)	Evaluate the contextual influences on the intervention at participating health centres	Examine the process of evaluating context and its influence on interpretations of intervention effects	

Each component of the framework brings together data from the design and evaluation of the PRIME intervention with methodological recommendations for examining the four areas considered central to complex intervention research.

<u>Intervention design</u>

Guidance recommends that interventions should be based on the available evidence, informed by theory, and tailored to the study context. I examine the methodologies used to design a complex intervention that is intended to meet these characteristics, could be evaluated within a randomised controlled trial, and had the potential to be scaled-up sustainably by the national government. Drawing on current recommendations (Möhler, Köpke, and Meyer 2015), I describe the content of the PRIME intervention and I also explore the influence of the intervention design methodologies and processes on the final

intervention content and suggest ways to improve the reporting of complex intervention design processes and content.

Evaluation of primary outcomes

RCTs are recommended as the gold standard study design to establish a casual effect of the intervention on the outcome of interest. I evaluate the effect of the PRIME intervention on the cRCT primary outcome defined as prevalence of anaemia in children under five years in communities surrounding health centres participating in the PRIME intervention. I examine the challenges and opportunities of using a clinical health outcome to assess the effectiveness of a complex health services intervention. The influences on the selection, definition, analysis and interpretation of the primary outcome are examined and suggestions for improving the selection and reporting of outcomes are presented.

Assessment of causal mechanisms

Guidance recommends that causal mechanisms should be evaluated in order to determine the processes through which the intervention may have produced an effect. Drawing on methodological recommendations (Bonell et al. 2012; Hennessy and Greenberg 1999; MRC Population Health Service Research Network 2014), I employ statistical mediation analysis to assess the hypothesised causal mechanisms linking the PRIME intervention's inputs and outcomes. I also examine the methodological practice of using statistical mediation analysis in the context of a complex health services intervention. The opportunities and challenges of applying mediation analysis for complex interventions are discussed and suggestions for considering the use of mediation analysis in future evaluations of complex interventions are presented.

Evaluation of context

Guidance recommends that the context into which interventions are implemented should be evaluated in order to establish the factors which may have influenced the intervention and its effects. Following examples from other assessments of context (Hoddinott, Britten, and Pill 2010; McMullen et al. 2015; Shoveller et al. 2007), I use a mix of qualitative data sources to evaluate the contextual influences on the effect of the PRIME intervention at participating health centres. I also examine the methodological practices of evaluating context and how different conceptualisations of context influence interpretations of intervention effect. The opportunities for improving evidence of intervention effects afforded by expanding our current conceptualisations of context are described.

Interpretations across methodological exercises

The guidance recommends that evidence from the areas of intervention design and evaluation described above can be used to inform a comprehensive assessment of not only if the intervention worked, but how, for whom and under what circumstances. I bring together the outputs of the methodological exercises including both substantive findings about the effect and functioning of the PRIME intervention, as well as findings about the practice of implementing and engaging with each methodology. I examine the points of connection between the methodologies and the evidence they produce in attempting to account for complexity, as well points where particular practices or interpretations may be contested. I consider how these findings from across the methodological exercises might enable better intervention design and evaluation. I situate these interpretations within the current global health climate and suggest opportunities and challenges for complex interventions research.

CHAPTER 2. Motivating case – The PRIME Intervention

2.1. Introduction

The aims of this thesis are explored using the case of the PRIME intervention. The PRIME intervention was designed to improve care for malaria at public health centres in Tororo District, eastern Uganda. The design and evaluation of the PRIME intervention was informed by the 2008 MRC guidance on designing and evaluating complex interventions (Medical Research Council 2008) making it a useful case for this study. Furthermore, malaria research has been proposed as an 'entry point' for making progress on other case management, health systems strengthening and disease surveillance initiatives in a global health context (World Health Organization 2015a). Therefore, the malaria and health services focus of the PRIME intervention makes this a useful case for examining the implications of improving the design and evaluation of interventions in a global health context.

In this chapter, I describe the contemporary framings of malaria control efforts and their role as an entry point for global health research. I outline malaria case management and health service provision in Uganda and provide a description of the study area followed by a brief description of the two studies used to evaluate the PRIME intervention. The studies used to evaluate the PRIME intervention are described in further detail in subsequent chapters.

2.2. Contemporary framings of malaria control efforts

Since the large scale public health efforts in 1950s, financial and operational efforts have been focused on strategic use of effective technologies to fight malaria. The malaria eradication campaigns launched in 1956 proposed an ambitious plan for interrupting malaria transmission (Nájera, González-Silva, and Alonso 2011). Achieving total coverage of indoor residual spraying with approved pesticides was seen as the 'silver bullet' to eradicate malaria within a span of eight years (Cueto 2013). However, by the early 1960s malaria resurged as countries lacked the financial commitments, political will and operational capacity to sustain the surveillance efforts needed to track and contain outbreaks (Nájera et al. 2011). Malaria was largely overlooked in the 1970s and 1980s as

the WHO underwent changes in leadership and organisation structure and declining country support in the wake of economic crises (ibid). Efforts were reoriented in the mid 1990s as international alliances were formed between pharmaceutical companies, private foundations and national governments. Many of these alliances are still operational today including the Multilateral Initiative on Malaria and the Medicine for Malaria Venture. They continue the emphasis on identifying the best technologies for malaria treatment and control (Cueto 2013).

The launch of the Global Fund to Fight AIDS, Tuberculosis and Malaria in early 2000s coinciding with establishing of the Millennium Development Goals saw a reinvestment towards malaria control and eradication initiatives (Cueto 2013). Since this time, there has been a marked return to the 'silver bullet' approach to malaria control and eradication efforts of the 1950s and 60s. Massive scale-up of malaria-related technologies and coordinated efforts at the international and national levels are promoted as the means of achieving malaria eradication (Alonso et al. 2011). These efforts have been supported by significant financial contributions from a range of actors in the global health landscape with global financing for malaria control increasing from an estimated US$ 960 million in 2005 to US$ 2.5 billion in 2014 (World Health Organization 2015b).

The increase in funding since the early 2000s has enabled countries to implement a range of life-saving technologies in the fight against malaria contributing to substantial declines in malaria morbidity and mortality. The WHO estimates that between 2000 and 2015, globally malaria incidence decreased by 37% and the number of death globally fell by 48% with 69% of cases averted due to insecticide treated nets, 21% of cases averted due to treatment with antimalarials, and 10% of cases averted due to indoor residual spraying (World Health Organization 2015b).

Today, malaria control efforts continue under the dominant framing of malaria as a biomedical and technical problem – a negative health state which can be prevented or alleviated to improve economic and social prosperity using life-saving technologies such as highly effective artemisinin combination therapies (ACTs), rapid diagnostic tests (mRDTs), bed nets and similar technological tools (Hausmann-Muela and Eckl 2015). From this framing, malaria control efforts remain focused on how to optimise these technologies and evaluations are focused on assessing their effect. Here, I focus specifically on the

implementation and evaluation of malaria case management, a key strategy for malaria control (World Health Organization 2015a).

In 2010, the WHO released new guidelines for malaria diagnosis and treatment recommending that suspected cases of malaria are confirmed with a parasitological test, and where positive, are treated with an ACT (World Health Organization 2010). ACTs are highly effective and when used rationally they have been shown to significantly improve health outcomes (Sinclair et al. 2009). mRDTs are proposed as being convenient to use in low resource settings and have made parasitological diagnosis of malaria possible in locations where poor infrastructure, resources and capacity make microscopy less feasible (Odaga et al. 2014). Moreover, use of mRDTs is considered a way to rationalise health care costs for malaria by reducing unnecessary ACT consumption (Lubell et al. 2008) and to prevent the spread of malaria parasite resistance to ACTs (Dondorp et al. 2010).

In 2012, the WHO launched the initiative, *T3: Test, Track, Treat*, to maximise the potential of diagnostic testing and treatment in the push towards achieving the Millennium Development Goal of reducing the malaria burden by at least 75% by 2015 (World Health Organization 2012). The objective of the T3 initiative was focused on clearing the parasite in affected persons and reducing the overall parasite reservoir in the community through operational and biotechnical activities implemented under the banner of health systems strengthening. These included improving patient and provider uptake and adherence of ACTs and mRDTs as well as improving point-of-care tracking of resources and malaria cases. Together, these activities were considered means to strengthen health system operations and surveillance in order to maximise coverage and improve the effectiveness of malaria control programmes. With the agreement of the Sustainable Development Goals, the WHO released the 2016-2030 Global Technical Strategy for Malaria (World Health Organization 2015a). Testing, treating and tracking malaria cases remain key activities of malaria case management in the new strategy.

Improving universal access to diagnostic testing combined with increased availability of ACTs and responsive surveillance of malaria epidemiology should translate into improved malaria control, however, several challenges have been identified that interfere with this goal. At the health system level, challenges including inadequately trained and insufficient availability of health workers, as well as poor quality and distribution of equipment,

supplies, and infrastructure have prevented community members from accessing good quality health care (Bhutta et al. 2010; Lozano et al. 2011; Reich et al. 2008). This can result in patients seeking malaria treatment in the informal healthcare sector where treatment is often inadequate, with ineffective or poor quality drugs given at incorrect doses (Goodman et al. 2004; Littrell et al. 2011). When patients do seek care in the formal sector, malaria diagnostics may only been available at higher level health centres and hospitals; lower level health centres have relied on clinical diagnosis of malaria. mRDTs offer promise for extending diagnosis to the primary health centres where many patients seek treatment. However, to achieve this goal, there is a need to strengthen health system activities including provider skills in malaria case management, management of health services, and access to ACTs and mRDTs (Asiimwe et al. 2012; Bastiaens et al. 2014).

The idea that malaria can be addressed through technical and operational health systems strengthening initiatives aligns with the wider discourses on improving health and access to care through health systems strengthening. Rather than being framed as political or social, the dominant discourse suggests operational and technical initiatives will lead to health systems solutions (van Olmen et al. 2012; Storeng and Mishra 2014). Thus, there is a proposal that malaria solutions can act as an 'entry point' to wider health systems solutions (World Health Organization 2015a). Understanding, therefore, how malaria control interventions are designed and evaluated, may provide insights into health systems interventions and global health research more widely.

2.3. Malaria case management in Uganda

Worldwide, malaria remains one of the most important global health challenges, with an estimated 214 million cases and 438 000 million deaths each year (World Health Organization 2015b). Recent intensification of efforts to reduce the burden of malaria have resulted in impressive progress including an estimated 18% decrease in the number of malaria cases globally from 2000 to 2015 (ibid). The majority of these successes have been achieved in settings with low malaria transmission (Greenwood and Koram 2014). In Uganda, however, a high transmission setting, the burden of malaria has remained high (Jagannathan et al. 2012; Kamya et al. 2015). Highly endemic areas require profound decreases in transmission in order to impact significantly on the incidence of disease. In Uganda, this requires coordinated and fully integrated vector control and case management systems at all levels of the health system. However, a lack of adequate health

care resources, ineffective health information management systems, and challenges with governance and accountability of both public and private actors have severely hindered progress on malaria control and public health more widely (Yeka et al. 2012).

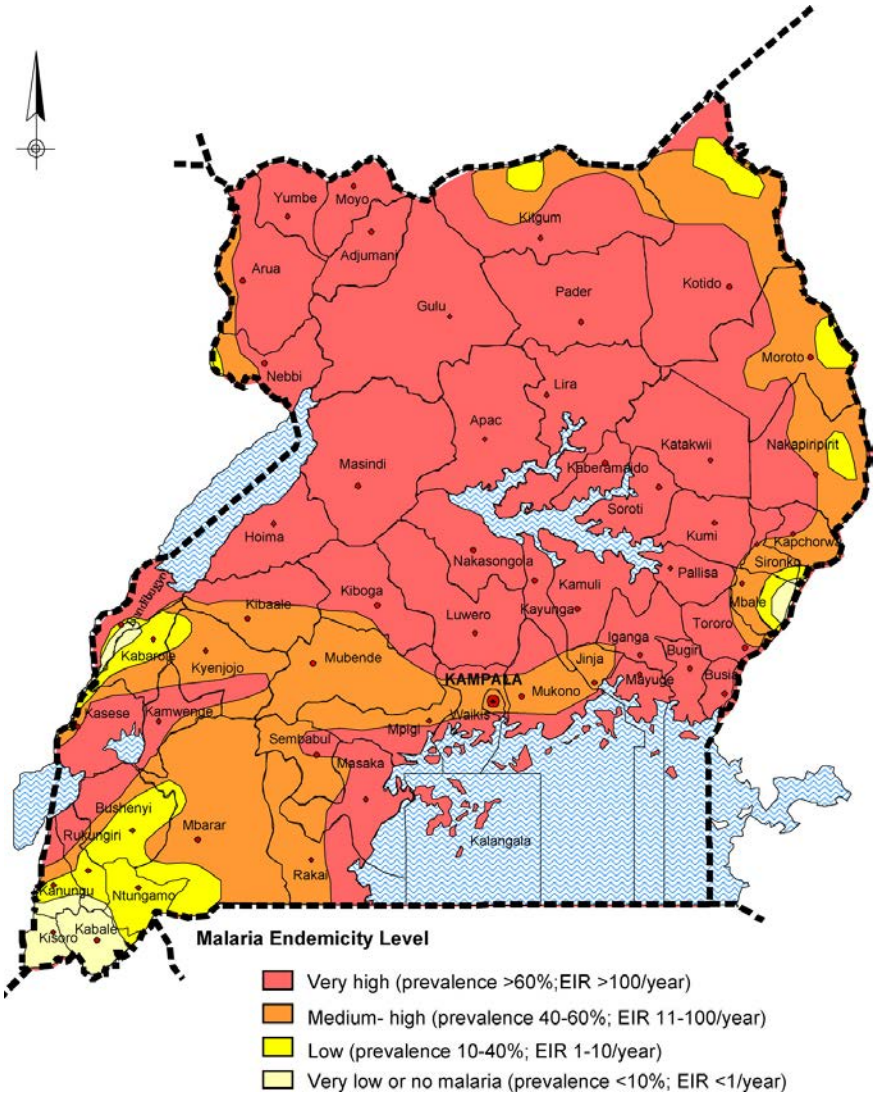
Uganda has the third highest number of total malaria infections worldwide, with 100% of Uganda's population at risk of malaria and 90-95% of the population residing in areas of highly endemic transmission representing approximately 90% of the country's total population of around 33 million (World Health Organisation 2014), Fugure 2.1. According to the Ugandan Ministry of Health, malaria is one of the most important health problems in Uganda and the leading cause of morbidity and mortality (NMCP 2014). There are approximately 8–13 million malaria episodes per year accounting for up to 30-50% of outpatient visits, 15-20% of hospital admissions, and 9-14% of inpatient deaths (ibid). Children under 5 years of age in Uganda experience an estimated average of six episodes of malaria each year, resulting in between 70,000 and 110,000 deaths annually (Uganda Ministry of Health 2008).

Malaria is transmitted by the bite of a mosquito infected with the malaria parasite. Some of the world's highest recorded rates of infective mosquito bites per person per year (entomological inoculation rates) have been recorded in Uganda, including rates of 1586 in Apac district and 562 in Tororo district (Okello and Bortel 2006), where the PRIME study was conducted. The most common malaria vectors in Uganda are *Anopheles gambiae s.l.* and *Anopheles funestus* (ibid). Both species usually feed and rest indoors making ITNs and IRS preferable vector control strategies.

In 2009, the estimated prevalence of malarial parasitaemia, assessed based on microscopy, was approximately 30–50% in children 6–59 months of age in 2009 (Uganda Bureau of Statistics (UBOS) and ICF Macro 2010). Anaemia was also very common with a haemoglobin <11 g/dl observed in more than half of children under 15 years of age. Prevalence of parasitaemia was low, 5%, in Kampala the capitol city and major urban centre of Uganda. In all other regions, including Tororo District where the PRIME study was conducted, prevalence was high ranging from 38 to 63%. Prevalence of parasitaemia was also lower as educational levels of mothers and household wealth increased (ibid). Since 2007 in Tororo District, the slide positivity rate, that is the percentage of individuals presenting to health facilities with suspected malaria who test positive by either a blood

smear or rapid diagnostic test has remained stable at 50–70% in children under 5 years of age (Yeka et al. 2012).

Figure 2.1 Malaria endemnicity in Uganda



Source (Yeka et al. 2012)

In 2004, artemether-lumefantrine (AL) was selected as the national first-line regimen for uncomplicated malaria. This was following documented high failure rates with widely used monotherapies, including chloroquine, amodiaquine, and sulfadoxine-pyrimethamine in the preceding decade (Dorsey et al. 2000; Staedke et al. 2001). In 2010, Uganda changed its malaria case management policy to align with the WHO guidelines for universal parasitological diagnostic testing of suspected cases of malaria, and where positive, treating cases with an ACT. Implementation of the policy included scaling-up provision of mRDTs in level II health centres (the lowest level health centre) and microscopy services in level III

health centres and above. At the community level, malaria case management remained as presumptive treatment provided through community health workers (CHWs) participating in village health teams (VHTs). At the time of the PRIME study, community-based health care was expanding from malaria-only to integrated community case management where CHWs would be trained to evaluate and provide presumptive treatment of malaria, pneumonia, and diarrhoea based on clinical criteria. The programme did not become operational during the timeframe of the PRIME study. In the private sector, a new financing mechanism, the Affordable Medicines Facility – malaria (AMFm) was piloted starting mid-2010. The initiative intended to increase access to ACTs and reduce access to less effective antimalarial treatments, particularly artemisinin monotherapies (http://www.theglobalfund.org/en/amfm/).

2.4. Health care service provision in Uganda

Since the 1970s, Uganda has struggled to provide free high quality health services and adequately support health workers and health centre infrastructure. While Uganda had an effective public health system in the 1960s, by the mid-1990s, after two decades of political strife and economic turbulence, provision of health care services was plagued by health system dysfunction (Iliffe 1998). In the mid-1990s, Uganda embarked on a programme of structural adjustment in response to availability of development funding from global actors such as the World Bank and various UN agencies. A component of this programme was the decentralisation of health service provision to districts to improve utilisation and access to health services (Kyaddondo and Whyte 2003). This included divesting responsibility and authority to set and collect fees for services provided to supplement district or health centre funds, and enable the recruitment of staff and allocation of resources at the local level which was intended to empower responsiveness to local needs (ibid). In practice, however, this programme did not yield the expected improvements in stable pay and improved opportunities for health workers (Ssengooba et al. 2007) which lead to mismanagement of health centre funds (Streefland et al. 1997), increased leakage of drugs, and informal requests for payment from patients, and reduced quality and accessibility of care (McPake et al. 1999).

The influx of development aid also saw the government of Uganda partnered with a range of international and local development agencies to plan, implement and monitor the provision of health services (Gonzaga et al. 1999). These efforts, however, were poorly

coordinated and were met with ongoing political and operational challenges at local and national levels sustained a poorly functioning public health system (Anokbonggo, Ogwal-Okeng, Ross-Degnan, et al. 2004; Kyaddondo and Whyte 2003; Whyte et al. 2013).

In 2001, following a presidential election campaign promise, user fees for all public health units were abolished (Nabyonga-Orem et al. 2008) with the intention of supporting the most finically-marginalised populations to access care (Nabyonga Orem et al. 2005). While more poor people sought care at public health centres following the removal of user fees, the proportion of poor households facing catastrophic health expenditures did not decrease (Xu et al. 2006). In addition, inadequate availability of drugs at local health centres prevented many from receiving adequate treatment (Anokbonggo, Ogwal-Okeng, Obua, et al. 2004; Burnham et al. 2004). In more recent years, Uganda has secured financing through multilateral initiatives such as the Global Alliance for Vaccines & Immunisations, The Global Fund to Fight AIDS, Tuberculosis and Malaria, and the AMFm. However, delays in processing funding meant that by 2007, 80% of health facilities had reported stock-outs of antimalarial over a six-month period (Ministry of Health (MOH) [Uganda] and Macro International Inc 2008). Such stock-outs persisted at the time of conducting the PRIME research project (Chandler, Kizito, et al. 2013).

Uganda's health care system is characterised by a strict hierarchy of institutions. At the highest level there are national and regional referral hospitals which have received the majority of government funding and support. At the district health system level, there are a network of district general hospitals, health centres levels IV, III and II, and the village health teams, when operational. These levels are closely linked to the political and administrative structures of local government. For example, HC II serves the parish or ward, HC III serves the sub-county and HC IV serves the county or parliamentary constituency (Ministry of Health (Uganda) 2009). The hierarchy is evident in the management of the health centres with health centre IIs managed by an enrolled nurse and providing basic services and treatment of some diseases; health centre IIIs headed by a clinical officer and providing additional services such as maternity services and laboratory services, when functional; and health centre IVs functioning as mini-hospitals headed by a medical doctor with inpatient wards and surgical services (ibid). This hierarchy is partly influenced by Uganda's colonial history where relatively sophisticated hospitals provided care to the elites and the colonial cadres and a network of smaller hospitals and dispensaries were

focused on delivering care to the rural population (Blaise and Kegels 2004). These were supplemented by vertical programs to deal with endemic diseases and vaccination programmes. This bureaucratic health care management structure with rigid hierarchical lines of command and control which supported these structures persist today. Centrally planned disease control programmes and retention of the highest trained health care providers in higher levels of the health care system leave lower level health centres at the periphery of the system (ibid). These lower level health centres, especially health centre IIs, continue to receive little investments or political support from the central government. At the same time, patients expect a range of curative services at these health centres despite their mandate being limited to providing prevention and referral services only (Medicines Transparency Alliance (MeTA) 2014).

2.5. Tororo District

In Tororo District, a history of health and development projects has influenced current efforts to improve health and access to care. Tororo district is located in eastern Uganda, on the border with Kenya, and is characterised as predominantly low-resource and rural with 90% of the population living outside of the urban centre, Tororo Town. The national decentralisation policies which were implemented n Tororo District in the mid-1990s have resulted in ongoing tensions in the public health care sector. The coverage of health centres has been low with only 50% of the desired health centres operational in 2003 with a staffing gap of 73% (Chandler, Kizito, et al. 2013). This disparity was again observed in 2009 with a lack of health centres in 44% of parishes and a staffing gap of 41% (Staedke and Uganda Malaria Surveillance Project 2010) compared with the staffing norms set out in the 2005 Health Sector Strategic Plan (The Republic of Uganda Ministry of Health n.d.). The distribution of health services and staff has also been skewed towards the two hospitals located in the urban centre with service in rural areas supported by a number of NGO and faith-based organisations at independently operated hospitals, health centres and dispensaries (Gonzaga et al. 1999).

The poor coverage of public health services by the government has been supplemented with financial and other resource supports from donors, NGOs and research programmes. The majority of these have been focused on programmes related to malaria prevention and control (Jagannathan et al. 2012; Yeka et al. 2015) and HIV/AIDS care (Whyte et al. 2013). There has also been a number of rural development initiatives ranging from agriculture

systems governance (Barungi 2013) to community activities for persons with intellectual disabilities (Moses 2009). These initiatives provide numerous material inputs and care opportunities at health centres and in the community. This mix of actors has been characterised as a crowded and projectified terrain in which many local and international organisations concurrently implement health and development projects (Whyte et al. 2013).

2.6. Tororo District - PRIME study formative research

In 2009-10, the PRIME study team conducted a study to characterise the local health services in Tororo, which informed the design of the PRIME intervention and evaluation activities. Methods included a census survey to enumerate the population, a situational assessment of health services, and a qualitative study with health workers, primary caregivers, and heads of households. The following sections reports a summary of the findings of this research drawn from a report of the study co-authored with the study team (Staedke and Uganda Malaria Surveillance Project 2010).

2.6.1. Health centre characteristics

There were 22 lower-level government run health facilities, including 17 level II health centers (HC), and 5 level III HCs. Most health centres lacked electricity (88%) and running water (94%). Less than half of staff members stationed at the centres were available each day. Nearly all health centres (94%) reported that they experienced stock-outs. Most centres, but not all, stocked artemether-lumefantrine (AL), the first-line recommended regimen for treatment of uncomplicated malaria in Uganda. However, only 29% of health centres reported that the supply of antimalarial drugs was adequate for treating their patients (23% HC II, 33% HC III, 100% HC IV). Most centres also stocked amoxicillin, mebendazone (antihelminthic), oral rehydration solution, vitamin A, and ferrous sulphate, but nearly all experienced stock-outs of these drugs.

Demographic information was collected on the majority of health workers stationed at the health centres. The mean age of health workers was 37.5 years; over half (60%) of health workers were women. Health workers based at HC IIs and IIIs were significantly more likely to be from the local area, than those based at the HC IV ($p<0.001$). The median number of years worked was 5 (range 0.1 to 37 years), and was consistent across health centre levels, but duration of employment varied with position. One-quarter of health workers

interviewed were volunteers with limited training. The volunteers were fairly evenly distributed across the health centres, and appeared to be actively involved in delivering health care including dispensing medications, immunizing children, delivering mothers, registering patients, and dressing wounds.

Overall, the knowledge of health workers about malaria case management was surprisingly poor. Out of a possible 178 points, the mean score was 51.6 (29%), ranging from 15 to 110. The in-charges of health centres scored unexpectedly low with a mean score of 60.5 (34%). Volunteers and vaccinators also scored poorly with mean scores of 35.7 (20%) and 31.4 (18%), respectively. When asked how to confirm the diagnosis of malaria, only eight (10%) health workers mentioned microscopy and two (2%) RDTs.

2.6.2. Household characteristics

In the census survey, a total of 144,216 residents were enumerated including 26,793 households. The findings suggested that the area is very rural, with limited infrastructure and education. Very few households had electricity or running water. One-quarter of households had no toilet facilities. One quarter of heads of households had no formal education. Most households were built with basic materials; less than 20% of few houses had cement floors or cement walls. Household asset ownership was also low, including mobile phones (31%), radios (43%) and television (2%) suggesting an overall low socioeconomic status in the area. The mortality rate in children under five was estimated at 11 % or 110 deaths per 1000 live births.

2.6.3. Community treatment seeking practices

Nearly all community members had visited their local health centre demonstrating fairly high interest in accessing care through the public sector. Nearly all households in the study area are within a 5km radius of a public health centre. Other sources of health care include CHWs (when operational), private clinics, and drug shops. Herbal medicine, shrines, churches and prayers were also important sources of treatment. Community members' choice of health care was influenced by: (1) initial perceptions and beliefs about aetiology and severity of the illness; (2) accessibility of the preferred treatment; and (3) trial and error in moving between treatment sources.

For illnesses perceived as mild, community members reported that they would first treat at home with tepid sponging, herbs or drugs obtained from CHWs or the private drugs shops and clinics. For illnesses considered to be severe, including excessive vomiting, high fever, and enlarged head (i.e. hydrocephalus), community members commonly sought care from public health centres, often without delay. However, delays in seeking care were commonly reported. After treating at home, caregivers may only present to health centres when child has become very sick. Delays might also result from fear and cultural beliefs. Community members may fear to seek care for certain diseases such as sexually transmitted infections and urinary tract infections. Some community members believe that delivering a baby at health centres is against the cultural norms, and prefer to deliver from home, only presenting to health centres if complications arise.

Accessibility of the preferred treatment was felt to be determined by multiple factors including distance to the provider, opening hours, spousal support in meeting costs, opportunity costs of leaving the home and travelling to the provider, ability to negotiate the logistical and social rules of the provider's institution, and availability of drugs at that provider. Government-run health centres were usually the first choice of treatment for community members that lived nearby. Community members from parishes without health centres reported that they would seek treatment from alternative sources like private clinics and drug shops that were closer, and only go to the health centre if they did not respond to the initial treatment. Primary caregivers, typically mothers, are left with the responsibility of taking care of children and of the household matters. Often caregivers do not have money or means to travel to the health centres, and are busy with household duties. As a result, they opt for sources of care closer to home only going to the health centre if the illness persists.

Caregivers appeared to rely on 'trial and error' to navigate health providers, moving from one provider to the next when initial treatment failed, rather than returning to the first provider for follow-up. Biomedical drugs were valued as a first port of call, but the wider process of care at health centres was often felt to be unsatisfactory leading caregivers to seek health care from alternative, non-medical sources. Community members also resort to traditional practitioners or religious healers when modern medicine fails.

2.6.4. Health care services in Tororo: Barriers to attending and providing care at health centres

Health workers and community members reported barriers which impact on getting to health centres and barriers that impact on attracting community members to attend health centres. Likewise, they also reported barriers which impact on the provision of services at health centres. These barriers to accessing and providing care are categorised into those affecting logistical and cultural processes, health centre management, therapeutic processes and interpersonal relationships.

Logistical and cultural barriers prevented community members from attending health centres. Community members reported that public health centres are far from many homes and that they often lack money for transport or a means of transport to the public health centre. As a result, community members opt to seek for care from nearer sources such as herbs or a traditional healer. At the health centre, some health workers charge patients for services which should be free. This occurs in part because the government provides few supplies, like syringes, so health workers have to ask the patients to buy their own. The volunteer health workers, who do not receive a salary, may also feel compelled to find other ways of earning money, including charging patients. While the majority of health workers denied charging the patients for services at the public health centres, simply knowing that payment may be required to access or receive care discourages community members from attending health centres. Being charged for services affects the nature of the interaction between health workers and patients, leading to mistrust and a feeling amongst community members that the priority of health workers is money rather than their health. Community members also described intra-household relationships as affecting their attendance at health centres reporting that in many households, men have left the responsibility of caring for sick children to women. In most cases women lack money and have many other household priorities such as providing food for the household which prevents them from attending public health centres.

Poor health centre management including lack of drugs, equipment, supplies and funding; poor health centre infrastructure; challenges with staffing, salaries and supervision; and influence by politicians impacted on access and provision of services at health centres. Community members and health workers describe that health centres lack drugs, equipment and supplies which results in frustrations because they are aware that this affects the provision of good quality care. Consistent and recurrent drug stock-outs result in patients sometimes being instructed to buy drugs from private clinics and drug shops

which negatively impacts patients' desire to attend health centres. To compensate, health workers prescribe drugs they know are available even though they may not be the most appropriate drug for the diagnosis. Additionally, health workers explained that a lack of diagnostic equipment to make and confirm diagnoses has a negative effect on their ability to accurately diagnose or confirm illnesses such as malaria. In addition, health workers believe that not being able to provide diagnostic services leads to mistrust in the health care system by patients. Finally, health workers complained that insufficient primary health care funds (PHC) funds makes management of health centres almost impossible. These funds are meant to pay for, among other things, support staff, cleaning materials, transportation of drugs, and photocopying documents. Because the PHC funds are insufficient, and fail to arrive on time, some health centres cannot pay support staff and the health centre remains untidy.

Health workers and community members also report that poor health centre infrastructure can affect the provision of care. Some health centres are renting their premises but long-term rentals may be unsustainable. Other health centres are using buildings offered by community members; however, these buildings can be of inadequate quality for a health centre. Health workers reported that health centres lack adequate security and fencing resulting in theft or damage of the property. Additionally, lack of nearby accommodation for health workers may impact on punctuality and availability of health workers.

Challenges with staffing, salaries and supervision are also described as important barriers because they impact on health worker motivation for providing care. Health workers and community members described insufficient staff in the majority of health centres. Health workers and community members report that this staffing shortage leads to longer wait times and some patients not being treated. Additionally, health workers describe being overworked and having to balance many competing roles and priorities. Most health workers focus on seeing as many patients as possible and limit the consultation time for each patient. This compromises the quality of the service they provide and as a result, some patients are given the wrong diagnosis and treatment. Health care workers mentioned that poor salaries and lack of allowances lead to loss of morale and poor performance at work including poor interpersonal skills. They cited problems in their remuneration including late arrival of allowances and salaries and no provision of meals or refreshments during the long working hours. Worse still volunteers receive very little if any

payment at all, these payments are also irregular. Health workers identified supervision as being infrequent and unhelpful. Some health centres would spend as long as eight months without supervision, others report that supervisors come in the evening hours when some health workers are not present. Health workers describe that supervisors do not help to constructively identify and resolve challenges in the workplace.

Health workers identified influence by politicians as a barrier to providing good quality care. They mentioned that politicians sometimes divert funds meant for health-related activities and accuse health workers of stealing drugs resulting in a poor reputation for health workers in the community. In addition, some politicians tell the community members that there are drugs at the health centres even if the drugs are out of stock. It was also identified that politicians have influence on the management of the health centres and can dictate the staffing at health centres without objection of staff or community members. It was also mentioned that when some politicians come with their patients to the health centre, they want to be attended to first and move to the front of the queue. Community members describe that preferential treatment of politicians or stock-outs believed to be the result of dishonest health worker actions creates mistrust in the health care and deters them from seeking care there again in the future, turning instead to alternative sources of care, even if charged for these services.

In terms of the therapeutic process, community members report previous experiences when appropriate care was not received or their illnesses were not relieved after visiting the health centre. These experiences lead to mistrust in the efficacy of clinical care and discourage community members from returning for subsequent illnesses. Some community members regarded illnesses that do not present initially with severe symptoms as non-serious illnesses and are reportedly managed at home. Yet still others mentioned that they may fail to seek health care because of the belief that some illnesses result from demonic attacks and are best treated using traditional medicines such as local herbs. This was corroborated by health workers who reported that some community members lacked knowledge of when to attend health centres, either because they believe it is more appropriate to seek care from alternative sources, such as witch doctors or traditional healers.

In terms of interpersonal relationships, community members described harassment and discrimination by health workers based on ethnicity, dress code, age, perceived socioeconomic status, and ability to speak English. Patients are reluctant to go to a health centre where they will not be able to communicate their symptoms and understand treatment information and instructions. Community members also report that they are treated inappropriately or are ignored by health workers; this treatment affects the entire health centre visit and creates a general dissatisfaction and anxiety towards interacting with health workers. Poor interpersonal interactions was echoed by health workers who expressed frustrations with not being able to adequately communicate with patients. Many health workers are not fluent in the local languages, and often community members cannot speak English. However, health workers suggest that their comments to improve hygiene or certain practices may be misunderstood by community members as rude and discriminatory.

2.6.5. Summary

In both health centres and communities, infrastructure is limited. Health centres are generally run by nurses or nursing assistants; many lack electricity, running water, functioning laboratories, and adequate staffing. There is a fairly high interest among community members in accessing care through the public sector, however, dissatisfaction with experiences is high. Community members report various and complex treatment seeking behaviours and outcomes which are largely driven by perceptions and understanding of illnesses and practical concerns, including accessibility, available resources, and prior experiences. Barriers that discourage treatment seeking include poor management of the health centre, previous negative experiences, a mistrust of the therapeutic process or lack of knowledge on appropriate treatment seeking as well as poor local referral system and political hindrances. At health centres, immediate barriers to quality care included drug stock-outs and lack of equipment; high patient to staff ratio; use of volunteer health workers; language barrier between health workers and patients and discriminatory treatment of patients. Underlying these barriers were poor motivation of staff; poor management of the health centre; lack of patient-centred culture and poor relationship between health workers and communities.

2.7. Design and evaluation of the PRIME intervention

2.7.1. Intervention design

The PRIME intervention was designed to attract patients to seek care and to improve the quality of care, including for the diagnosis and treatment of malaria, delivered at public health centres in Tororo district, eastern Uganda. The design and evaluation of the PRIME intervention is based on the framing of malaria control as a biomedical problem that can be addressed through improving access to life-saving technologies coupled with behaviour change and health system initiatives to ensure their successful implementation and sustained impact (Bastiaens et al. 2014; Greenwood and Koram 2014; Whitty et al. 2008). The PRIME intervention, therefore focused on ensuring access to ACTs and mRDTs at health centres through a range of components to improve provider behaviour and health centre operations creating a complex, multi-component intervention (DiLiberto et al. 2015). This framing made the intervention amenable to design and evaluation following the MRC guidance which conceives of complex interventions as consisting of several interacting components, targeting a variety of behaviours to produce several outcomes, and involving different groups of participants (patients and providers) (Medical Research Council 2008).

Following a systematic process, the intervention was designed to be evidence-based, grounded in theory, and appropriate to the study setting. The PRIME intervention consisted of four components: 1) training in fever case management and use of mRDTs; 2) workshops in health centre management (HCM); 3) workshops in patient-centred services (PCS); and 4) ensuring the supply of mRDTs and artemether-lumefantrine (AL, the first- line ACT for malaria in Uganda). Chapter 4 examines the intervention rationale and the multi-step design process which produced the final intervention content. While the account in Chapter 4 presents a 'streamlined' development process and final content, it is important to acknowledge this as the representation of an iterative process of overlapping and interconnected steps. It was through a reflection on the intervention development process that this multi-step process could be clearly articulated as presented in Chapter 4. A brief reflection is provided here to highlight the work and contributions that went into developing the final PRIME intervention content which were not captured in Chapter 4.

The PRIME study was one of 25 projects of the ACT Consortium, an international research collaboration aiming to answer key questions on malaria drug delivery in Africa and Asia

(http://www.actconsortium.org/). Specifically, there were eight studies in five countries in East and West Africa which developed complex interventions to improve care for malaria (Chandler et al. 2016). The social science lead for the ACT Consortium working across these eight studies was also a Co-Investigator of the PRIME study. This provided the opportunity to draw from the experiences of these other ACT Consortium projects. For example, working together with members of several study teams, and drawing on literature of theory and best practice in adult learning, the social science lead developed the six-step learning process which was used in several projects employing training workshops in their designs, including the PRIME intervention. In another example, the decision to work with an experienced public health consulting firm (WellSense, http://www.wellsense-iphc.com/) to fine-tune the intervention content and training manuals was based on another study's positive experience of working with this firm on a similar intervention. Several of the other ways in which the studies informed each other during the intervention development process have been documented elsewhere and are suggested to have been overall useful contributions (Chandler et al. 2016).

At the time of designing the PRIME intervention in 2010, there was a growing literature discussing the importance of designing interventions that were evidence-based and grounded in theory (Craig et al. 2008; ICEBeRG and Francis 2006; Michie et al. 2009). However, there was limited guidance describing how to design the components of such interventions in practice, especially interventions attending to the social nature of health care. For example, while there was guidance for selecting individually oriented behaviour change techniques informed by theories from health psychology (Abraham and Michie 2008), these proved to be less useful for the PRIME intervention which sought to engage the different ways that health workers may learn and change their practice in groups at health centres. Drawing on experiences from other ACT Consortium studies, as described above, the PRIME intervention design team found that the anthropological literature (Arhinful et al. 1996; Nichter, Acuin, and Vargas 2008) proved more useful by demonstrating how the extensive formative research in the study area could be used to identify target areas for potential intervention. A supplement to this relative lack of guidance in the literature was the PRIME study team's tacit knowledge of the health care system and service provision gained through years of experience as clinicians, social scientists, epidemiologists, health workers, and project managers living and working in Uganda. It is difficult to systematically categorise the extent and influence of this

knowledge on the development of the intervention, but like other projects embedded in the areas were interventions are being designed (Achonduh et al. 2014; Chandler et al. 2014; English 2013), we consider this input essential when developing a contextually relevant intervention and contend that it should be acknowledged when reporting on intervention designs and final content.

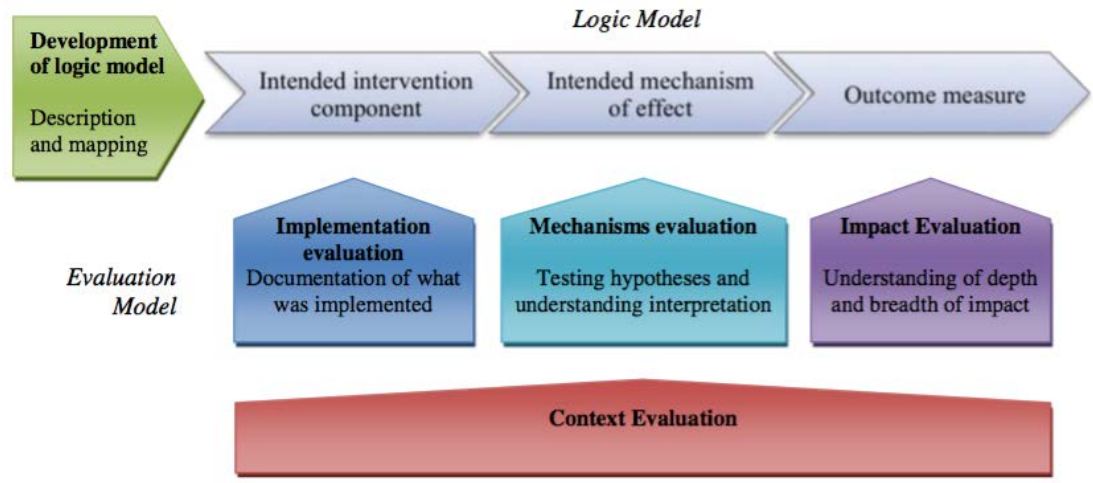
Finally, an iterative review process was necessary to articulate the PRIME intervention theories of change and logic model depicted in Chapter 4. Drawing on examples in the literature (Medical Research Council 2008), draft theories of change and logic model were developed throughout the intervention design process. These draft documents were reviewed amongst the PRIME study investigators and team members. Feedback from these reviews highlighted areas of the theories of change and logic model which were unclear either in the way they were articulated or in their visual representations. Through trial and error, different versions of the theories of change and logic model were developed with feedback from the PRIME study team informing subsequent versions of the documents. This review process served two useful functions. First, it was useful for arriving at the final version of the theories of change and logic model which most accurately represented how the intervention components were hypothesised to produce the desired outcomes. Second, it facilitated the intervention design process. Often theories of change and logic models are articulated after the intervention has been developed or even implemented (Van Belle et al. 2010; MRC Population Health Service Research Network 2014). However, we found that developing the theories of change and logic model throughout the intervention design process provided a point of reference for communicating ideas about the intervention rationale and ensuring that components being developed by different groups of study team members remained aligned to the overall objective of the intervention. This unintended positive outcome of articulating theories of change and logic models during intervention design should be highlighted in the intervention research literature.

2.7.2. Evaluation design

Informed by the MRC guidance, the impact of the PRIME intervention was comprehensively evaluated including a rigorous outcome evaluation and a parallel mixed-methods 'process' study. Together these two studies provide a rich set of data for each area of investigation central to complex interventions research examined in this thesis. The PRIME cRCT was

designed to evaluate the impact of the intervention on population-level health outcomes. The cRCT compared health centres that received the intervention with 'standard care' health centres that did not receive the intervention. The primary outcome was the prevalence of anaemia (haemoglobin <11.0 g/dL) in individual children under five and the secondary outcome was prevalence of malaria parasitaemia in the same population, both measured in annual surveys of communities surrounding health centres enrolled in the PRIME trial (Staedke et al. 2013). The mixed-methods PROCESS study was conducted alongside the cRCT. The PROCESS study was designed to examine the implementation of the PRIME intervention activities, as well as the mechanisms of change, contextual influences and wider impact within and outside of the intended consequences of the intervention (Chandler, DiLiberto, et al. 2013). A range of quantitative and qualitative methods were used to assess the different components of the PROCESS study. Each of these areas was conceived as part of an overall evaluation framework intending to provide a comprehensive assessment of the PRIME intervention, Figure 2.2. Further description of the PRIME trial and PROCESS study as well as the methods used in each are described in detail in subsequent chapters.

Figure 2.2: PROCESS study evaluation framework



CHAPTER 3. Overall methodological approach

3.1. Introduction

In this chapter, I describe the overall methodological approach that underpins this thesis. The specific methods applied to each area of investigation are described in detail in subsequent chapters. Here I also describe my motivation for undertaking this research and how this shaped the methodological approach taken.

3.2. Methodological approach

My overall methodological approach is framed as a series of methodological exercises undertaken in each area considered central to complex interventions research: intervention design, evaluation of primary outcomes, assessment of causal mechanisms, and evaluation of context. The exercises are intended as a way to work through each area by engaging deliberately both with the process of applying methodological recommendations for the design and evaluation of complex interventions in practice, as well as with the process of examining the processes through which the different methodologies attempt to account for complexity. To engage in these methodological exercises, I took the concepts underpinning each area of complex intervention research as well as their associated methodologies as the objects, or focus, of my research. Borrowing from anthropological practice, I examined these 'objects' with the objective of 'making the familiar strange and the strange familiar' (Hammersley and Atkinson 2007).

The practice of 'making the familiar strange and the strange familiar' is a legacy of the reflexive turn in anthropology and sociology around 1970-80s which suggested that any arena of the social world is open for inquiry, not just the so-called exotic tribes of other places (Clifford and Marcus 1986; Rosaldo 1989). In the study of sociology of science, many efforts have been directed towards interrogating the ontological, epistemological and methodological implications of this strange/familiar concept. This thesis is not a classic social study of science, but it draws from this field to examine the concepts and methodologies used to design and evaluate complex interventions. In line with social studies of science, this work considers where the different concepts and methodologies

come from, what they represent, and the implications of how they are used to examine interventions and their effects (Latour 2005).

Making the 'familiar strange' is the practice of interrogating the ideas, assumptions and objects that are usually taken for granted, or taken at face value, in the practice of doing analytical work. In so doing, the researcher seeks to apply an analytic perspective to explain familiar practices instead of simply describing them, or not noticing them at all. On the other hand, the notion of making the 'strange familiar' is to start from the perspective that ideas, assumptions and objects can be rationally and intelligibly explained, even those that seem strange or incomprehensible. In so doing, the researcher seeks to apply an analytic perspective to develop convincing explanations for what might initially appear puzzling (Hammersley and Atkinson 2007).

To apply this familiar/strange practice to my research, I examined each of the four areas of complex intervention research with the objective of examining their familiar practices and procedures and also examining the practices and procedures that initially appeared to me to be unusual or strange in the context of complex interventions. Through this exercise of working through each area, I examined the expectations of what each area will do; what definitions and values are embedded in its methodologies; what rules and assumptions are necessary; and what evidence is produced. I drew together the findings from each exercise with the aim of identifying points of connection across the concepts and methods applied in each area, as well as the points where particular practices or interpretations may be contested. This process enabled me to achieve the objective of examining what interpretations of complex interventions are brought about when comparing and contrasting the findings from across the four areas central to complex interventions research.

3.2.1. Methods employed in each chapter

Here I provide a brief summary of the methods employed and data used for each methodological exercise. A more detailed description follows in subsequent chapters.

In Chapter 4, I examine the methods used to design the PRIME intervention and describe the intervention rationale and final content. These methods include formative research in the study area, prioritisation exercises with key stakeholders, rapid literature reviews,

integration of behaviour change and adult learning theory, and piloting. I engage in a reflexive exercise to discuss the process of using these methods and how they influenced the final intervention content.

In Chapter 5, I present an analysis of the PRIME trial primary outcomes of prevalence of anaemia (hemoglobin < 11.0 g/dL) and prevalence of malaria parasitaemia in children under 5 years of age. Data are drawn from the PRIME trial community cross-sectional surveys conducted annually in households within 2 km of health centres participating in the PRIME intervention. Data are analysed on an intention-to-treat basis following best practice for cRCTs. An extended analysis is also conducted to examine different statistical and logistical influences on analysis and interpretation of the primary outcome.

In Chapter 6, I present an analysis of the PRIME intervention theory of change using statistical mediation to identify the impact of hypothesised causal mechanisms on the PRIME trial primary outcome as well as intermediary outcomes along the causal pathway. Data are drawn from across the PRIME trial and PROCESS study and include health worker and patient questionnaires, AL and mRDT stock data, and community cross-sectional surveys.

In Chapter 7, I present a qualitative analysis of contextual influences on the functioning of the intervention at health centres participating in the PRIME intervention. Data are drawn from the PROCESS study including in-depth interviews, a semi-structured contextual record, and field notes. A multiple case study is presented and data are analysed following a phased and iterative process of thematic analysis.

In Chapter 8, I present an interpretation of the commonalities and differences between the methodological approaches applied and the evidence they produce. Data are drawn from my experiences of working through each methodological exercise as well as the empirical findings produced. Analytical purchase is gained from comparing and contrasting these data under three areas: methodological challenges and contributions, ways of accounting for complexity, and integrating accounts of the intervention and its effects.

3.3. Researcher position and motivation

Reflecting on a researcher's values and experiences is acknowledged as an important practice in research and is suggested as means of contributing to the integrity and trustworthiness of the findings (Hammersley and Atkinson 2007; Robson 2011). In this section I describe my position and motivation for undertaking this research recognising that this has shaped the methodological approach taken and the interpretations that are presented.

My motivation for using the PRIME intervention for this research was based on my experiences with designing and evaluating the intervention as well as advances in the rapidly growing literature on complex interventions research. Prior to starting this PhD research, I worked as a Research Fellow with the PRIME trial and PROCESS study from 2010 to 2013 based in Uganda. In this role, I was involved with all aspects of designing, implementing and analysing these research projects. This included designing the PRIME intervention as well as the PRIME trial and PROCESS study research protocols. I was also responsible for overall management of the research projects in the field.

During this time, I gained first hand insight into the investments of time, materials and resources required to design and evaluate a complex intervention. I found the process exciting, but struggled at times to rationalise the investments made against the intended outputs of the PRIME trial – a single measure of effect demonstrating whether the intervention worked, or not. The inclusion of the PROCESS study, with the aim of explaining how the intervention functioned and its wider impacts, was a valuable counterpoint. Yet, I was uncertain as to how the two studies might support or unsettle each other during data collection, analysis and interpretation. My experiences were reflected in the expanding complex interventions literature as others were also engaging with and reporting on the challenges of complexity, the role of the randomised trial, and the contributions of process evaluations (Bird et al. 2011; Clark et al. 2012; Munro and Bloor 2010; Petticrew 2011). Although there was an increasing rhetoric on the importance of and challenges to accounting for complexity, I found it curious that this was not matched with the publication of empirical examples and consolidation of best practice. With these observations, I decided to pursue this PhD research.

With prior training in epidemiology and social science research methods, and having worked on the PRIME trial and PROCESS study under the guidance of both a clinical epidemiologist and an anthropologist, I acknowledged the opportunities and challenges presented by both disciplines for the design and evaluation of health interventions. In pursing this PhD, I therefore sought to develop my academic skills in both quantitative and qualitative analytical work engaging with the theoretical underpinnings and the methodological practices of trial analysis as well as social science informed by medical anthropology. My aim of developing these skills has been to push against singular methodological boundaries, as Hesse-Biber (Hesse-Biber 2012:888) says, to be "both an insider and an outsider to a given theoretical perspective—a double consciousness that provides for the unearthing of new knowledge by not allowing some forms of inquiry to be subjugated to any one dominant methodology". In practice, this position was achieved by conducting the methodological exercises described above which enabled me to examine each theoretical perspective and methodology in its own right. Then, bringing these together through a deliberate and reflexive familiar/strange practice enabled me to examine the points of commonality between each, as well as what might be highlighted by one perspective but missed out by another, and how these influence interpretations of the intervention.

3.4. Student role

From 2010 to 2013, I was employed as a Research Fellow on both the PRIME trial and PROCESS study. I started work on this thesis as a full-time PhD student in 2013. While this thesis draws on my experiences and utilises the data from the PRIME trial and PROCESS study, I have carried out the work presented in this thesis as an independent researcher seeking support from the PRIME trial and PROCESS study Principal and Co-Investigators as necessary when interpreting my findings within the overall context of the two studies.

3.5. Ethical approvals

This thesis was conducted under the ethical approvals granted to the PRIME trial and PROCESS study. The PRIME trial was approved by the Ugandan National Council for Science and Technology (UNCST Ref HS 794), the Makerere University School of Medicine Research & Ethics Committee (SOMREC Ref 2010–108), The London School of Hygiene and Tropical Medicine Ethics Committee (LSHTM Ref 5779), and the University of California San

Francisco Committee on Human Research (UCSF CHR Ref 006160). Sponsorship and insurance was provided by the LSHTM's Clinical Trials Sub-Committee (Ref QA292).

The PROCESS study was approved by the Ugandan National Council for Science and Technology (UNCST Ref HS 864), the Makerere University School of Medicine Research & Ethics Committee (SOMREC Ref 2011–103), and the London School of Hygiene and Tropical Medicine Ethics Committee (LSHTM Ref 5831).

Analysis of the PRIME trial and PROCESS study lead by the Principal Investigator ended in 2013. Since then, I have maintained active ethical approval for both projects through annual renewals at all institutions.

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RESEARCH PAPER COVER SHEET

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SECTION A – Student Details

Student	Deborah D DiLiberto
Principal Supervisor	Elizabeth Allen
Thesis Title	Accounting for complexity: An examination of methodologies for complex intervention research in global health

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	Global Health Action		
When was the work published?	2015		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
Have you retained the copyright for the work?*	Yes	Was the work subject to academic peer review?	Yes

**If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.*

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	Choose an item.

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I contributed to the development of the intervention described in the paper including data collection, analysis and interpretation. I conceived of, drafted and submitted the paper for publication.

Student Signature: D.DiLiberto **Date:** 5 October 2016

Supervisor Signature: Elizabeth Allen **Date:** 5 October 2016

CHAPTER 4. Examination of intervention design

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Abstract

Background: In Uganda, health systems challenges limit access to good quality health care and contribute to slow progress on malaria control. We developed a complex intervention (PRIME) which was designed to improve quality of care for malaria at public health centres.

Objective: Responding to calls for increased transparency, we describe the PRIME intervention's design process, rationale and final content, and reflect on the choices and challenges encountered when designing this complex intervention.

Design: To develop the intervention, we followed a multi-step approach, including: 1) formative research to identify intervention target areas and objectives; 2) prioritisation of intervention components; 3) review of relevant evidence; 4) development of intervention components; 5) piloting and refinement of workshop modules; and 6) consolidation of the PRIME intervention theories of change to articulate why and how the intervention was hypothesised to produce desired outcomes. We aimed to develop an intervention that was evidence-based, grounded in theory, and appropriate for the study context, which could be evaluated within a randomised controlled trial, and had the potential to be scaled-up sustainably.

Results: The process of developing the PRIME intervention package was lengthy and dynamic. The final intervention package consisted of four components: 1) training in fever case management and use of rapid diagnostic tests for malaria (mRDTs); 2) workshops in health centre management; 3) workshops in patient-centred services; and 4) provision of mRDTs and antimalarials when stocks ran low.

Conclusions: The slow and iterative process of intervention design contrasted with the continually shifting study context. We highlight the considerations and choices made at each design stage, discussing elements we included and why, as well as those that were ultimately excluded. Reflection on and reporting of 'behind the scenes' accounts of intervention design may improve the design, assessment, and generalisability of complex interventions and their evaluations.

4.1. Introduction

Good quality health care for malaria includes accurate diagnosis of suspected malaria cases and provision of prompt, effective treatment with artemisinin combination therapies (ACT) (World Health Organization 2010); however, in Uganda and elsewhere, health systems challenges often limit access to good quality care and contribute to slow progress on malaria control (Rao, Schellenberg, and Ghani 2013; Stratton et al. 2008; Yeka et al. 2012). In Uganda, good quality care has been described as appropriate clinical processes combined with respectful interpersonal interactions and adequate resources (Chandler, Kizito, et al. 2013). Benefits of providing good quality care include increased demand for services (Arifeen et al. 2004; McPake 1993; Wouters 1991), improved attendance at health centres (Mbaruku and Bergstrom 1995), better relationships between patients and health workers (Deyo and Inui 1980), and increased clinic loyalty (Vera 1993), potentially producing better health outcomes (Williams 1994). Interventions to improve the quality of care provided at health centres, increase patient attendance, and ultimately to improve health outcomes for malaria and other illnesses, are urgently needed (Kizito et al. 2012; World Health Organization 2008). However, the optimal approach to improving quality of care is not clear, particularly in low-resource settings (Pariyo et al. 2005). Provision of basic training and health education have been tried, but appear to have limited impact, prompting calls for more complex interventions targeting the multidimensional nature of patient treatment seeking (Smith et al. 2009), and provider practices (Grimshaw et al. 2001; Oxman et al. 1995).

For the PRIME trial (Staedke et al. 2013), we developed a complex intervention targeting malaria case management at public health centres in Uganda. Drawing on available literature (Campbell et al. 2000; Craig et al. 2008), we aimed to design an intervention that was evidence-based and grounded in theory, was tailored to our study setting, could be evaluated within a randomised controlled trial, and had the potential to be scaled-up

sustainably by the Ugandan Ministry of Health. The final PRIME intervention consisted of four components: 1) Training in fever case management and use of rapid diagnostic tests for malaria (mRDTs); 2) Workshops in health centre management; 3) Workshops in patient-centred services; and 4) Ensuring the supply of mRDTs and artemether lumefantrine (AL, the first line ACT for malaria in Uganda). The primary outcome for the evaluation of the PRIME intervention was the prevalence of anaemia (haemoglobin <11.0 g/dL) in individual children under five measured in annual surveys of communities surrounding health centres enrolled in the PRIME trial (Staedke et al. 2013).

Interventions such as PRIME can be considered 'complex' due to their multiple, interacting components which address multifaceted problems within dynamic systems (Hawe et al. 2009; Medical Research Council 2008). Responding to calls for more detailed and transparent reporting of intervention components (ICEBeRG and Francis 2006; Michie, van Stralen, and West 2011; Proctor, Powell, and McMillen 2013) and designs (Hoffmann et al. 2014; Michie et al. 2009), here we describe the process of designing the PRIME intervention, including the choices we made and the challenges we faced, and how this shaped the final intervention package.

4.2. Study setting

The PRIME intervention was designed for Tororo, Uganda, an area of high malaria transmission (Kamya et al. 2015). In both health centres and communities, infrastructure is limited. Health centres are generally run by nurses or nursing assistants; many lack electricity, running water, functioning laboratories and adequate staffing. As a result of system-wide reforms in the 1990s and early 2000s, public health care was decentralised and, in theory, provided free of charge (Burnham et al. 2004). Due to frequent stock-outs of essential drugs, including antimalarials, patients were often forced to purchase drugs, or go without adequate treatment (Anokbonggo, Ogwal-Okeng, Obua, et al. 2004).

4.3. Intervention development

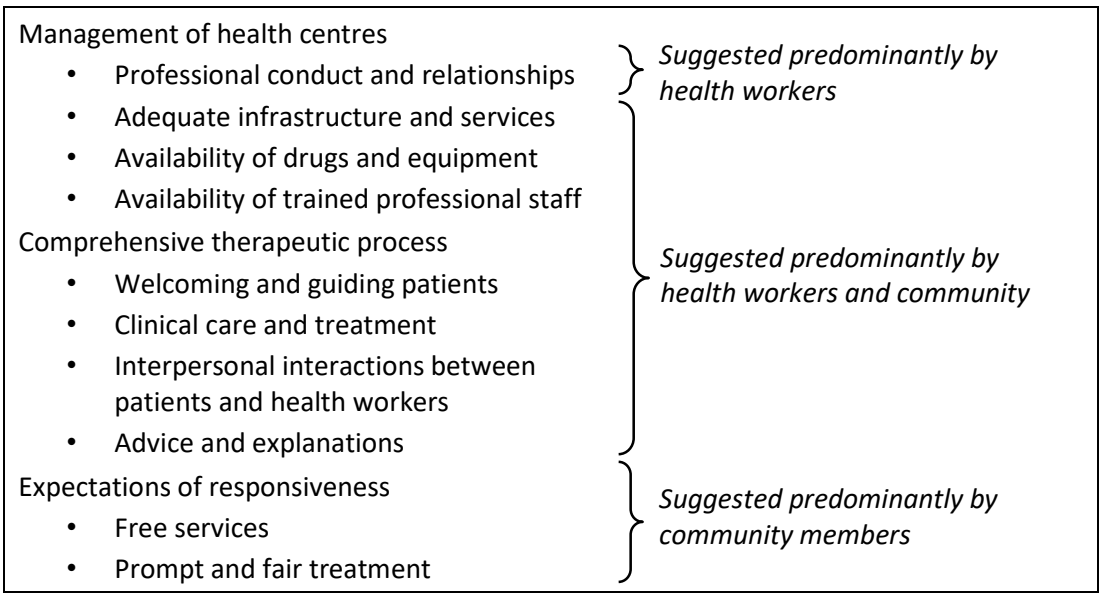
In developing the intervention, we followed a step-wise approach informed by the literature (Arhinful et al. 1996; Medical Research Council 2008; Nichter et al. 2008), including: 1) formative research to identify target areas and refine objectives; 2) prioritisation of intervention components; 3) review of relevant evidence to support

intervention content; 4) development of intervention components; 5) piloting and refinement; and 6) consolidation of the PRIME intervention theories of change.

4.3.1. Step 1. Formative research to identify target areas and refine objectives

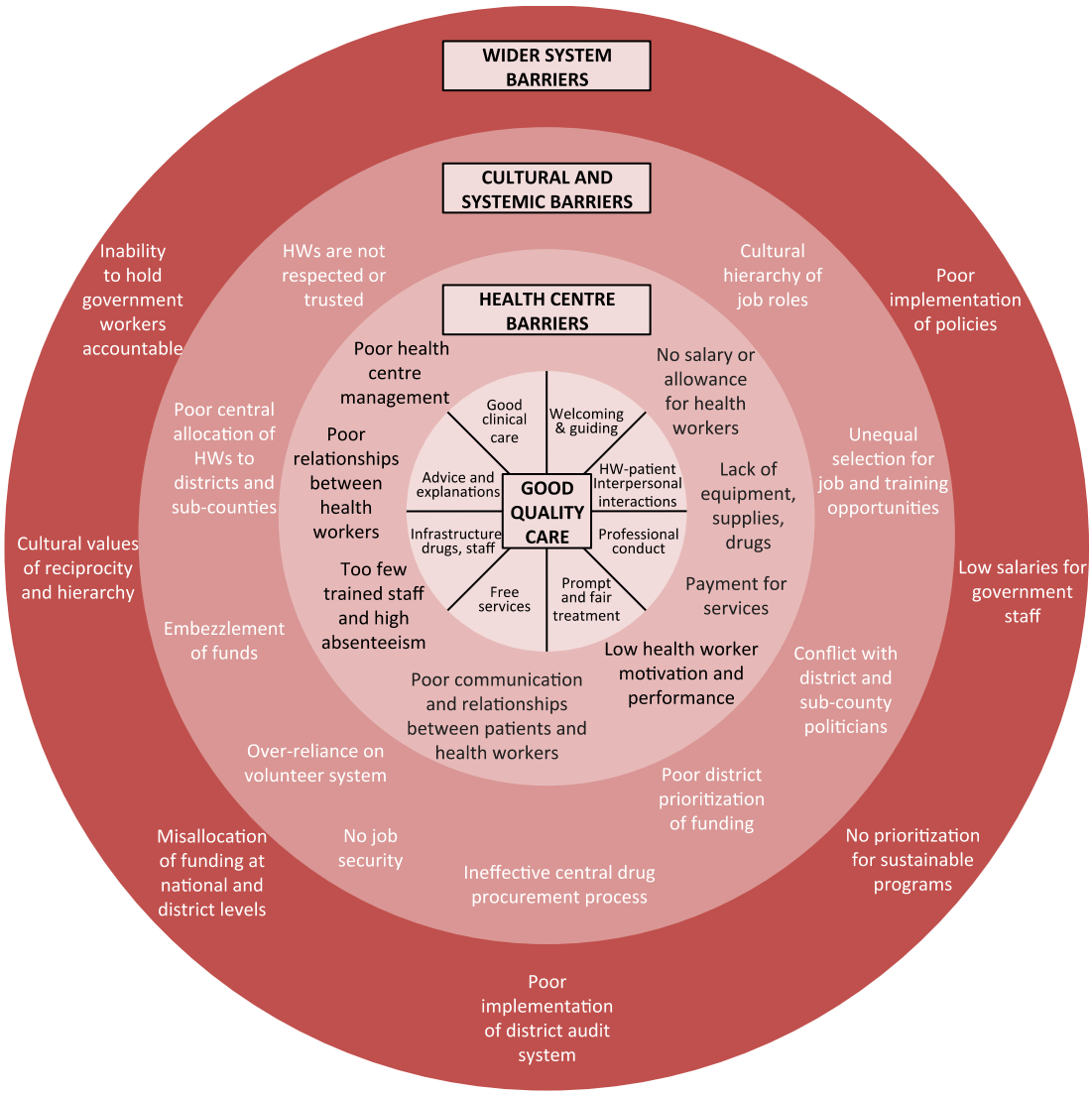
In 2009-2010, we conducted mixed-methods research to characterise the population and local health services using a household survey, situational analysis of government-run health centres, and qualitative assessment of health workers' and community members' experiences at health centres (Staedke and Uganda Malaria Surveillance Project 2010). Through an iterative thematic analysis, we identified aspirations for good quality care and malaria case management, and suggestions of how these might be achieved. Health workers and community members shared ideals of what constituted good care, suggesting that patients might be attracted to attend health centres if quality of care was improved, Figure 4.1. However, multiple challenges were identified, including lack of equipment and basic infrastructure, high patient to staff ratios, poor health centre management, and stock-outs of antimalarials and other drugs. Social challenges were also identified, including low health worker motivation, and difficult relationships between health workers and community members due to lack of trust, language barriers, discriminatory behaviours, and requests for informal payments for services.

Figure 4.1: Health workers' and community members' aspirations for good quality health care



We categorised the challenges identified, including health centre factors, cultural and systemic issues, or wider system factors. The results of our analysis identified eight key components of good quality care and corresponding target areas for potential intervention, Figure 4.2. Through this process, we differentiated challenges that were amenable to implementation research from those that were beyond the project's scope, thereby reducing a range of complex challenges into a definable set of factors for action at health centres.

Figure 4.2: Barriers to providing good quality care at health centres



4.3.2. Step 2. Prioritisation of intervention components

Prioritising components to include in the PRIME intervention was an iterative process. We conducted a workshop and follow-up meetings with stakeholders involved in malaria control and child health programmes including researchers and programme officers at the Ministry of Health, the National Malaria Control Programme, Makerere University and a local malaria-related non-governmental organisation. Together, we reviewed the findings of the formative research and prioritised potential interventions based on stakeholders' guidance. Overall, stakeholders agreed that we should target malaria case management, patient-centred care, and health centre management. However, some of the activities we proposed were deemed beyond the scope of our project. For example, to address staffing shortages and absenteeism, we suggested negotiating with district officials to increase salaries and hire additional staff. We also suggested supplementing the primary health care fund -- a small cash fund provided to health centre in-charges (often erratically) to pay for essential activities, including transportation of drugs, cleaning services, and necessary supplies. However, district officials were against these propositions, arguing that they would be difficult to administer and sustain. Table 4.1 outlines further details of these and other activities that were removed from consideration during this process.

Through this process of prioritisation we arrived at four intervention components (Table 4.2, Appendix 1), including: (1) Training in Fever Case Management and Use of mRDTs (FCM); (2) Workshops in Health Centre Management (HCM); (3) Workshops in Patient-Centred Services (PCS); and (4) Supporting the supply of mRDTs and AL.

Table 4.1: Activities considered but excluded as out of scope for the PRIME intervention

Potential intervention activity	Reasons considered drawn from formative research	Reasons not included in the PRIME intervention
Reinstate/ supplement the primary health care fund	• Insufficient funds to meet daily health centre costs including transporting drugs, paying for cleaning services, and purchasing supplies • Health workers request payment for services	• Bureaucratically and administratively challenging to implement • Opportunity for misappropriation • Unsustainable after the study period
Fill staffing gaps at health centres in accordance with Ministry of Health guidelines	• Many patients and too few staff • Low motivation of staff due to overburdened workloads • Health centres not fully functional due to insufficient availability of staff • Staff not at recommended levels	• Bureaucratically and politically challenging to implement • Limited availability of health workers nation-wide • Requires substantial funding • Unsustainable after the study period
Pay/supplement staff salaries	• Health workers not paid on time or in full • Low motivation of staff due to lack of pay • Time spent in alternative employment activities • Health workers request payment for services	• Bureaucratically and administratively challenging to implement • Not likely to be successful due to national payroll system challenges • Requires substantial funding • Unsustainable after the study period
Implement ICCM* through VHTs†	• Community medicine distributors/VHTs important source of care, treatment and referral in the community • Need to determine a sustainable VHT ICCM programme: community sensitisation, training, VHT kits, drug supply, supervision	• ICCM and VHT policy under revision and implementation timelines uncertain • Potential challenges with the operationalization of the new policy • Required drug formulations for pneumonia not yet available
Improve the drug supply chain for AL‡	• Frequent stock-outs of AL and other essential drugs leading community members to seek care elsewhere • Stock-outs due to challenges with quantification, ordering, storage, district level stock of AL, and numerous logistical barriers	• Other programmes already addressing the drug supply chain • Imminent implementation of new 'push' system, potential for misalignment • Unlikely to yield results due to challenges at higher levels of the system
Work with District and partners to ensure supply of mRDTs˅ and thermometers	• World Health Organisation guidelines for malaria case management, but limited supply of mRDTs to health centres • Thermometers not supplied or available in health centres	• No options for partnering with other stakeholders/partners providing mRDTs and thermometers identified; therefore, directly supplied by the PRIME intervention
Implement community sensitisation	• Attract patients to health centres by communicating new/improved services using local councillors, social gatherings, word of mouth, mass media, community dialogues	• Suggested to focus on word of mouth/VHTs to communicate information; however, VHT programme not implemented during study period
Include supervision and coaching as part of HCM˸ modules	• Supervision is described by health workers as 'fault finding, unsupportive and infrequent' leading to demotivation	• Weak evidence demonstrating effectiveness of supervision • Challenging logistics of implementing supervision activities
Implement 3-month self-observation activities to complement PCS˫	• Lack of patient-centred thinking due to low motivation and lack of awareness of how emotions can affect actions and relationships with others	• 3 month activities not aligned with other intervention training packages, therefore revised to weekly activities to fit within four PCS modules

* ICCM = integrated community case management
† VHT = village health team
‡ AL = artemether lumefantrine
˅ mRDT = malaria rapid diagnostic test
˸ HCM = health centre management
˫ PCS = patient-centred services

Table 4.2: PRIME training and workshop modules

Training in Fever Case Management		
Aim: To train health workers in use of mRDTs and build clinical skills for managing malaria and other febrile illnesses.		
Barriers addressed	Module	Topic
• Poor knowledge of malaria case management • Inadequate/unavailable infrastructure or diagnostic laboratory facilities	Training module	• How to evaluate patients with fever and select patients for mRDT[ˇ] testing • Performing and reading an mRDT • Management of a patient with fever and a positive or negative mRDT • Recognition and referral of patients with severe illness • mRDT storage and monitoring

	Supervision visits	• Observation and feedback on:
		  • Use of mRDTs
		  • Skills in fever case management
		  • Stock management of AL and mRDTs
		  • Recording mRDT results in patient registers

Workshop in Health Centre Management		
Aim: To develop in-charge health workers' accountable practices in management of finances, supplies, and health information.		
Barriers addressed	Module	Topic
• Poor management of resources by in-charges • Low motivation of staff due to poor health centre administration • Under-utilization or lack of appropriate tools to appropriately mange health centres • Low use of records to monitor and manage resources and report to local and district stakeholders	HCM[˛] 00: Introduction to HCM	• The role of accountability as a health worker
	HCM 01: Primary Health Care Fund management	• Budgeting and accounting using the Primary Health Care Fund management tool • Budgeting and accounting -- putting it all together
	HCM 02: Drug Supply Management	• Principles of the drug distribution system • Forms required in drug distribution cycle • The ACT Drug Distribution Assessment Tool
	HCM 03: Health Information Management	• Why quality information matters • The information cycle -- from patient to patient
Workshop in Patient-Centred Services		
Aim: To improve health workers' interpersonal communication with patients and other health centre staff and to build consultation skills.		
Barriers addressed	Module	Topic
• Lack of patient-centred thinking • Communication problems including language barrier • Discrimination/preferential treatment of patients • Inappropriate use of volunteers • Poor relationships between staff and communities • Poor patient flow and management	PCS[˙] 00: Introduction to PCS and Self Observation Activities	• Thinking about my role as a health worker • Introduction to patient-centred services • Introduction to Self-Observation Activities
	PCS 01: Communication Skills Part 1	• Building rapport • Active listening
	PCS 02: Communication Skills Part 2	• Asking good questions • Giving good information
	PCS 03: Building a positive work environment	• Health centre management changes • Dealing with stress at work
	PCS 04: Improving the Patient Visit	• Communication review • Patient welcome and orientation

[ˇ] mRDT = malaria rapid diagnostic test

[˛] HCM = health centre management

[˙] PCS = patient-centred services

4.3.3. Step 3. Review of relevant evidence to support intervention content

We searched for existing training packages in the published and grey literature, both online and in local library collections, prioritising interventions that had been evaluated and found to be effective in Uganda or similar low-resource contexts.

4.3.3.1. Fever case management (FCM) module

For the FCM module, we identified a training package developed by the Joint Uganda Malaria Training Program (JUMP) team utilising mRDT training guidelines and job aids adopted by Uganda's Ministry of Health (National Malaria Control Program 2009). The training consists of lectures and practical sessions, followed by three rounds of support supervision by the JUMP team on-site at health centres (1 and 6 weeks, and 6 months post-training). The training has been shown to improve fever case management and reduce the number of unnecessary antimalarial treatments when implemented in public health centres in Uganda (Hopkins, unpublished observations) (Odaga et al. 2014).

4.3.3.2. Health centre management (HCM) and Patient-centred services (PCS) modules

For the HCM and PCS modules, we were unable to identify suitable pre-existing interventions. Although interpersonal interactions between health workers and patients are considered to be central to good quality care (Chandler, Kizito, et al. 2013; Haaland and Vlassoff 2001; Kizito et al. 2012; Stewart 2001), the philosophy of patient-centred services is not as prominent in African health care (Nayiga et al. 2014), as it is elsewhere (Balint 1957; Mead and Bower 2000). In addition, most health centre management interventions we identified were large-scale, and implemented in a top-down format. The Securing Uganda's Right to Essential Medicines (SURE) programme is an example (SURE - Securing Ugandans' Right to Essential Medicines n.d.), see also (Benavides 2009; EngenderHealth 2003; Langley et al. 2009; Management Sciences for Health 2005; Shabahang 2003). Because rigorous evaluations of these programmes have been limited, there was little evidence to inform the PRIME intervention. Thus, we opted to design the HCM and PCS modules ourselves.

Our HCM and PCS modules are based on concepts and resources originally developed by A. Haaland for a health provider communication training model in collaboration with health providers in seven countries in Eastern Europe and Africa, and with the Kenya Medical

Research Institute (KEMRI)/Wellcome Trust Research Programme (Haaland, personal communication, 15 May 2010). The HCM modules were designed to align with existing health centre management processes. For the PCS modules, we aimed to strengthen providers' relationships with patients, colleagues, and the community (Stewart 2001), by reorienting the care-seeking experience towards patients' aspirations for good quality care (Chandler, Kizito, et al. 2013).

4.3.3.3. Supply of mRDTs and AL

We aimed to align the PRIME supply component with Uganda's existing supply system and the SURE programme (SURE - Securing Ugandans' Right to Essential Medicines n.d.). However, while we were developing the intervention, Uganda's National Medical Stores (NMS) distribution system changed from a 'pull' system, in which drugs were ordered by health centres, to a 'push' system, with regular delivery of a pre-determined package of drugs, requiring us to revise the PRIME supply component. We identified an existing health worker to act as a liaison, who was responsible for gathering stock information from health centres, and facilitating delivery of mRDTs and AL from PRIME when the NMS supply was inadequate, or failed. The SURE programme, introduced in 2009, aimed to gather drug stock information and minimise stock-outs through supervision visits. The PRIME intervention utilised SURE's pharmaceutical management information system forms and procedures.

4.3.4. Step 4. Development of intervention components: HCM and PCS modules

To develop the HCM and PCS modules, we reviewed evidence on successful intervention activities; translated evidence into content; incorporated behaviour change theory, adult learning cycles, and learning activities; and created workshop manuals.

4.3.4.1. Reviewing evidence on successful intervention activities

We reviewed the literature to identify activities targeting health worker communication and interpersonal relationships, patient satisfaction, health worker supervision and coaching, and management of health centres. We focused on low-cost and low-resource interventions, prioritising interventions that had been successfully implemented and evaluated. The review methods are described elsewhere (Chandler, unpublished observations).

Several activities have been shown to improve communication between health workers and community members, producing a positive effect on patient satisfaction and health outcomes, including enabling clinicians to give patients 'time to talk' during a consultation by asking good questions (Haaland, Molyneux, and Marsh 2006), and employing active listening (Fassaert et al. 2007; Krasner et al. 2009) to elicit better information from patients (Marvel et al. 1999). Activities to build rapport and support emotional care by reassuring patients (Neumann et al. 2009), have also been shown to facilitate patients' therapeutic reactions (Di Blasi et al. 2001; Fassaert et al. 2008; Leventhal, Leventhal, and Contrada 1998). Likewise, activities promoting 'positive communication' may improve team work by recognising how personal circumstances and work environment affects emotions and communication (Neumann et al. 2009; Thomas 1987). Activities to improve relationships between health workers include building self-awareness and constructive communication through vignettes which are used to identify and resolve sources of conflict (Kozub and Kozub 2004). Notably, of these activities, only 'time to talk' was drawn from a low-income setting.

Activities shown to improve patient satisfaction with experiences at health centres include greeting patients (Makoul, Zick, and Green 2007), and guiding patients through the health centre (EngenderHealth 2003). Interventions promoting supervision and coaching were also identified, although evidence that these activities change provider performance was weak (Bosch-Capblanch and Garner 2008; Bosch-Capblanch, Liaqat, and Garner 2011). We also considered health worker performance management programmes, including the SURE programme, and the Uganda Malaria Surveillance Programme's (UMSP) Continuous Quality Improvement Project, which demonstrated that providing health status reports and regular supervision with constructive feedback improved health worker performance (Mpimbaza, personal communication, 10 June 2010). However, the UMSP activities had not been systematically evaluated. Thus, we were forced to weigh the available evidence and decide which best informed the design of our intervention package. We ultimately chose not to include coaching or supervision due to the concerns about sustainability, both during the trial and if scaled-up, and the limited evidence base supporting coaching and supervision in our setting (Rowe et al. 2009, 2010).

4.3.4.2. Developing intervention content

For drug supply management, we drew on literature to develop the ACT Drug Distribution Assessment Tool, a one-page tool to support health workers with resolving everyday distribution bottlenecks that are not tracked in standard monitoring tools, but are often the cause of health centre drug stock-outs (DiLiberto 2009). For financial management, we developed the Primary Health Care Fund Budgeting and Accounting Tool, a one-page tool to assist health workers with managing the health centre primary health care fund.

For the PCS modules, we adapted activities to improve health worker communication developed mainly in high-income settings to our study setting by using local cultural and social references drawn from our formative research. We deconstructed concepts contained in activities such as giving 'time to talk', 'building rapport and emotional care' and 'self-awareness', and reconstituted these in forms and definitions meaningful to the study context. Thus, activities maintained their intended purpose but were communicated using scenarios and discussion points relevant to health workers' everyday experiences.

4.3.4.3. Incorporating behaviour change theory

The HCM and PCS modules are underpinned by behaviour change theory to initiate the intended pathway of effect. Both modules aimed to build a supportive community of practice. The 'Communities of Practice' behaviour change theory posits a cyclical process of change, where individuals' frames of reference are transformed through participation in a community of peers, and their participation in turn transforms the community (Wenger 1998). This process serves to create an 'informal curriculum' for health workers in addition to the existing overarching core curricula (Hafferty 1998). Through this process, learners engage with other community members and reflect critically on their practice through a social process of individual and collective learning (Mann 2011).

The theory of Communities of Practice resonated in our setting where many health workers learn primarily 'on the job'. Likewise, our setting lacks many external motivators that have been shown to promote health worker performance, such as financial incentives, constructive supervision, professional accreditation and opportunities for promotion (Chandler et al. 2009; Dieleman et al. 2006; Mathauer and Imhoff 2006; Sodhi et al. 2014; Willis-Shattuck et al. 2008). Therefore, we sought to balance the limitations of the context with the opportunity to stimulate health workers' internal motivations for providing good

quality care (Franco, Bennett, and Kanfer 2002), which included the desire to be viewed as professional, to be respected by colleagues and community members, and to be valued for providing good health care services (Staedke and Uganda Malaria Surveillance Project 2010). We theorized that as health workers built, demonstrated and received positive feedback on their clinical, interpersonal and managerial skills, the social processes emerging from participation in the community of practice would help them to develop their professional identity, and sustain positive skills and behaviours (Lingard et al. 2003).

4.3.4.4. Incorporating an adult learning cycle and learning activities

The HCM and PCS modules were designed as interactive weekly 3-hour workshops to promote group learning, contributing to the development of a community of practice. The structure was designed to allow time to reflect and practice skills in between workshops and to get feedback at subsequent workshops. Small groups of health workers were selected to enhance participation and encourage peer support in the future. The workshops were led by three members of the PRIME research team, with medical backgrounds but little experience in interactive training methods, as is the norm in Uganda (Ssekabira et al. 2008).

The workshops were framed as continuing professional development with interactive learning activities which have been shown to improve health worker knowledge, skills, attitudes and behaviours leading to improved patient outcomes (Forsetlund et al. 2009; Mansouri and Lockyer 2007; Robertson, Umble, and Cervero 2003). The workshops were structured as a *6-step adult learning cycle* drawn from Kolb's (Kolb 1984) experiential learning theory which includes four stages of experience, reflection, conceptualisation and planning; and from Knowles' (Knowles, Holton, and Swanson 2005) theory of adult learning which asserts that adults must first establish why they should learn something before proceeding to acquiring new knowledge. The 6-steps involve: developing a 'need to know', individual reflection, conceptualisation, experimentation, group reflection, and planning. To activate this learning cycle, the workshops employ a variety of participatory learning methods drawn from training modules in similar contexts (Appendix 2), (Haaland, personal communication, 15 May 2010) (Haaland et al. 2006; Haaland and Vlassoff 2001).

The PCS module also included weekly self-observation activities (SOA) which aimed to stimulate learners' purposeful critical analysis of their knowledge and experience (Schön

1983) enabling them to engage and deal with their emotions (Lewin 1951), and develop appreciation and respect for others (Branch 2006). Semi-structured SOAs followed by feedback in groups provided opportunities for both individual learning and change as a community (Mann 2011). The SOAs were adapted from tasks designed and tested in a number of other health care settings (Haaland, personal communication, 15 May 2010) (Haaland et al. 2006).

4.3.4.5. Creation of Workshop Manuals

For each HCM and PCS workshop, we created corresponding Trainer and Learner Manuals - -18 in total (Appendix 1). We contracted with an experienced public health consulting firm (WellSense n.d.) to fine-tune the learning activities and typeset the manuals. This was a collaborative effort, requiring significant input on a new layer of design considerations, including the colours and fonts that would best communicate the ethos of the workshops, and how pictures and layout of activities could support learning retention. We also considered how the trainer instructions would encourage active facilitation but also support trainers in drawing-out learners' reflections and experiences.

4.3.5. Step 5. Piloting and refinement: HCM and PCS modules

We conducted two rounds of piloting the HCM and PCS modules with 10 health workers from outside of the study area. We administered questionnaires to learners and trainers; gathered daily feedback from trainers and the piloting team; and conducted focus group discussions with participants at the end of the modules. The piloting evaluated the relevance and applicability of the learning objectives and content, and delivery of the training (Haaland 2001). The piloting proved to be an invaluable exercise, revealing, unexpectedly, that the learning capacity of our intended learners was not in line with our expectations. While the 6-step learning process and interactive activities appeared to support learning, some of the module concepts and language were too advanced, requiring us to readjust our expectations of how these concepts could be feasibly introduced. The trainers, who had more experience with didactic approaches, also reported challenges with the interactive format of the manuals. Thus, we revised the modules, aiming to 'hit the mark' with our intended learners by simplifying the language, reducing the number of new concepts and learning objectives per module, including more interactive activities, and revising the prompts and instructions throughout the trainers' manuals. See Table 4.3 for examples of revisions made. The second round of piloting indicated that the revised

modules did meet our intended objectives. However, the piloting and subsequent revisions added significant and unexpected delays to the design process. The final learning objectives are in Appendix 1 and final versions of the modules can be found online (Infectious Diseases Research Collaboration & ACT Consortium 2011).

Table 4.3: Example of revisions made to the PCS and HCM modules as a result of piloting

Description of revisions made	Reason for revision	Example of revisions made
Reduced the total number of objectives across the modules so that only one or two new concepts were introduced per module	The total number of learning objectives and content was ambitious for the 3-hour module format. Learning was best taken-up when there were only one or two concepts per module.	• Concepts for improving communication with patients were introduced over two modules with two concepts per module: – PCS 01: Communication Skills Part 1 introduced building rapport and active listening – PCS 02: Communication Skills Part 2 introduced asking good questions and giving good information
Simplified language and revised learning objectives to only introduce only one new word per module	Overall, the language needed to be reduced to meet the education level of the learners (average level = primary school). New words required time and expertise to introduce and be taken-up by learners.	• Reduced number of new words such as: building rapport, triage, open/closed questions, or automatic emotional responses, to one or two per module
Revised learning objectives to include more group work activities	Learners responded well to group work activities, were more engaged with each other and retained more learning points, compared to didactic teaching activities. For example, learners struggled to understand and perform calculations required for drug supply management when these were taught didactically.	• Revised learning objective for drug supply management to 'Accurately complete the forms required in the drug distribution system'. Calculations for the forms were completed as group work, and more information was provided in the Learners' Manual for later reference when completing forms at the health centre.
Rephrased objectives with abstract concepts into simpler ideas communicated with activities or games	Abstract concepts took a long time to introduce and give adequate examples; learners understood concepts better when they had an example or activity to describe the concept.	• Learning objective about appreciating 'barriers' to attending the health centre, both logistical (transportation, time, etc.) and emotional (anxiety, confusion), was introduced using a maze activity to demonstrate how these barriers prevent access to health services.

4.3.6. Step 6. Consolidation of the PRIME intervention theories of change

Drawing on complex intervention design and evaluation guidance (Judge and Bauld 2001; Medical Research Council 2008; Weiss 1995; White 2009b), we articulated two complementary intervention theories -- a programme theory and an implementation theory. These theories make explicit how and why we hypothesised the PRIME intervention components would combine to produce desired outcomes (Weiss 1998). The programme theory, represented in a logic model describes why the four intervention components are anticipated to produce specific outcomes, hypothesising that an intervention addressing the barriers to providing good quality care for malaria and febrile illnesses will improve appropriate malaria case management and patient satisfaction, leading to repeat attendance at health centres, and ultimately, improved health outcomes in community children, Figure 4.3. The implementation theory articulates how the intervention will stimulate behaviour change, hypothesising that a learning process stimulating health workers' cognitive, emotional and social learning processes through interactive workshops reinforced within a community of practice, will lead to immediate and sustained change in health worker motivation, behaviour and practice for providing good quality care, Figure 4.4.

Figure 4.3: PRIME intervention programme theory and logic model

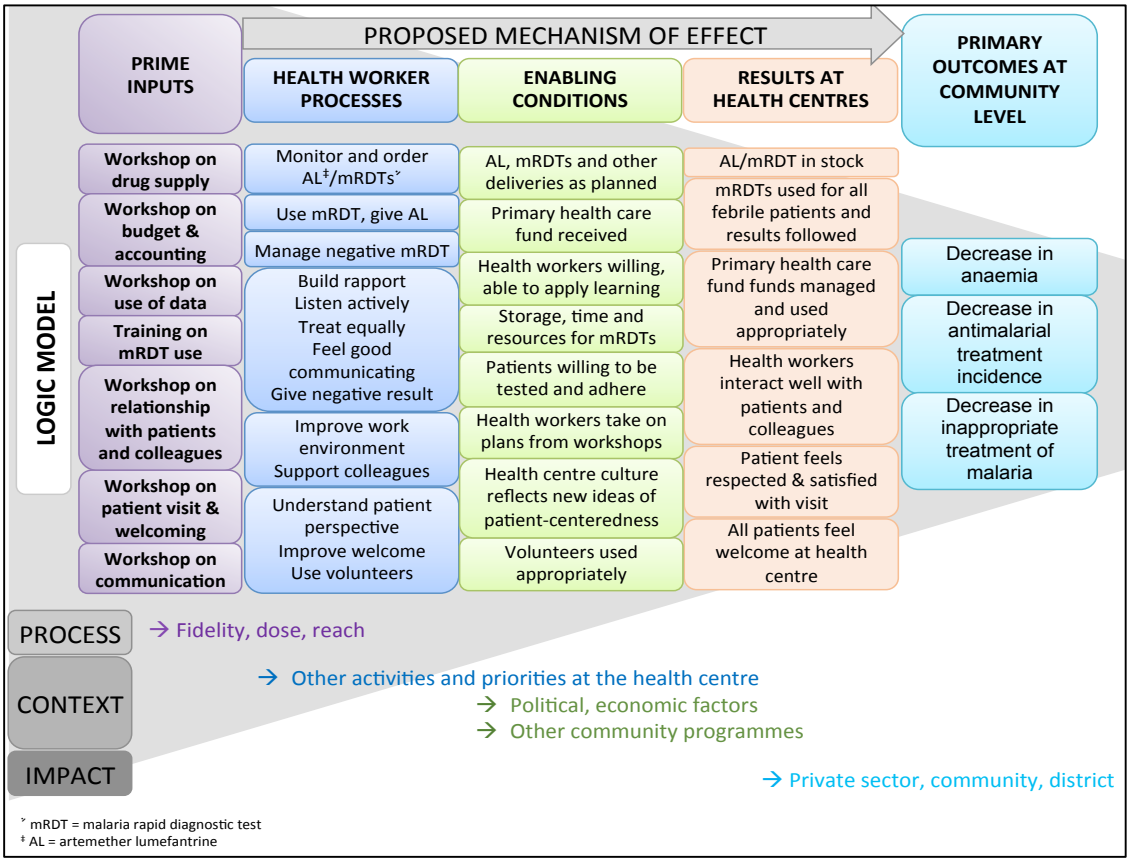


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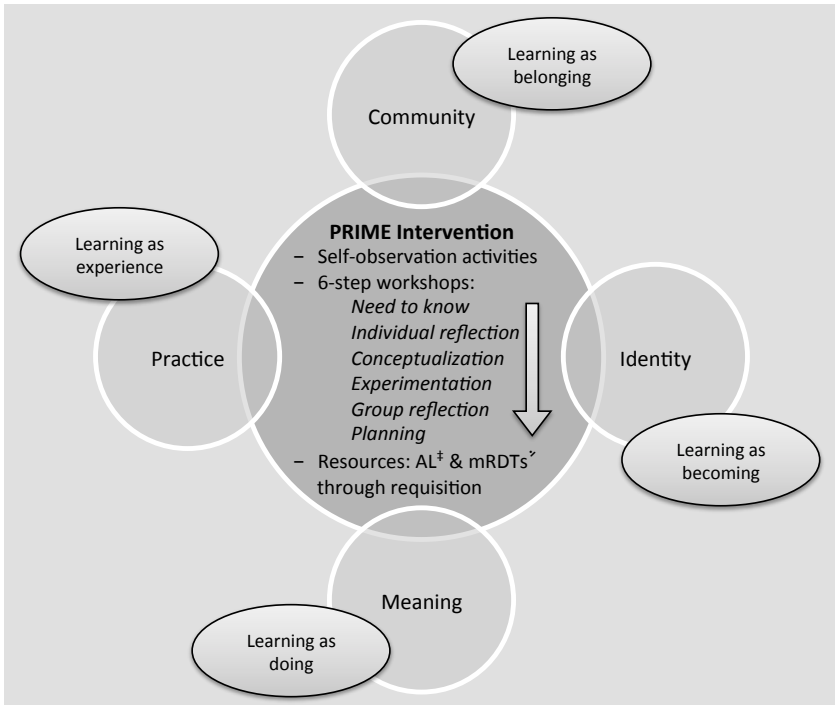
Figure 4.4: PRIME implementation theory



‡ AL = artemether lumefantrine
˅ mRDT = malaria rapid diagnostic test

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4.4. Discussion

We designed a complex intervention targeting delivery of care for malaria at public health centres in Uganda (Chandler, DiLiberto, et al. 2013; Staedke et al. 2013). Informed by best practice, we aimed to develop an intervention which was evidence-based, grounded in theory, and appropriate for our study setting using a systematic approach. In the process, we learned several important lessons related to the scope of the intervention and necessary compromises, the tension between static interventions and dynamic contexts, and the challenges of rigorously designing a behaviour change intervention for low-resource settings. By transparently reporting our 'behind the scenes' accounts, we hope to inform the design and content of future complex interventions.

Our formative research identified several challenges to providing good quality care at different levels of the health system. Many of these challenges were interpreted to be rooted in wider health system norms which prioritise technical skills and technologies over a patient-centred approach to care. Likewise, our context is characterised by ineffective political systems, and a deeply embedded hierarchical structure which perpetuates power imbalances throughout the health system (Chandler, Kizito, et al. 2013). In an attempt to define factors for action at the health centre level, we found it necessary to bracket out much of the complexity and the political-economic reality underlying health service provision in Uganda. As a result, we focused on intervention components that had the highest likelihood of success and buy-in from stakeholders within the constraints of a focused project, which others have noted as a critical factor for success when designing health services interventions (English 2013). However, this choice meant that the deeper social, political and economic challenges which underlie poor health care quality and lack of progress on malaria, remained unaddressed by our intervention(Okwaro et al. 2015). Rather than ignore these challenges as being out of scope of the intervention design process, engaging with them was required situate the intervention within the wider health system context and to provide deeper insight into how the intervention components might operate within this system. Recognising that interventions are a part of complex health systems (Hawe et al. 2009), we urge intervention designers to consider and report on the process of negotiating wider social, political and economic realities, and how this influenced intervention content and design.

The slow and iterative process of intervention design contrasted with the continually shifting study context. During the intervention design process, which took almost one year, several changes in the study context occurred that had significant impacts on the intervention. The integration of the SURE programme and implementation of NMS's 'push' delivery system required a reconceptualization of the HCM modules and the supply component. A policy introduced by the District Health Office to remove untrained volunteers from health centres required an adaptation of the PCS module to suit other authorised support staff. This ever-changing context created a 'moving target' with which to align the intervention, and contrasted with the need to develop standardised content suitable for evaluation in a cluster-randomised trial. To accommodate this, the modules were designed as a structured framework complemented by reflective learning activities to engage with learners' everyday experiences. In this way, the structure of the modules were standardised and reproducible, but the learning points could be adapted to the local context (Hawe, Shiell, and Riley 2004). While the challenge of implementing and evaluating static interventions in dynamic contexts has been considered (Bird et al. 2011; Hoddinott et al. 2010; Kok et al. 2012; Vahedi Nikbakht-Van de Sande et al. 2014), we encountered similar tensions during intervention design. To resolve these issues, flexibility and responsiveness were needed. Although this required additional investments of time and resources, we found this was essential to designing an intervention appropriate for our study setting.

Developing the PRIME intervention required a diversity of expertise, including clinicians, social scientists, epidemiologists, health workers, trainers, project managers, and training consultants. Team members approached the design of the intervention from different epistemological and disciplinary backgrounds. Developing the logic model suited the positivist perspective favouring a representation of the intervention as discrete components leading to pre-defined measurable outcomes. The process of developing the logic model provided an opportunity for the team to share and consolidate ideas, and emerged as a convenient communication tool. However, the static nature of the model did not adequately capture the way we expected change to occur, recognising that change processes would be dynamic, emergent and contingent on links between the intervention, individuals and society (Cohn et al. 2013). By utilising both text and visual models as part of our intervention theories, we endeavoured to articulate a specific intervention theory while acknowledging that the intervention would be enacted in a dynamic context which would

create many unique change processes, both intended and unintended. Our different disciplinary perspectives also led us to engage with questions of what the intervention 'is' – for example, rather than simply a composition of training materials and events, we began to conceive it as a series of interactions embedded in social relationships through which its meaning would emerge. This raised the possibility that the meaning of the intervention could be constructed differently by different actors, which was important to capture in our evaluation activities. Our experience concurs that an interdisciplinary approach appears to be essential for making meaningful progress towards improving population health (Dean and Hunter 1996); however, it should be recognised that this approach is time and resource intensive (Achonduh et al. 2014; Chandler et al. 2014; English 2013) requiring concerted effort to align perspectives into a shared understanding of the intervention (Clarke et al. 2012).

Our experience designing the PRIME intervention reflected a process that is more interactive and demanding than the available evidence and theory suggest (Craig et al. 2008). While the literature guiding intervention design is expanding (English 2013; Nutley et al. 2014), few authors discuss the construction process we found necessary to reach the final intervention package. The importance of reporting 'insider accounts' of intervention implementation and evaluation activities to better interpret trial outcomes has been noted (Reynolds et al. 2014; Wells et al. 2012). We argue that this same reflective and transparent reporting practice should apply to intervention design. Guidelines for reporting complex intervention content ask authors to describe the reasons for selecting intervention components which may include "experience of or evidence on the suitability of the component to achieve the intended change process" (Möhler et al. 2015). Our experiences reveal manifold reasons influencing the processes through which intervention content was considered, shaped, and integrated (or discarded), in light of research aims, available evidence, and resource constraints. Sharing accounts of activities that were considered but omitted, and why these decisions were made, may be as informative as descriptions of final intervention packages. Thus, we argue that describing these 'behind the scenes' accounts of the intervention design process should be considered a key 'experience' included in guidelines for reporting intervention content and their evaluations. A reflective and transparent reporting of the design process may promote assessments of the intervention's internal validity, facilitate interpretation and generalisability of results, and inform future interventions. As complex interventions gain momentum in health care, guidelines for

developing interventions and reporting on the design process will need to evolve, consistent with current debates of how complex interventions should be conceptualized and evaluated (Cohn et al. 2013; Hawe et al. 2009; Petticrew 2011).

Addendum

This chapter outlines the aspirations for good quality care described by health workers and community members. Due to the focus of this published paper on methods for designing the intervention, space was limited to develop in full how the content of the intervention responded to local concerns. For example, participants desired that services should be 'free' and 'fair', reflecting concepts of justice and fairness. In this addendum, I will describe how the PRIME intervention design addressed these concerns and the extent to which these were addressed in the evaluation.

4.4.1. The PRIME intervention

The PRIME intervention was designed to address the barriers to providing good quality care and improve patient satisfaction with their care seeking experience, leading to repeat attendance at health centres, and ultimately, improved health outcomes in community children. In so doing, the intervention sought to achieve principles of justice, equity and fairness by redirecting treatment seeking towards public health centres, where in line with national policies, treatment is provided free at the point of care. To support these principles, the intervention sought to address barriers to providing and accessing care by enabling a 'patient-centered' health care experience that focused on the relations between patients and providers and built interpersonal qualities for successful health seeking experiences. This is in contrast to the more common 'biomedical model' in which the emphasis is on technologies and technical skills for identifying standard disease entities and do not address the social processes that underlie health and access to care (Chandler, Kizito, et al. 2013).

Reorienting services towards patients required an approach that built health workers' motivations for providing good quality care including their desire to be viewed as professional, to be respected by colleagues and community members, and to be valued for providing good healthcare services. This was achieved through the interactive workshop format and employing participatory learning principles employed successfully elsewhere (Fonn et al. 2001; Haaland and Vlassoff 2001). The PRIME intervention activities supported health workers to address the different components of quality of care by exploring provider–client relations within a gender-sensitive context. These included self-observation activities, interactive group discussions, role playing, and problem solving activities. Through these activities, health workers learned to reflect on their personal motivations,

attitudes and behaviours, and through supportive discussions with colleagues, develop action plans to address problems at their health centres.

In the PCS module, health workers developed strategies for treating patients with dignity and respect. This included interpersonal skills for making patients feel welcomed at the health centre, building rapport, employing active listening skills, and providing good information. These sought to address the social gap between health workers and patients with the intention of making the health centre visit a more positive and accessible experience for patients encouraging them to attend regardless of their gender or socioeconomic position, for example. Health workers also developed strategies for managing their emotions at work and understanding how these might affect their interactions with patients and other health workers.

In the HCM module, health workers developed strategies for demonstrating professionalism and accountability in their role as managers. This included skills for managing health centre finances, supplies, and health information. These sought to address the challenges of managing a health centre in a hierarchal system where health workers have little power to negotiate for resources. Additionally, ensuring good management also sought to encourage patients to attend health centres knowing that they would be clean, organised and in good working order.

In the FCM module, health workers developed clinical skills to manage malaria and other febrile illnesses in line with national policies. To support implementation of these skills, the PRIME intervention ensured supply of mRDTs and antimalarials when stocks ran low. This sought to address health workers' and patients' aspirations for good clinical care which included appropriate testing and provision of treatment. Additionally, ensuring good stocks also sought to encourage patients to attend health centres knowing that drugs and supplies would be available.

4.4.2. Evaluation of the PRIME intervention

While principles of social justice were implicit in the way the PRIME intervention was designed and its final content, these principles are less visible in the evaluation of the intervention. The evaluation of the PRIME intervention was informed by MRC guidance for complex interventions research (Craig et al. 2008). The objectives of the evaluation were to

assess the impact of the intervention on a clinically defined primary outcome and a process evaluation to further our understanding about why the PRIME intervention was effective, or not (Chandler, DiLiberto, et al. 2013; Staedke et al. 2013). Some social justice concepts, such as fairness and access, were addressed in some of the PRIME evaluation activities such as the exit interviews with care givers which explored satisfaction with services at the health centre; indepth interviews with key stakeholders which explored the effects and factors shaping interpretation and integration of the intervention into practice; and focus group discussions with community members which explored their interpretation of the PRIME intervention. However, these activities were not designed from a social justice framework explicitly and these concepts, therefore, were not included as specific outcomes in the evaluation. As a result, these concepts did not feature in the analyses conducted in this thesis. Acknowledging certain concepts and in or out of scope reflects the limits that are encountered when applying a particular lens to the design of evaluation methods and tools. This speaks to the different ideas and interests that comprise contemporary conceptualisations of global health.

CHAPTER 5. Evaluation of primary outcomes

5.1. Introduction

The PRIME cRCT was designed to evaluate the impact of the PRIME intervention on population-level health outcomes. Yet, there is increasing recognition that the characteristics of complex interventions pose challenges for the design and analysis of RCTs and interpretation of their outcomes. Critiques to date have focused on the mismatch of logistical requirements of randomised designs to dynamic contexts and complex health systems (English, Schellenberg, and Todd 2011; Ranson et al. 2006), the challenges of establishing and maintaining a viable control arm (Hawe, Shiell, and Riley 2004; Okwaro et al. 2015), and the lack of responsiveness to adaptive system-wide changes (Hawe et al. 2009; Pawson and Tilley 1997). However, few studies have focused on the nature of the outcomes themselves used in randomised trials of complex health service interventions are needed (Datta and Petticrew 2013; O'Cathain et al. 2013). This gap in the literature is curious given the central importance that the choice of outcome measure, or trial endpoint, plays in establishing the intervention's effect. A recent example in *The Lancet* demonstrates the challenge and importance of selecting outcomes in response to the null results of a large randomised trial evaluating the impact of an intensive home-visiting intervention for teenage first-time mothers published in *The Lancet* (Robling et al. 2016), three separate commentaries highlighted that the choice of outcome measures was inappropriate considering the intervention goals, change processes and study participants, and was thought to severely limit the interpretation and transferability of evidence generated from the trial (Barlow et al. 2016; Barnes 2016; Olds 2015). The authors of the commentaries warned that basing policy decisions on the evidence from the trial would be unwise. While there is an increasing demand for evaluations to produce additional evidence to define how, where, and for whom an intervention works (Craig et al. 2008; Moore et al. 2015), it appears more work is required to understand how measures used define 'what works' are constructed and applied in evaluations, and with what effect.

Clinical or biomarker outcomes, such as the anaemia measurement used to evaluate the PRIME intervention, or also blood pressure, or weight, are favoured when assessing the impact of an intervention on individual-level health because they are considered to be valid, reliable, precise, and sensitive to change (Bowling 2009). This is contrasted with 'soft' endpoints such as participant-reported satisfaction or service uptake which may be more subject to human-influenced biases (Will and Moreira 2010). However, in complex health interventions research, other considerations may also need to be taken into account. Outcomes should be considered in terms of appropriateness, that is how sensitive outcomes are to the complexities of interventions intending to change multiple care processes and also specific to the health problem under investigation (Feldman 1997). To be useful, outcomes should be consistently defined (Clarke 2007) but also reflect the most efficient study design and use of resources (Julious and Senn 2010; Lilford et al. 2010). Outcomes should be valid producing results robust against the biases introduced by the context of different study settings (English, Schellenberg, et al. 2011). Finally, outcomes should be relevant to different stakeholders, such as service users, clinicians, and decisions makers (Glasgow, Brownson, and Kessler 2013; Loudon et al. 2015; Stewart et al. 2011; Uhm et al. 2012). Each of these considerations can differently influence the choice of outcomes used to evaluate the effect of an intervention. However, these considerations do not appear to be robustly discussed when reporting findings from trials of complex interventions. As a result, it is difficult to determine how the considerations and compromises made when selecting, defining, analysing and interpreting outcomes may themselves have affected the evidence being reported. This suggests that further empirical examples are needed to examine the importance of such considerations and how they might contribute to improving the interpretation of evidence from evaluations of complex interventions.

The methodological exercise presented in this chapter is a secondary analysis of the PRIME cRCT outcomes. An analysis of the implementation of the PRIME intervention indicates that the intervention was implemented as intended with high achievement of the learning objectives by most health workers at all health centres participating in the intervention (Chandler, Nayiga, et al. 2013). The published findings of the original cRCT analysis showed no effect of the intervention on the outcomes of prevalence of anaemia and parasitaemia in children under 5 years and 5-15 years of age (Staedke et al. 2016). The extended analysis presented in this chapter integrates additional data and outcomes with the aim of

examining the different influences on the outcomes used to evaluate the effect of the PRIME intervention and how these may have affected the interpretation of results. Considerations of appropriateness, usefulness, validity and meaningfulness are discussed in relation to the complexity of study context and PRIME intervention theory of change, as well as the design and analysis of the cRCT.

5.2. Methods

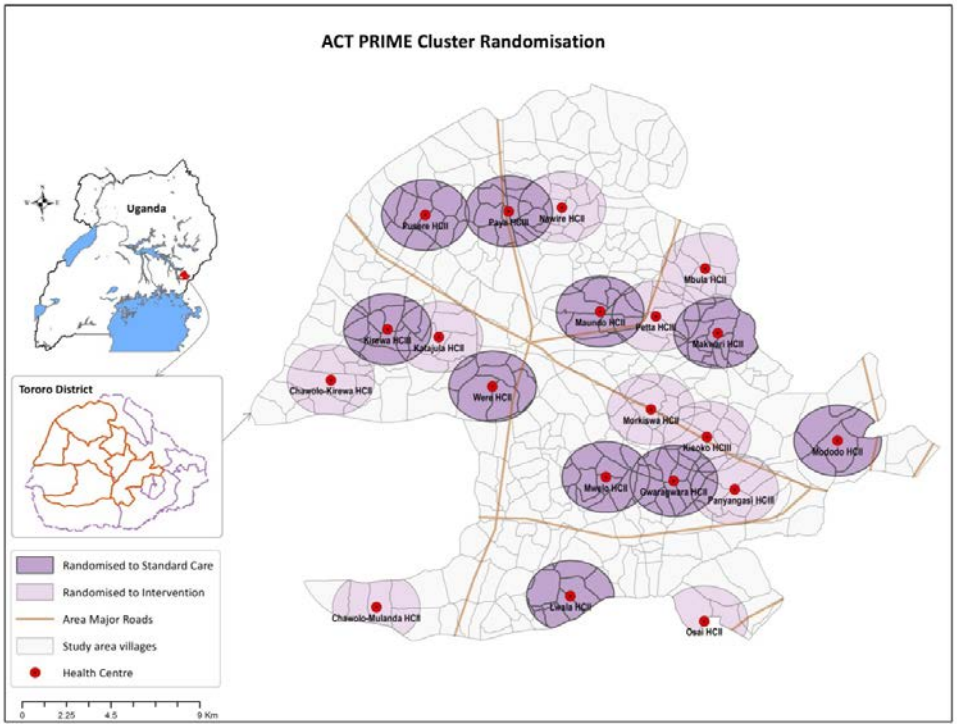
5.2.1. PRIME cRCT design

The following description of the design of the PRIME cRCT is also published in a manuscript co-authored with the study team (Staedke et al. 2016). Additional details have been added where necessary for this chapter.

5.2.1.1. Design

The PRIME study was a cluster-randomised trial. Twenty government-run health centres (level II and III) in seven sub-counties were included in the study, Figure 5.1. The cluster-randomised design was selected to test the hypothesis that implementing the PRIME intervention at health centres would improve malaria-related health outcomes in communities.

Figure 5.1: PRIME study area, health centres and clusters in Tororo, Uganda



5.2.1.2. Participants

From 2009 to 2010, all health centres and households in the study area were enumerated and mapped using hand-held global positioning satellite receivers (Garmin eTrex Legend H®). Of 22 health centres in the study area, two pairs of health centres had substantially overlapping catchment areas; one facility from each pair was randomly excluded. All other health centres were eligible for participation. Households located within 2 km of the selected health centres formed the clusters. If a household was within 2 km of more than one health centre, the household was assigned to the cluster of the closest health centre. Prior to the start of the study, study personnel met with health leaders, health centre in-charges, and community representatives to inform them about the study. An information sheet was used to describe the intervention, and verbal consent to participate in the study was obtained from the health centre in-charges.

5.2.1.3. Randomisation and masking

The 20 public health centres and their surrounding households formed the clusters, which served as the units of randomization and were assigned in a 1:1 ratio to intervention or control. Health centres were stratified by level (II or III), and restricted randomization was employed to ensure balance on geographical location and cluster size. The trial statistician generated the allocation sequence using random number generation in R (http://www.r-project.org/), and assigned health centres to trial arms. Study personnel enrolled health centres after randomization; allocation was not masked.

5.2.1.4. Cross-sectional community survey

Community surveys were conducted at baseline, with follow-up community surveys one and two years later, in children from randomly selected households in each cluster. Using the census database, a random sample of households with at least one child under 15 years of age was selected to generate a list for each cluster of households to be approached. Separate recruitment lists were generated for each community survey. Study personnel conducted door-to-door recruitment, which continued until the target sample size for participants was reached for each cluster. At each household, one child under-five and one aged 5-15 years were eligible for participation. If multiple children of appropriate age resided in the household, one child from each age category was randomly selected for recruitment. Selection criteria included: (1) appropriate age, (2) agreement of parent/guardian to provide written informed consent, (3) agreement of child aged eight

years or older to provide written assent, (4) ability to locate child. Participating children underwent a history and examination. Blood was collected by finger-prick for thick blood smear and haemoglobin. Primary caregivers were asked about bednet use and management of febrile children.

5.2.1.5. Laboratory procedures

Thick blood smears were stained with 2% Giemsa for 30 minutes and read by experienced laboratory technologists. For quality control, all slides were read by a second microscopist and a third reviewer settled any discrepant readings. Haemoglobin was measured from finger-prick blood samples using a portable spectrophotometer (HemoCue, Anglom, Sweden).

5.2.1.6. Outcomes

The primary outcome for the trial was prevalence of anaemia (haemoglobin < 11.0 g/dL) in children under-five, assessed in the final community survey. Secondary outcomes also assessed in the community survey were prevalence of anaemia in children aged 5-15, and prevalence of parasitaemia in under-fives and 5-15 year olds.

5.2.1.7. Sample size

Children were sampled from each cluster in proportion to the total cluster size, with a harmonic mean of 200 children per cluster for the two age strata. Assuming control arm anaemia prevalence in children under-five of 65%, and coefficient of variation k=0.2, this would give 80% power to detect an absolute difference in anaemia prevalence between trial arms of 17% (or more) at 5% significance level, allowing for the stratified, cluster-randomized design. A relatively low coefficient of variation k of 0.2 was assumed for the sample size calculations and was found to be reasonable, with observed k for the primary outcomes in the community survey of 0.12. Thus, the trial had good power to detect any potential effect of the intervention.

5.2.2. Statistical methods

This section describes the two analytical approaches conducted for this chapter. The first followed the original trial analysis outlined in Staedke et al (2016) which examined the effect of the intervention at the final community survey. This approach was repeated for this chapter and was also extended to include an evaluation of outcomes at the midline

community survey. The second approach to analysis was designed and implemented specifically for this chapter using a different modelling strategy to examine the effect of the intervention at the midline and final community surveys as well as trends within each community survey and across the study population. Both approaches are described below. All analyses were done using Stata version 14 (STATA Corp Lp, College Station, Tx).

The original trial analysis was conducted using cluster-level summaries which is recommended when there are a small number of clusters, i.e. 15 or fewer clusters per treatment arm (Hayes and Moulton 2009). However, in this approach, effects of covariates are removed in the cluster-level summaries; as a result, it is not possible to explore the effect of individual-level covariates (Eldridge and Kerry 2012). More importantly for the secondary analysis presented in this chapter, the cluster-level approach is not efficient and does not readily support exploratory analyses.

The exploratory analysis was conducted using individual level observations which allows greater flexibility to model and present cluster and individual level covariates alongside intervention effects. However, the individual level approach does not perform as reliably when there are a small number of clusters per arm. Hayes and Moulton (2009) suggest at least 15 clusters per arm are required, while more recent work suggests a minimum of 10 clusters per arm, which suggests that the number of clusters in the PRIME study is sufficient for the analysis (Eldridge and Kerry 2012). Given the potential for bias in the individual-level results, the analysis with cluster-level summaries was conducted to check that conclusions from the individual-level analysis were robust (Hayes and Moulton 2009).

5.2.2.1. Analysis with cluster-level summaries – original trial analytical approach

The effect of the intervention at the midline and final community surveys in children under 5 years and 5-15 years was analysed following the procedures for unadjusted and adjusted analysis described by Hayes and Moulton (2009). Analysis was conducted on an intention to treat basis, where data was analysed according to the cluster assigned at randomisation.

The prevalence of anaemia and parasitaemia was summarised for each cluster as well as a weighted average of the cluster prevalences, with the weights derived from the sample size for each cluster. Because most outcome distributions of the cluster level summaries were positively skewed, a logarithmic transformation was applied before analysis to normalize

cluster-specific prevalences. A crude risk ratio (RR) for the effect of the intervention was calculated directly from the cluster-based point estimates. A stratified t-test was used to compare the means of the cluster-specific proportions, where the within-stratum between-cluster variance was estimated as the residual mean square from a two-way analysis of variance of the log-prevalences on stratum and treatment arm, including an interaction term. A 95% confidence interval (CI) for the risk ratio, adjusting for stratum, was calculated from this variance using a t-statistic with 16 degrees of freedom (Hayes and Moulton 2009).

A two-stage analysis process was conducted to adjust for the cluster-specific prevalence of anaemia or parasitaemia collected at the baseline community survey, and *a priori* individual level factors including age, gender and use of ITNs. In the first stage, a logistic regression model, including terms for stratum and the covariates for adjustment, but excluding the intervention effect, were fitted to calculate cluster-specific predicted prevalences with ratio-residuals between the observed and predicted prevalence estimated. In the second stage, methods described above for estimating the 95% CI and performing a stratified t-test were conducted with the cluster-level prevalences replaced with the covariate-adjusted ratio-residuals (Hayes and Moulton 2009).

5.2.2.2. Analysis with individual level observations – secondary exploratory analytical approach

Several exploratory analyses using the individual level observations were conducted. First, anaemia and parasitaemia were modelled using multilevel regression. A mixed effects logistic regression, with cluster as the random effect, was conducted to estimate the effect of the intervention on prevalence of anaemia and parasitaemia in each age group at the midline community survey and repeated for the final community surveys. An initial crude odds ratio (OR) for the effect of the intervention was estimated. In an adjusted model, covariates of cluster-specific prevalence for anaemia or parasitaemia at baseline and individual level factors of age, gender, and use of ITNs where included (Hayes and Moulton 2009). Because the model contains a combination of binomial variation within clusters and normal variation between clusters, likelihood methods do not apply; therefore, the model was approximated by adaptive Gaussian quadrature (Eldridge and Kerry 2012).

Secondly, the analysis sought to explore the effect of dichotomising haemoglobin into anaemic or not anaemic at the cut-point of haemoglobin < 11g/dL. Drawing on the work of

Senn and Julious (Julious and Senn 2010; Senn 2003) dichotomising a continuous variable into a binary variable may present a challenge for analysis and interpretation of outcomes. A dichotomised outcome has been shown to result in a loss of information and therefore decrease in precision of estimates. When the mean of the continuous variable is close to the cut-point, a dichotomised variable is prone to demonstrate variation in the outcome where there is none, or to miss variation when it does exist. Considering these challenges of using a dichotomised outcome, the continuous outcome of haemoglobin was also modelled.

A mixed effects linear regression with cluster as the random effect was conducted to estimate the difference in mean haemoglobin in both age groups at the midline and final community surveys. An initial crude effect of the intervention was estimated. Next covariates of cluster-specific mean haemoglobin at baseline and individual level factors of age, gender, and use of ITNs where included (Hayes and Moulton 2009). The model was bootstrapped at the cluster level to approximate normality and to obtain bias-corrected confidence intervals. The model was fitted using maximum likelihood; however, since estimates from unrestricted maximum likelihood are known frequently to be biased downwards when there are a small number of clusters, restricted maximum likelihood was applied (Eldridge and Kerry 2012).

Next, the analysis also sought to take advantage of the availability of data from the repeated community surveys which provided greater power to detect an effect of the intervention and provided the opportunity to explore changes in the entire study population over time. Modelling all of the community surveys together and including a parameter for each time point distinguished between the intervention effect and any temporal trends which were estimated using data from the control clusters (Hayes and Moulton 2009). As such, a single model provided estimates of effects of the intervention at the midline and final community survey and changes in the entire study population over time. To achieve this, the fully adjusted mixed effect regression models for each of the outcomes described above were fitted with an interaction term representing the trial arm and the community survey time point. In this approach, the data were modelled to allow for any imbalances at baseline.

Next, the models were also constrained to remove the effect of any observed imbalances at baseline. Following the theory of randomisation, any differences observed at baseline between the trial arms were due to chance, rather than a true effect in the population. However, when imbalances are observed, they can be accounted for in the models by statistically constraining the baseline observations to zero in order to artificially achieve a balanced baseline. To constrain the baselines, the variable representing the trial arm was re-parameterised to create a variable that ignored treatment arm allocation at baseline in the regressions for the repeat community surveys.

Based on the results of these models, a final analysis sought to explore the temporal effects within each community survey and each age group by adding a covariate for month recruited to the survey to the models assessing mean haemoglobin and prevalence of parasitaemia described above.

5.3. Results

5.3.1. Recruitment and follow-up

The baseline cross-sectional community survey was conducted from December 2010 to June 2011. The midline community survey was conducted from January to May 2012. Of the 7,390 households visited in the midline survey, 2,024 were excluded for the reasons outlined in Figure 5.2. A total of 8,785 children were screened, and 8,777 were enrolled, including 4,391 children under 5 years and 4,386 aged 5–15 years. The final community survey was conducted from January to April 2013. Of the 7,170 households visited in the final survey, 2,037 were excluded for the reasons outlined in Figure 5.3. A total of 8,766 children were screened, and all were enrolled, including 4,383 children under 5 years and 4,383 aged 5–15 years.

Figure 5.2 Trial profile for midline community

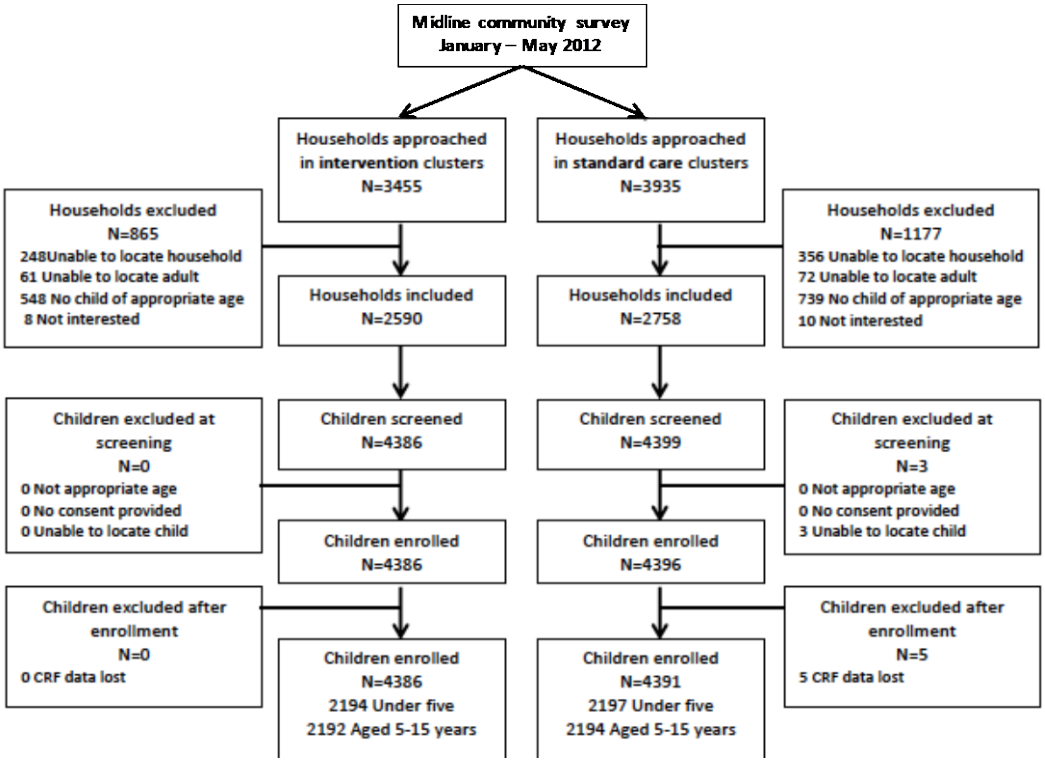
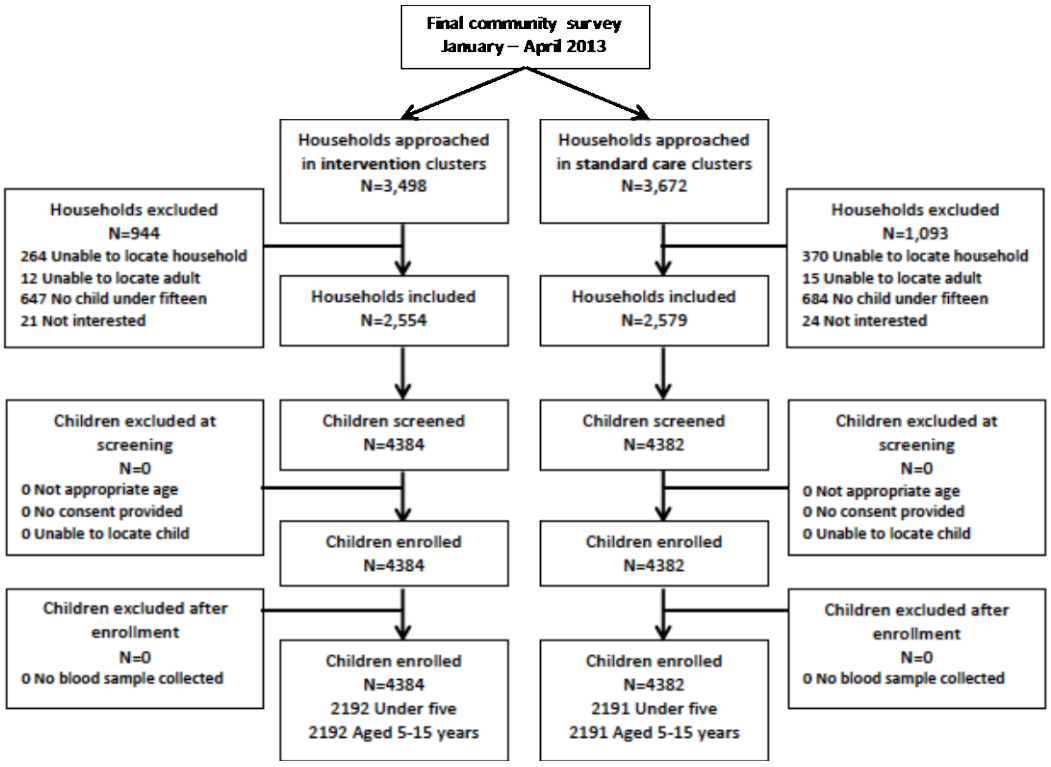


Figure 5.3 Trial profile for final community survey



5.3.2. Population characteristics at baseline

In the baseline survey, in children under 5 years, the mean age was 2.5 years (standard deviation (SD) 1.4 years), and 9 years (SD 2.9 years) in children 5-15 years. Mean haemoglobin was 10.7 (SD 1.5) in the children under five years where anaemia was more common (2,552 [58.2%]) than in those aged 5-15 years (1,016 [23.1%]) with a mean haemoglobin of 11.9 (SD 1.2). In contrast, children under-five years were less likely to have a parasite positive blood smear (2,515 [57.5%]), than older children (3,164 [72.0%]), Table 5.1.

5.3.3. Baseline imbalance

In the baseline community survey, in children 5-15 years, there was an imbalance in prevalence of anaemia between the two trial arms; prevalence was lower in the intervention arm, 20.7%, compared to the standard care arm, 25.5%, Table 5.1. There were no discrepancies with the randomization procedures, thus this imbalance was assumed as occurring by chance. Nevertheless, this imbalance was accounted for in the models using the two approaches described in 5.2.2 Statistical methods above.

Table 5.1: Baseline, midline and final community survey population characteristics

	Baseline				Midline				Final			
	< 5 years		5-15 years		< 5 years		5-15 years		< 5 years		5-15 years	
Characteristic	Standard care	Intervention	Standard care	Intervention	Standard care	Intervention	Standard care	Intervention	Standard care	Intervention	Standard care	Intervention
N	2192	2200	2207	2199	2197	2194	2194	2192	2191	2192	2191	2192
Age, years mean (SD)	2.49 (1.4)	2.57 (1.38)	9.0 (2.82)	9.0 (2.86)	2.62 (1.40)	2.72 (1.39)	9.07 (2.85)	8.62 (2.79)	2.64 (1.4)	2.66 (1.41)	8.4 (2.77)	8.1 (2.77)
Sex, female %	49.4%	48.1%	50.4%	49.2%	50.1%	49.1%	50.8%	51.7%	47.1%	50.1%	49.3%	49.9%
Slept under ITN previous night	67.7%	58.6%	44.2%	37.3%	69.2%	53.7%	48.7%	37.5%	56.3%	57.9%	44.6%	41.2%
Haemoglobin, mean (SD)	10.55 (1.61)	10.67 (1.54)	11.73 (1.23)	11.95 (1.31)	10.59 (1.5)	10.76 (1.46)	11.75 (1.34)	11.92 (1.22)	10.33 (1.58)	10.37 (1.51)	11.51 (1.35)	11.54 (1.33)
Anaemia (haemoglobin < 11g/dL)	59.9%	56.5%	25.5%	20.7%	58.0%	52.4%	26.4%	19.3%	64.2%	64.2%	31.4%	30.8%
Parasitaemia (blood slide positive)	52.6%	53.9%	69.0%	66.8%	43.8%	45.9%	53.6%	55.2%	49.7%	50.7%	64.6%	65.7%
Temperature (^{o}C), mean (SD)	37.13 (0.53)	37.12 (0.5)	37.19 (0.42)	37.17 (0.43)	37.25 (0.48)	37.17 (0.51)	37.27 (0.37)	37.21 (0.41)	37.27 (0.54)	37.31 (0.51)	37.3 (0.4)	37.31 (0.4)
Febrile (temperature ≥38^{o}C) and/or history of fever in last 48 hrs	60.9%	44.3%	32.0%	26.9%	70.7%	72.5%	56.4%	54.8%	81.7%	78.6%	62.8%	62.1%
Rapid diagnostic test positive	74.3%	82.1%	80.7%	85.7%	79.8%	82.0%	85.2%	88.9%	87.1%	86.9%	89.8%	87.1%

5.3.4. Exploring anaemia and haemoglobin

At baseline, in children under 5 years, the cluster-level prevalence of anaemia ranged from 34.4% with a mean haemoglobin of 11.42 g/dL (SD 1.36) to 69.8% with a mean haemoglobin of 10.25 g/dL (SD 1.51), Table 5.2. The majority of cluster-level mean haemoglobin measures were below the anaemia cut-point of 11g/dL and their standard deviations were spread across the cut-point, Figure 5.4. Thus, despite a difference in prevalence of anaemia of more than 30% between the highest and lowest clusters, the relatively narrow distribution of mean haemoglobin across clusters, and their proximity to the anaemia cut-point, indicated that clusters may have been more similar than their anaemia prevalences suggested.

Figure 5.4: Baseline mean haemoglobin by cluster, under 5 years

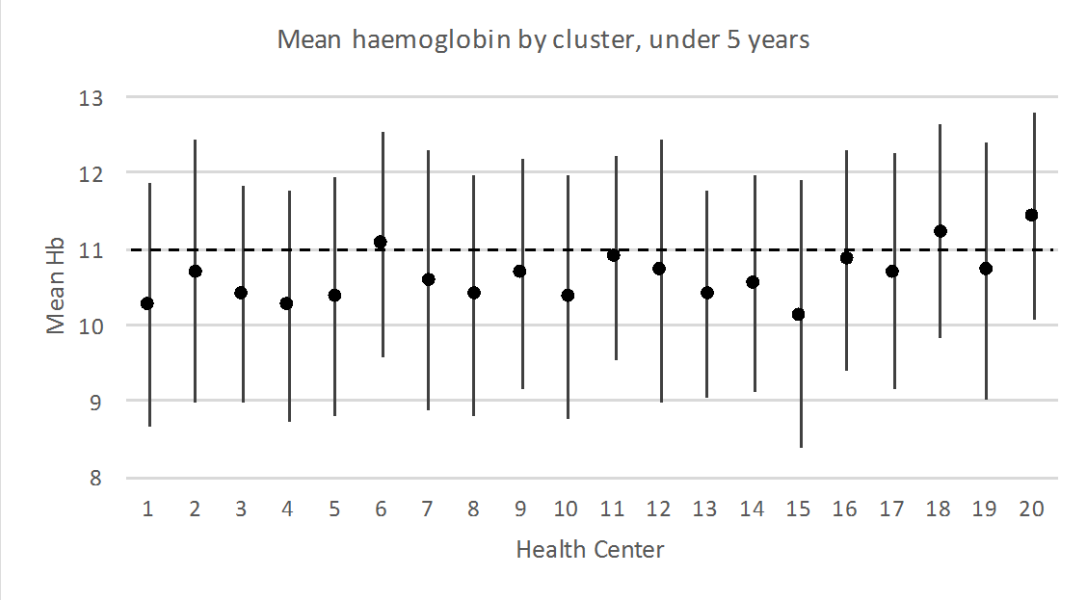
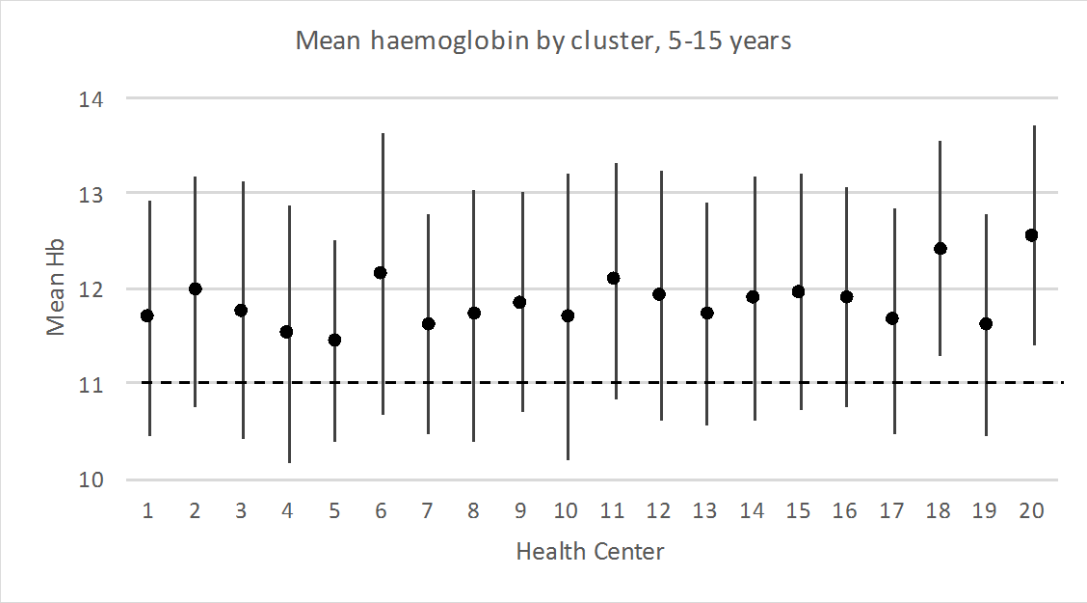


Table 5.2: Prevalence of anaemia and mean Hb by cluster, under 5 years

	Baseline				Midline					Final				
	Anaemia			Hb	Anaemia				Hb	Anaemia				Hb
HC	n	N	%	Mean (SD)	n	N	%	% diff from baseline	Mean (SD)	n	N	%	% diff from baseline	Mean (SD)
Standard care														
1	166	262	63.6%	10.25 (1.6)	142	261	54.4%	-9.2%	10.69 (1.43)	199	261	76.2%	12.6%	9.92 (1.39)
2	114	217	52.5%	10.7 (1.72)	145	217	66.8%	14.3%	10.37 (1.31)	159	216	73.6%	21.1%	9.95 (1.62)
4	150	215	69.8%	10.25 (1.52)	122	215	56.7%	-13.0%	10.48 (1.69)	136	215	63.3%	-6.5%	10.42 (1.63)
5	136	216	63.3%	10.37 (1.58)	109	217	50.2%	-13.0%	10.82 (1.52)	138	216	63.9%	0.6%	10.27 (1.66)
7	132	226	58.4%	10.58 (1.7)	107	231	46.3%	-12.1%	10.96 (1.51)	145	227	63.9%	5.5%	10.42 (1.49)
12	132	227	58.4%	10.7 (1.73)	139	228	61.0%	2.6%	10.63 (1.45)	146	228	64.0%	5.6%	10.37 (1.46)
14	166	261	63.6%	10.54 (1.42)	140	261	53.6%	-10.0%	10.81 (1.5)	150	261	57.5%	-6.1%	10.55 (1.56)
16	108	221	48.9%	10.86 (1.44)	171	221	77.4%	28.5%	9.8 (1.49)	117	221	52.9%	4.1%	10.75 (1.63)
17	56	107	52.3%	10.69 (1.55)	48	106	45.3%	-7.1%	11 (1.21)	56	106	52.8%	0.5%	10.72 (1.78)
19	149	240	62.6%	10.71 (1.68)	152	240	63.3%	0.7%	10.45 (1.43)	160	240	66.7%	4.1%	10.21 (1.5)
Overall			59.9%	10.55 (1.61)			58.0%		10.59 (1.5)			64.2%		10.33 (1.58)
Intervention														
20	32	93	34.4%	11.42 (1.36)	40	93	43.0%	8.6%	11.25 (1.35)	42	93	45.2%	10.8%	11.2 (1.65)
3	163	247	66.3%	10.39 (1.43)	147	247	59.5%	-6.7%	10.64 (1.68)	154	247	62.3%	-3.9%	10.43 (1.6)
18	102	255	40.0%	11.23 (1.4)	114	255	44.7%	4.7%	10.96 (1.36)	143	255	56.1%	16.1%	10.81 (1.47)
15	95	137	69.3%	10.14 (1.77)	60	136	44.1%	-25.2%	10.98 (1.31)	84	136	61.8%	-7.6%	10.45 (1.32)
13	143	218	65.6%	10.42 (1.36)	109	218	50.0%	-15.6%	10.73 (1.42)	148	218	67.9%	2.3%	10.09 (1.45)
8	169	260	65.0%	10.39 (1.59)	156	256	60.9%	-4.1%	10.35 (1.46)	170	255	66.7%	1.7%	10.22 (1.49)
9	184	324	57.0%	10.67 (1.53)	192	323	59.4%	2.5%	10.64 (1.57)	211	323	65.3%	8.4%	10.27 (1.47)
10	151	245	61.9%	10.38 (1.61)	109	245	44.5%	-17.4%	10.97 (1.25)	171	245	69.8%	7.9%	10.15 (1.5)
11	98	194	50.5%	10.89 (1.35)	98	192	51.0%	0.5%	10.9 (1.23)	125	192	65.1%	14.6%	10.39 (1.44)
6	105	227	46.3%	11.07 (1.48)	124	229	54.1%	7.9%	10.71 (1.56)	159	228	69.7%	23.5%	10.19 (1.52)
Overall			56.5%	10.67 (1.54)			52.4%		10.76 (1.46)			64.2%		10.37 (1.51)

The same narrow distribution of means applied to children 5-15 years where the cluster-level prevalence of anaemia ranged from 8.6% with a mean haemoglobin of 12.55 g/dL (SD 1.15) to 34.9% with a mean haemoglobin of 11.45 g/dL (SD 1.06), Table 3. However, the important difference is that all measures of mean haemoglobin were above the anaemia cut-point, Figure 5.5, and the prevalences of anaemia were relatively low, Table 5.3. This suggested a potential challenge with detecting any change in anaemia, as on average, children were already above the anaemia cut-point and there was relatively little scope for further improvements within and across clusters.

Figure 5.5: Baseline mean haemoglobin by cluster, 5-15 years



Taken together, these distributions suggest, in line with arguments by Senn (2013), that dichotomizing haemoglobin into anaemia may have provided an illusion of variation in prevalence of anaemia when in fact there was relatively little difference between levels of mean haemoglobin across the clusters. This suggests that additional information may be gained from assessing changes in mean haemoglobin alongside changes in prevalence of anaemia.

Table 5.3: Prevalence of anaemia and mean Hb by cluster, 5-15 years

	Baseline				Midline					Final				
	Anaemia			Hb	Anaemia				Hb	Anaemia				Hb
HC	n	N	%	Mean (SD)	n	N	%	% diff from baseline	Mean (SD)	n	N	%	% diff from baseline	Mean (SD)
Standard care														
1	77	266	28.9%	11.69 (1.24)	61	261	23.4%	-5.6%	11.84 (1.29)	143	261	54.8%	25.8%	10.76 (1.29)
2	37	216	17.1%	11.98 (1.22)	74	217	34.1%	17.0%	11.45 (1.25)	76	216	35.2%	18.1%	11.48 (1.46)
4	75	215	34.9%	11.52 (1.36)	67	215	31.2%	-3.7%	11.63 (1.41)	67	215	31.2%	-3.7%	11.67 (1.36)
5	60	217	27.6%	11.45 (1.06)	38	218	17.4%	-10.2%	11.93 (1.23)	59	216	27.3%	-0.3%	11.54 (1.2)
7	61	229	26.9%	11.62 (1.16)	28	227	12.3%	-14.5%	12.41 (1.39)	52	227	22.9%	-4.0%	11.71 (1.26)
12	59	235	25.1%	11.92 (1.3)	56	228	24.6%	-0.5%	11.81 (1.21)	59	228	25.9%	0.8%	11.67 (1.33)
14	58	261	22.3%	11.89 (1.29)	71	261	27.2%	4.9%	11.77 (1.29)	72	261	27.6%	5.3%	11.57 (1.29)
16	40	222	18.1%	11.9 (1.15)	85	221	38.5%	20.4%	11.28 (1.39)	57	221	25.8%	7.7%	11.79 (1.38)
17	30	106	28.3%	11.65 (1.19)	21	106	19.8%	-8.5%	11.93 (1.21)	26	106	24.5%	-3.8%	11.69 (1.12)
19	64	240	26.7%	11.61 (1.17)	78	240	32.5%	5.8%	11.49 (1.36)	77	240	32.1%	5.4%	11.43 (1.37)
Overall			25.5%	11.73 (1.23)			26.4%		11.75 (1.34)			31.4%		11.51 (1.35)
Intervention														
20	8	93	8.6%	12.55 (1.15)	10	93	10.8%	2.2%	12.38 (1.11)	24	93	25.8%	17.2%	11.8 (1.38)
3	22	255	8.6%	12.41 (1.12)	48	255	18.8%	10.2%	12.01 (1.12)	68	255	26.7%	18.0%	11.7 (1.35)
18	28	136	20.6%	11.96 (1.25)	24	136	17.6%	-2.9%	12.04 (1.3)	33	136	24.3%	3.7%	11.7 (1.25)
15	52	218	24.0%	11.73 (1.17)	51	218	23.4%	-0.6%	11.87 (1.17)	61	218	28.0%	4.0%	11.65 (1.29)
13	66	256	25.8%	11.72 (1.32)	38	255	14.9%	-10.9%	12.02 (1.16)	76	255	29.8%	4.0%	11.57 (1.29)
8	71	323	22.0%	11.85 (1.16)	54	323	16.7%	-5.3%	11.97 (1.21)	82	323	25.4%	3.3%	11.7 (1.34)
9	74	245	30.5%	11.71 (1.51)	57	245	23.3%	-7.2%	11.74 (1.43)	111	245	45.3%	14.9%	11.1 (1.36)
10	28	195	14.4%	12.08 (1.23)	30	192	15.6%	1.3%	11.88 (1.15)	72	192	37.5%	23.1%	11.43 (1.17)
11	44	230	19.1%	12.15 (1.48)	35	228	15.4%	-3.8%	12.1 (1.08)	86	228	37.7%	18.6%	11.26 (1.36)
6	62	248	25.1%	11.76 (1.36)	77	247	31.2%	6.1%	11.5 (1.27)	62	247	25.1%	0.0%	11.66 (1.34)
Overall			20.7%	11.95 (1.31)			19.3%		11.92 (1.22)			30.8%		11.54 (1.33)

5.3.5. Results at the cluster level

5.3.5.1. Intervention effect

In both age groups, in the final community survey, there were no statistically significant differences in the overall prevalence of anaemia or parasitaemia between the trial arms, after adjusting for differences in age, gender, ITN use, and either baseline cluster-level prevalence of anaemia or parasitaemia, Table 5.4, as reported in Staedke et al (2016). The exploratory analysis for this chapter revealed that in the midline community survey, in children 5-15 years, there was a positive effect of the intervention. There was a 29% decrease in the risk of anaemia in the intervention arm (RR 0.71; CI 0.55, 0.92; p=0.01) corresponding to an absolute decrease in prevalence of anaemia of 7.1%. There were no other significant effects of the intervention in the midline community survey, Table 5.4.

5.3.6. Results at the individual level

This section presents results of the exploratory analyses at the individual level for the outcomes of prevalence of anaemia and parasitaemia, and mean haemoglobin, including the effect of the intervention at each community survey and temporal changes within the community surveys and across the study population. The comparison of results of the analysis at the cluster level (Table 5.4) aligned with results of the analysis at the individual level (Table 5.5) indicating that the mixed effects multilevel modelling approach was robust and suitable for the exploratory analyses.

5.3.6.1. Intervention effect

Results of the intervention effect at the midline and final community surveys including the crude and adjusted analysis on prevalence of anaemia and parasitaemia are presented in Table 5.5, and effects for mean haemoglobin are presented in Table 5.6. Results from the fully adjusted models with all community survey time points and the constrained baseline are presented below.

In the midline community survey, in children 5-15 years, there was evidence that the odds of being anaemic were 0.41 times lower in the intervention arm compared to the standard care arm (CI 0.4, 0.87; p=0.01) corresponding to an absolute decrease in prevalence of anaemia of 7.1%, Table 5.5. There were no other effects of the intervention in either age group on prevalence of anaemia, Table 5.5; or parasitaemia, Table 5.5; or mean

haemoglobin, Table 5.6. These results correspond to the model allowing for any imbalances at baseline.

When examining the results in the intervention arm at the midline community survey in children under 5 years by cluster, half of the clusters showed a decrease in prevalence of anaemia suggesting a positive effect of the intervention; however, the other half showed an increase in prevalence of anaemia suggesting that these clusters may have cancelled out any potential effect of the intervention, Table 5.2. The same trend was observed in the intervention arm at the midline community survey in children 5-15 years, Table 5.3. However, a positive effect of the intervention was also observed, as described. In the more restrictive model with the constrained baseline, the odds of being anaemic were reduced, but still remained significant (OR 0.69; CI 0.56, 0.84; p=0.001), Table 5.7. By the final community survey, in both age groups, the majority of clusters in the intervention arm showed an increase in prevalence of anaemia suggesting that there was no sustained effect of any changes observed at the midline community survey.

Surprisingly, although there was an observed effect of the intervention on prevalence of anaemia in the midline community survey in children 5-15 years, there was no effect in the same age group on mean haemoglobin, Table 5.9. This contradiction points to the challenge of dichotomizing continuous outcomes which may have produced an illusion of a variation in the outcome when there was none. Because mean haemoglobin was clustered around the anaemia cut-point, small changes in haemoglobin could result in a change in anaemia classification (moving from being anaemic to being non-anaemic) causing change in prevalence of anaemia despite a relatively small and insignificant difference in mean haemoglobin of 0.17 g/dL between trial arms.

Thus there are three possible explanation of the observed effect of the intervention at the midline community survey in children 5-15 years. First, the observed effect may be interpreted as a genuine effect of the intervention. Second, the observed effect may have been due to the baseline imbalance in the prevalence of anaemia despite deliberately exploring the imbalance using the two different statistical approaches. Third, the observed effect may have been due to the illusion of variation as a result of using the dichotomised variable.

Table 5.4: Effect of the PRIME intervention on anaemia and parasitaemia – Analysis at the cluster level, crude and adjusted

	Midline community survey						Final community survey					
	n/N	Prevalence	Crude risk ratio (95% BC CI*)	P	Adjusted risk ratio (95% BC CI*)	P	n/N	Prevalence	Crude risk ratio (95% BC CI*)	P	Adjusted risk ratio (95% BC CI*)	P
Anaemia												
Under 5 years												
Control	1275/2197	58.0%	1		1		1406/2191	64.2%	1		1	
Intervention	1149/2194	52.4%	0.89 (0.77, 1.02)	0.11	0.89 (0.78, 1.03)	0.1	1407/2192	64.2%	0.99 (0.87, 1.13)	0.89	1.01 (0.91, 1.13)	0.82
5-15 years												
Control	579/2194	26.4%	1		1		688/2191	31.4%	1		1	
Intervention	424/2192	19.3%	0.72 (0.56, 0.93)	0.02	0.71 (0.55, 0.92)	0.01	675/2192	30.8%	1.00 (0.80, 1.26)	0.97	1.03 (0.84, 1.27)	0.75
Parasitaemia												
Under 5 years												
Control	963/2197	43.8%	1		1		1088/2191	49.7%	1		1	
Intervention	1007/2194	45.9%	1.02 (0.93, 1.12)	0.67	0.98 (0.90, 1.06)	0.52	1112/2192	50.7%	1.01 (0.88, 1.16)	0.90	1.01 (0.90, 1.13)	0.86
5-15 years												
Control	1175/2194	53.6%	1		1		1415/2191	64.6%	1		1	
Intervention	1210/2192	55.2%	1.03 (0.90, 1.18)	0.56	1.01 (0.89, 1.14)	0.87	1441/2192	65.7%	1.02 (0.92, 1.13)	0.75	1.02 (0.93, 1.11)	0.70

- BC CI = bias corrected confidence interval

Table 5.5: Effect of the PRIME intervention on anaemia and parasitaemia – Analysis at the individual level, crude and adjusted

	Midline community survey						Final community survey					
	n/N	Prevalence	Crude odds ratio (95% CI)	P	Adjusted odds ratio (95% CI)	P	n/N	Prevalence	Crude odds ratio (95% CI)	P	Adjusted odds ratio (95% CI)	P
Anaemia												
Under 5 years												
Control	1275/2197	58.0%	1		1		1406/2191	64.2%	1		1	
Intervention	1149/2194	52.4%	0.77 (0.57, 1.03)	0.08	0.76 (0.56, 1.03)	0.07	1407/2192	64.2%	0.98 (0.76, 1.28)	0.91	1.05 (0.81, 1.35)	0.72
5-15 years												
Control	579/2194	26.4%					688/2191	31.4%				
Intervention	424/2192	19.3%	0.66 (0.47, 0.93)	0.02	0.59 (0.4, 0.87)	0.01	675/2192	30.8%	1 (0.73, 1.37)	0.98	1.03 (0.74, 1.43)	0.86
Parasitaemia												
Under 5 years												
Control	963/2197	43.8%	1		1		1088/2191	49.7%	1		1	
Intervention	1007/2194	45.9%	1.09 (0.96, 1.23)	0.21	0.98 (0.86, 1.12)	0.74	1112/2192	50.7%	1.03 (0.83, 1.27)	0.8	0.99 (0.8, 1.23)	0.93
5-15 years												
Control	1175/2194	53.6%					1415/2191	64.6%				
Intervention	1210/2192	55.2%	1.06 (0.82, 1.36)	0.66	1.01 (0.79, 1.29)	0.92	1441/2192	65.7%	1.06 (0.83, 1.35)	0.65	1.13 (0.95, 1.35)	0.16

Table 5.6: Effect of the PRIME intervention on haemoglobin – Analysis at the individual level, crude and adjusted

	Midline community survey results					Final community survey				
	Mean (SD)	Crude regression coefficient (95% CI)	P	Adjusted regression coefficient (95% CI)	P	Mean (SD)	Crude regression coefficient (95% CI)	P	Adjusted regression coefficient (95% CI)	P
Haemoglobin										
Under 5 years										
Control	10.59 (1.5)	1		1		11.75 (1.34)	1		1	
Intervention	10.76 (1.46)	0.21 (0.02, 0.43)	0.13	0.19 (-0.11, 0.48)	0.17	11.92 (1.22)	0.06 (-0.15, 0.23)	0.68	-0.02 (-0.17, 0.2)	0.85
5-15 years										
Control	10.33 (1.58)	1		1		11.51 (1.35)	1		1	
Intervention	10.37 (1.51)	0.19 (-0.03, 0.36)	0.12	0.22 (0.02, 0.41)	0.12	11.54 (1.33)	0.03 (-0.14, 0.21)	0.83	-0.01 (-0.18, 0.16)	0.96

Table 5.7: Effect of the PRIME intervention on anaemia – Analysis at the individual level, adjusted with constrained baseline

			Under 5 years				5-15 years			
			n/N	Prevalence	Adjusted odds ratio (95% CI)	P	n/N	Prevalence	Adjusted odds ratio (95% CI)	P
Survey population compared to baseline		Baseline	2551/4392	58.2%	1		1016/4406	23.1%	1	
		Midline	2424/4391	55.2%	0.98 (0.87, 1.09)	0.68	1003/4386	22.9%	1.13 (0.98, 1.31)	0.1
		Final	2813/4383	64.2%	1.26 (1.12, 1.42)	0.003	1363/4383	31.1%	1.25 (1.08, 1.45)	0.000
Intervention effect	Midline	Control	1275/2197	58.0%	1		579/2194	26.4%	1	
		Intervention	1149/2194	52.4%	0.87 (0.75, 1.01)	0.06	424/2192	19.3%	0.69 (0.56, 0.84)	0.001
	Final	Control	1406/2191	64.2%	1		688/2191	31.4%	1	
		Intervention	1407/2192	64.2%	1.1 (0.95, 1.28)	0.20	675/2192	30.8%	1.17 (0.96, 1.42)	0.11

Table 5.8: Effect of the PRIME intervention on parasitaemia – Analysis at the individual level, adjusted with constrained baseline

			Under 5 years				5-15 years			
			n/N	Prevalence	Adjusted odds ratio (95% CI)	P	n/N	Prevalence	Adjusted odds ratio (95% CI)	P
Survey population compared to baseline		Baseline	2340/4392	53.3%	1		2991/4406	67.9%	1	
		Midline	1970/4391	44.9%	0.67 (0.6, 0.74)	0.000	2385/4386	54.4%	0.53 (0.47, 0.59)	0.000
		Final	2200/4383	50.2%	0.83 (0.74, 0.92)	0.001	2856/4383	65.2%	0.79 (0.71, 0.89)	0.000
Intervention effect	Midline	Control	963/2197	43.8%	1		1175/2194	53.6%	1	
		Intervention	1007/2194	45.9%	0.98 (0.86, 1.12)	0.82	1210/2192	55.2%	1.1 (0.96, 1.26)	0.19
	Final	Control	1088/2191	49.7%	1		1415/2191	64.6%	1	
		Intervention	1112/2192	50.7%	1.01 (0.88, 1.15)	0.94	1441/2192	65.7%	1.12 (0.97, 1.29)	0.13

Table 5.9: Effect of the PRIME intervention on haemoglobin – Analysis at the individual level, adjusted with constrained baseline

			Under 5 years			5-15 years		
			Mean (SD)	Adjusted regression coefficient (95% BC CI*)	P	Mean (SD)	Adjusted regression coefficient (95% BC CI*)	P
Survey population compared to baseline		Baseline	10.61 (1.57)	1		11.84 (1.28)	1	
		Midline	10.68 (1.48)	-0.01 (-0.36, 0.23)	0.88	11.83 (1.29)	-0.01 (-0.26, 0.19)	0.72
		Final	10.35 (1.54)	-0.25 (-0.45, -0.11)	0.003	11.52 (1.34)	-0.30 (-0.43, -0.01)	0.000
Intervention effect	Midline	Control	10.59 (1.5)	1		11.75 (1.34)	1	
		Intervention	10.76 (1.46)	0.09 (-0.28, 0.39)	0.14	11.92 (1.22)	0.06 (-0.21, 0.30)	0.24
	Final	Control	10.33 (1.58)	1		11.51 (1.35)	1	
		Intervention	10.37 (1.51)	-0.06 (-0.33, 0.18)	0.32	11.54 (1.33)	-0.12 (-0.38, 0.20)	0.01

- BC CI = bias corrected confidence interval

5.3.6.2. Temporal effects

Modelling the community survey time points together provided the opportunity to explore changes in the study population over time. There were no changes in prevalence of anaemia at the midline community survey compared to baseline, Table 5.7, Figure 5.6. However, by the final community survey, across both trial arms, there was 1.26 times the odds of having anaemia among children under 5 years (CI 1.12, 1.42; p=0.003) corresponding to an absolute increase of 6% from the baseline community survey, Table 5.7, Figure 5.6. Likewise, there was 1.25 times the odds of being anaemic among children 5-15 years (CI 1.08, 1.45; p<0.001) corresponding to an absolute increase of 8% from the baseline community survey – suggesting a worsened health status, Table 5.7, Figure 5.6. Contrary to expectations (Kamya et al. 2015), parasitaemia displayed the opposite trend to anaemia. By the midline community survey, across both trial arms, there was an 8.4% absolute decrease (OR 0.67; CI 0.60, 0.74; p<0.001) in prevalence of parasitaemia among children under 5 years, and a 13.5% absolute decrease (OR 0.53; CI 0.47, 0.59; p<0.001) among children 5-15 years, compared to prevalences at the baseline community survey – suggesting an improved health status, Table 5.8, Figure 5.7. In the final community survey, differences in prevalence of parasitaemia were less pronounced, but still significant, with a 3.1% absolute decrease (OR 0.83; CI 0.74, 0.92; p=0.001) in children under 5 years, and 2.7% absolute decrease (OR 0.79; CI 0.71, 0.89; p<0.001) in children 5-15 years, compared to the baseline community survey, Table 5.8, Figure 5.7.

Figure 5.6 Observed prevalence of anaemia, by trial arm

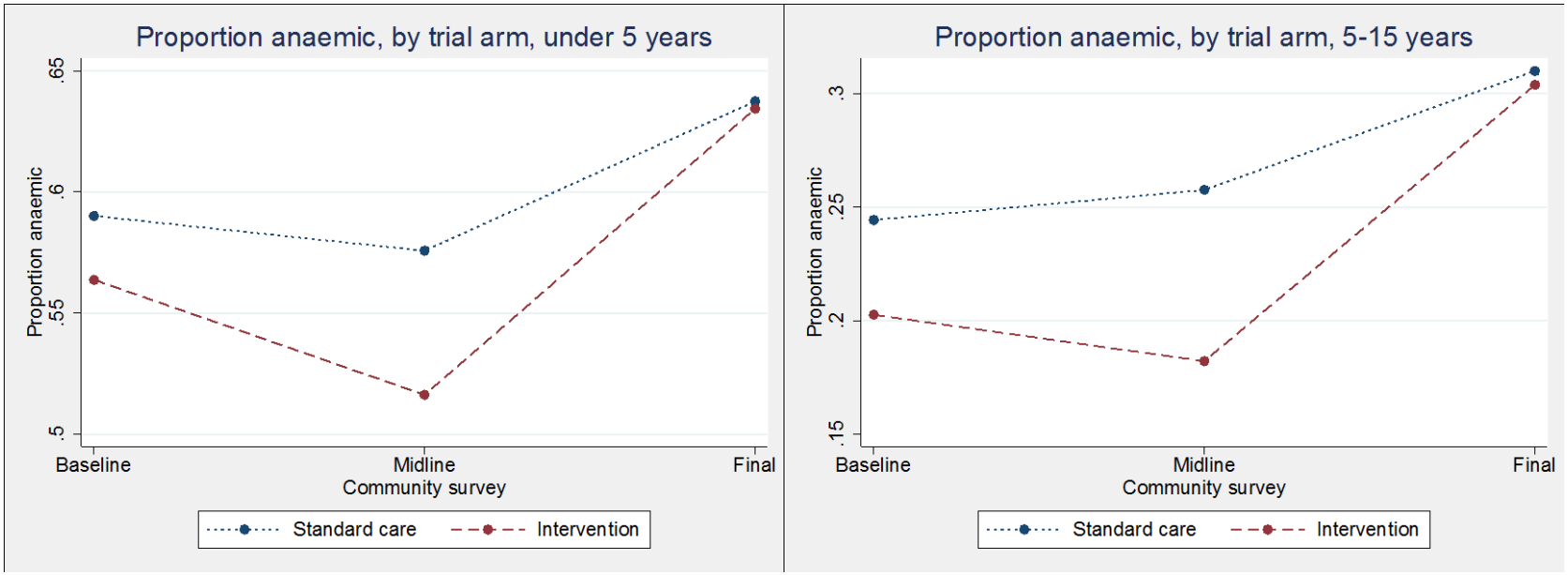


Figure 5.7 Observed prevalence of parasitaemia, by trial arm

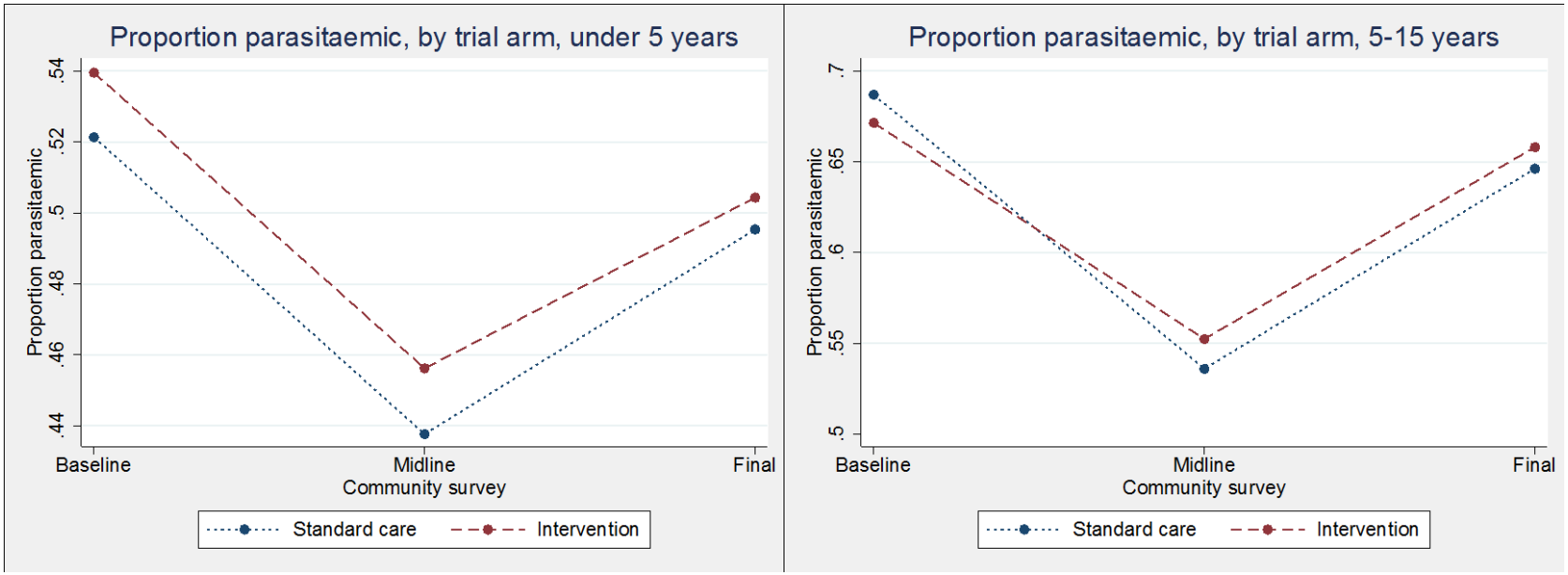
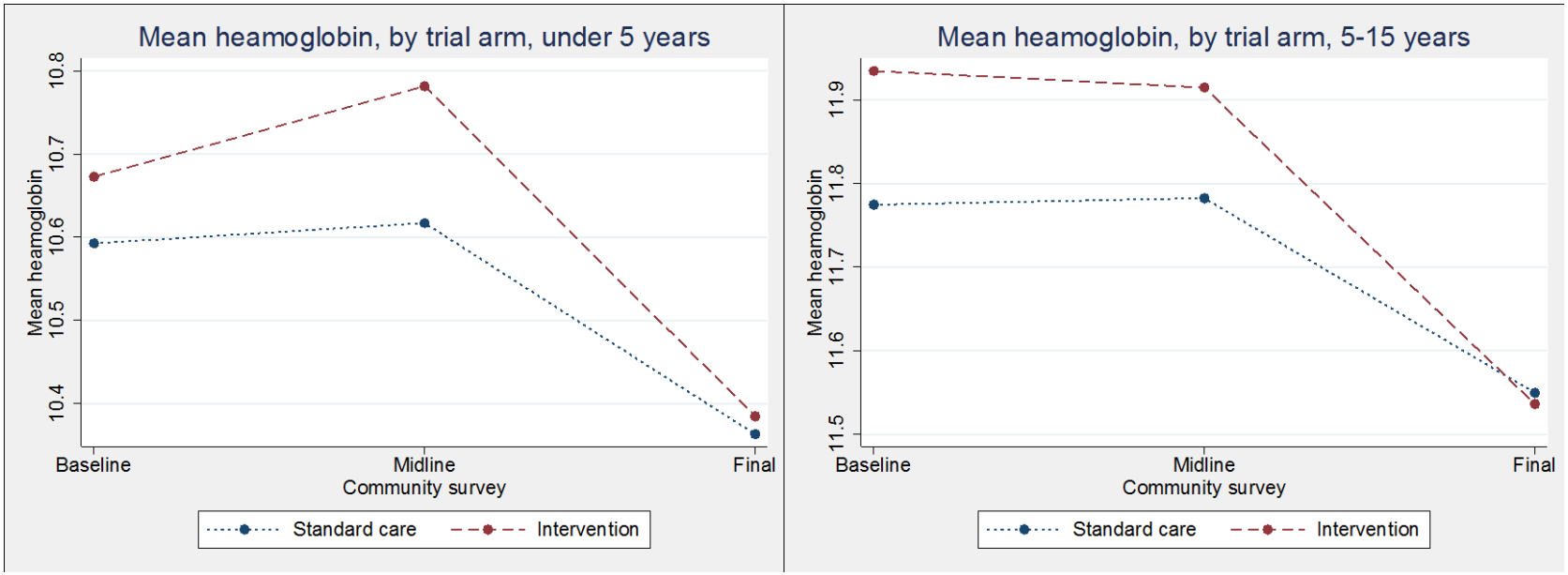


Figure 5.8 Observed mean haemoglobin, by trial arm



To explore these trends further, changes over time within each community survey were assessed (baseline survey December – June; midline community survey January – May; final community survey January – April). In Tororo, due to malaria seasonality, parasitaemia is expected to be highest in the months of November to January and April to June when malaria infection is highest (Jagannathan et al. 2012). Monthly prevalences of parasitaemia in the baseline community survey, in children under 5 years, corresponded with these seasonal trends in both age groups, Figure 5.9, Figure 5.10. Prevalence of parasitaemia was significantly lower in February, March and April, compared to prevalences in December, January, May and June when prevalence of parasitaemia is expected to be higher; however, these seasonal trends were not observed in the midline and final community surveys, Table 5.10. These two community surveys were conducted over shorter periods of time and mostly between the two malaria seasonal peaks. It is possible to consider that had the community survey run for the same length of time as the baseline community survey, 6.5 months, more seasonal variation in the outcome may have been observed. Furthermore, it is possible to hypothesise that the observed decreases in prevalence of parasitaemia compared to baseline levels may have been due to a shorter community survey length when data was collected during the lower transmission season.

Trends in mean haemoglobin were also explored. In the baseline community survey, in children under 5 years, mean haemoglobin was significantly higher in the months of February to June compared to levels measured in December, the first month of recruitment. In the midline and final survey, mean haemoglobin was also higher only in the months of March and April, compared to December, Table 5.11. Without a longer community survey time, it is difficult to ascertain the effect of any within-survey seasonal trends on changes in population-wide mean haemoglobin between community surveys. Furthermore, despite the relatively large observed changes in prevalence of anaemia in each community survey and age group compared to baseline, the changes in mean haemoglobin were relatively small with an adjusted mean decrease in haemoglobin of 0.25 g/dL (CI -0.45, -0.11; p=0.003) in children under 5 years, and an adjusted mean decrease of 0.30 g/dL (CI -0.43, -0.01; p<0.001) in children 5-15 years in the final community survey compared to the baseline community survey, Table 5.9, Figure 5.8.

Table 5.10: Prevalence of parasitaemia by recruitment month

			Under 5 years				5-15 years			
			n/N	Prevalence	Adjusted odds ratio (95% CI)	P	n/N	Prevalence	Adjusted odds ratio (95% CI)	P
Baseline		Baseline	1154/2192	52.6%	--		1522/2207	69.0%	--	
		Intervention	1186/2200	53.9%	--		1468/2199	66.8%	--	
	Recruitment month	Dec 10 (reference)	71/118	60.2%	1		94/127	74.0%	1	
		Jan 11	268/433	61.9%	0.97 (0.63, 1.51)	0.89	379/514	73.7%	1.07 (0.68, 1.68)	0.79
		Feb 11	178/342	52.0%	0.64 (0.41, 1.00)	0.05	278/406	68.5%	0.82 (0.52, 1.29)	0.39
		Mar 11	550/1122	49.0%	0.54 (0.36, 0.81)	0	786/1240	63.4%	0.68 (0.44, 1.03)	0.07
		Apr 11	623/1213	51.4%	0.57 (0.38, 0.86)	0.01	721/1074	67.1%	0.83 (0.54, 1.26)	0.38
		May 11	537/947	56.7%	0.68 (0.45, 1.03)	0.07	642/922	69.6%	0.81 (0.52, 1.24)	0.33
		June 11	113/217	52.1%	0.53 (0.33, 0.86)	0.01	91/123	74.0%	0.92 (0.52, 1.64)	0.77
Midline		Control	963/2197	43.8%	1		1175/2194	53.6%	1	
		Intervention	1007/2194	45.9%	0.98 (0.86, 1.12)	0.75	1210/2192	55.2%	1.01 (0.78, 1.32)	0.94
	Recruitment month	Jan 12 (reference)	128/285	44.9%	1		161/331	48.6%	1	
		Feb 12	611/1363	44.8%	1 (0.77, 1.3)	0.99	849/1574	53.9%	1.25 (0.98, 1.59)	0.07
		Mar 12	717/1630	44.0%	0.95 (0.73, 1.23)	0.67	783/1455	53.8%	1.22 (0.91, 1.62)	0.18
		Apr 12	496/1075	46.1%	1 (0.76, 1.31)	0.99	573/990	57.9%	1.57 (1.14, 2.17)	0.01
		May 12	18/38	47.4%	1.03 (0.51, 2.1)	0.93	19/36	52.8%	1.31 (0.62, 2.80)	0.48
Final		Control	1088/2191	49.7%	1		1415/2191	64.6%	1	
		Intervention	1112/2192	50.7%	0.99 (0.81, 1.21)	0.93	1441/2192	65.7%	1.13 (0.95, 1.34)	0.15
	Recruitment month	Jan 13 (reference)	351/679	51.7%	1		485/766	63.3%	1	
		Feb 13	857/1625	52.7%	1.05 (0.87, 1.26)	0.61	1170/1735	67.4%	1.15 (0.96, 1.38)	0.12
		Mar 13	733/1527	48.0%	0.89 (0.73, 1.1)	0.29	895/1398	64.0%	0.92 (0.75, 1.13)	0.42
		Apr 13	259/552	46.9%	0.91 (0.69, 1.21)	0.52	306/484	63.2%	1.01 (0.77, 1.32)	0.93

Table 5.11: Mean haemoglobin by recruitment month

			Under 5 years				5-15 years			
			N	Mean (SD)	Adjusted regression coefficient (95% BC CI)	P	N	Mean (SD)	Adjusted regression coefficient (95% BC CI)	P
Baseline		Baseline			--				--	
		Intervention			--				--	
	Recruitment month	Dec 10 (reference)	118	9.93 (1.67)	1		127	11.57 (1.28)	1	
		Jan 11	433	10.08 (1.72)	0 (-0.39, 0.33)	0.99	514	11.54 (1.41)	-0.17 (-0.49, 0.10)	0.27
		Feb 11	342	10.59 (1.46)	0.57 (0.32, 0.88)	0.001	406	11.85 (1.29)	0.15 (-0.24, 0.44)	0.39
		Mar 11	1122	10.7 (1.5)	0.62 (0.19, 1.03)	0.000	1240	11.84 (1.25)	0.1 (-0.28, 0.44)	0.6
		Apr 11	1213	10.71 (1.55)	0.56 (0.18, 0.97)	0.000	1074	11.94 (1.24)	0.05 (-0.30, 0.40)	0.8
		May 11	947	10.68 (1.55)	0.48 (0.14, 0.87)	0.002	922	11.92 (1.21)	0.02 (-0.37, 0.33)	0.91
		June 11	217	10.81 (1.69)	0.5 (0.04, 0.99)	0.005	123	11.85 (1.45)	0.08 (-0.40, 0.56)	0.75
Midline		Control	2197	10.59 (1.5)	1		2194	11.75 (1.34)	1	
		Intervention	2194	10.76 (1.46)	0.21 (-0.07, 0.47)	0.14	2192	11.92 (1.22)	0.28 (0.01, 0.53)	0.04
	Recruitment month	Jan 12 (reference)	285	10.44 (1.53)	1		331	11.82 (1.22)	1	
		Feb 12	1363	10.61 (1.54)	0.18 (-0.2, 0.44)	0.23	1574	11.85 (1.27)	0.01 (-0.24, 0.31)	0.92
		Mar 12	1630	10.66 (1.44)	0.33 (-0.25, 0.64)	0.13	1455	11.69 (1.31)	0.24 (-0.25, 0.65)	0.01
		Apr 12	1075	10.84 (1.46)	0.52 (-0.01, 0.85)	0.02	990	12.01 (1.27)	0.6 (-0.01, 0.96)	0.004
		May 12	38	10.87 (1.39)	0.17 (0.45, 0.72)	0.6	36	12.12 (1.21)	0.37 (-0.16, 0.89)	0.11
Final		Control	2191	10.33 (1.58)	1		2191	11.51 (1.35)	1	
		Intervention	2192	10.37 (1.51)	-0.01 (-0.21, 0.18)	0.9	2192	11.54 (1.33)	0.02 (-0.19, 0.21)	0.88
	Recruitment month	Jan 13 (reference)	679	10.18 (1.6)	1		766	11.56 (1.46)	1	
		Feb 13	1625	10.24 (1.53)	0.04 (-0.13, 0.29)	0.53	1735	11.43 (1.33)	-0.04 (-0.17, 0.11)	0.43
		Mar 13	1527	10.42 (1.46)	0.21 (-0.02, 0.48)	0.01	1398	11.56 (1.26)	-0.01 (-0.27, 0.33)	1.0
		Apr 13	552	10.68 (1.66)	0.33 (0.06, 0.77)	0.003	484	11.73 (1.39)	0.16 (-0.15, 0.49)	0.12

Figure 5.9: Prevalence of parasitaemia, by trial arm and recruitment month, under 5 years

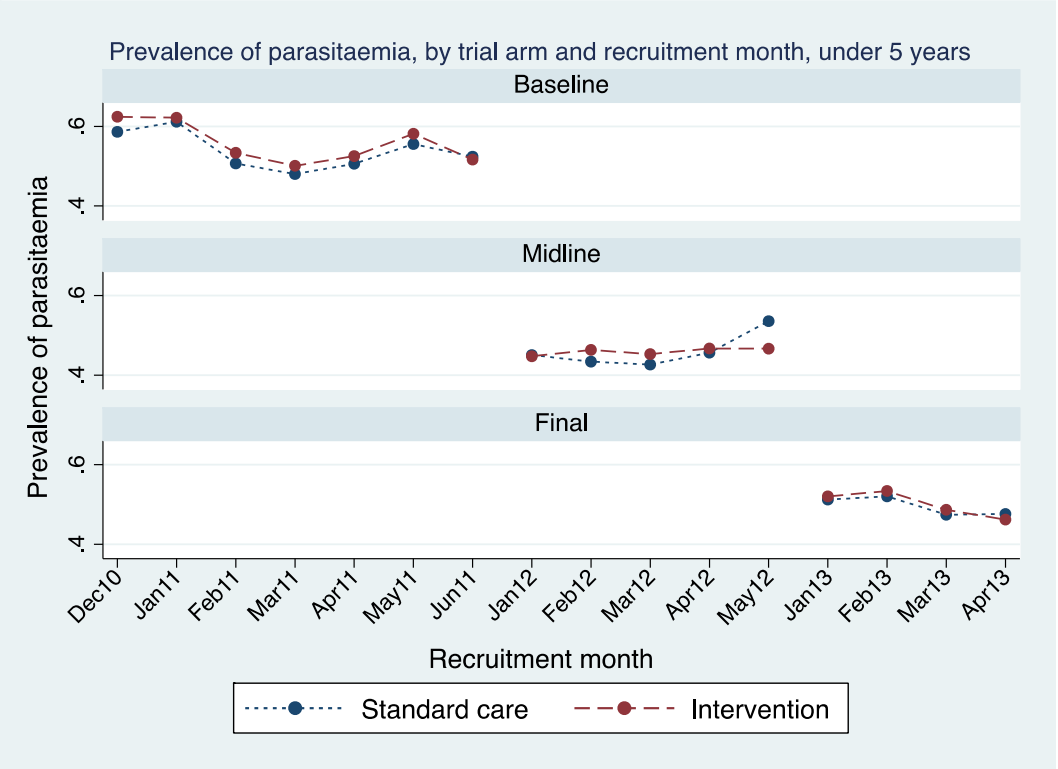
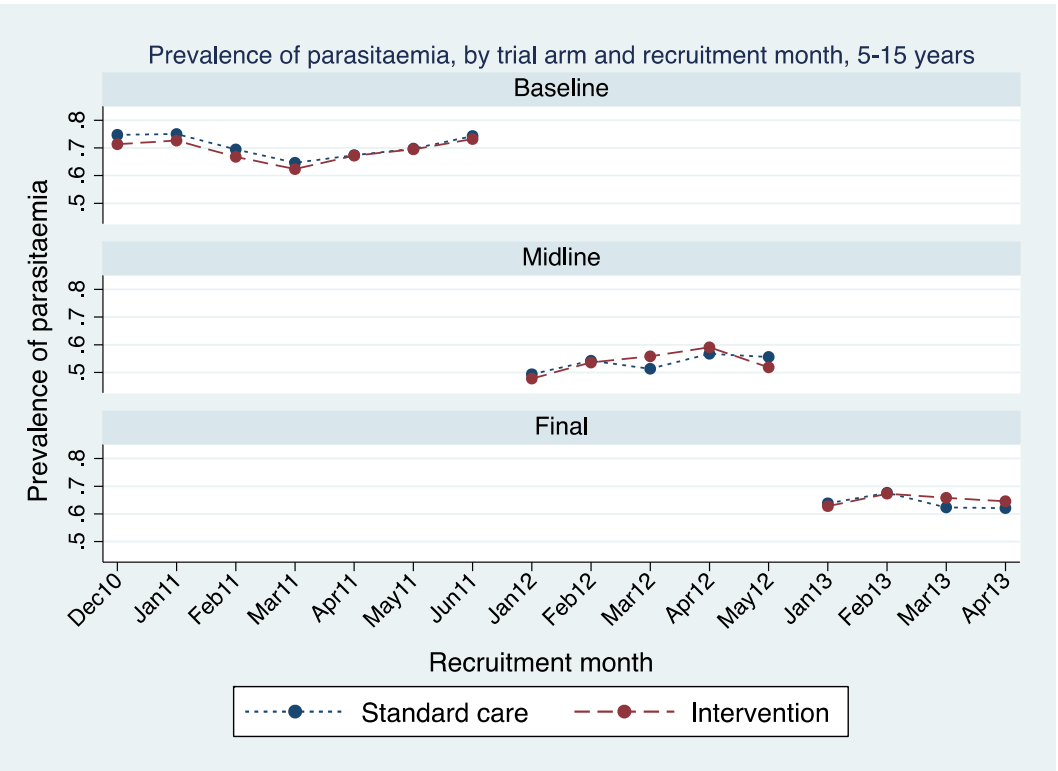


Figure 5.10: Prevalence of parasitaemia, by trial arm and recruitment month, 5-15 years



5.4. Discussion

The published results of the PRIME cRCT indicate that the PRIME intervention did not improve malaria-related health outcomes of children in the study area. By the final community survey, in both age groups, there were no statistically significant differences in prevalence of anaemia or parasitaemia between the two trial arms, as has been reported by Staedke et al (2016). The exploratory analyses conducted for this chapter sought to unpick the different influences on the PRIME cRCT outcomes. This exercise revealed that varied and contrasting results can be produced using different outcome measures. In the midline community survey, in children 5-15 years, there was evidence of a positive effect of the intervention on prevalence of anaemia. However, this effect may have been due to issues that arise when dichotomising the haemoglobin variable into a binary anaemia variable, or due to an imbalance in prevalence of anaemia at baseline, rather than a true effect of the intervention. In addition, in each community survey, the monthly prevalence of parasitaemia appeared to follow expected seasonal trends, however, it was not possible to draw similar parallels for the prevalence of anaemia. Moreover, changes in the study population over time demonstrated an overall decrease in the prevalence of parasitaemia, yet a contrasting increase in prevalence of anaemia and decrease in mean haemoglobin compared to baseline. Although exploratory, the results are statistically valid drawing on robust, but unconventional, approaches to analysing trial outcomes.

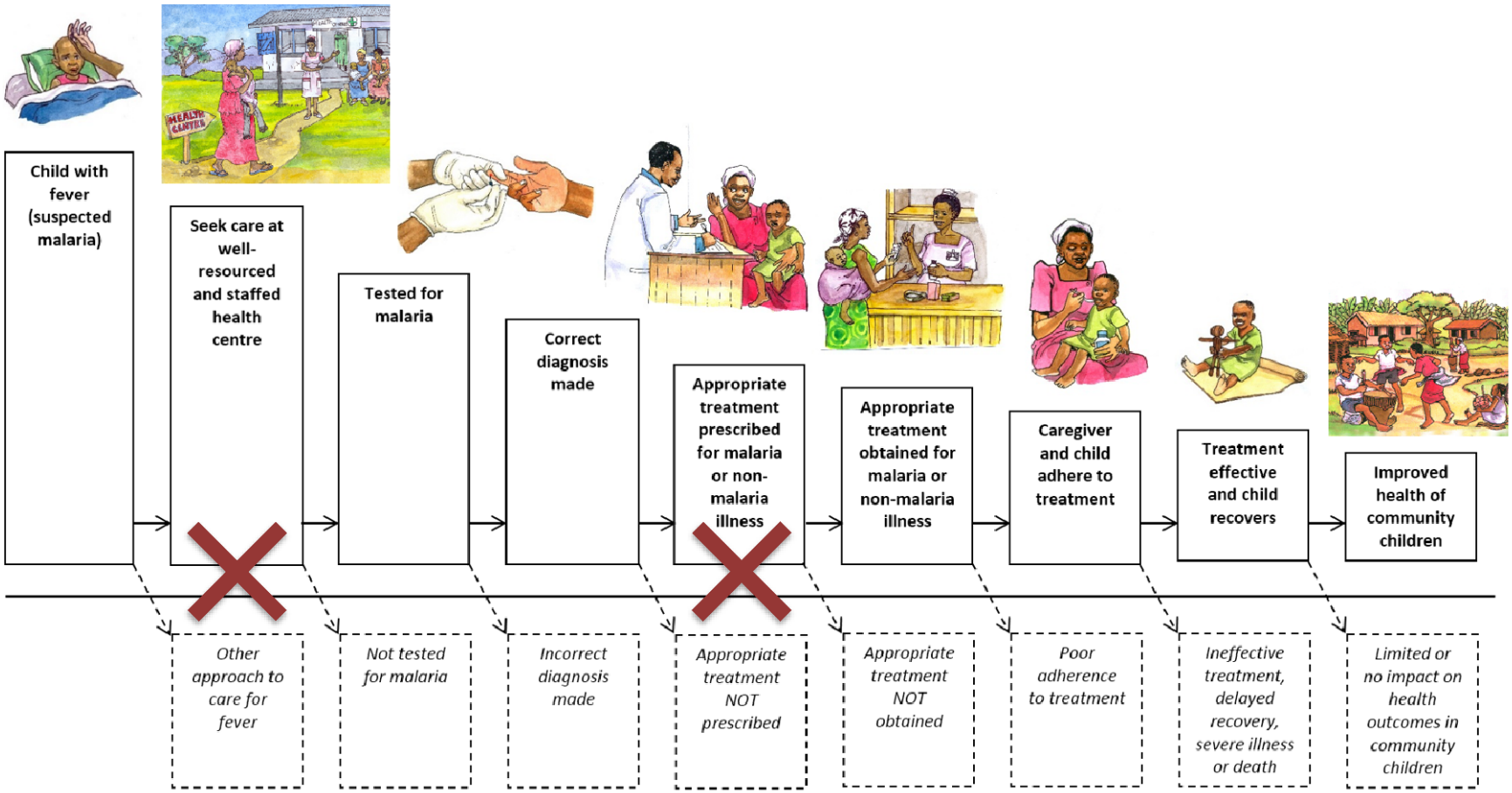
Based on these results of the primary outcomes, the PRIME intervention would be described as 'ineffective', despite some positive impacts of the intervention on health worker communication with patients (Nayiga et al. 2014), community perceptions of care (Okwaro et al. 2015), and appropriate treatment of malaria (C. Chandler, personal communication, 15 Jan 2015). The original analysis of the PRIME cRCT led to the interpretation that the intervention's lack of effect was due to breakdowns in intervention's pathway of effect including at the point of changing treatment seeking and attendance practices at health centres, and at the point of improving fever case management by health workers – see Figure 5.11 (Staedke et al. 2016). While a range of practical, social and political realities haven been be identified as limiting the intervention's effect (ibid), a recent critique suggests that this lack of effect could have been anticipated given the relatively narrow intervention package compared with scale of the problem (Hawe 2015b), and therefore the issue is with the intervention design rather than the context. This argument can also be made of other complex intervention studies that have cited similar

reasons for interventions not being 'strong enough' to overcome challenges and achieve their intended impacts – see for example, the study of community health interventions in Guinea-Bissau which suggested that the intervention was insufficient to overcome contextual challenges and, therefore, failed to reduce under 5 mortality (Boone et al. 2016). A further interpretation, beyond focusing on the failure of the intervention or its suitability to the context, is to foreground the suitability of the outcomes chosen to define the success of the intervention. This discussion examines the appropriateness, usefulness, validity and meaningfulness of the outcome measures used to define success of the intervention in relation to the complexity of the study context, the intervention's theory of change, and the cRCT study design and analysis.

5.4.1. Influence of study area context on appropriateness of outcomes

Anaemia is an accepted proxy indicator to measure the impact of malaria control programmes on health outcomes of children. For example, anaemia is used as a key indicator of malaria-related morbidity in children in the *Roll Back Malaria* national Malaria Indicator Surveys conducted in malaria endemic countries (http://www.malariasurveys.org/). Although the aetiology of anaemia is multifactorial, in Tororo, where malaria transmission is high, malaria is considered an important contributor to anaemia in children under 5 (Uganda Bureau of Statistics (UBOS) and ICF Macro 2010). Thus anaemia was chosen as a suitable outcome to assess the effect of the PRIME intervention (Staedke et al. 2013). However, over the past decade, several epidemiological studies have demonstrated a dynamic landscape of malaria-related health outcomes in Tororo. A study of children from birth to 10 years conducted in 2011-2013 demonstrated a decrease in annual infective mosquito bites per person, an increase in malaria incidence, no change in malaria parasite prevalence, and a decrease in prevalence of anaemia (Kamya et al. 2015). Another study conducted in 2012 found that prevalence of anaemia did not correspond well with level of malaria transmission intensity measured by annual number of infective mosquito bites (Yeka et al. 2015). Furthermore, at the national level in Uganda, it appears that despite a persistent high burden of malaria, the prevalence of anaemia in children under 5 years has declined since 2000 (Yeka et al. 2015).

Figure 5.11 Breakdowns in the cascade of care



Reproduced and adapted with permission from (Staedke et al. 2016)

A number of other issues have also been linked to anaemia in this area, including red blood cell disorders, intestinal helminths and malnutrition, as well as climate variability (Yeka et al. 2015). Research in similar settings has noted the interaction of malnutrition, sanitation and hygiene practices, and malaria on anaemia outcomes (Coffey 2014; Druilhe 2006; Ehrhardt et al. 2006; Nussenblatt and Semba 2002). Therefore, in this setting, anaemia may not be as closely related to malaria as has been understood. This suggests that the anaemia outcome may have lacked the specificity necessary for identifying the impact of the intervention on malaria case management and related health centre activities.

5.4.2. Influence of the PRIME intervention theory of change on appropriateness of outcomes

The PRIME intervention theory of change hypothesised that an intervention addressing the barriers to providing good quality care for malaria and febrile illnesses will improve appropriate malaria case management and patient satisfaction, leading to repeat attendance at health centres, and ultimately, improved health outcomes in community children (DiLiberto et al. 2015). This pathway of effect suggests that anaemia and parasitaemia as end-point measures of success are very distal to the everyday realities the intervention was intending to influence at health centres and in communities. Indeed, a number of factors may have influenced the pathway from intervention implementation to community outcomes. Throughout implementation of the PRIME trial, a number of potential influencing factors in the community and at health centres were observed. These included immunization, deworming and bednet distribution campaigns, health promotion and malaria control activities, and health worker training programmes conducted by research groups and non-governmental organizations operating in the study area – these are outlined in Table 5.12. Similar types of contextual influences on study outcomes have been noted in other trials conducted in low resources settings (English, Schellenberg, et al. 2011). Capturing this context revealed a complex 'biocultural dynamic' wherein social practices, population characteristics and physiological responses interact with each other in emergent and contingent ways (Worthman and Kohrt 2005). This suggests that a number of factors and complex biocultural pathways, in addition to the intervention, were interacting with each other and likely influencing the trial outcomes. As a result, the outcomes may not have been responsive to, or appropriate for, capturing the relatively specific changes to quality of care for malaria initiated by the intervention.

Table 5.12 Example of contextual factors in the study area, 2010-2012

Health centre resources	• Stock-outs of antibiotics and analgesics • Excessive supply of contraceptives • New supply of mRDTs by government • Safe delivery kits provided by World Vision • ACTs donated by Finnish donor • Health workers accused of stealing drugs, new labels on government supplied drugs to prevent stealing
Health centre infrastructure	• No pit latrines, running water or electricity at health centres • Repair of health centre pit latrines by World Vision • Road to the health centre has been affected by heavy rains, health centre inaccessible • Health worker given a bicycle to facilitate transportation
Health centre activities	• Staff members absent leaving health centre short staffed • Health workers reprimanded for arriving late and leaving early • Supervision visit by Health Sub-District Officer • Received posters on hand washing campaign
Health worker activities	• Training on treatment of neglected tropical diseases by the Health Sub-District • Training on management of malnutrition among children by World Vision • Training on health centre management by Plan international • Training on use of mRDTs by Joint Uganda Malaria Program
Community health interventions	• Mosquito net distribution and education to pregnant mothers and children under 5 years • Community Led Total Sanitation meetings to discuss health issues with community leaders and health workers by PLAN International • Health workers participate in mass treatment of Vitamin A and Zinc • ChildPlus immunization campaign at schools • Distribution of kits including water guard, nets, condoms and water vessels for HIV + patients • Home visits, HIV testing and referral for services by THETA and CDC • Measles & polio immunisation, mass deworming, Vitamin A in schools by UNICEF, WHO & Ministry of Health • Door to door mass polio immunisation by WHO • Suspected outbreak of measles, increased attendance t health centres and hospitals • Heavy rains contaminated water sources increasing diarrhoeal diseases • Increased cases of malnutrition among children due to famine
Community education and information	• Radio talk shows on malaria prevention and treatment • Community dialogue meetings on malaria prevention • Campaign delivered through radio talk shows and spot messages on STD & HIV prevention • Press briefing at local radio stations to inform the public about availability of cheap ACTs • Campaign about immunisation for polio & measles through radio & VHTs home visits by MoH

5.4.3. Influence of statistical and clinical definitions on usefulness of outcomes

Interpreting the effect of the intervention at the midline community survey in children 5-15 years raises questions about the statistical usefulness of the dichotomised anaemia outcome. There appeared to be two compounding methodological issues contributing to the observed effect at the midline community survey. The dichotomised anaemia variable created a statistical difference between clusters and trial arms at baseline when there was actually little difference in mean Hb between clusters and trial arms. This imbalance in turn created the illusion of a difference in prevalence of anaemia in children 5-15 years in the midline community survey. As a statistical function, there was no statistical usefulness to dichotomising the outcome; furthermore, this type of outcome may have led to false interpretation of the impact of the effect of the intervention. In addition to these interpretation challenges, Senn and Julious (2010) have demonstrated a loss of precision when using a dichotomised outcome resulting in the need for a larger sample size to obtain the same precision that would have been obtained from a continuous outcome. For cRCTs specifically, it has been demonstrated that an increase in sample size of more than 60% is required to make the same inferences from a dichotomised variable compared to a continuous variable (Caille, Leyrat, and Giraudeau 2012). This suggests that the PRIME trial could have had a smaller sample size using haemoglobin as an outcome which would have had important influences on the logistics and resources needed for the trial. Thus, the decision to use a dichotomised outcome, such as anaemia, influences both the interpretation of outcomes and trial design challenging the statistical usefulness of using such outcomes.

On the other hand, using the outcome of anaemia may support clinical interpretation of outcomes. Anaemia as a health state is associated with specific morbidities. As such, changes in mean haemoglobin may not have clinical relevance, or impacts on health, unless associated with changes in anaemia status. Regardless of the statistical relevance of using a continuous haemoglobin outcome, the clinical interpretability of the dichotomised anaemia outcome may to be more relevant for public health. Furthermore, the evidence generated from the PRIME cRCT was intended for an audience including public health researchers, funders and policy makers. Because anaemia is widely used as an indicator for malaria and other infectious diseases, as well as a marker of overall health, the categorisation and analysis of anaemia as an outcome representing malaria morbidity, may be more useful and produce more transferable evidence for a wider audience.

5.4.4. Influence of design externalities on validity of outcomes

Randomly assigning clusters to trial arms minimises selection bias and ensures internal validity by eliminating the chance that any other factors could be causally attributed to the observed outcomes (Hayes and Moulton 2009). While this is a lauded feature of the cRCT, the scale of operations necessary to collect the required sample size for achieving this aim can impact on the logistical processes of data collection. The PRIME cRCT required a large sample size to achieve an appreciable improvement in the prevalence of anaemia. Recruiting this sample size was time intensive and required a significant investment of financial, human and material resources over three years. With each community survey, the trial team became more efficient at conducting field work. They also welcomed the opportunity to improve efficiency and accuracy of data collection, and to conserve limited resources by switching to electronic tablets for the midline and final community surveys. However, it appears that the efficiency gained in terms of reducing the time taken for each community survey may have introduced a bias in the evidence produced.

In the baseline community survey, data were collected over 6.5 months covering two malaria seasons. Examining data within this community survey demonstrated that parasitaemia followed the expected seasonal trends. The midline and final community surveys were conducted between the peaks of the two malaria seasons making it difficult to determine if there were any seasonal trends in parasitaemia outcomes in the community surveys. This raises the question as to whether there would have been any impact of the intervention if the community surveys had covered the seasonal peaks when people were more likely to seek care for malaria and therefore would have been exposed to the intervention including treatment with ACTs. Furthermore, the prevalence of parasitaemia and anaemia displayed contradicting trends in the midline and final community surveys. It is not expected that parasitaemia and anaemia will align because of the time lag between parasite infection and onset of anaemia and other malaria-related symptoms. However, the difference in community survey lengths makes it challenging to unpick whether these opposite trends are spurious and to determine any potential explanations. Despite the PRIME trial being carefully designed to accommodate malaria seasonality, the externality of improved efficiency of data collection may have undermined these efforts. However, these challenges are raised here are not to suggest fault – the cRCT was well executed and the decision to switch to tablets was carefully considered against the competing challenges of time and resources required to complete the trial. Rather, the aim is to draw attention to

the vulnerability of well-designed trials and objective outcomes to a range of unintended sources of bias. The choice of using a cRCT to detect individual-level effects may itself have introduced bias as a result of the large sample size and length of time required to recruit the community surveys. The priority of minimising contamination and selection bias through use of a cluster randomised design may have inadvertently introduced other unintended sources of bias influencing the validity of the outcomes produced.

5.4.5. Influence of evidence use on meaningfulness of outcomes

The cRCT was powered to detect an absolute difference in prevalence of anaemia of 17% or more, after accounting for intracluster correlation and variable clusters sizes. This is arguably a large effect size to achieve in practice, especially considering the range of challenges described in this chapter. However, the decision to use this outcome measure depends on its meaningfulness, or relevance, to different stakeholders. Like other projects funded by government or philanthropic organisations, the outcomes and effect size for the PRIME intervention were determined at the research proposal and funding stage. At this stage, the intervention was not yet designed but the proposal had to be compelling to the funders who were interested in interventions that made health gains. The anaemia outcome was therefore a relevant choice for demonstrating health gains of a malaria-related study. This need for an outcome measure that was acceptable to the funders may have overshadowed other considerations such as the size and structure of the study population and what effect size might be possible to achieve in practice. A similar scenario was found in the Building Blocks trial described in the introduction to this chapter. The authors pointed out that the choice of outcome measure was selected by the Department of Health suggesting, implicitly, that the selection of other more attainable and meaningful outcomes may not have been politically acceptable (Barlow et al. 2016). The priorities of funders can influence the choice of outcome measure and potential effect size, which in turn can affect the functioning of the trial and evidence produced. Yet the impact of these priorities on the conclusions drawn about the effectiveness of the intervention is often unrecognised and therefore unexamined.

Yet, it is also necessary to examine the choice of outcome from the perspective of research users. Considering that the PRIME intervention was designed to be scaled up sustainably by the Ugandan Ministry of Health within the existing health system structure, it is not evident that a 17% change in prevalence of anaemia represented a compelling and sizable impact

when considered alongside the investments into health services and the resources that would be required to sustain the PRIME intervention. Research on evidence use has demonstrated that evidence produced by large externally-funded effectiveness studies is not as valued by in-country government staff and policy makers who prefer applied, operational research that will produce findings quickly for more immediate application to health services and policies (Burchett et al. 2015). This suggests that the evidence produced from the anaemia outcome may not have been meaningful to the research users and therefore, may not have been a useful measure to define the effectiveness of the intervention.

5.4.6. Summary and some considerations

This chapter produced a detailed, exploratory analysis of the PRIME cRCT outcomes and revealed a number of considerations and decisions that can influence the interpretation of the intervention as effective, or not. The interpretations of the findings suggests that the anaemia outcome may not have been as specific to malaria as originally thought and it may not have been responsive to the intervention given the complex biocultural context into which it was implemented. Likewise, its use for interpreting changes in health status was affected by different statistical and clinical definitions, and its measurement required a large, clustered sample size where the logistics necessary may have introduced bias. Finally, its relevance was influenced by the priorities of different stakeholders. These considerations call into question whether the choice of anaemia outcome was the most appropriate way of defining whether the intervention worked, or not.

This chapter has been useful in demonstrating that outcomes are shaped by a number of theoretical, statistical and logistical processes and everyday realities of evaluating health service interventions that intended to change individual-level health outcomes. From this perspective, even clinical outcomes that are considered to be objective measurements are shown to be influenced by the subjective, human processes inherent in defining, collecting, analysing and interpreting outcomes. The advantage of this position is the opportunity for researchers to engage with outcome-based research as an active process that can be interrogated and made stronger, more useful, and more informative for interpreting the complexities of intervention effects and transferability of these findings.

There is now an increasing variety of approaches for engaging with the selection and application of outcomes. For example, the formalised 'Theory of Change' (ToC) method employs a 'ceiling of accountability' for selecting outcomes which describes the level at which the intervention can no longer specifically influence or accept responsibility for the observed effects (De Silva et al. 2014). The PRECIS-2 tool assists trialists in considering how outcomes identified are pragmatic and meaningful to different intervention stakeholders (Loudon et al. 2015). The MRC guidance for developing and evaluating complex interventions suggests considering how clusters of outcomes, rather than a single primary outcome, may be more informative (Medical Research Council 2008), and work has been undertaken to develop composite outcomes capturing multiple services delivered in interventions (Watt et al. 2015). Finally, modelling of the intervention, outcome measures and anticipated effect sizes prior to undertaking a full-scale evaluation can be used to determine weak points in the causal logic and re-deign studies with more achievable outcomes (Eldridge et al. 2005; Hardeman et al. 2005).

This chapter suggests that the selection and application of outcomes appears more complex than is currently acknowledged in health interventions research. Ideally, the justification for the choice of outcomes would be reported in trial protocol papers so that their suitability can be assessed before trials begin. This chapter suggests that there are also a number of influences that arise while trials are in progress which should be reported in reports of trial findings. These influences are not currently required in trial reports according to the CONSORT statement which describes what information about trials should be reported to assess the validity of the evidence being reported (Campbell et al. 2012; Schulz, Altman, and Moher 2010). This chapter, however, argues that engagement with the considerations and compromises influencing how and why outcomes were chosen, applied and interpreted provides additional contextualised information to promote more informed assessments of why interventions are judged as effective, or not. Increased reflexive and transparent reporting of this information will contribute rich empirical examples helping to navigate the challenges and opportunities of using individual-level health outcomes to evaluate complex health service interventions.

5.5. Limitations

The focus of this chapter has been on exploring the potential limitations and biases affecting the interpretation of the results of the PRIME cRCT. Areas that might usually be commented on as limitations have been discussed at length such as baseline imbalance, contextual influences and changes in participant recruitment protocols. There is one additional limitation, however, concerning the interpretation of the findings that can be drawn from the extended analysis presented in this chapter. The extended analysis was developed for this thesis and was therefore was not included in the cRCT analytical plan. Analyses that are conducted post-hoc can be subject to data dredging, or attempting to identify a significant effect through manipulation of measures or analytical modes (Ioannidis 2005). Any post-hoc analysis of trial data must therefore be interpreted with caution. The findings of this analysis do not contradict the findings of the main cRCT analysis, but rather provide further potential explanations for the observed lack of effect of the intervention on the cRCT outcomes. Nevertheless, the findings presented in this chapter should be considered as illustrative, and readers should consider the findings of the published trial paper the formal interpretation of the cRCT findings (Staedke et al. 2016).

Another limitation is that the analysis was not disaggregated by sex. In recent years, there has been an increasing emphasis on improving the analysis and reporting of clinical trial data that has been disaggregated by sex in order to explore the potential differential effects of public health interventions and understand how to reduce health inequities between different groups of people in society (Heidari et al. 2016; Schiebinger et al. 2016). However, when such analyses are not included in the study protocol and sample size calculation, they can lack sufficient power or precision to estimate intervention effects and may produce misleading results (Hayes and Moulton 2009). An analysis disaggregated by sex was not included in the PRIME trial protocol and therefore, was not conducted for the analysis presented in this chapter. The analysis would have lacked sufficient power and precision to make any statistically valid interpretations of the results. It is acknowledged that this may present a potential limitation of this analysis to provide a greater understanding of whether the PRIME intervention may have differentially improved health outcomes for males or females.

CHAPTER 6. Assessment of causal mechanisms

6.1. Introduction

While the RCT is considered the most rigorous experimental design to assess intervention effect, it is criticised for perpetuating the 'black box' effect – it does not reveal the processes through which interventions may have worked (Anderson 2008). As a result, researchers are increasingly interested in isolating casual mechanisms that produce intervention effects in order to understand not only if interventions work, but how (Craig et al. 2008). Evaluation of mechanisms can test an intervention's hypothesised causal pathways identifying pathways which are most effective in producing the intended outcomes or those which may have had unexpected effects (Bonell et al. 2015). With information on which mechanisms are effective, it is believed that interventions can be tailored to strengthen these pathways and thereby amplify intervention effects. Recent guidance from the MRC on evaluating complex interventions suggests that RCTs should be complemented by process evaluations to provide evidence of the causal mechanisms that produce intervention effects (Moore et al. 2015). Process evaluations often include the development of an intervention theory of change – a description of how the intervention inputs, change mechanisms and context are hypothesised to produce the intended outcomes. It is recommended that these intervention theories are represented and evaluated using 'logic models' which visually demonstrate the pathway of effect between intervention inputs and intended outcomes (Funnell and Rogers 2011). While process evaluations and accompanying logic models are encouraged as key tools for evaluating casual mechanisms, they have been reported infrequently alongside outcome evaluations in health services research (Carroll et al. 2007). Integration of data from process evaluations, including information on casual mechanisms, with analyses of intervention outcomes is even rarer (Stern, Saunders, and Stame 2015). One reason for this may be the lack of guidance supported by empirical examples informing which analytical approaches are best suited to conducting these comprehensive evaluations.

Among the available literature on assessing causal mechanisms, the MRC guidance on conducting process evaluations has suggested that statistical mediation analysis can be used to assess mechanisms and provide "valuable insights into how an intervention

produces impacts" (MRC Population Health Service Research Network 2014:43). This follows the same recommendation within the programme evaluation literature, from which many approaches for evaluating public health interventions have been drawn (Shadish, Cook, and Campbell 2002; Weiss 1997a). The aim of mediation analysis is to isolate the causal mechanisms through which the intervention produces the outcome of interest. Mediation frameworks are considered to be particularly useful for complex interventions because of their proposed ability to represent multiple mediating processes in a single comprehensive model (Hennessy and Greenberg 1999; Lipsey and Pollard 1989) and therefore generate precise and rigorous tests of the intervention theory of change (Chen 1990, 2010; MacKinnon, Fairchild, and Fritz 2007). Mediation analysis is gaining momentum in public health research and efforts are underway to determine how best to maximise its application to evaluations of complex interventions (Bonell et al. 2012; Fletcher et al. 2016; Littlecott et al. 2014). Anecdotally, interest in mediation analysis for intervention research has been increasing amongst researchers at LSHTM and other universities as funders have been demonstrating interest in exploring the potential of this methodology for complex interventions research.

Despite this enthusiasm for applying mediation analysis to complex interventions research, there are relatively few examples of this in the literature. Evaluations to date have used relatively simple logic models with only one process component, for example either intervention implementation (Campbell et al. 2015; Trigwell et al. 2015) or mechanisms of change (Protheroe et al. 2007; Strange et al. 2006) integrated into the explanation of intervention effect. The limited use of mediation analysis may be due in part to the types of data needed to develop valid mediation models and to the advanced nature of the statistical theory and analysis underpinning the methodology. Thus, while mediation analysis may be a promising tool for the evaluation of complex interventions, more empirical examples are needed to determine if and how this methodology may be usefully employed.

The aim of this chapter is to undertake an evaluation of the PRIME intervention's theory of change by assessing the hypothesised causal mechanisms using statistical mediation analysis. The PRIME intervention's detailed theory of change and accompanying logic model (described in the previous chapter), plus the availability of data on hypothesised mechanisms from the PROCESS study as well as outcome data from the PRIME trial, makes

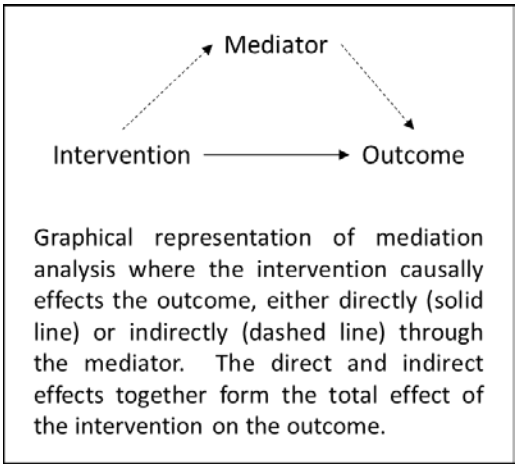
the PRIME intervention an ideal opportunity for applying mediation analysis methodology to the evaluation of a complex intervention. The chapter concludes with a discussion of the challenges and opportunities of applying mediation analysis to the evaluation of complex interventions.

6.2. Methods

6.2.1. Methodological approach – An introduction to mediation analysis

Mediation analysis seeks a causal explanation of the intervention effect, that is, the causal mechanism explaining how the intervention produced the intended outcome. A mediator is a variable representing this process which lies on the causal pathway between the intervention and the outcome of interest. A mediator is in contrast to a moderator (or effect modifier) which can vary the size or direction of the effect of the intervention on the outcome, but does not have causal properties (Baron and Kenny 1986). In health intervention research, the inferential goal is to determine the causal effect of an intervention on an outcome, ideally assessed using a RCT. Mediation analysis extends this goal by providing an estimate of the relative contribution of hypothesised causal pathways to the outcome of interest (MacKinnon et al. 2007). To achieve this estimate, mediation analysis deconstructs the casual effect of the intervention on the outcome into two pathways of interest: 1) the direct effect of the intervention on the outcome, and 2) the indirect effect of the intervention on the outcome through the mediator variable, Figure 6.1. Mediation analysis is therefore considered a causal inference, rather than exploratory or descriptive analysis (Keele 2015).

Figure 6.1: Diagram representing mediation analysis



Graphical representation of mediation analysis where the intervention causally effects the outcome, either directly (solid line) or indirectly (dashed line) through the mediator. The direct and indirect effects together form the total effect of the intervention on the outcome.

The traditional framework for mediation analysis applies structural equation modelling (SEM) based on the approach popularised by the seminal work of Baron and Kenny (1986). Baron and Kenny's work has been highlighted as influential within psychology, political science and social policy (MacKinnon et al. 2007), and has gained favour amongst notable evaluation theorists (Chen 1990; Shadish et al. 2002; Weiss 1997a). More recently, the work is cited in the MRC process evaluation guidance (MRC Population Health Service Research Network 2014) and has been applied in evaluations of complex health interventions (Gardner et al. 2010; Littlecott et al. 2014). In SEM, the direct and indirect effects are estimated as a function of the coefficients drawn from regressions estimating the effect of the intervention on the outcome, the intervention on the mediator, and the intervention and mediator on the outcome (Baron and Kenny 1986). While SEM has been valuable because of its relatively simple approach to analysing mediators, recent advances in mediation theory have shown that the SEM approach has theoretical limitations which make it insufficient for identifying causal pathways (Imai, Keele, and Tingley 2010) Furthermore, the approach is based on a linear framework; it is extremely limited for any non-linear models (ibid).

An alternative nonparametric approach employed in this chapter is based on the 'potential outcomes framework' and applies the logic of counterfactuals to identify direct and indirect effects (Holland 1986; Rubin 1974). The counterfactual framework is familiar in traditional epidemiological analyses as it forms the inference framework for RCTs. Take for example participants randomised to the intervention and control arms of a trial. The outcome of each group remains potential (unrealised) until the intervention is implemented. Once implemented, the outcome for participants in the intervention arm can be observed. Because all participants are randomised and therefore are the same with the exception of the intervention, the observed outcome from the intervention arm can be compared to the counterfactual outcome from the control arm to determine if the observed outcomes might be different to what might have happened had there been no intervention (Imai et al. 2011).

Identifying a mediator follows a similar logic. A mediator is potential until the intervention is implemented. Once the intervention is implemented, the mediator in the intervention arm can be observed. However, in the counterfactual scenario, participants are exposed to the intervention, but the mediator remains unobserved and represents what would have

been observed had participants been in the control arm. The indirect effect of the mediator on the outcome is the difference between the observed and the unobserved counterfactual outcomes; the direct effect is the effect of all other potential mediators (Imai et al. 2011). Unlike RCTs where the intervention and counterfactual scenarios can be directly compared, it is not possible to observe the counterfactual mediator – that is, it is not possible to observe a value of the mediator for a participant in the intervention arm but assuming that the participant was not exposed to the intervention. Therefore, the observed mediator data needs to be connected to the unobservable counterfactual mediator in order to compare the observed and counterfactual scenarios and determine the direct and indirect effects. To make this connection, strong assumptions are needed to make inferences about the effect of mediation from the observed data (Keele 2015).

The set of assumptions required are called 'assumptions of sequential ignorability' (Imai, Keele, and Yamamoto 2010). Sequential ignorability makes two assumptions in order to make claims about true effect of mediation from the observed data. Part one of sequential ignorability requires that assignment to the intervention and control trial arms is unaffected by potential mediators and outcomes. This assumption is satisfied when participants are randomised to trial arms which rules out confounding – that is, mediators do not influence how participants are randomised. Part two requires that the mediator must be distributed between trial arms as if it were randomised to ensure that there is no confounding of the relationship between the intervention and outcome, and between the mediator and outcome. To satisfy part two, the complete set of covariates that could confound the relationship between the mediator and outcome must be measured and these covariates must also not be affected by the intervention. In other words, there must be no unmeasured confounding anywhere along the causal pathway (Imai, Keele, and Tingley 2010). This is a strong assumption and there is no 'gold standard' method, like randomisation, to distribute and rule-out the presence of confounding. Thus, this assumption must be evaluated through statistical sensitivity analyses which can provide an indication of whether results may be violating sequential ignorability (Keele 2015). Sensitivity analysis is a crucial step of mediation analyses as previous studies have produced contradicting evidence of intervention effect when the assumption of no unmeasured confounding was made and when it was not (Ten Have and Joffe 2012).

It is this second assumption of no unmeasured confounding that poses challenges to the traditional SEM approach for mediation analysis. The multiple regressions used in SEM are insufficient for connecting the observed and unobserved counterfactual mediation scenarios making claims of direct and indirect effects invalid (Imai, Keele, and Yamamoto 2010). Furthermore, because SEM is based on a linear parametric estimation framework, all regression models must be linear otherwise the comparison between coefficients will no longer be valid and estimates of indirect effects will be biased (Keele 2015). Finally, the SEM approach does not permit sensitivity analyses to check whether the assumptions of sequential ignorability have been violated (Hicks and Tingley 2011). While these are important limitations of SEM, they are only recently being addressed in mediation literature (VanderWeele 2016) and recognition of these limitations does not appear in the complex interventions literature. However, complex interventions will potentially include a variety of types of mediator and outcome variables making SEM invalid in many circumstances. Thus, this chapter employs the potential outcomes approach advanced by Imai et al (2010). Finally, while the previous chapter identified that there was no effect of the intervention on community health outcomes, this does not preclude the application of mediation analysis using the potential outcomes framework. This methodology applies a different analytical logic and computational approach to evaluate the effect of the intervention on an outcome of interest by identifying the indirect effects isolated from direct effects and the competing effects of other mediators.

6.2.2. Statistical methods

The analysis followed a three stage approach to undertake the mediation analysis of the PRIME intervention theory of change: 1) Operationalization of the logic model, 2) Development of logic model measures, and 3) Mediation analysis of logic model pathways. As there is currently no guidance on applying mediation analysis to complex interventions, these stages represent a pragmatic approach developed for the analysis of the PRIME intervention.

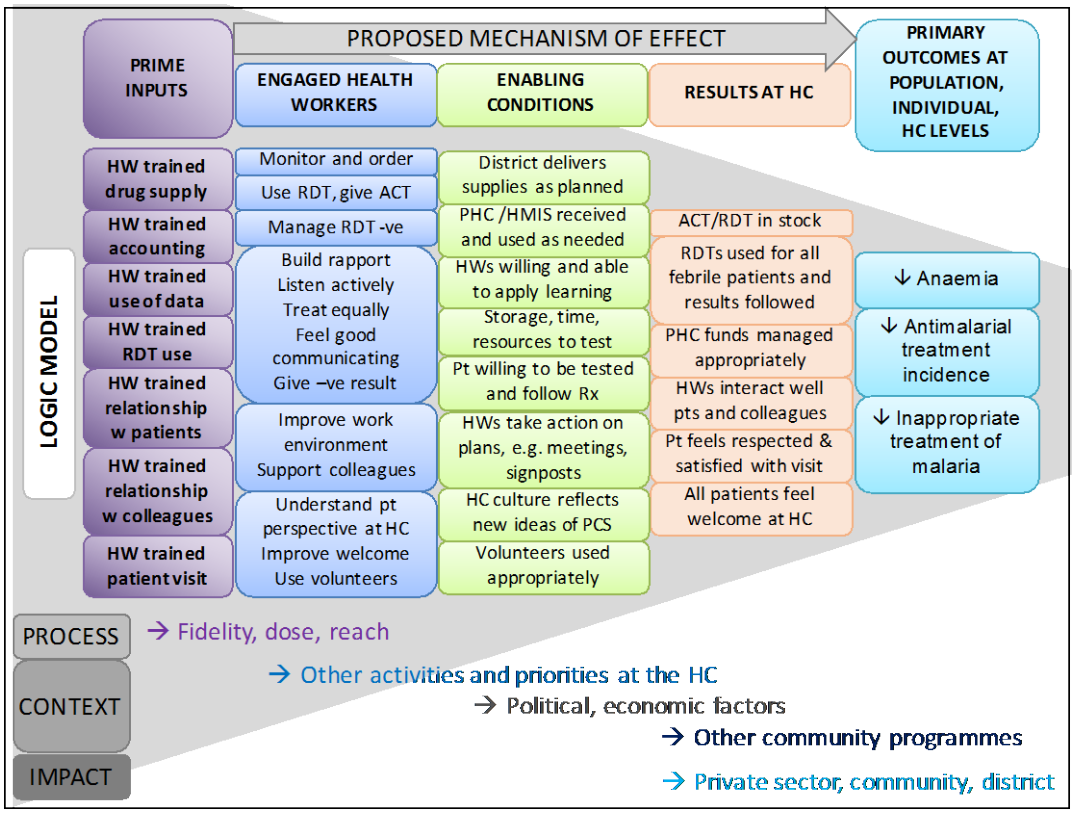
6.2.2.1. Operationalization of the logic model

Previous attempts at integrating process and outcome evaluations describe the need for a theoretical explanatory model to guide statistical analyses (Strange et al. 2006). The PRIME intervention was underpinned by an intervention theory of change described narratively and in an accompanying logic model, Figure 6.2, which described how and why the

intervention inputs would influence mechanisms and lead to the intended outcomes (DiLiberto et al. 2015). The logic model formed the basis of the explanatory model to guide the analysis.

To operationalize the logic model into a format suitable for statistical analysis, data on the hypothesised mechanism and outcome measures from across the PRIME trial and PROCESS study were identified and arranged into a directed acyclic graph (DAG). DAGs are the visual format used to represent the pathways between exposure (intervention), outcome and mediating variables. Being acyclic, all pathways between variables must be drawn in a single forward direction. Figure 6.1 is an example of a DAG. In addition, for mediation analysis, there must be temporal primacy between variables starting from the exposure variable. That is, all mediators must follow in a forwards chronological order from the exposure variable such that a mediator farthest from the exposure could not have influenced a mediator closer to the exposure (Greenland, Pearl, and Robins 1999).

Figure 6.2: PRIME logic model



6.2.2.2. Development of logic model measures

Measures to populate the operationalized logic model were drawn from across the PRIME trial and PROCESS study data under two categories: 1) Mechanism measures, and 2) Outcome measures.

6.2.2.2.1. Mechanism measures

Mechanism measures were defined as the mediating variables representing the causal pathway through which the intervention was hypothesised to produce change including: 1) Health worker attitude, 2) Patient satisfaction, 3) Appropriate treatment of fever, and 4) Health centre stock of AL and mRDTs.

Health worker attitude: The measure for health worker attitude assessed health workers' knowledge, opinions and confidence to perform activities in line with the intervention objectives including improving health centre management, fever case management and patient centred services, as well as motivations and feelings towards their work at the health centre. The health worker attitude measure was drawn from semi-structured questionnaires self-completed by all health workers in both arms of the trial. The questionnaire was piloted and revised by a team of social scientists. All health workers who participated in the PRIME cRCT were eligible to complete the survey. Questions to assess health worker attitude were responses to statements with four-point Likert scale ranging from 'strongly agree' to 'strongly disagree'. However, due to low variation in responses, and to facilitate analysis and aggregation, Likert scale responses were converted to binary responses such that 'strongly disagree' and 'disagree' were treated as 'no' responses, and 'strongly agree' and 'agree' were treated as 'yes' responses. A mean score of the proportion of 'yes' responses for each health worker was calculated and an overall health worker attitude score was calculated for each health centre as the average of health worker means scores.

Patient satisfaction: The measure for patient satisfaction assessed caregivers' opinions on three domains of patient-centeredness of health worker communication and satisfaction with the consultation including: 1) the health worker's history taking and efforts to understand the patient's illness experience, 2) how the health worker attempts to see the 'whole patient' looking beyond the disease to include the patient's personal life context, and 3) the health worker's explanation of the diagnosis and treatment plan including

medications, lifestyle management and follow-up. A structured questionnaire assessing these domains, adapted from an existing questionnaire developed in Canada (Stewart et al. 1995), was conducted with caregivers on exit from their consultation with the health worker. The questionnaire was piloted and revised by a team of social scientists. Eligible caregivers were those seeking care for a child under five years with a fever but no sign of severe disease. The sample size was calculated at 100 caregiver exit interviews and across both study arms (Chandler, DiLiberto, et al. 2013). As above with health worker attitude, Likert scale responses were converted to binary yes/no responses. A mean score of the proportion of 'yes' responses for each caregiver was calculated and an overall patient satisfaction score was calculated for each health centre from the average of care giver mean scores.

Appropriate treatment of fever: The measure for appropriate treatment of fever was assessed as a composite measure of health workers' adherence to malaria treatment guidelines – the proportion of children tested who had a positive mRDT and were prescribed AL or who had a negative mRDT and were not prescribed AL. An exit interview and clinical assessment were conducted on children under five on exit from their visit to the health centre. Caregivers of children under five were asked a short series of questions about their visit to the health centre including information on testing, diagnosis and treatments prescribed and given, followed by a physician review of the child including a mRDT for children with fever or history of fever. Appropriate treatment was determined by comparing the medication prescribed by the health worker as reported by the caregiver to the reference mRDT conducted in the clinical assessment. The sample size was calculated at 50 assessments per health centre, 1000 total to detect a difference in proportion inappropriately treated of 12% (or more) with 80% power at the 5% significance level (Chandler, DiLiberto, et al. 2013). A mean score for health centre was calculated from the proportion of children that were appropriately treated.

Health centre stocks of AL and mRDTs: The measure for health centre stocks of AL and mRDTs was drawn from a questionnaire with the health worker incharge of stock management conducted at monthly surveillance visits to health centres for the duration of the study period. Health workers were asked a series of questions regarding their stocks of AL and mRDTs including stock levels, periods of stock-outs and re-stocking procedures. For AL, which was supplied in four package sizes for dosing according to patient weight and

age, stock questions were asked for each package size. Total months stock-out measure was created for two time periods – from baseline to the midline community survey and from baseline to the final community survey. Total months stock-out for each package size of AL and for mRDTs was calculated by diving the total days stock-out in each time period by 30 days.

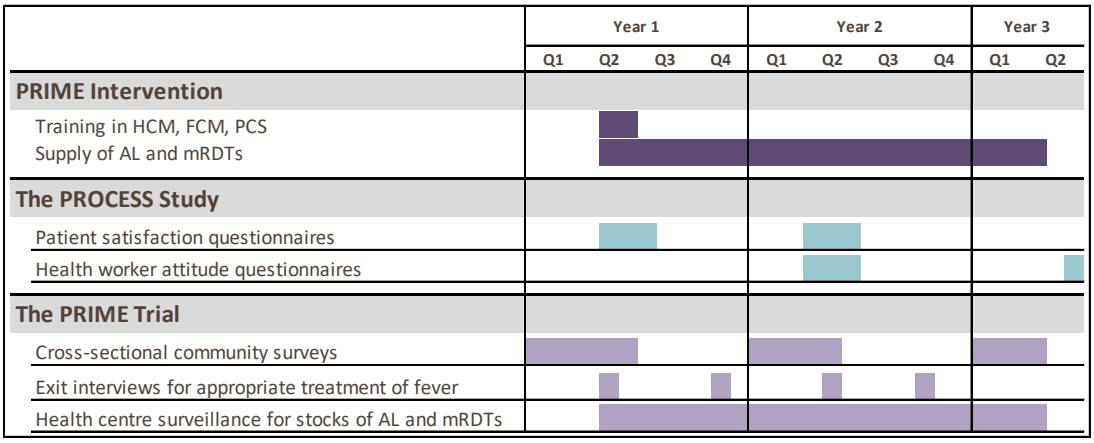
6.2.2.2.2. Outcome measures

Community-level health outcome: The measure used for the community-level health outcome was prevalence of anaemia, the primary outcome of the PRIME trial as reported in the previous chapter. The prevalence of anaemia, defined as haemoglobin <11g/dL, was measured in community clusters surrounding the health centres enrolled in the trial. Anaemia was assessed using cross-sectional community surveys of children under five and 5 to 15 years randomly selected from households in each cluster conducted at baseline and then annually for two years. Haemoglobin measured from fingerprick blood samples using a portable spectrophotometer (HemoCue, Anglom, Sweden). The sample size per cluster was proportional to the total cluster size from a planned harmonic mean of 200 children per cluster, totalling 8766 participants per cross-sectional survey. The sample size was calculated to detect an absolute difference in anaemia prevalence between study arms of 17% (or more) with 80% power at a 5% significance level (Staedke et al. 2013). A cluster-level proportion of anaemia in each age group was calculated for the baseline, midline and final community surveys.

6.2.2.2.3. Timeline of data collection for mechanism and outcome measures

Measures of health worker attitude, patient satisfaction and appropriate treatment of fever mediators were collected at 12-14 months post implementation of the intervention. Stocks of AL and mRDTs were collected for 24 months post implementation of the intervention. The community health outcome was collected at baseline, and at 12 and 24 months post implementation of the intervention representing the midline community survey and final community survey, respectively. See Figure 6.3 for a timeline of the data collection activities.

Figure 6.3: Data collection timeline



6.2.2.3. Mediation analysis of logic model pathways

The mediation analysis of the logic model pathways followed a two-stage approach: 1) Analysis of individual mechanism measures, and 2) Analysis of logic model pathways. All analyses were done using Stata version 12 (STATA Corp Lp, College Station, Tx).

6.2.2.3.1. Analysis of individual mechanism measures

The first stage of the analysis evaluated the impact of the intervention on the individual mechanism measures. An intention-to-treat analysis was used to estimate intervention impact on the individual mechanism measures. The analysis was performed separately for each measure. The mechanism measures were calculated as mean scores at the health centre level. Where the score was a proportion, the means were far from the bounds of 0 and 100% therefore linear regression were acceptable and performed using mean difference in scores as the measure of intervention impact. Individual crude analyses of the effect of the intervention on each mechanism were followed by analyses adjusted for health centre monthly average patient load and number of health workers stationed at the health centre.

6.2.2.3.2. Analysis of logic model pathways

The second stage of the analysis sought to test two hypothesised pathways. The first pathway drew on the hypothesis that the health centre stocks of AL and mRDTs themselves mediated the effect of the intervention on health worker attitude, patient satisfaction and appropriate treatment of fever. That is, the intervention was hypothesised to lead to improved stocks of AL and mRDTs which would lead to improved health worker attitude,

patient satisfaction and appropriate treatment of fever. The second pathway drew on the hypothesis that the intervention would influence each mechanism and these would each subsequently influence the community health outcomes. That is, the intervention would improve health worker attitude, patient satisfaction, appropriate treatment of fever, and stocks of AL and mRDTs and through each of these mediators there would be an improvement in health outcomes in the community. For this second pathway, the analysis was conducted separately for the community-level health outcome of anaemia in children under 5 and 5-15 years with the exception of the models for patient satisfaction and appropriate treatment of fever which was restricted to children under 5 years. It is important to note that because the mechanism measures of health worker attitude, patient satisfaction and appropriate treatment of fever were assessed just after the midline community survey was completed, the outcome rom the final community survey was used to ensure a chronological path between the intervention, mediator and outcome. However, because stocks of AL and mRDTs were collected continuously from baseline, it was possible to include these as mediators of the health outcome from both the midline and final community survey. Table 6.1 outlines each pathway tested including a description of the temporal ordering of data to ensure a chronological path and avoid chances of reverse causation in the analysis.

The pathways were analysed using the Stata 'mediation' package designed specifically for mediation analysis based on the potential outcomes framework (Hicks and Tingley 2011). Within the package, the 'medeff' command was used to implement the algorithm designed by Imai et al (2010) in four steps. In the first step, models were fitted following the algorithm for a continuous mediator and continuous outcome variables. For this analysis, the linear regression models were fitted using mean difference in scores for each mechanism measure as the measure of intervention impact. In steps 2 and 3, the model parameters were simulated from their sampling distribution to determine the potential (unobserved) values of the mediator and the resulting average causal mediated effect (indirect effect), the average direct effect, and the average total effect of the intervention on the outcome of interest. In the fourth step, summary statistics including average mean point estimates and confidence intervals were calculated. A second command, 'medsens', runs the sensitivity analysis to investigate if the results were subject to violations of the assumptions of sequential ignorability (Hicks and Tingley 2011). Individual crude analyses

of the effect of each pathway were followed by analyses adjusted for health centre monthly average patient load and number of health workers stationed at the health centre.

Table 6.1**: PRIME intervention pathways for mediation analysis**

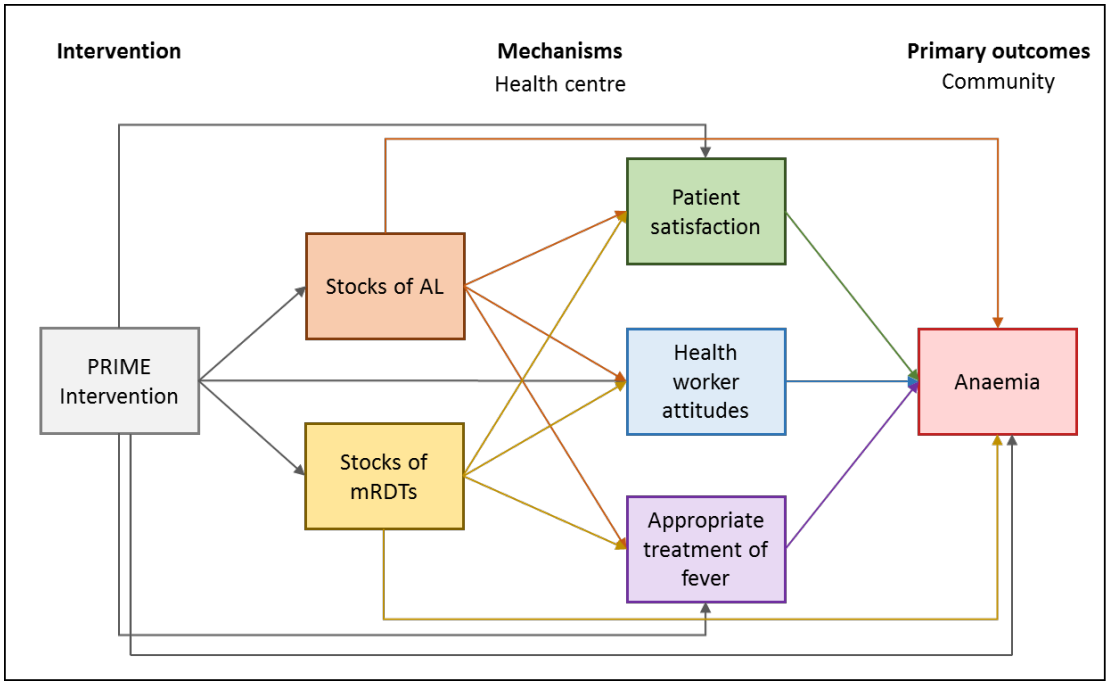
Exposure	Mediator			Outcome		
	Measure	Measured at	Applies to age group	Measure	Measured at	For age group
Pathway 1: Effect of intervention on mechanisms mediated by AL and mRDT stocks						
Trial arm: PRIME Intervention or Standard care	Stocks of AL	12 months preceding midline survey	Under 5 & 5-15 years	Health worker attitude	Midline survey	Under 5 & 5-15 years
				Patient satisfaction	Midline survey	Under 5 years
				Appropriate treatment of fever	Midline survey	Under 5 years
	Stocks of mRDTs	12 months preceding midline survey	Under 5 & 5-15 years	Health worker attitude	Midline survey	Under 5 & 5-15 years
				Patient satisfaction	Midline survey	Under 5 years
				Appropriate treatment of fever	Midline survey	Under 5 years
Pathway 2: Effect of intervention on community health outcomes mediated by mechanisms						
Trial arm: PRIME Intervention or Standard care	Health worker attitude	Midline survey	Under 5 & 5-15 years	Proportion anaemic	Final survey	Under 5 & 5-15 years
	Patient satisfaction	Midline survey	Under 5 years	Proportion anaemic	Final survey	Under 5 years
	Appropriate treatment of fever	Midline survey	Under 5 years	Proportion anaemic	Final survey	Under 5 years
	Stocks of AL	12 months preceding midline survey	Under 5 & 5-15 years	Proportion anaemic	Midline survey	Under 5 & 5-15 years
		24 months preceding final survey	Under 5 & 5-15 years	Proportion anaemic	Final survey	Under 5 & 5-15 years
	Stocks of mRDTs	12 months preceding midline survey	Under 5 & 5-15 years	Proportion anaemic	Midline survey	Under 5 & 5-15 years
		24 months preceding final survey	Under 5 & 5-15 years	Proportion anaemic	Final survey	Under 5 & 5-15 years

6.3. Results

6.3.1. Operationalized logic model

The operationalized logic model in DAG format representing the mechanism and outcome measures and the hypothesised pathway of effect is represented in Figure 6.4. The intervention was intended to work comprehensively to improve mediating outcomes at the health worker and health centre level, and ultimately improve health outcomes in the community. The operationalised logic model demonstrated the two hypothesised pathways of effect distilled from the PRIME intervention theory of change: 1) the effect of the intervention on health worker attitude, patient satisfaction and appropriate treatment of fever mediated by health centre stocks of AL and mRDTs, and 2) the effect of the intervention on community health outcomes mediated by the mechanism measures of health worker attitude, patient satisfaction, and health centre stocks of AL and mRDTs.

Figure 6.4: Operationalized logic model



6.3.2. Logic model measures

6.3.2.1. Health centre characteristics

Average monthly patient load and number of health workers stationed at each health centre was similar between health centres in each study arm, Table 6.2. Average monthly

patient load was 194 in the standard care arm and 203 in the intervention arm. Average number of health workers stationed at the health centres was 2.7 in the standard care arm and 2.6 in the intervention arm.

Table 6.2: Health centre, health worker and patient characteristics

Health centre	Average monthly patient load	Total number of health workers
Standard care		
1	183.18	1
2	178.18	2
4	243.47	5
5	164.71	2
7	249.65	6
12	186.88	2
14	162.71	2
16	225.47	2
17	128.94	2
19	124.47	3
Overall	193.77	2.7
Intervention		
20	144.24	2
3	230.47	1
18	279.82	5
15	183.59	2
13	144.41	2
8	160.41	1
9	216.00	6
10	193.76	2
11	236.88	3
6	232.24	2
Overall	202.18	2.6

6.3.2.2. Mechanism and outcome measures

Response rates for all mechanism measures were high with similar health centre characteristics between the intervention and standard care trial arms, Table 6.3. Scores for health worker attitude, patient satisfaction and appropriate treatment for fever were similar between health centres in each study arm, Table 6.3. Health worker attitude scores were 45% in the standard care arm and slightly higher at 50% in the intervention arm. Overall, these scores suggest that health workers had neither extremely positive nor extremely negative attitudes regarding their motivations and feelings towards their work at the health centre. Patient satisfaction scores were similar between arms at 82% in the standard care arm and 83% in the intervention arm suggesting that overall patients were

satisfied with their experiences at the health centre. Appropriate treatment scores were also similar between arms at 72% in the standard care arm and 75% in the intervention arm suggesting that overall, health workers were appropriately treating around three quarters of children under 5 presenting at the health centre with a fever.

In both time periods, total duration of AL stock-outs in months was similar between trial arms – 8.4 months in the standard care arm and 7.76 months in the intervention arm between baseline and the midline community survey, and 18.56 months in the standard care arm and 17.45 months in the intervention arm in between baseline and the final community survey, Table 6.3. While these figures appear high, it is important to note that this measure represents stock-outs of any package size of AL, not all package sizes of AL. It was common practice by health workers to 'cut-up' 24 tab packages of AL to meet the demand for 8 and 12 tab packages. While this practice was common, it was not ideal since AL is specially packaged by dose with instructions indicating how many tabs to administer and at what times of the day which is intended to improve adherence, an important component of ensuring parasite clearance and recovery (Connor, Rafter, and Rodgers 2004). There were no periods of complete stock-out of all AL packages at any health centres during the study period. This was expected due to the increased supply of AL to all health centres by the Government of Uganda corresponding with the implementation of the intervention. The measure of stock-outs of any package of AL was used to examine the potential influence of variability in different packages of AL.

In both time periods, total duration of mRDT stock-outs in months was different between trial arms – 4.78 months in the standard care arm and 0.67 months in the intervention arm between baseline and the midline community survey, and 7.61 months in the standard care arm and 1.4 months in the intervention arm in between baseline and the final community survey, Table 6.3. In the first time period, some health centres had 0 months stock-out of mRDTs. While it would be expected that health centres in the standard care arm should report complete stock-outs of RDTs, it is important to note that the Government of Uganda intermittently supplied mRDTs to health centres during the study period. These mRDTs were variously used by health workers – in some cases health workers reported that they did not use the mRDTs and therefore they remained 'in-stock' while in other cases health workers reported that mRDTs were used occasionally between intermittent supply by the

government. Months stock-out of mRDTs were low across all health centres in the intervention arm in both time periods.

Table 6.3: Mechanism and outcome measures by health centre

	Mechanism measure							Outcome measure			
Health centre	Health worker attitude score	Patient satisfaction score	Appropriate treatment score	Months stock-out of AL, Baseline to midline survey	Months stock-out of mRDTs, Baseline to midline survey	Months stock-out of AL, Baseline to final survey	Months stock-out of mRDTs, Baseline to final survey	Proportion anaemic, Under 5, Midline	Proportion anaemic, 5-15 yrs, Midline	Proportion anaemic, Under 5, Final survey	Proportion anaemic, 5-15 yrs, Final survey
Standard care											
1	55%	87%	77%	8.87	14.8	8.03	12.27	54.4%	23.4%	76.2%	54.8%
2	39%	74%	74%	15.37	26.77	0	1.33	66.8%	34.1%	73.6%	35.2%
4	40%	84%	71%	6.5	10.47	6.77	8.1	56.7%	31.2%	63.3%	31.2%
5	47%	74%	70%	8.1	21.07	0	1.1	50.2%	17.4%	63.9%	27.3%
7	50%	82%	67%	5.93	15.33	0	1.57	46.3%	12.3%	63.9%	22.9%
12	49%	94%	44%	4.83	14.63	0.97	3.73	61.0%	24.6%	64.0%	25.9%
14	48%	74%	71%	12.93	22.83	8	11.23	53.6%	27.2%	57.5%	27.6%
16	39%	88%	71%	5.3	18.8	7.43	11.9	77.4%	38.5%	52.9%	25.8%
17	41%	79%	88%	4.93	11.43	8.4	13.17	45.3%	19.8%	52.8%	24.5%
19	44%	82%	85%	11.23	29.47	8.23	11.7	63.3%	32.5%	66.7%	32.1%
Overall	45%	82%	72%	8.4	18.56	4.78	7.61	58.0%	26.4%	64.2%	31.4%
Intervention											
20	52%	80%	50%	12.83	23.43	0.03	0.3	43.0%	10.8%	45.2%	25.8%
3	37%	80%	77%	10.63	22.17	0.2	0.37	59.5%	18.8%	62.3%	26.7%
18	50%	87%	87%	5.83	17.5	0.7	1.23	44.7%	17.6%	56.1%	24.3%
15	54%	89%	64%	5.87	16.97	0.6	2.67	44.1%	23.4%	61.8%	28.0%
13	55%	76%	78%	8.87	19.83	1	1	50.0%	14.9%	67.9%	29.8%
8	54%	81%	68%	5.7	14.93	0.73	2.33	60.9%	16.7%	66.7%	25.4%
9	61%	83%	74%	10.87	20.5	2.1	2.3	59.4%	23.3%	65.3%	45.3%
10	53%	80%	90%	5.9	18.37	0.37	0.97	44.5%	15.6%	69.8%	37.5%
11	46%	88%	77%	5.87	9.13	1	2.33	51.0%	15.4%	65.1%	37.7%
6	42%	89%	87%	5.27	11.7	0	0.5	54.1%	31.2%	69.7%	25.1%
Overall	50%	83%	75%	7.76	17.45	0.67	1.4	52.4%	19.3%	64.2%	30.8%

6.3.3. Logic model pathways

6.3.3.1. Individual logic model pathways

There was some evidence to indicate that health worker attitude scores were on average 5 points higher (CI -0.01, 0.11; p=0.08) in the intervention health centres compared to the standard care health centres. After adjusting for monthly average patient load and number of health workers stationed at the health centre, health worker attitude scores were 6 points higher in the intervention arms (CI -0.01, 0.12; p=0.09), Table 6.4. In the period between the baseline and midline community survey, after adjusting for monthly average patient load and number of health workers stationed at the health centre, there was strong evidence of an average of 5.96 months fewer stock-outs of mRDTs (CI -9.66, -2.26; p=0.004) in the intervention health centres compared to the standard care health centres, Table 6.4. In the period between the baseline and final community survey, after adjusting for monthly average patient load and number of health workers stationed at the health centre, there was strong evidence of an average of 4.46 months fewer stock-outs of mRDTs (CI -7.46, -1.46; p=0.01), Table 6.4. There was no effect of the intervention on the other hypothesised mechanism measures.

6.3.3.2. Mediated logic model pathways

For the first pathway analysed, there was no evidence of a causal pathway between the intervention and the measures of health worker attitude, patient satisfaction and appropriate treatment of fever mediated by health centre stocks of AL or mRDTs, Table 6.5. For the second pathway analysed, there was no evidence of a causal pathway between the intervention and community health outcomes mediated by either health worker attitude or health centre stocks of mRDTs, Table 6.6. Even though there appears to be evidence of a total effect of the intervention on community health outcomes mediated by health centre stocks of AL and mRDTs in children 5-15 years (based on the confidence interval of outcome 'percentage of total effect mediated'), because the evidence of 'average causal mediated effect' is not significant, there is no evidence of an overall mediated effect. Furthermore, because there were no mediated effects, the sensitivity analysis was not performed.

Table 6.4: Effect of the intervention on mechanism measures

			Crude		Adjusted	
Mechanism measure		Mean (SD)	Regression coefficient (95% CI)	P	Regression coefficient (95% CI)	P
Health worker attitude	Control	0.45 (0.05)	1		1	
	Intervention	0.5 (0.07)	0.05 (-0.01, 0.11)	0.08	0.06 (-0.01, 0.12)	0.09
Patient satisfaction	Control	0.82 (0.07)	1		1	
	Intervention	0.83 (0.05)	0.01 (-0.04, 0.07)	0.61	0.02 (-0.03, 0.08)	0.42
Appropriate treatment of fever	Control	0.72 (0.12)	1		1	
	Intervention	0.75 (0.12)	0.03 (-0.08, 0.15)	0.54	0.04 (-0.08, 0.16)	0.52
Stock-outs of AL, baseline to midline survey	Control	9.2 (4.51)	1		1	
	Intervention	8.91 (3.43)	-1.11 (-6.3, 4.09)	0.66	-1.24 (-6.56, 4.08)	0.63
Stocks-outs of RDTs, baseline to midline survey	Control	5.46 (4.22)	1		1	
	Intervention	0.75 (0.65)	-6.21 (-9.66, -2.76)	0.001	-5.96 (-9.66, -2.26)	0.004
Stock-outs of AL, baseline to final survey	Control	18.56 (6.39)	1		1	
	Intervention	17.45 (4.51)	-0.29 (-4.05, 3.48)	0.88	-0.36 (-4.28, 3.57)	0.85
Stocks-outs of RDTs , baseline to final survey	Control	7.61 (5.1)	1		1	
	Intervention	1.4 (0.92)	-4.7 (-7.54, -1.86)	0.003	-4.46 (-7.46, -1.46)	0.01

Table 6.5: Mediated effect of the intervention on mechanism measures

		Regression coefficient (95% CI)
Effect of the intervention on mechanism measures mediated by stocks of AL		
Intervention → HW attitude mediated by Stocks of AL	Indirect effect	0.01 (-0.01, 0.01)
	Direct effect	0.05 (0 , 0.11)
	Total effect	0.05 (0, 0.11)
	% of total effect mediated	0.01 (-0.01, 0.01)
Intervention → Patient satisfaction mediated by Stocks of AL	Indirect effect	0.01 (-0.03, 0.03)
	Direct effect	0.01 (-0.03, 0.06)
	Total effect	0.01 (-0.04, 0.07)
	% of total effect mediated	0.04 (-0.95, 0.59)
Intervention → Appropriate treatment of fever mediated by Stocks of AL	Indirect effect	0.01 (-0.03, 0.03)
	Direct effect	0.04 (-0.07, 0.15)
	Total effect	0.04 (-0.07, 0.14)
	% of total effect mediated	0 (-0.04, 0.03)
Effect of the intervention on mechanism measures mediated by stocks of mRDTs		
Intervention → HW attitude mediated by Stocks of mRDTs	Indirect effect	0.01 (-0.05, 0.04)
	Direct effect	0.06 (-0.01, 0.13)
	Total effect	0.05 (0, 0.11)
	% of total effect mediated	-0.07 (-0.5, 0.16)
Intervention → Patient satisfaction mediated by Stocks of mRDTs	Indirect effect	-0.01 (-0.06, 0.02)
	Direct effect	0.03 (-0.03, 0.1)
	Total effect	0.01 (-0.04, 0.06)
	% of total effect mediated	-0.42 (-8.28, 9.58)
Intervention → Appropriate treatment of fever mediated by Stocks of mRDTs	Indirect effect	-0.06 (-0.17, 0.02)
	Direct effect	0.1 (-0.03, 0.24)
	Total effect	0.04 (-0.08, 0.14)
	% of total effect mediated	-0.87 (-14.93, 12.74)

Table 6.6: Mediated effect of the intervention on community health outcomes

		Under 5	5-15 years
		Regression coefficient (95% CI)	Regression coefficient (95% CI)
Mediated effect of the intervention on anaemia prevalence at the midline community survey			
Intervention → Anaemia mediated by Appropriate Stocks of AL	Indirect effect	0 (-0.03, 0.02)	-0.01 (-0.04, 0.03)
	Direct effect	-0.06 (-0.13, 0.02)	-0.07 (-0.12, -0.01)
	Total effect	-0.06 (-0.14, 0.01)	-0.07 (-0.14, -0.01)
	% of total effect mediated	0.05 (-0.22, 0.44)	0.08 (0.04, 0.37)
Intervention → Anaemia mediated by Appropriate Stocks of mRDTs	Indirect effect	-0.01 (-0.07, 0.05)	-0.03 (-0.09, 0.01)
	Direct effect	-0.05 (-0.15, 0.05)	-0.04 (-0.11, 0.04)
	Total effect	-0.06 (-0.14, 0.01)	-0.07 (-0.14, -0.01)
	% of total effect mediated	0.12 (-0.86, 1.2)	0.46 (0.22, 2.22)
Mediated effect of the intervention on anaemia prevalence at the final community survey			
Intervention → Anaemia mediated by Health worker attitude	Indirect effect	0.03 (0 , 0.08)	0.01 (-0.02, 0.06)
	Direct effect	-0.03 (-0.1, 0.04)	-0.01 (-0.09, 0.07)
	Total effect	0 (-0.07, 0.06)	0 (-0.07, 0.07)
	% of total effect mediated	-0.43 (-11.39, 12.68)	-0.19 (-6.32, 3.4)
Intervention → Anaemia mediated by Patient satisfaction	Indirect effect	0 (-0.03, 0.02)	--
	Direct effect	0 (-0.07, 0.07)	--
	Total effect	0 (-0.07, 0.07)	--
	% of total effect mediated	0.07 (-1.83, 1.32)	--
Intervention → Anaemia mediated by Appropriate treatment of fever	Indirect effect	0 (-0.03, 0.02)	--
	Direct effect	0 (-0.07, 0.07)	--
	Total effect	0 (-0.07, 0.07)	--
	% of total effect mediated	0.06 (-1.46, 1.23)	--
Intervention → Anaemia mediated by Stocks of AL	Indirect effect	-0.01 (-0.04, 0.03)	0 (-0.02, 0.02)
	Direct effect	0 (-0.06, 0.07)	0 (-0.07, 0.08)
	Total effect	0 (-0.07, 0.06)	0 (-0.08, 0.07)
	% of total effect mediated	0.09 (-2.07, 2.59)	-0.02 (-0.74, 0.57)
Intervention → Anaemia mediated by Stocks of mRDTs	Indirect effect	0.03 (-0.03, 0.09)	-0.03 (-0.1, 0.03)
	Direct effect	-0.03 (-0.12, 0.06)	0.03 (-0.07, 0.13)
	Total effect	0 (-0.08, 0.06)	0 (-0.08, 0.07)
	% of total effect mediated	-0.41 (-13.99, 17.86)	-0.24 (-11.5, 16.38)

6.4. Discussion

With the goal of identifying the processes through which interventions work, mediation analysis seems a promising approach for opening the 'black box' between interventions and their outcomes. With complex interventions like PRIME, it is believed that mediation analysis could be used to produce evidence demonstrating effective causal pathways in order to improve targeting of intervention inputs leading to more sustainable and scalable interventions (Craig et al. 2008; Moore et al. 2015). The mediation analysis of the PRIME intervention attempted to identify an effect of the intervention attributed to a specific mediator by isolating individual pathways from amongst the competing effects of the multiple hypothesised pathways of effect. However, despite some evidence of improvements in health worker attitude scores and stocks of mRDTs in intervention health centres, there was no evidence linking these to improvements in community health outcomes. Despite not identifying evidence of causal pathways, the process of conducting a mediation analysis of the PRIME intervention was a valuable opportunity to consider the usefulness of promoting this methodology to meet the need for more comprehensive evaluations of complex interventions. The process of operationalizing the logic model and conducting the mediation analysis revealed that the strong assumptions required to make claims of mediation may actually limit what can be known about interventions and how they function. Here, the challenges of mediation analysis are considered and a cautious approach for incorporating the ideas of mediation analysis into evaluations of complex interventions is suggested.

The main assumption underling causal mediation methodology, whether using the Baron & Kenny (1986) approach or the potential outcomes framework (Imai, Keele, and Tingley 2010), is that the causal pathway is non-recursive. However, complex interventions are generally accepted to be multidimensional and synergistic activities implemented into dynamic and unpredictable contexts (Craig et al. 2008). Indeed, it has been remarked that the precision required to define an intervention and a mediator for causal mediation does not align with the type of processes and evidence valued in evaluations of real world complex social and policy interventions (Cartwright 2007). The PRIME intervention was intended to work dynamically, igniting social and emotional processes to stimulate and sustain new skills and behaviours (DiLiberto et al. 2015). When operationalizing the logic model, several attempts were required to reduce this complexity inherent in how the

intervention would produce change into an ordered causal pathway. Versions of the operationalized logic model were cross-referenced to the theories of change, logic model, other study documents, and with the PRIME trial and PROCESS study investigators in an attempt to arrive at an 'accurate' operationalized logic model. The resulting operationalised logic model was a very simplified version of the theory of change and omitted the recursive and synergistic processes of how the intervention was hypothesised to have an effect. This challenge of reducing the complexity of the intervention change processes is acknowledged as problematic by authors within the causal mediation literature who suggest further efforts are needed to understand and accommodate the temporal and recursive dynamic changes of real world scenarios (Aalen et al. 2012). While initially considered a process that could 'clarify' the intervention mechanisms and outcomes, during this process, it became clear that the operationalised logic model represented just one of many potential interpretations of the intervention change process.

The effect of confounding, although a standard consideration in epidemiological analyses when making causal inferences between the intervention and the observed outcomes, is amplified in mediation analyses. The introduction of a mediator introduces a second consideration – that there is no confounding between the mediator and the outcome. This additional 'entry point' for confounding presents a serious threat to interpretations of mediation that cannot be satisfied through randomisation (Imai, Keele, and Tingley 2010). With complex interventions operating in complex settings, it is likely that there will be many sources of confounding between the mediator and outcome that cannot be measured and accommodated in analyses of mediation. For example, in the PRIME intervention, because the mediators were not randomised, they cannot be assumed to have been evenly distributed between the intervention and standard care health centres and therefore are subject to confounding. Consider the causal pathway between the intervention and patient satisfaction mediated by stocks of mRDTs: Some health centres received supplies of mRDTs from the government throughout the study period. This activity would have had an effect on the mediator by decreasing stock-outs of mRDTs thereby confounding the outcome of improved appropriate treatment of fevers if health workers used the mRDTs to diagnose patients. Consider another example of the causal pathway between the intervention and community health outcomes mediated by health worker attitude: Some health centres and surrounding community areas were supported by

NGOs, for example World Vision. This activity would have had an effect on health worker attitude through provision of additional deworming medications, equipment and supplies (constructs measured in the health worker questionnaire) and would have also had an effect on community health outcome of anaemia through provision of deworming medication and support campaigns. Both of these examples demonstrate how activities that independently influenced the mediator and the outcome and would have introduced bias into evidence of mediated effects. These types of 'confounding activities' occurred intermittently at baseline and throughout the study period making it difficult to measure and include them as covariates in the mediation analysis. In the crowded landscape of low resource settings where numerous government, NGO and research initiatives are working to improve health and health services (Whyte et al. 2013), it is inevitable that initiatives will interact with each other in significant and 'confounding' ways. Some authors have argued that this landscape distorts the ideals of randomised designs by questioning the reality of maintaining 'intervention' and 'control' sites (Hawe, Shiell, and Riley 2004; Okwaro et al. 2015), here it presents an additional challenge for assessments of mediation which cannot be overlooked.

Another challenge of applying mediation analysis to the evaluation of complex intervention is the assumption that mediators are independent, that is, mediating variables do not influence each other (Imai and Yamamoto 2013). This assumption presents two challenges. First, it appears that this assumption negates the intention of using mediation analysis to conduct a comprehensive analysis modelling the effect of all hypothesised mediators comprehensively. Secondly, it severely limits the interpretation of any effects generated from mediation analyses. For example, applying this assumption would require assuming that the mechanisms of health worker attitude and patient satisfaction did not interact with each other. However, the PRIME intervention theory of change hypothesised that by establishing a community of practice at health centres, the intervention would produce multiple effects at the health worker and health centre level which together would lead to improved health outcomes in the community. Indeed these contingent and emergent interactions have been considered as necessary to how interventions function and are encouraged in intervention design and evaluation (Cohn et al. 2013; Hawe 2015a). Yet, these interactions between multiple mediators can introduce unexpected sources of bias and confounding into analyses. As a result, most researchers conducting mediation analysis

proceed with a single mediator model which assumes that there is no relationship among the multiple mediators and analyse pathways separately (Imai and Yamamoto 2013), as was done with this analysis. However, analysing pathways separately without taking into account the confounding effect of different mediators can lead to biased estimates of the mediated effect (Imai and Yamamoto 2013). Yet, moving from single mediator analysis to multiple mediator analysis is a statistically complex and ambitious process. As Daniel et al (2015) demonstrate, when applying the potential outcomes framework to the analysis of two causally related mediators, there are 24 possible ways to decompose the total causal effect into direct and indirect effects. Extrapolating this process to the PRIME's five mediating variables would yield myriad results that would likely be challenging to disentangle into a meaningful interpretation of mediated effects. While methods are emerging to accommodate two or more mediators (Daniel et al. 2015; Imai and Yamamoto 2010), further work is needed to determine the theoretical and empirical application of these methods to the inevitabilities of accommodating multiple mediators in complex interventions.

6.4.1. Proceeding with caution

This chapter has evaluated the PRIME intervention using mediation analysis, a methodology that has been recommended as an ideal approach for conducting comprehensive evaluations of an intervention's theory of change. However, as Keele (2015) notes, while mediation analysis may appear a promising and simple methodology at first, many hidden complexities belie its successful implementation. Furthermore, negotiating these complexities gives pause to what mediation theorists have acknowledged as a naïve notion that applying the methodology can unlock "special access to the causal truth" demonstrating if and how interventions work (Aalen et al. 2012:6). Indeed, as this chapter demonstrated, many choices and compromises were necessary in the process of evaluating causal mechanisms suggesting a more subjective process than is usually acknowledged in statistical analyses. As such, this chapter contributes to the mediation literature urging researchers to "recognise that mediation effects are not simple by-products that can be produced for any intervention" (Keele 2015:511). In a more extreme warning, some researchers have suggested that the extent of the challenges warrants abandoning the search for mechanisms (Bullock, Green, and Ha 2010). Yet, within the complex health interventions literature, there does not appear to be a recognition, or even discussion, of

this restricted application and interpretive value of mediation analysis. Thus, further critical engagement with the theory and assumptions underpinning mediation analysis is required if this methodology is to be pursued for the evaluation of complex health interventions. To this end, the next section outlines a cautious approach which may assist researchers wanting to use mediation analysis for the evaluation of complex interventions.

First researchers should be made aware that the standard RCT is not the ideal study design for assessments of mediation because mediators are not randomised and therefore the mediators themselves may be subject to confounding. Imai et al (2013) have designed a set of alternative study designs which address this issue by randomising assignment to the intervention as well as the mediator and comparing these outcomes with the outcomes from a standard RCT. These are new designs and have not been widely applied, although there appears to be a growing interest for alternative types of designs and analyses for the evaluation of complex interventions (Cousens et al. 2011; Lamont et al. 2016). Thus as a first consideration, researchers must decide their primary objective – either analysis of intervention effect or analysis of mediation – and design their study to maximise this objective.

Secondly, researchers should consider how their interventions and accompanying theories of change might be conceptualised in such a way as to align with the acyclical logic necessary for statistical mediation analyses. As an example, Angeles et al (2013) present an approach to intervention design that is based on identifying variables (independent, dependent, mediating, moderating, and control), postulating how these variables are related, and developing a logic model by linking the variables in a series of if-then logic statements. This type of approach appears to be aligned with the conventions and requirements for mediation analysis.

Thirdly, instead of attempting to assess the complete causal pathway between intervention, mediator and outcome, researchers should consider the suggestion from within the mediation literature of limiting their analyses to only modelling the intervention effects on mediators, but not extending the analyses to include outcome measures (Keele 2015). Applying this approach to the PRIME intervention would mean only conducting the first stage of the analysis (Analysis of individual mechanism measures). As another

example, this approach was applied to the evaluation of the SASA! Intervention to reduce occurrence of intimate partner violence against women in Uganda (Abramsky et al. 2016). In this study, the authors evaluated the effect of the SASA! Intervention on the intimate partner violence outcomes and then conducted a separate analysis of the influence of the intervention on hypothesised community-, partner- and individual-level mechanisms. The authors hypothesised how the significant mechanisms might have influenced the intimate partner violence outcomes drawing on other studies to support their ideas. Importantly, and appropriately, the authors explained that the findings suggested potential mechanisms rather than provided evidence of causal pathways of effect.

Finally, researchers are urged to engage with and learn from the growing literature on mediation, much of which is published outside of public health and health services research, for example in the disciplines of psychology (Emsley et al. 2010; Imai, Keele, and Tingley 2010) and political science (Imai et al. 2011), as well as in statistical journals such as the Journal of the Royal Statistical Society (Imai et al. 2013). Likewise, researchers are encouraged to transparently report their attempts at applying mediation analysis to complex interventions. This chapter is one of several attempts amongst a group of researchers who have subsequently abandoned their mediation analyses due to conceptual and statistical limitations, and lack of results. Without these examples in the literature, there is the risk that researchers and funders will continue to naïvely promote the use of mediation analysis despite several significant statistical and conceptual challenges that have yet to be resolved. While mediation analysis may appear a promising methodology, researchers must be prepared to first tackle the theoretical underpinnings of the methodology, and then contribute empirical examples scrutinising its statistical and conceptual challenges in order to determine the usefulness of applying this methodology to the evaluation of complex health interventions.

6.5. Limitations

A limitation is that this analysis was somewhat constrained by the statistical computing package used. As described, the analysis for this chapter was conducted using the 'mediation' package in Stata (Hicks and Tingley 2011). The package is convenient because the mediation analysis and accompanying sensitivity analysis can each be easily implemented. However, it is also limited in that it does not enable analyses that account

for the clustering of data. A more robust mediation analysis package has been developed for use in the statistical package 'R' (www.r-project.org/). The R 'mediation' package implements a general algorithm for estimating causal mediation effects with a variety of statistical models and has several features that are not available in the Stata package (Tingley et al. 2014). Given this, applying the R 'mediation' package could have enhanced the analysis applied in this chapter. First, using the R package would have allowed for a nonparametric bootstrap to estimate confidence intervals which is the approach recommended by Imai and colleagues (Imai, Keele, and Tingley 2010). Additionally, using the R package would have produced p-values for the various estimates of average indirect, direct and total effects. While these enhancements would have provided additional information to support interpretation, it is not believed that they would have changed the overall findings of the analysis.

Second, using the R package would have supported a multilevel modelling approach to analyse the data at the individual level and account for clustering at the health centre level. This chapter applied an analysis aggregated at the health centre (cluster) level in keeping with the overall intervention theory of change which hypothesised that the intervention would have health centre level effects on the mediators such as ensuring health centre stocks of AL and mRDTs and improving and sustaining health worker attitude and skills by creating a community of practice. Therefore, assessing the overall impact of the intervention on these mediators and outcomes at the health centre level aligned with the theory of how the intervention was hypothesised to work and was a relevant approach for this analysis. However, because cluster-level summaries are suggested by some as being less efficient meaning that the results they produce are less precise (Eldridge and Kerry 2012), a multilevel model accounting for clustering may have been preferable. To implement a multilevel analysis using the R package, the mediator and outcome variables would have been modelled using individual level observations rather than cluster-specific proportions, where possible. For example, in mediation pathway 1 (Table 6.1), the model would have been fitted using the mediator variable of stocks of AL and mRDTs at the health centre level (in keeping with how the data was observed) to estimate the effect of the intervention on mean health worker attitude, patient satisfaction and appropriate treatment of fever using data for these outcomes observed at the individual level. In mediation pathway 2 (Table 6.1), the model would have been fitted using the mediator

variables of health worker attitude, patient satisfaction and appropriate treatment of fever observed at the individual level and stocks of AL and mRDTs at the health centre level to estimate the effect of the intervention on prevalence of anaemia using data observed at the individual level. For both of these scenarios, a mixed effects regression model with cluster as the random effect would have been used. It is important to note, however, that there are limitations with the multilevel model mediation analysis. First, the bootstrap-based uncertainty estimates for the mediation effects that could have been employed to enhance the aggregated cluster level analysis are not yet available for multilevel models. Second, the sensitivity analysis using the R package's medsens function (Tingley et al. 2014) cannot be applied to multilevel models. Without the ability to implement a sensitivity analysis, it is not possible to test the robustness of the findings to the potential violations of the assumptions of sequential ignorability.

While the R package offers some improved functionalities compared to the Stata package, it is not believed that it would have significantly changed the analytical approach or findings produced. Additionally, it is important to note that the validity of the estimates still crucially rests on meeting the assumptions of sequential ignorability. The R package does not resolve or provide a bypass of the assumptions necessary to make valid causal claims of mediated effects. The warning remains that mediation analysis must be applied and interpreted with caution regardless of the statistical package used and especially when applied post-hoc to trials of complex interventions.

CHAPTER 7. Evaluation of context

7.1. Introduction

In the pursuit of refining RCT designs to account for complexity or applying methodologies to identify mechanisms, the element of context can go unexamined. Yet, the rising rhetoric in the complex interventions literature is that 'context matters' (Edwards and Di Ruggiero 2011; Victora et al. 2005), encouraging researchers to integrate context in assessments of how, for whom and under what circumstances interventions produce effects, or not (Craig et al. 2008; Moore et al. 2015). Context is commonly defined as an external factor that that may act as a barrier or facilitator to the implementation or interpretation of intervention effects (Moore et al. 2015:6). Some suggest that this definition casts context as a noisy externality, or bias, threatening the expected outcome of the well-planned intervention (Lindsay 2004) or as all-encompassing and nonspecific operating in a black box and exerting influences that defy identification and measurement (Bate et al. 2014). Methodologically speaking, proponents of the RCT suggest that the effects of context can be minimised through randomisation, which is understood to distribute contextual influences across the study area, or through statistical analyses that adjust for the effects of context on trial outcomes, or both (Bonell et al. 2012; English, Schellenberg, et al. 2011). For others, the RCT is seen as a antithetical to accommodating context because it is considered to minimise, or bracket-out social complexities in order to produce objective assessments of intervention outcomes (Montgomery and Pool 2011). It is argued by some that these definitions are denuded of the social processes underlying the interaction between context and interventions and much could be gained from greater recognition of competing and conflicting interests within society and of the methodological implications of such differences (Hawe 2015a; Shoveller et al. 2015).

Despite a lack of methodological clarity on assessing context, there appears to be some commonalities regarding the factors that are considered in discussions of context. These include what are commonly referred to as the social, political, economic, cultural, geographical, organisational or biological factors that explain disparities in health and access to care. To provide conceptual clarity, these factors are usually considered to

operate at different levels of social organisation which provide a type of framework for understanding the role and influence of different factors. These levels might be arranged and presented differently (Neudorf et al. 2015), but mainly follow a stratification into orders of magnitude such as macro to micro levels of society. Factors considered to operate at the macro level might describe how global and national policies distribute resources among different social groups. The meso level might describe how the political and administrative organisation of the health system influences the provision of health care services. The micro level might describe how demographic, cultural and socioeconomic characteristics within society influence access to care and health outcomes.

At a general level, frameworks of contextual factors can be used to describe the characteristics of where interventions are being implemented and their target populations in order to develop explanations of intervention effects and how these might relate to other places with similar contextual characteristics. A more critical approach proposed by Farmer and colleagues (Farmer et al. 2006), and taken up more widely (Solar and Irwin 2010), examines context at these different levels to describe the forces in society that prevent people from achieving good health and wellbeing. These forces include the unequal distributions of power, narratives of blame, and exclusions based on gender or economic position, for example, that permeate economics, politics, institutions and social relationships (Farmer et al. 2006, 2013). When applied to intervention research, such an approach seeks to move beyond oversimplified designs and evaluations which focus only on biomedical causes of ill health. Instead, this approach provides a framework for deconstructing the social conditions that enable or prevent interventions from achieving desired impacts on health and related outcomes.

This chapter argues, however, that examining context through levels of social organisation is one of many ways through which context can be conceptualised and sense made of complex social realities. There are indeed other imaginations of the social and ways through which it might be rendered visible. Adopting new approaches provides the opportunity to foreground things not normally attending to and examine those that might be taken for granted. An alternative account might consider context as relational arguing that it cannot be disentangled into social strata. Such an approach starts with a proposition that interventions themselves are composed of social processes that are intertwined with

the social world into which they are implemented (Hansen and Tjørnhøj-Thomsen 2015). In addition, more mundane physical and environmental elements are also considered to have agency influencing relations in the social world (Shareck, Frohlich, and Kestens 2014). From this perspective, context takes on a more nuanced and fluid meaning recognising the inter-relationships between actors, settings and the messiness of real life (Bate et al. 2014; George et al. 2015). By foregrounding context in this way, attention is diverted from identifying specific contextual factors that determine success or failure of the intervention towards exploring it as part of the interactions between human, material and structural elements operating in dynamic systems (Cohn et al. 2013).

One approach to exploring context from this different perspective is to 'zoom in' on the people and places enrolled in the intervention to reveal the elements of their everyday realities. Drawing from Strathern's work on exploring complexity (2004), the act of zooming in enables elements to be examined closely revealing details which are not visible at other scales of observation. Rather than a factor, context shifts to being a quality of relationships between humans, the intervention, the environment, and even material objects. In so doing, the complex linkages between elements are revealed generating different interpretations than would have otherwise been considered. The advantage afforded by zooming in is the ability to uncover different ways of seeing and thinking about phenomena. This magnified perspective may help to explore the complexity of so-called 'factors' and the complex linkages between these to generate more locally specific understandings of the elements influencing how interventions are taken-up in different places.

Given that these different perspectives nevertheless recognise context as paramount raises theoretical, conceptual and methodological challenges for accommodating it in evaluations of complex interventions (Datta and Petticrew 2013; Pfadenhauer et al. 2015; Shoveller et al. 2015). Consequently, there is a need to reflect critically on how context is constructed and integrated into evaluations and with what effect. The aim of this chapter is to explore what happens to constructions of context and the intervention when explored at different scales of observation, and specifically, when zooming in on the everyday realities of health workers enrolled in the PRIME intervention.

7.2. Study setting

Health and access to care to good quality health care have remained elusive in Uganda for the past several decades (Kiwanuka et al. 2008). The examination of health care service provision in Uganda outlined in Chapter 2 described the historical and contemporary processes which have contributed to this lack of progress. This review highlighted that a history of reforms has resulted in a decentralised but dysfunctional national health system (Iliffe 1998). The health system continues to operate under a legacy of hierarchy where lower level health centres operate at the periphery of the system and receive limited investment and political support (Blaise and Kegels 2004). The removal of user fees for public health units in 2001 increased the overall number of poor people seeking care at public health centres (Xu et al. 2006), however, perceptions of quality of care (Kiguli et al. 2009) and satisfaction with services has remained low (Medicines Transparency Alliance (MeTA) 2014). Persistent health system challenges including low and unstable salaries (Ssengooba et al. 2007), poor management of health centre funds (Streefland et al. 1997), stock outs of essential medicines (Jitta, Whyte, and Nshakira 2003; Ministry of Health (MOH) [Uganda] and Macro International Inc 2008), and poor supervision and management of health workers (Lutwama, Roos, and Dolamo 2013) have contributed to poor quality care.

In Tororo District, health service provision is characterised as a projectified terrain where a range of health and development projects provide care services in the community (Whyte et al. 2013). These health projects have not had lasting impacts on improved health and access to care (Kiwanuka et al. 2008). These have included projects focused on inputs such as intermittent investment in health centres, training of some health workers, and changes in fees for services. For example, improvements in availability of drugs (Jitta et al. 2003) or removal of user fees (Rutebemberwa et al. 2009) at health centres have not been seen to translate into lasting impacts on equitable access to care for the poor (Kwesiga et al. 2015). Likewise, access to care is not fully realised when community members are unsure of how to navigate the unspoken, hidden rules present in health centres (Mogensen 2005). Additionally, health system reforms, while intending to improve responsiveness to local health care needs, may in fact weaken health workers' identity as professionals with

negative consequences on their motivation to provide quality care (Kyaddondo and Whyte 2003). These studies suggest that interventions focusing on operational inputs, such as resources or financing mechanisms, may fail to take more local priorities, and realities, into account (Chandler, Kizito, et al. 2013).

These local priorities for good quality care at public health centres in Tororo were found to be oriented around a compound of three factors related to a comprehensive therapeutic process – technical factors, including good clinical care and the right treatment; interpersonal factors including a positive health worker attitude conveyed through welcoming patients, providing explanations and reassurance; and resource factors including availability of drugs, equipment and staff (Chandler, Kizito, et al. 2013). As described in Chapter 2, there are a number of determinants which impact on provision and access to good quality care. There is a fairly high interest among community members in accessing care through the public sector, however, community members may not seek care if the illness is perceived as mild, if the health centre is far from their home, or if they lack spousal support in meeting financial and opportunity costs. Additionally, community members may not seek care if they feel unable to negotiate the logistical and social rules of the health centre, or believe they will not receive treatment due to unavailability of drugs and supplies. Both community members and health workers report that poor management of the health centre, previous negative experiences, a mistrust of the therapeutic process, lack of knowledge on appropriate treatment seeking, as well as poor local referral systems and political hindrances discourage treatment seeking at health centres. Additionally, community members and health workers report that drug stock-outs and lack of equipment, a high patient to staff ratio and discriminatory treatment of patients impacts negatively on the quality of care provided at health centres. Overall, dissatisfaction with care provided at health centres is high which is interpreted to be a function of poor health worker motivation and poor management of the health centre combined with a lack of patient-centred culture and poor relationship between health workers and communities (Staedke and Uganda Malaria Surveillance Project 2010).

These findings echo patterns in barriers to treatment seeking and provision of care elsewhere in Uganda. Barriers which have been consistently reported as impacting on community members' treatment seeking at public health centres include lack of knowledge

about when to attend, costs of care (Kiwanuka et al. 2008), long distances to health centres and perceived lack of skilled staff in health centres (Kiguli et al. 2009; Kiwanuka et al. 2008). Barriers which impact on quality of care received at health centres include poor health worker attitude and interpersonal relations between health workers and community members (Kiguli et al. 2009; Kiwanuka et al. 2008). Additionally, stock-out of drugs and supplies are consistently reported as challenge to good quality care (Jitta et al. 2003; Kiguli et al. 2009; Kiwanuka et al. 2008; Rutebemberwa et al. 2009) and motivation of health workers remains low due to ineffective reforms persistent health system challenges (Kyaddondo and Whyte 2003; Nabyonga-Orem et al. 2008).

7.2.1. Context examined through social structures

The section that follows examines context through three levels of social organisation to describe the factors which may have influenced how the intervention was delivered and taken-up at health centres and in the community. Different social, political and economic factors at each level that form the structures within which health services, health workers and care seekers operate are examined. Findings which are presented later in this chapter are drawn on here for illustrative purposes. This includes health workers' narratives regarding the PRIME intervention examined through four health centre cases. These are supplemented with findings from other analyses of the PRIME intervention documented elsewhere (Chandler et al. 2017; Nayiga et al. 2014; Okwaro et al. 2015).

7.2.1.1. National level

In a decentralised health system, health workers play a major role in operationalising the national level policy of improved service delivery and reduced costs (Kyaddondo and Whyte 2003). Health worker motivation, and how this affects service quality, efficiency, and equity has therefore been an important focus of research (Bukuluki et al. 2013; Franco et al. 2002; Mbindyo et al. 2009). Components of national level policies which are considered important positive motivators include, for example, clear employment terms, regular and fair remuneration, constructive performance appraisals, and access to training and promotion opportunities (Okello and Gilson 2015). These have been consistently absent or inadequately implemented in Uganda resulting in the demoralisation of health workers, a theme which has become common in discussions of the national health care system (Kyaddondo and Whyte 2003; Lutwama et al. 2013). As it will be demonstrated later in this

chapter, this theme was echoed strongly in two of the cases examined in which health workers reported high levels of job dissatisfaction. Interestingly, health workers in the other cases examined did not appear as demotivated by these same deficiencies and instead looked to experiences such as the promise of a new health centre building and the regular presence of the PRIME research team as alternative sources of positive motivation. Differential influence of national level context on health worker have been reported in other low resource settings. Research conducted in Kenya, for example, demonstrated that the deterioration of working conditions as a result of health system reforms left some health workers demotivated whereas other health workers were motivated by the opportunity to build their skills in preparation for other work opportunities, despite lack of pay and other de-motivators (Mbindyo et al. 2009).

Differential motivation of health workers can also have knock-on impacts on services provided and treatment seeking practices. Although the health workers in the cases examined in this chapter described persevering with their jobs and provided little indication that overall satisfaction affected the quality of services provided, these findings were not universal across the health centres in the study nor were they echoed by community members. Analyses conducted by the PRIME study team, and documented elsewhere (Nayiga et al. 2014; Okwaro et al. 2015), demonstrated that while there were some improvements in quality of care these were not consistent in all intervention health centres. Community members, describing services at some intervention health centres for example, reported demands by health workers for illegal payments for drugs, not being given complete doses of prescribed drugs, or being told to buy drugs at private clinics or drug shops. These types of strategies for coping with lack of pay, have a long history in Uganda (Burnham et al. 2004; Streefland et al. 1997). These strategies in turn deter patients who do not have the economic means to seek care at health centres (Chandler, Kizito, et al. 2013; Jitta et al. 2003; Rutebemberwa et al. 2009). The dysfunction at the national level can be said to have an insidious and diffuse effect. Once it takes root in health workers' personal motivation, it instigates different coping strategies affect the equity and fairness of services provided at health centres. The intervention attempted to improve health worker motivation through training, provision of resources and building a community of practice. However, the intervention's relatively narrow focus on malaria care left many of the root causes of dissatisfaction – including economic resources for health

workers and their health centres – untouched. These findings suggest that in this context improving health worker motivation and directing treatment seeking towards health centres would require substantial improvements to the operationalisation of national level policies through systemic change in health systems rather than being addressed through single-disease focused programmes.

7.2.1.2. District level

At the organisational level in Tororo District, a level more proximal to the PRIME intervention, the influence of a projectified setting compounded by physical and political constraints appeared to affect engagement with the research project in the cases examined. This setting manifested a careful negotiation of power structures between health workers and the research project as each group of actors sought to maximise their respective priorities. Two major power differentials were observed: between health workers and the research project and between health workers and the district administrative structures.

For research projects in low resource settings with physical and political constraints, like Tororo District, health workers, the research project and the district administration operate in a type of multidirectional power structure. On one hand, research projects, although not positioned as development initiatives, nevertheless fill gaps in health service delivery through the provision of, for example, financial and material resources and biomedical expertise. In a projectified setting, health workers have ever more access to these types of resources from a variety of government, research and NGO initiatives. Vian and colleagues (Vian et al. 2013), for example, observed that health workers in Uganda often attend numerous training workshops offered by different research and NGO projects as a way of earning a per diem – a small cash supplement for health workers' time and participation. A situation which has become common in many African public health projects (Ridde 2010). Likewise, it has been observed that initiatives often target the same disease in the same health centre following the same pattern: identification of health problem of interest, provision of product, training, implementation, monitoring and evaluation (Whyte et al. 2013). In this context of repetition and oversupply, health workers may be in more of a position to tailor their engagement with the different research and development projects taking on or discarding parts relevant to them in relation to other opportunities. In the

present study, health workers demonstrated this agency through their engagement with parts of the research project relevant to them, for example selectively using mRDTs or fastidiously completing research data collection tools, rather than taking on the intervention wholesale as was intended by the research project.

On the other hand, research and development projects are reliant on the engagement of one group of health workers, patients or other target group in a specific setting – both as intervention participants and as providers and collectors of data demonstrating intervention effect. Indeed, the endeavour of global health would not be possible without 'vulnerable populations' with problems to be solved. As Crane notes in her ethnography of transnational research partnerships between Uganda and the US, countries in east and southern Africa, as a result of colonial ties, have come popular locations for global health initiatives with their populations providing certain kinds of 'valuable opportunities' for researchers in the global north (Crane 2013). Research and development projects therefore utilise different strategies to secure participant engagement and ensure the success of their endeavours. For the PRIME project, this included strategies such as providing specialised 'research only' registers to health centres, installing a liaison person to ensure an effective drug supply system, conducting repeated visits to the health centre by clinically trained research staff, and moving around the study area in project branded vehicles. Although not an overt intention, these strategies were a means through which the research project established and maintained a position of power within the administrative and organisational health system structures in the study area thereby securing health worker participation. Interestingly, these strategies in turn became ways through which health workers could establish strategic engagements to negotiate some of the physical and political constraints. For example, engaging the research project as an advocate to address longstanding infrastructure issues or using good performance on the research activities as corollary for upgrading the health centre. However, despite these opportunities provided by the research project, health workers were still operating in a deeply hierarchical power structure. Their narratives described being unable to negotiate power held by district level health officials in accessing other resources, including PHC funds and additional staff members, and resolving accusations of stealing drugs for personal gain. These findings suggest that interventions intending to empower health workers to negotiate organisational level constraints may be diluted by the

multidimensional power relationships at play in a projectified setting and deeply hierarchical system. Reorienting these relationships would require substantial reorganisation of research and development priorities to focus on the social and organisational supports needed by health workers to navigate systemic power imbalances rather than simply focusing on the provision of training, resource and technical inputs.

7.2.1.3. Community level

At the community level, analysis of community members' responses to the intervention, documented elsewhere (Chandler et al. 2017; Nayiga et al. 2014; Okwaro et al. 2015), suggests that a context of poor health care provision appears to have become normalised rendering poor services 'business as usual'. Community members attending standard care health centres, and some intervention health centres, described persistent challenges including discriminatory and disrespectful health worker attitudes, demands for illegal payments for drugs, and inappropriate or dangerous treatment. Community members developed a way of overcoming these challenges by engaging in a number of positioning strategies to get better services including attempting to be served by friendlier health workers or finding ways to 'get tough' with health workers by reporting them to the local council or demanding to be served. Yet, there were some noticeable improvements in some intervention health centres, and exceptionally one standard care health centre. Here, community members' narratives suggest that the introduction of mRDTs was largely seen as positive and reinforced some of the desirable aspects of providing and accessing biomedical care. They also described improvements in health worker attitudes and interpersonal communication, and in availability of antimalarials and mRDTs. Despite these improvements, community members on the whole did not report changing where they sought care describing that they continued to seek care from the same sources regardless of whether the care received was of good or poor quality, including community members living beyond the research project catchment areas. Their reasons for maintaining existing care seeking practices included the renewed availability of antimalarials and mRDTs, and qualified though 'harsh' health workers. Moreover, community members described a narrative of desperation revealing that as a result of 'being poor' and disenfranchised, they had few better alternatives. These reflect the persistent observation that those in the weakest position to navigate power have the poorest ability to access good quality health care. It appears, therefore, that the intervention was 'not sufficient enough' to address the

social and economic determinants affecting treatment seeking practices in order to elicit a major change in the choice of where community members access health care. These findings suggest that interventions attempting to shift treatment-seeking patterns toward health centres must address a broad range of community level determinants in order to enable improved local access to better health care.

7.2.1.4. Summary

This account of the study context and its influence on how the intervention was delivered and taken up at health centres and the community followed the approach common in the intervention research and development literature which seeks to understand how contextual factors at different levels of social organisation provide explanations of intervention effects, or lack thereof. In so doing, it produced certain valuable insights suggesting that the intervention may have had little sustainable impact on improving quality of care and directing treatment seeking towards health centres because it failed to address systemic political challenges affecting health worker motivation, power imbalances affecting access to health centre resources, or a broad range of community level determinants necessary to enable improved local access to better health care. However, in providing these insights, it takes for granted and reinforces a specific way of conceptualising reality. Taking the approach of 'zooming in' on everyday realities offers an opportunity to mix and unsettle these existing categories and conceptualisations which may uncover alternative ideas about how the intervention and its effects. The remainder of this chapter applies this alternative approach of zooming in and in so doing, it seeks to re-problematise context by foregrounding health workers' everyday realities and their interactions with the research project that might not normally be attended to.

7.3. Methods

7.3.1. Data

The findings presented in this chapter derive from data collected during the three years of developing, implementing and evaluating the PRIME intervention and include reported and observational field data. In-depth semi-structured interviews with health workers were conducted by research assistants trained in conducting qualitative interviews as part of the PROCESS study (Chandler, DiLiberto, et al. 2013). Employing a topic guide (Appendix 3), the

interviews aimed to elicit health workers' narratives of the intervention and objectives, and its effects on everyday practices. In addition, the interviews explored experiences and factors shaping the enactment and integration of the intervention such as personal motivations, resources, research activities, and interactions at the health centre and in the community. As part of the interviews, demographic data were collected. Interviews were conducted at the health centres during normal working hours and were between 1 to 2 hours in length. Interviews were conducted one year following the implementation of the PRIME intervention. Interviews were conducted in English and were tape-recorded and transcribed verbatim.

A semi-structured contextual record questionnaire was administered every three months for the first year following implementation of the PRIME intervention. A purposively selected cohort of 20 key informants identified as being knowledgeable about local health activities at the district level, health centre and community level were interviewed to collect information on activities that may have affected implementation and impact of the PRIME intervention. The questionnaire sought information on activities, events, policies, infrastructure, human resources, media stories, environmental or other changes that may have impacted on health workers' ability to engage with the PRIME intervention and to provide quality care (Appendix 4). Reponses were collated and typed with responses from different informants triangulated to verify consistency and validity. Responses were entered into an excel database organised by time, source of information, and category (health campaigns, activities/training, resources, health worker and patient practice, policy, other).

The author's (DD) field notes were gathered in a non-structured format from a number of sources. These included first-hand observations from visits to health centres, formal discussions at study team meetings, experiences at the field site including information gathered from the news media, and informal discussions with health workers and study team members. These observations provided rich accounts of the functioning of the PRIME intervention and evaluation activities in everyday situations.

Field notes and reports from the PRIME trial and PROCESS study research teams were generated over numerous visits to health centres to conduct study activities. Specifically,

field notes were recorded from interactions before, during and after different data collection activities including health worker communication assessments, in-depth health worker interviews, patient exit interviews, and monthly health centre surveillance interviews. During these visits, informal interactions took place with health workers, patients and other community members regarding aspects of the implementation of the PRIME intervention, as well as general activities influencing the provision of services or other aspects of the health centre. These interactions and observations were recorded as field notes supplementing the formal PRIME trial and PROCESS study data gathering activities and were discussed in fieldwork debriefing meetings and in regular research team meetings.

Of note, the term 'research project' used throughout this chapter refers to all intervention and evaluation activities conducted as part of the PRIME trial and the PROCESS study (Chandler, DiLiberto, et al. 2013; DiLiberto et al. 2015; Staedke et al. 2013). Data were imported into NVivo version 8 (QSR International) to support data management and analysis.

7.3.2. Approach to analysis

The initial aim of this chapter was to identify contextual factors that could explain differences in outcomes at health centres following the approach which views context as external to the intervention (MRC Population Health Service Research Network 2014). The two intermediate outcomes of health worker appropriate treatment of fever and patient-rated satisfaction with the health centre visit were selected and arranged in a matrix of high and low performance on the two health centre outcomes. A set of four initial cases were selected, one from each quadrant of the matrix. Appendix 5 presents these cases relative to the other health centres enrolled in the study. Following the approach outlined in Yin (2009), initial coding of the cases attempted to define a framework of themes and factors representing similarities and differences at health centres, for example: health worker belief in mRDT outcomes, generic or individualised interactions with patients, health centre infrastructure, availability of resources, and health worker relationship with the community. The intent was to define a theory of contextual factors supporting or hindering the intervention which could then be tested against the remaining cases (Yin 2009). Other studies have applied a similar approach to using case studies to examine context and

determine reasons for differences in outcomes at different locations participating in the intervention (Hoddinott et al. 2010; McMullen et al. 2015)

However, as the analysis progressed, it became increasingly evident that it was not possible to isolate context as factors separate from the intertwining processes and relationships through which health workers made meaning of the research project in relation to their lived realities. Instead, what emerged was the notion of context as relative to social and material processes. Examining context from the perspective of health workers' everyday realities foregrounded a different view of context than what has usually been applied which projects context as a generic background in relation to the intervention of interest (Shoveller et al. 2015). Thus the analysis shifted to a different approach where cases were used as an instrument to explore context in relation to health workers' everyday realities and the intervention (Stake 1995). This type of exploratory case study is advantageous when studying evolving and complex phenomena (Stake 1995). Whereas the explanatory approach to case studies intends to identify a unifying theory of a phenomena (Yin 2009), the exploratory approach applied in this chapter to intends to identify convergent and divergent experiences, in order to generate new ways of thinking about a phenomena and its influence on interpretations of the social world (Law and Mol 2002).

The analysis and interpretation was underpinned by a social constructivist perspective which acknowledges that there is no single objective reality, but rather that realities are constructed by and are dependent on individuals' lived experiences. Knowledge about these realities can be gained though interaction with and observations of experiences in the social world (Guba and Lincoln 1994). Applying this perspective to the analysis was achieved by using an interpretive approach that acknowledged cases as comprising health workers' specific and locally constructed experiences of participating in the research project in relation to their everyday realities.

The analysis followed a phased and iterative process of thematic analysis (Denzin and Lincoln 2011). In the first phase, each case was individually analysed. Interview transcripts and supplementary data were coded iteratively with ideas labelled and grouped according to emerging theme. Particular attention was paid to understanding health worker's individual and collective descriptions of what and how changes were perceived to have

occurred, as well as the similarities and differences in how health workers' everyday realities shaped how the research project was enacted and what it became as a result.

An initial framework of themes for each case was developed and discussed with another researcher which stimulated deeper exploration and consideration of underlying social processes related to health workers' enactment of the research project. These interpretations were applied in the next round of coding to generate higher order concepts that could account for multiple codes illustrating wider, shared interpretations among cases. Concepts identified included health workers' emotional and practical experiences with the research project in relation to the surrounding human, material and structural elements.

This analysis was again followed by discussions and an examination of the emerging findings alongside the theoretical and empirical literature to inform and situate the interpretation in an understanding of how wider structural issues influenced health workers' experiences of the research project. In particular, texts by Law and Mol (2002) and Strathern (2004) helped to extend the examination of complexity and context beyond the boundaries of material objects. In this way, immaterial features of space, time and place came to feature as important concepts to understanding experiences of the research project alongside the materiality of settings, objects and research activities.

In a final round of engaging with the data, the concepts arising were organised into an overarching analytical scheme that combined interpretations of health workers' experiences, the research project, and descriptions of broader structural issues. In this round, the analytical scheme was informed by the empirical and theoretical literature on socio-spatial locations which juxtaposed notions of context, which is often considered as 'setting' or 'place', with a different perspective that considers space as the product of interactions between features of time, actors, physical and social structures (Massey 2005; Shoveller et al. 2004, 2007).

7.4. Results

7.4.1. Description of cases

Four cases are presented based on the experiences related by the health workers stationed at four of the health centres: Mark (Health Centre 10), Halima (Health Centre 9), Godfrey (Health Centre 1), and Constance (Health Centre 2). Pseudonyms and only general demographic details from across the four cases are used to preserve anonymity. All of the health workers interviewed were in-charges responsible for overseeing the functioning and clinical service at the health centre. Of the four health workers, three were Nursing Assistants with highest education level achieved ranging from middle school to a vocational certificate in nursing; one health worker was a Clinical Officer with a university certificate. The health workers had been stationed at the health centres between 8 to 15 years. All health workers approached agreed to be interviewed and also participated in the other research project activities. A brief description of each case and illustrative photos are provided to situate the findings:

7.4.1.1. Mark, Health Centre 10

Health centre 10 was situated off of a rural, dirt road near the local trading centre. The health centre building was a rented house, not a standardised government-issued building, and was in a state of disrepair. Overgrown bushes surrounding the health centre were explained by a lack of funds to pay for a groundskeeper. Leading away from the building was a path to the once-functional pit latrine, which on account of not being emptied for some time, was over full and was not in use. The same scenario applied to the water pump and as a result, there was no clean water available at the health centre, Photo 7.1. Instead, water was collected from a nearby borehole and stored at the health centre in jerry cans. The veranda served as the waiting area where patients sat on the ground shaded by a corrugated tin awning, Photo 7.2; there was little other space to wait, which at times could be several hours before seeing the health worker. Just inside the front door of the building was the consultation room furnished with a table and a few chairs. Patients moved in and out of the consultation room to speak with the health worker, collect medication, or determine when their consultation would take place. Privacy in consultations was not attempted, nor possible. The attic area was home to an infestation of bats leaving a damaged ceiling made worse by the heavy rains, Photo 7.3. One room functioned as a

storage area with a large cupboard for storing drugs, neatly organised. In the absence of a laboratory in this rented house, another room was used as a makeshift testing area where mRDTs were performed. Some days there were two staff who worked together who alternated patient intake, testing, diagnosis and dispensing of medication, but most days the work was done by the in-charge health worker, Mark.

Photo 7.1: Health centre 10 – Water at the health centre

Photo 7.2: Health centre 10 – Building exterior

Photo 7.3: Health centre 10 – Damaged ceiling

7.4.1.2. Halima, Health Centre 9

Health centre 9 was located just off the main road running through the sub-district and was in close proximity to other places of interest such as a church and some small shops selling phone cards, snacks and soda. The building was government-issued and followed the standard layout complete with a maternity wing, inpatient beds, a laboratory and staff quarters. The building was located next to the sub-county government offices and the grounds of both buildings were well maintained, Photo 7.4. There was a functioning pit latrine and running water. Inside, the building was spacious and light with ventilation blocks in the walls. Upon entering, there was a patient waiting area with wooden benches along the walls. The floors and walls were concrete, smooth and clean; a few health promotion posters hung alongside hand-drawn graphs of health surveillance activities, Photo 7.5. Patients waited on the benches before being called into their consultations which were held in a separate room with a closed door. mRDTs are performed in the laboratory where there were work tops, sinks and good lighting; although water and electricity were only intermittently available, Photo 7.6. Drugs were stored in the dedicated store room on wooden shelves and were issued from a dispensing window; patients waited to be called to approach the window and receive their medication. Of the five health workers stationed at the health centre, usually 2-3 were recorded as being absent from the health centre.

Photo 7.4: Health centre 9 - Building exterior

Photo 7.5: Health centre 9 – Patient waiting area

Photo 7.6: Health centre 9 – Area for performing mRDTs

7.4.1.3. Godfrey, Health Centre 1

Health centre 1 was located along an unpaved road a fair distance from the local trading centre and main road. Like health centre 10, the health centre building was a rented house, not a standardised government-issued building, and was old, but in fine condition. The grounds were well maintained and there was a functioning pit latrine, but no electricity or running water. Patients waited on the veranda under the shade of a tin roof and mature mango tree, Photo 7.7. As patients left the building after their consultation, others waiting on the veranda would shift into a room inside where patients waited on wooden benches or on the floor, Photo 7.8. Inside, the building was dark and stuffy with few windows and no ventilation. The walls were covered with health promotion posters, although many of them were out of date. Consultations were held around the corner in a room off of the waiting area; there was no door, but a degree of privacy was afforded. Patients moved in and out of the consultation room to speak with the health worker, collect medication, or determine when their consultation would take place. One room functioned as a storage area with wooden shelves for storing drugs; other rooms were empty. mRDTs were performed in the consultation room under the light from a window in the absence of electricity, Photo 7.9. Drugs were also dispensed from the consultation table, Photo 7.10. The in-charge health worker, Godfrey, worked alone at the health centre.

Photo 7.7: Health centre 1 – Building exterior

Photo 7.8: Health centre 1 – Patient waiting area

Photo 7.9: Health centre 1 – Performing mRDT by a window

Photo 7.10: Health centre 1 – Dispensing area on consultation desk

7.4.1.4. Constance, Health Centre 2

Health centre 2 was located along a dusty, dirt road a fair distance from the local trading centre and main road, Photo 7.11. The health centre building was a rented mud brick building, not a standardised government-issued building, and was in a state of disrepair. The grounds were well maintained, but there was no running water or electricity; water was fetched from a nearby well. There was no laboratory, but at times a midwife attended to perform maternity services. The building was smaller than the standard government-issued or similar rented buildings. Waiting patients queued on the small veranda and continued into the consultation room just inside the main door. Patients sat on wooden benches around the health worker's consultation desk, and as a result, there was no privacy during consultations, Photo 7.12. The consultation room was hot and stuffy, with few windows and no ventilation. Health promotion posters were falling off the crumbly surface of the exposed mud brick and dusty walls, Photo 7.13. mRDTs were done in a separate room from the consultations; after testing, patients returned to the consultation desk where drugs were dispensed. There were a few wooden cupboards in the testing room to store drugs. There were two health workers stationed at the health centre, although one was often sick leaving the in-charge, Constance, to work on her own.

Photo 7.11: Health centre 2 – Dirt road leading to health centre

Photo 7.12: Health centre 2 – Consultation room

Photo 7.13: Health centre 2 – Posters on brick wall

7.4.2. Introduction to cases

The exploration of the cases includes descriptions of the health centre and health workers' experiences noting that at the local level, narratives shifted between these two elements seamlessly. Health workers' narratives were underpinned by intertwining processes and relationships through which they described locating themselves not just geographically, but socially and temporally in relation to the research project and their local circumstances. Drawing on the concept of socio-spatial locations (Shoveller et al. 2007) provides a frame with which to explore health workers' narratives as the intersection of social processes, settings and broader social structures. This concept acknowledges that everyday practices emerge from experiences of time, space and place and seeks to understand the relationship between material and immaterial features in everyday surroundings (Shoveller et al. 2007). Health workers' socio-spatial locations were articulated in two key ways – temporally and structurally. Thus, the results are presented in two sections to illustrate the points of divergence and converge among these socio-spatial locations. First, socio-spatial locations are presented as a function of time – health workers' narratives of past, present and future experiences in relation to the research project. Second, socio-spatial locations are

presented as a function of social structures – health workers' narratives of different social hierarchies in relation to the research project.

7.4.3. Finding locations in time

In this section, each of the four cases explores how the health workers described themselves, the health centre, and as a consequence the research project, through a temporal location – past, present or future. Each describes a different narrative of health workers' temporal locations shaping how the research project became part of their everyday realities in divergent and unexpected ways. Two components of the research project are highlighted – the introduction of mRDTs and the PRIME trial and PROCESS study evaluation activities – as an illustration of how different processes of integration emerged. Although from the formal description of the intervention and study protocols these activities were assumed to have a clear and singular purpose – diagnosis and treatment of fevers and data collection – they took on additional roles and values as they became enmeshed in health workers' everyday lives.

7.4.3.1. Drawing on the past

The first two cases, Mark and Halima, illustrate how past experiences became central in their everyday practice of engaging with the research project.

<u>Mark, Health Centre 10</u>

Mark, a health worker close to retirement, experienced a long history of health system challenges with few resolutions during his tenure. Uganda's health system, like that of many low resource settings, remains poorly functioning. Decades of failed economic and social policies, coupled with intermittent NGO and research programmes, have left gaps in availability of infrastructure, resources, salary, and personnel (Chandler, Kizito, et al. 2013). Mark cited the lasting impact of these past and ongoing challenges including heavy workload due to insufficient staffing, low salary, poor health centre infrastructure, and inadequate resources. Mark's description that his job is good 'and there is no problem apart from maybe the problem of Uganda', made explicit his exasperation with these entrenched economic, social and political issues plaguing the country. As a result, Mark described feelings of hopelessness coupled with being dissatisfied in his role as a health worker, for example questioning the purpose of 'wasting time doing work which cannot pay'.

Mark's feelings of hopelessness and dissatisfaction underscored his engagement with the research project. Mark expressed exasperation at the introduction of mRDTs as he was already facing challenges including managing a heavy workload without support or appropriate compensation. An exasperation compounded by other additional activities introduced by the government which Mark was required to do including mobilization activities in the community to encourage participation in polio immunization and home visits to distribute zinc and deworming tablets. However, despite the additional workload from increased volume and time spent with patients, Mark nevertheless decided to use the mRDTs for all patients with fever because, as he described:

> *'Patients love this system which you (the research project) have brought to the health centre … If the mRDT will go away, people will again not be happy treated like that'. (Mark)*

mRDTs thereby became a means to provide a valued service to patients against a backdrop of health centre challenges. Moreover, Mark described trusting and following the results of the mRDTs as they appeared to offer information and immediate feedback in a system where Mark felt otherwise alone and neglected. For Mark, the use of mRDTs became more than the implementation of a diagnostic tool, rather they appeared to give him a sense of agency against the intractable challenges at the health centre.

Where mRDTs provided a counterpoint to Mark's longstanding frustrations, the research project evaluation activities themselves became an attempt to resolve some of his challenges. Over the course of the research project, Mark developed an increasingly close relationship with the research project team. The monthly health centre data collection visits became an opportunity for Mark to discuss his on-going challenges such as lack of clean water, an infestation of bats in the ceiling, a heavy workload, and altercations with local politicians. Over time, as the research team continued to enquire about challenges, the monthly visits evolved into an outlet for Mark's grievances. The responsiveness and attentiveness of the research project was in stark contrast to Mark's enduring distrust and frustrations. Eventually, Mark asked for the research project to act on behalf of the health centre and communicate his challenges to the government and other organisations in hopes of identifying resolutions.

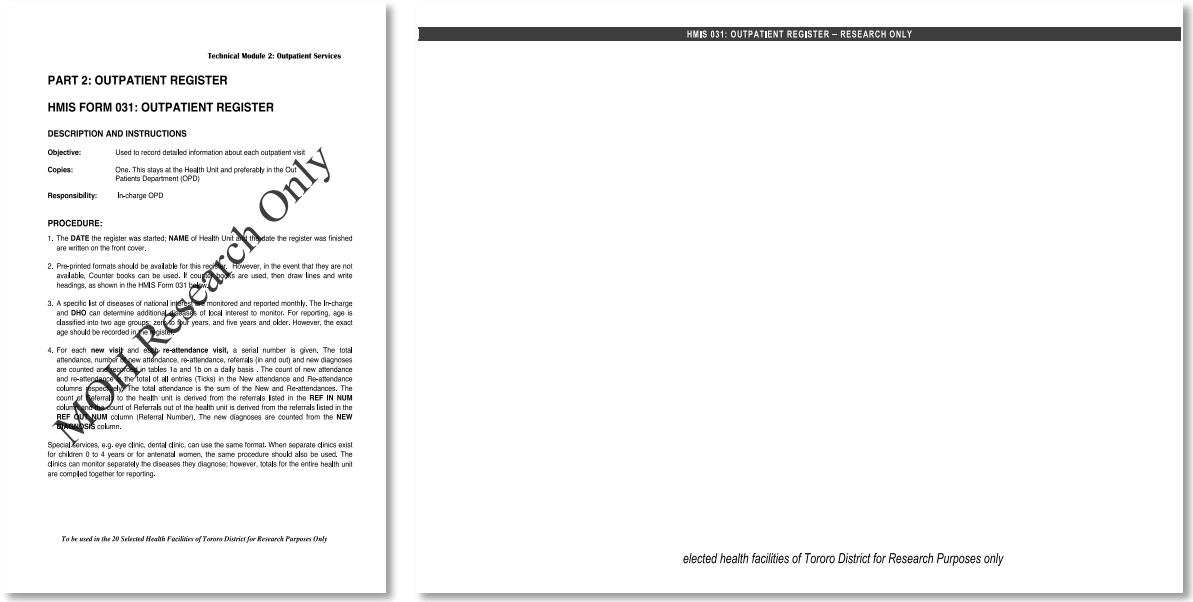
Halima, Health Centre 9

Like Mark, Halima also described feelings of hopelessness and long-term consequences when reflecting on her experiences with repeated failed government policies contributing to the dysfunction of the health system 'from the time (she) started doing (her) job'. Like Mark's reference to 'the problem of Uganda', Halima also described the challenges of being a civil servant highlighting the entrenched political and economic structural challenges affecting the state. For example, Halima described how persistent low salary has meant prioritising family expenses over funding further training which had severely limited her career progression. Her lack of recourse against accusations and bullying by local politicians were also witnessed during visits to the health centre. However, rather than just feeling hopeless and apathetic, Halima described persevering and taking pride in her role as a civil servant seeking motivation from her professional identity. In so doing, she attempted to draw on the intrinsic personal benefits of serving patients to compensate for failures. However, these feelings of perseverance and resilience never entirely overcame her sense of past frustrations:

> *"I would say the only thing that motivates me to continue doing my work is because it is my profession and I would also love to help people who are sick and seek care and I see them improve, but there are so many others that make me be dissatisfied."*

However, unlike Mark, Halima was apprehensive about engaging with mRDTs because she was concerned that they would not be sustained after the research project. This fear appeared to be reproduced from the simple fact that the health centre registers in which the trial required health workers to record patient information and mRDT results were watermarked with 'For research purposes only', Photo 7.14. Likewise, the sporadic supply of mRDTs to health centres by the government throughout the implementation of the research project may have signalled to Halima that supply of mRDTs may not continue once the research project ended in line with the number of other activities taking place intermittently at the health centre and in the community by research, development and NGO groups such as the Centres for Disease control, the United States aid agency (USAID), Plan International, and Marie Stopes. As a result, mRDTs were cast as yet another initiative that the government was unlikely to sustain into the future as part of a health worker's routine duties of care.

Photo 7.14: ‘For research purposes only’ health centre patient register



Technical Module 2: Outpatient Services

PART 2: OUTPATIENT REGISTER

HMIS FORM 031: OUTPATIENT REGISTER

DESCRIPTION AND INSTRUCTIONS

Objective: Used to record detailed information about each outpatient visit

Copies: One. This stays at the Health Unit and preferably in the Out Patients Department (OPD)

Responsibility: In-charge OPD

PROCEDURE:

1. The **DATE** the register was started; **NAME** of Health Unit and the date the register was finished are written on the front cover.

2. Pre-printed formats should be available for this register. However, in the event that they are not available, Counter books can be used. If counter books are used, then draw lines and write headings, as shown in the HMIS Form 031 (overleaf).

3. A specific list of diseases of national interest are monitored and reported monthly. The In-charge and **DHO** can determine additional diseases of local interest to monitor. For reporting, age is classified into two age groups; zero to 4 years, and five years and older. However, the exact age should be recorded in the register.

4. For each **new visit** and each **re-attendance visit**, a serial number is given. The total attendance, number of new attendance, re-attendance, referrals (in and out) and new diagnoses are counted and recorded on tables 1a and 1b on a daily basis . The count of new attendance and re-attendance is the total of all entries (Ticks) in the New attendance and Re-attendance columns respectively. The total attendance is the sum of the New and Re-attendances. The count of referrals to the health unit is derived from the referrals listed in the **REF IN NUM** column. The count of Referrals out of the health unit is derived from the referrals listed in the **REF OUT NUM** column (Referral Number). The new diagnoses are counted from the **NEW DIAGNOSIS** column.

Special services, e.g. eye clinic, dental clinic, can use the same format. When separate clinics exist for children 0 to 4 years or for antenatal women, the same procedure should also be used. The clinics can monitor separately the diseases they diagnose; however, totals for the entire health unit are compiled together for reporting.

To be used in the 20 Selected Health Facilities of Tororo District for Research Purposes Only

Not to be used for Research Only

HMIS 031: OUTPATIENT REGISTER – RESEARCH ONLY

elected health facilities of Tororo District for Research Purposes only

Halima was also dubious about the validity of mRDT results for identifying malaria as the cause of fever. She nevertheless described using them as a way to support her challenges with negotiating results of diagnoses with patients. The mRDT appeared an objective ally in detecting ‘fake patients’ who attended the health centre in order to collect drugs on behalf of a sick person at home. However, when the workload became too heavy, Halima said she would forego the use of mRDTs and prioritise what she described as the official health worker tasks of ‘recording, providing treatments and injections’. mRDTs, associated with her past experiences of unsupported and unsustainable government policies, appeared to be adopted simply as another tool to confirm her professional identity in the present and persevere with providing care in the midst of adversity.

7.4.3.2. Engaging with the present

<u>Godfrey, Health Centre 1</u>

This case, with few references to the past or the future, presents a temporal location strongly rooted in present opportunities. Godfrey already had high status and respect in the community due in part to him being male, older and a health worker serving the community in which he lived. He appeared motivated by this status which he described having obtained through service and sacrifice to the community. He described the various ways in which he went beyond the expectations of his role including not taking leave for a

year, juggling the pressures of keeping the health centre open with needing to attend community events, and keeping-up with an expanding workload despite it making him feel unwell. Yet he also appeared to enjoy the status this hard work manifested, for example taking pride when he was praised by patients and notable community members, and citing increased patient attendance as evidence of his commitment. These immediate benefits appeared valuable to Godfrey – they reinforced his professional identify of 'being a nurse' and manifested benefits and status beyond the health centre. Godfrey described being satisfied in his role drawing on his ongoing work which were not marred with accounts of challenges from the past.

Like Mark, Godfrey also noted the paradox that mRDTs present – that they are liked by patients, but have negative impacts on workload. Godfrey, however, constructed mRDTs as part of his service to patients and integrated mRDTs into his practice regardless of the personal cost:

> *"That one (using mRDTs) make me feel tired though I please them (the patients), it makes me to become even sick because you over work the the head. That one makes me to become very tired. Though I try to please the patient, I get more more tiredness." (Godfrey)*

Despite the work required, mRDTs appeared to provide yet another an opportunity for Godfrey to prove his ongoing efforts. He appeared motivated by the opportunity to maximise his status and secure benefits realised from the carrying the 'heavy burden' which mRDTs manifested. The mRDTs, coupled with the other research and NGO activities taking place at the health centre, became part of Godfrey's narrative of obligation and reward, and a resource which reinforced his status and position at the health centre, and by extension, with the community.

7.4.3.3. Imagining the future

Constance, Health Centre 2

In this final case, the temporal location emerged as an imagined future where beneficial opportunities were almost palpable. Constance was stationed at a health centre where, at the time of the research project, a new standard-issue health centre building was being constructed by the government to replace the existing rented mud brick building.

Constance hoped that this official building would provide legitimacy and the physical space to become 'more' and enact the health worker qualities she perceived as valuable:

> *"Even the the health centre I know when we move to this place here we are going to be more more than we are here because this place here also you cannot place things in a right way there. I have known that each part each things has to have its place so at least from here we are not being going to be like the same … eeeh, we are going to be more organised there."*

Constance also described that 'being chosen' to participate in the research project was also an important source of confidence and motivation. For health workers like her, participation in research or NGO programmes can bestow a range of benefits and opportunities. The material objects provided (for example drugs and supplies, equipment, infrastructure t-shirts, notebooks), the virtue of 'being chosen', and access to organisations serve to raise the health centre's profile and the health worker's agency. Constance believed the government and others would recognise her chosen status and reward good performance similar to other health centres in the area that had been improved by research and NGO groups. She described being 'very satisfied' with her job. Taken together, the new building, 'being chosen', and recognition of performance were demonstrations to Constance of an imagined future of possibilities.

Constance believed that upgrading the health centre from a level II to a level III was a corollary of increased patient attendance due to good use of mRDTs. As such, Constance readily engaged with mRDTs, describing that they have been 'tremendously useful' and were used on all patients with fever. Constance recognised the immediate benefits of increased confidence and power that mRDTs afforded. Constance described that by using mRDTs she was performing the same clinical skills as the doctors leading the mRDT training – powerful and prestigious skills for a nursing assistant with minimal clinical training. Unlike the other health workers presented here, Constance was guarded in any unfavourable descriptions of mRDTs and their impact on her and the health centre. Perhaps this was because the benefits of using mRDTs far outweighed any negative impacts, or because Constance recognised the importance of maintaining the appearance of a good and obliging performance as a health worker in order to secure favour and future opportunities. For Constance, mRDTs supported her current and future motivations and became embedded in her identity and clinical practice. As Constance noted, 'they (mRDTs) have become part of us'.

From Constance's perspective, the research project evaluation activities provided an opportunity for her to demonstrate good performance to outsiders. For example, Constance sought information from a patient who had participated in an evaluation activity in order to know what was being evaluated and mould her consultation activities in response. Similarly, Constance described the research team as 'testing' her performance in line with the research project's expectations:

> *"Also they were they came they came also to see what we are doing and also to interview us on the test we did. … And also the after testing they also go and test to see whether our test was right."*

The health centre patient register from which the research project extracted information on a monthly basis also became a means through which Constance demonstrated her competence to people in authority. As she described, 'those people of of the district, … the researchers, and … other bodies', are the people who had the power to grant her and the health centre benefits such as upgrading or being selected to participate in research. Thus, for Constance, the research project became an opportunity to position herself and the health centre as deserving of recognition and benefits:

> *"You know right now because you have given us much work than what we had, so at least you tell, you tell the boss that, 'Aaa the the health centre needs at least upgrade, to be upgraded to certain level'."*

The research project, merging with Constance's everyday realities, became an ally in securing her future hopes.

7.4.3.4. Summary

The four cases demonstrate how health workers described aspects of their everyday realities in relation to where they placed themselves in time – ranging from embittered recollections of health system challenges to capitalising on present opportunities and imagining future benefits. More than simply a feature of their everyday realities, temporal locations became enmeshed with how the health workers enacted different aspects of the research project, influencing what was missed, discarded, attempted or embedded. mRDTs, a new technology, featured across all narratives, but health workers' engagements with them were contingent on emotional and practical justifications, transforming them into something other than their assumed purpose for the PRIME intervention. Interactions

with the research project became part of a wider narrative – a configuration of relationships manifesting expectations of frustration, status or recognition. Health workers shaped the elements of their everyday realities such that the formal description of the PRIME intervention was barely represented within their narratives.

7.4.4. Finding locations in social structures

This section explores the health workers finding ways to locate themselves not through the narrative of time, but in reference to two social structures – the national structure of policies determining health worker roles, and the community structure of personal, patient and community relations and expectations. The same four cases are presented together to illustrate the common tensions experienced as the health workers navigated the different sets of relationships in their everyday lives. Their experiences of two drug supply systems – the national system and the PRIME supply system – are highlighted to demonstrate the shifting and reconfiguring of the research project as it interacted with existing social structures.

7.4.4.1.1. Contrast between social structures

In Uganda, health workers appear to occupy contrasting positions in the national and community structures. From the national perspective, health workers stationed at health centre IIs and IIIs are socially and professionally at the bottom of the hierarchy. These lower level health centres are known to be politically and economically disadvantaged, especially compared to higher level health centre IVs and hospitals. Like many low-resource settings with a command and control culture, such hierarchies are strongly rooted and perpetuate power imbalances throughout the health system (Blaise and Kegels 2004). As one health worker explained, being transferred from a health centre IV to a more prestigious position but in a lower level health centre III, was considered a 'demotion'. Position within the hierarchy is an important lever of social capital and status. In contrast, health workers' professional role and activities in managing most of the community's primary health care needs engenders health workers to a high social status within the community. As health workers described, this status provides them with opportunities to reinforce their social capital by being an honourable guests at community functions or a representative on community committees.

In consideration of these two structures – national and community – health workers appeared to prioritise their location in the latter. They described the most important aspect of their job was to provide the correct diagnosis and treatment to patients. By doing so, they described being able to address the community's problems by 'curing' or 'healing' patients. These acts of care are seen as benevolent and specialised acts which go beyond the notion of simply providing treatment and point to the importance and power health workers ascribed to their role. Performing good diagnosis and treatment was therefore coupled with descriptions of listening to patients, providing information and counselling, and extending care to include social services beyond health workers' clinical remit:

> *"They (patients) are sick and they are not only sick of diseases but they also have other surrounding social problems which we have to take care of." (Halima)*

Health workers recognised that these practices helped to make patients feel comfortable with the services while at the same time contributed to manifesting their personal motivations for power, status and recognition. As a result, health workers located themselves and the health centre within the opportunities of the local community structure.

While health workers oriented their priorities towards managing their location in the community system, having to negotiate their inferior position in the national system hierarchy resulted in unresolvable tensions. Health workers described challenges in dealing with political decisions and bureaucratic processes which prevented access to much needed health centre resources. For example, health centre volunteers were described as 'very important' in supporting activities such as recording patient information, dispensing medication, and general cleaning and administrative activities. However, just prior to implementing the intervention, the district health administration removed volunteers stationed at health centres leaving health workers without any support. In addition, health workers described that the national policy to provide a small cash 'primary health care fund' to support operational activities at the health centre was insufficient for their local needs and protracted bureaucratic processes further prevented them from accessing it:

> *"January, Feb and March that money came but now I don't have the signatory who can go and pick it because I am I should write what we call requisition through the sub county chief to the sub county chief then through my immediate in-charge, which is which was Mr. Okama in the health centre III, then they are the one to go and pick those that money. But the health the in-charge of health centre III is not around since those month I don't know where he is." (Godfrey)*

The health workers all described trying to resolve these challenges by raising them with local officials, but invariably, their attempts were futile and did not yield solutions. The government's culpability and unresponsiveness to health workers' concerns and health centre challenges was seen as a betrayal and an intractable position:

> *"It has taken long, maybe I can call it deceiving language that we are going to repair this house [health centre]. It has taken almost 3 years. There is no way out. The officers come, they check, they say 'we are coming', and there is nothing done." (Mark)*

Threats to health workers' position and inability to operate in the community structure because they lacked agency and power in the national structure appeared demoralising and paralysing.

7.4.4.1.2. Contrast between supply systems

The national supply of drugs to health centres is highlighted as a specific illustration of health workers' frustrations in negotiating their structural locations. The government supply of essential medicines to health centres, especially antimalarials, improved nation-wide during the time of the research project. This was due to the implementation of a 'push' supply system which provided pre-defined kits of drugs and resources to health centres on a quarterly basis – see also Bukuluki et al (2013). While health workers appreciated the improved supply, new challenges emerged. The introduction of this strategy was seen as undermining health workers' independence and the government's trust in their ability to forecast or order drugs as they were no longer responsible for performing these tasks. Further, with the predefined kits, health centres received unnecessary drugs and insufficient supply of those that were required. While the availability of antimalarials improved, there were still stock-outs of antibiotics, analgesics and other essential medicines. As a result of the new national push supply system, health workers described feelings of powerlessness to resolve stock-outs and meet the specific needs of their community:

> *"We cannot go and request for supplementary [drugs], so what you are given you use it [the drug], and when it gets finished then you sit. But formerly when they were giving us money we make our request equivalent to the amount they give us … Now as per now there is no way out. When it [the drug] is finished, it is finished." (Constance)*

The push supply system also perpetuated a poor image of health workers in the community. The government and local politicians often accused health workers of stealing drugs for private retail – see for example reports in the news media Kiwanuka (2010), Monitor Reporter (2010), Oketch (2010), and Olupot (2009). The public nature of the national drug supply logistics sustained these accusations. For example, the arrival of trucks delivering drug kits signalled to the community that the health centre was re-stocked. So, when community members were not given drugs at their health centre visit, perhaps because the required drug was not supplied or had run out, the health workers described being accused of withholding the drugs for private gain. Similarly, according to the new supply policy, when health workers were required to return overstocked drugs to the health sub-district office, the sighting of a health worker transporting drugs was reported to further perpetuate a sense of mistrust:

> *"I get challenges from patients or from the villagers. They say that we sell drugs because … if I carry them [overstocked drugs] to Nagongera [health centre IV], they say 'oho today he has carried box of medicine he is going to sell'." (Godfrey)*

The drug kits and push supply system aptly demonstrated the tensions that arose for health workers between navigating locations in the community structure and the hierarchical and unaccommodating nature of the national system. Increased availability of drugs through the standardised kits supported health workers with treating patients. However, this benefit was counteracted by health workers' feelings of powerlessness, poor image, and inability to negotiate the national system when stock-outs or political interference threatened their priorities within the community.

7.4.4.1.3. PRIME, an inadvertent solution

This final section focuses on the PRIME supply system to demonstrate how health workers variously and unpredictably furnished the research project as a potential solution to overcoming the specific difficulties of the national supply system. The PRIME supply system was designed to provide antimalarials and mRDTs to health centres when supply by the government was inadequate or failed. In coordination with the research project, the PRIME supply system operated under the auspices of its implementing partner, the Infectious Diseases Research Collaboration (IDRC), a prominent research organisation, and the Ministry of Health. Project information forms with IDRC and Ministry of Health logos, a fleet of IDRC branded trucks and motorbikes, and project visits by doctors and expat

researchers had the effect of casting the research project as part of the national system of organisational hierarchies, structured policies, formalised processes, and specific expectations. A health officer at the sub-district level acted as a liaison person and was responsible for gathering stock information from health centres and facilitating delivery of antimalarials and mRDTs from the research project to health centres. In contrast to the government push system, the PRIME supply system operated on-demand – health workers could access antimalarials and mRDTs at any time required. But the distribution system was not formally evaluated as part of the trial as it was not intended to inform scale-up or implementation elsewhere. However, it was the distribution system itself that came to represent and address the contradictions health workers faced when having to navigate their positions within the two social structures.

The PRIME supply system appeared to operate within a network of human, material and structural elements which promoted health workers' engagement, trust and cooperation. Across the four cases, the PRIME supply system re-empowered health workers to take an active role in securing antimalarials and mRDTs for their health centres. Health workers praised being able to request specific quantities of drugs and that the drugs came in a timely manner with no additional transportation costs. With the PRIME supply system, health workers described developing a 'comfortable relationship' with the liaison person. Regular phone calls from the liaison person to check on stock levels, forecast needs, and place orders for drugs transformed supply logistics into a responsive relationship-based service that could be easily navigated:

> *"It makes also me also have enough time, I just expect when it's not there I just ring that Aaa, it's getting over. So not like those those days I have to report, make requisitions and so forth, make reorder forms, all those other things. So at least things have become a bit easy." (Constance)*

Likewise, health workers appreciated the transparent ordering and delivery note system which built trust and ensured both parties in the system were held accountable:

> *"The useful thing is that you just you just write what you are seeing or what you were given. So you, it is good that you can't forge or they can't forge something from there because it's written there, the amount you are to get that is what you're to use." (Mark)*

While the top-down national push supply system did not appear to trust or require health workers' involvement, in the PRIME supply system health workers felt that their active role

was necessary. More than just logistical conveniences, the PRIME supply system came to represent an alternative way of interacting with, and being treated by, an agent of the national system.

7.4.4.1.4. Summary

Health workers described experiences navigating the community and national structures, revealing inherent contradictions between the socio-spatial locations. Whereas the national structure threatened health workers' central importance in the community system, the PRIME supply system reinstated it. The research project, although positioned as part of the national system, endorsed the behaviours that aligned with health workers' motivations and priorities – establishing and managing relationships, autonomy to access resources, transparent and trustworthy mechanisms, responsive service, and cooperative problem solving. As a result, health workers engaged with a process that supported performance of what they considered was their most important task – diagnosing and treating patients – without the negative consequences of having to operate within a system which undermined their power and authority. The PRIME supply system supported health workers' priority to the community, and as a result, came to be seen as a partial solution to the challenges experienced with the national system. Unbeknownst to the trial, the PRIME supply system merged with health workers' everyday realities to address a set of challenges and barriers that were not anticipated when the intervention was designed.

7.5. Discussion

By focusing on four cases, this chapter took an unconventional approach to examining context as relational by zooming in on health workers' everyday realities. This approach reveals how health workers' socio-spatial locations influenced, and were influenced by, the research project. Health workers' temporal locations shaped how the research project emerged for each of them – a representative for action, an affirmation of professional identity, a means of maintaining power and status, and an opportunity for promotion. Additionally, exploring health workers' locations in the community revealed sources of tensions when interacting with the national structures. Likewise, with its liminal position between the community and national structures, the PRIME supply system became a potential means of navigating the contradictions between the different relationships and expectations of the two. These findings demonstrate the dynamic interactions between

socio-spatial locations and the research project and the ensuing difficulty in identifying the original outline of the intervention within and across cases once it merges with everyday realities. The presentation of findings in this way was a deliberate choice so as to not readily invoke the 'levels of social organisation' approach to conceptualising context common in the intervention research and development literature. These findings, therefore, run contrary to the received view in much of the health interventions literature which promotes context as merely the local environment for a standardly applied intervention. Acknowledging these different perspectives calls for more reflection on how 'context' is constructed and applied, and its role in the evaluation of complex interventions that aim to improve delivery of health services.

The concept of socio-spatial locations drawn on in this chapter foregrounds notions of space, time and place, but is not limited by reductionist definitions that might consider only physical locations or linear timescale (Shoveller et al. 2007). Health workers' temporal locations enmeshed into present realities, while invisible hierarchical social systems manifested in everyday challenges. In this way, this influence of socio-spatial locations only became apparent through health workers' accounts of their involvement with the research project. At the same time, material places and spaces also played an important role. The people, infrastructure, training materials, medical commodities, research vehicles, and so forth, were all part of the ways in which health workers attempted to situate themselves and makes sense of their everyday realities. Thus, socio-spatial locations emerge as an assemblage of health workers' immaterial and material realities of which the research project – both intervention and evaluation activities – is a part. This idea aligns with the proposal by Hansen and Tjørnhøj-Thomsen (2015) that context can be considered a social process of composition and joining together of practices and surroundings into meaningfulness. As health workers fashioned the research project into their everyday practices, the boundaries between the intervention and 'context' blur such that one is not distinguishable from the other, and trying to separate them becomes irrelevant. As the categories of 'context' and 'intervention' disappear, health workers' everyday interactions are foregrounded as they draw on a variety of resources and relationships in the course of providing care at their health centres.

In health intervention research, participants are often reified into a homogenous group and assumed to act in a standardised way to a well-defined intervention. This view, however, masks the social embeddedness that underpins how interventions are produced (Cohn, 2014). As Rod and colleagues (2014) describe, interventions are not just the material things described in protocols and training manuals, but also the social practices that imbue these things with meaning through a cycle of exchange between intervention participants, researchers and the material environment. Interventions emerge out of the actions and interactions of autonomous individuals. In this study, health workers, acting as autonomous agents, recognised the benefits of participating in a standardised research project because of the predictability, frequency and ease of access to research project resources and staff which the research project provided as per the study protocols and standard operating procedures. These interactions became meaningful as health workers adapted the research project to their own desires for autonomy, responsiveness and trusting relationships within the national system hierarchy. What emerged in this examination of the research project was a partial solution to the challenges experienced with the national system and was unpredictable. This was not because the intervention was poorly defined or theorised, but because interventions will inevitably take on different forms through the course of social exchanges that produce them. Similar processes of local tailoring of the intervention have been documented elsewhere and deemed necessary in order to produce the intervention (Belaid and Ridde 2014; Hawe, Riley, et al. 2015; Hawe et al. 2009; Wells et al. 2012). Recognising this local tailoring of interventions requires making an active decision to expect unpredictability as an integral component of the change process.

Exploring cases from health workers' perspectives revealed everyday practices that might otherwise not have been foregrounded. The accepted view within the health interventions literature promoted by recent guidance conceives of context as a static background external to the intervention, or as enumerable factors evenly distributed among clusters through randomisation (Moore et al. 2015). Context then becomes a generic list of 'usual suspects' influencing intervention implementation, uptake and outcomes. For example, a recent literature review of contextual factors affecting interventions to improve health worker performance included supply stock-outs, inadequate supervision or management, staffing challenges including shortages, lack of skills and motivation, and poor relationships with local leadership (Blacklock et al. 2016). However, in this chapter, examining these

factors ‘close up’ as part of the way health workers project and make sense of their everyday realities invites a rethinking of the concept of context. Relative to the two research components examined, factors such as ‘poor health centre infrastructure’, ‘lack of resources’ or ‘inadequate support’ became intrinsic to how health workers integrated the research project components into their practices at the health centre and came to have quite different influence on health worker behaviours, practices and motivations in each case. From this perspective, what might be taken to be a contextual ‘factor’ that is considered stable and generic, emerges as active and contingent on a network of human, material and structural elements.

As Strathern (2004) describes, exploring phenomena from different perspectives and scales shapes what can be known about them and what is therefore considered relevant. She specifies that complexity can be perceived at any scale of observation provided the observer chooses to explore the detail at that level. Thus, how researchers choose to look at and construct ‘context’ in the evaluation of complex interventions is a decision with tangible implications. The decision implied in the health interventions literature is taken from a perspective where context appears as a smooth terrain, stable and similar across sites. Settings, features or actors are often constructed unproblematically in trials which are focused on evaluating pre-defined outcomes through an objective scientific method in order to generalise effects across places (Victora et al. 2005). This decision and its implications for what can be known about interventions aiming to improve health services is rarely questioned – namely that it obscures the detail of the political, economic and social realities that shape provision of care and access to health services (Adams 2013). Yet this chapter has demonstrated how exploring the detail at a local level reveals a terrain that can be realised as quite bumpy and heterogeneous at many levels. Therefore, how context is observed and perceived to matter, and gets addressed and evaluated in complex health interventions, is relative to the scale of inquiry applied and the categories used to construct ‘context’, ‘intervention’, ‘participants’ and ‘evaluation’.

The emergence of frameworks and tools for exploring the context and implementation of interventions signals an important move towards acknowledging and interrogating the different dimensions of how and why interventions produce effects (Bergström et al. 2015; Chaudoir, Dugan, and Barr 2013; Grant et al. 2013; Luoto et al. 2014). However, these

frameworks with validated domains, pre-defined questions and specific criteria, are based on the implicit, and therefore rarely questioned, assumption of context as a stable factor. The result is a missed opportunity to interrogate how these frameworks may be concealing relevant details, and to promote different conceptualisations of context that explore the more fluid and complex interactions emerging from the social realities that produce interventions. The details contained in these social realities including the local tailoring of interventions, the navigation of social hierarchies, and the relationships between participants, researchers, and non-human actors may be both productive and practical. By resisting the current motivation in interventions research to develop a single account of why interventions work, or not, alternative approaches to conceptualising context can instead be a means through which different aspects of the intervention and evaluation activities might come under scrutiny. This can provide alternative accounts and identify new insights to inform the design of more resilient and relevant interventions.

This chapter presented two different approaches to conceptualising context – one exploring contextual factors by levels of social organisation and the other exploring context as relational by zooming in on everyday realities. Both are informed by social scientific perspectives for understanding how context might influence interventions and therefore provided gains over more quantitatively oriented approaches. Both, for example, identified the social embeddedness of interventions and the important social exchanges between a variety of actors. The 'levels of social organisation' approach was productive in that it provided an interpretation of the intervention that aligned to wider explanations of disparities in health and access to care. Namely, that the intervention was unable to address systemic political challenges affecting health worker motivation, power imbalances affecting access to health centre resources, and a broad range of community level determinants necessary to enable improved local access to better health care. When interventions are evaluated within this multilevel approach to framing context, however, there is a risk that they will continue to describe a lack of impact because the determinants of ill health remain too deeply embedded for meaningful and sustainable action by relatively small disease-specific interventions (Hawe 2015b).

Alternatively, the approach of zooming in and conceptualising context as relational offered a reframing of the interaction between context and the intervention and in so doing

foregrounded new ideas. While narrow in its focus on the everyday realities of health workers, the analysis was still situated within and drew on knowledge about the wider social and political setting. In this way, it was able to reconfigure the role of different human and non-human actors in this setting and the relationships between them producing productive findings. It foregrounded the agency of a variety of actors, including research project team members and local politicians, as well as mRDTs, health centre buildings, and research data collection tools, in shaping the way health workers enacted the intervention. Likewise, it uncovered an unpredictable, yet useful role of the research project in becoming a partial solution to strained relationships throughout the health system. While this approach is different from the more common approach based on factors organised by levels of social organisation, its productive potential is in providing alternative arrangements of the social to uncover new ideas about where and how we might intervene to improve health and access to care. To this end, this chapter offers one way of reframing context recognising that it will nevertheless continue to shift in light of its importance for complex interventions. As such, this chapter encourages researchers to reflect on and report their implicit or active decisions taken to define how 'context matters' and to consider how alternative approaches might be productive in shaping their approach to investigating context and the interpretations produced as a result.

7.6. Limitations

Any research involving interviews and participant observation may be affected by the issue of social desirability response bias, or the possibility that respondents will act or respond in a way that they feel is socially acceptable or desired by the interviewer/observer (Denzin and Lincoln 2011). It is possible that the health workers may have refrained from being overly critical of the PRIME intervention, may have been overly emphatic in the descriptions of their challenges in hopes to secure future benefits from the study team, or may have chosen not to expose their own personal or professional shortcomings in relation to their provision of care. However, the combination of data sources, the multiple interactions with the health workers, and the length of time over which the study took place mitigate this concern. These activities served to build relationships and trust between the health workers and study team which are believed to have encouraged health workers to report honestly and freely, including both positive and negative experiences. Likewise, there was consistency between the various interactions, behaviours, and

incidents that were reported in the interviews, witnessed in various observations, and collected in the context record. Together, this suggests that data sources are not overly affected by the social desirability response bias.

That the analysis was limited to four of ten health centres participating in the PRIME intervention may be seen as another limitation of the study. However, the objective was not to generalise interpretations of the intervention itself, but rather to examine the nature of the context concept. The cases served as instruments to explore convergent and divergent experiences between context, the intervention, the health workers and the health centres. The interpretation of context which emerged is argued to represent a particular relationship between these elements mirrored in wider social structures. It is argued therefore that examining four cases was sufficient for arriving at an interpretation of context as socially contingent and heterogeneous which can be abstracted as a more general interpretation of the context concept.

A final limitation to this analysis may be a lack of expanded engagement with the notion of temporality by not integrating an analysis of the history of clinical care and health service provision in Uganda at local and national levels alongside health workers' experiences. This approach may have provided a more fulsome interpretation of how aspects of temporality and social space as functions of immaterial context influenced the enactment of the research project and with what effect. Indeed, as Strathern (2004) argues, there is detail in every scale of observation. Zooming out to explore the intervention alongside a wider historical and social lens, but engaging closely with the detail at that scale, may have enhanced interpretation of the interaction and integration of the research project into everyday life.

CHAPTER 8. Discussion

8.1. Introduction

This concluding chapter seeks to draw together the processes and findings of the methodological exercises implemented in this thesis – examination of intervention design, evaluation of primary outcomes, assessment of causal mechanisms, and evaluation of context. Through implementing these exercises, I aimed to examine methodological approaches used in complex interventions research drawing on the example of the PRIME intervention. In each chapter, I have already provided a discussion on the process of applying each methodology and the conceptual and methodological contributions emerging as a result. I will first briefly summarise these discussions and their key contributions and also discuss my more practical experiences from across the four chapters and how they might inform future work on complex interventions research. Next, I will examine the processes through which the different methodologies attempted to account for complexity drawing out the points of connection between the methodologies and the evidence they produce, as well points where particular practices or interpretations may be contested. In so doing, I will examine the limitations of the current guidance for complex interventions research and the possible consequences in global health research. From here, I will consider the overall findings of this thesis in relation to the continued relevance of the 'what works' framework suggesting new directions for better intervention design and evaluation in global health. Moving on from the empirical findings of the thesis, I will offer some reflections on the limitations, strengths and reflections on the overall approach to this interdisciplinary thesis. Finally, I will present some concluding statements about what this thesis adds to current debates over methodologies for the design and evaluation of complex interventions in global health.

8.2. Methodological challenges and contributions

Through the research described in this thesis, I examined the processes involved in applying methodological recommendations for the design and evaluation of complex interventions across four areas of investigation – examination of intervention design, evaluation of primary outcomes, assessment of causal mechanisms, and evaluation of context. In each

chapter, I discussed the conceptual and methodological challenges that I encountered in the process of undertaking each methodological exercise. I also discussed the conceptual and methodological contributions emerging as a result. These are summarised in Table 8.1. In this section, I draw together my experiences from across the four chapters suggesting that work necessary in applying the methodological recommendations was more involved than is currently acknowledged in the literature.

Across each of the methodological exercises, I found that translating the purpose for evaluating each area of investigation and its associated methodological approach into an analytical strategy required more time and effort than originally envisaged. While the processes, analyses and investments of time and effort varied across the methodological exercises, there were similarities in the types of activities on which these investments were focused. These included revisiting the literature to recontextualise my evolving interpretation of the concepts underlying the areas of investigation, reconceptualising previously defined understandings of the areas of investigation, testing out different analytical strategies, and discussing concepts and emerging findings with other PRIME intervention team members. The process of working through these different activities was fruitful and contributed significantly to the new conceptual and methodological contributions for each area of investigation.

In drawing together my experiences from across the methodological exercises, I suggest that the current recommendations for intervention design and evaluation cannot be applied 'off the shelf'. Substantial intellectual and resource investments are necessary to operationalise the recommendations into practical methodological strategies. Conducting this work as part of my PhD research invariably allowed the methodological exercises to expand and be more exploratory than might otherwise be expected. However, the heterogeneous conceptualisations in the literature around each area investigated and the relatively few methodological examples suggests that a degree of uncertainty and experimentation will be necessary in 'regular' studies. Indeed, my experiences are similar to others who have remarked on the work necessary to design interventions (Chandler et al. 2016) and conduct comprehensive evaluations (Clarke et al. 2012; Reynolds et al. 2014) suggesting that this phenomenon is likely more commonplace than is currently acknowledged in the literature. However, continued ambivalence about these experiences

risks researchers continuing to apply the MRC guidance and undertake indepth outcome and process evaluations without appreciating and planning for the resources and expertise required. I suggest, therefore, that greater reflection and reporting on the processes of conducting complex interventions research is necessary. A reflexive and transparent reporting of the processes taken and work involved to translate current recommendations into practical methodological strategies may promote increased awareness of the investments of time and expertise necessary. Such information will be beneficial to evaluators looking to the literature for methodological guidance and will also provide evidence to funders to inform allocation of resources for complex interventions research.

Table 8.1 Conceptual and methodological challenges and contributions to complex interventions research

Area of investigation	Conceptual or methodological challenges	Contributions to complex interventions research
Intervention design	– Negotiating the wider social, political, and economic realities relative to the narrow scope necessary to evaluate the intervention in a cRCT – Recognising and accommodating the influence of the shifting study context – Negotiating different epistemological and disciplinary backgrounds of team members requiring the development of both a linear logic model and conceiving the intervention as interactions embedded in social relationships – Identifying and reflecting on insider accounts of how the intervention was constructed	– Designing the interventions are more interactive and demanding than the available evidence and theory suggest – 'Behind the scenes' accounts of the intervention design processes should be included in guidelines for reporting intervention content and their evaluations
Evaluation of primary outcomes	– Disentangling the various contextual and biocultural influences on the appropriateness of the outcome measures – Examining the influence of different statistical and clinical definitions of the usefulness of the outcome measures – Disentangling the different design externalities on the validity of the outcome measures – Examining how features of the cRCT itself may have influences the meaningfulness of outcome measures to different actors	– Outcome measures are shaped by a number of theoretical, statistical and logistical processes and everyday realities which influence the appropriateness, usefulness, validity and meaningfulness of outcomes used to assess intervention effect – Decisions on choice of outcome measures and their relevance relative to the intervention's theory of change, study design and priorities of actors involved should be considered and transparently reported in descriptions of trial outcomes
Assessment of causal mechanisms	– Operationalising the logic model into a format suitable for mediation analysis – Negotiating statistical assumptions with the reality of a complex trial in a complex setting – Interpreting findings in light of violations of statistical assumptions	– The complexity of interventions and their settings makes it challenging to meet the statistical assumptions necessary to make valid causal inferences using mediation analysis – Caution is needed when applying the methodology and interpreting findings – Further engagement with the theoretical literature is necessary in order to design interventions and studies that align with the conventions and procedures of mediation analysis

Continued – **Table 8.1**

Area of investigation	Conceptual or methodological challenges	Contributions to complex interventions research
Evaluation of context	– Recognising an inability to identify contextual factors that are stable across cases – Reconceptualising context as relational to the intervention and to notions of time, space and place – Investigating multiple unpredictable and different effects of the intervention within and across cases	– Examining context at the local level reveals intervention effects in relation to political, economic and social realities that might otherwise be obscured when context is viewed as stable across intervention settings – Different conceptualisations of context will reveal different effects of the intervention; researchers are encouraged to reflect on and report their decisions taken to define, apply and interpret context

8.3. Methodological limits when accounting for complexity

My second observation emerging from across the methodological exercises concerns the ways in which the methodologies employed accounted for complexity and produced evidence about the intervention and its effects. For each methodological exercise, I observed that a number of assumptions, choices and considerations were necessary during implementation and interpretation of the evidence produced. The reflexive process of 'making the familiar strange and strange familiar' was instrumental in arriving at this interpretation both within and across the methodological exercises. Working through each exercise with the intention of paying close attention to the processes and practices involved afforded me the opportunity to examine the assumptions, choices and considerations that may not be surfaced during routine analyses. Despite being 'hidden', or their role in knowledge production not usually considered in such detail, these actions were demonstrated to be influential in making sense of the complexity of the intervention and the setting into which it was implemented. I discussed these actions and their influence on the interpretation of evidence in each chapter; these discussions are synthesised in Table 8.2, Table 8.3, Table 8.4 and Table 8.5.

Here I consider the points of connection and contrast of these actions across the methodological exercises. Although the actions were different across the different methodologies, they all required the inclusion and exclusion of certain data, ideas and interpretations. In so doing, different and partial accounts of the intervention and its effects emerged from each methodological exercise. For example, designing an intervention amenable to evaluation in a cRCT meant that wider social and political challenges interpreted to underlie provision of poor health care could not be addressed by the intervention. The selection of a clinical outcome measure and approaches to its measurement and analysis provided a single measure of intervention effect, but may have been unresponsive to the biocultural dynamic inherent in changing health practices in a dynamic context. Similarly, ordering variables into the operationalised logic model for the mediation analysis required deciding on a single interpretation of the intervention theory of change. These decisions meant that the multiple theories of how the intervention was hypothesised to change were excluded from the analysis. Finally, choosing to zoom in on context and apply a conceptualisation of context as relational meant that local

interpretations of time, space and place were revealed. This analysis, however, meant that it was not possible to identify a theory of how study-wide contextual 'barriers' or 'facilitators' may have influenced the effect of the intervention on hypothesised outcomes, as is recommended in the current guidance.

Table 8.2: Synthesis of learning points from Chapter 4 – Intervention design

Actions considered by taking a reflexive approach	Decisions taken that came into view as a result of reflecting on actions	Impact of decisions on intervention content and design process
– **Refining the intervention**: Intervention had to be multicomponent to meet the challenges of delivering quality health care but also amenable to evaluation in a cRCT, scalable and sustainable	– Focused on intervention components that had the highest likelihood of success and buy-in from stakeholders within the constraints of a focused project	– Deeper social, political, and economic challenges that underlie poor healthcare quality and lack of progress on malaria remained unaddressed
– **Prioritising components**: Stakeholder guidance and buy-in was important to the political success of the trial	– High degree of emphasis placed on stakeholder opinions despite contrary opinions by the research team	– Several activities were removed from consideration as potential intervention components
– **Appraising evidence**: Intervention should be evidence-based using best available evidence from peer-reviewed research	– Considered evidence from peer-reviewed journals, mostly in high income settings, as more legitimate compared to years of experience in the study area by the research team	– Activities that had shown impacts in the study area, were not corroborated in the available literature and were removed from consideration
– **Readjusting assumptions**: Piloting was an important step of the research design process	– Piloting had an important influence and served to readjust our assumptions about the capacity of the health workers in the study area	– Final intervention package covered less objectives than planned based on formative research and intervention goals
– **Shifting context**: Intervention design had to adapt to changes in the study area	– Continually shifting study context was challenging to align with the standardisation necessary for an intervention evaluated in a cRCT	– Standardised the structure of the intervention, but kept the learning points adaptable to changes in the local context
– **Negotiating epistemologies**: Diverse team from disciplinary backgrounds needed to assist with different intervention components	– An interdisciplinary approach was necessary to align different perspectives into a comprehensive understanding of the intervention and how it would function	– Developed two interpretations of the intervention – the logic model representing the intervention as discrete components leading to predefined measurable outcomes and also the intervention conceived as a series of interactions embedded in social relationships through which its meaning would emerge

Table 8.3: Synthesis of learning points from Chapter 5 – Evaluation of primary outcomes

Assumptions and actions revealed by taking a reflexive approach	Challenges that come into view once assumptions are recognised	Impact of assumptions on interpretation of the evidence
– **Outcome specificity**: Anaemia outcome chosen because it is an accepted proxy indicator to measure the impact of malaria control programmes on health outcomes of children	– Malaria landscape in Tororo was more dynamic than previously understood	– Anaemia may have lacked specificity for measuring changes in malaria-related morbidity influencing interpretation of the effect of the intervention
– **Outcome appropriateness**: Anaemia and parasitaemia outcomes represented the intervention change at health centres and in communities	– Study context was a complex 'biocultural dynamic' wherein social practices and physiological responses interacted with each other in emergent and contingent ways	– Outcomes may not have been responsive to, or appropriate for, capturing the complexities inherent in changing health practices in a dynamic context
– **Outcome interpretability**: Anaemia outcome is a more meaningful and interpretable outcome versus a continuous haemoglobin outcome	– Dichotomised anaemia outcome may have created the illusion of a difference in prevalence of anaemia – Dichotomised outcome required a larger sample size impacting on logistics and resources required to conduct the cRCT	– Observed intervention effect may have been a statistical artefact of a dichotomised variable, but a continuous outcome may not have been interpretable or transferable for a wider audience
– **Externality bias**: cRCT was considered the best study design and individual-level health outcomes suitable despite large investment of time and resources required	– Decisions to conserve limited resources may have introduced bias through changes in length of time required to recruit the community surveys	– Scale of operations necessary to collect the required sample size may have influenced the outcome
– **Outcome meaningfulness**: Outcome and effect size were determined by funding requirements and availability	– Outcome and effect size not did not account for policy-makers' preferences or the potential investments into health services and the resources introduced by the PRIME intervention	– Evidence of effect may not be meaningful and interpretable in a policy context

Table 8.4: Synthesis of learning points from Chapter 6 – Assessment of causal mechanisms

Assumptions considered by taking a reflexive approach	Challenges that come into view once assumptions are recognised	Impact of assumptions on interpretation of the evidence
– **Linear change pathway**: Causal mechanisms can be isolated and made to fit a linear and non-recursive representation of the intervention change process	– The intervention's theory of change was dynamic and was difficult to reduce to fit the conventions necessary for mediation analysis	– The operationalised logic model, and therefore results produced, represented just one of many potential interpretations of the intervention change process and are therefore not comprehensive
– **No confounding**: All of the possible influences on the intervention can be accounted for, measured and included in the model	– Mediators were not randomised and confounding occurred at baseline and throughout the study period making it difficult to measure and include them as covariates in the mediation analysis	– Impossible to make assumption that there is no unmeasured confounding therefore difficult to make valid inferences of mediate effect
– **Independence of mechanisms**: Mediators are independent and do not interact with each other	– The theory of change hypothesised that mechanisms would work together to produce change making it hard to consider mediators and pathways as independent	– Challenging to meet assumption that there is no relationship between the intervention's different change processes therefore limiting the interpretation of any effects generated from mediation analyses

Table 8.5: Synthesis of learning points from Chapter 7 – Evaluation of context

Assumptions revealed by taking a reflexive approach	Challenges that come into view once assumptions are recognised	Impact of assumptions on interpretation of the evidence
– **Context external to the intervention**: Context is anything external to the intervention that may act as a barrier or facilitator to its implementation, or its effects and could explain differences in outcomes at health centres which could be tested in other cases	– The intervention was not a bounded entity separate from the context into which it was implemented – It was not possible to isolate context as factors separate from the intertwining processes and relationships through which health workers made meaning of the research project in relation to their lived realities	– Context and the intervention enmeshed making it difficult to identify the original outline of the intervention within and across cases once it merged with everyday realities
– **Participants as homogenous group**: Intervention participants are assumed to respond to the context and the intervention in a standardised way	– The intervention took on different, unpredictable meanings for each health worker through the course of social exchanges with patients, the research project, and others	– Health workers' socio-spatial locations influenced, and were influenced by, the research project; temporal locations shaped how the research project emerged differently for each of them; PRIME supply system became a potential means of navigating social structures
– **Context as static background**: Context is a static background or is a set of enumerable factors evenly distributed among clusters through randomisation	– Factors emerged as active and contingent on a network of human, material and structural elements	– Factors such as 'poor health centre infrastructure', 'lack of resources' or 'inadequate support' became intrinsic to how health workers integrated the research project components into their practices at the health centre
– **Context can be enumerated and generalised**: Context can be integrated into assessments of the cRCT measures of effect in order to generalise effects across places	– Details at a local level revealed a terrain that was realised as quite bumpy and heterogeneous at many levels	– Exploring local details revealed the political, economic and social realities shaped provision of care and access to health services which might have otherwise been obscured

This notion of inclusion and exclusion suggests a process of selection, or pruning, in order to make sense of complexity and produce knowledge of the intervention and its effects. In other words, the methods applied for making sense of complexity rendered complexity simplified. This simplification, in turn, suggests that there are limits as to what each methodology can reveal about the effect and functioning of the intervention. Yet, there does not appear to be an acknowledgement of these methodological limits in the current guidance and complex interventions literature, more widely.

Recent discussions suggest that our ability to account for complexity has been limited by a lack of methodological and conceptual advancements (Hawe 2015a; Stern et al. 2015). The implication here suggests that once these limitations are overcome, we will have study designs and methods that are able to more comprehensively account for complexity in order to produce objective, generalizable and transferable evidence of intervention effects. In response, there has been some work towards identifying, applying and advancing more sophisticated study designs and methodologies.

For example, recent work advanced in partnership with the Health Foundation, the Medical Research Council, the National Institute for Health Research and different academic stakeholders proposes a number of innovative study designs, computer applications and advanced statistical methodologies to account for complexity in health interventions research (Raine et al. 2016). This includes for example, the use of Bayesian analysis to synthesise multiple sources of evidence along the intervention's causal pathway (Watson and Lilford 2016). Elsewhere, work is advancing on the use of social network analysis to model the effect of an intervention operating in a complex system (Hawe, Bond, et al. 2015), and on integrating more ethnography into process evaluations (Bunce et al. 2014). Lamont and colleagues (2016) recently provided a compilation of potential methodological solutions to current barriers to healthcare evaluation.

The contributions of this thesis seek to temper, or offer some perspective on the expectations of what might be achieved as we endeavour to advance different methodologies for complex interventions research. I suggest that my interpretation of methodological limits experienced in this thesis applies to methodologies more broadly –

all methodologies will inevitably comprise actions that simplify complexity and therefore provide only partial accounts of the intervention and its effects. I join others in arguing that more methodological sophistication is not likely to provide the solution to comprehensively account for complexity in health interventions research (Cohn et al. 2013; Mowles 2014). However, I acknowledge that this is an active area of research that is continually evolving and innovating. It remains to be seen, therefore, if any of these emerging methodologies will eventually become a sufficient solution to accounting for complexity in complex interventions research.

While individual methodologies are insufficient to account for complexity, it may be reasonable to consider that evidence from multiple methodologies can be added together. This is indeed the more common approach in complex interventions research and assumes that that each methodology will 'fill the gaps' of the others, or 'add up', such that a comprehensive description of the intervention and its effects will be produced. In the next section, I explore the possibility of overcoming partial accounts by combining evidence from multiple methodologies.

8.4. Combining accounts of the intervention and its effects

The potential for combining of multiple methodologies is informed by the MRC guidance on conducting comprehensive evaluations (Medical Research Council 2008) which implies that the different areas of investigation (intervention design, outcomes, mechanisms, context) are envisaged as pieces of a puzzle drawn together by the intervention theory of change and logic model. Together the evidence from these investigations would produce a 'complete picture' of the intervention effect such that it would be possible to establish how it was that the intervention worked (or not), in what settings, and where in the hypothesised pathway of effect successes or failures could be attributed. This type of work is driven by a mixed or multidisciplinary approach where the different methodological approaches applied are drawn from different disciplinary fields following their respective conventions and interpretive strengths with the evidence produced brought together under a common framework. Although this is the central recommendation of the MRC guidance, there remain few examples where this has been achieved and reported comprehensively in a single manuscript. The current tendency is for outcome and process evaluations to be conducted by separate teams and reported in different journals and reporting different

evaluation objectives. This makes it difficult for the reader to determine if there is a 'complete picture', or coherent story, explaining the intervention and its effects.

My approach of having conducted the different investigations as a single investigator and looking across the methodologies applied appears relatively unique. To examine the implications of this work, I will first summarise the findings from each chapter and then consider what can be brought about from examining the commonalities and contested findings of the different methodological exercises.

My examination of the process and methodologies used to design of the PRIME intervention suggest that the intervention was well designed following best available guidance resulting in an intervention package that could appropriately and effectively target a set of factors identified as barriers to delivery of good quality care for malaria at public health centres. It was acknowledged, however, that the intervention may not have been able to address the deeper social, political, and economic challenges that underlie poor healthcare quality and lack of progress on malaria. The intervention was proposed to work both as a set of products that would initiate change and as a series of social relationships that would evolve over time. The evaluation of the intervention implementation process suggested that the interactive learner-centred workshops supported by supply of AL and mRDTs were implemented as intended and were well received and considered useful by participating health workers (Chandler, Nayiga, et al. 2013).

The evaluation of certain outcomes, however, showed limited or no effect of the intervention. First, the analysis of the cRCT primary and secondary outcomes suggested that there were no effects of the intervention on community level health outcomes of anaemia and parasitaemia. Rather than concluding that the intervention was ineffective, however, my extended analysis of the cRCT outcomes suggests that there were a range of statistical, contextual and practical considerations influencing the choice, analysis and interpretation of the outcome measures. Examining these considerations highlighted that outcomes chosen may have been inappropriate for defining if the intervention worked, or not. Second, the analysis of the causal mechanisms intended to identify pathways through which the intervention may have worked but which are obscured when looking at cRCT

outcome measures only. The findings suggested that the intervention had a positive effect on the mechanisms of worker attitude scores and stocks of mRDTs, but not on patient satisfaction, appropriate treatment of malaria, and stocks of AL. The successful mechanisms, however, could not be linked to an impact of the intervention on improvements in population-level health outcomes. While the analysis highlighted some possible effects of the intervention, I demonstrated that the complexity of the intervention and context may have undermined the statistical assumptions required to infer a valid causal effect.

On the other hand, evaluation of context revealed a different narrative about how the intervention functioned amidst health workers' everyday realities of providing care. The findings suggested that the intervention had important influences on how health workers negotiated the entrenched socio-economic challenges and hierarchical structures influencing their care practices and working lives. Features of the intervention were taken-up differently by each health worker and became part of their wider narratives of frustration, expectation and recognition. At the same time, the intervention became in inadvertent solution to navigating a health system which undermined the health workers' power and authority. These findings contrast with those which suggest that the intervention was ineffective. Instead, this perspective revealed multiple important and locally relevant effects of the intervention on health workers' motivations and care practices.

The findings from across the four chapters suggest that despite having assessed each of the areas following the framework promoted by the MRC guidance documents, the evidence does not cohere to produce a 'complete picture' that describes the intervention and how it functioned. Each methodology told different parts of different stories of the intervention. Each set of evidence is distinctive in its area of focus and level of detail or abstraction and does not easily map on to each other. The findings are somewhat incommensurable and produce a fragmented and still incomplete picture of the intervention and its effects. These findings suggest problems with the notion that evaluating different areas of investigation will unlock pieces of evidence that can 'add-up' to an explanation of whether the intervention was effective or not, and why.

I suggest that this incommensurability reflects the different epistemological perspectives that underpin each methodology applied (Guba and Lincoln 1994), as outlined in Table 8.6. The findings of the chapters underpinned by a postpositivist epistemology were oriented towards producing objective, quantitative and representative knowledge on how the intervention functioned. The findings of these analyses were considered to represent the 'truth' about whether the intervention was effective or not. To produce this knowledge, the randomisation and statistical modelling techniques were considered to 'adjust for' or minimise the effect of complexity when interpreting intervention effects (Guba and Lincoln 1994). The more constructivist epistemology underpinning the approach to designing the intervention and assessing context did not suppose that a single 'truth' could be distilled. The approaches therefore explored and examined the interactions between the complexity of the social world and the intervention acknowledging that there will be many equally valid processes and effects (ibid). I suggest, therefore, that there is a disconnect between the reductionist or 'single story' view of examining *if* the intervention works as produced by the statistical analyses and the multiple views of *how* the intervention was hypothesised to work and was found to produce diverse effects in different places under more constructivist perspectives.

Table 8.6: Methodologies and epistemological perspectives

Area of investigation	Epistemology applied	Description of epistemology	Methods applied	Area of focus	Interpretation
Intervention design (Chapter 4)	Informed by social constructivist perspective	Seeking subjective, relational meanings of the social world	Formative research, literature review, stakeholder meetings, questionnaires and focus groups for piloting	Development of an intervention that could be evaluated in cRCT	The intervention was proposed to work both as a set of products that would initiate change and as a series of social relationships that would evolve over time
Evaluation of primary outcomes (Chapter 5)	Post positivist	Seeking to test a scientific hypothesis, outcome-driven	Repeat cross-sectional surveys	Prevalence of anaemia and parasitaemia, mean haemoglobin	Intervention effect can be assessed by comparing the difference between outcomes in the intervention and control trial arms
Assessment of causal mechanisms (Chapter 6)	Post positivist	Seeking to test a scientific hypothesis, outcome-driven	Repeat cross-sectional surveys, health worker and patient questionnaires, stock records	Identification of causal mechanisms leading to specific outcomes	Causal mechanisms can be isolated to explain the effect of the intervention
Evaluation of context (Chapter 7)	Social constructivist	Seeking subjective, relational meanings of the social world	Interviews, observations, context record	Health workers' everyday realities in relation to context and the intervention	Context and the intervention interact to produce unpredictable effects

These epistemological tensions have been noted in other evaluations of complex interventions. Recently, Toye and colleagues (2016) found that patients' and caregivers' diverse experiences and perceived value of a scoliosis treatment intervention did not easily map onto the intended clinical outcomes of the trial. The lack of cohesion led the researchers to consider their findings as independent contributions to knowledge, rather than as explanatory annexes to the trial outcomes (ibid). Munro and Bloor (2010) likewise found that while interpretative qualitative process evaluations provided multiple rich understandings of how a school-based drug prevention programme functioned, the findings did not provide a determinate explanation of the trial outcomes. As a result, they contend that process evaluation may not be the 'miracle' solution for providing explanatory accounts of why interventions work, or not, as is currently expected in the literature (ibid). These epistemological tensions are also a focus of ongoing debates in the mixed methods literature more generally (Small 2011) reflecting a wider recognition that incommensurabilities may be an inevitability of taking seriously the epistemological perspectives employed by different disciplines and their methodologies.

Despite these ongoing discussions in the literature, there is surprisingly little discussion of the potential for competing and contested interpretations in the recent versions of the MRC guidance. Within the guidance, there appears to be an assumption that different methodologies and the evidence they produce can be combined unproblematically under the RCT framework. I suggest that this assumption is a by-product of the assimilation properties of the evidence-based movement described in the literature review in Chapter 1. There I suggested that contestations of the RCT's ability to navigate complexity have been absorbed into the dominant frame as new parameters of complex interventions research in the form of 'process evaluations'. As a result, the types of methods used in process evaluations are taken up as 'handmaidens' in service to outcome-driven approaches (Béhague, Gonçalves, and Victora 2008; Petticrew 2015). For example, qualitative methodologies are considered a method to generate hypotheses about which groups of participants should be included as subgroups in outcome analyses, to identify barriers and facilitators that influenced the outcomes, or to provide narratives describing variations in outcomes (MRC Population Health Service Research Network 2014). This suggests that while the dominant approach to complex interventions research is becoming more diverse

in method, it seeks to integrate these methods into a singular epistemological approach focused on answering 'what works'.

By rendering methodologies into a single perspective, however, we lose the opportunity to learn from the more interpretive and critical knowledge that comes from taking different forms of knowledge production seriously (Béhague et al. 2008). In global health, this has consequences on our ability to engage with the local realities and deeper social, political, and economic challenges that underlie poor health and access to care. For example, Adams (2013) has described how designing interventions that are amenable to standardisation and evaluation in experimental designs often eliminates the opportunity to design interventions based on evidence derived from ethnographic and participatory action research. Such interventions, however, are often considered by community members and local stakeholders to be more well-suited to addressing the inequalities and injustices hampering improvements in health and wellbeing (ibid). Likewise, Biehl and Petryna (2013) have demonstrated how the process of producing single quantifiable measures of effect through experimental designs ignores the deeper social complexities causing ill health. When experimental designs are emphasised at the expense of other approaches, these social complexities remain unaddressed and consequently reinforced (ibid). At the same time, this type of outcome-based evidence is not always considered useful by policy and programme decision makers at the local and national levels. Such evidence has been described by these stakeholders as being undermining of local contexts and expertise (Behague et al. 2009) and not being relevant and responsive to everyday realities of health programming in low resource settings (Burchett et al. 2015).

This suggests, together with the findings of this thesis, that there is a disconnect between approaches that prioritise a singular perspective in order to identify 'what works' and the diversity of perspectives on intervention research and evidence that may be necessary for affecting and sustaining changes to health and wellbeing. In the next section, I consider this disconnect alongside the continued relevance of the 'what works' framework and the implications for improving complex interventions research in global health.

8.5. Future directions for better intervention design and evaluation in global health

The conceptual and methodological challenges raised throughout this thesis invite reflection on whether assessing intervention effectiveness by asking 'what works', remains a relevant paradigm for complex interventions research in global health. I contend that the evidence-based global health science paradigm driven forward by the pursuit of objective evidence and a push for accountability of investments through quantitative metrics may be insufficient for accommodating the concepts and methodologies that employ different approaches to understanding how interventions are taken up and produce effects. While extending the 'what works' question to ask 'how, for whom and under what circumstances interventions work, or not', as suggested by the MRC guidance, might be seen as an opportunity for accommodating different methodologies, these extensions remain within the hypothesis-testing approach to evidence production and interpretation. Such an approach does not appear to support serious examination and integration of the evidence produced by different methodologies and epistemological positions that are now proliferating in the complex interventions literature.

I acknowledge, however, that taking different perspectives seriously will produce incommensurable forms of evidence which the framework promoted by the MRC guidance may not currently be equipped to navigate and negotiate. The framework, therefore, needs to adapt to acknowledge and value epistemological diversity. It does not appear, however, that doing so will be possible within the guidance's current remit. Indeed, its authors may have inadvertently foreshadowed the unresponsiveness of the guidance to future evolution by equating it to the design of the bicycle suggesting that once the bicycle frame was set, any subsequent changes have been minimal, not radically innovative (Craig and Petticrew 2013). Relating this to the MRC guidance they explain that "we can expect further improvements (and further revisions to the guidance), but they are likely to be within rather than beyond the current framework" (Craig and Petticrew 2013:586). This type of tinkering with the guidance is not likely to lead to the types of changes necessary to advance intervention design and evaluation beyond the current *status quo*.

There are, however, recent examples of shifts towards evaluation frameworks that accommodate multiple perspectives. For example, Jones and colleagues (2016), Hansen

and Tjørnhøj-Thomsen's (2015) and Hutchings and colleagues (2016) have each proposed multimethod evaluation frameworks for complex interventions that seek to integrate different epistemological and methodological positions including from RCTs and interpretive qualitative studies. Crucially, these frameworks aim to capture the multiple confirming and opposing effects that arise when taking different epistemological perspectives seriously. In so doing, they aim to produce a coherent and balanced interpretation of the intervention with the intention of not over-emphasising or reducing findings from any one epistemological perspective. However, there are not yet any empirical examples applying these frameworks in practice.

Nevertheless, these frameworks signal a new direction for complex interventions research. They suggest a movement away from the simple hypothesis-testing approach of 'what works' towards a more dynamic and multi-perspective question of 'what happens' – that is, examining different perspectives on what and how effects emerge locally across places and people when an intervention is introduced. Asking 'what happens' may be a more responsive and informative question for complex interventions research (Petticrew 2015). Widening the scope of the evaluative frame may provide the opportunity for conceptual, methodological and evidentiary contributions from different knowledge bases.

Towards asking 'what happens'

Asking a different question embedded in epistemological diversity suggests that there may need to be re-arrangements to some aspects of current practice and thinking in complex health intervention research. This includes reframing what is considered as the 'best' way of producing evidence and the types of intervention effects we consider relevant for improving health and wellbeing. This may include changes to the way evidence is produced and used, and to the types of study design, data collection and analytical approaches that are valued. Likewise, commitment to new forms of intervention research will require individual and institutional investment in order to meaningfully engage with the theoretical and practical aspects of interdisciplinary work. This might include, for example, more focus on building interdisciplinary teams, scholars and practitioners engaged in complex interventions research (Miller et al. 2013), especially in low income settings where such expertise is lacking (English, Nzinga, et al. 2011). More fundamentally, asking new

questions and examining problems from multiple perspectives may require a different, 'slower' approach to research.

This notion of 'slow research' in global health has recently emerged as a response to the normative practices of the fast-paced and accountability-driven evidence-based global health research paradigm anticipated in the literature review, Chapter 1 (Adams, Burke, and Whitmarsh 2014). 'Going slow' is not considered simply a temporal readjustment; it focuses on reimagining and refashioning the qualities that underpin our actions as producers and consumers of research (Mountz et al. 2015). It values a deep engagement with the people and places where research is conducted to produce, and demand, locally specific and relevant evidence (Adams et al. 2014). Drawing from Adams and colleagues' (ibid) work on elaborating a movement for slow research in global health, I have outlined some ideas for shifting towards an agenda of slow research for the design and evaluation of complex interventions in global health, Figure 8.1.

The aim of asking 'what happens' and engaging in an agenda of slow research is not to replace the current evidence-based global health paradigm. Yet, it acknowledges that such an approach may render approaches to examining 'what works' more tenuous and discordant with everyday realities. Taking seriously and enacting the qualities of slow research may raise challenges to the notion that one mode of producing evidence and one knowledge system represents a universally applicable truth, and therefore solution, to challenges of complex interventions research in global health. However, this instability can be productive in fostering constructive debates leading to critical insights, and the development of more locally relevant and specific methodological approaches to complex interventions research. To achieve this ambition, we must be willing to make the reputational investment of self-critique, both of ourselves and of our disciplines, in order to promote an open and humble discourse on the challenges and opportunities that arise in our attempts at addressing the myriad challenges facing global health today.

Figure 8.1 Thoughts on engaging in slow research for the design and evaluation of complex interventions

Slow research for the design and evaluation of complex interventions is:

- Local: Instead of focusing solely on providing evidence that can be used to explain primary outcomes, value methodologies that elaborate the particularities and specificities of a place even if this means these details may destabilise the outcomes from RCTs or undermine the priorities of an evidence-based paradigm.
- Embedded: Instead of focusing on ways to improve, innovate and streamline intervention design and evaluation practices such that the same practices can be applied everywhere, empower researchers to work locally with stakeholders to identify what practices are productively suited to producing the types of information valued by constituents directly affected by research activities, such as patients, health workers, and local and national government decisions makers.
- Slow and deliberate: Instead of focusing on methodologies, project operations, and modes of communication that valorise speed and efficiency, design processes that specifically take time and require engagement and interaction with people, surroundings and processes to allow space to learn things that are not directly sought, but are likely important in understanding interventions and how they function.
- Focused on knowledge over information: Instead of focusing on producing manuscripts that can communicate a single message about the intervention findings (i.e. did the intervention work or not?), acknowledge that describing and communicating complex and in-depth knowledge about the many perspectives on the intervention and how it functions may require longer manuscripts with mixed media such as images, sounds, videos, maps and so forth, and different types of engagement with research participants and users.

8.6. Summary and implication of findings for global health researchers and practitioners

The findings of this thesis encourage both global health researchers, practitioners and commissioners to examine the current priorities driving complex intervention research and consider new ways of thinking about how we apply methodologies for the design and evaluation of complex interventions in global health. Researchers are considered to be those 'doing' designing and evaluating complex interventions, for example researchers at universities and research-oriented departments within health and development organisations. Practitioners are considered to be those using the evidence from research to inform global health programmes, policy, and research initiatives. Commissioners include

those who might fund or commission complex intervention research in global health, like the MRC or the Gates Foundation, for example. The findings are specifically relevant to those who currently rely on the MRC guidance to inform their thinking on the design and evaluation of complex interventions in global health contexts. As such, the most immediate implications of this work are for researchers, as outlined first below, but I go on to argue for longer term implications for researchers, practitioners and commissioners working in complex interventions research in global health.

8.6.1. Immediate implications for researchers

The first set of implications for researchers draws from each of the methodological exercises of examining intervention design, evaluating outcomes, assessing mechanisms, and evaluating context. These were outlined earlier in this chapter and in Table 8.1. In summary, researchers are encouraged to reflect on and report their 'behind the scenes' accounts of the intervention design processes; consider how their decisions on choice of outcome measures might influence interpretation of trial results; be cautions of applying mediation analysis to complex interventions research and engage with the theoretical literature to understand the opportunities and challenges of using this method; and acknowledge how different conceptualisations of context might productively lead to new ideas about the intervention and evidence produced as a result. These considerations intend to facilitate the use of different methods but also encourage researchers to acknowledge that recommended methodologies can be difficult to implement in practice and therefore greater awareness is needed to identify which methods may or may not be productively applied to complex interventions research.

The second set of implications for researchers draws from across the findings of each methodological exercise and concerns both methodological and epistemological challenges. The methods applied in this thesis aligned with those recommended in the MRC guidance. A careful examination of the processes of applying each method revealed that they simplified complexity and, as a result, produced a specific narrative of intervention effectiveness and change processes. This finding emerged when taking seriously the epistemological approach underpinning each methodology. Methods underpinned by a reductionist, or single story view of assessing 'what works, how, for whom and in what settings' were unable to account for the multifaceted and synergistic processes interpreted

to underlie the way complex interventions produce change. Methods applying a more constructivist frame accounted for complexity through acknowledgement of multiple stories of change concerning the interactions between people, the intervention and different social realities. When brought together, the evidence produced through these different approaches were found to be incommensurable. Each set of evidence was distinctive in its area of focus and level of detail or abstraction and did not easily map on to each other. This suggests problems with the notion promoted in the MRC guidance that evidence from the different areas of investigation can produce a 'complete picture' that describes the intervention and how it functioned. Researchers, therefore, may need to reconsider their expectations about what can be achieved both by individual methods and by the type of multi-method approach to complex interventions research promoted in the MRC guidance.

Regarding individual methods, there appears to be an expectation amongst some researchers working on complex interventions that we might identify a way to comprehensively account for the effects multiple, interacting causal processes in a single methodological approach (Keele 2015; Watson and Lilford 2016). The results of this thesis suggest, however, that it is unlikely that methodological sophistication to develop more sensitive, accurate or robust analytical strategies will yield a solution that might account for the multidimensional and entangled nature of complexity. This also aligns with discourses which argue that a repertoire of methods working together is necessary for complex interventions research and for global health more widely (Bardosh 2014; Panter-Brick et al. 2014). The implication for researchers, therefore, is to reconsider whether it is valuable, and indeed practical, to pursue efforts to identify such 'comprehensive' methodologies or whether efforts are better spent working to reduce methodological and disciplinary silos in order to build the repertoire of methodologies called for.

Regarding multi-method approaches, the expectation about how multiple methods might be combined and the evidence they might produce also requires reconsideration by researchers. The MRC guidance recommends a multi-method, or multidisciplinary, approach where the evidence produced by different methodologies can be brought together under a common framework. However, there is little reflection in the MRC guidance of the different epistemologies underpinning these methodologies and the

potential to produce incommensurable interpretations of intervention effectiveness and change processes as a result. It can be argued that this ambivalence of the MRC guidance to epistemological diversity is reflective of the biomedical paradigm within with the MRC guidance was developed and promoted. This works well for providing a single framing and narrative that appears to accommodate complexity and context, but in practice it is rare to find examples of successful implementation. The findings in this thesis suggest that this lack of success may in part be due to problems with glossing over the differences in methodological and epistemological positions. Rather than simply suggesting that these differences then render collaboration impossible, this thesis shows the value in exploring and embracing these differences as multiple lenses which can reveal different accounts. Recent frameworks by Jones and colleagues (2016), Hansen and Tjørnhøj-Thomsen's (2015) and Hutchings and colleagues (2016) have been proposed to allow for multiple epistemological perspectives in evaluation, although there are not yet any empirical examples applying these frameworks in practice. Experimenting with these and other frameworks alongside or instead of the MRC guidelines may prove worthwhile, however, to address the challenges of implementation that attempts and often fails to develop a single account of whether interventions work or not.

The third implication for researchers concerns how we reflect and report on the processes and investments necessary when conducting complex interventions research. Guidelines for improving the reporting of complex interventions have been proposed (Abraham 2008; Hoffmann et al. 2014; Möhler et al. 2015). These guidelines, however, fall short of acknowledging the assumptions, choices and considerations, as well as the investments of time and expertise, that are necessary when employing a range of methodologies to design and evaluate complex interventions. Encouraging a reflexive and transparent account of these actions and investments can, however, serve two important functions. First, reporting the actions necessary to produce and interpret findings provides additional contextualised information that may be useful for situating interpretations within the larger social, political, and economic contexts in which the research project was conducted. This information may facilitate interpretation and promote transferability of findings to other similar contexts. Second, reporting the time and resources required may promote greater awareness and encourage researchers to adequately plan for the investments necessary to conduct comprehensive complex interventions research. Researchers are therefore

encouraged to recognise the value of such reports and argue for their inclusion included alongside results papers or in specific sections of journals to support and promote both publication and debate over methodologies for complex interventions research.

8.6.2. Longer-term implications for researchers, practitioners and commissioners

The longer-term implications of this thesis apply to both researchers and practitioners as a community engaged in complex interventions research. The implications concern the direction in which debates over methodologies for complex interventions research should evolve and argues for a re-problematisation of complex interventions research in global health. This research has argued that the hypothesis testing logic underlying the MRC guidance – that is, asking 'what works' and also 'how interventions work, for whom and in what settings' is still relatively narrow compared to the acknowledgment of complexity as the social, political and economic entanglements of the social world. Researchers and practitioners are therefore urged to consider a reframing of the kinds of questions we ask in complex interventions research in global health. This thesis has proposed that we might instead adopt the dynamic and multi-perspective question of 'what happens'. The question of 'what happens' is interdisciplinary at its root acknowledging and incorporating different perspectives on what and how effects emerge locally across places and people when an intervention is introduced. It may be a more responsive and informative question for complex interventions research (Petticrew 2015). This new question may seem like a semantic turn, but the implications for researchers and practitioners are much more profound. This new question aligns with an emerging discourse concerning the need for a new approach to global health that seeks to reframe and re-problematise the current fixation with magic bullet approaches both in terms of the types of interventions that are promoted and the ways in which they are evaluated (Adams 2013; Bardosh 2014; Panter-Brick et al. 2014).

In asking 'what happens', practitioners are urged to embrace epistemological diversity and promote more methodological risk taking in complex interventions research instead of requiring methodological standardisation that produces specific types of evidence that might facilitate aggregation but obscure local realities (Adams 2013). This has several implications. For practitioners using evidence from complex interventions research to inform decision making on directions for global health policies, programmes and research

initiatives, asking a 'what happens' may require new arrangements to the types of evidence that are valued. This means valuing and incorporating non-RCT and non-quantitative forms of evidence, which have hereto had little purchase in global health science (Béhague and Storeng 2013), into decision making processes rather than considering them as handmaidens or anecdotal descriptions in service to outcome-driven approaches (Behague and Goncalves 2008; Petticrew 2015). As a result, practitioners should expect that gathering and consolidating evidence for decision making may be more complex and the answers produced may not be simple. But the 'rich' array of evidence produced as a result may inform decisions that more meaningfully take the social entanglements of complexity into account. For commissioners funding research initiatives, asking 'what happens' may require new schemes and incentives to promote disciplinary diverse research teams and value additional time and resources that may be needed to engage with complexity through interdisciplinary research. The implication is not necessarily an increase in financial investments, but rather a rearrangement of funding priorities as it has been argued that interdisciplinary research can be a cost-effective strategy for improving global health programmes if findings are incorporated into intervention design and decision making (Bardosh 2014).

For researchers, asking 'what happens' will require maintaining and elaborating the strategies discussed above. This includes pursing an epistemologically diverse methodological approach as well as building a reflective practice that examines and reports on the processes and investments necessary when conducting complex interventions research. Such activities will provide researchers with the experience and expertise needed to identify the challenges and opportunities of asking 'what happens', and in so doing, inform future directions of complex interventions research in global health.

For both practitioners and researchers, encouraging risk-taking requires a reframing of the value systems that underpin different research paradigms in global health science and how these shape the production and use of evidence to improve health and wellbeing. As Herrick and Reubi (2016) have eloquently expressed, such an reframing requires,

> *"a commitment to 'making intelligible what often remains obscured, reformulating problems to allow alternative solutions, resisting individualistic and technical models to highlight the social mechanisms and political issues of global health'* (Fassin 2012:115)*. In doing so, it then might be possible to counter the biomedical tendency to 'project coldness and abstraction, faceless publics [and] anonymous*

> *populations' to develop a concept of health that 'emphasises the connectedness of each of us to each other, one that understands how our future depends upon extraordinary cooperation between us'* (Horton 2014:218)*" (Herrick and Reubi 2016:np).*

The implications for both researchers and practitioners of adopting a new framing of complex interventions research in global health are not easy nor do they come with a set of prescriptive recommendations. I have suggested, however, that the notion of 'slow global health' may provide some ideas. 'Going slow' seeks to challenge the normative practices embedded in the biomedical paradigm and encourages us to reframe approaches to producing evidence and the types of interventions that are valued. These challenges seek to draw knowledge from a practice that values a deep engagement with the people and places where research is conducted to produce, and demand, locally specific and relevant evidence (Adams et al. 2014). Adopting a 'slow' approach to global health research is a long-term commitment. The research community engaged in complex interventions research can start by promoting an open and humble discourse amongst disciplines on the challenges and opportunities that arise in our attempts at addressing the myriad challenges facing global health today.

8.7. Strengths, limitations and reflections

Limitations specific to each methodological exercise have already been discussed in each chapter. Here, I present the strengths and limitations on the overall methodological approach and further reflections on undertaking interdisciplinary research.

The approach of examining the methodological exercises through the practice of 'making the strange familiar and the familiar strange' was useful for achieving the aims of this thesis. This practice afforded me the time and space to work through each methodology and also provided the motivation for engaging with the processes and practices involved in implementing each methodology. At the same time, it provided a way of examining and making sense of these experiences and a means for doing so in the same way across each methodological exercise. A strength of this research, therefore, was having a platform from which I could develop and embody a 'double consciousness' where I was able to engage in and examine each methodology such that I considered each equally and none were subjugated to any one perspective. Certainly, the familiar/strange practice was especially

useful in the absence of any accepted way of undertaking interdisciplinary methodological critique.

Despite having an approach for framing this interdisciplinary work, there were limitations with 'doing' interdisciplinary work in practice. Balancing the depth necessary to do rigorous research in each discipline with the breadth of theoretical thinking needed to bridge learning from across the methodologies was challenging. As other doctoral students have acknowledged, the processes of engaging with disparate literatures, learning and applying the languages, assumptions and values of different knowledge bases, and working rigorously according to the expectations of each discipline was at times unexpectedly time consuming and disorienting (Carey and Smith 2007). As a result, there was a limit to the depth of analysis I was able to apply in each chapter. For example, with the mediation analysis in Chapter 6, I could have taken the analysis deeper by engaging with alternative approaches to causal mediation analysis, such as those based on instrumental variables or principal component analysis, which may have resolved some of the limitations encountered with the Stata mediation package applied. Likewise, as I already described with the evaluation of context in Chapter 7, I could have further engaged with the historical literature of health services in Uganda to extend the examination of context as part of the assemblage of material and immaterial realities influencing the research project. However, negotiating this limitation with the investment of time and resources necessary to work across methodological boundaries was a necessary and worthwhile trade-off. Doing so lead to the interpretations presented in this thesis which may not necessarily be revealed when analyses are conducted by different researchers with relatively little emphasis spent on cross-boundary methodological critique and learning.

Learning to balance depth and breadth of research skills and theoretical thinking has been an important output of my doctoral training. As I have presented in this discussion, I believe that engaging in explicitly integrated interdisciplinary work has advantages for global health intervention research. Therefore, developing an interdisciplinary expertise as 'jack of all trades' may be particularly useful as complexity increasingly becomes a feature of interventions research in our globalising world. However, this position of being 'jack of all trades' also alludes to being 'master of none'. This position may be seen as a disadvantage in the academy which remains organised along disciplinary boundaries and

where success often depends on developing specific and in-depth expertise in one discipline. This suggests that further work is needed to examine how universities and funders are responding to increasing demands for interdisciplinarity in complex health intervention research and how this can be facilitated and promoted at the doctoral level and throughout academic careers.

8.8. Conclusion

The turn to complexity in interventions research has reshaped the approaches seen as appropriate for evaluating 'what works'. Driven by the MRC guidance on designing and evaluating complex interventions, there is now an emphasis on accounting for complexity by producing explanations of how an intervention works, or not. Four areas of investigation are considered central to producing these explanations – examination of intervention design, evaluation of primary outcomes, assessment of causal mechanisms, and evaluation of context. This thesis set out to examine the methodological approaches recommended in each of these areas.

In each of the areas of investigation, there were different conceptual, analytical, and practical considerations which influenced the way in which the recommended methodologies were applied in practice, and likewise, how evidence was produced and interpreted. I offered ideas to facilitate the conceptualisation and implementation of each methodology in practice. In addition, I suggested that greater reflection and reporting on the processes taken and work involved to translate current recommendations into practical strategies will benefit both researchers and funders in future complex interventions research endeavours.

Across the areas of investigation, I also identified points of connection in how the methodologies applied accounted for complexity, but also incommensurabilities in the evidence they produced. This has several implications. First, I suggested that all methods render complexity simplified and in the process produce different and partial accounts of the intervention and its effects. Given that accounts are only every partial, it does not appear that more methodological sophistication will provide the solution to comprehensively account for complexity in health interventions research. Second, I suggested that the incommensurabilites in the evidence produced resulted from taking

seriously the different epistemologies underlying each methodological approach. These differences made it challenging to produce a 'complete picture' of the intervention where evidence from the different areas of investigation could 'add-up' to an explanation of whether the intervention was effective or not, and why.

My findings of incommensurability point to a disconnect with the MRC guidance which appears to suggest that different types of evidence can be integrated to produce a complete picture of the intervention provided they are made to align with a singular epistemological approach focused on answering 'what works'. I argued however, that by rendering methodologies into a single perspective, we lose the more interpretive and critical knowledge that comes from taking the different epistemological perspectives seriously. This has consequences on our ability to gather and produce locally relevant and meaningful evidence.

This thesis demonstrated the conceptual and methodological challenges with designing and evaluating interventions under the narrow 'what works' approach rooted in a medicalised and metricised view of global health. In response, I suggested the need for a shift towards emphasising a more dynamic and multi-perspective question of 'what happens'. Asking 'what happens' widens the scope of the evaluative frame and provides the opportunity for contributions from different knowledge bases. However, shifting the current paradigm will require re-arrangements to some aspects of current practice and thinking in complex health intervention research in global health. This shift may be enabled by taking a 'slow approach' to global health research. Such an approach may be particularly useful for gaining local knowledge and understanding the multiple and varied effects of complex interventions and their role in improving health and wellbeing.

CHAPTER 9. References

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Appendices

Appendix 1 PRIME intervention components

Training in Fever case management		
Aim: To train health workers in use of mRDTs and build clinical skills for managing malaria and other febrile illnesses.		
Barriers targeted: • Poor knowledge of malaria case management • Inadequate/unavailable infrastructure or diagnostic laboratory facilities		
Module	**Topic**	**Learning outcomes** By the end of this module, participants should be able to:
Fever case management training module	How to evaluate patients with fever and select patients for Rapid Diagnostic testing	• Describe fever and explain how this symptom is important in selecting a patient for mRDT´ testing • List signs of severe illness in a patient with fever • Outline important questions to ask when taking a history from a patient with fever • Describe how to carry out a physical examination of a patient with fever • Describe how to select a patient for mRDT testing based on the history and physical examination
	Performing and reading a mRDT	• Describe a mRDT and how it works • Perform a mRDT correctly and safely • Read a mRDT accurately and record the result as positive or negative • List some important tips for using mRDTs • Describe safe handling of blood and sharps
	Management of a patient with fever and a positive mRDT	• Explain the meaning of a positive mRDT result in a patient with fever • Describe how to treat a patient with fever and a positive mRDT • Outline supportive treatments for a patient with fever and positive mRDT
	Management of a patient with fever and a negative mRDT	• Outline the benefits of treating patients on the basis of mRDT results • Explain the meaning of a negative mRDT in a patient with fever • Describe the management of a patient with fever but a negative mRDT • List and describe the management of some common non-malaria febrile illnesses
	Recognition and referral of patients with severe illness	• List danger symptoms and signs of severe illness • Outline the steps to refer severely ill patients to higher level health facilities • Describe pre-referral treatments that may be given to severely ill patients before transfer to a higher level health centre
	Patient education	• List 5 good communication skills • Outline important messages to give to a patient/caregiver to encourage adherence to treatment • Outline important messages to give a patient/caregiver on

		symptoms that indicate a need to return to for further care • Outline important messages to give a patient/caregiver on malaria prevention
	mRDT storage and monitoring	• Describe the proper storage conditions for mRDTs • Explain how to monitor mRDT expiry dates with the first expiry, first out' principle
Fever case management supervision visits	First supervision visit: within 1 week of training	• Observe and mentor health workers on how to: • Manage fever patients with positive or negative results • Set the working area • Record mRDT results in the registers • Assess and replenish stocks of AL and mRDTs
	Follow-up supervision visit: 6 weeks and 6 months after initial training	• Observe and mentor how health workers are: • Evaluating patients with fever. • Performing the mRDTs 6 weeks after the training. • Reading the results • Managing the results of mRDTs • Recording the results and treating patients • Identify and address weakness and challenges of mRDT use in fever patient management.

Workshop in Health Centre Management

Aim: To develop in-charge health workers' accountable practices in management of finances, supplies, and health information.

Barriers targeted:
- Poor management of resources by in-charges at health centres
- Low motivation of staff due to poor health centre administration
- Under-utilization or lack of appropriate tools to appropriately mange health centres
- Low use of health centre records to monitor and manage health centre resources and report to local and district stakeholders

Module	**Topic**	**Learning outcomes** By the end of this module, participants should be able to:
HCM[-1] 00 Introduction to HCM	Accountability	• Understand the meaning and role of accountability for in-charges • Recognize how being accountable impacts on others' perception of in-charges • Describe the role of accountability in good health centre management
HCM 01 Primary Health Care Fund management	Budgeting and accounting using the Primary Health Care Fund management tool	• Describe the Ministry of Health policy for Primary Health Care Funds for health centres II/IIIs • Understand the rationale for training in budgeting, accounting, and Primary Health Care Fund management • Describe how the health centre uses its Primary Health Care Funds • Recognize how in-charges can build trust and accountability in their roles through good Primary Health Care Fund management • Describe the principles of budgeting and accounting • Develop and apply budgeting and accounting skills using the Primary Health Care Fund Management Tool
	Budgeting and accounting -- putting it all	• Describe the importance and benefit of budgeting and accounting for the Primary Health Care Fund

	together	• Understand how budgeting and accounting contributes to showing accountability and skill as an in-charge • Plan and commit to completing the Primary Health Care Fund Management tool regularly at their health centres
HCM 02 Drug Supply Management	Principles of the drug distribution system	• Describe the main components of the drug distribution system • Be motivated to actively participate in and keep the drug distribution system on track
	Forms required in drug distribution cycle	• Describe the purpose and benefit of completing forms required in the drug distribution system including the Out-Patient Department register, Stock-card (Form 015), Order Form (Form 085) • Accurately complete the forms required in the drug distribution system • Put in place a plan for completing the forms regularly at the health centre
	The ACT Drug Distribution Assessment Tool	• Identify issues that prevent drugs from reaching the health centre • Identify and implement solutions to the issues that prevent drugs from reaching the health centre • Be motivated to complete the ACT Drug Distribution Assessment Tool regularly
HCM 03 Health Information Management	Why quality information matters	• Understand why we collect patient information
	The information cycle -- from patient to patient	• Understand how collecting information can beneficial to the health centre (drug quantification, predicting future needs) • Understand how collecting information improves patient management
Workshop in Patient-Centred Services		
Aim: To improve health workers' interpersonal communication with patients and other health centre staff and to build consultation skills.		
Barriers targeted: • Lack of patient-centred thinking • Communication problems including language barrier • Discrimination/ preferential treatment of patients • Inappropriate use of volunteers • Poor relationships between staff and communities Poor patient flow and management		
Module	**Topic**	**Learning outcomes** By the end of this module, participants should be able to:
PCS+ 00 Introduction to PCS and Self-Observation Activities	Thinking about my role as a health worker	• Identify one's own motivations for work.
	Introduction to PCS	• Understand the meaning and importance of providing patient centred services.
	Introduction to SOAs	• Start developing self-awareness through self-observation activities.
PCS 01 Communication Skills Part 1	Building Rapport	• Recognise the impact of non-verbal and verbal behaviour on the patient and consultation outcome. • Strengthen non-verbal and verbal skills in building

		rapport. • Recognise that we think of different people in different ways, and this affects how we behave towards them. • Understand that respect is a core value for how we can put patients at ease. • Strengthen skills to show respect to patients.
	Active listening	• Strengthen skills in self-reflection. • Strengthen non-verbal and verbal skills in active listening. • Recognise the consequences of listening well, and less well, on the patient and consultation outcome. • Identify ways to listen actively in spite of busy work environments.
PCS 02 Communication Skills Part 2	Asking good questions	• Understand the importance of getting good information. • Be aware of the way and consequences of how they ask questions. • Know how to formulate open questions. • Ask questions without showing judgement.
	Giving good information	• Understand the importance of giving good information. • Be aware of the way and consequences of how they give information. • Know how to give good information to patients. • Understand how to empower patients to follow advice.
PCS 03 Building a positive work environment	Health Centre Management Changes	• Recognise their challenges at work. • Know about planned Health Centre Management changes. • Know their role in Health Centre Management changes.
	Dealing with stress at work	• To recognise stress by how we feel and behave. • To understand the effect of automatic reactions on us and others. • To know how to 'step back' and stop automatic reactions. • To carry a picture of best practice in dealing with difficult patients and situations.
PCS 04 Improving the Patient Visit	Communication Review	• Become aware of ways to invite their patients and colleagues to co-operate and the impact of doing this.
	Patient Welcome and Orientation	• Recognise that we all have different perspectives, including as health workers and patients. • Put themselves into the shoes of a patient approaching a health centre as an organisation with unspoken 'rules'. • Explore reasons why patients have to wait long, and develop strategies that meet health workers' as well as patients' needs better. • Implement strategies to improve the welcome of patients at health centres. • Implement strategies to improve the orientation of patients at health centres. • Implement strategies to ensure patients are seen fairly.

[x] PCS = patient-centred services
[xi] HCM = health centre management
[xii] mRDT = malaria rapid diagnostic test

Appendix 2 PRIME Intervention Learning & Design Principles

The PRIME Intervention Learning & Design Principles

The structure, design and layout of the Patient-Centred Services (PCS) and Health Centre Management (HCM) manuals was designed to assist trainers with facilitating the interactive group-style learning and to assist learners with actively engaging with the trainer and the manuals including:

1. Formatting and typeset principles
2. 6-step adult learning cycle
3. Participatory training activities
4. Icons to facilitate use of manuals

1. Formatting and typeset principles

The learner manuals were designed as workbooks with space allocated for answering questions posed by the trainer, completing activities, taking notes, and recording reflections. A workbook-style manual was created to improve engagement and retention of learning and provides a reference for learners' responses for reference after the training.

The visual format of the manuals was designed to communicate a positive and motivating learning process. The page layout, colour schemes, and fonts were designed to be inviting, friendly, and visually appealing. The manual design is also suitable for printing in greyscale on standard A4 paper in order to provide a lower cost option for reproducing the training manuals on a large scale.

A consistent structure for title page, introductions, training agenda, description of learning activities, learning summary boxes, and conclusion were used throughout each manual to create a professional product which intended to be easily taken-up by trainers in Uganda, and potentially elsewhere.

2. PRIME 6-step adult learning cycle

Step 1: Need to know

In order for the learner to become engaged, the individual must understand why they should participate in the learning, building on their own experiences.

Step 2: Individual reflection

Deep learning involves reflecting on experiences, analysing patterns of behaviour and identifying consequences. The team followed the appreciative inquiry approach to facilitation which intends to identify and focus on positive behaviours and build on these in moving forward.

Step 3: Conceptualisation

If learners can identify a pattern in their experiences (of either 'old' behaviour or 'new' ideas from learning) then the learner can form a generalisation and a set of concepts to define the situation.

Step 4: Experimentation

Once solutions have been identified in theory to problems identified from experience, these solutions need to be tested in practice.

Step 5: Group reflection

Learning is not an isolated experience but a collective process involving cultural formation and shifts in perspectives of groups.

Step 6: Planning
After learning something new, it is necessary to complete the cycle by identifying how the learning can be applied to the learner's job, to solve their problems, including setting commitments for future learning and changes and mechanisms to monitor and support peers in achieving these commitments.

3. Participatory learning activities

The following outlines the participatory learning activities in the PCS and HCM modules. Activities such as group presentation and group discussion are used during the 'Principles' step of the learning cycle. Skill-based activities such as role-play and demonstrations are used during the 'Conceptualisation' and 'Experimentation' steps of the learning cycle to practice and discuss new skills. Group participation activities such as group discussion and small group work are used during the 'Group reflection' and 'Planning' steps of the learning cycle to foster teamwork and a community of practice. Throughout the modules, interactive activities such as buzzing, question and answer, flip chart, the parking lot, and energisers are used to keep learners active and engaged.

Drawings are included to communicate practices of good quality care to health workers (1) and act as a reminder when text may be daunting to read. We applied principles of picture design following (2) to create a visual representation of the main learning outcome for each PCS and HCM module.

Group presentation by the trainer is used to present theory or concepts to the group in plenary. Active listening and participation is encouraged through asking questions to the group, placing information on the flip chart, reading aloud from the Learner Manual, and writing in the Learner Manual.

Group discussion is used to gather information, thoughts, and responses to questions or activities from the group. By discussing with others in a 'safe space', participants are able to justify their own learning experiences and learn from the experiences of others. This helps participants to feel that their new ideas, skills, or behaviours are acceptable to their peers, making them more likely to be applied in everyday situations.

Small group work is used to increase understanding of a topic or concept, discuss participant experiences, and to practice new skills. Constructive feedback is encouraged to improve group dynamics and promote teamwork, build participants' confidence in their new skills or behaviours, and provide a foundation for group work or discussions in the workplace.

Role play a dramatic acting of a scenario or behaviour and is used to help discuss sensitive issues which can be difficult to address in plenary and to assess whether participants have acquired the knowledge and are able to apply it in practice.

Demonstrations are used by the trainer or learner to show how to perform a skill correctly. Demonstrations are an effective way of teaching skills that are hard to describe in words or involve body actions, for example communication skills, or for practicing how to complete tasks correctly, for example completing routine forms.

Buzzing is used as a quick method to have participants, usually pairs or up to groups of four, discuss together and then write responses in their Learner Manual or feedback responses to the group. Buzzing encourages participation and active learning with peers.

Questions and answers are used to encourage participation and active learning by assessing learners' level of knowledge or learning on a topic or concept or to gain learners' feedback. Trainers encourage learners to think of and provide their response by 'giving time' to participants after asking questions.

Flipchart papers are used to present information or record responses provided by learners. Flipchart headings or content are prepared ahead of the training to save time and help keep the trainer on-track.

The Parking Lot is a blank flipchart paper used to acknowledge and record learners' questions or observations, which do not relate to the topic at hand but may be addressed in a previous or subsequent topic or module. Trainers 'park' the question and address anything outstanding by the end of the training or by the next training session to show learners that their contributions are values and appreciated.

Energisers are included to combat restlessness or boredom by introducing an activity that encourages learners to move and become more alert. Short energisers such as a two-minute exercise or dance are encouraged.

4. Icons to facilitate use of manuals

The following icons are used throughout the PCS and HCM manuals to signpost key activities to trainers and learners. Icons were developed and used throughout the manuals to signpost key activities. The icons are simple black and white line drawings and were placed in the margins of the manuals for easy identification.

Talking Point: This icon indicates text for the trainer to speak to the participants. These are the sections of text you should be familiar with and perhaps use a highlighter pen to emphasize the most important sections of the text you want to present to the participants.

Asking point: This icon indicates text for the trainer to ask to the participants. Try to use the questions written in the training manual – these are 'open-ended' questions that allow participants to think of and give a 'rich' response, rather than a quick 'yes or no' response.

Activity: This symbol indicates that an activity is to take place and should remind you that materials or special instructions may be needed.

Summary box: This icon indicates a box with a summary has been included in the manual, for reference for trainers and learners.

Flipchart: This icon is used to show you when you should be writing or placing items on the flipchart.

References

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Haaland A. Reporting with Pictures. A concept paper for researchers and health policy decision-makers [Internet]. Geneva: UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases; 2001 [cited 2014 Mar 15]. Available from: http://www.who.int/tdr/publications/documents/pictures.pdf

Appendix 3 Health worker in-depth interview topic guide

IDI DATA COLLECTION TOOL - HEALTH WORKERS (HFI)		
Health centre code [_____|_____]	**Study ID** [_____|_____]	***Date*** *[_____/_____]/[_____/_____]/[_____/_____]* day month year

Position:

1 = In-charge	5 = Clinical officer	9 = Public health nurse	13 = Health assistant
2 = Senior medical officer	6 = Nursing officer	10 = Nursing aide/assistant	14 = Health educator
3 = Medical officer	7 = Enrolled nurse	11 = Laboratory technician	15 - Volunteer
4 = Senior clinical officer	8 = Midwife	12 = Laboratory assistant	15 = Other_____

[_____|_____]

DEMOGRAPHIC INFORMATION		
1. Age	Years [_____|_____]	**5. Highest level of education or qualification achieved** 1 = Primary (P1 — P7) 2 = Secondary (S1 — S6) 3 = Certificate 4 = Diploma 5 = Bachelor's degree 6= Master's degree 99 = Refused to answer 77 = Other_____ [_____|_____]
2. Gender	1 = Male 2 = Female [_____]	
3. Originally from this area?	1 = Yes 2 = No [_____]	
4. Number of years worked in this job	[_____|_____]	**6. Year graduated** [_____|_____|_____|_____]

PART 1: INTRODUCTION

Conduct the interview according to the directions below and record information as indicated.

Introduction to in-depth interview

"Hello my name is _____ and I am interested in interviewing you. This interview will ask you to express your own views and experiences about your work and role at this health centre. We are interested in knowing whether improving the health services at this health centre has improved children's health in this area. We are specifically asking you about the ACT PRIME study activities which include 1) health center management training, 2) information management, 3) health worker training in fever case management and patient-centered services, and 4) supply of consumables, including malaria diagnostics and antimalarial drugs.

A note-taker will be writing down what you say for our records, and we will record the interview using a digital recorder; these notes will be kept securely and your name will not be used anywhere. Your answers will be looked at together with those of many other health workers from different facilities and you will not be identifiable in any reports that are published.

It is very important for us to hear your views and experiences because you have experience working here and can give us this insight. We hope you will have time to spend with us now to complete this interview. The interview will take about 45 minutes; if you prefer we can reschedule the interview for tomorrow or another day of your convenience.

Do you have any questions? Do you agree to continue before we start?

Now we request that we all switch off our mobile phones so that we are not distracted."

NOTE TO INTERVIEWER: For this interview, bring a copy of the ADDAT form, Stock Card, Order Form for EMHS and the two instruction sheets: 'using the stock card' and 'using the order form'

PART 2: IN-DEPTH INTERVIEW – HEALTH WORKERS (HFI)	
Domains, topic questions, and probes: Use the table below to help you administer the questions during the interview.	
Domain	**Topic and Probes**
1. Your role at work	a) What does your usual day consist of at the health centre these days?
	b) What is the most important thing to you personally about doing this job?
	c) How do you feel about this job now? How has this changed over time?
2. Significant events	a) Looking back over the past year, what do you think was the most significant change in the way you managed illness in your health centre?
	b) Why is this significant to you?
	c) What difference has this made now or will it make in the future?
3. Reflection on HFI	a) The ACT PRIME project has carried out some activities at your health facility and others in this area since April 2011. Can you tell me about any that you have been involved with or that have affected you? *Probe for all aspects of the intervention they can recall, and what they remember about each (it may be different from the way we frame the intervention, but we want to hear their description of what it meant to them)*
4. Reflection on training	a) What training did you attend with the ACT PRIME project since April last year? *Probe for a list of all components they can recall, in their own words.* *Once they have listed them all, prompt them to see what they recall about: PCS training, PCS self-observation tasks, HCM training, RDT training, RDT supervision* 'Between the PCS workshops, there were some suggestions for things to think about when you return to your individual health facilities that were written in your learner manuals. What can you tell me about those?'
	b) How do you feel the ACT PRIME study training you attended has impacted on your work?
	c) Was there anything that you learnt during the training that you have found difficult to put into practice? *Probe for each of the training sessions they can recall attending above- but further probes can be brought in under subsequent domains for each intervention components*
	d) Have you attended any other training courses or received any materials or tools from other organizations to help you do your job? *If yes, please list, and let us know what was most useful about each of those courses, materials or tools.*
5.A Health centre management: Staffing	a) How would you describe the staffing levels at your health centre right now? *Probe for number of staff, qualifications and status e.g permanent vs locum or temporary*
	b) Have there been any changes recently to the staffing at this health centre? *Probe: specifics and who effected these changes (district or Sub County)? How does the leave system operate, and how do you feel about this?*

	c) What difference have these changes made to your work? *Probe: Which part of your every day work is greatly affected by the staffing levels at your facility*
	d) What is the role of volunteers at your health centre? *Probe: how do you feel about the use of volunteers here?*
	e) What challenges do you still face in staffing at this health centre? *(try to keep this brief- there will be many challenges!)*
5.B Health centre management: Drug stocking implementation	a) Can you describe the way that drugs are stocked at this health centre? *Probe: how has this changed over the past year – including when changes were implemented.*
	b) Can you describe your relationship with the health sub-district (HSD) liaison, and what role he plays in stocking at your health facility?
	c) How often do you use the stock card? What do you think of this as a method to keep track of stocks? *NB: bring the one-pager instructions 'using the stock card' and see if they are familiar with this. What is useful/not useful about this instruction sheet? What was most useful for knowing how to complete the stock card?*
	d) How often do you use the 'order form for EMHS'? What do you think of this as a method to order supplies? *NB: bring the one-pager instructions 'using the order form' and see if they are familiar with this. What is useful/not useful about this instruction sheet? What was most useful for knowing how to complete the order form?*
5.C Health centre management: Drug stocking impact	a) How have any changes in stocking at your health facility affected your work? *Probe: What is the impact on hours spent at work, patient attendance etc?*
	b) What has been the effect of stocking by both NMS through the push system and ordering drugs from the HC IV on the management and dispensing of drugs? *Probe for sharing of drugs and RDTs and which HCs they usually share drugs with (between HFI and Standard care facilities?)*
	c) What challenges do you still face in stocking of drugs at this health centre?
	d) How would you describe the function of the ADDAT form for re-stocking activities? *Probe for whether they are using the ADDAT for restocking activities – show the ADDAT form if necessary and see if they recognize it.*
	e) When you run out of Lumartem or Coartem and RDTs, what method is your first choice for getting more supplies? What is the process of that method, and how did you learn about that process? *Probe for any trickle down of training on how to requisition for supplies from in-charges to other health workers at the health centre*
	f) How does the system for requisitioning supplies through the HC IV compare with other methods you use to get supplies including the the NMS system? *Probe for preferences and reasons; how could ordering supplies from the HC IV system be integrated with the NMS system?*
5.D Health	a) How would you describe the financial situation at this health centre

centre management: Budgeting and accounting	right now?
	b) How would you describe the accounting and budgeting for PHC funds or other funds at this health centre right now?
	c) Have you made any changes over the past year to the way you undertake accounting and budgeting of PHC funds or other funds at this health centre? *Probe for specifics.*
	d) What difference, if any, have these changes made to your work? *Probe: where do you see the greatest impact of accounting and budgeting in your every day work?*
	e) How would you describe the function of the PHC Fund Accounting Tool for accounting for activities at the health facility? *Probe for specifics.*
	f) How has the requisition for and delivery of PHC funds for your health centre been working in the past year? *Probe: what impact has this had on the operation of your health centre?*
5.E Health centre management: Information management	a) What is the information you collect about patients at your health centre in the OPD register used for?
	b) (How) have you and your colleagues at your health centre used the information documented in the OPDs? *Probe: how has the way you have used this information changed in the past year?*
	c) What impact does the way this information is used have on your work?
	d) What problems did or have you experienced in completing the OPD for recording fever, malaria tests and treatment at your health centre?
6.A Reflection on Patient-Centered Services: Communication with patients	a) How would you describe your relationship with the different types of patients who come to this health centre? *Probe for different types of patients (age, gender, type of illness, perceived social status) and how the relationship varies. Probe for the relationships they observe that their colleagues have with patients.*
	b) What is the most significant change in the past year in the way you interact with patients? *Probe: why do you think this change occurred and how did you achieve it?*
	c) Have you noticed any differences in the types of patients who attend at your health centre in the past year? *Probe: any differences in the socioeconomic status, catchment area or social group of patients coming now? If so, how are these different groups treated by colleagues at the health centre?*
	d) Can you describe the impact your relationship with patients has on your work? *Probe for any changes to this relationship. Probe for impact on own sense of wellbeing.*
	e) The unsalaried staff at different health centres were invited to some training last year about improving the way they welcome and interact with patients. Have you noticed any changes in these behaviours since then? *Probe for stories of examples of change/no change; probe for why they think these changes occurred and if they think the training was worthwhile*
	f) Have there been any changes in the order in which patients are seen at your health centre? If so, what is the reason, and what have been the consequences?
6.B Patient-	a) How would you describe your relationship with your colleagues at your

Centered Services: Communication with colleagues	health centre?
	b) What do you think are the reasons for the nature of this relationship with colleagues, as you described it?
	c) What is the most significant change you have experienced in the past year in the way you and your colleagues interact? *Probe: why do you think this change occurred and how are you all achieving it?*
	d) Can you describe the impact your relationship with colleagues has on your work?
7.A Fever case management	a) Can you tell me about your experiences with the RDT trainers since last year? *Probe for what their interactions with the RDT trainers consisted of (i.e. training, supervision, time points)*
	b) Can you tell me what were the most important things that you learned from the RDT trainers? *Probe for each: can you remember when you learnt that? Why do you think you can still remember that now?*
	c) Were there any parts of the recommendations made by the RDT trainers that you have found hard to put into practice? *Probe for any difficulties with mechanisms of doing the different types of tests (pf/pan (2 lines) vs bioline (3 lines), including loop vs dropper); how did these different methods affect your use of the tests (frequency/ inclination)*
	d) Did you receive a visit from the RDT trainers to your health facility? Can you tell me what they did when they came? What was most useful to you, and why?
	e) Can you make any recommendations for what could be improved about the RDT training?
8. Satisfaction	a) How would you describe your personal satisfaction with your job at this health centre? *Probe for reasons for satisfaction/dissatisfaction*
	b) Can you describe what impact your satisfaction/dissatisfaction has on your work?
9. Closing	Is there anything else you think is important about working at this health centre that we have not talked about? (*Probe for challenges like interference by political leaders, faultfinding supervision)*
✓ **Summarise** ✓ **Thank participant**	

PART 3: CONTACT SUMMARY FORM (1)	
Interviewer to complete this form after the interview	
Study ID [_____ | _____]	***Date*** *[_____ /_____] / [_____ /_____] / [_____ /_____]* day month year
1. How would you describe the atmosphere and context of the interview (*Include interview location and how this may have affected responses)*?	
2. What were the main points made by the respondent during this interview?	

PART 3: CONTACT SUMMARY FORM (2)	
Study ID [_____|_____]	***Date*** *[_____/_____] / [_____/_____] / [_____/_____]* day month year
3. What new information did you gain through this interview compared to previous interviews?	
4. Was there anything surprising to you personally? Or that made you think differently?	
5. What messages did you take from this interview to improve the intervention design?	
6. Were there any problems with the topic guide (e.g. wording, order of topics, missing topics) you experienced in this interview?	

Appendix 4 Semi-structured contextual record questionnaire

STRUCTURED CONTEXTUAL RECORD (Form 1, Part A, Page 1)			
DISTRICT LEVEL: *To be administered to the DHO and DHI*	**Staff ID** [_____|_____]	***Date completed*** *[_____|_____] / [_____|_____] / [_____|_____]* day month year	
TIME PERIOD COVERED:	1 = Baseline 2 = 0-3 months 3 = 4-6 months	4 = 7-9 months 5 = 10-12 months 6 = 13-15 months	7 = 16-18 months 8 = 19-21 months 9 = 21-24 months	[___|___]

SECTION 1: RESPONDENT INFORMATION		
1. Respondent name	***2. Contact information*** *(cell phone or email address)*	
3. Respondent position	*1 = DHO 77 = Other (list)* *2 = DHI* _____	*[___|___]*

SECTION 2: INTERVENTIONS		
(1) BEDNETS		
1. Have bednets been distributed in the study area in the last 3 months? *If YES, go to Qn 2 (and complete Part B #1), otherwise skip to Qn 5.*	*1 = Yes* *2 = No* *88 = Don't know*	*[___|___]*
2. Who was responsible for the distribution?		
3. Where were the nets distributed?		
4. Who do you suggest that we talk to for more information about the bednet distribution?		
(2) INDOOR RESIDUAL SPRAYING (IRS)		
5. Has IRS been conducted in the study area in the last 3 months? *If YES, go to Qn 6 (and complete Part B #2), otherwise skip to Qn 9.*	*1 = Yes* *2 = No* *88 = Don't know*	*[___|___]*
6. Who conducted the IRS campaign?		
7. What areas were sprayed?		
8. Who do you suggest that we talk to for more information about IRS?		

(3) ARTEMISININ COMBINATION THERAPY (ACTs)		
9. Have any programs to distribute ACTs been conducted in the study area in the last 3 months? *We are particularly interested in ACT distribution outside of the existing NMS supply to the public health centers, including the ACT study.* *If YES, go to Qn 10 (and complete Part B #3), otherwise skip to Qn 13.*	*1 = Yes* *2 = No* *88 = Don't know*	*[___|___]*
10. Who distributed the ACTs?		
11. Where were the ACTs distributed?		
12. Who do you suggest that we talk to for more information about ACT distribution?		
(4) RAPID DIAGNOSTIC TESTS (RDTs)		
13. Have RDTs been distributed in the study area in the last 3 months? *We are particularly interested distribution of RDTs outside of the NMS supply to the public health centers, including the ACT Study.* *If YES, go to Qn 14 (and complete Part B #4), otherwise skip to Qn 17.*	*1 = Yes* *2 = No* *88 = Don't know*	*[___|___]*
14. Who distributed the RDTs?		
15. Where were the RDTs distributed?		
16. Who do you suggest that we talk to for more information about RDT distribution?		
(5) SCHOOL-BASED INTERVENTIONS		
17. Have any interventions targeting schools and/or school-aged children been conducted in the study area in the last 3 months? *Probe for programs involving health education, vaccination, deworming, malaria, nutrition, sanitation, etc.* *If YES, go to Qn 18 (and complete Part B #5), otherwise skip to Qn 21.*	*1 = Yes* *2 = No* *88 = Don't know*	*[___|___]*
18. What was the program(s) and who conducted it?		
19. What schools were involved?		
20. Who do you suggest that we talk to for more information about school-based interventions?		
(6) COMMUNITY-BASED INTERVENTIONS		
21. Have any interventions targeting the community been conducted in the study area in the last 3 months? *Probe for*	*1 = Yes* *2 = No*	*[___|___]*

programs involving VHTs, ICCM, HBMF, CHWs, and/or those that target vaccination, deworming, malaria, nutrition, sanitation, etc. *If YES, go to Qn 22 (and complete Part B #6), otherwise skip to Qn 23.*	*88 = Don't know*	
22. What was the program(s) and who conducted it?		
23. Where were the program(s) conducted?		
24. Who do you suggest that we talk to for more information about community-based interventions?		
(7) HEALTH IEC CAMPAIGNS		
25. Have any IEC (information, education, and communication) campaigns been conducted in the study area in the last 3 months? *Probe for campaigns that target malaria treatment, prevention, or diagnostics (RDTs), and other health-related issues such as vaccination, deworming, nutrition, sanitation, etc.* *If YES, go to Qn 26(and complete Part B #7), otherwise skip to Qn 29.*	*1 = Yes* *2 = No* *88 = Don't know*	*[___|___]*
26. What was the campaign(s) and who conducted it?		
27. Where were the campaigns conducted?		
28. Who do you suggest that we talk to for more information about the IEC campaigns?		
(8) DISTRICT & HEALTH SUB-DISTRICT ISSUES		
29. Have any new policies been introduced at the district or health sub-district level in the last 3 months? *Probe for policies that might affect health.* *If YES, go to Qn 30 (and complete Part B #8), otherwise skip to Qn 31.*	*1 = Yes* *2 = No* *88 = Don't know*	*[___|___]*
30. Who do you suggest that we talk to for more information about the policy changes?		
31. Have there been any important changes in guidelines for health centers, health workers, CHW, or on malaria diagnosis and treatment in the last 3 months? *If YES, go to Qn 32, otherwise skip to Qn 33.*	*1 = Yes* *2 = No* *88 = Don't know*	*[___|___]*
32. Who do you suggest that we talk to for more information about the guideline changes?		
33. Have there been any important changes or gaps in staffing at the district or HSD level in the last 3 months? *If YES, go to Qn 34, otherwise skip to Qn 35.*	*1 = Yes* *2 = No* *88 = Don't know*	*[___|___]*

34. Who do you suggest that we talk to for more information about district and HSD staffing?		
35. Have there been any important changes or gaps in staffing at the health centers in the study area in the last 3 months? *If YES, go to Qn 36, otherwise skip to Qn 37.*	*1 = Yes* *2 = No* *88 = Don't know*	*[___|___]*
36. Who do you suggest that we talk to for more information about health center staffing?		
35. Have there been any important changes in supervision of health centers or health workers in the study area in the last 3 months? *If YES, go to Qn 36, otherwise skip to Qn 37.*	*1 = Yes* *2 = No* *88 = Don't know*	*[___|___]*
36. Who do you suggest that we talk to for more information about supervision?		
(9) ECONOMIC AND POLITICAL FACTORS		
37. Have there been any significant changes in economic or political factors that may have affected the performance of health workers, access to health centers, or health of the population (particularly children) in the last 3 months? *If YES, go to Qn 38 (and complete Part B #9), otherwise skip to Section 3.*	*1 = Yes* *2 = No* *88 = Don't know*	*[___|___]*
38. Who do you suggest that we talk to for more information about these factors?		

SECTION 3: ADDITIONAL COMMENTS
39. Is there anything that you think is important for us to know about the study area in the last 3 months that we've not asked?
THANK YOU FOR YOUR TIME AND SUPPORT

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #1, Page 1)		
(1) BEDNETS: ***To be completed if bed nets have been distributed in last 3 months***	**Staff ID** [____|____]	***Date completed*** [____|____] / [____|____] / [____|____] day month year
TIME PERIOD COVERED:	1 = Baseline 2 = 0-3 months 3 = 4-6 months	4 = 7-9 months 5 = 10-12 months 6 = 13-15 months	7 = 16-18 months 8 = 19-21 months 9 = 21-24 months	[____|____]

SECTION 1: RESPONDENT INFORMATION	
1. Respondent name	***2. Contact information*** *(cell phone or email address)*
3. Respondent organization and position	

SECTION 2: BEDNET DISTRIBUTION		
Introduction: *We understand from our meeting with the DHO (or representative) that you or your organization have been involved with distributing bed nets in Tororo District. We would like to learn more about the bed net distribution.*		
1. What organization(s) were responsible for distributing the bed nets?		
2. Where were the nets distributed?	*Probe for sub-county, parish, villages, if known.*	
3. When were the nets distributed?	**Date started** [____|____] / [____|____] / - [____|____] *day month year*	**Date completed** [____|____] / [____|____] / - [____|____] *day month year*
4. What type of nets were distributed?	*1 = Long lasting net (Permanet, Smartnet, Olyset, etc)* *2 = Net with insecticide kit (KO, Kooper, Ico, Safi, etc)* *3 = Net with no insecticide* *77 = Other* _____	***[____|____]***

5. How were the nets distributed? *Probe: Were nets distributed to the community (households), schools, health centers, antenatal clinics? Was an education program included in the campaign? Was any follow-up provided?*

6. How many nets were distributed?

If more detailed information on number of nets distributed is available, record in Section 3 on page 2.

Total nets[_____|_____|_____|_____|_____|_____]

7. Who funded the bed net program?

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #1, Page 2)

Staff ID	***Date completed***
[_____|_____]	*[_____|_____] / [_____|_____] / [_____|_____]* day month year

SECTION 3: ADDITIONAL COMMENTS

8. Is there anything that you think is important for us to know about the distribution of bed nets by your organization in the last 3 months that we've not asked?

THANK YOU FOR YOUR TIME AND SUPPORT

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #2, Page 1)		
(2) IRS: ***To be completed if IRS has been conducted in last 3 months***	**Staff ID** [____|____]	***Date completed*** [____/____] / [____/____] / [____/____] day month year
TIME PERIOD COVERED:	1 = Baseline 2 = 0-3 months 3 = 4-6 months	4 = 7-9 months 5 = 10-12 months 6 = 13-15 months	7 = 16-18 months 8 = 19-21 months 9 = 21-24 months	[____|____]

SECTION 1: RESPONDENT INFORMATION	
1. Respondent name	***2. Contact information*** *(cell phone or email address)*
3. Respondent organization and position	

SECTION 2: IRS CAMPAIGNS		
Introduction: *We understand from our meeting with the DHO (or representative) that you or your organization have been involved in conducting IRS in Tororo District. We would like to learn more about the IRS campaign.*		
1. What organization(s) were responsible for conducting the IRS campaign?		
2. What areas were sprayed?	*Probe for sub-county, parish, villages, if known.*	
3. When was the spraying conducted?	**Date started** [____|____] / [____|____] / - [____|____] *day month year*	**Date completed** [____|____] / [____|____] / - [____|____] *day month year*
4. What class of insecticide was used?	*1 = DDT (Organochlorine)* *2 = Organophosphate (Malathion, Fenitrothion, etc)* *3 = Carbamate (Bendiocarb, Propoxur)* *4 = Pyrethroid (Lambda-cyhalothrin [ICON], Deltamethrin, etc)* *88 = Don't know*	***[____|____]***
5. What was the name of the insecticide used?		
6. Can you describe the details of the IRS campaign? *Probe for information about community*		

sensitization, education programs, challenges faced, etc.
7. What was the total population targeted? *Total population*[_____|_____|_____|_____|_____|_____] *If more detailed information on target populations is available, record in Section 3 on page 2.*
8. What proportion of the target population was sprayed? [_____|_____] %
9. Who funded the IRS campaign?

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #2, Page 2)	
Staff ID [_____|_____]	***Date completed*** [_____/_____] / [_____/_____] / [_____/_____] day month year

SECTION 3: ADDITIONAL COMMENTS
10. Is there anything that you think is important for us to know about IRS in the study area in the last 3 months that we've not asked?
THANK YOU FOR YOUR TIME AND SUPPORT

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #3, Page 1)		
(3) ACTs: ***To be completed if ACTs have been distributed in last 3 months***	**Staff ID** [____|____]	***Date completed*** [____/____] / [____/____] / [____/____] day month year
TIME PERIOD COVERED:	1 = Baseline 2 = 0-3 months 3 = 4-6 months	4 = 7-9 months 5 = 10-12 months 6 = 13-15 months	7 = 16-18 months 8 = 19-21 months 9 = 21-24 months	[____|____]

SECTION 1: RESPONDENT INFORMATION

1. Respondent name	***2. Contact information*** *(cell phone or email address)*
3. Respondent organization and position	

SECTION 2: ACT DISTRIBUTION

Introduction: *We understand from our meeting with the DHO (or representative) that you or your organization have been involved in distributing ACTs in Tororo District. We would like to learn more about the ACT distribution.*

1. What organization(s) were responsible for distributing the ACTs?

2. In what areas were the ACTs distributed? *Probe for sub-county, parish, villages, if known.*

3. When were the ACTs distributed?	**Date started** [____|____] / [____|____] / - [____|____] *day month year*	**Date completed** [____|____] / [____|____] / - [____|____] *day month year*

4. What levels or programs were targeted for the ACT distribution? [____\|____]

1 = Private sector (drug shops, clinics, hospitals)
2 = Community level (VHTs, CHWs)
3 = Public health centers (HC Iis, IIIs, IVs)
4 = Public hospitals (TDH, etc)
77 = Other _____
88 = Don't know

5. Can you describe the details of the ACT distribution? *Probe for information about how and where the ACTs were distributed, and associated sensitization, education, or training programs.*

6. How many ACTs were distributed?

If more detailed information on number of ACTs distributed is available, record in Section 3 on page 2.

Total ***[***_____|_____|_____|_____|_____|_____***]***

7. Who funded the ACT distribution?

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #3, Page 2)

Staff ID	***Date completed***
[_____|_____]	*[_____/_____] / [_____/_____] / [_____/_____]* day month year

SECTION 3: ADDITIONAL COMMENTS

8. Is there anything that you think is important for us to know about ACT distribution in the study area in the last 3 months that we've not asked?

THANK YOU FOR YOUR TIME AND SUPPORT

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #4, Page 1)		
(4) RDTs: ***To be completed if RDTs have been distributed in last 3 months***	**Staff ID** [____|____]	***Date completed*** [____/____] / [____/____] / [____/____] day month year
TIME PERIOD COVERED:	1 = Baseline 2 = 0-3 months 3 = 4-6 months	4 = 7-9 months 5 = 10-12 months 6 = 13-15 months	7 = 16-18 months 8 = 19-21 months 9 = 21-24 months	[____|____]

SECTION 1: RESPONDENT INFORMATION	
1. Respondent name	***2. Contact information*** *(cell phone or email address)*
3. Respondent organization and position	

SECTION 2: RDT DISTRIBUTION		
Introduction: *We understand from our meeting with the DHO (or representative) that you or your organization have been involved in distributing RDTs in Tororo District. We would like to learn more about the RDT distribution.*		
1. What organization(s) were responsible for distributing the RDTs?		
2. In what areas were the RDTs distributed? *Probe for sub-county, parish, villages, if known.*		
3. When were the RDTs distributed?	**Date started** [____|____] / [____|____] / - [____|____] *day month year*	**Date completed** [____|____] / [____|____] / - [____|____] *day month year*
4. What levels or programs were targeted for the RDT distribution?	*1 = Private sector (drug shops, clinics, hospitals)* *2 = Community level (VHTs, CHWs)* *3 = Public health centers (HC Iis, IIIs, IVs)* *4 = Public hospitals (TDH, etc)* *77 = Other _____* *88 = Don't know*	[____|____]
5. Can you describe the details of the RDT distribution? *Probe for information about how and where the RDTs were distributed, whether supporting supplies (lancets, gloves, etc) were also distributed, and associated sensitization, education, or training programs.*		
6. How many RDTs were distributed?		

If more detailed information on number of RDTs distributed is available, record in Section 3 on page 2.	*Total* ***[_____|_____|_____|_____|_____|_____]***
7. Who funded the RDT distribution?	

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #4, Page 2)	
Staff ID [_____|_____]	***Date completed*** *[_____/_____] / [_____/_____] / [_____/_____]* day month year

SECTION 3: ADDITIONAL COMMENTS
8. Is there anything that you think is important for us to know about RDT distribution in the study area in the last 3 months that we've not asked?
THANK YOU FOR YOUR TIME AND SUPPORT

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #5, Page 1)		
(5) SBIs: ***To be completed if interventions targeting schools have been implemented in last 3 months***	**Staff ID** [_____|_____]	***Date completed*** [_____/_____] / [_____/_____] / [_____/_____] day month year
TIME PERIOD COVERED:	1 = Baseline 2 = 0-3 months 3 = 4-6 months	4 = 7-9 months 5 = 10-12 months 6 = 13-15 months	7 = 16-18 months 8 = 19-21 months 9 = 21-24 months	[_____|_____]

SECTION 1: RESPONDENT INFORMATION	
1. Respondent name	***2. Contact information*** *(cell phone or email address)*
3. Respondent organization and position	

SECTION 2: SCHOOL-BASED HEALTH INTERVENTIONS		
Introduction: *We understand from our meeting with the DHO (or representative) that you or your organization have been involved in implementing school-based health interventions in Tororo District. We would like to learn more about the programs.*		
1. What organization(s) were responsible for implementing the interventions?		
2. In what areas or schools were the interventions conducted? *Probe for sub-county, parish, villages, if known, plus school names.*		
3. When was the intervention conducted?	**Date started** [_____|_____] / [_____|_____] / - [_____|_____] *day month year*	**Date completed** [_____|_____] / [_____|_____] / - [_____|_____] *day month year*
4. What was the focus of the intervention? *Include all that apply.*	*1 = Malaria treatment (including ACTs)* *2 = Malaria prevention (including ITNs)* *3 = Malaria diagnosis (including RDTs)* *4 = Health education*	***[_____|_____]*** ***[_____|_____]***

5 = Vaccination **[_____|_____]**

6 = Deworming

7 = Nutrition

8 = Sanitation

77 = Other _____

88 = Don't know

5. Can you describe the details of the intervention? *Probe for information about intended impact on health, age groups (or school classes targeted), schools included, duration of the program, etc.*

6. How many students were included?

If more detailed information on number of students is available, record in Section 3 on page 2.

Total **[_____|_____|_____|_____|_____|_____]**

7. Who funded the intervention?

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #5, Page 2)

Staff ID	***Date completed***
[_____|_____]	*[_____|_____] / [_____|_____] / [_____|_____]* day month year

SECTION 3: ADDITIONAL COMMENTS

8. Is there anything that you think is important for us to know about school-based health interventions in the study area in the last 3 months that we've not asked?

THANK YOU FOR YOUR TIME AND SUPPORT

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #6, Page 1)		
(6) CBIs: ***To be completed if interventions targeting communities have been implemented in last 3 months***	**Staff ID** [_____|_____]	***Date completed*** [_____/_____] / [_____/_____] / [_____/_____] day month year
TIME PERIOD COVERED:	1 = Baseline 2 = 0-3 months 3 = 4-6 months	4 = 7-9 months 5 = 10-12 months 6 = 13-15 months	7 = 16-18 months 8 = 19-21 months 9 = 21-24 months	[_____|_____]

SECTION 1: RESPONDENT INFORMATION	
1. Respondent name	***2. Contact information*** *(cell phone or email address)*
3. Respondent organization and position	

SECTION 2: COMMUNTIY-BASED INTERVENTIONS		
Introduction: *We understand from our meeting with the DHO (or representative) that you or your organization have been involved in implementing community-based interventions in Tororo District. We would like to learn more about the programs.*		
1. What organization(s) were responsible for implementing the interventions?		
2. Where were the interventions conducted? *Probe for sub-county, parish, villages, if known.*		
3.When was the intervention conducted?	**Date started** [_____|_____] / [_____|_____] / - [_____|_____] *day month year*	**Date completed** [_____|_____] / [_____|_____] / - [_____|_____] *day month year*
4. What was the focus of the intervention? *Include all that apply.*	*1 = Malaria treatment (including ACTs)* *2 = Malaria prevention (including ITNs)* *3 = Malaria diagnosis (including RDTs)* *4 = Health education* *5 = Vaccination* *6 = Deworming*	***[_____|_____]*** ***[_____|_____]*** ***[_____|_____]***

7 = Nutrition

8 = Sanitation

77 = Other _____
88 = Don't know

5. Can you describe the details of the intervention? *Probe for information about intended impact on health, how the program was delivered (using VHTs? CHWs?), duration of the program, etc.*

6. What population was covered?

If more detailed information on population is available, record in Section 3 on page 2.

Total **[**_____|_____|_____|_____|_____|_____**]**

7. Who funded the intervention?

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #6, Page 2)

Staff ID	***Date completed***
[____|____]	*[____/____] / [____/____] / [____/____]* day month year

SECTION 3: ADDITIONAL COMMENTS

8. Is there anything that you think is important for us to know about community-based interventions in the study area in the last 3 months that we've not asked?

THANK YOU FOR YOUR TIME AND SUPPORT

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #7, Page 1)		
(7) IEC: ***To be completed if IEC campaigns have been implemented in last 3 months***	**Staff ID** [____|____]	***Date completed*** *[____|____] / [____|____] / -* *[____|____]* day month year

TIME PERIOD COVERED:	1 = Baseline	4 = 7-9 months	7 = 16-18 months	
	2 = 0-3 months	5 = 10-12 months	8 = 19-21 months	[____|____]
	3 = 4-6 months	6 = 13-15 months	9 = 21-24 months	

SECTION 1: RESPONDENT INFORMATION	
1. Respondent name	***2. Contact information*** *(cell phone or email address)*
3. Respondent organization and position	

SECTION 2: HEALTH IEC CAMPAIGNS		
Introduction: *We understand from our meeting with the DHO (or representative) that you or your organization have been involved in delivering information, education, and communication (IEC) campaigns in Tororo District. We would like to learn more about the programs.*		
1. What organization(s) were responsible for conducting the campaign?		
2. Where were the campaigns conducted? *Probe for sub-county, parish, villages, or other unit of delivery (schools, health centers, etc).*		
3. When was the campaign conducted?	**Date started** [____|____] / [____|____] / - [____|____] *day month year*	**Date completed** [____|____] / [____|____] / - [____|____] *day month year*

4. What was the focus of the campaign? *Include all that apply.*	*1 = Malaria treatment (including ACTs)* *2 = Malaria prevention (including ITNs)* *3 = Malaria diagnosis (including RDTs)* *4 = Health education* *5 = Vaccination*	*[____|____]* *[____|____]* *[____|____]*

6 = Deworming

7 = Nutrition

8 = Sanitation

77 = Other _____
88 = Don't know

5. Can you describe the details of the campaign? *Probe for information about intended impact on health, how the program was delivered (using VHTs? CHWs?), duration of the program, etc.*

6. What population was covered?

If more detailed information on population is available, record in Section 3 on page 2.

Total [_____|_____|_____|_____|_____|_____|_____]

7. Who funded the campaign?

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #7, Page 2)

Staff ID	***Date completed***
[_____|_____]	*[_____|_____] / [_____|_____] / [_____|_____]* day month year

SECTION 3: ADDITIONAL COMMENTS

8. Is there anything that you think is important for us to know about IEC campaigns in the study area in the last 3 months that we've not asked?

THANK YOU FOR YOUR TIME AND SUPPORT

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #8, Page 1)		
(8) District & HSD: ***To be completed if changes have been implemented in last 3 months***	**Staff ID** [_____|_____]	***Date completed*** *[_____|_____] / [_____|_____] / -* *[_____|_____]* day month year
TIME PERIOD COVERED:	1 = Baseline 2 = 0-3 months 3 = 4-6 months	4 = 7-9 months 5 = 10-12 months 6 = 13-15 months	7 = 16-18 months 8 = 19-21 months 9 = 21-24 months	[_____|_____]

SECTION 1: RESPONDENT INFORMATION	
1. Respondent name	***2. Contact information*** *(cell phone or email address)*
3. Respondent organization and position	

SECTION 2: DISTRICT & HEALTH SUB-DISTRICT ISSUES		
Introduction: *We understand from our meeting with the DHO (or representative) that changes have been made recently at the district and/or HSD level in Tororo District. We would like to learn more about these changes.*		
1. What was the nature of the change? *Include all that apply.*	*1 = New policy introduced* *2 = Changes in guidelines* *3 = Changes or gaps in staffing at district or HSD level* *4 = Changes or gaps in staffing at health centers* *5 = Changes in supervision of HCWs or health centers* *77 = Other _____* *88 = Don't know*	*[_____|_____]* *[_____|_____]* *[_____|_____]*
2. At what level was the change made? *Include all that apply.*	*1 = District* *2 = Health sub-district* *77 = Other _____* *88 = Don't know*	*[_____|_____]* *[_____|_____]*
3. To what areas did the changes apply? *Probe for sub-county, parish, villages, or health centers, etc.*		
4. When was the change implemented?	**Date started** [_____|_____] / [_____|_____] / -	**Date completed** [_____|_____] / [_____|_____] / -

	[_____|_____] *day* *month* *year*	[_____|_____] *day* *month* *year*
5. Can you describe the details of the change?		
6. What was the intended impact of the change?		

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #8, Page 2)	
Staff ID [_____|_____]	***Date completed*** *[_____|_____] / [_____|_____] / [_____|_____]* day month year

SECTION 3: ADDITIONAL COMMENTS
7. Is there anything that you think is important for us to know about changes at the district or health sub-district level in the last 3 months that we've not asked?
THANK YOU FOR YOUR TIME AND SUPPORT

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #9, Page 1)		
(9) Economic & political: ***To be completed if changes have been implemented in last 3 months***	**Staff ID** [____|____]	***Date completed*** *[____|____] / [____|____] / -* *[____|____]* day month year
TIME PERIOD COVERED:	1 = Baseline 2 = 0-3 months 3 = 4-6 months	4 = 7-9 months 5 = 10-12 months 6 = 13-15 months	7 = 16-18 months 8 = 19-21 months 9 = 21-24 months	[____|____]

SECTION 1: RESPONDENT INFORMATION	
1. Respondent name	***2. Contact information*** *(cell phone or email address)*
3. Respondent organization and position	

SECTION 2: ECONOMIC & POLITICAL FACTORS		
Introduction: *We understand from our meeting with the DHO (or representative) that economic and political factors that might impact on the health of the population have recently changed in Tororo District. We would like to learn more about these changes.*		
1. To what areas do the factors or changes apply? *Probe for national level, sub-county, parish, villages, if known .*		
2. When were the factors or changes introduced?	**Date started** [____|____] / [____|____] / - [____|____] *day month year*	**Date completed** [____|____] / [____|____] / - [____|____] *day month year*
3. What is the source the information? *Include all that apply.*	*1 = Newspaper* *2 = Radio* *3 = TV* *77 = Other* _____ *88 = Don't know*	***[____|____]*** ***[____|____]***
4. Can you describe the details of the factors and changes?		
5. What was the potential impact of these		

factors and changes?

STRUCTURED CONTEXTUAL RECORD (Form 1, Part B, #9, Page 2)	
Staff ID [_____|_____]	***Date completed*** *[_____|_____] / [_____|_____] / [_____|_____]* day month year

SECTION 3: ADDITIONAL COMMENTS
6. Is there anything that you think is important for us to know about economic and political factors in the last 3 months that we've not asked?
THANK YOU FOR YOUR TIME AND SUPPORT

Appendix 5 Patient satisfaction and inappropriate treatment outcomes

Health Centre	Percentage of patients treated inappropriately for malaria (relative rank)	Patient-rated satisfaction with health centre visit (relative rank)
1	12% (high)	78% (high)
2	12% (high)	51% (low)
3	17%	80%
4	22%	44%
5	19%	54%
6	25%	76%
7	23%	72%
8	32%	56%
9	36% (low)	75% (high)
10	43% (low)	54% (low)