Evaluation of proactive community case management to accelerate access to care and reduce under-five mortality in Mali: a cluster randomised trial and process evaluation

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Declaration

I, Caroline Whidden, 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.

Abstract

Background: Low- and middle-income countries (LMICs) are scaling up community health worker (CHW) programmes. Research is needed to understand how CHWs can be integrated into, and supported by, health systems and communities, including evaluation of different approaches to delivering CHW services. This thesis synthesises the evidence, quantifies the impact, and evaluates the process of a proactive CHW workflow designed to reduce treatment delays and under-five mortality.

Methods: We first conducted a systematic review of the effects of proactive case-finding home visits by CHWs in LMICs on mortality, morbidity, and access to care for common childhood illnesses. We then evaluated the effects of proactive CHW service delivery at patients' homes compared to passive CHW service delivery at fixed village sites in a cluster randomised trial in rural Mali. The primary outcome of the trial was mortality among children under five years of age. The main secondary outcomes pertained to children's health care utilisation, measured at baseline and 12, 24, and 36 months of follow-up. We conducted a mixed method process evaluation alongside the trial, with embedded realist approaches, to evaluate implementation, mechanisms, and context to explain trial results between and across arms.

Results: Our systematic review of 14 reports of 11 interventions found that proactive CHW home visits may improve treatment coverage (RR: 1.59–4.64; low certainty evidence) but effects on prompt treatment and under-five mortality were uncertain, due to limitations in study designs, indirect measures of effect, and unexplained heterogeneity. Our trial found that CHW home visits had no effect on under-five mortality compared to site-based delivery by CHWs. After 12 months, sick children had 22% higher odds of health sector treatment within 24 hours of symptom onset in intervention compared to control clusters (95% CIs: 1.06, 1.41), but no difference at 24 or 36 months. Over all three years, we found modest improvements in children's health sector consultation in intervention compared to control clusters (aOR=1.12; 95% CIs: 0.99, 1.26). In both arms combined, under-five mortality fell from 148.4 to 55.1 deaths per 1000 live births and

prompt health sector treatment more than doubled compared to baseline. Our process evaluation showed that user fee removal, professional CHWs, and upgrades to primary clinics—all in both trial arms—enabled providers to offer acceptable, quality services and trial participants to seek prompt care. In this context, proactive home visits improved access via mechanisms that had already been activated.

Conclusion: Proactive home visits may accelerate access to care, but user fee removal, professional CHWs, and systems strengthening at primary clinics are foundational to achieving UHC and child survival goals.

Acknowledgements

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Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal Care
AHR	Adjusted Hazard Ratio
AOR	Adjusted Odds Ratio
ARR	Adjusted Risk Ratio
ASACO	Community Health Association
ASHA	Accredited Social Health Activist
CBA	Controlled Before-After
CEA	Cost-Effectiveness Ratio
CENTRAL	Cochrane Central Register of Controlled Trials
CI	Confidence Interval
CIAMO	Context-Intervention-Actor-Mechanism-Outcome
CHW	Community Health Worker
CONSORT	Consolidation of Standards for Reporting of Trials
CRA	Clinical Research Associate
DALY	Disability Adjusted Life Year
DHIS2	District Health Information Software II
DHS	Demographic and Health Survey

DSMB	Data Safety and Monitoring Board
EMR	Electronic Medical Records
EPOC	Cochrane Effective Practice and Organisation of Care
FMPOS	Faculté de Médecine, Pharmacie et Odonto-Stomatologie
GOBI	Growth monitoring, Oral rehydration, Breastfeeding, and Immunisation
GPS	Global Positioning System
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HBNC	Home Based Newborn Care
HIC	High-Income Country
HIV	Human Immunodeficiency Virus
HR	Hazard Ratio
iCCM	integrated Community Case Management
ICC	Intracluster Correlation Coefficient
ICER	Incremental Cost-Effectiveness Ratio
IDI	In-Depth Interview
IMNCI	Integrated Management of Neonatal and Childhood Illness
ITS	Interrupted Time Series
ITT	Intention-To-Treat
LIC	Low-Income Country

LMIC	Low- and Middle-Income Country
MeSH	Medical Subject Headings
MD	Mean Difference
MDG	Millennium Development Goal
MSDS	Ministry of Health and Social Development
NCD	Non-Communicable Disease
NGO	Non-Governmental Organisation
NRCT	Non-Randomised Controlled Trial
ODK	Open Data Kit
ORS	Oral Rehydration Solution
PHC	Primary Health Care
PHC	Primary Health Centre
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
ProCCM	Proactive Community Case Management
RCT	Randomised Controlled Trial
RR	Risk Ratio
SAP	Statistical Analysis Plan
SDG	Sustainable Development Goals
SMC	Seasonal Malaria Chemoprevention

TBA   Traditional Birth Attendant

ToC   Theory of Change

UHC   Universal Health Coverage

UN   United Nations

UNICEF   United Nations International Children's Emergency Fund

USAID   United States Agency of International Development

WHO   World Health Organization

Chapter 1   Introduction

Background

Evidence-based preventive and curative interventions could avert many maternal, newborn, and child deaths globally, if scaled up to reach those who are systemically denied access (Jones *et al.*, 2003; Darmstadt *et al.*, 2005; Campbell and Graham, 2006; Bhutta *et al.*, 2014). In the Sustainable Development Goal (SDG) era, the United Nations (UN) and World Health Organization (WHO) have emphasised Universal Health Coverage (UHC) as both an intrinsic and instrumental goal to achieve health and survival. UHC envisions a world where all people have access to affordable, quality, and effective essential health services, treatments, and vaccines (United Nations, 2019). However, in 2019, the first UN High Level Meeting on UHC acknowledged that at least half of the world's population still lacked access to essential services and up to one third would remain uncovered by the 2030 deadline unless progress accelerated (United Nations, 2019). The same year, the Global Burden of Disease study showed that countries with the worst UHC effective coverage index were concentrated in West and Central Africa (Lozano *et al.*, 2020), and half of total Disability Adjusted Life Years (DALYs) among children under 10 years of age occurred in sub-Saharan Africa (Vos *et al.*, 2020). To close these coverage and equity gaps, facility-based care needs to be strengthened, but this alone will not achieve UHC and health and survival goals without integrating community-based care that can be delivered safely, effectively, and equitably by Community Health Workers (CHWs) (Black *et al.*, 2017; Schleiff *et al.*, 2017; Perry and Hodgins, 2021).

The first widespread recognition of the potential of CHWs occurred in the 1960s in the context of the global Primary Health Care (PHC) movement. PHC represented an "alternative" approach to health and development compared to the "medical elitism" of "Western" models that prioritised hospitals, curative care, disease-specific technologies, and vertical programmes (Cueto, 2004). Based on the concept of the socio-economic determinants of health, the PHC movement prioritised rural health centres, lay health workers to deliver basic services, and community participation. During the 1960s and

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1970s, many countries experimented with CHW programmes, including Tanzania, Niger, Venezuela, Indonesia, India, and most influentially, China. China's "barefoot doctor" programme had begun in the 1950s and, by the early 1970s, had expanded to include an estimated one million salaried CHWs serving a rural population of 800 million people (Lehmann and Sanders, 2007; Perry *et al.*, 2014). In Mali, the 1960 postcolonial, socialist government of Modibo Keita built and staffed rural health centres, a PHC agenda that continued after the 1968 *coup d'état* that placed Moussa Traoré in power until 1991 (Golaszewski, 2021). The first CHW programmes in Mali began in the early 1970s in the Koulikoro and Sikasso regions to train local young, literate women as *matrones* (auxiliary midwives) who were intended to work in rural maternity wards that were supposed to be constructed and equipped by the community's own resources (Golaszewski, 2021).

While the movement was already underway in Africa, Asia, and South America, policy makers in Europe and North America took up the PHC cause in the 1970s, including the director general of the WHO from 1973 (Cueto, 2004). In 1978, the WHO and UNICEF co-sponsored the International Conference on Primary Health Care in Alma Ata, Kazakhstan, which was attended by 134 governments representing almost all member countries, although China was notably absent (Cueto, 2004; Perry *et al.*, 2014). This conference produced the Declaration of Alma Ata, an ambitious document that proclaimed health as a human right, comprehensive PHC as the key to achieving "Health for All by 2020", and the foundational role of CHWs in that effort (World Health Organization, 1978). Consistent with the principles underpinning PHC, namely equity, preventive care, multisectoral approach, community participation, and appropriate technology, CHWs were expected to be "liberator" rather than "lackey" (Werner, 1977), broad agents of social change rather than more narrow health extension workers. Many ministries of health returned home enthusiastic about implementing PHC and scaled up national CHW programmes. In Mali, although there was no standard national policy, CHW initiatives expanded to include volunteer cadres of male *hygiénistes secouristes* who focused on health promotion and treating minor ailments (Ministère de la Santé et du Développement

Social du Mali, 2021), and female traditional birth attendants (TBAs) who could deliver babies in communities or work in rural maternity wards (Golaszewski, 2021).

However, the success of large-scale CHW programmes was almost immediately undermined by global economic pressures, neoliberal policies, and concerns about measurement and cost-effectiveness in health care (Cueto, 2004). One year later, the Rockefeller Foundation, USAID, and UNICEF, among others met in Bellagio, Italy and endorsed "selective primary health care", a package of low-cost interventions targeting the main health issues in low-income countries (LICs), such as growth monitoring, oral rehydration, breastfeeding, and immunisation, known as GOBI (Cueto, 2004). Contrary to these technical interventions with clear budgets and measurements, it was unclear how "comprehensive" PHC envisioned at Alma Ata and socio-economic development would be financed. These debates continued into the 1980s, against the backdrop of economic recession, a foreign debt crisis, and the rise of neoliberalism. Low- and middle-income countries (LMICs) were hit with structural adjustment programmes by the World Bank and International Monetary Fund, which considerably reduced the role of the state and financing in health, including national CHW programmes (Lehmann and Sanders, 2007).

In this context, during the 1980s and 1990s, nearly all African countries introduced user fees into the public health sector (Ridde and Morestin, 2011). In 1987, Mali hosted African Ministers of Health at a conference sponsored by the WHO and UNICEF on the financial sustainability of PHC, where they adopted the Bamako Initiative. The Bamako Initiative advocated that revenue generation and control should be de-centralised (Gilson, 1997), using PHC language of community participation in health care financing and management. The Bamako Initiative aimed, by introducing user fees for essential drugs and establishing a revolving drug fund managed at the community level, to finance and strengthen PHC, including CHWs (Kanji, 1989; Garner, 1989). Although primarily introduced to raise revenue, proponents of user fees also argued that they would lead to gains in efficiency and equity by incentivising service utilisation and resource allocation towards the primary care level (Gilson, 1997). Critics at the time raised concerns that the poorest would be unable to pay, doctors would overprescribe, local drug funds would be

mismanaged, and governments would become increasingly dependent on donors (Kanji, 1989; Garner, 1989). Several studies have since confirmed that user fees pose a major barrier to access to health services, especially for the poor, and their introduction has resulted in reduced and inequitable utilisation (Wiseman, 2005; James *et al.*, 2006; Lagarde and Palmer, 2008). Furthermore, exemption schemes, originally proposed to protect the most vulnerable, have largely been difficult to implement and ineffective (James *et al.*, 2006; Ridde, 2008; Ridde and Morestin, 2011). With regard to raising revenue, the Bamako Initiative expected countries to achieve self-sufficiency in drug purchasing by the end of 1993 (Kanji, 1989), but national fee systems generated only about 5% of total recurrent health system expenditure (not including administrative costs) during this time period (Gilson, 1997).

Fundamentally inhibited by insufficient planning and resources, several large-scale CHW programmes in the 1980s fell short of expectations and, by the end of the 1990s, had collapsed along with the optimism surrounding CHWs and comprehensive PHC (Lehmann and Sanders, 2007; Perry *et al.*, 2014). With the perception that CHW programmes were a panacea, a cheap or temporary fix to the health system (rather than an integral part of it), several programmes provided initial training and a minimal drug supply, but failed to anticipate recurring costs, such as salaries, supervision, and supplies (Berman *et al.*, 1987; Walt, 1990; Perry *et al.*, 2014). Many programmes, like those in Mali, relied on volunteers who were themselves poor (Mburu, 1994) and, in some cases, gained some remuneration by charging fees and selling drugs to patients (Berman *et al.*, 1987; Walt, 1990). Without the necessary support and empowerment, CHWs had all of the responsibility and none of the authority (Mburu, 1994). Their role as social change agents went largely unrealised. Case study evaluations showed that while CHWs could reach historically underserved populations and at a lower cost than facilities, many programmes suffered from high attrition and low quality of care (Berman *et al.*, 1987; Walt, 1990). As it became clear that CHW programmes were more difficult and costly than expected to implement at scale, they lost momentum and popular support.

The 2000s saw a global resurgence in the interest of CHWs in order to meet the Millennium Development Goals (MDGs) to reduce child mortality, improve maternal health, and combat HIV/AIDS, malaria, and other disease—all while facing a global health workforce shortage (Lehmann and Sanders, 2007; Schneider *et al.*, 2016). Inspiration came from recent successful CHW case studies in Brazil, Bangladesh, India, Pakistan, Iran, and Ethiopia (Lehmann and Sanders, 2007; Bhutta *et al.*, 2010; Perry, 2020), and from South Africa, where a grassroots CHW response to the HIV/AIDS epidemic had emerged (Schneider *et al.*, 2008; Tulenko *et al.*, 2013). Given the WHO's "task shifting" agenda (World Health Organization *et al.*, 2008), CHWs re-emerged with a more technical, "medically oriented" focus rather than a "socially oriented" one related to prevention, community mobilisation, and social change (Campbell and Scott, 2011). New actors with money and influence, including the Bill and Melinda Gates Foundation, the Global Alliance for Vaccines and Immunization, and the Global Fund to Fights AIDS, Tuberculosis and Malaria, oriented the global health agenda towards vertical programmes (Rifkin, 2018). During this period (2007 to 2017), only 2.5% of total development assistance for health was allocated to CHW programmes, with vertical CHW interventions targeting infectious diseases receiving the most funds (Lu *et al.*, 2020).

The MDG era established evidence of the effectiveness of CHWs to deliver a range of promotive, preventive, and curative primary care interventions. These interventions covered maternal, newborn, and child health, and the management of infectious diseases such as malaria, pneumonia, tuberculosis, and HIV. Compared to usual care at facilities, CHWs can increase the coverage and uptake of essential newborn care practices including breastfeeding (moderate quality evidence), malaria chemoprevention and bed net use, childhood immunisation, and care-seeking for neonatal morbidities and childhood illnesses (Bigirwa, 2009; Lewin *et al.*, 2010; Gilmore and Mcauliffe, 2013; Lassi and Bhutta, 2015). According to moderate quality evidence, CHWs can improve tuberculosis treatment outcomes (Lewin *et al.*, 2010) and increase the coverage and uptake of HIV prevention, management, and retention care without compromising quality or patient outcomes (Mwai *et al.*, 2013; Kredo *et al.*, 2014). CHWs may also alleviate symptoms of

mental, neurological, and substance use disorders (Mutamba *et al.*, 2013; van Ginneken *et al.*, 2013), with more recent evidence validating the potential of CHWs in mental health care (Barnett *et al.*, 2018; van Ginneken *et al.*, 2021). The 2013-2016 Ebola epidemic in West Africa reaffirmed CHWs' vital role in the surveillance of disease and mobilisation of communities to help contain outbreaks (Perry *et al.*, 2016). Ultimately, the synthesis of evidence with a high degree of internal validity suggests that CHWs contribute in much needed ways to reducing maternal morbidity, and neonatal and child morbidity and mortality (Haines *et al.*, 2007; Bigirwa, 2009; Lewin *et al.*, 2010; Christopher *et al.*, 2011; Lassi and Bhutta, 2015; Gogia and Sachdev, 2016). Investing in a strong CHW system at full scale across sub-Saharan Africa could generate an economic return of up to 10:1 (Dahn *et al.*, 2015).

The WHO and UNICEF recommended, in 2012, integrated Community Case Management (iCCM) by CHWs to diagnose and treat common childhood illnesses in LMICs in the community setting, including malaria, diarrhoea, pneumonia, acute malnutrition, and/or newborn illnesses (Young *et al.*, 2012). This recommendation was adopted by many African governments and iCCM was scaled up across the continent (Bennett *et al.*, 2014; Rasanathan *et al.*, 2014). While iCCM programmes in different countries are aligned with the international clinical guidelines and principles, they vary greatly in terms of their design and implementation—including financing mechanisms, health system and community support, and approach to CHW service delivery—to variable effects (Amouzou *et al.*, 2014; Bosch-Capblanch and Marceau, 2014; Hazel and Bryce, 2016; Oliphant *et al.*, 2021). In Mali, the first national community health strategy, which was launched in 2016, stationed CHWs (*agents de santé communautaire*) at sites in villages greater than five kilometres from a primary health centre to offer promotive services, basic newborn care, family planning, and iCCM (Ministère de la Santé et de l'Hygiène Publique du Mali, 2015). However, even within Mali, this plan has been implemented by different technical partners in various ways with mixed results.

In a periurban setting outside of Bamako, called Yirimadio, a non-governmental organisation (NGO) launched a small-scale CHW programme in 2008 in partnership with

the Malian Ministry of Health and Social Development (MSDS). The Proactive Community Case Management (ProCCM) programme included door-to-door home visits by CHWs to proactively identify childhood illnesses, diagnose and treat childhood malaria in the home, and refer all patients with other conditions to the primary health centre. ProCCM also included rehabilitation of health centre infrastructure, training health care providers, removal of user fees for patients who were unable to pay, and community mobilisation. Three years after the launch of ProCCM, under-five mortality in Yirimadio fell from 155 per 1000 live births to 17 per 1000 live births (Johnson *et al.*, 2013), and this fall was sustained over seven years of repeated follow-up (Johnson *et al.*, 2018). After three years, the prevalence of febrile illness among children under five decreased from 38% to 23% ($p<0.001$), and receipt of effective antimalarial treatment within 24 hours of symptom onset increased from 15% to 28% ($p<0.05$) (Johnson *et al.*, 2013). Given the observational design of the study, however, it was not possible to infer causality of the intervention or to deduce which components of the intervention may have been most responsible for its effects.

Proactive case-finding home visits by CHWs may be an effective strategy for delivering child health services (Freeman *et al.*, 2017) and may unlock the potential of iCCM to accelerate access to care, reduce the progression of disease, interrupt transmission, and reduce child mortality. Some of the world's most longstanding, comprehensive CHW programmes with evidence of impact on infant or child mortality over more than ten years include routine CHW contact with all households (Perry *et al.*, 2017). CHW home visits have been identified as a key component of community-based primary health care interventions that have evidence of effect on maternal and neonatal health outcomes (Lassi and Bhutta, 2015). Home-based neonatal care by CHWs, which includes health education and promotion and may sometimes include detection and management or referral of morbidities, has been associated with reduced neonatal and perinatal mortality (Gogia and Sachdev, 2010, 2016). In 2009, the WHO and UNICEF recommended home visits in the newborn baby's first week of life by skilled health workers, including CHWs linked to the health system (World Health Organization and UNICEF, 2009). However, a systematic

review on home visits in the early postpartum period (by health professionals or skilled attendants) found that the evidence was very uncertain about their effects on maternal and neonatal mortality (Yonemoto *et al.*, 2017, 2021). Importantly, most of this experience and evidence on comprehensive maternal, newborn, and child health comes from Asia, with less emerging from Africa.

With the global revitalisation of interest and investment in CHWs, policy debates have shifted from *whether* CHWs can effectively deliver health services to *how to design and implement* CHW programmes that bring about their full potential and optimise impact. CHW performance has been conceptualised at the centre of CHW programming, health and community systems, and context (Palazuelos *et al.*, 2013; Naimoli *et al.*, 2014; Kok *et al.*, 2017a). Systematic reviews of features that enable CHW performance or CHW programme impact have identified broad strategies related to incentives, continuous education, supportive supervision, logistics and supplies, and community engagement, and have concluded that rigorous research is needed on specific components, exact mechanisms, and contextual factors that contribute to success (Glenton *et al.*, 2013; Kok *et al.*, 2015a, 2015b; Scott *et al.*, 2018). In 2018, after the studies included in this thesis had begun, the WHO released the first evidence-based global guideline on health policy and system support to optimise CHW programmes (World Health Organization, 2018). The WHO guideline strongly recommends remunerating CHWs commensurate with their work, providing paid CHWs with a written contracting agreement, and involving communities in programme planning, CHW selection, and monitoring (Cometto *et al.*, 2018). It makes several other conditional recommendations based on the low or very low certainty of evidence, and highlights priorities for a future research agenda on CHWs, including:

1. "Further research is needed on CHW workflow for community engagement and care, including to measure the effect of home visits and in-home care by CHWs on access to care and mortality" (World Health Organization, 2018).
2. "There is a need to investigate not only what works, but also the contextual factors and enablers (how, for whom, under what circumstances), and the broader health

system requirements and implications of supporting the implementation of several interventions simultaneously" (World Health Organization, 2018).

Aims and objectives

The study described in this thesis aimed to test and understand a proactive approach to CHW service delivery in rural Mali in order to inform the design and implementation of CHW strategies, including iCCM, to meet national and international UHC and child health goals.

The study had the following objectives:

1. Synthesising the existing evidence for the effectiveness of proactive case detection at home by CHWs of common childhood illnesses in LMICs on mortality, morbidity, and access to care.

2. Determining whether adding proactive case-finding home visits to reinforced iCCM in rural Mali reduced mortality, reduced the prevalence of common illnesses, and improved the timeliness of health care among children under five years of age.

3. Evaluating the implementation, mechanisms of effect, and context of the proactive CHW home visit intervention and of the broader proactive community case management programme that included health systems support.

Overview of the thesis

To meet these study objectives, this thesis includes a systematic review (Chapter 2), trial protocol (Chapter 3), impact evaluation results (Chapter 4), outcome evaluation (Chapter 5), and process evaluation (Chapter 6).

Following the introduction to the thesis in Chapter 1, Chapter 2 comprises the systematic review that meets the first objective of the thesis and highlights the knowledge and methodological gaps pertaining to proactive case-finding home visits by CHWs (the "intervention") for child health care utilisation, morbidity, and mortality in LMICs.

Chapter 3 is the protocol that describes the methods of the cluster randomised trial in rural Mali, designed to assess the intervention's effects on under-five mortality (primary trial endpoint) and access to maternal, child, and reproductive health care (secondary trial endpoints) compared to fixed, village site-based CHW service delivery. The methods describe a large, three-year, parallel cluster randomised trial with before and after observations.

Chapters 4 and 5 report the primary and secondary trial outcome results, respectively. Chapter 4 reports the effects of adding proactive case-finding home visits to reinforced iCCM on under-five mortality. Chapter 4 also reports the changes in this outcome during the implementation period compared to the pre-implementation period, ignoring trial arm. Chapter 5 reports trial results pertaining to children's health (prevalence of common childhood illnesses) and service utilisation (24-hour treatment, health sector consultation) between and across trial arms. Both Chapters 4 and 5 provide intention-to-treat (ITT) and per-protocol estimates of intervention effects, as well as heterogeneous treatment effect analyses by equity dimensions of household wealth and distance to facility, and cluster population size. Together, Chapters 3, 4, and 5 meet the second objective of the thesis.

Chapter 6 reports the process evaluation that meets the third objective of the thesis. The process evaluation examined the implementation, mechanisms, and context of the intervention and health system support co-interventions to help to explain trial results between and across arms.

Finally, Chapter 7 provides a discussion that ties the results of the studies described in the thesis together, highlighting the key findings and their implications for policy, practice, and research.

Chapters 2, 3, and 5 are published papers. Chapters 4 and 6 are manuscripts that have been submitted and are under peer review. Given that each of these papers needs to stand on its own, some repetition across thesis chapters was inevitable. However, I have tried to limit this as much as possible.

Contributions of the candidate

This thesis contributed to the larger aims of the ProCCM trial. I was one of the key investigators of this trial, along with Kassoum Kayentao (University of Sciences, Techniques, and Technologies of Bamako) and Ari Johnson (University of California, San Francisco).

- I conceived the research question and developed the systematic review protocol, with input from my supervisors (Daniel Chandramohan and Brian Greenwood) and members of the trial team. I conducted the review, analysed the data, and wrote the manuscript.
- I wrote the ProCCM trial protocol manuscript, which is included in the thesis.
- Along with colleagues in Mali and the USA, I developed and tested the survey tools, trained data collectors, supervised annual data collection, and contributed to data management and data validation. Trial statisticians (Jenny Liu and Emily Treleaven) analysed intervention effects on under-five mortality. I contributed to writing the manuscript that reported these findings.
- I developed the statistical analysis plan for the trial's secondary outcomes related to children's health and access to care, with advice from my advisor Clémence Leyrat, supervisors, and trial team. I performed all analyses and wrote the manuscript.
- I designed the study for the process evaluation and wrote the protocol, with input from my advisor Jayne Webster, supervisors, and trial team. I developed and piloted the tools (survey, guides), trained the interviewers, and supervised

data collection. I coded qualitative interviews along with my co-coder (Faith Cole), conducted qualitative and mixed method analyses, and wrote the manuscript.

Chapter 2   Systematic review

Overview

This systematic review addresses the first objective of the thesis. It highlights the knowledge and methodological gaps in the field of study and sets up the rest of the thesis.

The paper is provided here in its published format. It is an open access article that falls under the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license. The online supplementary files 1-4 that are referenced in this paper are provided in Appendix A of this thesis, including the review's full search strategy and supplementary figures, tables, and results.

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed _for each_ research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1605048	**Title**	Ms
First Name(s)	Caroline		
Surname/Family Name	Whidden		
Thesis Title	Evaluation of proactive community case management to accelerate access to care and reduce under-five mortality in Mali: a cluster randomised trial and process evaluation		
Primary Supervisor	Daniel Chandramohan		

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?	BMJ Global Health		
When was the work published?	15 Dec 2019		
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?*	**No**	Was the work subject to academic peer review?	**Yes**

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Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	

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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 conceived the research question and developed the systematic review protocol, with input from my supervisors (Daniel Chandramohan and Brian Greenwood) and members of the trial team. I conducted the review and analysed the data. I wrote the manuscript and managed the peer review process.

SECTION E

Student Signature	Caroline Whidden
Date	12 Dec 2023

Supervisor Signature	Daniel Chandramohan
Date	12 Dec 2023

BMJ Global Health

Proactive case detection of common childhood illnesses by community health workers: a systematic review

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ABSTRACT

Introduction Identifying design features and implementation strategies to optimise community health worker (CHW) programmes is important in the context of mixed results at scale. We systematically reviewed evidence of the effects of proactive case detection by CHWs in low-income and middle-income countries (LMICs) on mortality, morbidity and access to care for common childhood illnesses.

Methods Published studies were identified via electronic databases from 1978 to 2017. We included randomised and non-randomised controlled trials, controlled before–after studies and interrupted time series studies, and assessed their quality for risk of bias. We reported measures of effect as study investigators reported them, and synthesised by outcomes of mortality, disease prevalence, hospitalisation and access to treatment. We calculated risk ratios (RRs) as a principal summary measure, with CIs adjusted for cluster design effect.

Results We identified 14 studies of 11 interventions from nine LMICs that met inclusion criteria. They showed considerable diversity in intervention design and implementation, comparison, outcomes and study quality, which precluded meta-analysis. Proactive case detection may reduce infant mortality (RR: 0.52–0.94) and increase access to effective treatment (RR: 1.59–4.64) compared with conventional community-based healthcare delivery (low certainty evidence). It is uncertain whether proactive case detection reduces mortality among children under 5 years (RR: 0.04–0.80), prevalence of infectious diseases (RR: 0.06–1.02), hospitalisation (RR: 0.38–1.26) or increases access to prompt treatment (RR: 1.00–2.39) because the certainty of this evidence is very low.

Conclusion Proactive case detection may provide promising benefits for child health, but evidence is insufficient to draw conclusions. More research is needed on proactive case detection with rigorous study designs that use standardised outcomes and measurement methods, and report more detail on complex intervention design and implementation.

PROSPERO registration number CRD42017074621.

INTRODUCTION

Community health worker (CHW) programmes are experiencing a resurgence as a strategy to achieve health-related sustainable development goals. Many low-income and middle-income countries (LMICs) have implemented integrated Community Case Management (iCCM) of common childhood illnesses,[1 2] a package of services delivered by CHWs to diagnose, treat and refer children under 5 with malaria, diarrhoea, pneumonia and malnutrition in the community setting.[3] This strategy has shown an increase in access to care and reduced child mortality.[4–12] However, the expected benefits have not been realised in all contexts.[13–18] Several recent evaluations of national iCCM programmes in

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Burkina Faso, Ethiopia and Malawi did not find impacts on care-seeking or child mortality.[19–22]

These programmes shared certain design features that may have contributed to the lack of overall effects by not addressing barriers to care, such as user fees for services,[23–25] lack of adequate CHW supervision,[26–28] or provision only for patients who sought care from a fixed site. As more countries scale up CHW programmes, it is critical to understand how to best design and implement iCCM, and CHW services more broadly, in order to realise their full potential.

A recent series of systematic reviews to inform WHO guidelines for optimising CHW programmes found a scarcity of evidence on best practices for several key policy areas, including CHW training, supervision and deployment, and calls specifically for more research on CHW workflow.[29] We conducted a systematic review of the evidence for the effectiveness of proactive case detection by CHWs to improve access to care and reduce morbidity and mortality. By proactively seeking out patients at home to offer diagnosis and treatment or referral, a proactive workflow has the potential to overcome barriers to care, including direct and indirect costs, distance, mistrust and gender inequality, reduce the time from onset of a condition to services, and consequently reduce disease progression and mortality.

METHODS
Inclusion criteria
Study designs
Studies from LMICs involving community-based, proactive case detection of common childhood illnesses were identified. Anticipating that randomised trials of healthcare service delivery would be very few, we included a broader range of study designs in line with Cochrane Effective Practice and Organisation of Care (EPOC) group recommendations.[30] These included randomised controlled trials (RCTs) and non-randomised controlled trials (NRCTs), controlled before–after (CBA) studies, interrupted time series (ITS) and repeated measure studies.

Interventions and comparisons
To be eligible for inclusion, studies needed to evaluate a primary healthcare intervention that included proactive case-finding home visits by CHWs for the purpose of searching for and identifying, through history and/or diagnostics, cases of common childhood illness, including malaria, diarrhoea, pneumonia, malnutrition, HIV or tuberculosis. These conditions were chosen because they are covered by international protocols for iCCM of common childhood illnesses[31] and/or contribute a substantial disease burden in LMICs. Studies needed to compare proactive healthcare delivery to usual or supplemented primary care available from facilities and/or CHWs that did not involve home visits for the purpose of identifying sick patients.

CHWs and trial participants
In accordance with earlier reviews, a CHW was defined as any lay health worker who received training to perform tasks related to primary healthcare delivery but had not received professional medical or paramedical education.[32] Recipients of proactive case-finding home visits had to include children under 5 years of age.

Outcomes
We included studies if they assessed any of the following outcomes: (1) mortality among children under 5 years of age or infants aged 0–11 months; (2) prevalence or incidence of disease; (3) hospitalisation; (4) access to healthcare services; (5) harms or adverse effects; (6) costs or economic effects.

Our review focused on assessing proactive case detection as an adjoint to iCCM. As causes of neonatal deaths in LMICs differ from those of post-neonatal child deaths, we did not include studies that were restricted to neonates, that is, intervening solely in the neonatal period and reporting solely on neonatal outcomes. Nevertheless, we retained studies from our search that assessed childhood illness starting from the first day of life and reported outcomes separately for neonates and infants.

Search strategy
We searched the following electronic databases for studies meeting the eligibility criteria, in addition to contacting researchers with expertise relevant to the review topic:
► MEDLINE Ovid (1946 to September Week 4 2017) (searched 10 October 2017);
► Embase (1947 to 2017 October 20) (searched 23 October 2017);
► Global Health Database (1910 to 2017 Week 41) (searched 23 October 2017);
► Cochrane Central Register of Controlled Trials (searched 9 November 2017);
► WHO Library (searched 30 November 2017).

The search strategy included terms to capture the following concepts describing the intervention: (i) proactive case detection—broad search terms were used to maximise sensitivity given a lack of MeSH terms for this concept; (ii) CHWs—search terms were adapted from a review by Lewin and colleagues[32] and (iii) condition. A combination of two methodological search filters was adapted to capture a fourth concept for appropriate study design: (iv) the sensitivity-maximising Cochrane MEDLINE filter for RCTs and an EPOC filter for non-randomised trials. The search included publications since 1978, the year of the Alma-Ata Declaration, which marked a restructuring of the global health agenda towards primary healthcare provision by CHWs. No language restrictions were applied. Full strategies and results are provided in online supplementary file 1.

Data collection and analysis
Selection of studies
Studies retrieved from the search were uploaded onto Covidence, a Cochrane technology platform for systematic reviews.[33] Two reviewers (CW and JT or JG) independently screened titles, abstracts and full-text articles

for eligibility. Inclusion was determined by consensus or in consultation with a third reviewer (JT or JG).

Data extraction and quality assessment

Two reviewers (CW and EW) independently extracted data from included studies related to study identification, methods, population, interventions, implementation of intervention, outcomes and results using a data extraction form designed in Covidence. Two reviewers (CW and EW) independently assessed the quality of included studies using the EPOC risk of bias tool for studies with a separate control group;[34] allocation concealment was removed from the quality assessment criteria as reviewers deemed this domain inapplicable due to the nature of the intervention under review. Consensus on data extraction and quality assessment was reached in discussion or in consultation with a third reviewer (JT or JG).

Data synthesis

We reported measures of effect in the same way that study investigators reported them and synthesised them by type of outcome. For studies with a separate control group, we included only the measure of effect derived by comparing the intervention group to the control group, if multiple comparisons were reported. For studies with no separate control group, we included baseline to end-line comparisons. We calculated risk ratios (RRs) for dichotomous data to allow for comparisons across studies. If appropriate denominators (eg, number of live births for mortality outcomes) were not reported, we used population estimates reported in the study to approximate the denominator. We calculated 95% CIs, adjusting for clustering using the intracluster correlation coefficient (ICC) reported in the study, if available.[35] If not available, we used a conservative ICC of 0.05 for all studies with a cluster design, as the ICC was <0.001 in the three studies for which it was reported. We assessed heterogeneity across studies for each outcome type both qualitatively and quantitatively using the I^2 statistic, which describes the percentage of total variation across studies that is due to heterogeneity rather than chance.[36] Two reviewers (CW and JT or JG) independently assessed the certainty of evidence for each analysis using the Grading of Recommendations, Assessment, Development and Evaluation approach,[37 38] which takes into account study design, risk of bias, inconsistency, indirectness/applicability, imprecision and strength of association. Consensus was reached through discussion or in consultation with a third reviewer (JT or JG).

RESULTS
Characteristics of included studies

Excluding duplicates, a total of 442 abstracts were screened for eligibility (figure 1 in online supplementary file 2). Fourteen studies were included, including five cluster RCTs (table 1). Complete information on the characteristics and risk of bias for each study is available in online supplementary file 3.

Study settings

Among the 14 included studies, seven were from Africa (three KwaZulu-Natal, South Africa,[39–41] two Mali,[42 43] one Ethiopia[44] and one Senegal.[45] The two reports from Mali[42 43] and the two from rural South Africa,[40 41] respectively, studied the same interventions delivered to the same populations, differing only with regard to when— and in South Africa, how—impact was assessed. Six studies were from Southeast Asia (three India,[46–48] one Bangladesh,[49] one Nepal[50] and one Pakistan.[51] Two reports from Haryana, India[47 48] evaluated the same intervention delivered to the same population but assessed different outcomes. One study was from the Americas, in Dominican Republic.[52] Four studies took place in urban or periurban settings,[39 42 43 52] and eight in rural settings;[40 41 44–46 49–51] the studies in Haryana[47 48] did not indicate whether the setting was rural or urban.

Study designs and outcomes

The KwaZulu-Natal, South Africa[39–41] and Haryana, India[47 48] studies were cluster RCTs that evaluated a range of access to care, morbidity and mortality outcomes; the rural South Africa study did not report outcomes separately for children under 5 years.[40 41] Two studies were NRCTs that measured morbidity outcomes;[49 52] the Bangladesh study did not report outcomes separately for children under 5 years.[49] The Nepal study[50] that used a non-randomised, stepped-wedge design to assess risk of death among infants and children did not compare results between early and late treatment groups. Instead, it compared annual risks to baseline and used a test for trend to assess programme maturity. This study was therefore considered in this review to be an uncontrolled before–after study from baseline to end-line.

Four studies used a CBA design[44–46 51] and reported percent differences or difference-in-differences for mortality, morbidity or access to care outcomes. However, some did not use the baseline or control group appropriately. The Pakistan study[51] reported different baseline years for intervention and control areas; therefore, this study was deemed a NRCT and only the postintervention comparison between groups was presented in this review. The Ethiopia study[44] presented a number of before–after access to care indicators for the intervention group, but only present before–after data for the comparison group for one outcome, the tuberculosis case notification rate; outcomes were not reported separately for children under 5 years. Finally, the Mali studies[42 43] were included as ITS designs; yet, with only one baseline, they lacked a comparative preintervention trend and thus were treated in the review as uncontrolled before–after studies from baseline to end-line.

Participants

Half of the studies extended CHW services to the entire population,[42–45 49 53 54] among which only the Mali

Table 1 Characteristics of included studies evaluating proactive case detection of common childhood illnesses by community health workers

Study	Study design (period)	Setting + unit of allocation	Participants + CHW sample	Description of proactive case detection intervention			Cointerventions	Description of control	Outcomes (timepoints)
				CHW profile	Conditions	Timing			
Bang, 1999	CBA (1993–1998)	Rural, Maharashtra, India; Area I: n=1 C: n=2	Mother–baby dyads I: n=38 998 C: n=42 149 CHWs I: n=? C: n=?	Educated female VHWs; recruited locally; trained 6months; supervised fortnightly; performance-linked payment	Doorstep detection of mother and infant danger signs/illnesses, and (in yr. 2–3) home-based management and follow-up of neonatal illnesses and sepsis	Newborn home visits on days 1, 2, 3, 5, 7, 14, 21, 28 and any day called on for 3year.	▲ Mother's health education (in year 3) ▲ User fee removal for VHW neonatal care ▲ CCM of childhood malaria, diarrhoea, pneumonia by male VHWs and TBAs	Routine care + CCM of childhood malaria and diarrhoea by male VHWs	Infant, neonatal, perinatal mortality (6 months)
Bhandari, 2012	Cluster RCT (2006–2010)	Faridabad, Haryana, India; PHC area I: n=9 C: n=9	Mother–baby dyads I: n=29 782 C: n=30920 CHWs I: n=601 C: n=?	Anganwadi workers trained additional 8 days in IMNCI; vacant supervisory roles filled (ASHAs); task-based pay; village drug depot	Doorstep detection, treatment and/or referral of newborn danger signs and infection, and infant diarrhoea, pneumonia and malnutrition	Newborn home visits on days 1, 3, 7; again if low birth weight on days 14, 21, 28	▲ IMNCI training for other public and private providers (eg, nurses) ▲ Quarterly mother's health education groups	Routine care at CHW and facility levels	Infant, neonatal, perinatal, postnatal mortality (1, 3, 6, 9, 12 months)
Chen, 1980	Cluster NRCT (05/1978–08/1978)	Rural, Bangladesh; Area I: n=1 C: n=1	Population I: n=1 57 381 C: n=1 34 249 CHWs I: n=160 C: n=130	Existing female VHWs trained for two half-days on indications, use, hazards of ORS	Doorstep detection (enquiry) and ORS treatment of simple diarrhoea; referral of severe diarrhoea or complications	Daily household visits	▲ ORS packets provided free-of-charge ▲ Diarrhoeal treatment facility and ambulance	Routine care at VHW and facility levels+diarrhoeal treatment facility and ambulance	Hospital admissions (0–4 months)
Johnson, 2013 and 2018	Repeated cross-sectional (2008–2015)	Periurban, Mali; PHC area I: n=1	Population I: n=56 000 CHWs I: n=20 C: n=NA	Educated female CHWs; recruited locally; 36-day training in iCCM; monthly dedicated supervision; paid monthly stipend	Doorstep detection, referral, follow-up for all cases of disease; doorstep detection and treatment of childhood malaria	Home visits for at least 2 hour/day, 6 days/week, aiming to visit all households 2x per month	▲ User fee removal at CHW and PHC levels ▲ PHC training and infrastructure improved ▲ Adult education and microenterprise groups ▲ LLIN distribution	NA	▲ Child mortality ▲ Prevalence of febrile illness ▲ Treatment rates (0, 12, 24, 36, 48, 60, 72 and 84 months)

Table 1 Continued

Study	Study design (period)	Setting + unit of allocation	Participants + CHW sample	Description of proactive case detection intervention				Description of control	Outcomes (timepoints)
				CHW profile	Conditions	Timing	Cointerventions		
Khan, 1990	CBA (1984–1987)	Rural, Pakistan; Village I: n=31 C: n=7	Under fives I: n=4665 C: n=1194 CHWs I: n=17 C: n=0	Educated CHWs recruited locally; trained in CCM of symptomatic ARI	Doorstep detection of ARI and treatment or referral for suspected pneumonia	Approx. 200 households visited every 10–14 days	▲ Standardised facility ARI treatment protocol ▲ Maternal health education programmes ▲ Vaccine campaign	Routine care at facility level + vaccine campaign	Infant and child mortality (I: 0–33 months C: quarterly from 0–33 months)
Linn, 2015	CBA (07–11/2013)	Rural, Senegal; Village I: n=15 C: n=15	Population I: n=4217 C: n=4747 CHWs I: n=? C: n=?	HCPs; 1-day training in active case detection; community-level and facility-level supervision; paid for added work	Doorstep detection, treatment and follow-up of malaria for individuals of all ages	Weekly sweeps to every household in the village	▲ Initial community mobilisation and health education ▲ LLIN distribution and SMC	Routine care at HCP and facility levels+LLIN distribution and SMC	▲ Malaria prevalence (I: 0–21 weeks C: 0, 12, 21 weeks) ▲ Care-seeking rates (0–21 weeks)
Mazumder, 2014	Cluster RCT (2006–2010)	Faridabad, Haryana, India; PHC area I: n=9 C: n=9	Mother–baby dyads I: n=29667 C: n=30813 CHWs I: n=601 C: n=?	Same as Bhandari, 2012	Same as Bhandari, 2012	Same as Bhandari, 2012	Same as Bhandari, 2012	Same as Bhandari, 2012	▲ Treatment rates ▲ Hospital admissions ▲ Disease prevalence (1, 6, 12 months)
Navarro, 2013	Cluster NRCT (2005–2007)	Urban, Dominican Republic; Parish I: n=8 C: n=8	Mother–child dyads I: n=266 C: n=337 CHWs I: n=? C: n=0	Community volunteers; mostly female; 60 hours basic training	Doorstep detection (weighing and plotting weight-for-age curve), follow-up and referral for childhood risk of overweight or malnutrition	Fortnightly home visits for first 1.5 month after birth, then monthly until age 2	Women's groups that met fortnightly during pregnancy, then monthly after childbirth, included newborn care and growth monitoring	Routine care at facility level	▲ Prevalence of malnutrition, wasting, stunting, overweight ▲ Hospital admissions (0–24 months)
Pandey, 1991	Non-randomised stepped-wedge trial (1986/1987–1989)	Rural, Nepal; Subdistrict I: n=8 C: n=10	Under fives I: n=3307 C: n=3377 CHWs I: n=1/1000 C: n=0	Literate CHWs recruited locally; 9-day training; supervised fortnightly; stocks ensured; salaried	Doorstep detection and treatment of childhood pneumonia	Daily visits to 10–15 child households, visiting all target homes every 2 weeks	User fees removed for pneumonia treatment	Routine care at facility level	Risk of death (0–36 months)

Continued

Table 1 Continued

Study	Study design (period)	Setting + unit of allocation	Participants + CHW sample	CHW profile	Conditions	Timing	Cointerventions	Description of control	Outcomes (timepoints)
				Description of proactive case detection intervention					
Tomlinson, 2014	Cluster RCT (2008–2010)	Periurban, KwaZulu-Natal, South Africa; Subplaces I: n=15 C: n=15	Mother–baby dyads I: n=1821 C: n=2136 CHWs I: n=? C: n=?	Literate female CHWs recruited locally; 10-day training in IMNCI and PMTCT; salaried	Doorstep detection and help seeking for mother and child danger signs/illnesses	two pregnancy + five postnatal home visits on days 1, 3–4, weeks 2, 3–4, 7–8; 2 extra week 1 if low birth weight	None reported	1 CHW home visit during pregnancy+2 postnatal to help with birth certificates and social grants	▲ Neonatal mortality ▲ Disease prevalence ▲ Care-seeking (Pregnancy+: I: 0–8 weeks C: 0–12 weeks)
Uwimana, 2012	Cluster RCT (2009–2010)	Rural, KwaZulu-Natal, South Africa; Village I: n=3 C: n=3	Population CHWs I: n=39 C: n=50	Former (NGO) CHWs recruited for 1 CCW cadre; 60-day training in TB/HIV/ PMTCT; supervised by CHFs at PHC; monthly stipend	Doorstep detection, referral and treatment adherence support for HIV, TB, STIs	Not reported	Initial community mobilisation that included HCT, TB and STI screening and referral	Home visits by CCWs promoting HCT and referring to clinic for HIV testing	Access to screening services (0–10 months)
Uwimana, 2013	Cluster RCT (2009–2011)	Same as Uwimana, 2012	Same as Uwimana, 2012	Same as Uwimana, 2012	Same as Uwimana, 2012	Not reported	None reported	Not reported	Access to screening services and treatment adherence support (14 months)
Yassin, 2013	CBA (2010–2011)	Rural, Ethiopia; Zone I: n=1 C: n=1	Population I: n>3.0m C: n>1.3m CHWs I: n=524 C: n=0	Females HEWs recruited locally; 1 year HSEP training; salaried; supported by lay volunteer CHPs and supervisors	Doorstep TB detection (enquiry), referral and follow-up/treatment adherence support	Not reported	▲ PHC training and laboratory equipment ▲ Community education via meetings, radio, etc. ▲ Contact screening and IPT for asymptomatic children by supervisors	Routine care at facility level	Case detection (0–14 months)

Notes: Unit of allocation is the geographic area allocated between intervention and control groups, even if the intervention was implemented at a smaller level (eg, village). *Participants* are those that received the proactive case detection intervention (n=sample at baseline); the CHW sample is provided where available. Health education/promotion activities are only listed under *cointerventions* if they took place outside of the proactive case detection home visits. *Outcomes* include those that are considered in this review. Fixed *time-points* are the time from intervention roll-out to survey measurement; where outcomes are measured throughout the intervention period from routine data, *time-points* are the range that the intervention was in effect.
ARI, acute respiratory infection; ASHA, accredited social health activists;C, comparison; CHW, community health promoter; CHW, community health worker; CBA, controlled before-after; CCM, community case management; CCW, community care worker; CHF, community health facilitator; CHP, community health promoter; CHW, community health worker; HBC, home-based carer; HCP, homecare providers; HCT, HIV counselling and testing;HEW, health extension worker; HSEP, health service extension programme;I, intervention; iCCM, integrated community case management; ICDS, integrated child development service; IM(N)CI, integrated management of (neonatal and) childhood illness; IPT, isoniazid preventive therapy; LLIN, long-lasting insecticidal bed net; NRCT, non-randomised controlled trial; ORS, oral rehydration solution; PHC, primary health centre; PMTCT, prevention of mother to child transmission; RCT, randomised controlled trial; SMC, seasonal malaria chemoprophylaxis;STI, sexually transmitted infection; TB, tuberculosis; TBA, traditional birth attendant; VHW, village health worker; yr, year.

studies[42 43] reported outcomes specifically for children under 5 years. Five studies recruited pregnant women and delivered a mother–child intervention during the neonatal period, and in some cases, into infancy and childhood.[39 46–48 52] The remaining two studies tested interventions that targeted children under 5 years of age during a period of 3 years.[50 51]

Characteristics of CHW programmes

The Bangladesh,[49] Ethiopia,[44] Senegal,[45] rural South Africa[40 41] and more recent India[47 48] studies provided supplemental training in the context of the study (two-half days in Bangladesh, 1 day in Senegal, 8 days in India, 60 days in South Africa and unreported in Ethiopia) to CHWs from an already established CHW cadre. The remaining studies evaluated CHW programmes initiated by a research institute, all of which recruited local, literate community members and trained them for a duration of 60 hours[52] to 6 months.[46] In half of all programmes, CHWs were exclusively or predominantly female. Reporting of recipient and CHW sample sizes, and therefore CHW to population ratios, was poor.

Eleven studies reported enhanced CHW supervision as an adjunct to the intervention. However, the supervision strategy and frequency were not adequately described. Supervisors included physicians,[46] nurses,[51] accredited social health activists[47 48] or senior project staff[42 50] who monitored CHW activities periodically. Other studies employed a dedicated cadre of CHW supervisors, either based at the facility[40 41] or in the community.[43 44] Eleven studies paid CHWs for their work, with a salary in-line with government standards,[39 43 44 50] a performance-linked[46] or task-based[47 48] remuneration scheme, or some other form of payment.[40 41 45]

CHWs provided services for the range of conditions eligible for inclusion in the review. CHWs in Mali,[42 43] India[46–48] and periurban South Africa[39] provided integrated management of common neonatal and childhood illnesses. CHWs provided care exclusively for diarrhoea in Bangladesh;[49] for pneumonia in Pakistan and Nepal;[50 51] for malaria in Senegal;[45] for malnutrition and at risk of being overweight in Dominican Republic;[52] for tuberculosis in Ethiopia;[44] and for HIV, tuberculosis, and sexually transmitted infections in rural South Africa.[40 41] In addition to proactive case detection, most studies included doorstep treatment by CHWs and referral to a facility if necessary, with the exception of the studies in Dominican Republic, Ethiopia and periurban South Africa,[39 44 52] which limited postdetection activities to referral for treatment and home-based follow-up.

Most studies compared proactive case detection by CHWs to the standard of care—passive case detection at public or private health facilities; six studies also included passive case detection by CHWs in the control arm. The South African studies included control CHWs who conducted home visits for purposes other than proactive case detection. Control arm CHWs conducted one pregnancy and two postnatal home visits to assist with securing identity documents and social grants in the urban study,[39] and home visits to promote and refer clients to HIV counselling and testing in the rural studies.[40 41]

Risk of bias of included studies

Risk of bias summaries are provided in online supplementary file 2 (figure 2 and figure 3). Risk of bias assessments for each study are provided in online supplementary file 3. These assessments were considered when interpreting the results and certainty of evidence for each outcome.

Selection bias

All studies, with the exception of those in Mali,[42 43] allocated the study area into intervention and control groups. Five studies used cluster randomisation to assign groups.[39–41 47 48] Among seven studies that did not use random allocation, sufficient evidence was provided in only two[45 46] that outcome measurements were similar between groups at baseline, and in only three[46 50 52] that population-level and/or cluster-level characteristics were similar between groups at baseline.

Performance bias and detection bias

Due to the nature of the intervention, blinding of participants and study personnel to allocation assignment was not possible and was scored high risk for all included studies. All six Southeast Asian studies[46–51] and the periurban South Africa study[39] blinded outcome assessors to allocation assignment, earning a low detection bias score.

Attrition bias

Reporting of incomplete outcome data varied considerably between studies. Studies involving pregnant women for a neonatal intervention discussed attrition bias with the use of a trial profile.[39 47 48 52] A Data Safety and Monitoring Board stopped the Haryana, India trials early after the required sample size had been met, but prior to about half of children completing the 12-month assessment.[47 48] Risk of attrition bias was high in the Dominican Republic study where roughly a quarter of mother–child dyads were lost, and there were statistically significant differences in some baseline characteristics that could be associated with the outcome between those who completed follow-up and those who did not.[52] Missing survey data for date of birth and death were imputed in the Mali studies, but the extent and patterns of missing data were explicitly reported.[42 43] Studies from India[46] and Nepal[50] did not comment on completeness of outcome data, but data were collected by an independent set of workers and analysed on an intention to treat basis. CBA studies in Pakistan[51] and Senegal[45] relied on CHWs to collect outcome data in intervention clusters and employed periodic surveys in control clusters. These studies did not discuss incomplete outcome data and were scored high risk due to the differences in data source and methods between the two groups.

Reporting bias

A published protocol was found for only one study.[39] No studies reported outcomes in the methods that were then subsequently omitted from the results and, therefore, no studies were scored as being at high risk of reporting bias. Some studies subsequently added outcomes from posthoc analyses, but provided justifiable reasons for inclusion of the additional outcomes that were not prespecified.[39 47 48]

Protection against contamination

Risk of bias due to contamination was scored as low when large units of allocation were chosen and efforts to minimise contamination were discussed and/or a map was provided showing geographic separation of groups.[44 46–50]

Effects of interventions

Eleven studies assessed the effects of proactive case detection of common childhood conditions by CHWs on mortality, morbidity or access to curative services and were included in the main analysis. Meta-analysis was deemed inappropriate as the studies in each analysis represented considerable clinical diversity with respect to intervention and participant characteristics, methodological diversity with respect to study design and risk of bias, and statistical heterogeneity as quantified by the I^2 statistic. We were unable to explore this heterogeneity by prespecified subgroup analyses due to the limited number of studies. Overall, the certainty of evidence is low or very low because of limitations in study design, indirect measures of effect due to cointerventions or comparisons and unexplained heterogeneity.

Mortality

Seven studies measured mortality outcomes (table 2; Figure 1). Proactive case detection may reduce neonatal mortality (low certainty evidence). However, the effects vary and it is possible that it makes little or no difference to neonatal mortality (calculated RRs: 0.43 to 1.07; I^2=79.1%). Proactive case detection may reduce infant mortality (calculated RRs: 0.52 to 0.94; I^2=61.9%) (low certainty evidence). It is uncertain whether proactive case detection reduces mortality among children under 5 years (calculated RRs: 0.04 to 0.80; I^2=94.4%) because the certainty of this evidence is very low.

Three studies assessed impact on neonatal mortality over a 2–3 year timeframe (table 2; Figure 1). It was the primary outcome in the Maharashtra[46] and Haryana[47] studies of proactive case detection of newborn and infant danger signs, infections and illnesses. In rural Maharashtra, there was a 62% reduction in intervention areas compared with control areas (p<0.001).[46] In Haryana, the neonatal mortality rate beyond the first 24 hours of life was lower in intervention clusters than in control clusters (adjusted HR=0.86; 95% CIs: 0.79 to 0.95), but not the case for the neonatal mortality rate overall—an effect, they explained, due to the higher than expected proportion of neonatal deaths occurring in the first 24 hours on which the intervention was unlikely to have had an

effect.[47] In both Maharashtra and Haryana, intervention groups included a mother's education component and system strengthening in terms of user fee removal for CHW care[46] or training of other provider cadres in Integrated Management of Newborn and Childhood Illnesses.[47] An exploratory analysis of the effect of a home visit programme in periurban South Africa to improve appropriate infant feeding and HIV-free infant survival[39] on neonatal mortality showed an increased risk of death in intervention compared with control clusters, although the effect was not statistically significant (RR=1.07; 95% CIs: 0.69 to 1.63).

Four Southeast Asia studies assessed infant mortality. The Maharashtra[46] and Haryana[47] studies found significant reductions (respectively, 45.7%; p<0.001 and AHR=0.89; 95% CIs: 0.78 to 1.00) in infant mortality between intervention and controls. Proactive case detection of childhood respiratory infection and doorstep treatment of suspected pneumonia compared with facility-based care led to reductions in infant mortality in rural Nepal,[50] where cotrimoxazole was provided at home free of charge, and in rural Pakistan,[51] where CHWs treated at home or referred to facilities where treatment protocols had been standardised. In Nepal, the greatest reduction in mortality after 3 years of intervention activities was seen in infants aged 6–11 months (RR=0.36; 95% CIs: 0.24 to 0.56). In Pakistan,[51] the infant mortality rate was 74/1000 in the intervention area during the first 2 years of the study compared with 93/1000 in the control area.

A reduction in mortality was seen for all children under 5 years of age in Nepal, with a relative risk reduction of 0.72 from baseline to year 3,[50] and in Pakistan, with a 26% reduction between intervention (29/1000) and control (39/1000) areas during the first 2 years of the study.[51] In periurban Mali, the under-5 mortality rate declined from 154/1000 at baseline to 25/1000 after 3 years of proactive case detection of common childhood conditions in addition to primary health centre reinforcements and removal of user fees, and to 7/1000 after 7 years.[43]

Morbidity

Six studies assessed prevalence of disease, and four assessed hospitalisation (table 3; Figure 2). Proactive case detection may improve nutritional outcomes (low certainty evidence), although the effects vary, and it is possible that it makes little or no difference to nutritional outcomes (calculated RRs range from 0.61 to 1.16; I^2=61.4%). It is uncertain whether proactive case detection reduces the prevalence of infectious diseases (calculated RRs: 0.06 to 1.02; I^2=90.6%) or hospitalisation (calculated RRs: 0.38 to 1.26; I^2=94.5%) because the certainty of this evidence is very low.

In Mali[42 43] and rural Senegal,[45] proactive case detection of malaria led to significant reductions in the odds of febrile illness among children under five (adjusted OR (AOR) after 7 years=0.45; 95% CIs: 0.32 to 0.62), and symptomatic malaria among the general population in intervention villages compared with control

Table 2 Intervention effects on mortality outcomes

Country	Design*	Reported measure of effect (95% CIs)†	Calculation of risk‡	Calculated RR§
Neonatal mortality				
India[46]¶	CBA	% diff=62.2%; p<0.001	I: 25/979 C: 66/1108	0.43 (0.27, 0.67)
India[47]¶	cRCT	AHR=0.91 (0.80 to 1.03)	I: 1244/29667 C: 1326/30813	0.97 (0.71, 1.33)
SA[39]	cRCT	RR=1.07 (0.69 to 1.63)	I: 20/1821 C: 22/2136	1.07 (0.58, 1.95)
Infant mortality				
India[46]	CBA	% diff=45.7%; p<0.001	I: 38/979 C: 83/1108	0.52 (0.36, 0.75)
India[47]¶	cRCT	AHR=0.89 (0.78 to 1.00)	I: 1925/29667 C: 2136/30813	0.94 (0.73, 1.20)
Nepal[50]	BA	0 to 6 days: RR=0.80 (0.59, 1.10) 0.25 to 5 months: RR=0.74 (0.58, 0.94) 6 to 11 months: RR=0.36 (0.24, 0.56)	I: 236/13406 C: 199/6684	0.60 (0.37, 0.96)
Pakistan[51]¶	cNRCT	% diff=21%; 'not significant'	I: 108/4665 C: 31/1194	0.87 (0.52, 1.46)
Child mortality				
Mali[42]	BA	HR=0.10; p<0.0001	I: 29/1390 C: 38/316	0.17 (0.11, 0.28)
Mali[43]	BA	HR=0.039 (0.013 to 0.116)	I: 5/1023 C: 39/330	0.04 (0.02, 0.10)
Nepal[50]¶	BA	RR=0.72 (0.63 to 0.82)	I: 409/13406 C: 301/6684	0.67 (0.46, 0.98)
Pakistan[51]¶	cNRCT	% diff=26%; p<0.001	I: 149/4665 C: 47/1194	0.80 (0.52, 1.22)

Neonatal period reported is 0–27 days. Infant period is 0–11 months. Child mortality period is 0–59 months. India[46] also reports mortality separately for early (0–6 days) neonates: % diff=57.3%; p<0.001; calculated RR=0.45, and late (7–27 days) neonates: % diff=51.6%; calculated RR=0.31. Study also found a reduction in perinatal mortality % diff=71.0%; p<0.001. A 2005 summary of this field trial reports that reductions in neonatal mortality and infant mortality reached 70% (95% CIs: 59, 81%) and 57% (95% CIs: 46, 68%), respectively, after 8 years postintervention.[65] India[47] also reports mortality for neonates after the first day of life: AHR=0.86 (0.79 to 0.95); calculated RR=0.93. Study also found a reduction in perinatal (AHR=0.89; 95% CIs: 0.78 to 1.00) and postneonatal (AHR=0.76; 95% CIs: 0.67 to 0.85) mortality. Nepal[50] reports no overall infant mortality, only by infant age brackets; denominators for calculated infant and childhood risks are based on study report that initial census registered[66] 84 children (control) and an additional 6722 were born during the study for a total of 13 406 children available (intervention). Pakistan[51] compares mortality rates between intervention and control periods for the 1985–1986 postintervention period; calculated risks are for 1985 only for which the study reports number of children per arm. Nepal[50] and Pakistan[51] also report disease-specific mortality rates; results not shown. The South Africa[39] study found no effect (RR=0.97; 95% CIs: 0.67 to 1.40) on the primary joint mortality–morbidity outcome: HIV-free infant survival at 12 weeks among HIV-positive mothers.
*The study design reported is the nature of the comparative data, not necessarily the design as described by study authors.
†The before–after (BA) studies[42 43 50] reported each annual time point compared with baseline; here we present end-line to baseline risk ratios.
‡Reviewer (CW) calculated risk of death for intervention (I) and comparison (C) groups by taking number of events over number of live births (or, if unavailable, over population). For CBA, cRCT and cNRCT study designs, risks were calculated and compared (ie, calculated risk ratio) for the postintervention period between intervention and control groups; for BA study designs, intervention risk was calculated at end-line and control risk at baseline.
§Risk ratios and 95% CIs are adjusted for clustering.
¶Study primary outcome(s).
AHR, adjusted HR; BA, before–after; CBA, controlled before–after; cNRCT, cluster non-randomised controlled trial; cRCT, cluster randomised controlled trial; RR, risk ratio.

villages (AOR=0.03; 95% CIs: 0.02 to 0.07), respectively. The Haryana[48] study found significant reductions in danger signs (adjusted RR (ARR)=0.82; 95% CIs: 0.67 to 0.99) and local infection (ARR=0.91; 95% CIs: 0.71 to 1.17) among neonates, as well as diarrhoea (ARR=0.63; 95% CIs: 0.49 to 0.80) and pneumonia

(ARR=0.60; 95% CIs: 0.46 to 0.78) among infants. The urban South Africa[39] and Dominican Republic[52] studies found no effects on childhood diarrhoea, a secondary intervention outcome.

The Dominican Republic[52] study found that monthly home visits and mother's groups to promote healthy
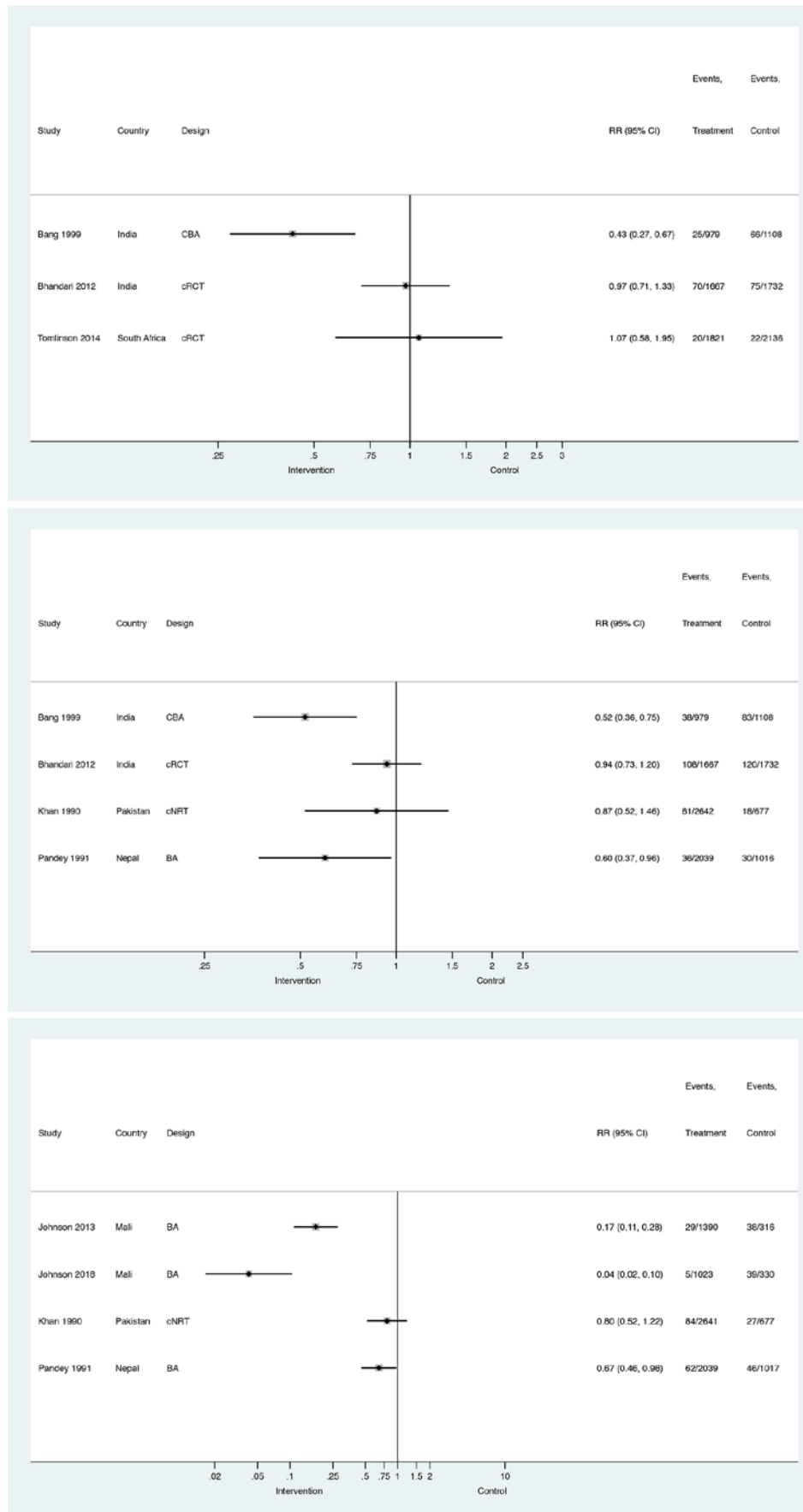
Figure 1 Forest plots for neonatal (top), infant (middle) and under 5 (bottom) mortality. CBA, controlled before–after; RR, risk ratio.

Table 3 Intervention effects on morbidity and access to care outcomes

Country	Design*	Population/condition†	Reported measure of effect (95% CIs)‡	Calculated RR (95% CIs)§
Prevalence of infectious diseases¶				
DR[52]	cNRCT	Diarrhoea, children under two	AOR=0.99 (0.59 to 1.67)	0.95 (0.61 to 1.47)
India[48]	cRCT	Infant** diarrhoea	ARR=0.63 (0.49 to 0.80)	0.63 (0.54 to 0.74)
India[48]	cRCT	Infant** pneumonia	ARR=0.60 (0.46 to 0.78)	0.56 (0.40 to 0.77)
Mali[42]	BA	Childhood febrile illness	PR=0.61; p<0.001	0.61 (0.51 to 0.73)
Mali[43]	BA	Childhood febrile illness	AOR=0.45 (0.32 to 0.62)	0.57 (0.47 to 0.68)
Senegal[45]††	CBA	Malaria, all ages	AOR=0.03 (0.02 to 0.07)	0.06 (0.02 to 0.18)
SA[39]	cRCT	Infant diarrhoea at 12 weeks	RR=1.01 (0.90 to 1.14)	1.02 (0.90 to 1.16)
Prevalence of nutritional outcomes‡‡				
DR[52]††	cNRCT	Stunting, children under 2	AOR=0.50 (0.22 to 1.10)	0.61 (0.33 to 1.11)
DR[52]††	cNRCT	Overweight, children under 2	AOR=0.43 (0.23 to 0.77)	0.69 (0.47 to 1.03)
DR[52]††	cNRCT	LAZ scores, children under 2	MD=0.21 (-0.02 to 0.44)	NA
DR[52]††	cNRCT	BAZ scores, children under 2	MD=−0.31 (-0.49 to -0.12)	NA
India[48]	cRCT	Infant stunting	ARR=0.99 (0.94 to 1.04)	1.03 (0.93 to 1.14)
India[48]	cRCT	Infant wasting	ARR=1.10 (0.90 to 1.36)	1.16 (0.93 to 1.46)
SA[39]	cRCT	Infant LAZ scores at 12 weeks	MD=0.11 (0.03 to 0.19)	NA
SA[39]	cRCT	Infant WLZ scores at 12 weeks	MD=0.01 (-0.07 to 0.09)	NA
SA[39]	cRCT	Infant WAZ scores at 12 weeks	MD=0.09 (0.00 to 0.18)	NA
Hospitalisation§§				
Bangladesh[49]††	cNRCT	For diarrhoea, all ages	% diff=29%; p<0.01	0.38 (0.34 to 0.41)
DR[52]	cNRCT	During first 2 years of life	AOR=1.09 (0.70 to 1.68)	1.07 (0.77 to 1.49)
India[48]	cRCT	During infancy**	ARR=0.67 (0.51 to 0.88)	0.65 (0.46 to 0.91)
SA[39]	cRCT	For infant diarrhoea at 12 weeks	RR=1.28 (0.75 to 2.19)	1.26 (0.67 to 2.39)
Access to effective¶¶ treatment				
DR[52]	cNRCT	Diarrhoea, children under two	AOR=3.86 (1.14 to 13.02)	1.29 (0.79 to 2.12)
India[48]††	cRCT	Infant** diarrhoea	ARR=1.22 (1.06 to 1.42)	1.25 (1.11 to 1.41)
India[48]††	cRCT	Infant** pneumonia	ARR=1.44 (1.00 to 2.08)	1.24 (0.71 to 2.14)
*Access to prompt*** treatment*				
India[48]††	cRCT	Infant** diarrhoea	ARR=0.99 (0.89 to 1.10)	1.00 (0.88 to 1.14)
India[48]††	cRCT	Infant** pneumonia	ARR=1.10 (0.96 to 1.25)	1.01 (0.84 to 1.22)
Mali[42]††	BA	Childhood malaria	PR=1.89; p=0.0195	1.89 (1.18 to 3.05)
Mali[43]††	BA	Childhood malaria	AOR=3.20 (1.75 to 5.85)	2.39 (1.49 to 3.83)

*The study design reported is the nature of the comparative data in this review.

†Neonatal period is 0–27 days, infant period is 0–11 months and childhood is under 5 years of age, unless otherwise indicated.

‡The BA studies[42 43 50] reported each annual time point compared with baseline; here we present effect estimates comparing end-line to baseline.

§For CBA, cRCT and cNRCT study designs, risks were calculated and compared for the postintervention period between intervention and control groups; for BA designs, intervention risk was calculated at end-line and control risk at baseline. Risk ratios and 95% CIs are adjusted for clustering.

¶For the Dominican Republic,[52] India,[48] Mali[42 43] and South Africa[39] studies, prevalence based on mother's reporting of condition during 2 weeks period preceding the interview; for the Senegal[45] study, prevalence measured at each time point by positive rapid diagnostic test of symptomatic community members.

**The India[48] study also reported effects of similar magnitude at 6 months of age; results not shown. Study found a reduction in neonatal morbidity: danger signs (ARR=0.82; 95% CIs: 0.67 to 0.99) and infection (ARR=0.91; 95% CIs: 0.71 to 1.17), and an increase in access to care for neonates: treatment by appropriate provider for danger signs (ARR=1.76; 95% CIs: 1.36 to 2.24), prompt treatment for danger signs (ARR=1.14; 95% CIs: 1.10 to 1.18), treatment by appropriate provider for infections (ARR=4.86; 95% CIs: 3.80 to 6.21) and prompt treatment for infections (ARR=1.97; 95% CIs: 1.71 to 2.27).

††Study primary outcome(s).

‡‡Based on anthropometric measures for all studies.

§§Measure based on mother's recall for Dominican Republic[52] (last 12 months), India[48] (last 3 months) and South Africa[39] (recall period not specified) studies; for the Bangladesh[49] study, measure based on hospital records. CHWs in the Dominican Republic[52] and South Africa[39] studies did not provide doorstep treatment but referred all cases detected; CHWs in the Bangladesh[49] and India[48] studies provided doorstep treatment and referral.

¶¶Defined for the Dominican Republic[52] study as oral rehydration for childhood diarrhoea, and for the India[48] study as treatment from an appropriate provider, which included physicians in government and private facilities, auxiliary nurse midwife, Anganwadi worker (CHW) or ASHA.[48]

***Defined as treatment within 24 hours of symptom onset for all studies.

AOR, adjusted OR; ARR, adjusted risk ratio; ASHA, accredited social health activists; BA, before–after; BAZ, Body Mass Index-for-age; CBA, controlled before–after; CHW, community health worker; cNRCT, cluster non-randomised controlled trial; cRCT, cluster randomised controlled trial; LAZ, length-for-age; MD, mean difference; NA, not applicable; RR, risk ratio; WAZ, weight-for-age; WLZ, weight-for-length.
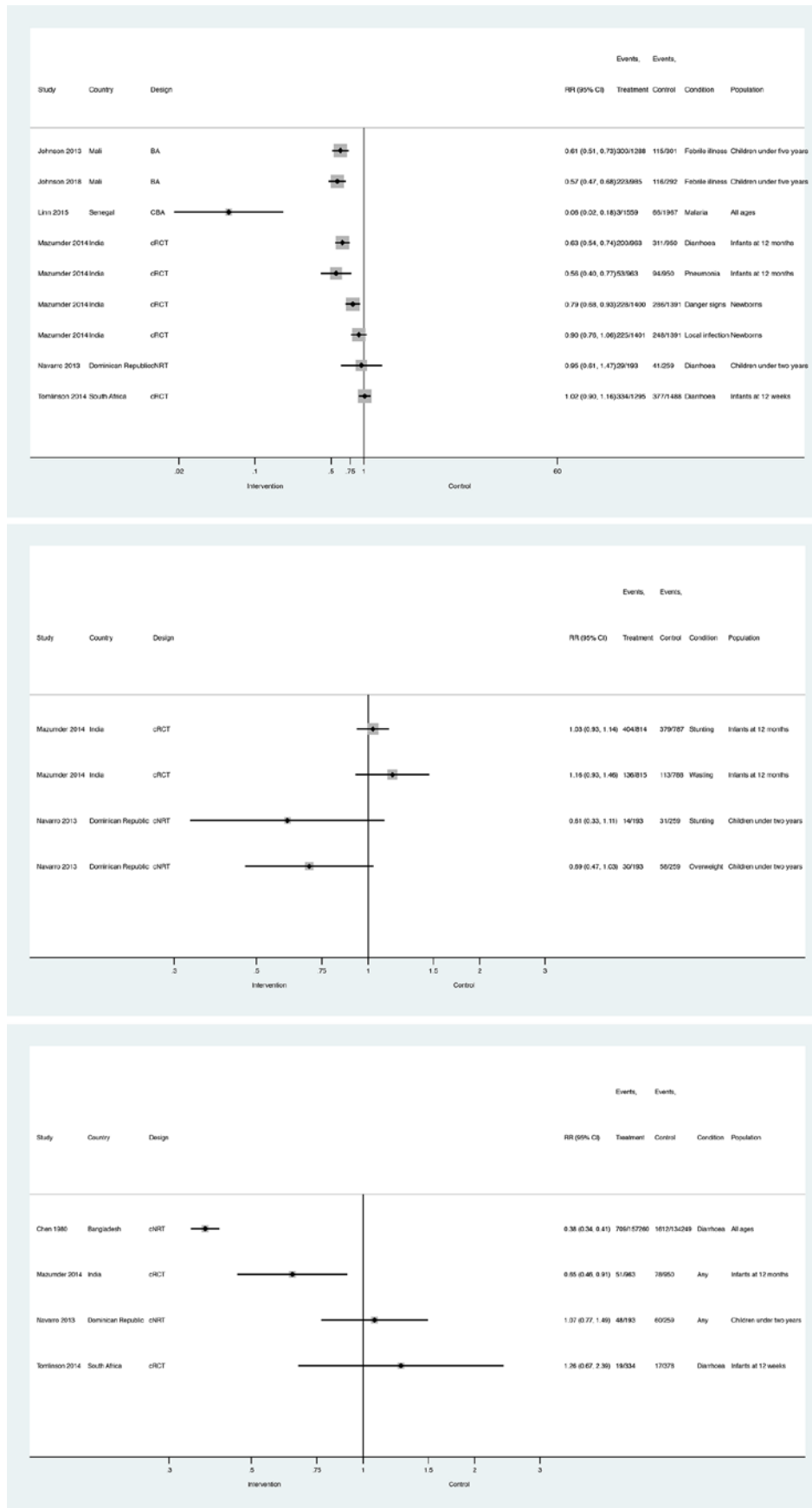
Figure 2 Forest plots for prevalence of common childhood infections (top) and nutritional conditions (middle), and hospitalisation (bottom). BA, before–after; CBA, controlled before–after; RR, risk ratio.

babies and monitor physical growth during the first 2 years of life led to reductions in stunting (AOR=0.50; 95% CIs: 0.22 to 1.10) and risk of overweight (AOR=0.43; 95% CIs: 0.23 to 0.77), compared with standard facility-based controls. The Haryana[48] study found no effect on wasting (ARR=0.99; 95% CIs: 0.94 to 1.04) or stunting (ARR=1.10; 95% CIs: 0.90 to 1.36) at 12 months of age in exploratory analyses. The South Africa[39] study found an increase in infant weight-for-age (mean difference (MD)=0.09; SD: 0.00, 0.18) and length-for-age (MD=0.11; SD: 0.03, 0.19) z-scores, but not weight-for-length (MD=0.01; SD: -0.07, 0.09).

In Bangladesh,[49] CHW home visits to inquire about diarrhoea and offer oral rehydration therapy packets free of charge were associated with a 29% reduction (p<0.01) in hospitalisation for diarrhoea compared with control villages with CHWs doing 'surveillance and health work'. In the Haryana[48] study, in which CHWs

assessed newborns for signs of illness at each visit and treated or referred them, caregivers in the intervention clusters reported fewer hospital admissions during infancy (ARR=0.67; 95% CIs: 0.51 to 0.88). In the South Africa[39] and Dominican Republic[52] studies, where proactive CHWs did not offer doorstep treatment but referred all cases detected, caregivers reported more hospital admissions for their children, although results were not statistically significant.

Access to treatment

Four studies assessed access to effective and/or prompt treatment (table 3; Figure 3). Proactive case detection may increase access to effective treatment (calculated RRs range from 1.59 to 4.64; I^2=97.0%) (low certainty evidence). It is uncertain whether proactive case detection increases access to prompt treatment (calculated RRs range from 1.00 to 2.39; I^2=84.9%) because the certainty

Figure 3 Forest plots for access to effective treatment (top) and prompt access to treatment (bottom). RR, risk ratio.

of this evidence is very low. Three studies assessed the effects of proactive case detection of HIV and/or tuberculosis on access to diagnostic services and/or treatment adherence support; these were excluded from the main analysis and summarised in online supplementary file 4.

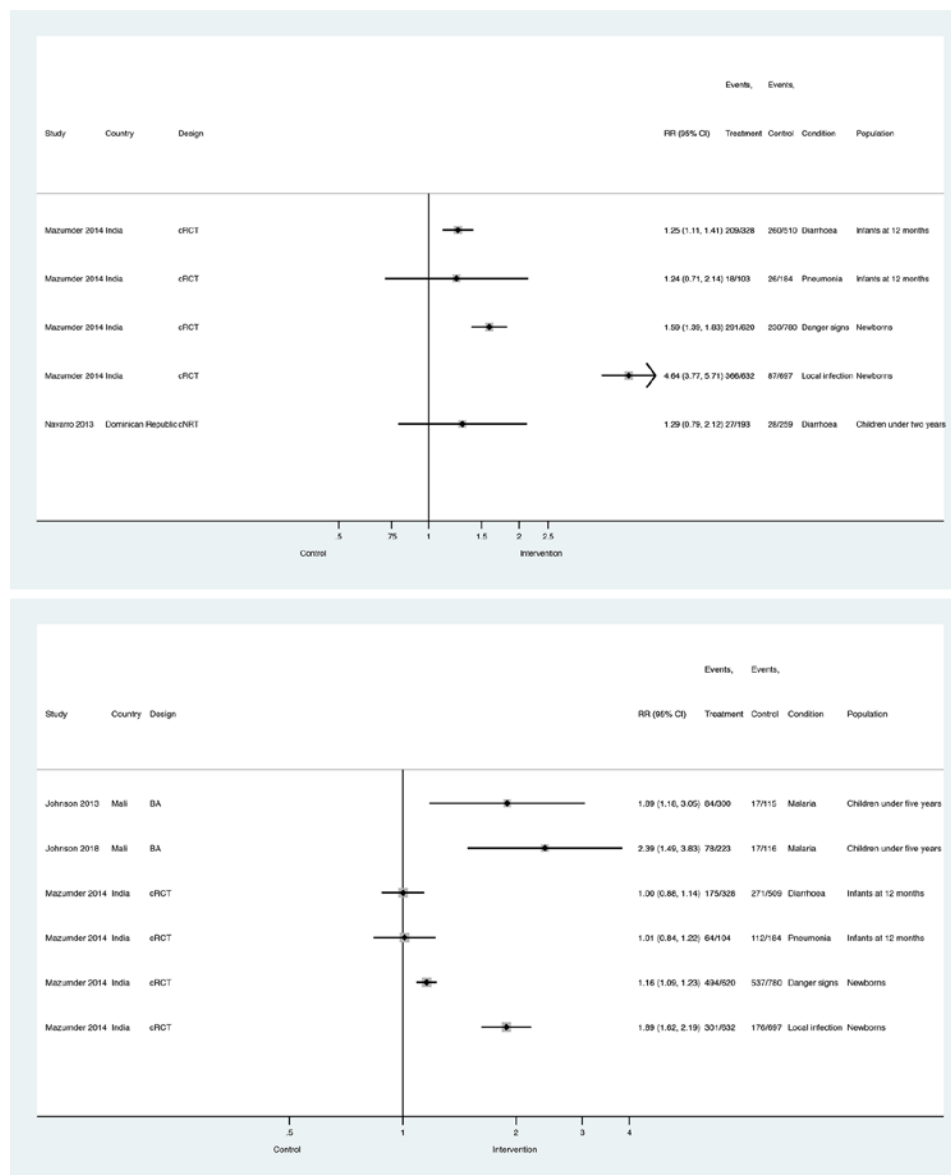In Dominican Republic,[52] proactive home visits increased the proportion of diarrhoeal children who received oral rehydration solution (AOR=3.86; 95% CIs: 1.14 to 13.02). In Haryana,[48] caregivers in intervention clusters were more likely to seek any treatment within 24 hours and treatment from an appropriate provider for newborns with danger signs (respectively, ARR=1.14; 95% CIs: 1.10 to 1.18 and ARR=1.76; 95% CIs: 1.36 to 2.24) and local infections (respectively, ARR=1.97; 95% CIs: 1.71 to 2.27 and ARR=4.86; 95% CIs: 3.80 to 6.21). Caregivers were no more likely to seek any treatment within 24 hours for infants with diarrhoea (ARR=0.99; 95% CIs: 0.89 to 1.10) or pneumonia (ARR=1.10; 95% CIs: 0.96 to 1.25), but more likely to seek treatment from an appropriate provider for diarrhoea (ARR=1.22; 95% CIs: 1.06 to 1.42) or pneumonia (ARR=1.44; 95% CIs: 1.00 to 2.08). In Mali,[42 43] a higher proportion of children with fever received antimalarial treatment within 24 hours of symptom onset compared with baseline (AOR=3.20; 95% CIs: 1.75 to 5.85).

DISCUSSION

Summary and quality of evidence

This review identified 14 studies of 11 different interventions involving proactive case detection of common childhood conditions by CHWs in nine LMICs. Findings are summarized in table 4. Proactive case detection may reduce infant mortality and increase access to effective treatment compared with conventional community-based healthcare delivery (low certainty evidence). Although our review suggests that proactive case detection may also reduce mortality among children under 5 years, prevalence of infectious diseases, hospitalisation and improve access to prompt treatment, it is uncertain because the certainty of this evidence is very low. Proactive case detection may reduce neonatal mortality and improve nutritional outcomes (low certainty evidence), although effects vary and it is possible that it makes little or no difference to these outcomes.

Three high-quality studies from India[46–48] provide evidence that proactive case detection of illnesses among newborns and infants reduced neonatal and infant mortality, morbidity, and improve treatment seeking, compared with a conventional community-based approach. Two moderate quality studies in Senegal[45] and Bangladesh[49] found that proactive case detection and doorstep treatment significantly reduced population-level morbidity, as measured by the prevalence of malarial fever and hospitalisation for diarrhoea, respectively. In these five studies, control groups received passive case detection and management from community-based CHWs and primary health facilities. This provides a more

direct assessment of the effectiveness of proactive case detection than studies that had no CHWs in control clusters (which are likely to overestimate its effects) as well as studies with control CHWs who conduct home visits for other purposes (which are likely to underestimate its effects). Activities in control clusters may partially explain the null effects on neonatal mortality and infant morbidity found in the periurban South Africa cluster RCT.[39] Home visits by control CHWs for the purpose of procuring identity documents and social grants may have served in practice to proactively identify sick children and encourage caregivers to seek care.

Our review extracted all study outcomes that met our inclusion criteria, even if those outcomes were the result of exploratory or posthoc analyses. This may account for some of the null effects in studies that reported numerous outcomes for which the study was not powered or for which the intervention had no clear pathway for impact. For example, finding no effect on prevalence of diarrhoea for visits targeting nutrition,[52] and no effect on stunting for visits to detect disease in infants were the results of exploratory analyses and small sample sizes.[47]

Although this review found large inconsistencies in results for hospitalisation, the two studies in which CHWs provided doorstep treatment found a significant reduction,[47 49] whereas the two urban studies[39 52] in which all cases were referred found an increase (although statistically not significant), as might be expected. These were the only studies included in the main analyses in which CHWs did not offer doorstep treatment following proactive detection of uncomplicated cases. In the studies concerning HIV and/or tuberculosis, CHWs referred cases detected and then conducted follow-up home visits for treatment adherence support.

Most studies evaluated complex interventions with multiple components, limiting our ability to draw conclusions about the isolated effects of proactive case detection. At a minimum, all studies likely included—whether or not explicit in the intervention description—health promotion and education messaging by CHWs at the time of home visitation, the benefits of which on child health have been documented.[55–57] Other cointerventions included additional support to proactive CHWs in the form of supervision and/or remuneration; systems strengthening such as facility-level improvements and/or user fee removal; community mobilisation and/or women's groups. Studies that found the intervention effective, such as those in India, Senegal, Bangladesh and Mali, offered more in terms of supportive cointerventions, suggesting these are important design features of successful CHW programmes.

Overall, the quality of studies evaluating proactive case detection was poor. Our review identified only three cluster RCTs that evaluated mortality, morbidity or access to treatment; two of which were the same trial reporting different outcomes.[47 48] Our results show clear design effect, with studies at higher risk of bias showing a larger magnitude of effect than the RCTs (tables 2 and

Table 4 Summary of findings for the main analysis

Proactive case detection of common childhood illnesses by CHWs compared with usual care for reducing mortality and morbidity and improving access to care in children under 5 years of age

Participants: children under 5 years of age accessing primary health services in LMICs
Settings: India (three studies), Mali (two studies), Bangladesh, Dominican Republic, Nepal, Pakistan, Senegal, South Africa
Intervention: home visits by CHWs for proactive detection of common childhood illnesses
Comparison: usual primary care (passive case detection) available from facilities and, in some cases, CHWs

Outcomes	Relative risk	Number of studies	Certainty of the evidence (GRADE)*	Comments
Neonatal mortality Verbal reports Follow-up: 0–12 months	0.43 to 1.07	3†	⊕⊕⊕◯ Low*§	Two Indian studies found proactive case detection of newborn illnesses reduced mortality, although only the non-randomised evidence was statistically significant. Proactive case detection may reduce neonatal mortality. However effects vary, and it is possible that it makes little or no difference to this outcome.
Infant mortality Verbal reports Follow-up: 0–36 months	0.52 to 0.94	4¶	⊕⊕⊕◯ Low**††	Four Southeast Asia studies found reductions in infant mortality, although not all were statistically significant. Two studies targeted various infant conditions, and two specifically targeted pneumonia among children under 5. Proactive case detection may reduce infant mortality.
Child mortality Verbal reports Follow-up: 0–84 months	0.04 to 0.80	4‡‡	⊕◯◯◯ Very low*†§§¶¶	Four studies found important reductions in under-5 mortality, although three were uncontrolled before–after analyses. It is uncertain whether proactive case detection reduces mortality among children under 5.
Prevalence of infectious diseases Verbal reports, diagnostic tests Follow-up: 0–24 months	0.06 to 1.02	6***	⊕◯◯◯ Very low*†††‡‡‡§§§¶¶¶	Three West African studies found significant reductions in fever or malarial fever. One study found reductions in both newborn and infant illnesses. Two studies found no effect on child diarrhoea, a secondary intervention outcome. It is uncertain whether proactive case detection reduces the prevalence of infectious diseases.
Prevalence of nutritional outcomes Anthropometric measurement Follow-up: 0–24 months	0.61 to 1.16	3****	⊕⊕⊕◯ Low§§§†††††	One study targeted childhood nutrition and found positive effects on length and BMI for age. Two studies that targeted various infant conditions found a range of nutritional effects. Proactive case detection may improve nutritional outcomes, although it is possible that it makes little or no difference to this outcome.
Hospitalisation Verbal reports, hospital records Follow-up: 0–24 months	0.38 to 1.26	4‡‡‡‡	⊕◯◯◯ Very low§§§†††††§§§§¶¶¶¶	Hospitalisation may reflect a higher severity of illness, improved treatment seeking, or both. In the two studies where CHWs provided doorstep treatment, hospitalisation significantly declined. In the two studies where all cases detected by CHWs were referred, hospitalisation increased, although results were not statistically significant. It is uncertain whether proactive case detection reduces hospitalisation.
Access to effective treatment Verbal reports Follow-up: 0–24 months	1.59 to 4.64	2*****	⊕⊕◯◯ Low§§§,††††,††††††	One study found that treatment was sought more often from an appropriate provider for neonatal illness and infection, and infant diarrhoea and pneumonia. One childhood nutritional intervention improved administration of ORS during diarrhoea. Proactive case detection may increase access to effective treatment.
Access to prompt treatment Verbal reports Follow-up: 0–84 months	1.00 to 2.39	3‡‡‡‡‡	⊕◯◯◯ Very low§,§§§,§§§§§,¶¶¶¶¶	One study found a significant improvement in the speed of treatment for newborns, but no effect for infants with diarrhoea and pneumonia. Uncontrolled before–after analyses in Mali found that the risk of prompt antimalarial treatment among children more than doubled. It is uncertain whether proactive case detection improves access to prompt treatment.

⊕⊕⊕⊕ High: this research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different‡ is low.
⊕⊕⊕◯ Moderate: this research provides a good indication of the likely effect. The likelihood that the effect will be substantially different‡ is moderate.
⊕⊕◯◯ Low: this research provides some indication of the likely effect. However, the likelihood that it will be substantially different‡ is high.
⊕◯◯◯ Very low: this research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different‡ is very high.

*GRADE, Working Group grades of evidence.
‡Substantially different=a large enough difference that it might affect a decision.
†Bang 1999, Bhandari 2012, Tomlinson 2014.
§The quality of evidence was downgraded for indirectness as the interventions in Bang 1999 and Bhandari 2012 included components other than proactive case detection, and comparison CHWs in Tomlinson 2014 conducted home visits for other purposes.
§The 95% CIs included both no effect and appreciable benefit.
¶Bang 1999, Bhandari 2012, Khan 1990, Pandey 1991.
**Risk of bias was assessed as low for Bang 1999 and Bhandari 2012, Khan 1990 and Pandey 1991 employed inappropriate analytical methods for their study designs. The quality of evidence was therefore downgraded for this limitation.
††The quality of evidence was downgraded for indirectness as the interventions in all studies included components other than proactive case detection, such as removal of user fees, facility-level capacity building, and/or women's education.
‡‡Johnson 2013, Johnson 2018, Khan 1990, Pandey 1991.
§§The quality of evidence was downgraded for risk of bias in Johnson 2013 and 2018 (shape of preintervention period not established and no control area for comparison) and in Khan 1990 and Pandey 1991 (inappropriate analyses for study designs).
¶¶The quality of evidence was downgraded for important inconsistency in results; many of the 95% CIs were not overlapping. Heterogeneity may be explained by differences in follow-up times (up to 84 months in Johnson 2018) and/or diseases targeted (only respiratory infection in Khan 1990 and Pandey 1991).
***Johnson 2013, Johnson 2018, Linn 2015, Mazumder 2014, Navarro 2013, Tomlinson 2014.
†††The quality of evidence was downgraded for limitations in design in Johnson 2013 and 2018 (shape of preintervention period not established and no control area for comparison), Navarro 2013 (outcome assessors not blind; high loss to follow-up and differences between lost and retained participants) and Linn 2015 (outcome assessors not blind; potential confounders not controlled for in analysis).
‡‡‡The quality of evidence was downgraded for important inconsistency in results. However, in the studies that showed a significant reduction in prevalence, the intervention targeted the diseases assessed for this outcome; in Navarro 2013 and Tomlinson 2014, CHWs conducted proactive case detection and management of conditions (nutritional and newborn, respectively) other than those assessed for this outcome.
§§§The quality of evidence was downgraded for indirectness due to cointerventions and differences in age groups.
¶¶¶The quality of evidence was upgraded for very large effects found in Lim 2015; weak study design may not explain all of the observed effect.
****Mazumder 2014, Navarro 2013, Tomlinson 2014.
†††††Risk of bias assessed as low for Mazumder 2014, unclear for Tomlinson 2014 (no baseline measurement of outcomes; unclear risk of contamination), and high for Navarro 2013 (outcome assessors not blind; high loss to follow-up and differences between lost and retained participants).
‡‡‡‡Chen 1980, Mazumder 2014, Navarro 2013, Tomlinson 2014. In Chen 1980, the intervention targeted and was assessed for the entire population; results not reported in such a way that the outcome could be calculated separately for children under 5.
§§§§Chen 1980 is a non-randomised trial with suggestion of important baseline imbalances in outcomes and confounding factors, although no statistical comparisons made at baseline. The quality of evidence was therefore downgraded for limitations in design.
¶¶¶¶Serious inconsistency in results, although likely due to whether CHWs provided doorstep treatment (likely to reduce hospitalisation), or referral only (likely to increase hospitalisation). The quality of evidence was therefore not downgraded for inconsistency, but for imprecision due to very wide 95% CIs.
*****Mazumder 2014, Navarro 2013.
‡‡‡‡‡Johnson 2013, Johnson 2018, Mazumder 2014.
¶¶¶¶¶Risk of bias was assessed as low for Mazumder 2014, but high for Johnson 2013 and 2018 (shape of preintervention period not established and no control area for comparison). The quality of evidence was therefore downgraded for this limitation in design.
†††††††The quality of evidence was downgraded for imprecision as studies had very wide 95% CIs.
§§§§§The quality of evidence was downgraded for imprecision due to very wide 95% CIs.
¶¶¶¶¶¶The quality of evidence was downgraded for important inconsistency in results; however, it may be explained by differences in intervention, target populations and follow-up times.
BMI, body mass index; CHWs, community health worker; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; LMICs, low-income and middle-income countries; ORS, oral rehydration solution.

3; Figures 1 and 2). Risk of bias was higher still where inappropriate analytical methods were employed for the study design.[50 51] Additionally, studies published before the year 2000 did not account for clustering in their analytical approaches.[46 49–51]

Limitations

Our synthesis of evidence was limited by the small number of eligible studies, and the considerable diversity between them. With only 11 studies included in the main analyses, we were unable to conduct subgroup analyses that would have tested for differences in effectiveness by features in study and intervention design, including setting, CHW characteristics, target populations, diseases detected or frequency of home visits. We could not explore how different health conditions in different transmission settings or health system contexts would have differential impacts on outcomes. We were also unable to assess publication bias due to the limited number of studies. However, our review included large trials reporting statistically non-significant results, so there are no specific reasons for suspecting a high risk of publication bias.

Our synthesis was further limited by inadequate reporting of methods and results in some studies. We had to make some assumptions in order to calculate a principal summary measure for between study comparisons, such as approximating the denominator or postulating the ICC. Features of CHW intervention design and implementation, including CHW recruitment and training, support and supervision and health system integration, were inadequately described. Comparisons were also inadequately described, making it difficult to understand the differences between the two groups. In some cases, it was not clear whether the control included CHWs at all,[44] what services were offered by control CHWs, including whether they conducted home visits for other purposes,[40 41 49] or whether they received the additional support, such as supervision or payment, offered to intervention CHWs.[45]

As there is no universally adopted terminology or strong indexation in health databases for the concept of proactive case detection, it is possible that some published or unpublished evaluations meeting the inclusion criteria were not identified through the search. There is a large body of evidence for the mortality, morbidity and access to care impacts of comprehensive community-based primary healthcare interventions,[58 59] including household and community integrated management of childhood illness[60–62] that may include home visits by community-based providers for the purpose of health promotion and education, vital registration and/ or proactive case detection. Some of these studies[56 57 63] may not have been included because insufficient information was available about the role of home visits in disease detection, study designs did not permit comparisons based on workflow and/or study designs were not sufficiently rigorous.

Implications for research and practice

The review process to inform the WHO guidelines for optimising CHW programmes found a scarcity of evidence for several areas reviewed, including recruitment and training, supervision and management, and health system integration.[29 64] Our review synthesising evidence around CHW workflow yielded similar conclusions regarding inadequate reporting of programme characteristics and lack of robust evidence. These features merit further consideration by programme architects and evaluators.

Standardising impact metrics for evaluating CHW programmes would greatly facilitate the synthesis of evidence in this field. Possible impact metrics include mortality among vulnerable groups, morbidity, as measured by disease prevalence, and access to prompt, effective treatment. Researchers should also consider process outcomes that provide an understanding of why and how a complex intervention did or did not work. None of the studies identified through the search provided a comparative costing analysis, or reported adverse effects of the intervention to patients, providers or the health system. These are important data points for practitioners and policymakers designing, implementing and scaling-up CHW interventions.

Finally, given that neonatal mortality is becoming an increasingly large proportion of mortality among children under 5 years of age, currently accounting for 45% of under-5 deaths,[65] a systematic review dedicated to appraising the evidence of the effects of proactive case detection of neonatal conditions by CHWs in LMICs is merited.

CONCLUSIONS

Proactive case detection by CHWs may reduce child mortality and morbidity and increase access to care. The certainty of this evidence is low due to limitations in study designs, inconsistency in results, indirect measures of effect and important diversity between a small number of included studies. More research is needed on proactive case detection with rigorous study designs, standardised outcomes and measurement, and detail on intervention design and implementation.

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Chapter 3   Trial protocol

Overview

This is the protocol that describes the methods of the cluster randomised trial that addresses the second objective of the thesis. The protocol also describes other trial objectives that are outside the scope of this thesis, such as intervention effects on other secondary endpoints (e.g., contraceptive use) or cost-effectiveness. Methods for the process evaluation that addresses the third objective of the thesis are not included in this protocol paper, as these were developed later. These methods are instead presented as part of the process evaluation paper in Chapter 6.

The paper is provided here in its published format. It is an open access article that falls under the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license. The online supplementary document referred to on page 3 of this paper is provided in Appendix B of this thesis for reference.

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed <u>for each</u> research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1605048	**Title**	Ms
First Name(s)	Caroline		
Surname/Family Name	Whidden		
Thesis Title	Evaluation of proactive community case management to accelerate access to care and reduce under-five mortality in Mali: a cluster randomised trial and process evaluation		
Primary Supervisor	Daniel Chandramohan		

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?	BMJ Open		
When was the work published?	26 Aug 2019		
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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)	As a key investigator of this trial, I contributed to its design. I wrote the trial protocol manuscript and managed the peer review process.

SECTION E

Student Signature	Caroline Whidden
Date	12 Dec 2023

Supervisor Signature	Daniel Chandramohan
Date	12 Dec 2023

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Proactive community case management and child survival: protocol for a cluster randomised controlled trial

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ABSTRACT

Introduction Community health workers (CHWs)—shown to improve access to care and reduce maternal, newborn, and child morbidity and mortality—are re-emerging as a key strategy to achieve health-related Sustainable Development Goals (SDGs). However, recent evaluations of national programmes for CHW-led integrated community case management (iCCM) of common childhood illnesses have not found benefits on access to care and child mortality. Developing innovative ways to maximise the potential benefits of iCCM is critical to achieving the SDGs.

Methods and analysis An unblinded, cluster randomised controlled trial in rural Mali aims to test the efficacy of the addition of door-to-door proactive case detection by CHWs compared with a conventional approach to iCCM service delivery in reducing under-five mortality. In the intervention arm, 69 village clusters will have CHWs who conduct daily proactive case-finding home visits and deliver doorstep counsel, care, referral and follow-up. In the control arm, 68 village clusters will have CHWs who provide the same services exclusively out of a fixed community health site. A baseline population census will be conducted of all people living in the study area. All women of reproductive age will be enrolled in the study and surveyed at baseline, 12, 24 and 36 months. The survey includes a life table tracking all live births and deaths occurring prior to enrolment through the 36 months of follow-up in order to measure the primary endpoint: under-five mortality, measured as deaths among children under 5 years of age per 1000 person-years at risk of mortality.

Ethics and dissemination The trial has received ethical approval from the Ethics Committee of the Faculty of Medicine, Pharmacy and Dentistry, University of Bamako. The results will be disseminated through peer-reviewed publications, national and international conferences and workshops, and media outlets.

Trial registration number NCT02694055; Pre-results.

Strengths and limitations of this study

► This is a cluster randomised controlled trial powered to detect a 25% relative difference in the incidence rate of under-five mortality between the two study arms.

► The trial will generate evidence on the efficacy, cost-effectiveness and equity of door-to-door proactive case detection by community health workers on access to care and child mortality.

► The intervention is designed to facilitate public sector adoption and scale-up if found to be effective.

► The large geographical area and 3-year time frame leave the study vulnerable to unexpected events that may influence the extent to which the intervention can be implemented per protocol.

► Changes to the health system or other contextual factors in the intervention area, such as drug stock-outs, health centre staff strikes, concurrent programme implementation by other actors, and political insecurity may be beyond the control of the study implementers.

INTRODUCTION

The vast majority of maternal, newborn and child deaths in low-income and middle-income countries are preventable. Evidence-based and cost-effective methods for prevention and treatment are available for the leading causes of death, yet many still face barriers to obtaining timely, quality and appropriate care. If community-based interventions, such as the treatment of malaria with artemisinin compounds, oral rehydration solution for childhood diarrhoea, oral antibiotics for pneumonia, nutritional interventions during pregnancy and hand washing with soap, were scaled to achieve 90% coverage in high-burden countries before 2020, an estimated 6.9 million maternal and child deaths could be averted.[1]

Integrated community case management (iCCM) of common childhood illnesses entails a package of services to diagnose, treat and refer children under 5 with malaria, diarrhoea, pneumonia or moderate malnutrition, delivered by community health workers (CHWs).[2] CCM of common childhood illnesses has been shown to improve access to

care[3–5] and treatment adherence,[3 6] and reduce mortality due to malaria,[7] diarrhoea,[3 8 9] pneumonia,[3 10 11] as well as all causes.[7 9 10]

Many countries in sub-Saharan Africa have adopted iCCM as an evidence-based strategy to improve child health.[12 13] However, the expected benefits of iCCM have not been realised in all contexts.[14–19] Several recent evaluations of national iCCM programmes did not find impacts on care seeking or child mortality, in part, study authors conclude, due to low demand for CHW services.[20–23] These national programmes shared certain design and implementation features that may have contributed to the lack of overall effects by not addressing barriers to care, such as user fees for services, lack of frequent and dedicated CHW supervision for quality assurance, and community care provision exclusively (or primarily) for patients that seek care from a fixed health site. As more countries commit to scaling up CHW-led healthcare systems, it is critical that we understand how to best design and implement iCCM and CHW services more broadly, in order to bring about their full potential.

To address this need, we designed a cluster randomised controlled trial to test door-to-door proactive case detection by CHWs compared with a conventional approach to iCCM service delivery, which relies on patient-initiated care seeking. In both arms of the trial, CHWs will provide an integrated package of child, reproductive and maternal health services, primary health centres (PHCs) will be reinforced in infrastructure and capacity, and user fees will be removed at all levels of care. The difference between the intervention (ProCCM) arm and the control (iCCM) arm is the proactive versus conventional approach to the delivery of community-based services. The comparator was chosen to isolate and assess the effects of one design feature of CHW service delivery: proactive case detection.

The ProCCM approach is designed to overcome additional social, structural and health system barriers that may impede or lead to delayed access, even under a community-based comprehensive iCCM approach. At a systems level, these include the direct and indirect costs of care, including distance to care. At the household level, lack of resources, mistrust in the healthcare system and complex familial decision-making dynamics due to in part to gender inequality can contribute to delays in reaching care.[24 25] By proactively seeking out patients and linking community members to the healthcare system, ProCCM is designed to reduce the time from onset of condition to utilisation of health services, including direct provision of comprehensive primary care services for all household members, ultimately reducing mortality.

METHODS AND ANALYSES
Study aims and hypothesis
Our cluster randomised controlled trial aims to:
1. Estimate the effect of adding door-to-door proactive case detection by CHWs to an enhanced iCCM
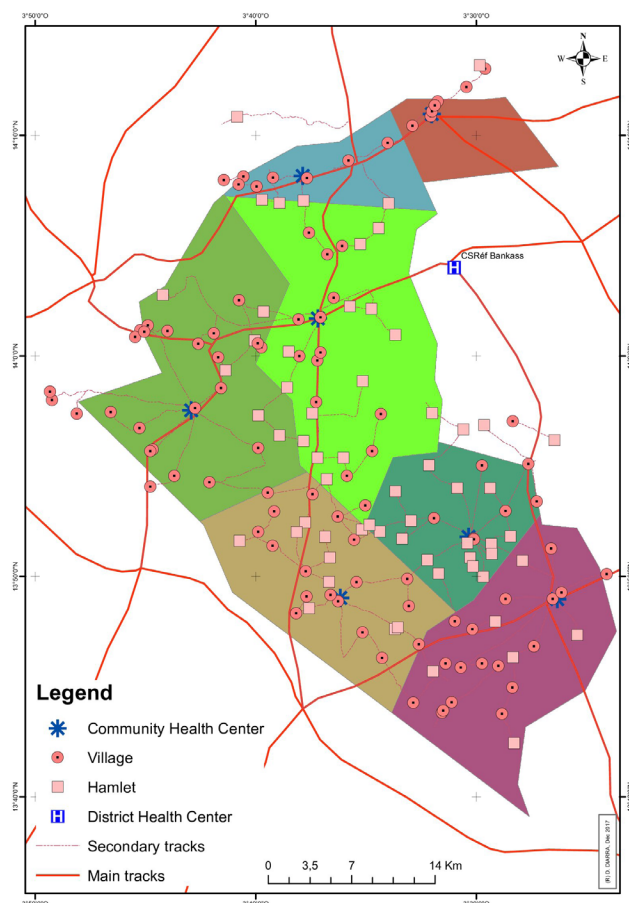
Figure 1 Map of study area; colours indicate the seven health catchment areas within which the trial is being conducted.

intervention on under-five child mortality; we hypothesise that, after 36 months, the relative difference in the incidence rate of under-five mortality between the two study arms will be greater than 25%.
2. Estimate the effect of adding door-to-door proactive case detection by CHWs to an enhanced iCCM intervention on utilisation of reproductive, maternal and child health services.
3. Evaluate the ProCCM intervention model, compared with the iCCM control model, in terms of cost-effectiveness, equity and affordability at scale.

Study site
The trial will be conducted in the Bankass health district of the Mopti region in eastern Mali, approximately 600 km east of the nation's capital, Bamako. The district has a 2016 population of approximately 300 000 people and is served by a public secondary referral hospital located in Bankass, the largest town in the district.[26] Within the Bankass health district, the study is being conducted in 7 (of 22) health catchment areas: Dimbal, Doundé, Ende, Kani Bozon, Koulongon, Lessagou and Soubala (figure 1). The study area has a 2016 population of approximately

100 000 people.[26] Each health catchment area is served by a PHC operated by the Ministry of Health.

Study design

This is an unblinded, pragmatic, cluster randomised controlled trial, with 69 village clusters in the intervention arm and 68 village clusters in the comparison arm. Clusters are randomised to receive either enhanced iCCM from stationary CHW(s) serving patients exclusively at a community health site (control) as per Mali's national iCCM strategy,[27] or ProCCM from CHW(s) conducting daily proactive case-finding home visits in addition to serving patients at a community health site. Only the intervention arm will receive door-to-door proactive case detection by CHWs, including doorstep care and home-based follow-up.

Intervention

Local community members—female candidates encouraged—who can read and write in French will be recruited, trained, supervised and supported as CHWs from the village cluster in which they will work. CHW coverage will be based on Mali's national iCCM strategy, which recommends one CHW for a population of 700 in the southern region where the study area is situated.[27] Clusters, therefore, may have one or multiple resident CHWs,

depending on the size of the cluster population. Clusters with less than 200 people and within 3 km of another cluster assigned to the same study arm will share a CHW, provided there is no geographic barrier (ie, river) between the two clusters and no linguistic barrier for the CHW.

In both arms, CHWs will provide a comprehensive set of primary care services, including iCCM in accordance with national and international standards,[2] as well as maternal and reproductive health for women of reproductive age (see table 1 for a full description of the CHW package of care). CHW services will include counselling, diagnostics, treatment, referral to reinforced PHCs and follow-up care. CHWs will be required to be on call, available to receive and care for patients who seek them out, 24 hours per day, 7 days per week. CHWs will receive a salary circa minimum wage (FCFA40 000 per month), and user fees will be removed for all CHW and referral services for all patients in the study area. A detailed description of the entire health system strengthening intervention in both arms is provided in the online supplementary document.

Control arm: conventional CHW service delivery

In clusters assigned to the control arm, CHWs will be stationed at a community health site to provide the

Table 1 Community health worker (CHW) package of care, provided at the patient's doorstep (intervention arm) or at the CHW's health site (both arms)

CHW services	Description
Diagnosis and treatment of malaria, all ages*	► Diagnosis and treatment of simple cases of malaria for patients of all ages, and accompaniment of patients of all ages with severe malaria to public PHC.
iCCM of common childhood illnesses*	► Diagnosis and treatment of malaria, diarrhoeal disease and acute respiratory infection for children 2–59 months, and acute moderate malnutrition for children 6–59 months according to standard iCCM protocols.[2]
Detection of pregnancy	► Pregnancy testing for women whose last menstrual period occurred more than 6 weeks before the date of the visit.
Family planning services*	► Contraceptive counselling, administration (oral contraceptives, depo provera, condoms) or referral (IUD, implants, sterilisation) for women who test negative for pregnancy and women or men who request family planning.
Accompaniment or referral to PHC for danger signs, all ages*	► Screening of sick patients of all ages for a list of predefined danger signs that indicate either immediate accompaniment or referral to public PHC. ► Referral of pregnant women to public PHC for prenatal consultation, facility-based delivery and postnatal care.
Follow-up care	► 24 hours follow-up for patients of all ages after referral to public PHC. ► 24, 48 and 72 hours follow-up after treatment of malaria (all ages) or iCCM (children under 5); additional follow-up according to standard iCCM protocols.[2] ► Follow-up and danger sign monitoring throughout pregnancy (2 weeks throughout her pregnancy, and every week in the final month until delivery) and postpartum period (24 hours, 48 hours, 5 days and once per week until 48 days after delivery).
Newborn assessment*	► Conduct of newborn assessment to provide counselling and screen for danger signs at 24 hours, 48 hours, 120 hours, 7 days, 14 days, 21 days and 28 days.
Health promotion and disease prevention*	► Counselling for patients and families for disease prevention using behavioural change communication techniques.

*These services are also offered by conventional CHWs in the Malian context, according to the Ministry of Health's policy on CHW care.[27]
iCCM, integrated community case management; IUD, intrauterine device; PHC, primary health centre.

comprehensive package of primary care services for at least 4 hours per day, 6 days per week, available to receive patients seeking care. The community health site is at the cluster level and separate from the PHC.

Intervention arm: proactive CHW service delivery

In clusters assigned to the intervention arm, CHW(s) will be trained and deployed to conduct proactive case finding, door-to-door home visits for at least 2 hours each day, 6 days a week, with the goal of visiting each household at least two times each month. During the home visit, CHWs will screen all household members for recent illness or symptoms and provide services at the home, including follow-up for sick children and adults, pregnant women, newborns and postpartum mothers. In addition to home visits, ProCCM CHWs will provide care at their community health site for at least 2 hours a day, 6 days per week, according to a calendar shared with the community. At the health site, CHWs will provide the same services as those offered by CHWs in the control arm to care-seeking patients.

Cluster definition and randomisation

In order to identify distinct clusters, a field team visited all villages and hamlets in the study area and collected global positioning system (GPS) coordinates at the public space where community-wide meetings, announcements and festivities are held. GPS coordinates were mapped and the cardinal distances between neighbouring villages and hamlets were calculated. Villages and hamlets 1 km or less from each another were grouped into clusters, resulting in 160 individual villages and hamlets grouped into 137 unique clusters. A cluster definition based in geographical reality rather than administrative delineation helps to mitigate against contamination.

Clusters located 1.0 or more km from a PHC were stratified by health catchment area and distance to the nearest PHC (1.0–5.0 km vs more than 5.0 km). The cut-off point of 5.0 km was defined in accordance with national iCCM guidelines,[27] which deploys CHWs to deliver iCCM services only in communities greater than 5.0 km from a PHC. An additional stratum included all villages where the PHC was located to ensure balanced assignment of PHC villages across arms. Within each stratum, clusters were randomly assigned to the control or treatment arm using a computer-generated random number. Randomisation was conducted by a member of the research team based in the USA who did not have any involvement in CHW recruitment or participant enrolment. Trial statisticians will remain blinded to cluster allocation until the end of the trial.

Sample size and primary and secondary endpoints
Primary endpoint

The primary endpoint is under-five mortality, measured as deaths among children under 5 years of age per 1000 person-years at risk of mortality. In Mopti, the region of the study site, the 10-year under-five mortality rate

(U5MR) was 111 deaths per 1000 live births during 2012–2013 Demographic and Health Survey (DHS), which is higher than the national U5MR.[28] Since the 2013 DHS, intermittent prophylactic therapy in children for malaria has been rolled out across the region. As intermittent preventive treatment in children is associated with a risk ratio of all-cause under-five mortality of 0.66 in areas of seasonal transmission of malaria,[29] we estimate that baseline U5MR in the area of the intervention will be 111*0.66=72.6/1000.

The sample size for the trial was based on this primary endpoint, derived using methods for cluster randomised trials[30] in which each cluster was treated as an observation and the cluster-level outcome was defined as the U5MR per person-years at risk. We used a negative binomial model to simulate the number of deaths among children under 5. According to 2014 national population estimates adjusted for 2016 using a 2.2% annual growth rate,[26] the seven health catchment areas encompassed a population of 103 848 inhabitants. Assuming that 20% of the population was children aged 0–59 months and 22% was women aged 15–49, we calculated a mean of 152 children and 167 women per cluster. Person-years at risk were calculated assuming 3 years of prospective study follow-up with 10% attrition based on experience with previous trials in Mali.[31 32] We used a coefficient of variation of k=0.29[30] to model the extra variation due to clustering ($1/k^2$ is the size parameter in the negative binomial model). With these parameters, the trial will be able to detect a relative difference of 25% (alpha=0.05, two-tailed test) in the under-five mortality incidence between treatment and control arms with 81.8% power after 36 months.

Secondary endpoints

We will also estimate the effect of the intervention on a number of secondary endpoints:

a. Infant mortality (deaths per 1000 live births among children aged 0–11 months).
b. Newborn mortality (deaths per 1000 live births among children aged 0–28 days).
c. Pregnancy-related mortality ratio (number of deaths among women while pregnant or within 42 days of delivery or termination per 100 000 live births per year) if there is sufficient and robust data to do so.
d. Receipt of oral rehydration therapy and zinc within 24 hours of diarrhoea onset among children under 5.
e. Receipt of diagnostic testing and/or effective treatment for malaria within 24 hours of fever onset among children under 5.
f. Evaluation by a qualified provider within 24 hours of symptom onset among children under 5 with cough and/or fast breathing.
g. Receipt of three or more doses of sulfadoxine–pyrimethamine as intermittent preventive treatment during a woman's most recent pregnancy.

h. Enrolment in antenatal care (ANC) with a skilled provider in the first trimester during a woman's most recent pregnancy.

i. Completing four or more ANC consultations with a skilled provider during a woman's most recent pregnancy.

j. Use of a modern method of contraception among women of reproductive age.

Inclusion criteria

Any individual in the study area at any point during the study period, including visitors, is eligible to receive the health services offered through the intervention. Only permanent residents of the study area are eligible to be included in the household survey. All women aged 15–49 permanently residing in the study area at baseline who provide consent or assent and report no foreseeable plans to leave the study area are eligible to participate in the women's questionnaire of the household survey—the data source used for the measurement of primary and secondary endpoints. Women who did not meet the inclusion criteria at baseline but who become newly eligible during the course of the study are invited to participate at follow-up household survey rounds.

Sources of data

The effects of the ProCCM model of service delivery, compared with the iCCM model, for the primary and secondary endpoints will be assessed using data from three sources: (1) household surveys, (2) the CHW mobile application and (3) facility records.

Household surveys

A household survey will be administered to all eligible women at baseline (prior to the launch of the intervention), and 12, 24 and 36 months after the intervention start. Surveyors will not be members of the villages they survey, nor will they be members of the intervention healthcare delivery staff. All surveyors will be female, as the survey tool contains sensitive questions regarding contraception and reproductive health. The survey includes a household roster, which may be completed by the female head of household, and a questionnaire administered to consenting or assenting women of reproductive age (15–49).

The household survey instrument was adapted from the Mali DHS and designed in Open Data Kit, which permits real-time quality and completeness control on data collection. The women's questionnaire will include a full birth history to capture all live births, which will then be updated during each of the follow-up survey rounds. To track maternal mortality, the survey will record all household deaths occurring the previous year, with additional information on timing of death (during pregnancy, childbirth, after childbirth) for women of reproductive age. The survey also captures detailed information on household and individual sociodemographic characteristics, access and utilisation of reproductive and maternal

healthcare, and care-seeking behaviours and investments for recently ill children under 5. Follow-up household survey rounds will add new household members to the study cohort (eg, due to births, migration) and record absences due to out-migration or death. Surveyors will attempt to contact each eligible woman up to three additional times if she is absent at the first visit.

CHW mobile application data

CHWs in both study arms will be equipped with an Android smartphone and trained to use a mobile application to track services rendered. The app is also designed to be a job aid with integrated data validation and prompts to guide the CHW through the appropriate case management protocol. Population census data collected at baseline, including individual unique identifiers and demographic information, will be prepopulated into the CHW application so that each CHW can access the records of families in his/her service delivery zone. During each encounter with a prospective patient, the CHW will either identify the individual in the application or register newborns, new arrivals or visitors, before selecting the appropriate form in the application for the specific health concern (eg, malaria case management). The types of actions displayed under a patient's profile are linked to her sex and age (eg, pregnancy follow-up is displayed only for women aged 15–49). The application will also alert the CHW of upcoming tasks related to patient follow-up, with an action calendar for 24-hour follow-up available starting at midnight each day.

Facility data

Each PHC will be equipped with five laptop computers, and the physician-in-chief, midwife, pharmacist, vaccine administration technician and receptionist will be trained in data collection on an Electronic Medical Records (EMR) system. Population census data collected at baseline will be imported into the EMR system, including individual unique identifiers and basic demographic information. When attending a PHC, patients will present first to reception, where their medical records will be identified using their unique identifier, name, family and/or village information. During the patient consultation, the service provider will record patient health information (ie, diagnostic tests, results, treatment, posology) in both the EMR and in the paper facility registers, the source documents of the Malian Ministry of Health and required by law. Referral by a CHW will be recorded.

Analytical plan

Analyses of the primary and secondary endpoints will estimate intention-to-treat (ITT) effects.

Analysis of primary endpoint

Using data collected prospectively in the 12, 24 and 36 months follow-up household surveys, we will test for the difference in the incidence of deaths among children under 5 across treatment and control arms using a Poisson regression model with cluster-level random

effects, controlling for household distance to PHC (less than 5 km vs 5 km or more). Children surveyed at baseline will contribute person-years of exposure from the start date of the trial's intervention launch; children born during the trial will contribute person-years of exposure beginning at birth. Children who enter the trial after baseline will contribute person-years of exposure beginning at the household survey interview date in which they are enrolled. All children included in the analysis will contribute person-years through the date of their death, or are right censored on their fifth birthday or the end date of the trial, whichever comes first. The coefficient of interest with be the incidence rate ratio estimated on a dichotomous variable that indicates the child's residence in a treatment versus control cluster. We will control for the non-constant risk of mortality in early childhood by controlling for age (in months) constant over time, and will control for any individual-level characteristics that are unbalanced at baseline. To estimate mortality, a child's date of birth, date of interview, vital status at interview, and if applicable, date of death are required. We will replicate the procedures for missing mortality data used in the DHS, described in detail elsewhere.[33]

Analysis of secondary endpoints

The same modelling approach will be used to estimate ITT effects for secondary endpoints (excluding the covariate for child's age); regression analyses will test the significance of the regression coefficient on the treatment assignment variable. Linking functions will be chosen based on the type of outcome variable analysed (ie, logit for dichotomous outcomes). If 10% or fewer observations have missing secondary outcome data, we will drop observations from analysis; otherwise, we will determine and apply sample weights to estimates derived from the complete sample of observations. For any secondary endpoints that differ significantly by arm at baseline, we will use a difference-in-differences estimation approach to account for this difference.

Per-protocol estimates

ITT estimates will be compared with estimates from a per-protocol analysis of primary and secondary outcomes. Our per-protocol analysis will estimate the effects of the intervention only for households that received the ProCCM CHW services according to the intervention protocol. This will be defined as households, which report they have received two or more visits from a CHW in the month preceding the household survey for each year they participated in the survey, regardless of treatment assignment. Finally, exploratory analyses will be conducted to assess the existence and magnitude of heterogeneous treatment effects according to village population size and household wealth.

Cost-effectiveness analysis

Cost-effectiveness analysis (CEA) compares different programme alternatives in terms of their cost-effectiveness ratio, which can be thought of as the average cost per unit of impact or benefit (eg, cost per life year saved). In most cases, CEA is used to determine whether or not a new alternative policy is better than the status quo, or whether the extra cost is worth the extra benefit. In such cases, the incremental cost-effectiveness ratio (ICER) is used, which takes the ratio between the incremental costs of the new programme with respect to the status quo, to the incremental benefits of the new programme with respect to the status quo. We will perform an ICER analysis to evaluate the relative cost-effectiveness of the ProCCM model with respect to the enhanced iCCM (control) model.

We will calculate the total economic costs of both programmatic models, which will reflect the monetary value of programme and household resources used to deliver and access services, respectively. From the programme perspective, these will include personnel and other recurrent costs such as drugs, laboratory tests and other inputs used to provide services. These data will come from three sources: (1) the CHW mobile application, which reflects all services and supplies used by CHWs for service provision; (2) PHC EMR, which include the services rendered at the PHC and resources will be valued at prices paid by the Ministry of Health; and (3) programme records, including CHW's time and value of work time vis-à-vis salaries. From the household perspective, costs include time used to access health services, valued at their opportunity costs (ie, time lost from work), as well as out-of-pocket expenses such as paying for drugs or health services. These data will be obtained from the household survey, which asks about out-of-pocket expenditures, time spent accessing services and earnings from paid work.

Patient and public involvement

The study was designed and implemented in partnership with national, district and local health officials of the Malian Ministry of Health. Bankass health district was chosen in consultation with the Ministry of Health for three reasons: (1) healthcare utilisation (prenatal and curative consultations) was low and under-five mortality was high; (2) there were no overlapping interventions by other non-governmental organisations at the time or intended for the period of the trial and (3) local authorities were highly engaged and interested in collaborating on study implementation. Research questions and outcome measures were also chosen in consultation, to answer questions of key concern to government partners for informing the design of the national strategic plan for iCCM scale-up, including whether the intervention is equitable, cost-effective and affordable at scale. Community consultation and permission will be sought prior to trial commencement in meetings with representatives of the village clusters, such as village chiefs and their advisories, politico-administrative authorities, religious leaders and representatives of women's and youth associations. Representatives will then communicate with community members via open public meetings. Once the study has

terminated, results will be disseminated to participants via dissemination workshops at all levels of local, regional, and national representation.

Ethics and dissemination

The University of California, San Francisco exempted secondary analysis of the trial data from ethical approval. External monitoring of the study will be assured by a Clinical Research Associate (CRA) external to the trial team. Any substantial protocol amendments or deviations, or any unintended effects of trial interventions or conduct, will be submitted to the Ethics Committee and records reviewed by the CRA.

Surveyors will obtain informed consent from all household survey respondents prior to enrolment in the trial, or from the respondent's parent or guardian if she is a minor. Identifying information (ie, proper name, phone number) will be stored separately from the survey data, linked by the registration ID. Access to identifying information will be restricted to the data collection and management team; trial statisticians and other external collaborators will access only de-identified data.

An independent Data Safety and Monitoring Board (DSMB) will provide oversight throughout the trial. The DSMB will oversee participant safety and evaluate interim results to determine if the trial should be stopped early. Interim analyses of the primary endpoint (under-five mortality) will be performed at 12 and 24 months, estimated using data from the first and second follow-up household surveys. The DSMB will terminate the study early if a 50% relative difference in under-five mortality is detected after 12 months (statistical significance at p<0.001) or a 35% relative difference in under-five mortality after 24 months (p<0.001), a stopping rule more stringent than Haybittle-Peto stopping rules.[34 35] At the end of the trial period, or if the trial is terminated early, all participating villages will receive the care with the condition identified in the superior study arm.

Trial results will be published in peer-reviewed journals following the International Committee of Medical Journal Editors guidelines. Findings will be disseminated via conferences and workshops with national and international stakeholders in community-based healthcare delivery including researchers, policy-makers and practitioners. De-identified data will be made publicly available after the conclusion of the trial and publication of the main effects.

DISCUSSION

Supported by the emergence of global health guidelines and the accumulation of rigorous evidence on the efficacy of iCCM, countries across sub-Saharan Africa are scaling up iCCM to improve child health.[12 13] Yet, the most recent evaluations of national iCCM programmes suggest further improvements in the delivery of iCCM programmes are necessary to reduce under-five mortality.[20–23] Because the core design and implementation of CHW services vary across health systems, their optimal features must be identified and evaluated for iCCM to realise its full potential. This includes identifying how financing mechanisms, health system integration, packages and delivery of care, and CHW recruitment, training, supervision and compensation relate to care outcomes where CHWs are deployed as front-line health workers. The current trial aims to address one of these gaps by testing door-to-door proactive case detection by CHW against a conventional CHW service delivery approach on reducing under-five mortality risk. The results of the trial will, thus, be pertinent to policy-makers and implementers to determine how CHWs may be better deployed for amplifying public health impact.

The current study was designed and will be implemented in partnership with the Mali Ministry of Health to facilitate adoption of lessons learnt and scale-up in the public sector if the intervention is found to be effective. In addition to the primary objective related to CHW service delivery mechanisms, secondary objectives explore questions of key concern to ministerial partners for informing the design of the national strategic plan for iCCM scale-up, including whether the intervention is equitable, cost-effective, affordable at scale. The intervention itself is designed to be scalable as the planning and implementation of the intervention was executed in partnership with the Ministry of Health and district health officials, including operating through government PHCs. Findings from this study could have important policy implications for CHW-led iCCM scale up across sub-Saharan Africa.

Limitations

The large geographical area and 3-year time frame leave the study open to a number of potential confounding effects. Although contingency measures have been put into place for various situations that may arise, unexpected events may occur that influence the extent to which the study can be implemented per protocol. CHWs may have avenues for interacting with each other outside the structures of the intervention which may lead to contamination. Changes to the health system or other contextual factors in the intervention area, such as drug stock-outs, health centre staff strikes, concurrent programme implementation by other actors, and political insecurity may be beyond the control of the study implementers. However, close partnership with national and local health authorities during study preparation will enable us to proactively track these events, implement contingency steps and/or otherwise document them for later sensitivity analyses of the trial's effects.

Trial status

The household baseline survey was carried out from December 2016 to February 2017. Health facility improvements, CHW trainings and provider trainings were completed by December 2016. Implementation of the intervention including the removal of user fees began in February 2017.

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Chapter 4   Impact evaluation

Overview

This paper reports the effects of the addition of proactive case-finding home visits to reinforced iCCM on under-five mortality, which addresses part of the second objective of the thesis.

At the time this thesis was finalised, this paper was under peer review at the Bulletin of the World Health Organization. The paper is presented here in the format in which it was submitted to the Bulletin. The appendices referred to in this manuscript are provided in Appendix C of this thesis for reference.

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed <u>for each</u> research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1605048	**Title**	Ms
First Name(s)	Caroline		
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Thesis Title	Evaluation of proactive community case management to accelerate access to care and reduce under-five mortality in Mali: a cluster randomised trial and process evaluation		
Primary Supervisor	Daniel Chandramohan		

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?			
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	Choose an item.	Was the work subject to academic peer review?	Choose an item.

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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	Bulletin of the World Health Organization
Please list the paper's authors in the intended authorship order:	Jenny Liu*, Emily Treleaven*, Caroline Whidden, Saibou Doumbia, Naimatou Kone, Amadou Beydi Cisse, Aly Diop, Mohamed Berthé, Mahamadou Guindo, Ibrahim M Koné, Michael P. Fay, Ari Johnson⚭, Kassoum Kayentao⚭

	*Co-first authors ⇞Co-senior authors
Stage of publication	**Undergoing revision**

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)	Along with teammates in Mali and the USA, I developed and tested the survey tools, trained data collectors, supervised annual data collection, and contributed to data management and data validation. Trial statisticians (Jenny Liu and Emily Treleaven) conducted the analyses on under-five mortality. I contributed to writing the manuscript that reported these findings.

SECTION E

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Date	12 Dec 2023

Supervisor Signature	Daniel Chandramohan
Date	12 Dec 2023

Title	**Effect of community health worker home visits on child survival: a cluster randomised trial in rural Mali**
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Abstract

Objective: To test the effectiveness of proactive home visits by trained community health workers on all-cause mortality among children under five years of age.

Methods: We conducted a two arm, parallel, unmasked cluster-randomised trial in 137 village-clusters in rural Mali. From February 2017 to January 2020, 31,761 children enrolled at the trial start or at birth. Village-clusters were randomised 1:1 to receive comprehensive primary care services by CHWs providing regular home visits (intervention) or by CHWs providing care at a fixed post (control). In both arms, user fees were removed and primary health centres received staffing and infrastructure improvements prior to the trial start. Using lifetime birth histories from women aged 15-49 surveyed annually, we estimated incidence rate ratios for intention to treat and per protocol effects of the intervention on U5M in time updated Poisson models.

Findings: Over three years, we observed 52,970 person years (27,332 intervention; 25,638 control). During the trial, 909 children in the intervention arm and 827 children in the control arm died. In the intervention arm, the U5M rate declined from 142.8 to 56.7 deaths per 1,000 live births (95% CI 133.3 to 152.9; 48.5 to 66.4, respectively) and from 154.3 to 54.9 deaths per 1,000 live births in the control arm (95% CI 144.3 to 164.9; 45.2 to 64.5, respectively). Intention to treat (IRR 1.019, 95% CI 0.87 to 1.19, *P*=.81) and per protocol estimates (IRR 1.021, 95% CI 0.87 to 1.20, *P*=.80) showed no difference between study arms.

Conclusion: Though no difference in U5M was attributable to CHW proactive home visits, there was an overall rate reduction in U5M during the trial despite the onset of armed conflict. Systems strengthening measures to accelerate access to care deployed in both arms may have contributed to this decline.

Trial registration: ClinicalTrials.gov NCT 02694055

Introduction

Despite recent declines globally, under-five mortality (U5M) remains unacceptably high in many of the poorest countries [1]. In Mali, U5M was 101 deaths per 1,000 live births in 2018, with sub-national rates as high as 152 deaths per 1,000 live births [2,3]. The leading causes of death among young children—malaria, diarrhoea, pneumonia, and malnutrition—progress rapidly, but are curable when diagnosed and treated early [4,5]. Direct and indirect barriers to timely and quality care, including user fees, distance to facilities, and the availability of trained health workers and medical supplies, stymie progress in further reducing morbidity and mortality [6,7].

Community health worker (CHW) led care can improve access to health services and treatment adherence, and reduce disease specific and all-cause mortality [8–10]. Based on this evidence, more than 25 countries have created national community health programs [11]. However, CHW interventions can yield varying impacts [10,12–16], attributable to differences in program design and implementation [17]. In particular, it is unclear how CHW workflows should be specified to overcome barriers to care and reduce U5M [18,19]. Conventionally, CHWs operate at a fixed health site [11]. Proactive case detection—via systematic home visits—may improve timely access to care and reduce mortality by bringing services directly to patients, although the certainty of existing evidence is very low [19].

This study aims to analyse the effect of proactive case detection via home visits for reducing U5M compared to a fixed, site-based passive workflow, delivered by professional community health workers (CHWs) integrated into the public sector health system in rural Mali [20].

CHWs in both arms were trained, paid, supervised, and received regular supplies to carry out their work. We report the estimated intention to treat and per protocol effects of the intervention on U5M. We also compare U5M in the pre-trial and trial periods across all clusters.

Methods

Study design

The Trial of Proactive Community Case Management to Reduce Child Mortality (ProCCM) is a two arm, parallel, unmasked cluster randomised controlled trial testing the effectiveness of proactive case detection home visits (intervention) versus a passive workflow (control) delivered by CHWs [20]. The trial was carried out over a three-year period from February 2017 through January 2020 in seven[1] of 22 health catchment areas in the Bankass district in central Mali, approximately 600 kilometres northeast of Bamako. Each catchment area is served by a public sector PHC. A public sector secondary referral hospital is located 35 kilometres outside the study area. At baseline, the study area had a population of approximately 100,000 people, a higher U5M rate, and a lower child healthcare utilization rate relative to the nation and globally [2,3,18]. The trial was powered to detect a 25% relative difference (alpha=0.05, two tailed test) in the incidence rate of U5M between study arms [20].

Participants

All individuals in the study area, regardless of residency status, were able to receive health services from study CHWs or at referral PHCs. All women of reproductive age (15-49 years) who self-reported no plans to move away from the study area in the next three years and were

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[1]Dimbal, Doundé, Ende, Kanibozon, Koulongon, Lessagou, and Soubala

permanent residents of the study area (defined as residing in the area for at least six months with no other primary residence) were eligible to participate in annual household surveys to assess primary and secondary trial endpoints.

Randomisation and masking

After mapping all settlements within the study area, clusters (N=137) were defined as a grouping of villages and/or hamlets less than one kilometre apart and at least one kilometre from the next nearest grouping of villages and/or hamlets. Trial statisticians stratified village-clusters along two dimensions: health catchment area and distance to the nearest PHC (<1.0 kilometres, 1.0–5.0 kilometres, and >5.0 kilometres). A distance of five kilometres was chosen as it emulates national guidelines that deploy CHWs in communities more than five kilometres from a health facility [22]. The villages less than one kilometre from the nearest PHC are the villages where the PHCs are located. Using a computer generated random allocation, village-clusters within each strata were randomly assigned to the intervention or control arm. The randomisation procedure was performed by an investigator based in the United States who did not have any contact with study implementation. Trial statisticians were masked to cluster allocation until the end of the trial and unmasked only after approval by the trial's independent Data Safety and Monitoring Board (DSMB). The original randomisation scheme included 15 strata, with all villages <1.0 kilometre from a PHC grouped into a single stratum. However, the randomisation scheme implemented included 21 strata, with each village <1.0 kilometre grouped in its own strata (Appendix A). The trial data analysis follows the randomisation assignment as implemented by and verified with the field team, as recommended and approved by the DSMB.

Procedures

Per Mali's national community health strategy, trained CHWs offer a comprehensive package of community-based primary care services from a fixed site in the community [22]. To maintain equipoise, control arm CHWs replicated this model, providing health promotion, preventive, and curative services via a passive workflow to patients who sought care from the CHW at the fixed community site. CHWs in the intervention arm offered the same services via a proactive workflow, by conducting case detection visits to households in their jurisdiction, with the goal of visiting each household at least twice per month.

CHWs in both arms referred patients requiring higher-level care to the participating PHCs, which received systems strengthening measures prior to the trial launch. These included removing all user fees and expanded staffing and training, equipment, and infrastructure. Thereafter the study instituted salaried, professional CHWs to provide care at a CHW:population ratio of approximately 1:700 to align with the national strategy, with supervisors providing monthly visits to CHWs in both trial arms. The study protocol includes a detailed description of the intervention and activities in the control arm [20].

Annual household surveys were conducted at baseline (December 2016–January 2017), and nominally 12 months (February–March 2018), 24 months (March–May 2019), and 36 months (February–April 2020). Surveys were administered to consenting or assenting women of reproductive age (15-49 at enrolment) at their home by female interviewers who were not a resident of study area. The survey instrument was adapted from the Mali Demographic and

Health Survey (DHS) questionnaire, encoded in ODK, and loaded onto mobile tablets for use by interviewers. GIS locations of each PHC and each concession (i.e., extended family grouping of households) at the time of enrolment were obtained to generate measures of household distance to the nearest PHC.

Each survey included a household roster and modules on sociodemographic characteristics, reproductive and maternal health, and recent illness and healthcare utilization among children under five. At follow up surveys, respondents reported their lifetime birth histories and the number of CHW home visits their household received in the preceding month. Household rosters were updated at each survey round to identify new members (due to births, migration, marriage, adoption) and those absent due to migration or death. Newly eligible women at each time point (due to aging or migrating in) were invited to participate. In all surveys, up to three attempts were made to contact each eligible household and woman.

Outcomes

The trial's primary endpoint is all cause U5M, defined as the death of a child under five years of age (age 0-59 months). Information about children's vital status was obtained prospectively in each follow up survey from birth histories. Children are at risk of death beginning at their date of birth, the start of the trial for those born before the baseline survey, or the interview date in which they are first reported as present in the household. Children are lost to follow up (LTFU) when the household could not be located in a subsequent household survey and no household member was available to participate. Children are right censored at the end of the trial, their fifth birthday, or when LTFU, depending on which occurred first.

Statistical analysis

Details of our analytical approach and sample size calculations are given in the trial statistical

analysis plan (Appendix B). Observable cluster and individual characteristics at trial start were

systematically tested for differences by arm accounting for the clustered nature of the data. We

calculated crude death rates as the number of deaths among children under five years of age per

1,000 person years of exposure to the risk of mortality. We estimated the under-five mortality

rate (U5MR) as the probability of dying between birth and the fifth birthday per 1,000 live

births. To estimate the U5MR for the three-year periods prior to and during the study period, we

used a life table approach with lifetime birth history data to estimate mortality probabilities in

eight age segments to account for non-proportional differences in age-specific mortality rates

across early childhood [23].

We used a time updated Poisson model at the child-month level to estimate the effect of the

intervention on the incidence rate ratio (IRR) of U5M using an intention to treat (ITT) approach

(primary effect analysis). We adjusted for non-constant risk of mortality in early childhood by

controlling for age (months) and sex of the child. Models also adjusted for household distance

to the nearest PHC ($\leq$ 5 kilometres vs. >5 kilometres), cluster population at baseline (<=700

people vs. >700 people), and household wealth at study entry. Household wealth was estimated

using a principal component analysis of household ownership of durable goods, livestock, and

physical housing characteristics [24]. All models used robust standard errors adjusted for

clustering at the village-cluster level to account for correlation among observations at the unit of

randomisation. We report the ITT as the IRR between intervention and control arms with 95% confidence intervals.

We also estimated the per protocol (PP) effect of the intervention. For the intervention arm, treatment adherence was defined as receiving two or more home visits from a CHW in the month preceding the survey for all years in which the household was enrolled [20]. In the control arm, adherence was defined as receiving no home visits in the preceding month in any year in which the household was enrolled. We estimated stabilized inverse probability (IP) weights for protocol deviation using pooled logistic regression fit by maximum likelihood, where the denominator included individual, household, and village-level covariates [25,26]. We then estimated the IRR of U5M using the time updated Poisson models described above with stabilized IP weighting.

Lastly, we examined the possibility of heterogeneous treatment ITT and PP effects along three pre-specified dimensions measured at baseline by interacting our intervention arm indicator with subgroup indicators as defined above. These include distance to PHC, village-cluster population size, and household wealth. All analyses were conducted in Stata Version 17.1.

Ethical approvals and trial oversight
The Ethics Committee of the Faculty of Medicine, Pharmacy and Dentistry at the University of Bamako approved the trial (2016/03/CE/FMPOS; ClincialTrials.gov NCT02694055). Secondary analysis of trial data was exempted from ethical review by the University of California, San Francisco (Ref: 154824) and approved by the Observational/Interventions

Research Ethics Committee at the London School of Hygiene & Tropical Medicine (Ref: 13832). All participants gave written informed consent for each annual household survey.

The trial was externally monitored by Pharmalys, a clinical research organization (CRO). Participant safety and evaluation of interim results was overseen by an independent DSMB. Since 2012, Mali has experienced increasing instability and violence in northern regions, subsequently spreading throughout the country. Since 2018, the study area experienced a marked increase in armed conflict-related events and fatalities. Subsequent protocol amendments and deviations to assure the safety of participants, providers, and study personnel were reviewed by the CRO and DSMB and approved by the governing Ethics Committee (Appendix A).

Results

Figure 1 presents the trial profile for children under five. A total of 137 village-clusters from the seven health catchment areas were enrolled and randomised. Six clusters were lost to follow up over the course of the trial due to armed conflict (Appendix A). Prior to the trial, 19,864 children under five years of age were enumerated (10,233 intervention; 9,631 control). Over the three-year trial period, 31,587 children were enrolled (16,248 intervention; 15,339 control), totalling 52,970 person years (635,644 person months) of observation (27,333 intervention; 25,637 control). By the end of the trial, there were a cumulative 1,736 deaths (909 intervention; 827 control), 9,463 children who aged out of the sample (4,959 intervention; 4,504 control), and 5,659 LTFU (2,657 intervention; 3,002 control).

Characteristics of individuals at the start of the trial are given in Table 1. We did not identify

any significant imbalances across study arms. Table 2 disaggregates reported deaths among

children under five and presents these per 1,000 person years (PY) of exposure to the risk of

mortality (i.e., crude death rates). For the three-year trial period, there were similar rates across

arms (33.26 per 1,000 PY intervention vs. 32.36 per 1,000 PY control). Deaths declined over

the course of the trial (February 2017 through January 2020) in both arms: from 42.90 (year 1)

to 25.71 per 1,000 PY (year 3) in the intervention arm, and from 41.52 (year 1) to 25.97 per

1,000 PY (year 3) in the control arm.

The U5MR declined by more than half over the three-year trial period (Figure 2). Across arms,

the U5MR declined from 148.4 (95% CI 141.5 to 155.7) deaths per 1,000 live births at study

baseline (encompassing the three-year period prior to trial launch; February 2014 through

January 2017), to 55.1 (95% CI 48.6 to 62.4) deaths per 1,000 live births over the three-year

trial period. Similar declines in the infant and newborn mortality rates were observed in both

arms. No rates differed by arm in the pre or post trial period. The U5M rate declined from 142.8

to 56.7 deaths per 1,000 live births in the intervention arm (95% CI 133.3 to 152.9; 48.5 to 66.4,

respectively) and from 154.3 to 54.9 deaths per 1,000 lives births in the control arm (95% CI

144.3 to 164.9; 45.2 to 64.5, respectively).

ITT estimates do not show a difference in the incidence rate of U5M between the intervention

and control arms (Table 3, IRR=1.019, 95% CI 0.87 to 1.19), or by distance to PHC, cluster

population size, or household wealth (Appendix C). As expected, the IRR declines with

increasing age.

Notably, 25.0% of children in the intervention arm met the per protocol criteria, while 73.5% of children in the control arm met the per protocol criteria (Appendix A). All intervention and all but one control clusters included children who met the per protocol definition. Per protocol estimates show no difference in mortality associated with intervention exposure (Table 3; IRR=1.021; 95% CI 0.87 to 1.20).

These results are robust to a variety of sensitivity analyses, including ways to account for potential biases resulting from missing data for children's age, date of birth, and date of death (Appendix D). Despite notable LTFU, we find no differential entry or LTFU by arm. We find no substantive difference in effect estimates when restricting to the sample of children born at least nine months after trial launch, that is, children who were exposed to the intervention in utero and whose entry into the trial was not conditional on survival to trial launch. Finally, conducting the ITT analysis at the village-cluster level yielded the same null effect as did individual-level specifications using Cox proportional hazard models.

Discussion

Our three-year cluster RCT to test the effectiveness of CHW home visits compared to passive site based care did not show an attributable difference in all cause U5M between arms in ITT or per protocol analyses. However, compared to the three-year period prior to the trial, we observed over a 60% decline in the U5MR in both arms to a rate lower than for almost all other regions in Mali [2]. Our pragmatic trial was conducted in real world conditions, affected by migration and the onset of armed conflict, reflected in our losses to follow up and moderate

adherence. The observed U5M decline is notable given that exposure to armed conflict is associated with persistent and diffuse increases in U5M [27].

The ProCCM trial addresses a critical gap in the literature by providing rigorous evidence about the impact of CHW workflow organization on all cause U5M [19]. Prior studies identifying positive effects of CHW home visits focused on disease or period specific effects. For example, home visits in the postpartum period reduced newborn mortality [28]; home visits for proactive malaria case detection and management led to increased treatment [29]. In making decisions about community health workflow, policymakers must consider costs and benefits of CHW home visits for multiple outcomes. Analyses of trial secondary endpoints show that though there was no difference by arm in prevalence of diarrhoea, febrile illness, or acute respiratory infections, at 12 months, children under five in the intervention arm were more likely to promptly access health services than children in the control arm [30]. Though this effect did not persist at 36 months, child healthcare utilization in both arms increased from 19% at baseline to 52% at trial completion despite the onset of armed conflict. The intervention also increased early initiation and uptake of antenatal care (ANC) relative to the control arm, though it did not impact facility delivery [31]. Both ANC and facility delivery increased across arms relative to the pre-trial period. That we did observe some intervention effects across trial arms suggests that the null effect of the intervention on under-five mortality is a product of a lack of effect of CHW workflow on U5M rather than poor adherence. However, we will test spatial and dose-response relationships on U5M in future analyses.

The overall U5MR decline suggests that systems strengthening measures deployed in both arms—including user fee removal; redesigned, improved, and expanded PHCs; and stationing a salaried, trained, supervised CHW in every village, regardless of distance to the nearest PHC—could be more important for child survival than CHW workflow modality. User fee removal and locating professionalized CHWs in communities were associated with increased healthcare utilization and reduced U5M in other studies, including in Mali [13,32–38]. Prior to the trial, CHW services were inconsistently provided in communities only five or more kilometres from the nearest PHC, though an analysis of pre-trial data showed significantly lower child healthcare utilization among children in villages just two kilometres from a PHC, relative to those living within two kilometres [18]. Addressing cost, distance, and clinical capacity, key determinants of healthcare utilization and U5M [6,39–42], may have been particularly salient in the context of armed conflict, which disrupts healthcare delivery and access [43–45]. To contextualize the trial results, this decline was far greater than that observed nationally in Mali over the trial period [2]. The presence of armed conflict may reduce the generalizability of our findings to settings not affected by armed conflict. However, because the conduct of this type of intervention is rare in conflict-affected settings, lessons from the trial's implementation and results can inform healthcare design and delivery in other conflict-affected settings. Moreover, lessons from the trial may be applicable to rural areas in other settings with similarly high rates of under-five mortality, where many cannot afford user fees or other costs associated with health care, and face long distances to access care [39,46–48].

Strengths of the trial include its sample size, rigorous measurement of endpoints, and longitudinal design. Limitations include the potential for errors in annually following up

participants in a highly mobile population and lack of data on cause of death, in addition to the low adherence observed in the intervention arm and loss to follow up in both arms. Pretrial U5MR estimates may be subject to recall bias, though we do not expect that recall bias varies by arm. Analysis of CHW mobile application data and program costs will provide further insight into fidelity to protocols, quantify CHW services delivered, and characterize the dose response relationship to health outcomes. Our process evaluation will further contextualize study results, including mechanisms of effect for systems strengthening measures.

The ProCCM Trial found that CHW proactive home visits did not reduce U5M, addressing a key question for dozens of national health systems in low and middle-income countries seeking to optimize CHW programs for impact. Deployment of professionalized CHWs in all communities, user fee removal, and other systems strengthening measures may have contributed to overall declines in U5M; further analyses of trial data will help elucidate the specific aspects that contributed to increased child survival.

Contributors

KK, AJ, CW, JL, ET, ABC, and MG designed the trial; MPF conducted the sample size calculations. AJ acquired funding for the trial, with grant writing and reporting help from JL, ET, CW, SD, NK, and KK. SD, NK, KK, and CW trained and supervised data collectors. SD, KK, CW, and AJ provided trial supervision. ABC and MG oversaw the intervention and MB, AD, and IMK provided additional local resource support for intervention implementation, with validation by JL, MPF, and CW. ET, SD, and NK managed trial data, with input from CW, KK, and JL. JL and ET developed the statistical methods for the analysis, with input from CW, MPF, AJ, and KK. ET analysed the data, with validation by JL, MPF, and CW. ET and JL generated data visualizations and wrote the first draft of the manuscript. CW contributed additional writing. All authors helped interpret results or edited the manuscript directly. All authors reviewed and approved the final version for publication.

Declaration of interests

CW, SD, NK, ABC, AJ, and KK were employed by Muso at the time of the trial and publication. JL, and ET received grants from Muso to contribute to the trial. Muso designed and implemented the trial and the intervention evaluated. Muso received funding to support the trial from USAID Development Innovation Lab, Johnson & Johnson Foundation, CRI Foundation, and Grand Challenges Canada. AD, MB, MG, and BMK were employed by the government of Mali at the time of the trial. All other authors declare no competing interest or other financial relationships with any organisations that might have an interest in the submitted work in the previous three years. All authors have completed the unified competing interest form (available

on request from the corresponding author), and declare no other relationships or activities that could appear to have influenced the submitted work.

supervisors in the trial area, listed by name in Appendix E, without whom the trial would not be possible.

Funding

Trial registration

The Trial of Proactive Community Case Management to Reduce Child Mortality (ProCCM Trial) is registered with ClinicalTrials.gov, NCT02694055. The trial was registered on February 26, 2016, prior to the trial start in February 2017. We affirm that registration was prospective prior to the enrolment of any trial participants.

Transparency statement

Drs. Liu and Treleaven, the co-lead authors, affirm that this manuscript is an honest, accurate, and transparent account of the ProCCM Trial. We have not omitted any aspects of the study. All discrepancies from the trial protocol and changes to the statistical analysis plan after the start of

the trial are reported with justifications in the manuscript or supplementary materials

(Appendices A and B).

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Tables

Table 1. Individual-level characteristics in intervention and control arms at trial start (February 2017).

	Intervention arm (N=10,196)		Control arm (N=9,585)		Total (N=19,781)	
	N	%	N	%	N	%
Number of households	5,267	50.83	5,097	49.17	10,366	100.0
Median number of children under 5 per household (SD)	2.57 (1.38)		2.48 (1.30)		2.53 (1.34)	
Child age						
0-5 months	1,297	12.72	1,179	12.30	2,476	12.52
6-11 months	1,002	9.83	1,013	10.57	2,015	10.19
12-23 months	2,000	19.62	1,884	19.66	3,884	19.64
24-35 months	2,006	19.67	1,893	19.75	3,899	19.71
36-59 months	3,891	38.16	3,616	37.73	7,507	37.95
Child sex						
Male	5,159	50.60	4,881	50.92	10,040	50.76
Female	5,037	49.40	4,704	49.08	9,741	49.24
Median household size (SD)	9.97 (4.73)		9.78 (4.76)		9.88 (4.75)	
Mother has attended any school	599	6.29	682	7.68	1,281	6.96
Mother's marital status						
Single[1]	104	1.02	98	1.02	202	1.02
Married, monogamous	5,398	52.94	5,173	53.97	10,571	53.44
Married, polygynous	4,574	44.86	4,208	43.90	8,782	44.40
Missing	120	1.18	106	1.11	226	1.14
Household wealth						
Poorest	1,758	17.24	1,515	15.81	3,273	16.55
Poor	1,835	18.00	1,905	19.87	3,740	18.91
Middle	2,039	20.00	1,966	20.51	4,005	20.25
Rich	2,175	21.33	2,125	22.17	4,300	21.74
Richest	2,389	23.43	2,074	21.64	4,463	22.56
Cluster distance to health facility (km)						
<=5 km	4,175	40.95	4,582	47.80	8,7957	44.27
> 5 km	6,021	59.05	5,003	52.20	11,024	55.73
Cluster population at baseline						
<700	2,873	28.18	3,287	34.29	6,160	31.14
700+	7,323	71.82	6,298	65.71	13,621	68.86

Notes:
[1] Single = never married, widowed, divorced

Table 2. Crude deaths per 1,000 person years among children under five.

Trial period	Intervention			Control		
	Deaths	Person years	Deaths/1,000 person years	Deaths	Person years	Deaths/1,000 person years
Year 1	408	9,511.17	42.90	372	8,959.08	41.52
Year 2	278	9,148.17	30.29	246	8,630.33	28.50
Year 3	223	8,673.25	25.71	209	8,048.33	25.97
Years 1-3 combined	909	27,332.58	33.26	827	25,637.25	32.36

Table 3. Estimated ITT and per protocol effects of the ProCCM intervention on under-five mortality (N=52,970 person years).

	ITT[a]			Per protocol[a,b]		
	IRR[c]	95% CI	p	IRR	95% CI	p
Intervention arm	1.019	0.87 – 1.19	0.811	1.021	0.87 – 1.20	0.802
Child age						
0 months	1055.375	830.43 – 1341.25	<0.001	1098.836	853.28 – 1415.06	<0.001
1-2 months	40.921	29.03 – 57.69	<0.001	39.806	28.44 – 55.70	<0.001
3-5 months	14.004	10.03 – 19.55	<0.001	13.012	9.15 – 18.51	<0.001
6-11 months	7.868	5.73 – 10.80	<0.001	7.960	5.71 – 11.09	<0.001
12-23 months	5.481	4.23 – 7.09	<0.001	5.489	4.18 – 7.21	<0.001
24-35 months	3.438	2.61 – 4.53	<0.001	3.477	2.63 – 4.60	<0.001
36-47 months	2.107	1.58 – 2.82	<0.001	2.134	1.58 – 2.88	<0.001
48-59 months	reference			Reference		
Child sex						
Female	0.916	0.82 – 1.02	0.120	0.897	0.80 – 1.00	0.055
Male	reference			reference		

[a]Estimated via a time-updated Poisson regression adjusted for facility distance, cluster population at baseline, and household wealth at baseline; robust standard errors adjusted for clustering at the village-cluster level.
[b]Estimated with stabilized inverse probability of treatment weights.
[c]IRR = incidence rate ratio

Figures

Figure 1. Enrollment, randomization, and treatment.
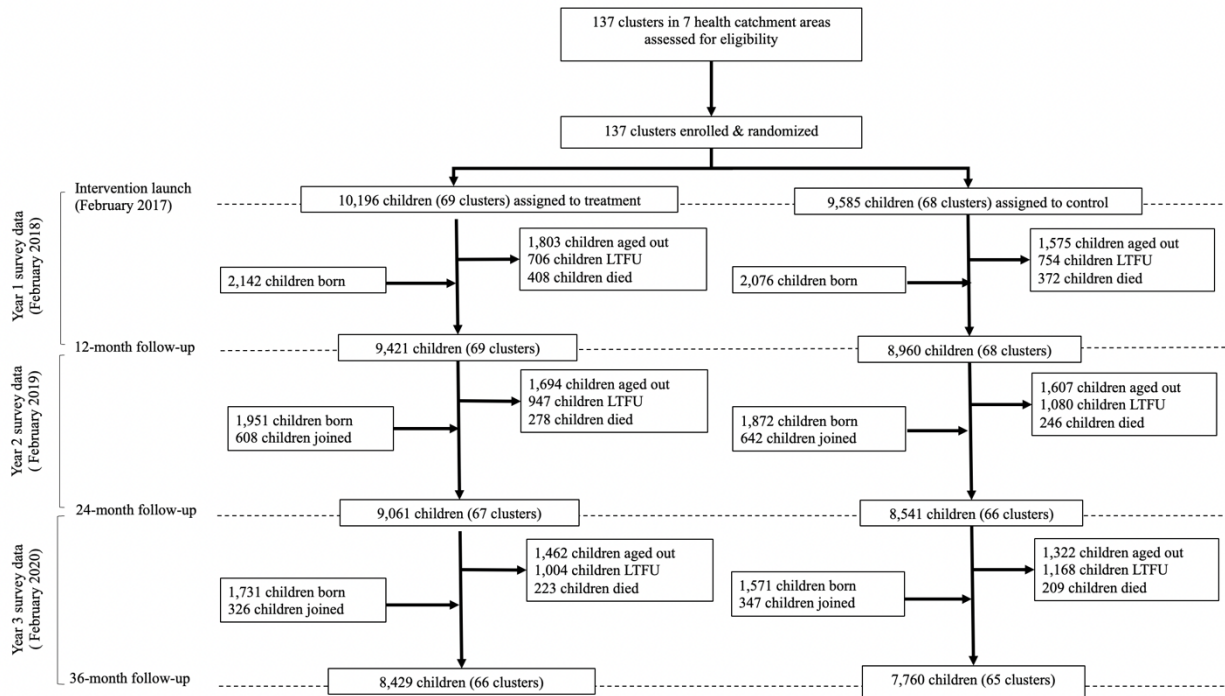
Data sources: Household rosters from baseline, 12-, 24-, and 36-month surveys; lifetime birth histories from all women aged 15-49 at enrollment surveyed annually at 12-, 24-, and 36-months.

Figure 2. Under-five, infant, and newborn mortality rates by arm in the three-year pre-versus post-trial periods.
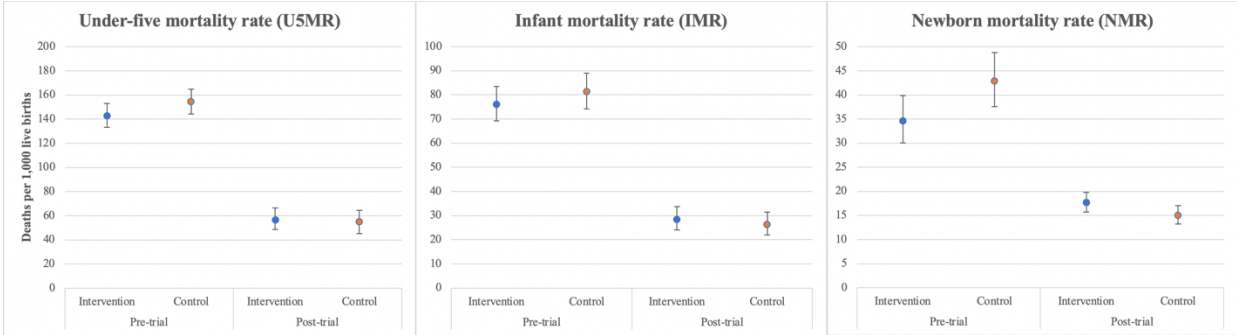
Notes:
1. Data source: Lifetime birth histories from all women aged 15-49 at enrollment surveyed annually at 12-, 24-, and 36-months.
2. U5MR is the probability of dying between birth and the fifth birthday per 1,000 live births; IMR is the probability of dying between birth and the first birthday per 1,000 live births; NMR is the probability of dying between birth and the 28th day of life per 1,000 live births.
3. The pre-trial period is the three-year period prior to the trial launch, February 2014–January 2017. The post-trial period is the three-year trial period, February 2017–January 2020.

Chapter 5   Outcome evaluation

Overview

This paper reports the effects of the addition of the proactive case-finding home visits to reinforced iCCM on secondary trial endpoints pertaining to children's health and health care utilisation, which addresses the rest of the second objective of the thesis. I developed a detailed statistical analysis plan (SAP) for the analysis of these secondary trial endpoints, which is presented in Appendix D of the thesis.

The paper is provided here in its published format. It is an open access article that falls under the Creative Commons Attribution (CC BY 4.0) license. The Online Supplementary Document referred to in this paper is provided in Appendix E of this thesis. This includes all additional analyses in supplementary tables and figures, as well as an author reflexivity statement for research from international partnerships between HICs and LMICs (Sam-Agudu and Abimbola, 2021; Morton *et al.*, 2022).

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed <u>for each</u> research paper included within a thesis.

<u>SECTION A – Student Details</u>

Student ID Number	1605048	**Title**	Ms
First Name(s)	Caroline		
Surname/Family Name	Whidden		
Thesis Title	Evaluation of proactive community case management to accelerate access to care and reduce under-five mortality in Mali: a cluster randomised trial and process evaluation		
Primary Supervisor	Daniel Chandramohan		

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

<u>SECTION B – Paper already published</u>

Where was the work published?	Journal of Global Health		
When was the work published?	April 21 2023		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	**No**	Was the work subject to academic peer review?	**Yes**

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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 developed the statistical analysis plan, with input from my advisor Clémence Leyrat, supervisors, and trial team. I prepared the data sets for analysis, performed all analyses, and wrote the manuscript.

SECTION E

Student Signature	Caroline Whidden
Date	12 Dec 2023

Supervisor Signature	Daniel Chandramohan
Date	12 Dec 2023

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PAPERS

Effects of proactive vs fixed community health care delivery on child health and access to care: a cluster randomised trial secondary endpoint analysis

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Background Professional community health workers (CHWs) can help achieve universal health coverage, although evidence gaps remain on how to optimise CHW service delivery. We conducted an unblinded, parallel, cluster randomised trial in rural Mali to determine whether proactive CHW delivery reduced mortality and improved access to health care among children under five years, compared to passive delivery. Here we report the secondary access endpoints.

Methods Beginning from 26-28 February 2017, 137 village-clusters were offered care by CHWs embedded in communities who were trained, paid, supervised, and integrated into a reinforced public-sector health system that did not charge user fees. Clusters were randomised (stratified on primary health centre catchment and distance) to care during CHWs during door-to-door home visits (intervention) or based at a fixed village site (control). We measured outcomes at baseline, 12-, 24-, and 36-month time points with surveys administered to all resident women aged 15-49 years. We used logistic regression with cluster-level random effects to estimate intention-to-treat and per-protocol effects over time on prompt 24-hour treatment within the health sector.

Results Follow-up surveys between February 2018 and April 2020 generated 20 105 child-year observations. Across arms, prompt health sector treatment more than doubled compared to baseline. At 12 months, children in intervention clusters had 22% higher odds of receiving prompt health sector treatment than those in control (cluster-specific adjusted odds ratio (aOR) = 1.22; 95% confidence interval (CI) = 1.06, 1.41, P = 0.005), or 4.7 percentage points higher (adjusted risk difference (aRD) = 0.047; 95% CI = 0.014, 0.080). We found no evidence of an effect at 24 or 36 months.

Conclusions CHW-led health system redesign likely drove the 2-fold increase in rapid child access to care. In this context, proactive home visits further improved early access during the first year but waned afterwards.

Registration ClinicalTrials.gov NCT02694055.

Ensuring that all people have access to quality health services without financial hardship is central to achieving universal health coverage (UHC) and other health-related targets of the Sustainable Development Goal (SDGs). Despite progress to date, up to one-third of the world's population may not benefit from UHC by 2030 [1]. Achieving these goals requires a fundamental shift in how primary care is organised, managed, and delivered.

Community health workers (CHWs) have the potential to contribute to the diverse, sustainable health workforce required to deliver integrated, people-centred primary care [1]. Low and middle-income countries (LMICs) are increasingly adopting integrated community case management (iCCM) (comprising the diagnosis, treatment, and referral in the community for childhood malaria, diarrhoea, pneumonia, acute malnutrition, and/or newborn illnesses [2]) as a CHW-led strategy to improve service coverage and health outcomes among children under five years of age [3,4]. This scale-up is motivated by substantial evidence that CHWs can deliver a range of preventive and curative primary care services [5-7], including community case management for malaria [8,9], diarrhoea [10], and pneumonia [10-12] to increase utilisation, improve health, and reduce mortality among under-five children in many settings.

However, iCCM programme design and implementation vary greatly between settings, to variable effects [13,14]. Evaluations of scaled iCCM in Burkina Faso, Ethiopia, and Malawi found implementation shortcomings related to CHW training and deployment, health systems, and community mobilisation, and no effects on care-seeking, treatment coverage, or child mortality [15-17]. A systematic review of iCCM found moderate quality evidence that care-seeking from an appropriate provider increased by 68%, compared to facility-based care, yet inconsistent effects on the receipt of adequate treatment from an appropriate provider and under-five mortality among included studies, few of which included payment, supervision, or information systems to support CHWs [18].

Optimising iCCM means moving beyond training and deploying CHWs to ensure that these frontline health workers are integrated into and adequately supported by the health system [18]. The World Health Organization (WHO) guidelines released in 2018 recommend CHW remuneration, functioning referral systems, supply chain management, and supportive supervision, among other health system enablers [19]. However, existing gaps in the evidence do not allow for the recommendation of specific programme design features such as CHW workflow or approaches by which community-based services like iCCM are delivered [18,19].

Across sub-Saharan Africa, including in Mali, CHWs are stationed in community health sites to provide iCCM and other community-based services to patients who seek care. An alternative to this conventional, passive approach to service delivery is a proactive workflow in which CHWs conduct routine door-to-door home visits, searching for and identifying prospective patients. Proactively offering promotive, preventive, and curative services at patients' doorsteps may improve community engagement, service coverage, and treatment outcomes, and especially the speed with which evaluation and treatment are received.

Ensuring prompt treatment, particularly within the crucial 24-hour window after symptom onset in children under five, is a cornerstone of global iCCM and malaria control programmes. A meta-analysis estimated that almost half of severe childhood malarial anaemia cases in the included studies could have been averted if children had accessed facility-based treatment within the first day of symptom onset [20]. From Brazil to Uganda, studies using verbal and social autopsy data have uncovered how delays at various points along the trajectory to care contribute to child death due to diarrhoea, acute respiratory infection, and newborn illnesses [21-23].

Based on existing evidence, it is uncertain whether proactive case-finding home visits by CHWs can improve prompt treatment and reduce the prevalence of infectious diseases or under-five mortality [24]. We implemented a cluster randomised trial to evaluate the effects of proactive CHW home visits on child mortality (primary trial endpoint) and access to care in rural, central Mali [25]. The primary trial endpoint results will be reported separately (unpublished data). Here we report the secondary trial endpoint analysis on child health and service utilisation over the three-year trial period, including the receipt of prompt treatment within the health sector, receipt of recommended case management according to iCCM protocols, and the prevalence of common childhood illnesses in this context. We assessed whether effects differed according to population size, distance to primary health centre (PHC), or household wealth, to determine the equity of this approach.

METHODS

Study design and participants

We conducted a pragmatic, cluster randomised controlled trial, with a stratified, two-arm, parallel group design in a rural setting in the Bankass health district of central Mali's Mopti region. The district, served by one public secondary referral hospital and 22 PHCs was chosen in partnership with the Malian Minis-

try of Health and Social Development based on its high under-five mortality and low health care utilisation [26,27], with few concurrent health interventions and a high interest from local authorities in collaborating. From initial geo-mapping across seven contiguous PHC catchment areas, villages and hamlets one kilometre or less apart were grouped into clusters. We randomised clusters in a 1:1 allocation to intervention and control arms to receive CHW services delivered via proactive home visits (n = 69 clusters) or only at a fixed community health site (n = 68 clusters), respectively.

To assess outcomes, we censused all permanent residents and surveyed all resident women aged 15 to 49 years at baseline and annually at 12, 24, and 36 months. Respondents provided written, informed consent (or assent, if aged 15 to 17 years and unmarried) at their first enrolment and were included in follow-up surveys if present (including those who were aged above 49 years). Any individual who sought care from study providers was eligible to receive health care throughout the trial, regardless of residency, survey enrolment, or arm assignment.

Randomisation and masking

We used the timeline cluster graphical tool to describe the sequencing and blinding of the different recruitment, randomisation, and assessment procedures implemented during the trial, and whether they were conducted at the cluster or participant level, or both (Figure S1 in the **Online Supplementary Document**) [28]. We stratified the randomization by health catchment area and distance to the nearest PHC. In total, we had 21 strata. Each of the seven catchment areas had three strata: one for the cluster where the PHC was located, one for clusters within five kilometres from the PHC, and one for clusters beyond this distance. Given the nature of the intervention, we could not blind the participants, providers, or outcome assessors. Statisticians were blinded throughout the trial, until the data were fully cleaned and locked by the Data Safety & Monitoring Board (DSMB).

Procedures

In each cluster, community leaders nominated individuals aged 18 to 45 years who could read and write in French to be trained, selected, and deployed as CHWs. Nominees were divided by study arm and trained separately over six weeks, with annual one-week refresher training, based on the same clinical protocols (that covered preventive and curative primary care for reproductive, maternal, newborn, and child health, including iCCM for diarrhoea, pneumonia, malaria, acute malnutrition, and newborn illnesses) and the delivery approach to which their clusters were allocated. CHWs were ultimately selected based on a post-training evaluation and deployed to serve approximately 700 people, in line with Mali's 2016-2020 national community health strategy [29].

CHWs in the intervention arm were instructed to conduct door-to-door proactive case-finding home visits for at least two hours per day, six days per week, with the goal of visiting every household at least twice per month. In the control arm, CHWs were instructed to station themselves at community health sites for four hours per day, six days per week, to provide the same package of services to care-seeking patients. CHWs in both arms were expected to be available on-call to provide care as needed, at all times.

CHWs in both arms received the same systems support, in accordance with WHO guidelines [19]. All CHWs signed contracts with the Community Health Associations (ASACO) that manage public-sector PHCs, received part-time salaries and benefits that met local minimum wage requirements, and had performance-based opportunities to advance into the cadre of dedicated CHW supervisors. All CHWs received individual, monthly supervision that included house calls without the CHW to solicit patients' perspectives, direct observation while conducting home visits or stationed at their site (depending on which arm they were allocated to), and one-on-one feedback aided by a personalised performance dashboard [30]. Dedicated supervisors also held group supervision meetings twice per month, separately by arm. Supervisors monitored CHWs' supplies and equipment, including the CHW smartphone-based mobile application for recording patient encounters. All CHWs were supported by a functioning referral system, as all study PHCs received reinforcements in infrastructure (e.g. waiting area, separate general and maternity wards), equipment, supplies, and human resources (e.g. recruitments and training). Finally, user fees were removed at all points of care, from CHW to tertiary hospital, for patients in both arms. The redesigned CHW-led health system in both arms was launched February 26-28, 2017.

We assessed the outcomes at baseline (December 2016 to January 2017) and approximately 12 (February to March 2018), 24 (March to May 2019), and 36 months (January to April 2020) via surveys administered at respondents' homes by female surveyors who were neither community residents nor involved in health

care delivery. We adapted the household and women's surveys from Mali's Demographic and Health Survey (DHS) and programmed in Open Data Kit. They included a household roster (census) and modules on migration, mortality, and socio-economic characteristics. The women's survey included socio-demographic characteristics, current contraceptive use, most recent pregnancy and childbirth, lifetime birth history, and symptoms and service utilisation in the two weeks preceding the survey for all the woman's co-residing children under five years of age.

Outcomes

We assessed all outcomes using the women's survey, measured at the child level and analysed at the child-year level. The primary outcome was prompt treatment within the health sector, defined as a child aged 0-59 months with any symptom at any time in the two weeks preceding the survey who had received CHW or public or private health centre evaluation and any treatment, including traditional or home remedies, the same or next day after symptom onset. Secondary outcomes included any prompt treatment (from any source), health sector evaluation (CHW or public or private health centre consultation, with or without prompt treatment), and any care (inside or outside the home). As the intervention was designed to improve UHC, we defined (in an appendix to the trial statistical analysis plan that was approved by the DSMB prior to unblinding) composite utilisation outcomes that assessed access to care for all sick children, regardless of illness. Consistent with endpoints defined in the trial protocol [25], we included as secondary outcomes recommended case management and prompt. According to iCCM clinical protocols [2], we defined recommended case management as a child aged 3-59 months with fever, and/or diarrhoea without blood, and/or cough with fast breathing (i.e., suspected pneumonia) who had received a rapid diagnostic test for malaria, and/or oral rehydration solution (ORS) and zinc, and/or antibiotics, respectively; newborns were excluded as their clinical protocol was different. We were unable, however, to conduct stratified analyses by illness due to fewer clusters with cases and events per illness. To contextualise the access to care results and assess intervention effects on child morbidity, we also included the prevalence of fever, diarrhoea, cough, and suspected pneumonia in the two weeks preceding the survey among all children under five years.

Statistical analysis

We based the sample size calculation, planned interim analyses, and stopping guidelines on the trial's primary endpoint (deaths among children under five years of age per 1000 person-years at risk of mortality), as reported in the protocol [25].

For all ten outcomes, we first generated cluster-specific summaries (means) by calculating the proportion in each cluster at each time point and plotting the median per arm and cluster-level variability over time. We then estimated the intervention effects using the following mixed effects logistic regression model on the intention-to-treat (ITT) population:

$$logit\left(\pi_{ijkt}\right) = log\left(\frac{\pi_{ijkt}}{1-\pi_{ijkt}}\right) = \alpha + \beta_i + \delta_t + \eta_i t + \sum_l \gamma_l z_{ijkl} + u_{ij}$$

Here, π_{ijkt} is the probability for the kth individual in the jth cluster in the ith treatment arm, at the tth time point. α is the constant, representing the mean outcome among individuals in the control arm. (β_i) is the cluster-specific odds ratio (OR_{CS}) representing the outcome in the intervention arm ($i=1$) compared to the control arm ($i=0$). δ_t represents the time effect, with $t=1, 2, 3$ corresponding to three consecutive follow-up surveys. $\eta_i t$ is the interaction term that estimates the differential effect of the intervention arm relative to the control arm across the three time points. For each outcome, we fit an additional model without the interaction term that estimated an overall cluster-specific effect throughout the three-year trial, controlling for the linear effect of time. γ_l is a vector of the estimated coefficients for the following set of covariates, represented by z_{ijkl} ($l=1,2,...,L$): a cluster-level summary of the baseline value of the outcome, baseline cluster-level summaries of sample characteristics that were deemed imbalanced at baseline and likely to influence the outcome, individual's age and sex, and variables on which randomisation was stratified. Cluster-level random effects, υ_{ij}, accounted for within-cluster correlation. For prevalence outcomes, we included an additional random intercept, v_{ijk}, to account for repeated measure and within-individual correlation over time. We conducted all statistical analyses using Stata version 15 (StataCorp, College Station TX, USA). We reported the results following the CONSORT guidelines [31], including the presentation of both relative and absolute effect sizes (using the margins post-estimation command) and the intracluster correlation coefficient (ICC) per arm (taking the rho coefficient of models run separately by arm, or using the estat post-estimation command with multilevel models).

We assessed heterogeneous treatment effects by fitting models that included an interaction term between an arm and prespecified effect modifiers at each time point separately (to facilitate the interpretation of interaction effects; prespecified analysis) and during the three-year period overall (controlling for the linear effect of time; post-hoc analysis). We used likelihood ratio tests to determine if there was evidence to reject the assumption of no interaction/effect modification. As potential modifiers, baseline cluster population size and distance to PHC were chosen to critically examine design features of Mali's community health strategy [29], which recommends one CHW per 700 people only in villages more than five kilometres away from a PHC. Household wealth was chosen to permit an equity sub-analysis, examining differential effects for children living in households in the poorest wealth quintile.

We conducted a prespecified per-protocol subgroup analysis by excluding (from the main model/equation above) child-year observations in the intervention arm if no female respondent in the household reported receiving at least two CHW home visits in the month preceding the survey, and then by additionally excluding child-year observations in the control arm if any female respondent in the household reported a home visit in the last month.

The main intervention effect models used complete-case analysis. However, due to missing treatment data at the 24-month time point caused by a data capture coding error, we performed multiple imputation by chained equations (MICE) in sensitivity analyses on related outcomes: primary outcome, any prompt treatment, recommended case management, and prompt, recommended case management. Furthermore, because missing outcome data exceeded the predefined 10% threshold for the 24-month subset, we performed MICE prior to assessing heterogeneous treatment effects at 24 months. Due to correlation between outcomes, we ran separate MICE models, each generating 20 imputed data sets. We included all variables and interaction terms that appeared in one or more subsequent regression analyses and two auxiliary variables (any treatment received and CHW care received) associated with missing data. Due to strong clustering for outcomes and missing data, we were unable to impute data separately by cluster or include indicator variables for clusters. Instead, we captured between-cluster variability by including all baseline cluster-level covariates and outcome summaries when creating imputations.

Patient and public involvement

We involved national and district level authorities from the Malian Ministry of Health and Social Development in the study design, implementation, and dissemination. We chose research questions (including an embedded costing analysis) and outcomes for the trial (including the primary outcome on under-five mortality) that were of key interest to our government partners. We also involved national and district health authorities in study site selection, including both the rural district within the country and the seven PHC catchment areas within the district. Within each catchment area, we held public consultation meetings with community representatives, including village chiefs and their advisors, women's and youth association leaders, religious leaders, and politico-administrative authorities (such as mayors, PHC directors, and ASACOs), where we discussed and obtained verbal permission to conduct the trial. Communities nominated CHW candidates who participated in the training and provided a fixed health site for control arm CHWs, as well as a house if the CHW was not a resident of the village-cluster.

Once we conducted the analysis on the trial's primary and secondary endpoints, including child health and access to care, we held results dissemination workshops with local, district, regional, and national level stakeholders, starting at the district and local level with community representatives (as listed above), including study CHWs and their dedicated supervisors.

Role of the funding source

The funders had no role in study design, data collection, analysis, interpretation, or writing of this paper. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Ethics

The trial received ethical approval from the Faculty of Medicine, Pharmacy and Odonto-Stomatology Ethics Committee at the Université des Sciences, des Techniques et des Technologies of Bamako (Ref: 2016/03/CE/FMPOS). Secondary analysis of trial data was approved by the Observational/Interventions Research Ethics Committee at the London School of Hygiene & Tropical Medicine (Ref: 13832) and exempted by the University of California, San Francisco (Ref: 154824)

RESULTS

Baseline data collection covered 137 clusters, censused 99 576 people, and surveyed 15 884 women of reproductive age who provided outcome data on 15 855 children under five years (Figure S2 in the **Online Supplementary Document**). Clusters , children under five years of age, sick children under five years, and children aged 3-59 months with iCCM illnesses had similar characteristics between arms at baseline (**Table 1**, Table S1-S3 in the **Online Supplementary Document**). All clusters contributed observations to the analysis. However, between the 12- and 24-month surveys, due to escalating violent conflict in the study area, three intervention and three control clusters, all relatively small and remote , were lost to follow-up (Table S4 and Figure S2 in the **Online Supplementary Document**). Sample characteristics were similar between observations with complete vs missing outcome data (Tables S5-S7 in the **Online Supplementary Document**). Analyses included 46 789 child-year observations, 20 105 sick child-year observations, and 15 278 child-year observations with iCCM illnesses during the three-year trial period. Among all child-year observations, 57% were repeated measures on the same child; 28% of sick child-year and 22% of child-year observations with iCCM illnesses were repeated measures.

Prompt treatment within the health sector increased from a median of 19% across all clusters at baseline to 61% at 12 months, 44% at 24 months, and 52% at 36 months, with similar trends in both arms (**Figure 1**). Similarly, one in five children at baseline received health sector evaluation, which increased to two-thirds at 12 and 24 months and over one-half at 36 months across arms. Recommended case management also

Table 1. Baseline cluster-level characteristics and summaries of the outcomes of interest*

	Intervention	Control
Characteristics, n (%)	n = 69 clusters	n = 68 clusters
Population size, median (IQR)	532 (305.0-1087.0)	564 (243.5-984.0)
<700	38 (55.1)	40 (58.8)
≥700	31 (44.9)	28 (41.2)
Distance from PHC in kilometres, median (IQR)	6.3 (4.2-8.6)	5.8 (3.5-8.6)
≤5.0	28 (40.6)	29 (42.7)
>5.0	41 (59.4)	39 (57.4)
Topography		
None	63 (91.3)	64 (94.1)
On clifftop	1 (1.5)	2 (2.9)
PHC inaccessible during rainy season (June, July, August)	5 (7.3)	2 (2.9)
CHW services available†		
None	51 (73.9)	51 (75.)
Satellite village	14 (20.3)	14 (20.6)
Posted village	4 (5.8)	3 (4.4)
PHC catchment area		
Dimbal	15 (21.7)	15 (22.1)
Lessagou	14 (20.3)	12 (17.7)
Doundé	8 (11.6)	7 (10.3)
Ende	2 (2.9)	3 (4.4)
Soubala	11 (15.9)	13 (19.1)
Kanibozon	9 (13.0)	8 (11.8)
Koulongon	10 (14.5)	10 (14.7)
Outcomes, median (IQR)		
Prevalence	n = 69 clusters	n = 68 clusters
Fever	0.12 (0.05-0.24)	0.12 (0.06-0.22)
Diarrhoea	0.14 (0.08-0.28)	0.16 (0.08-0.26)
Cough	0.10 (0.06-0.15)	0.11 (0.04-0.18)
Suspected pneumonia	0.03 (0-0.05)	0.03 (0.00-0.05)
Health care utilisation median (IQR)	n = 67 clusters‡	n = 68 clusters
Prompt treatment within health sector	0.19 (0.09-0.31)	0.19 (0.06-0.27)
Any prompt treatment	0.48 (0.29-0.60)	0.45 (0.33-0.55)
Health sector evaluation	0.21 (0.14-0.37)	0.20 (0.08-0.33)
Any care	0.55 (0.38-0.68)	0.50 (0.42-0.66)
Recommended case management, median (IQR)	n = 67 clusters	n = 68 clusters
Recommended case management	0.21 (0.93-0.30)	0.16 (0.08-0.27)
Prompt, recommended case management	0.16 (0.08-0.25)	0.12 (0.05-0.21)

CHW – community health care workers, IQR – interquartile range, PHC – primary health centre

*Data are presented as n (%) unless otherwise specified.

†CHWs are stationed/posted in some communities at baseline and may also serve members from neighbouring/satellite communities.

‡There are two intervention clusters with no sick children at baseline.

increased two-fold compared to baseline, and similarly between arms (**Figure 1**), but did not reach half of the children with iCCM illnesses during the trial. Whether sick children received any prompt treatment (from any source) or any care varied considerably between clusters at baseline, but less so during the trial, reaching as many as 66% or 72%, respectively, at 12 months across arms.

At the 12-month follow-up, the odds of receiving prompt treatment within the health sector were 22% higher in intervention compared to control clusters (AOR_{CS} = 1.22; 95% confidence interval (CI) = 1.06, 1.41, P = 0.005) (**Table 2**). At 12 months, children in intervention clusters were 4.7 percentage points more likely to receive prompt health sector treatment than those in control clusters (adjusted risk difference (ARD) = 0.047;
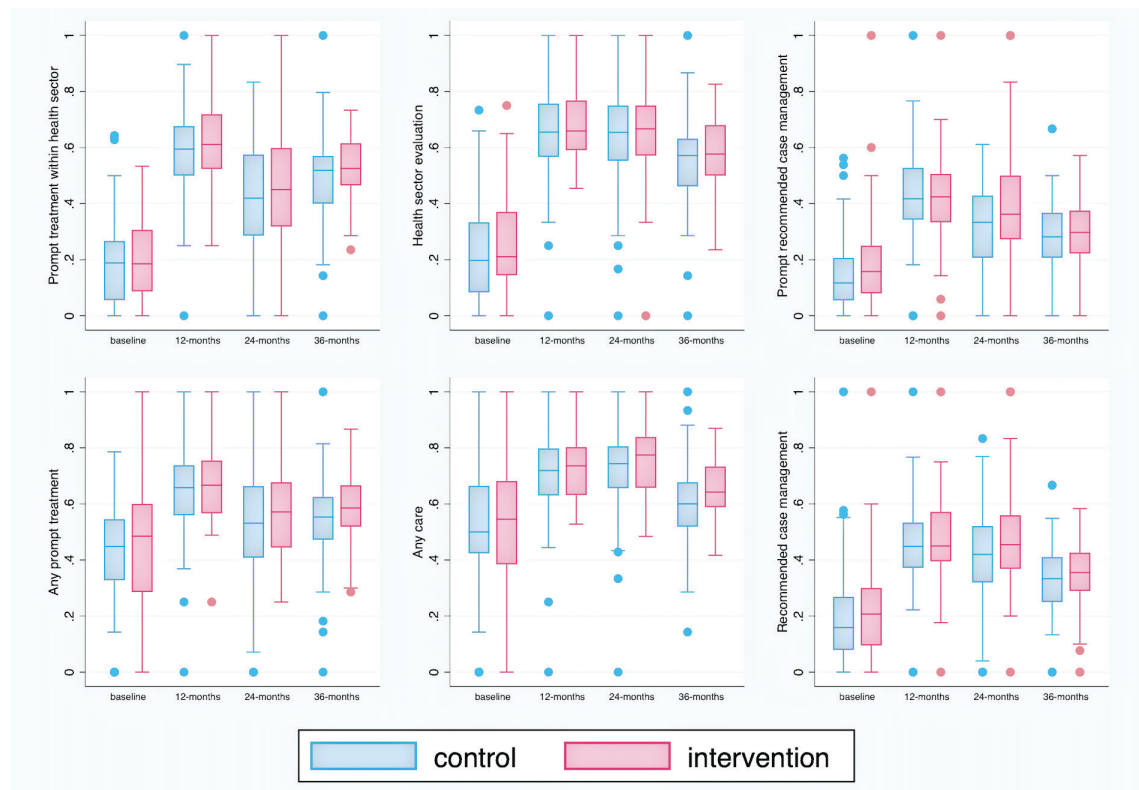

Figure 1. Box plots representing the variability in cluster summaries of the primary and secondary health care utilisation outcomes in intervention and control arms at each time point.

95% CI = 0.014, 0.080). However, there was no evidence of an intervention effect at 24 or 36 months. Findings were similar for any prompt treatment. Furthermore, the results were consistent in sensitivity analyses dealing with missing data, including multiple imputation (Table S8 in the **Online Supplementary Document**). The ICC for the primary outcome was 0.017 (95% CIs = 0.010, 0.029) in the intervention arm and 0.019 (95% CI = 0.010, 0.035) in the control arm.

The results suggested no differential effect by time point for health sector evaluation and any care, although the largest effects were seen at 12 months (**Table 2**). During the three-year period overall, the odds of receiving any health sector evaluation was 12% higher in intervention compared to control clusters (AOR_{CS} = 1.12; 95% CI = 0.99, 1.26, P = 0.072), corresponding to an absolute difference of 2.5 percentage points (ARD = 0.025; 95% CI = -0.002, 0.052). Results were similar for any care. There was no evidence of an effect on recommended case management or prompt, recommended case management. We did not find statistical evidence for effect modification by cluster size, distance to PHC, or household wealth. However, estimated magnitudes suggest that the intervention may have been more effective in improving prompt treatment within the health sector (**Table 3**) and access to care across outcomes and time points (Tables S9-S10 in the **Online Supplementary Document**) in smaller, more remote clusters, and in the poorest households.

During the trial, 47% of sick child-year observations met the per-protocol definition (at least two CHW home visits in the preceding month) in the intervention arm, while 78% met the definition (no CHW home visits in the preceding month) in the control arm (Table S11 in the **Online Supplementary Document**). The proportion that met the per-protocol definition waned over time in the intervention arm (53% at 12, 49%

Table 2. Cluster-specific intervention effects on primary and secondary health care utilisation outcomes, including absolute risks in each arm, during the three-year trial period overall and at each follow-up time point*

	ARC	ARI	C vs I, AOR_CS (95% CI)	P-value		ARC	ARI	C vs I, AOR_CS (95% CI)	P-value
Prompt treatment within the health sector (n = 18 765)					Time point‡				
Overall†	0.52	0.55	1.10 (0.98-1.24)	0.103	12 mo	0.46	0.47	1.07 (0.92-1.25)	0.399
Time point‡					24 mo	0.39	0.41	1.14 (0.97-1.34)	0.109
12 mo	0.58	0.62	1.22 (1.06-1.41)	0.005	36 mo	0.38	0.38	1.02 (0.87-1.20)	0.812
24 mo	0.46	0.45	0.99 (0.85-1.15)	0.887	ICC				
36 mo	0.52	0.54	1.08 (0.94-1.25)	0.290	Control			0.010 (0.003-0.028)	
ICC					Intervention			0.008 (0.003-0.022)	
Control			0.019 (0.010-0.035)		LR test				0.5361
Intervention			0.017 (0.010-0.029)		**Prompt, recommended case management (n = 14 612)**				
LR test				0.016	Overall†	0.36	0.37	1.09 (0.97-1.22)	0.164
Any prompt treatment (n = 18 753)					Time point‡				
Overall†	0.59	0.61	1.12 (1.00-1.25)	0.054	12 mo	0.42	0.44	1.08 (0.93-1.26)	0.332
Time point‡					24 mo	0.31	0.34	1.21 (1.03-1.42)	0.024
12 mo	0.64	0.69	1.24 (1.08-1.42)	0.003	36 mo	0.33	0.33	0.98 (0.83-1.16)	0.787
24 mo	0.55	0.55	0.98 (0.85-1.13)	0.792	ICC				
36 mo	0.56	0.59	1.13 (0.98-1.30)	0.100	Control			0.008 (0.023- 0.025)	
ICC					Intervention			0.011 (0.005- 0.026)	
Control			0.016 (0.008-0.032)		LR test				0.1106
Intervention			0.013 (0.007-0.025)						
LR test				0.009					
Health sector evaluation (n = 20 088)									
Overall†	0.62	0.64	1.12 (0.99-1.26)	0.072					
Time point‡									
12 mo	0.63	0.67	1.19 (1.03-1.38)	0.016					
24 mo	0.65	0.66	1.06 (0.91-1.22)	0.463					
36 mo	0.57	0.60	1.10 (0.95-1.27)	0.216					
ICC									
Control			0.020 (0.011-0.036)						
Intervention			0.019 (0.011-0.033)						
LR test				0.232					
Any care (N = 20 104)									
Overall†	0.69	0.72	1.15 (1.03-1.28)	0.017					
Time point‡									
12 mo	0.70	0.74	1.20 (1.04-1.38)	0.010					
24 mo	0.73	0.75	1.07 (0.92-1.23)	0.386					
36 mo	0.63	0.66	1.17 (1.01-1.34)	0.032					
ICC									
Control			0.017 (0.009-0.032)						
Intervention			0.014 (0.007-0.027)						
LR test				0.282					
Recommended case management (n = 14 613)									
Overall†	0.41	0.42	1.08 (0.96-1.21)	0.208					

AOR_CS – cluster-specific adjusted odds ratio, LR – likelihood ratio, ARC – absolute risk of events in the control arm, ARI – absolute risk of events in the intervention arm, C – control clusters, CI – confidence interval, I – intervention clusters, ICC – intracluster correlation coefficient, mo – months
*Two regression models are presented here: regression model 1 controlled for the time effect $t = 1, 2, 3$, to estimate the intervention effect during the three-year follow-up period overall. Regression model 2 included the interaction term η_t that estimated the intervention effect at each time point. The likelihood ratio test corresponds to the interaction term in model 2. Adjusted models controlled for child's age (0-11, 12-23, 24-35, 36-59 mo) and sex; baseline cluster-level summary of the outcome; baseline cluster-level summary of household wealth (quintiles), mother's decision-making power (any, none), and mother's mobility (none, dependent mobility, independent mobility), which were deemed imbalanced at baseline and likely risk factors; PHC catchment area and cluster distance to PHC (coded as a continuous variable in the models for prompt treatment within the health sector, any prompt treatment, prompt, recommended case management, and pneumonia where the relationship with distance was linear, and otherwise coded as a dichotomous variable using a five-kilometre cut-off), which were the variables on which randomisation was stratified; and symptom (fever, diarrhoea with no blood, cough with fast breathing, combination), only for recommended case management outcomes.
†Regression model 1.
‡Regression model 2.

at 24, 39% at 36 months) and increased in the control arm (72% at 12, 81% at 24, 83% at 36 months). Restricted to the per-protocol subgroup, the intervention effect on prompt treatment within the health sector increased to 45% higher odds at 12 months (AOR_CS = 1.43; 95% CI = -1.21, 1.69, P < 0.001) and 22% over the three years (AOR_CS = 1.22; 95% CI = -1.06, 1.40, P = 0.005), compared to control clusters (**Table 4**). Health sector evaluation odds were 29% higher in the intervention compared to control clusters over the three years (AOR_CS = 1.29; 95% CI = -1.12, 1.48, P < 0.001). Per-protocol analyses also yielded significant effects over the three years on recommended case management (AOR_CS = 1.20; 95% CI = -1.06, 1.37, P = 0.005). Results were consistent whether or not we excluded control arm observations that did not meet per-protocol (Table S12 in the **Online Supplementary Document**).

Finally, infectious disease prevalence increased in both arms compared to baseline, two-fold for cough and suspected pneumonia (Figure S3 in the **Online Supplementary Document**). There was no intervention effect on any disease prevalence during the three years overall, although the odds of cough and suspected pneumonia were 1.16 times (95% CI = 1.04, 1.30) or 2.2 percentage points and 1.22 times (95% CI = 1.07, 1.40) or 1.6 percentage points higher, respectively, at 12 months in the intervention compared to control clusters, with consistent results in the per-protocol analyses (Table S13, S16, and S17 in the **Online Supplementary Document**).

Table 3. Heterogeneous treatment effects by cluster population size, cluster distance to nearest PHC, and household wealth on the primary outcome, prompt treatment within the health sector, during the three-year trial period overall*

	ARC	ARI	C vs I, AOR$_{CS}$ (95% CI)	*P*-value
Cluster distance to PHC				
≤5.0 km	0.54	0.55	1.01 (0.84-1.22)	0.918
>5.0 km	0.50	0.54	1.18 (1.01-1.38)	0.039
LR test				0.2193
Cluster population size				
<700 people	0.53	0.57	1.18 (0.99-1.41)	0.072
≥700	0.51	0.53	1.07 (0.91-1.24)	0.419
LR test				0.4132
Household wealth†				
Less poor	0.53	0.55	1.08 (0.95-1.22)	0.243
Poorest	0.49	0.54	1.23 (1.03-1.46)	0.022
LR test				0.1000

PHC – public health centre, LR – likelihood ratio, AORCS – cluster-specific adjusted odds ratio, ARC – absolute risk of events in the control arm, ARI – absolute risk of events in the intervention arm, C – control clusters, CI – confidence interval, I – intervention clusters

*We ran three separate models, one for each of the predefined effect modifiers that included an interaction term between treatment arm and the modifier. We report the results of the LR tests for interaction between arm and modifier in each model. All models controlled for the same covariates as the main model for overall effects during the three-year trial period; we removed the baseline cluster-level summary of wealth in the models that assessed heterogeneous effects by this variable at the household level.

†For 20% of sick child-year observations included in the analysis, their household wealth was measured during the follow-up period rather than at baseline. The co-intervention in both arms to remove user fees could have influenced household wealth in the follow-up period.

Table 4. Per-protocol subgroup estimates for the primary and secondary health care utilisation outcomes, excluding observations in the intervention arm that did not receive at least two CHW home visits in the month preceding the survey, during the three-year trial period overall and at each follow-up time point*

Outcome	ARC	ARI	C vs I, AOR$_{CS}$ (95% CI)	*P*-value
Prompt treatment within the health sector (n = 13 500)				
Overall†	0.52	0.57	1.22 (1.06-1.40)	0.005
Time point‡				
12 mo	0.58	0.66	1.43 (1.21-1.69)	<0.001
24 mo	0.46	0.48	1.07 (0.89-1.28)	0.453
36 mo	0.52	0.55	1.13 (0.94-1.35)	0.184
LR test				0.0036
Any prompt treatment (n = 13 493)				
Overall†	0.59	0.64	1.26 (1.09-1.44)	0.001
Time point‡				
12 mo	0.64	0.72	1.43 (1.21-1.69)	<0.001
24 mo	0.55	0.58	1.10 (0.92-1.32)	0.315
36 mo	0.56	0.61	1.23 (1.03-1.47)	0.023
LR test				0.0205
Health sector evaluation (n = 14 518)				
Overall†	0.62	0.68	1.29 (1.12-1.48)	<0.001
Time point‡				
12 mo	0.63	0.70	1.38 (1.17-1.65)	<0.001
24 mo	0.65	0.71	1.30 (1.09-1.55)	0.003
36 mo	0.58	0.61	1.17 (0.97-1.39)	0.094
LR test				0.1736
Any care (n = 14 527)				
Overall†	0.69	0.75	1.35 (1.17-1.55)	<0.001
Time point‡				
12 mo	0.70	0.76	1.37 (1.16-1.63)	<0.001
24 mo	0.73	0.79	1.35 (1.13-1.62)	0.001
36 mo	0.63	0.69	1.31 (1.10-1.57)	0.003
LR test				0.8945
Recommended case management (n = 10 569)				
Overall†	0.42	0.45	1.20 (1.06-1.37)	0.005
Time point‡				
12 mo	0.46	0.49	1.19 (0.99-1.42)	0.061
24 mo	0.39	0.45	1.35 (1.12-1.63)	0.001
36 mo	0.38	0.39	1.06 (0.86-1.30)	0.592
LR test				0.1435
Prompt, recommended case management (n = 10 569)				
Overall†	0.36	0.39	1.15 (1.01-1.32)	0.040
Time point‡				
12 mo	0.43	0.46	1.19 (0.99-1.43)	0.062
24 mo	0.31	0.36	1.26 (1.04-1.53)	0.017
36 mo	0.33	0.33	0.99 (0.80-1.22)	0.890
LR test				0.1280

AORCS – cluster-specific adjusted odds ratio, ARC – absolute risk of events in the control arm, ARI – absolute risk of events in the intervention arm, C – control clusters, CI – confidence interval, I – intervention clusters, ICC – intracluster correlation coefficient, LR – likelihood ratio, mo – months

*Two regression models are presented here: regression model 1 controlled for the time effect t = 1, 2, 3, to estimate the intervention effect during the three-year follow-up period overall. Regression model 2 included the interaction term $\eta_i t$ that estimated the intervention effect at each time point. The likelihood ratio test corresponds to the interaction term in model 2. Adjusted models controlled for child's age (0-11, 12-23, 24-35, 36-59 mo) and sex; baseline cluster-level summary of the outcome; baseline cluster-level summary of household wealth (quintiles), mother's decision-making power (any, none), and mother's mobility (none, dependent mobility, independent mobility), which were deemed imbalanced at baseline and likely risk factors; PHC catchment area and cluster distance to PHC (coded as a continuous variable in the models for prompt treatment within the health sector, any prompt treatment, prompt, recommended case management, and pneumonia where the relationship with distance was linear, and otherwise coded as a dichotomous variable using a five-kilometre cut-off), which were the variables on which randomisation was stratified; and symptom (fever, diarrhoea with no blood, cough with fast breathing, combination), only for recommended case management outcomes.

†Regression model 1.
‡Regression model 2.

DISCUSSION

Early access to health sector treatment more than doubled for sick children when study communities received care from professional CHWs and upgraded primary care clinics without user fees. In 2018, the Mali DHS found that only 21% and 55% of children under five with fever in the Mopti region received any prompt treatment and any care, respectively [32]. In that same year, our 12-month survey found that any prompt treatment and any care reached two-thirds or more of all sick children under five in the trial area of Mopti. Health care utilisation peaked at 12 months and waned over time, and many sick children still did not receive prompt, health sector, or recommended care. Nevertheless, this overall improvement in child access to care is remarkable in the context of the performance of large-scale iCCM programme [15-17] and the armed conflict that emerged after 12 months in the trial area, imposing challenges to delivering and receiving services. It is in this redesigned health system context that the results between arms on the effects of proactive CHW home visits should be interpreted.

Proactive CHW service delivery improved early health sector treatment further, compared to the fixed approach, after 12 months, but not after 24 or 36 months of implementation. These findings suggest that home visits were most important during the first year after launching the redesigned CHW-led health system, possibly by mobilising care-seeking, reinforcing the importance of prompt treatment, or building trust in the health system. After more than a year of experiencing accessible, high-quality care without fees, control communities with fixed CHWs may have themselves mobilised, adopted rapid care-seeking, and gained trust in the system, though not as quickly. There was some evidence that, over all three years, proactive CHW service delivery improved access to health sector evaluation and any care, suggesting that home visits may have helped to overcome persistent indirect cost, distance, or social barriers to care, even where fixed CHW services were available without fees. Subgroup estimates suggested that proactive home visits may improve child access to care best in smaller communities, where a CHW can achieve greater home visit coverage, in those farther from a PHC, where utilisation was lowest at baseline [27], and in the poorest households, by overcoming indirect costs to even frontline services or women's limited resources to make health care decisions. Although these subgroup results should be interpreted with caution, they may contribute to the evidence that home visits enhance equity benefits of CHW programmes, along with the important equity impacts of free, proximal, quality service provision [33,34].

For maternal health care, our analysis of other secondary trial endpoints (reported elsewhere) [35] found that proactive CHW home visits increased the likelihood of first trimester antenatal care (ANC) by 11% (risk ratio (RR) = 1.11; 95% CI = 1.02, 1.19) and of four or more ANC visits by 25% (RR = 1.25; 95% CI = 1.08, 1.43), but had no effect on institutional delivery (RR = 1.06; 95% CI = 0.91, 1.20). Across trial arms relative to baseline, any ANC attendance increased by 83% (RR = 1.83; 95% CI = 1.78, 1.86), first trimester ANC by 15% (RR = 1.15; 95% CI = 1.06, 1.25), four or more ANC visits by 2.6 times (RR = 2.59; 95% CI = 2.28, 2.91), and institutional delivery by 54% (RR = 1.54; 95% CI = 1.41, 1.66) [35]. These maternal care results are consistent with the child health care utilisation results insomuch that the bulk of the improvements occurred across both arms, with the proactive service delivery intervention yielding modest incremental benefits, which are nonetheless important for achieving timely, universal health coverage.

CHW adherence to the proactive workflow protocol, as reported at survey time points by respondents, reached only half of sick children in the intervention arm and waned over time. This could be intervention fatigue or the conflict making the proactive workflow difficult to deliver. This likely biased ITT intervention effect estimates towards the null, as per-protocol subgroup analyses showed stronger magnitudes and significance of effects across children's utilisation outcomes at 12 months and during the trial overall. These findings suggest that had households in the intervention arm received a proactive CHW home visit at least once every two weeks throughout the trial period, home visits may have had more effect on children's health care utilisation.

The proactive service delivery intervention effects found in this trial should be understood within the context of the co-interventions in both trial arms, including user fee removal, professional CHWs, and upgraded primary care clinics. Proactive CHW home visits' effects may be different in other health system or social contexts. Our forthcoming process evaluation paper used mixed methods to elucidate the implementation, mechanisms, and context of the proactive home visits and co-interventions in both arms and to help to explain these trial outcome results (unpublished data).
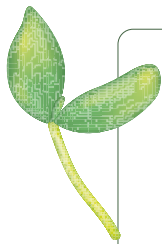
Child morbidity, measured as disease prevalence, did not decrease over time or more so in the intervention arm as we expected it to. Rather, reported prevalence of all four illnesses increased during the trial

period compared to baseline (descriptive), and cough and suspected pneumonia increased statistically at 12 months in intervention compared to control clusters. These increases could reflect mothers' improved illness recognition given CHW care and, additionally, home visits. Mothers who received routine counselling during home visits on disease prevention, illness recognition, and rapid care-seeking may have been more likely during the first year than their control arm counterparts to recognise cough as an illness and fast breathing as an alert, and thus report it during a survey. Our study did not measure progression or severity of disease, which may link health care utilisation to survival in the pathway of change, and this is a limitation. In Ghana, home visits by volunteer CHWs focusing on health education, but who also tested febrile children for malaria and treated childhood diarrhoea with ORS, had no effect on the prevalence of these illnesses (primary outcomes) or case detection/management, compared to no volunteer CHWs [36]. Although our trial also did not find expected reductions in the prevalence of these illnesses, we did find that recommended case management of iCCM illnesses doubled during our intervention of paid, professional CHWs, compared to baseline.

With its randomised design, large number of clusters, and rigorous, baseline, and repeated outcome measurement, this trial addressed common risks of bias found in studies in this domain [24]. Contamination between arms is an important concern and could have occurred because CHWs did not always adhere to their workflow protocol; co-interventions may have triggered mechanistic pathways of proactive home visits, such as supervisor house calls without the CHW or community mobilisation by village chiefs; or study participants could have migrated between clusters. The armed conflict that emerged led to devastating death and displacement, contributing to our loss to follow-up, but all clusters and participants contributed data to the analysis. We also had missing treatment data for some sick children at 24 months, which is an important limitation, but our complete-case analysis results were robust to multiple imputation.

CONCLUSIONS

This analysis showed that proactive CHW service delivery can improve the timeliness of children's curative treatment within the first year of implementing a redesigned CHW-led health system, and may increase sick children's health care utilisation relative to a fixed CHW approach. In the context of user fee removal, professional CHWs, and upgraded primary care clinics, proactive CHW home visits yielded modest improvements in access to child and maternal health care. While policy-makers, public health practitioners, and clinicians may consider proactive home visits to be a low-cost intervention for optimising CHW programmes, the UHC and equity impact they seek will be primarily driven by health system enablers, such as user fee removal, professional CHWs, and reinforced primary care clinics.

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PAPERS

Chapter 6   Process evaluation

Overview

This is the final research paper that reports the results of the process evaluation that addresses the third objective of the thesis. This process evaluation brings together research methods from different traditions to create an in-depth understanding of ProCCM trial results between and across trial arms.

At the time this thesis was finalised, this paper had been revised and resubmitted (twice) and recommended for publication by peer reviewer(s) at Health Policy and Planning. The paper is presented here in the format in which it was resubmitted. Supplementary figures referenced in this paper are provided in Appendix F of this thesis, along with an author reflexivity statement for the process evaluation research.

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed <u>for each</u> research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1605048	Title	Ms
First Name(s)	Caroline		
Surname/Family Name	Whidden		
Thesis Title	Evaluation of proactive community case management to accelerate access to care and reduce under-five mortality in Mali: a cluster randomised trial and process evaluation		
Primary Supervisor	Daniel Chandramohan		

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?			
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	Choose an item.	Was the work subject to academic peer review?	Choose an item.

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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	Health Policy and Planning
Please list the paper's authors in the intended authorship order:	Caroline Whidden, Amadou Beydi Cissé, Faith Cole, Saibou Doumbia, Abdoulaye Guindo, Youssouf Karembé, Emily Treleaven, Jenny Liu, Oumar Tolo, Lamine Guindo, Bréhima Togola, Calvin Chiu, Aly Tembely, Youssouf

	Keita, Brian Greenwood, Daniel Chandramohan, Ari Johnson, Kassoum Kayentao, Jayne Webster
Stage of publication	**Undergoing revision**

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 designed the study and wrote the protocol, with input from my advisor Jayne Webster, supervisors, and trial team. I developed and piloted the tools (survey, guides), trained the interviewers, and supervised data collection. I coded qualitative interviews along with my co-coder (Faith Cole), conducted qualitative and mixed method analyses, and wrote the manuscript.

SECTION E

Student Signature	Caroline Whidden
Date	12 Dec 2023

Supervisor Signature	Daniel Chandramohan
Date	12 Dec 2023

1 **Title**

2 Process evaluation of the proactive community case management intervention to accelerate

3 access to healthcare in Mali: a mixed methods evaluation using realist approaches within a

4 cluster randomized trial

5

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19 **Abbreviated title**

20 ProCCM process evaluation

21

22 **Keywords**

2

Process evaluation, Health services research, Health systems evaluation, Primary health care, Community health workers, Realist evaluation, Cluster randomized trials

Key messages

- The WHO recommends health policy and system support to optimise CHW programmes, but evidence gaps persist to recommend specific interventions, including how to deliver CHW services, the role of context, and implications of implementing multi-component CHW interventions.

- This study brings together different research methodologies in new ways to enhance a process evaluation and accommodate the complexity inherent in community health systems interventions.

- Within a cluster randomized trial, we demonstrate how proactive CHW home visits accelerated maternal and child healthcare utilization via mechanisms that were also activated by health system support co-interventions in both arms of the trial, which had changed the context within which the home visit intervention was implemented.

- By addressing multiple structural barriers to care, user fee removal, professional CHWs, and upgraded primary care clinics in both trial arms interacted in complex ways with providers' and patients' agency to achieve rapid care and child survival across arms over three years, despite the onset of armed conflict.

Abstract

The Proactive Community Case Management (ProCCM) trial in Mali reinforced the health system across both arms with user fee removal, professional Community Health Workers (CHWs), and upgraded primary health centres (PHCs)—and randomized village-clusters to receive proactive home visits by CHWs (intervention) or fixed site-based services by passive CHWs (control). Across both arms, sick children's 24-hour treatment and pregnant women's four or more antenatal visits doubled, and under-five mortality halved, over three years compared to baseline. In the intervention arm, proactive CHW home visits had modest effects on children's curative and women's antenatal care utilization, but no effect on under-five mortality, compared to the control arm. We aimed to explain these results by examining implementation, mechanisms, and context in both arms. We conducted a process evaluation with a mixed method convergent design that included 79 in-depth interviews with providers and participants over two time-points, surveys with 195 providers, and secondary analyses of clinical data. We embedded realist approaches in novel ways to test, refine, and consolidate theories about how ProCCM worked, generating three context-intervention-actor-mechanism-outcome nodes that unfolded in a cascade. First, removing user fees and deploying professional CHWs in every cluster enabled participants to seek health sector care promptly and created a context of facilitated access. Second, health systems support to all CHWs and PHCs enabled equitable, respectful, quality healthcare, which motivated increased, rapid utilization. Third, proactive CHW home visits facilitated CHWs and participants to deliver and seek care, and build relationships, trust, and expectations, but these mechanisms were also activated in both arms. Addressing multiple structural barriers to care, user fee removal, professional CHWs, and upgraded clinics interacted with providers' and patients' agency to achieve rapid care and child survival in both arms.

1   Proactive home visits expedited or compounded mechanisms that were activated and changed the

2   context across arms.

3

1 Introduction

2 Governments around the world are scaling up community health worker (CHW) programmes to

3 improve service coverage and health outcomes (Hodgins et al. 2021). Further research is needed

4 to understand how CHWs can be integrated into, and supported by, health systems and

5 communities (World Health Organization 2018). Specifically, research is needed on how to

6 organize CHW workflows and approaches to delivering CHW services that optimize impact

7 (World Health Organization 2018).

8

9 Proactive Community Case Management (ProCCM) is a multi-component intervention based on

10 formative research that identified financial, health system, and social barriers to care in periurban

11 Mali (Johnson et al. 2012). ProCCM includes (Johnson et al. 2018):

12   1) Proactive home visits: CHWs conduct routine door-to-door home visits, identifying

13   prospective patients and proactively offering promotive, preventive, and curative care at

14   patients' doorsteps.

15   2) Professional CHW care: CHWs are salaried, trained, and supervised to provide

16   comprehensive primary healthcare in communities, including reproductive, maternal, and

17   integrated Community Case Management services (Young et al. 2012).

18   3) Reinforced primary care clinics: public sector primary health centres (PHCs), to which

19   CHWs refer cases outside their scope, receive improvements in infrastructure, equipment,

20   supplies, recruitment, and training.

21   4) User fee removal: all fees are removed at all points of care, including ambulatory

22   evacuation and care at secondary or tertiary referral hospitals.

23

1   We conducted the ProCCM trial (Figure S1) in Bankass, Mali from February 2017 to April 2020.

2   This cluster randomized trial had two arms, which both received ProCCM components two to

3   four listed above. In the intervention arm only, village-clusters received proactive CHW home

4   visits (two hours per day, six days per week). In the control arm, village-clusters received

5   ProCCM without component one listed above, where CHWs provided care exclusively at a

6   community health site (four hours per day, six days per week). We designed the trial to isolate a

7   single component of ProCCM, proactive home visits by CHWs, and assess its effectiveness to

8   reduce under-five mortality (primary endpoint) and increase child, maternal, and reproductive

9   healthcare utilization (secondary endpoints) compared to a fixed site-based approach to CHW

10   service delivery (Whidden et al. 2019). We also assessed trial outcomes across both arms over

11   time, comparing the three-year implementation period to the baseline period.

12

13   Between trial arms, we found no difference in the incidence rate of under-five mortality (Liu et

14   al. 2023). After 12 months, sick children had 22% higher odds of prompt (24-hour) treatment

15   from the health sector in intervention compared to control clusters (95% Confidence Intervals

16   (CIs): 1.06, 1.41), but no difference at 24 or 36 months (Whidden et al. 2023). Over all three

17   years, we found some evidence that home visits increased children's health sector consultation

18   (Odds Ratio=1.12; 95% CIs: 0.99, 1.26). We found no difference between arms in institutional

19   delivery, although pregnant women were 11% more likely to initiate antenatal care (ANC) in the

20   first trimester (95% CIs: 1.02, 1.19), and 25% more likely to receive four or more ANC visits

21   (95% CIs: 1.08, 1.43) in intervention compared to control clusters (Kayentao et al. 2023).

22

1 Across trial arms, we found marked improvements in child survival and healthcare utilization

2 compared to the baseline period, despite the escalation of armed conflict. Under-five mortality

3 reduced by more than 60%, from 148.4 to 55.1 deaths per 1000 live births (Liu et al. 2023), and

4 sick children's prompt treatment more than doubled (Whidden et al. 2023). Any ANC increased

5 by 83% (95% CIs: 1.78, 1.86), first trimester ANC by 15% (95% CIs: 1.06, 1.25), four or more

6 ANC visits by 2.59 times (95% CIs: 2.28, 2.91), and institutional delivery by 54% (95% CIs:

7 1.41, 1.66), compared to baseline (Kayentao et al. 2023).

8

9 We embedded a process evaluation to explain the results of the trial of the home visit

10 intervention and to determine whether and how ProCCM as a whole could be effective in a rural

11 and remote Malian context. Guided by the process evaluation framework of the United

12 Kingdom's Medical Research Council (Moore et al. 2014) and an adaptation for cluster trials

13 (Grant et al. 2013), the ProCCM process evaluation thus examined implementation, mechanisms,

14 and context in both arms of the ProCCM trial. This is the process evaluation of a health system

15 intervention (ProCCM) in the context of a trial that quantified the impact of the service delivery

16 component (home visits) of that system.

17

18

19 **Methods**

20 **Study design**

21 We conducted a mixed method process evaluation with a convergent design, in which we

22 collected and analysed quantitative and qualitative data separately, then compared and

23 interpreted the results together (Creswell and Plano Clark 2018). Data sources included a close-

1   ended survey with providers (CHWs, CHW supervisors, and PHC staff), two rounds of

2   qualitative in-depth interviews (IDIs) with trial providers and participants (community

3   members), and clinical data collected by CHWs and PHCs.

4

5   We embedded realist approaches within this process evaluation conducted alongside a cluster

6   randomized trial (Bonell et al. 2012), because these methods have been developed precisely to

7   scrutinize how, why, for whom, and in what contexts complex interventions work (Pawson and

8   Tilley 1997). At different stages in the evaluation, we used both Theory of Change (ToC) and

9   Realistic Evaluation approaches (Blamey and Mackenzie 2007). We started with a ToC logic

10   model depicting an implementation theory that linked ProCCM's activities to intended outcomes,

11   which we workshopped with programme designers and managers. We then used the ToC to map

12   what mixed method data to assemble, and complimented it with realist approaches in data

13   collection, analysis, integration, and interpretation. This allowed us to iteratively test, refine, and

14   consolidate programme theories that linked ProCCM's causal mechanisms and context to

15   outcomes, which we report as context-intervention-actor-mechanism-outcome (CIAMO)

16   configurations (Hamon et al. 2020).

17

18   **Study site**

19   The study was conducted in seven contiguous, rural health catchment areas home to

20   approximately 100,000 people, each serviced by a public sector PHC, in the Bankass district in

21   central Mali. PHCs are managed by Community Health Associations (ASACO), elected

22   committees of local community members, and linked to the district referral hospital outside the

23   study area. At baseline, 17 CHWs (*agents de santé communautaires*) stationed at fixed sites

1   serviced some villages greater than five kilometres from a PHC and worked with community

2   health volunteers (*relais communautaires*) who engaged in health education, promotion, and

3   mass distribution campaigns. Prior to ProCCM, CHWs and PHCs charged user fees to care-

4   seeking patients. Healthcare utilisation and under-five mortality were worse in this setting at

5   baseline than national and regional averages (Treleaven et al. 2021, Whidden et al. 2021,

6   Boettiger et al. 2021).

7

8   Approximately one year into the ProCCM trial, armed conflict spread and intensified in central

9   Mali (Human Rights Watch 2020), affecting the lives of trial providers and participants.

10   Minority communities enrolled in the trial (four entire clusters and ten partial clusters) were

11   destroyed or displaced. Starting in December 2018, we adapted the programme in nine of the 137

12   clusters to mitigate the security risks in accessing or delivering services, by deploying a mobile

13   PHC clinic and/or relocating CHWs who travelled into their clusters.

14

15   **Data collection**

16   *Providers' survey*

17   We developed a short, structured questionnaire that covered health worker characteristics. We

18   administered the survey during the trial period (April, May 2019) to all CHWs (N=168) and

19   dedicated CHW supervisors (N=10); we added PHC workers (N=20), including technical

20   directors, maternity ward providers, and pharmacists, after the trial period (November 2020). We

21   administered the survey at a place of work in French or Bambara, depending on the respondent's

22   choice.

23

1   *In-depth interviews*

2   We conducted a total of 79 IDIs over two time-points, at a midline point during the trial (July

3   2019) and at an endline point after the trial (August 2020), with different respondents to explore

4   changes over time and glean and refine theories about how ProCCM worked (Manzano 2016).

5   At each of the two qualitative data collection rounds, we selected a purposive sample of CHWs

6   (N=12), CHW supervisors (N=5), PHC providers (N=4) and trial participants (N=15). Within

7   each respondent type, we sampled to ensure variability in gender, geography, and trial arm

8   (CHWs) or role (in the PHC, community, or household). Respondent availability, insecurity, and

9   road conditions limited access to some targets; thus, we added seven interviews in January 2021

10   with CHWs (N=2) and female participants (N=5), all from geographically remote clusters.

11

12   Prior to each qualitative data collection round, we developed a semi-structured qualitative

13   interview guide for each respondent type that we piloted outside the study area. Midline

14   interview guides asked respondents to share experiences and perspectives about the programme

15   and its outcomes, mechanisms, and context. Endline interview guides incorporated realist

16   interviewing techniques, where tentative theories about how ProCCM worked were presented to

17   respondents, eliciting reactions and stories to refine programme theories (Manzano 2016). Two

18   Malian, male anthropologists who were not from the study area or part of the trial or

19   implementation teams conducted IDIs in French or Bambara or, if this was not possible, an

20   interpreter (also not from the trial area or team) provided translation in real time via a local

21   language. Interviews lasted between 45 and 120 minutes; longer interviews tended to be those

22   requiring translation or with supervisor respondents. All interviews were audio-recorded and

23   transcribed in French.

1

2   *Clinical data*

3   PHCs collected patient data in paper registers, which were aggregated monthly and entered into

4   the District Health Information Software II (DHIS2). We extracted PHC-month-level count data

5   on facility service utilization approximately one year before and three years during the trial.

6   CHWs collected patient data during routine encounters, including proactive home visits, on a

7   mobile phone application (Community Health Toolkit). We extracted de-identified encounter-

8   level data on CHW service utilization in both trial arms.

9

10 **Analysis**

11 We coded qualitative data using a hybrid deductive and inductive approach to thematic analysis.

12 We developed an initial hierarchical coding frame based on the evaluation's aims and

13 frameworks, which we revised and supplemented based on themes that emerged in the data.

14 Three investigators independently coded the same five midline and endline interviews. Two

15 investigators divided the remaining transcripts equally, coding all interviews using NVivo 12

16 (QSR International 2017). Coders maintained personal reflexive journals and met weekly to

17 ensure intra and intercoder consistency, iteratively update the coding frame, and share reactions

18 to data excerpts or patterns in the dataset. In addition to interview summaries, coders wrote

19 analytic memos to capture emerging ideas or higher level thinking while coding (Miles,

20 Huberman and Saldaña 2013).

21

22 Once the midline dataset was coded, we consolidated analytic memos into propositions or initial

23 programme theories. We iteratively tested and refined our theories using realist retroduction that

1   moves back and forth between inductive and deductive logic (The RAMESES II Project 2017,

2   Gilmore et al. 2019), including discussions with programme managers and researchers, realist

3   interviews with providers and trial participants, and interrogating quantitative data. We

4   descriptively analysed provider survey, CHW application, and DHIS2 data using Stata 15

5   (StataCorp 2017), Stata 17 (StataCorp 2021), and Excel (Microsoft Corporation 2021),

6   respectively.

7

8   We compared mixed methods evidence against these emerging theories to see whether it

9   reaffirmed, reshaped, or contradicted our understanding. We generated three CIAMO nodes that

10   each include multiple contextual factors (C), intervention components (I), actors (A),

11   mechanisms (M), and/or outcomes (O) that act inter-dependently, reflecting the complex analytic

12   reasoning that people engage in when they interact with health system interventions. These nodes

13   relate to each other in a cascade (Webster et al. 2021), as each one triggered mechanisms and/or

14   led to outcomes that changed the context within which the next node operated. The first two

15   nodes encompass CIAMOs that were present in both arms of the trial to explicate how and why

16   changes occurred in both arms relative to baseline. The third node contains CIAMOs specific to

17   proactive CHW home visits to explicate the effects and null effects in the intervention arm

18   relative to the control, in the context engendered by the first two CIAMO nodes.

19

20

21   **Results**

22   Providers had a median age of 26 years (Table 1). More than half (58%) of CHWs were female,

23   and almost all were either from the village (44%), district (29%), or region (7%) within which

1 they were deployed. Three supervisors (30%) and 20 CHWs (12%) had previous work

2 experience or training in health. CHW characteristics were similar between arms.

3

4 **CIAMO node 1: PHC and CHW care available without fees enabled care-seeking without**

5 **delay**

6 In the prevailing health system context (user fees, distance to PHC, insecurity, poverty, and

7 gender inequality or gendered social norms (C1)), removing user fees and deploying salaried

8 CHWs linked to the formal health system (I) immediately led to more universal, frequent, and

9 rapid public sector care-seeking (O) by expanding the healthcare options readily available to

10 participants and empowering them, especially women (A), in their ability to make strategic

11 choices and act on their healthcare needs and desires (M) (Table 2). This CIAMO node was

12 activated in both trial arms, fundamentally changing the context in which healthcare was

13 delivered and received (C2).

14

15 Previously, due to user fees and distance, participants recalled having 'no choice' other than to

16 wait to seek care from the public health system when faced with illness. They would first see if

17 symptoms resolved on their own, '*se débrouiller*' (manage) with traditional medicines, and/or

18 mobilize sufficient resources to reach and receive PHC care. A female control arm participant

19 contextualized people's care-seeking 'preferences' prior to the programme: 'people had

20 difficulty paying for care, which is why they preferred to heal the sick with traditional medicines,

21 without any guarantee they would improve, than to travel kilometres for care they could not

22 afford' (#41-endline). In the first month of implementation, CHWs recorded over 10,000 sick

23 patient diagnostic assessments, and PHCs registered over four times as many initial curative

consultations with sick patients compared to the previous month (Figure 1). Overall, new

curative consultations with public sector providers increased by 8.8 times, comparing the trial

period to the 14 months prior (Figure 1). Participants reported that care had become 'easier' to

access because there were no fees and CHW services were available close to or at home,

enabling participants to choose care from within the public health system as a first recourse. A

village chief in an intervention cluster explained: 'nowadays, we have CHWs in the villages and

dogotorow [providers] in the PHCs and all the care is free, so people no longer stay a long time

at home with their illness' (#19-endline).

Removing user fees and deploying CHWs in every cluster enabled some women to take and act

on decisions pertaining to their and their children's health more autonomously and quickly.

Whereas many women previously asked male heads of household for the means to reach and pay

for health sector care, respondents reported that women could now seek care on their own,

simply 'inform', or request only 'accompaniment' and/or transport. Female participants from

intervention and control clusters, respectively, explained: 'now, even if your husband is not

there, you have the possibility to go to the health centre because it's free. Plus, we benefit from

certain services at home from our CHW' (#27-endline). 'If the husband is nearby, it would be

good to inform him, this is normal. If not, the ideal is to go without informing him because [...]

some diseases require a quick intervention' (#38-endline). Another participant described how no

fees and a (fixed) CHW reduced treatment delays:

> *Before, when you got sick, you would tell your husband. He would respond clearly that*
> *there is no money to treat you. You could stay cloistered in your room during two, three*
> *days, even a week. Eventually, you would go to your parents' house to get care. It was*
> *the same for the children, it was the mother who suffered alongside her child. But all*
> *these are bad memories for us. Now, once you get sick, you take a day to observe your*

1   *condition. If it doesn't improve, the next day you go to* [CHW] *to get care or a referral*

2   *form* (#19-midline).

3

4 Women's care-seeking autonomy depended on household relationships and structures, gendered

5 power dynamics, distance to PHC, and insecurity. Critically, in areas and moments of heightened

6 insecurity, temporary laws prohibited motorcycles and the PHCs' moto-ambulances would not

7 service villages after dark. These restrictions inhibited access to PHC services in important ways,

8 including rapid referral to obstetric care. The chief of a remote village explained: 'With this

9 insecurity, at night people are afraid to go [to the health centre]. It's especially the women that

10 are affected. At night the motos can't leave and if we call the ambulance, it also doesn't come.

11 To go by donkey cart is also difficult. […] At that moment when the situation was *chaud* [hot,

12 meaning intense], people didn't leave, so we couldn't have the health we wanted' (#16-midline).

13

14 Removing ANC fees (less than USD$2) doubled women's first ANC visits at PHCs in the first

15 month of implementation (Figure S2). Over the trial period, first ANC visits was 23% higher on

16 average compared to the 14 months prior (p<0.001), when providers recalled being unable to

17 convince many women to attend. They would conduct village outreach campaigns and 'women

18 would run and hide because money had to be taken' (midwife, #35-endline). A male ASACO

19 member and former *relais* recalled 'we used to sensitize pregnant women to come to the centre

20 for prenatal follow up, but they told us their husbands didn't have the money. […] Now if a

21 woman gets pregnant, she gets up of her own accord to come and see us' (#18-endline).

22

23 According to providers and participants, user fee removal also had direct economic and social

24 impacts. Respondents reported less 'conflict' or '*mankan*' (noise) and more 'cohesion' or

25 '*entente*' (understanding) between couples and within families because they were no longer

confronted with difficult decisions about healthcare expenses and could allocate more resources

to feeding the family or supporting children. As a male control arm participant explained:

> *The standard of living has increased in the community. We are farmers, after the harvest*
> *we used to put the grain at the women's disposal and that was it. In case of illness, we*
> *had no money to care for our wives and our children. This naturally created small*
> *conflicts within the couple. But all these problems are over […]* *Now, heads of families*
> *have no more healthcare worries. The children are well and the women are also able to*
> *do their small business activities* (#17-midline).

CIAMO node 2: Systems support enabled respectful, quality PHC and CHW care that

motivated utilization

In the context of facilitated access and increased, rapid utilization (C2), upgraded PHC and

professional CHW support in both trial arms (I) motivated more universal and rapid healthcare

utilization and engendered new care-seeking norms (O) as providers and patients (A) built

relationships, trust, expectations, and social networks (M) through a mutually acceptable, quality

experience delivering and receiving care (C3) (Table 2).

When participants sought and reached public sector healthcare, they experienced an intake

reception that they perceived as 'welcoming', 'organized', and equitable, which 'prevents

frustration between people, discrimination, and encourages us to seek care' (female control arm

participant, #30-endline). This included having a comfortable place to wait, being consulted in

order of arrival or urgency, and receiving treatment or referral quickly and at no cost. Patients

used to be seen based on who could pay, and thus, the poor used to experience delays or were

denied care once they reached the clinic. 'Nothing is more frustrating than seeing someone, who

came to find you at the health centre, access care before you. If this happens to me, I will no

longer return to that place unless I have no other choice' (#19-endline). Now, 'it is the [referral]

forms that talk. There is no need to say 'I have money' or 'I am poor'. It's by order of arrival'

(head of household, #22-endline). This was so important to participants that providers and

ASACO members recalled having to explain initially why emergency cases jumped ahead of the

queue, a practice that then became widely accepted. 'Today, the most urgent cases are seen first.

This does not affect human dignity, it has nothing to do with disrespect. But before, when you

had no means, there was no respect, no dignity on human life' (female *relais, #29-endline*).

Providers and participants reported 'respect', compassion, and patience in their interactions with

each other, which was enabled, according to providers themselves and ASACO members, by

health system inputs, namely: financing (e.g., reliable salaries, user fee removal), infrastructure

(e.g., reception), human resources (e.g., recruitment), equipment (e.g., ambulance), and stocks

and supplies (e.g., reliable drugs). Even with five times more curative visits to PHCs (Figure 1),

the programme offered the resources providers needed to feel supported, capable, and proud in

their ability to provide care and be accountable to their patients. An auxiliary midwife (*matrone*)

explained:

> *Before, our health centres were not well equipped. This caused a lot of problems for us.*
> *Often, faced with certain situations, you would ask yourself how to manage.* […] *When*
> *you meet the patient she will say that you are not welcoming. But she doesn't know all the*
> *problems you are going through. You are there wondering how to do your job, but she*
> *doesn't see all that.* [...] *Now that the* [healthcare] *workers are everywhere and we have*
> *equipment, our comportment has also changed. We are more welcoming now that we*
> *have everything we need to do our job* (#30-midline).

In this enabling environment, providers emphasized the importance of '*l'accueil*' (the welcoming

reception). For a PHC deputy technical director, 'a patient well received is a patient half cured. A

good reception incites other patients to come to the health centre' (#34-endline). For a female

fixed CHW, 'when women come, I smile with them, I welcome them well, until we become

intimate friends. This is how I instill confidence between them and me' (#9-midline). A female

participant experienced this: 'the *dogotorow* [providers] receive us well and they respect us.

Everything happens with transparency, in communicating with the patient. Before, […] the

doctor would treat you without telling you what you were suffering from. But now, […] the

doctor takes all his time to explain to you all about your illness' (#36-midline).

Trust in the health system care was instilled over time as participants experienced services to be

effective, as well as respectful, available, and affordable. 'When you manage to cure a person of

their illness, they will trust you' (proactive CHW, #6-endline). 'At the beginning, no one

believed in free care. We mistrusted the medicines that the CHWs proposed. But, as time went

on, we realized that the treatments were not only free but effective. This is how the people

started to adhere […] to the care offered by CHWs' (#19-endline). Through their personal and

shared experiences, participants came to expect respectful, rapid, effective care once reached,

which encouraged care-seeking. 'Everyone knows that if you go hunting today and find game,

you'll go back tomorrow. It's the same thing. When people are well received at the health centre

and the treatments are effective, they will go every time they are sick' explained a CHW

supervisor (#14-endline). They will also encourage others to go, such as this female control arm

participant:

> *I took my sick child to the health centre and they gave me medicine and 'peanut paste'* [Plumpy'Nut]. *Some days later, my child's condition improved significantly. Sometime later, I noticed the same signs in the child of a neighbour. Immediately, I suggested to her to take her child to the health centre to benefit from the same treatment. She took her child, he got the same treatment, and his condition improved* (#38-endline).

From traditional to health sector treatments, from delayed to rapid care-seeking, from home

births to ANC and institutional delivery, were among the most common 'surprising changes'

reported by respondents. Providers and participants explained that women now attended ANC 'in great numbers' (*matrone*, #36-endline) or 'preferred to deliver at the health centre' (female participant, #32-endline) because 'they found their importance in it' (#36-endline), or 'as time went on, they realized the benefits' (#32-endline). Stories about women who attended ANC and saw their baby on the ultrasound, or who did not attend ANC and had a complicated delivery, or who delivered at a PHC and received postnatal and newborn care, 'served as examples' for other pregnant women, orienting them towards the health system.

PHC providers were encouraged by the increased utilization, which in turn provided opportunities to develop their skills and serve their community. 'Before, […] I came to the maternity and patients didn't come, or very little. Plus, our bosses were tapping us on the head telling us the ANC rate was low, while I was crumbling under the weight of the work. But now, women come for consultation, all the numbers are up, and I find this very motivating' (#30-midline). 'I can say that I have 55 namesakes. These are girls that came into my hands or who I helped the parents to deliver […] My husband also has at least ten namesakes because of me!' (#36-endline).

CIAMO node 3: Proactive CHW home visits facilitated service delivery and utilization in an already facilitated context

In an accessible, quality health system context (C3), proactive CHW home visits (I) prompted slightly more and earlier utilization in the intervention arm (O) by enabling participants' and providers' (A) abilities to seek and deliver services, and to build relationships, mutual trust,

1   expectations, and social networks (M), but these mechanisms were already activated in both trial

2   arms (Table 2).

3

4   From September 2017 to March 2020, intervention arm CHWs registered a median of 28,486

5   total home visits per month (205 per CHW per month), and control arm CHWs registered 2690

6   total per month (four per CHW per month) (Figure S3; Figure S4). Among new sick child

7   consultations with CHWs, 76% occurred at the caregiver's home in the intervention arm

8   compared to 4% in the control arm, and the rest at the CHW's site/home (Figure 2).

9

10 With a proactive CHW, participants appreciated that sick patients were 'treated at home without

11 having to travel', which they found to be accommodating, respectful, and confidential. Home

12 visits 'not only save us the trip, but also guarantees medical confidentiality' (#31-endline), and 'I

13 find that the one that comes to you accords you an importance' (#29-endline), reported two

14 female intervention arm participants. Having heard about proactive CHWs in other villages, a

15 male control arm participant liked 'that you don't tire yourself. Plus, when elders are sick, it is

16 difficult to take them to the CHW. If the CHW could come to the house […] not everyone would

17 see your sick patient' (#17-midline). Participants in control clusters did not initially 'accept' the

18 fixed workflow, and supervisors and PHC representatives were called in to defend it. Over time,

19 control participants came to appreciate, and some prefer, the passive workflow because 'at any

20 moment we can find [CHW] at their site to treat certain illnesses that cannot wait' (#37-endline)

21 and expressed concern that 'if the CHW was mobile, some people would surely find them

22 absent' (#41-endline). However, in both arms, participants reported that their CHW was

23 available when needed, by phone or at home. The proactive CHW 'does his rounds morning and

evening. If someone is sick, they call him and he comes immediately' (head of household, #35-midline).

Supervisors and CHWs in both arms believed that proactive CHWs 'had more patients' and 'treated patients faster'. Proactive CHWs 'discovered' sick people during home visits who they believed would have otherwise waited to seek care or not sought care, while fixed CHWs were discouraged that people seemed to not seek care until the condition was more 'serious'. For those with limited mobility, such as the very sick, the elderly, and postpartum mothers and newborns, it could be 'difficult' to seek fixed site care. Those with labour burdens 'might cancel their appointments with me to go to the field or tend to livestock' (fixed CHW, #1-endline). 'Because people have other occupations, they often wait until after work to come to the fixed CHW, and in the meantime the illness gets worse. Whereas proactive CHWs consult them even while they are working at home' (fixed CHW, #12-endline). Many proactive CHWs adapted their home visit hours during the rainy season, so they would find women at home 'pounding millet together' (proactive CHW, #4-midline) rather than out in the fields. Among new sick child consultations recorded by CHWs, two thirds (67%) in the intervention arm occurred the same/next day as symptom onset, compared to one third (36%) in the control arm (Figure S5). Furthermore, 28% in the intervention arm were diagnosed with danger or referral signs, compared to 38% in the control arm (Figure S6). According to supervisors, fixed CHWs were 'perceived as being there only to deliver the referral form' or as gatekeepers to the PHC: 'when sick people go to the fixed CHW, they often ask for the referral form [to the PHC] and not healthcare services for treatment or the medical visit. [...] The fact that proactive CHWs conduct active case finding, it's when the case exceeds their competence that they give the referral form' (#14-endline).

A proactive CHW describes her responsibility as an active agent within the health system:

> *We, the proactive CHWs, cover the village searching and if we find a case, we don't*
> *abandon them. Whereas fixed CHWs are immobile, as long as patients don't come to*
> *them, they don't go to patients.* […] *There are some pregnant women who don't go to the*
> *health centre unless they fall sick. So, it's up to us to go towards them, side by side, so*
> *that they come regularly to do their ANC* (#6-endline).

Home visits enabled proactive CHWs to better ensure patient follow up compared to fixed

CHWs (Figure S7), who 'sensitized in vain that [patients] come for follow up. Tired, we left it

alone' (#10-endline). A male intervention arm participant reported 'when [CHW] starts to treat a

patient, he comes every day to see them until they are completely cured. […] When he starts to

treat a child, he doesn't leave him, deh! He follows him right up until the end of his treatment'

(#15-midline). However, some proactive CHWs reported challenges in finding their target

patient during follow-up home visits.

Home visits helped CHWs build relationships, trust, and embed within communities by inquiring

about people's health, 'going toward' the sick, following up, demonstrating the services on offer,

and counseling to promote health. Proactive CHWs were in 'constant contact' with their

community and knew all the 'worries' and 'secrets' of the village. 'It's easier for a proactive

CHW to gain someone's trust since they communicate together every day, than a fixed CHW

who people see only when they're sick. Even if trust will establish between them, it will be

slower than with proactive CHWs' (female control arm participant, #25-endline). Through more

regular and universal contacts (80% of CHW encounters with women were in the intervention

arm), proactive CHWs could 'encourage' or 'motivate' care-seeking by reinforcing what

participants could expect from the redesigned health system.

1

2

Discussion

4   Central to the ProCCM trial, we hypothesized that CHW home visits would proactively detect

5   sick patients and pregnant women, lead to earlier treatment and ANC initiation, and thereby

6   improve child survival and birth outcomes. Our process evaluation found that, while home visits

7   may have accelerated access to care, ProCCM regardless of CHW workflow dismantled

8   structural barriers to care that transformed the context in which we implemented and evaluated

9   the home visit intervention. Together, user fee removal, professional CHWs, and upgraded PHCs

10   addressed direct costs, indirect costs (transport, time), and quality of healthcare, and interacted in

11   multifaceted ways with people's agency. Co-interventions in both trial arms enabled participants'

12   abilities and motivated their choices to seek care from within the public health system, resulting

13   not only in more utilization but faster utilization, which is crucial for child survival and

14   understudied in health policy and systems research.

15

16   Elimination of fees empowered participants when it came to healthcare, or activated 'the process

17   by which those who have been denied the ability to make strategic life choices acquire such an

18   ability' (Kabeer 1999). With salaried, integrated CHWs in every cluster, public sector healthcare

19   became as affordable and available as traditional or informal care, expanding the options with

20   which participants could strategically engage. We saw large, immediate increases in maternal

21   and children's curative healthcare utilization, as seen in other user fee removal studies (Lagarde

22   and Palmer 2011). In our context, participants' 'capability space' – their choice, ability, and

23   opportunity (Frediani 2010) – to seek affordable, available public sector care was influenced by

24

the conflict, distance to PHC, gendered social norms, and individual relationships. As experts on

their body, their children, their context (Abimbola 2023), participants navigated this space as

'active patients' (Leonard 2014), seeking ProCCM services because they experienced them to be

organized and fair, welcoming and respectful, rapid and effective. Financial, human, and

material resources enabled CHW and PHC providers' ability and self-efficacy to deliver

equitable, respectful, high-quality care, which reinforced trust relationships with patients. Our

findings, remarkable given the nine-fold increase in curative caseload and escalating security

crisis, contribute to evidence that links health systems support, trust, respect, motivation, and

performance of health workers (Okello and Gilson 2015, Munabi-Babigumira et al. 2017),

including CHWs (Glenton et al. 2013, Kok, Dieleman, et al. 2015, Kok, Kane, et al. 2015, Scott

et al. 2018). Participants' perceptions and expectations of the quality of healthcare, rooted in

their experiential learning and social networks, drive child (Colvin et al. 2013, Scott et al. 2014)

and maternal (Freedman and Kruk 2014) utilization in other disadvantaged contexts. We

contribute novel findings about speed to care: via multiple pathways to impact, ProCCM

engendered a context of facilitated access, quality care, and prompt utilization, as participants

sought curative child healthcare faster and preventive maternal healthcare earlier. Across trial

arms, 24-hour treatment among children more than doubled (Whidden et al. 2023) and first

trimester ANC increased by 15% (Kayentao et al. 2023).

Proactive CHW home visits triggered mechanisms that were already activated in both trial arms,

which explains the modest improvements in utilization and no effect on under-five mortality

attributable to home visits. First, doorstep care further reduced distance and opportunity costs to

CHW services, enabling marginalized participants who faced poverty, time constraints, gendered

1   social norms, and/or limited mobility to make/realize healthcare choices. This process evaluation

2   indicated that, in the intervention arm compared to control, more sick children were assessed by

3   CHWs, assessed earlier, had less severe symptoms, and were followed up more. In our trial

4   outcome evaluation, sick children in intervention clusters were more likely to receive healthcare

5   overall compared to control (Whidden et al. 2023), and subgroup analyses suggested that home

6   visits may have improved child access to care most in remote communities and the poorest

7   households (Whidden et al. 2023). CHW home visits have been found in other contexts to have

8   pro-equity effects (McCollum et al. 2016, Schleiff et al. 2017, Blanchard, Prost and Houweling

9   2019). Second, home visits helped CHWs build relationships, trust, and social capital (Kane et

10   al. 2020, Schaaf et al. 2020, Ndambo et al. 2022), and patients learn about quality of healthcare

11   and what they should expect. As these processes take time (Leonard 2014), home visits may

12   have made a difference in curative care utilization at the beginning of the programme, while

13   feedback loops (Marchal et al. 2013) and social networks via participants' own and shared

14   experiences sustained and ultimately overtook its effects. In the trial, children were more likely

15   due to home visits to receive prompt treatment at 12 months but not thereafter (Whidden et al.

16   2023). Home visits may also have more effect via these relational and experiential mechanisms

17   on early preventive or complete follow-up care (Gilmore and Mcauliffe 2013, Yonemoto, Nagai

18   and Mori 2021, Wroe et al. 2021), than time to treatment. The trial found 11% and 25%

19   increases in first trimester ANC and four or more ANC, respectively, in the intervention arm

20   compared to control (Kayentao et al. 2023), and CHW home visits during pregnancy have

21   improved antenatal care attendance in other contexts (Edmond et al. 2018, Katzen et al. 2020).

22

1   Although we quantified home visits conducted by CHWs (Figures S3 and S4), we were unable to

2   measure fidelity to the workflow protocol at the household level: at least two home visits per

3   household per month in the intervention arm and no home visits per household per month in the

4   control arm, continuously throughout the trial. IDIs suggested good adherence to the CHW

5   workflow, but survey responses from the ProCCM trial indicated that only 47% and 78% of

6   child-year observations in intervention and control arms, respectively, met the per protocol

7   definition in the preceding month. The trial's per protocol analyses suggested that, while poor

8   adherence may partially account for the subdued effects on child healthcare utilization between

9   arms (Whidden et al. 2023), they do not explain the null effects of home visits on under-five

10   mortality (Liu et al. 2023). Our forthcoming dose-response analysis aims to generate a reliable

11   denominator between CHW mobile application data and trial survey data and assess the

12   relationship between home visit 'dose' and mortality outcome. Nevertheless, this process

13   evaluation shows how the ProCCM trial's null main effects are due, at least in part, to the co-

14   interventions and overlapping mechanisms across both trial arms. Poor adherence in intervention

15   arms and 'exceptional' services in control arms, which overlap with and dilute the primary

16   interventions being tested, have been found to explain null results of other trials (Padian et al.

17   2010).

18

19   We note that IDIs with participants and providers were overall positive about ProCCM, and we

20   need to conduct further investigation to better understand how or why many children still did not

21   access care or died during the trial. Some respondents could have been inclined to give biased

22   responses out of loyalty to their CHW (such as how frequently their proactive CHW visited their

23   home) or to ensure the programme continued. Furthermore, power imbalances could have come

into play between interviewers and respondents, intimidating some respondents and hindering

collaborative theory refinement. Interviewers used traditional qualitative interview techniques of

building rapport, body language, tone, and active listening to put respondents at ease, and we

only incorporated realist interviewing techniques after asking open ended questions (Gilmore

2019). We also observed that some respondents contradicted initial programme theories that we

put to them, including reactions of female respondents to theories that had to do with gender.

Some of our tentative theories were not understood well by respondents, and we considered this

to be evidence that the theory did not resonate, which helped us refine our overall CIAMOs. We

noted that the use of translators during some interviews could have led to misunderstandings or a

loss of information or nuance, and it would have strengthened our study had we involved

translators directly in the interpretation of data and consolidation of theories (Gilmore 2019).

Finally, although we consider the two rounds of IDIs a strength of this evaluation, we lacked

baseline interviews, which is an important limitation given how central context was in this

evaluation and is in realist evaluations more broadly. However, we were able to capture

important elements of the baseline context by asking questions about changes.

CHW interventions need to be evaluated with frameworks that address complexity inherent in

community health systems. Trialling individual components in isolation, like CHW home visits,

may not reflect real life programme implementation or accommodate multiple components

working together in nonlinear ways (Hargreaves et al. 2019). In this process evaluation, we were

able to explain ProCCM trial results between and across arms, and generate ProCCM programme

theories that link outcomes to contexts and mechanisms, by combining theory of change and

realist approaches and embedding them within a process evaluation framework. We propose a

1   cascade of CIAMO nodes that interact within and between each other to hold the interplay

2   between multiple ProCCM components together, centre the expertise of both providers and

3   participants as actors who interpret and construct health system, and reflect the dynamic,

4   nonlinear processes that are healthcare-seeking decisions. Although the changes in outcomes

5   across trial arms compared to baseline are observational results, this process evaluation

6   contributes to the plausibility that ProCCM led to these improvements, which specific

7   components drove effects, and how. We treated context as dynamic, that interacted with the

8   implementation process, activated mechanisms (or not), and affected outcomes in our trial. Thus,

9   our empirical theories can be used to elaborate midrange theories that can be tested in other

10   contexts to consider the transferability of ProCCM and CHW home visits (Nilsen 2015).

11

12

13   **Conclusion**

14   ProCCM's user fee removal, professional CHWs, and upgraded PHCs in both trial arms

15   accelerated access to healthcare and cut under-five mortality by more than a half via multiple

16   pathways to impact that interacted in complex ways with both structural barriers and people's

17   agency, and reshaped the broader health system and social context. In the intervention arm,

18   proactive CHW home visits prompted increased, rapid child and maternal healthcare utilization

19   via similar mechanisms, thus diminishing expected effects of this singular component. Our

20   findings contribute to research and policy discussions on how to design, implement, and evaluate

21   community health systems that support CHWs, serve the most marginalized, and optimize

22   impact and learning.

23

1 **Abbreviations**

2 ANC Antenatal Care

3 ASACO Community Health Association

4 CI Confidence Interval

5 CIAMO Context-Intervention-Actor-Mechanism-Outcome

6 CHW Community Health Worker

7 DHIS2 District Health Information Software II

8 IDI In-Depth Interview

9 PHC Primary Health Centre

10 ProCCM Proactive Community Case Management

11 ToC Theory of Change

12

1   **Declarations**

2   **Reflexivity statement**

3   Over half of the 19 authors are Malian researchers, including the second and penultimate-senior

4   authors. Five authors are female, including the first, third, and senior authors, but none of the

5   female authors are Malian and this is a critical gap. Six authors are early career researchers (three

6   female and three male) and these authors led data analysis. The authors reflect a range of

7   expertise and contributions to this research. A longer author reflexivity statement is provided as a

8   supplementary file.

9

10   **Authors contributor statement**

11   Conception or design of the work: CW, ABC, FC, SD, AG, YK1, ET, JL, YK2, BG, DC, AJ, KK

12   JW

13   Data collection: AG, YK1, SD

14   Data analysis: CW, FC, LG, BT, CC

15   Data interpretation: CW, ABC, FC, SD, AG, YK1, ET, JL, OT, LG, BT, CC, AT, YK2, BG, DC,

16   AJ, KK, JW

17   Drafting the article: CW

18   Critical revision of the article: CW, ABC, FC, SD, AG, YK1, ET, JL, OT, LG, BT, CC, AT,

19   YK2, BG, DC, AJ, KK, JW

20   Final approval of the version to be submitted: CW, ABC, FC, SD, AG, YK1, ET, JL, OT, LG,

21   BT, CC, AT, YK2, BG, DC, AJ, KK, JW

22

23   **Ethics approval**

1 The process evaluation received ethical approval from the ethics committee at the Université des

2 Sciences, des Techniques et des Technologies of Bamako (Ref: 2018/185/CE/FMPOS) and the

3 Observational/Interventions Research Ethics Committee at the London School of Hygiene &

4 Tropical Medicine (Ref: 15923). All respondents provided written informed consent prior to

5 their participation in the close-ended survey or qualitative interview. The Technical Director at

6 each participating PHC provided written permission for secondary analysis of PHC and CHW

7 clinical data.

8

15

16 **Conflicts of interest**

17 All authors have completed the ICMJE uniform disclosure form at

18 http://www.icmje.org/disclosure-of-interest/ and declare: AJ, CW, ABC, SD, OT, LG, BT, YK2,

19 KK were employed by Muso. JL, ET, FC, AG, YK1, CC received grants from Muso to

20 contribute to the study. Muso designed and implemented ProCCM. AT is employed by the

21 Government of Mali.

22

23 **Data availability statement**

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2 Table 1: Socio-demographic and work-related characteristics of trial providers

| | PHC provider N=20 | Supervisor N=10 | CHW | | Total N=195 |
			Intervention N=82	Control N=83	
	n (%)	n (%)	n (%)	n (%)	n (%)
Age					
Median (IQR)	30 (26.5, 36.5)	32 (28, 36)	25 (23, 28)	26 (24, 28)	26 (24, 29)
Sex					
Male	10 (50)	8 (80)	36 (44)	34 (41)	88 (45)
Female	10 (50)	2 (20)	46 (56)	49 (59)	107 (55)
Education					
Primary (years 1-9)	2 (10)	0 (0)	13 (16)	16 (19)	31 (16)
Secondary (years 10-12)	10 (50)	3 (30)	66 (80)	63 (76)	142 (73)
Higher education	8 (40)	7 (70)	3 (4)	4 (5)	22 (11)
Marital status					
Not married	4 (20)	2 (20)	20 (24)	13 (16)	39 (20)
Polygynous	5 (25)	4 (40)	17 (21)	22 (26)	48 (25)
Monogamous	11 (55)	4 (40)	45 (55)	48 (58)	108 (55)
Household size					
Median (IQR)	4.5 (3, 6.5)	1 (1, 4)	4 (3, 6)	4 (3, 6)	4 (3, 6)
Religion					
Muslim	19 (95)	9 (90)	67 (82)	74 (89)	169 (87)
Christian	1 (5)	1 (10)	15 (18)	9 (11)	26 (13)
Cultural origin					
Dogon	10 (50)	5 (50)	79 (96)	76 (92)	170 (87)
Other	10 (50)	5 (50)	3 (4)	7 (8)	23 (12)
Relocated to catchment area					
Born/before trial	6 (30)	1 (10)	40 (49)	32 (39)	79 (41)
For trial from within district[†]	4 (20)	2 (20)	24 (29)	24 (29)	54 (28)
For trial from within region[†]	2 (10)	2 (20)	4 (5)	8 (10)	16 (8)
For trial from outside region[†]	8 (40)	5 (50)	2 (2)	0 (0)	15 (8)
Missing	0 (0)	0 (0)	12 (15)	19 (23)	31 (16)
Engages in other paid work[‡]	1 (5)	2 (20)	11 (13)	13 (16)	27 (14)
Previous work experience[§] or training in health prior to trial	18 (90)	3 (30)	10 (12)	10 (12)	36 (19)
Current/ongoing stockout[¥]	2 (10)	8 (80)	73 (89)	70 (84)	145 (78)
Mean (min, max) weeklong stockouts[¥,£] since trial launch	1.3 (0, 3)	1.9 (0, 4)	1.2 (0, 3)	1.1 (0, 3)	1.2 (0, 4)
Mean (SD) clinical protocol knowledge score (max 19)	17 (2.1)	NA	16 (1.5)	16 (1.9)	16 (1.8)
Mean (SD) gender norms and attitudes scale[¤] (max 14)	12.4 (1.1)	12.2 (1.4)	12.2 (1.2)	12.2 (1.4)	12.2 (1.3)
Mean (SD) work days per week	6.4 (0.5)	3.0 (1.1)	5.6 (2.1)	5.8 (0.8)	5.6 (1.2)
Mean (SD) work hours per day	8.2 (0.9)	6.3 (1.4)	4.0 (0.7)	4.0 (0.6)	4.6 (1.6)
Mean (SD) times contacted by patients the previous work day	2.0 (2.6)	NA	2.6 (3.8)	2.9 (4.3)	2.7 (3.9)

3   Notes: Characteristics are at the time of the survey (May-Apr 2019 for CHWs and supervisors, Nov 2020 for PHC).

4   [†]From within the Bankass health district, or within or outside the Mopti region.

5   [‡]Two thirds of CHWs who reported other paid work were women and they reported small business activities

6   (*commerce*) or housework; men were involved in *commerce* or herding.

1   §This includes the 17 CHWs at baseline who are all ProCCM CHWs.
2   ¥CHWs reported vitamin A and artesunate suppository stockouts; supervisors reported a vitamin A stockout.
3   £Five out of 14 PHC providers who reported a stockout specified an antimalarial.
4   ¤Higher scores are more egalitarian, source: [52].

1   Table 2: Context-intervention-actor-mechanism-outcome nodes

CIAMO node 1	In the prevailing health system context (user fees, distance to PHC, insecurity, poverty, and gender inequality or gendered social norms (C1)), removing user fees and deploying salaried CHWs linked to the formal health system (I) immediately led to more universal, frequent, and rapid public sector care-seeking (O) by expanding the healthcare options readily available to participants and empowering them, especially women (A), in their ability to make strategic choices and act on their healthcare needs and desires (M).
Context	- Public-sector user fees - Poverty, rural setting - Intensive labour/time-constrained agricultural livelihoods - High absolute poverty and wealth tied up in assets e.g., animals - Donkey cart transportation, wealthier households may have motorcycle - Remote - Median distance to nearest PHC of 6 kilometres (min <1, max >12) - Poor road conditions, some cliffs and rivers - Insecurity - Unsafe to travel, especially after dark - Temporary laws against motorcycle transport - Gender inequality and/or gendered social norms - Women ask male heads of household for money, transport, and permission to seek care for their own and their children's health - Women's labour burden/time poverty, including household chores, caregiving, agriculture, commerce
Interventions	1. User fee removal 2. Salaried CHWs in every cluster, integrated within the formal health system 3. Referral system, including ambulatory service
Mechanisms and Actors	- Participants' ability to choose public-sector care among the care options affordable and available to them - Participants' ability to act quickly on their wants/needs, without having to assemble the means to pay or reach public-sector care - Women's ability to seek care more autonomously - Participants' social networks: other family members' ability to support, encourage, or participate in women's and children's care-seeking
Outcomes	- Facilitated access to public-sector care - Removed direct costs and reduced distance and indirect (transport, time, opportunity) costs - Improved affordability, availability (proximity) and accommodation of public-sector care - Increased public-sector utilization and prompt utilization - More universal, frequent, and faster curative care-seeking from within the health sector - More and earlier maternal care-seeking from within the health sector, including ANC and institutional delivery - Health and wellbeing - Less suffering - Fewer child deaths - Empowerment (ability to make strategic life choices related to health) - Less conflict, more social cohesion - Less poverty, more resources (money, time) to invest elsewhere

CIAMO node 2	In the context of facilitated access and increased, rapid utilization (established by CIAMO node 1) (C2), upgraded PHC and professional CHW support in both trial arms (I) motivated more universal and rapid healthcare utilization and engendered new care-seeking norms (O) as providers and patients (A) built relationships, trust, expectations, and social networks (M) through a mutually acceptable, quality experience delivering and receiving care (C3).
Context	▪ Poverty, rural, remote, insecurity, gendered inequality and/or social norms (C1) ▪ Facilitated access to public-sector care created by CIMAO node 1 (C2)

Interventions	▪ Upgraded PHCs
	   ▪ Financing (user fee removal, reliable HW salaries)
	   ▪ Infrastructure, equipment, and supply chain
	   ▪ Recruitment (including a midwife) and training
	   ▪ Referral system to hospital care
	▪ Professional CHWs
	   ▪ Financing (user fee removal, reliable HW salaries)
	   ▪ Stocks and supply chain
	   ▪ Recruitment, training, and dedicated supervision
	   ▪ Referral system to PHC care

Mechanisms and Actors	▪ Patients felt they were treated equitably at reception and with dignity ▪ Providers' ability to provide care and self-efficacy (feeling they were able to do what they needed to do) ▪ Providers' motivation due to system resources and patients' utilization/gratitude ▪ Mutual respect and relationship building between providers and patients ▪ Participants' trust and expectations in the health system ▪ Participants' social networks circulated motivating examples
Outcomes	▪ Improved acceptability and quality of healthcare ▪ More universal, frequent, and faster curative care-seeking (and treatment adherence) from within the health sector ▪ More and earlier maternal care-seeking from within the health sector, including ANC and institutional delivery ▪ Improved health knowledge, disease prevention, and symptom recognition
CIAMO node 3	In an accessible, quality health system context (established by CIAMO nodes 1 and 2) (C3), proactive CHW home visits (I) prompted slightly more and earlier utilization in the intervention arm (O) by enabling participants' and providers' (A) abilities to seek and deliver services, and to build relationships, mutual trust, expectations, and social networks (M), but these mechanisms were already activated in both trial arms.
Context	▪ Poverty, rural, remote, insecurity, gender inequality and/or gendered social norms, and social values toward the elderly (C1) ▪ Facilitated access to public-sector care created by CIMAO node 1 (C2) ▪ Acceptable, quality public-sector care created by CIAMO node 2 (C3) ▪ Increased, rapid health service utilization created by CIAMO nodes 1 and 2
Interventions	▪ Proactive CHW home visits
Mechanisms and Actors	▪ Perceived opportunity cost and ability to reach public-sector care ▪ Participants felt accommodated and respected when treated at home ▪ CHWs' ability to deliver promotive, preventive, and follow-up services ▪ CHWs' and participants' perceptions of the CHW's role/responsibility ▪ Relationship building and community embeddedness ▪ Participants' trust and expectations in the health system ▪ CHWs ability to more actively participate in social networks

Outcomes	- Improved accommodation and acceptability of healthcare - Trust relationships and embeddedness between CHW and community - Slightly more heath sector care utilization among sick children - Slightly faster curative care-seeking among sick children, especially initially - More and earlier ANC, including community ANC contacts - More complete follow ups after treatment/referral - Improved health knowledge, disease prevention, and symptom recognition

1

2

1   **Figures**

2   Figure 1: Number of PHC and CHW new curative consultations during the 14 months prior to

3   ProCCM launch and the trial period
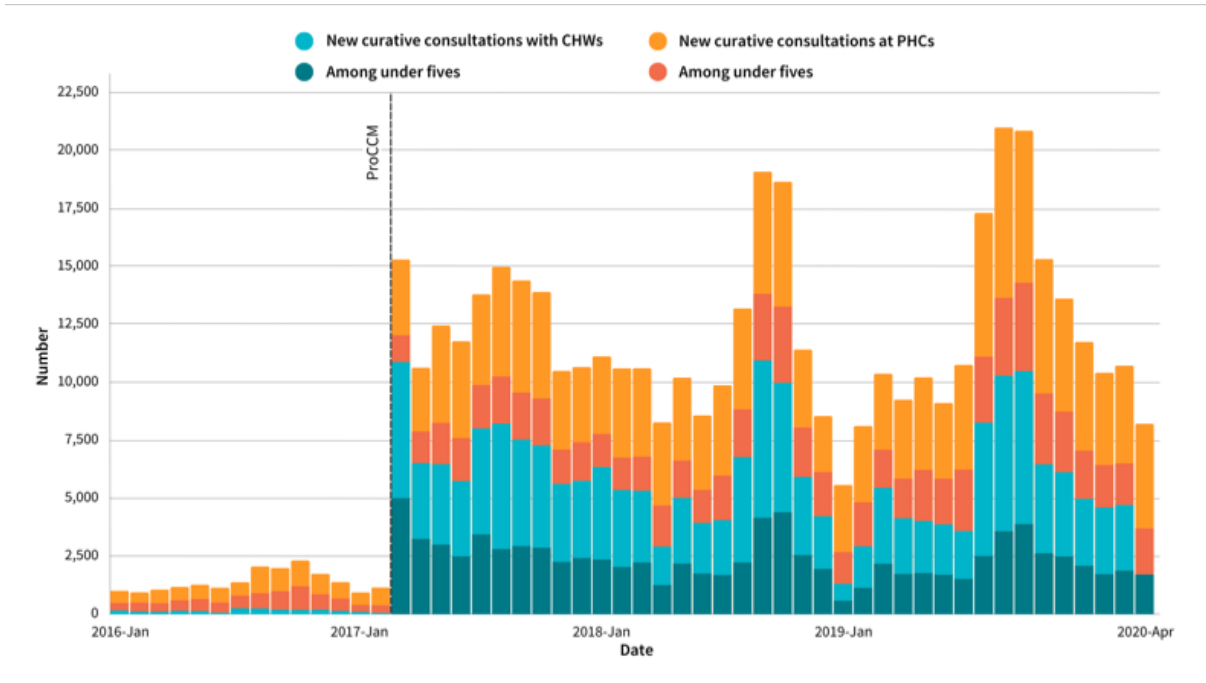
4

5   Notes: New curative consultation refers to sick patient assessments/diagnostic visits with CHWs or PHCs.

6   Orange counts were derived from DHIS2 and blue counts from the CHW application (except for the blue

7   counts prior to ProCCM which came from district health quarterly reports). Consultations with sick under

8   five-year-olds are layered over top of the totals in a darker colour. A patient who was assessed by a CHW

9   and referred to the PHC (and completed that referral) would be included in both orange and blue counts.

10   No other follow-up visits were included at either CHW or PHC level.

11

1   Figure 2: CHWs' new curative consultations/diagnostic assessments with sick children under

2   five by location (child's home or accompanied by caregiver) by arm during the trial period
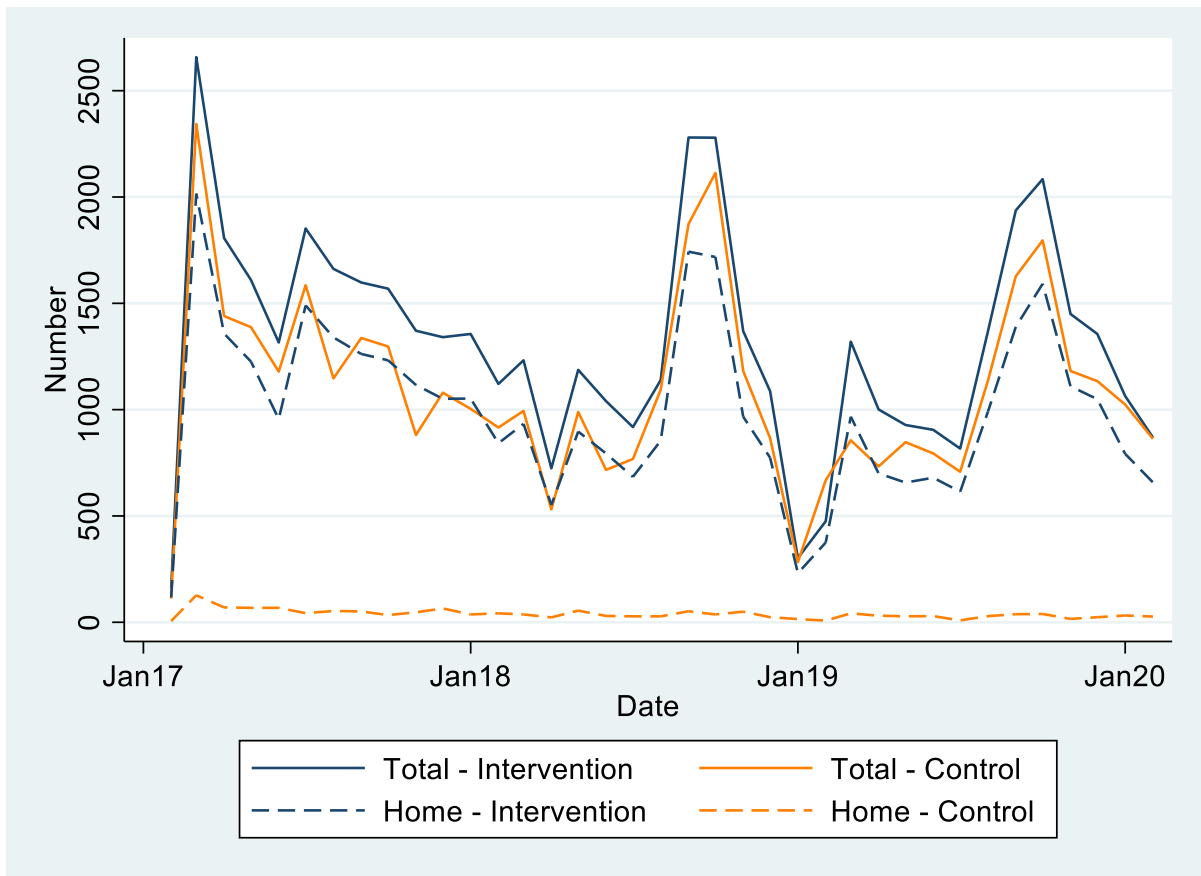
3

4   Source: CHW application. CHWs recorded the location of the sick under-five patient assessment. Home

5   refers to the child's home. Other response options were accompanied by a parent, accompanied by a

6   community member, and other.

Chapter 7   Discussion

Key findings

The studies described in the thesis sought to generate robust evidence about proactive CHW service delivery to inform community health policies and systems in Mali and other LMICs. First, our systematic review identified 14 studies of diverse multi-component CHW interventions that included proactive case-finding home visits of childhood conditions and concluded that CHW home visits may improve treatment coverage among children under five years of age in LMICs (low certainty evidence), but the effects on prompt treatment, prevalence of infectious diseases, and mortality were uncertain (very low certainty evidence) (Chapter 2). Second, we designed the first trial to evaluate the effectiveness of the proactive CHW home visit intervention on these outcomes, in rural, central Mali (Chapter 3), with an embedded process evaluation (Chapter 6).

We found that, in the context of the reinforced community health system across both trial arms (user fee removal, professional CHWs, and upgraded PHCs), proactive CHW home visits did not reduce under-five mortality compared to fixed, village site-based CHW service delivery (Chapter 4). Proactive CHW home visits did increase prompt treatment within the health sector among sick children under five at 12 months, but not at 24 or 36 months after implementation, and increased children's health care utilisation (any care) overall (Chapter 5). These improvements in children's health care utilisation (over all three years) and prompt treatment (at 12 months) were small in absolute terms, and we found no effects on recommended case management outcomes, which could explain the null effect of home visits on under-five mortality. Although poor intervention adherence at the household level contributed to the limited effects on children's health care utilisation, prompt treatment, and recommended case management (Chapter 5), these limited effects are also explained by complex mechanistic pathways and the changing nature of context (Chapter 6). Our findings indicated how proactive CHW home visits increased rapid utilisation via causal mechanisms that were also activated by co-

interventions in both trial arms, which changed the health system context and ultimately drove down mortality across the trial area (Chapter 6).

We observed marked improvements in health care utilisation and child survival over the three-year trial period in both arms of the trial compared to baseline, that well exceeded national and regional estimates (Institut National de la Statistique (INSTAT) *et al.*, 2019). We found that under-five mortality fell over 60% within three years across both trial arms, from 148.4 per 1000 live births to 55.1 per 1000 live births, despite the onset and escalation of armed conflict in the trial area (Chapter 4). During the trial period, over a half of sick children received prompt treatment from the health sector, compared to one in five at baseline (Chapter 5). We found that user fee removal, professional CHWs, and upgraded PHCs in both trial arms worked together to dismantle multiple structural barriers to care and interacted in multifaceted ways with the agency of both providers and patients to reduce treatment delays and save child lives (Chapter 6). Removing user fees and deploying professional CHWs in every cluster created a context of facilitated access to public sector care and enabled trial participants, especially women, the poorest, and most remote, to seek health care promptly. Furthermore, upgrades to PHCs and professional support to CHWs enabled these providers to deliver equitable, respectful, high-quality care, which motivated more, earlier utilisation and changed social norms around health care seeking.

Implications for policy and practice

Since the studies included in this thesis began, a global movement to "institutionalise" or "professionalise" CHWs has gathered momentum, based on historical experience, emerging evidence, and a moral imperative. Framing of the policy and research questions has shifted from how to optimise (individual) CHW performance, to how to support CHWs as an equity issue and to optimise programme impact. The research included in this thesis responds to several calls to address gaps in the evidence base to inform CHW

policy and practice, including effective approaches to support CHWs and optimise CHW programmes, the broader health system requirements, questions of "how, for whom, under what circumstances", and the role of context (Cometto *et al.*, 2018; Rowe *et al.*, 2018; Scott *et al.*, 2018; Agarwal *et al.*, 2019). The joint effect of eliminating user fees, integrating CHWs within the health system, and increasing the resources available at the primary health care level on child survival has important policy implications. In Mali, the government announced sweeping health system reforms in 2019, which included free primary care for pregnant women and children under five and universal coverage of CHWs—changes expected to be rolled out by 2022 or 2023 (Adepoju, 2019). However, the country has since experienced two *coup d'états*, economic sanctions, and an ongoing security and humanitarian crisis, and the implementation of these policies in practice is far behind schedule. In April 2022, the government approved a decree that legally recognised CHWs as professionals within Mali's health system pyramid, paving the way for their salaries to be included in the national budget in the future. Our findings also provide context specific evidence to help understand whether and how these policies will increase the acceptability and utilisation of Mali's public health services, and ultimately reduce the country's high burden of child deaths, including in areas directly affected by the conflict.

Our findings do not recommend proactive CHW home visits to achieve reductions in under-five mortality, but proactive CHW home visits could, nevertheless, be considered to achieve UHC or equity targets where this is the goal. In the outcome and process evaluations, we found that more children overall accessed health care in the intervention arm compared to control. Effect modification analyses and qualitative data suggested that the proactive CHW workflow may have improved health service coverage and utilisation best for members of the most remote communities, the poorest households, the most disempowered women, and the elderly. These findings thus contribute to the evidence that CHW home visits can enhance the overall equity benefits of CHW programmes (McCollum *et al.*, 2016; Schleiff *et al.*, 2017; Blanchard *et al.*, 2019). Furthermore, the evidence of effect of home visits on children's health care utilisation, prompt treatment,

and recommended case management was stronger when the analysis was restricted to the subgroup that had received the intervention per protocol in the preceding month. In the process evaluation, we found that home visits worked via multiple mechanisms, including people's capabilities, which were also activated by user fee removal in both arms and fixed professional CHWs in the control arm. Therefore, while we cannot know what the effects of home visits would have been under "standard of care" conditions, we can speculate that the effects of home visits via these mechanisms may be more pronounced under circumstances where access to "passive" care is not well facilitated.

Proactive CHW home visits may especially help to achieve timely, universal, and equitable coverage and uptake of health promotive, preventive, and other interventions that require repeat contacts with a health provider. These types of interventions were not included in our systematic review because our study focused on home visits to proactively detect and manage cases of childhood illnesses, to accelerate time to treatment onset, and avert deaths among children under five. Nevertheless, in secondary trial endpoint analyses on maternal health care utilisation (outside the scope of this thesis) and in the process evaluation, we found that the proactive CHW workflow facilitated patients' access to follow-up care, including women's antenatal care (ANC) (Kayentao *et al.*, 2023) and sick children's check-up visits, compared to the passive workflow. The WHO recommends eight or more ANC contacts (including with CHWs) and CHW postnatal home visits during the first week after birth (World Health Organization, 2014, 2016). However, many LMICs have encountered serious challenges with implementation and coverage of these interventions (McPherson and Hodgins, 2018; Guenther *et al.*, 2019; Tesfau *et al.*, 2022). Furthermore, prevention and management of infectious diseases, such as malaria chemoprevention, tuberculosis control, and HIV treatment adherence, which require continuity of care, are usually delivered via vertical CHW programmes to a target population. Meanwhile, disability from non-communicable diseases (NCDs), also requiring long term care, is becoming an increasingly large component of the burden of disease globally and in LMICs (Vos *et al.*, 2020). Given these trends, our results suggest that these types of interventions could achieve greater coverage, uptake, and impact if

integrated within a proactive CHW workflow that delivers comprehensive services to all homes. For example, in southern Mali, a cluster randomised trial found that coverage was 74% in villages where CHWs delivered seasonal malaria chemoprevention (SMC) door to door, compared to 60% in villages where CHWs delivered SMC at a fixed point (p=0.009) (Barry *et al.*, 2018). In rural Malawi, an HIV and tuberculosis disease-specific CHW programme was expanded to include comprehensive proactive CHW home visits, and resulted in a 20% decrease in default rates from chronic NCD care and a 30% increase in first trimester ANC attendance, while maintaining already low default rates for HIV patients (Wroe *et al.*, 2021). In all contexts, care needs to be taken to avoid overloading CHWs. This can be achieved by empowering CHWs and communities in strategic decision making about programme priorities, resource allocation, and planning, especially CHWs' task mix and target population size.

Since we observed that home visit implementation and effectiveness on children's service utilisation waned over the three-year study period, a recommendation of CHW home visits to improve access to care should include tools to monitor frequency and reach of home visits. In a randomised controlled trial in Yirimadio, Mali, our team showed that a CHW performance dashboard that was used to provide personalised feedback during dedicated supervision sessions increased the mean number of home visits conducted by proactive CHWs by 40 visits per month (p=0.031) without compromising timeliness or quality of care (on which there was no significant effect) (Whidden *et al.*, 2018). Our team also tested a new user interface of the CHW mobile-phone application, called UHC Mode, to help CHWs track their proactive home visit coverage. In a randomised controlled trial in Yirimadio and a site in Bankass (separate from the ProCCM trial area), we found that households whose CHWs used UHC Mode were more likely to receive at least two home visits per month, compared to households whose CHWs did not use the feature (OR=2.41; p<0.0005) (Yang *et al.*, 2021). These interventions can be integrated into the digital job aid tools of proactive CHWs (UHC Mode) and their dedicated supervisors (CHW Dashboard) to optimise home visit quantity and coverage.

The results presented in this thesis could also recommend proactive home visits as an intervention to enable professional CHWs to integrate within formal health systems *and* embed within community systems (Schneider and Lehmann, 2016), to navigate their "unique intermediary position" between the health sector and communities (Kok *et al.*, 2017b). Both health system integration and community embeddedness are considered foundational to successful CHW programmes, but there is limited evidence on how to achieve both (Scott *et al.*, 2018; Agarwal *et al.*, 2019). We showed that proactive home visits can facilitate or expedite the process of building relationships, trust, expectations, and social networks in communities that encourage people's utilisation of services, particularly during the first year of deploying a new health system or professional CHW programme. This is an important message for the deployment of newly institutionalised CHWs in Mali: proactive home visits could help CHWs to build relationships in their communities and the public's trust in the reformed health system, and ultimately increase prompt utilisation within the first year of implementation of the reforms. However, our results also showed that the potential of proactive CHW home visits to work via these relational or "software" mechanisms was inextricably linked with context, and with health system inputs or "hardware" (Kok *et al.*, 2017a). Our findings indicated that people adhered to health education, counselling messages, or encouragement to seek care over the long term because they had established trusted relationships with their CHW and PHC providers, and trusted expectations of the health system. This trust had been built up through their lived and shared experiences with equitable, respectful, quality care. This is consistent with qualitative findings from a recent systematic review on the equitability of CHW interventions in LMICs, which found that members of disadvantaged groups were less able than their more privileged counterparts to follow CHW advice and take up referrals to other services, due to costs, poor quality, and disrespectful care (Ahmed *et al.*, 2022). Therefore, even where CHWs conduct home visits, one might expect effects on people's uptake of health promotive practices or utilisation of health services via these software mechanisms to improve and be sustained if intervention and health system hardware are also in place.

Regardless of the CHWs' workflow, our findings across trial arms contribute to the growing body of evidence and consensus that "professional" CHWs who are "salaried, skilled, supervised, and supplied" (Community Health Impact Coalition, 2023) can achieve overall improvements in health service utilisation and child survival. A cluster randomised trial in Tanzania found that paid CHWs who conducted home visits that included doorstep iCCM yielded no overall effects on mortality after four years (Kanté *et al.*, 2019). However, subgroup analyses revealed that mortality reduced among post neonates during the first two years of implementation (Hazard Ratio (HR)= 0.85; p=0.008), an effect that then disappeared in the latter two years of implementation due to stockouts of essential CHW supplies (Kanté *et al.*, 2019). An interrupted time series analysis showed that CHWs across 27 districts in four African countries, who were supported in line with WHO guidelines (including ProCCM CHWs in Yirimadio, Mali), maintained coverage and speed of iCCM services throughout the first 15 months of the COVID-19 pandemic, while disruptions to UHC were occurring at a global scale (Ballard *et al.*, 2022). In the studies included in this thesis, professional CHWs improved the accessibility of health sector care and provided services that patients experienced as reliable and effective, which increased utilisation in both trial arms. However, removing user fees and equipping PHCs (including recruiting and paying clinical staff) also contributed to facilitating access and providing services that patients experienced as equitable, respectful, and effective. These three components of ProCCM worked together to double rates of health care utilisation and cut in half the child mortality rate. Our findings caution against looking to professional CHWs as a panacea, much like the misguided expectations that were placed on volunteer CHWs during previous waves of interest. Professional CHWs are as strong as the health system to which they are linked and should not be expected to overcome all structural determinants of health inequities, such as direct and indirect costs, poor quality and disrespectful care at referral clinics (Blanchard *et al.*, 2019; Ahmed *et al.*, 2022).

Our findings demonstrate that CHWs can receive professional health system support and still build trust and embed within communities. Rather than compromising trust and

embeddedness, the integration of CHWs within a resourced health system extended coverage of highly acceptable and quality services and *as a result* fostered sustained trusting relationships between CHWs and their community members. These findings support the idea that, rather than the old dichotomy of "lackey or liberator" (Werner, 1977), CHWs "bridge" the formal health system and communities along a spectrum of health service extender, cultural broker, and social change agent (Schaaf *et al.*, 2020). In our studies, the "community health system" (Schneider and Lehmann, 2016), comprised of and constructed by clinic-based providers, professional CHWs, and the population, achieved "social change" along the lines of new norms around health care utilisation (such as childbirth at PHCs), women's empowerment related to health care seeking, and reduced financial hardship and social conflicts. The Alma Ata ideal of community participation or empowerment does not require volunteerism, and can be achieved by an integrated community health system that overcomes structural barriers and determinants of health inequities, with professional CHWs as "influential actors" within that system (Kane *et al.*, 2021).

Gender shapes CHWs' experiences and interactions at the individual, community, and health system levels in LMICs (Steege *et al.*, 2018)—including in our study setting—but we found that professional support to CHWs may have tempered the role of gender in health care delivery and utilisation in one of the least gender equal countries in the world (*Global Gender Gap Report 2023*, 2022). In our study context, where only 10% of all women had ever attended school (Whidden *et al.*, 2021), the literacy and educational requirements of the CHW and CHW supervisor cadres systematically disadvantaged women in the local recruitment and promotion processes. Over half of all CHWs in our study were women, though men held eight out of the 10 supervisor positions. Both male and female CHWs reported that they were more "acknowledged" and "listened to", with a more active role to play, in their households and communities now with their CHW work. This work included a salary, career progression opportunities (to CHW supervisor), regular training and supervision, supplies, and linkages to referral facilities. According to both CHW and patient respondents, CHWs' embeddedness, relationships, and trust in the

community depended more on the "quality" of how they treated patients (such as with patience, respect, confidentiality, speed, and effectiveness) than on their personal characteristics (such as gender, age, or place of origin). We saw how this quality of care was enabled by the professional and health system support that all CHWs received. Nevertheless, gender, age, and place of origin intersected to shape CHWs' interactions with patients in our study; some CHWs reported that they or their patients experienced "shame" discussing certain topics or delivering certain services across gender and age/generational divides, especially related to sexual and reproductive health (e.g., pregnancy tests, male condom use, women's convert contraceptive use). The proactive workflow may have helped CHWs bridge these differences, especially male CHWs to establish trusting relationships and open communication with women by regularly visiting and chatting with them in their homes. Our study contributes evidence that professional, health system support promotes gender equity and empowerment among CHWs (Steege *et al.*, 2018) and may help to overcome gender barriers to care in LMICs.

A key feature that made the community health system accessible, acceptable, and effective in our context was the free provision of services, from adequately supported CHWs and PHCs. Since user fee debates returned to global and national health agendas in the 2000s (James *et al.*, 2006), evidence has accumulated to confirm that the removal of user fees increases service utilisation (Lagarde and Palmer, 2011; Ridde and Morestin, 2011). However, several studies in sub-Saharan Africa concluded that user fee removal alone is insufficient to improve health where distance and geography, travel and indirect costs (including opportunity costs), poor quality of care, or social barriers persist (James *et al.*, 2006; Ansah *et al.*, 2009; McKinnon *et al.*, 2015; Witter *et al.*, 2016; Zombré *et al.*, 2019). Our intervention of ProCCM addressed all of these structural barriers to care simultaneously, leading to sustained improvements in health care utilisation and child survival. Furthermore, countries that have implemented national user fee removal policies have experienced increases in utilisation but challenges with maintaining quality of care, such as the availability of drugs or the accountability of providers (Ridde and Morestin, 2011). On the contrary, ProCCM providers and patients in our study context reported

improved structural quality, process quality, and accountability because the programme ensured resources that the health workers needed to do their work, including salaries, colleagues, training, supervision, equipment, and supplies. These findings provide evidence as to how free care policies can be designed and implemented to optimise sustainable impact. In particular, free care policies should consider reinforcing the work environment to enable providers' ability, self-efficacy, and motivation to deliver both technical and interpersonal quality of care.

We evaluated context, interventions, and outcomes in ways that enable decision makers to assess the applicability and transferability of ProCCM and proactive home visits to other LMIC settings (Burchett *et al.*, 2011). First, we described contextual factors that facilitated and hindered implementation, mechanisms of effect, and outcomes that would help to make these assessments. However, we also went a step further and developed realist programme theories that link outcomes to their context and mechanisms. This means that our empirical theories can be used to elaborate midrange theories that would be testable in other contexts (Nilsen, 2015). We did this because our data depicted context as something much more active and changing than our initial conception. Decision makers in other settings might opt to implement similar interventions in similar contexts to ProCCM (and assume similar mechanisms of effect), different interventions in different contexts to trigger similar mechanisms of ProCCM (e.g., trust and expectations), or different interventions to create a similar ProCCM context (e.g., facilitated access) via different mechanisms. In this sub-section of the thesis, I hypothesised (above) how one might expect the effects of home visits by CHWs to be different under different circumstances. Second, in terms of interventions, our findings emphasised their acceptability and perceived quality by the study population as drivers of effect. We described what characteristics of the interventions were perceived as acceptable or high quality (such as their accommodation, fairness, respect, speed, etc.). These findings are useful for assessing the potential acceptability of ProCCM and home visits in other settings. Finally, with regard to outcomes, we measured the sustainability of effect on children's service utilisation over three years. Furthermore, ProCCM has been adapted,

implemented, and evaluated in northern Togo. Over five years, under-five mortality fell by 30%, from 51.1 per 1000 live births at baseline in 2015 to 35.8 per 1000 live births in 2020, compared to the estimated 14% decline nationally during the same period (Fiori *et al.*, 2021). Health care utilisation within 24 hours among children with fever increased from 52% at baseline to 65% after one year and to 80% after five years (Fiori *et al.*, 2021). This observational study strengthens the case for the transferability of ProCCM within West Africa, and in contexts where baseline child health care utilisation is not as low, or mortality not as high, as in Bankass.

In Bankass, the implementing NGO and Ministry of Health and Social Development (MSDS) have continued ProCCM beyond the end of this research and converted all fixed clusters to proactive clusters given the acceptability of the home visit intervention and its effectiveness for prenatal care. ProCCM was designed and implemented within the public sector health system so that it could be sustainable and scalable within Mali via government adoption. The Government of Mali has already adopted some elements of ProCCM nationally, in policy if not yet in practice, including free primary maternal and child health care (policy phase), paying CHW salaries (planning phase), expanding coverage of CHWs (deployment phase), and dedicated supervision of CHWs (implementation phase). In the process evaluation, we identified and examined the important role in the pathways of change of the availability of financial, human, and material resources, which are structural factors that can make or break the successful scale-up of public health interventions (Bulthuis *et al.*, 2020). Our trial team is also undertaking a costing evaluation (alongside the impact, outcome, and process evaluations presented in this thesis) that compares the incremental costs between trial arms. We cannot conduct the cost-effectiveness analysis as planned in the trial protocol due to the null effect of home visits on under-five mortality. Nevertheless, our comparative costing analysis will help determine whether proactive CHW home visits should be scaled up to improve UHC. We will also estimate the overall costs of ProCCM as a whole to help make its investment case in the context of limited fiscal space and competing health priorities (Gichaga *et al.*, 2021). Unfortunately, we cannot conduct a cost-effectiveness analysis of

ProCCM across trial arms compared to the baseline standard of care due to limited cost data prior to the trial. These different features of our intervention design, implementation, and evaluation create opportunities for scale-up. However, challenges throughout history of scaling up niche CHW programmes point to the need for sufficient financing, careful planning, and process monitoring and evaluation.

Reflections on the research methodologies

The ProCCM trial was originally designed to address the limitations of the observational study on ProCCM in periurban Yirimadio, and to determine whether ProCCM could also be implemented and effective in a different, rural Malian context. We thus employed the "gold standard" randomised controlled trial (RCT) design, which minimises bias and confounding, to test the effectiveness of an innovative component of the ProCCM programme: proactive case-finding home visits by CHWs. We randomised groups, or clusters, of villages/hamlets (one kilometre or less apart) because the proactive CHW home visit intervention was to be implemented at the community level and there was a need to reduce the risk of contamination between randomised units. In addition to the methodological advantages inherent in the cluster RCT design, our trial had several strengths, including its large size of 137 enrolled clusters, outcome measurement in the entire population, and three-year duration. We powered the trial to be able to measure under-five mortality as the primary outcome, which is rare among iCCM studies in Africa (Christopher *et al.*, 2011; Amouzou *et al.*, 2014; Oliphant *et al.*, 2021). We included a range of health service utilisation and treatment coverage endpoints, as these proximal outcomes are preconditions for achieving a mortality impact (Amouzou *et al.*, 2014) and intrinsically valuable as UHC targets. We included outcomes that assessed timeliness of health service utilisation and treatment, which is also understudied in iCCM research (Diaz *et al.*, 2014; Oliphant *et al.*, 2021) and critical for child survival. We collected data that permitted equity sub-analyses of intervention effects by geography and wealth. Our baseline and three annual follow-up measures enabled the assessment of how intervention

effects varied over time as well as the before-after comparisons across arms. Effects of user fee removal interventions, for example, are rarely studied beyond one year or on health outcomes (Zombré *et al.*, 2019). Finally, much needed data on CHW programme implementation, mechanisms, and context were incorporated with the embedded process evaluation.

The ProCCM process evaluation was added roughly halfway through the trial to expand the scope of the PhD. In developing the protocol for the process evaluation, I met with ProCCM designers, managers, and researchers to develop a theory of change (ToC) in the form of a logic model. Prior to this, the set of theories, conditions, and assumptions (Mills *et al.*, 2008) about how or why proactive CHW home visits were expected to work— above and beyond, or in the context of, the other ProCCM co-interventions—was not explicit. The ToC revealed how the outputs and outcomes that proactive CHW home visits were expected to generate (such as prompt treatment) were also derived, in part, by other ProCCM activities (such as professional CHWs in each cluster). In the end, our study found no effect of home visits on under-five mortality, partly because the intervention activated similar processes and produced similar outputs to the co-interventions in both arms. This study thus demonstrates the importance of developing a clear ToC at the outset when designing complex interventions and their evaluations.

While attempting to use the ToC as the analytic framework in conducting the process evaluation, it became clear that the logic model was not well suited to explaining how or why inputs lead to outputs. The mechanisms of effect that the process evaluation sought to bring to the surface appeared buried in the arrows that linked inputs, activities, outputs, outcomes, and impacts in the logic model. As I tested and refined theories about causal mechanisms of effect, I found that the logic model framework was unable to accommodate the complexity of the pathways, with arrows that looped backward, amplified each other, were bigger or smaller in magnitude/importance, or linked outputs to other outputs rather than to outcomes downstream. I learned about realist evaluation and discovered that their methods could be applied to enhance a process evaluation, because they were developed specifically to address questions of how, why, for whom, to what extent, and under what

circumstances complex interventions work (Pawson and Tilley, 1997). I found realist evaluation's context-intervention-actor-mechanism-outcome (CIAMO) framework to be better suited to rendering explicit the underlying causal processes that generate outcomes. Yet, I still found that CIAMO was limited in its ability to capture the complex analysis that people undertook when making decisions about health care (holding multiple considerations at once), or the dynamic nature of context. I thus designed CIAMO nodes, each with multiple interrelated C's, I's, A's, M's, and O's that related to each other in a cascade, to reflect the changing nature of things. This study demonstrates how realist approaches can be applied in new ways to improve the development and evaluation of CHW programmes and community health system interventions.

Over the course of this thesis work, my conception of the research I was conducting evolved from iCCM intervention research, to CHW service delivery research, to community health systems research. The systematic review and trial design work highlighted the need to consider the design and implementation of the whole CHW programme in order to understand iCCM intervention effectiveness. To make sense of ProCCM trial results and process evaluation data, I realised that I needed to consider all of the building blocks of the health system rather than only the service delivery block (Gilson, 2012). I also had to consider the full range of actors within the health system, who interacted with and shaped ProCCM and the changing context that generated outcomes. These actors were not only implementers of the health system (CHWs, CHW supervisors, PHC providers) but also community members, who were not under the direct "influence" of the intervention (Schneider and Lehmann, 2016). In our trial's context of facilitated access to care, patients and caregivers were also "proactive" and, together with providers, created a new social context of "rapid care" in both trial arms with or without home visits.

In hindsight, it appears the process evaluation—with its mixed methods, critical realist approaches, and comprehensive systems lens—was better suited to deducing which components of ProCCM drove impact than the RCT that isolated and tested a single component. The trial design failed to account for the features that make a complex

intervention like ProCCM "complex": the interconnection and nonlinear interactions between its various components to achieve something greater than the sum of its parts (Hawe *et al.*, 2004; Rifkin, 2018; Hargreaves *et al.*, 2019). In the end, our study showed how multi-component ProCCM was more effective at changing health care utilisation and impacting child mortality than any one of its components. A different study could have randomised clusters to receive complete ProCCM or current standard of care in order to infer causality of ProCCM (rather than proactive CHW home visits), with an embedded process evaluation (like the one we did) to deduce how ProCCM worked. However, because complete ProCCM included interventions at the facility level, this other study would have had to randomise PHC catchment areas rather than village units. It would have had far fewer clusters to randomise, and consequentially, reduced power and ability to detect a mortality differential. In our trial, we did not include a standard of care control group due to ethical concerns about collecting data from participants who would not receive any intervention, and about withholding life-saving interventions like user fee removal and health system strengthening. Cluster randomised trials with stepped wedge or waitlist controls are alternative designs that could relieve some concerns and be used to compare a complex intervention to a randomised, concurrent control group that would later receive the intervention.

In adopting a critical realist perspective, I have engaged in a continuing reflexive process of the ways in which the knowledge I produced is dependent on the theories we used and the questions we asked, and how these methodological choices were influenced by power and positionality. Critical realism assumes a realist ontology and a subjectivist epistemology; in other words, it acknowledges that the world is real (that scientific experiment is possible) and that knowledge production is subjective (that the researcher cannot simply observe the world) (Fryer, 2022). I have reflected on how the research included in this thesis was shaped by our research group's pre-existing notions about how the interventions would work and what evidence was most relevant for the range of stakeholders involved: donors, researchers, implementing NGO, government, and participating communities. Protocols, indicator lists, and data collection tools were end

products of complex social processes (Mosse, 2004). For example, I led a back and forth discussion with seven signatories to negotiate and arrive at a final indicators list of 10 different endpoints, their definitions, and statistical analysis plan related to children's health and health care utilisation (Appendix D).

While pursuing this PhD, I have been a foreign researcher (Gilmore, 2019), and there are limits to what a foreign researcher can perceive relative to a local expert (Abimbola, 2019). I am white, female, early in my career, and from a high-income country (HIC). I have been living in Mali prior to and throughout this research (eight years), embedded within a local research team. I believe this experience has made me a somewhat well "engaged" foreign researcher, who has a (limited) understanding of the research setting and can use this to interpret data and consolidate realist theories in collaboration with local partners (Gilmore, 2019). However, due to escalating armed conflict and security threats, I spent less time at the research sites in rural, central Mali where people have unique history, language, and cultural identity. From my perspective, I cannot fully understand how social norms, power dynamics, and relationships play out in Mali, which makes it difficult to pinpoint context and mechanisms that generate outcomes. Furthermore, my pre-conceived values shaped what I emphasised or de-emphasised in the interpretation of data. For example, because I believe that focusing on people's knowledge and behaviours is a colonial legacy in global health, I tended to focus my analysis on structural and systems changes that are implementable and interact with people's agency, and dismissed claims that rural Malian people were "ignorant" or "lazy". Although I led this process, I iteratively tested theories with local researchers and programme managers, as well as with respondents themselves during the second round of qualitative data collection. Because the second round built reflexivity into the process and solicited the expertise of patients and providers on the theories, it turned out to be much more valuable than originally conceived, which was to capture changes in implementation over time.

While I developed and piloted the data collection tools used in this thesis and trained data collectors, Malian researchers collected both trial and process evaluation data, which could have improved the trustworthiness of data. Trial surveyors were women because the

respondents were women and the survey included potentially sensitive questions about reproductive health. We organised the trial survey teams to match surveyors and communities based on their linguistic and cultural identities, which was especially sensitive in the context of the conflict during the last two survey waves. For the qualitative interviews, the anthropologists were male, PhD-educated, and although they were from the Mopti region and of the predominant cultural origin in the area, they spoke a different language and lived in the capital city. Power imbalances due to these different characteristics between interviewers and respondents could have played out during qualitative interviews, comprising the trustworthiness of the data, especially the data derived using realist techniques. However, the anthropologists were experienced interviewers, and used classic qualitative interview techniques to put respondents at ease and started all interviews with open ended questions. I observed in the data that some respondents, including women, contradicted programme theories that the interviewers proposed to them using realist techniques. The anthropologists were unwilling to hold frequent debriefing sessions with me during data collection, and it could have been related to my age, gender, and academic qualifications relative to theirs. This impeded my ability to engage in the processes of collecting qualitative data, including reflexivity, reorienting lines of questioning, and refining CIAMOs in real time.

Although our research consortium had several systems in place to ensure health and safety, ethical conduct, and scientific quality and integrity, we did not explicitly use the framework of safeguarding in international development research, which encompasses any physical, sexual, or psychological violence, abuse, exploitation, or neglect (Aktar *et al.*, 2020). The local programme and research teams were committed to preventing and addressing different concerns that would fall under a safeguarding definition, including adapting interventions and data collection procedures to ensure the health and safety of trial participants, providers, and researchers in the context of armed conflict (e.g., deploying mobile clinics, hiring a trauma psychologist, relocating CHWs, changing when and where data collectors travelled and lodged). We received clinical oversight from several independent bodies, including ethics committees, a Contract Research

Organisation, and a Data Safety and Monitoring Board. At every trial survey wave, we met with community representatives, trained surveyors in Good Clinical Practice, and obtained informed consent from participants. However, we did not have a team or officer with the explicit mandate of setting, implementing, and monitoring a safeguarding agenda reflective of the concerns of the most marginalised partners in this research. This matters because all global health research interacts with, perpetuates, or subverts extant power relations, such as those between researchers and participants, members of international research consortiums, and development organisations and communities (Aktar *et al.*, 2020). In our study, these power relations were complicated by the fact that (1) trial communities and participants depended on the global health organisation for service provision (and providers and researchers depended on it for work), and (2) the site became an active conflict zone midway through the trial. In this context, and in the context of hierarchical and patriarchal relations in rural Mali, we could have had a more robust system in place to empower and manage the reporting of safeguarding concerns by community members and frontline providers. CHW supervisors conducted home visits without the CHW to solicit patient perspectives, and data collectors asserted the principles of confidentiality and anonymity, but these actors were affiliated with the organisation that provided services free of charge.

Finally, as this thesis was written to obtain a PhD from an HIC institution, it was "written with a foreign pose for a foreign gaze", which is far from the "ideal of local people writing about local issues for a local audience" (Abimbola, 2019). Importantly, the research included in this thesis contributes to the broader work of the ProCCM trial consortium, which includes Malian researchers sharing Malian research findings with Malian audiences. Throughout this collaboration, we engaged in continuing reflexive dialogue and action (Liwanag and Rhule, 2021) to reconcile these different poses and gazes in an effort to contribute to decolonising global health (Abimbola and Pai, 2020; Richardson, 2020; Hirsch, 2021; Olufadewa *et al.*, 2021).

Future research directions

Researchers working on complex problems (like child health) or complex interventions (like CHW service delivery) are confronted with the challenge of having so much information to gather and process, requiring extraordinary resources (Marchal *et al.*, 2013). Given this complexity, I have identified some future directions for research (involving new data or secondary analyses of this study's data sets) that would be of particularly high value in addressing outstanding or emerging questions from this research and gaps in the wider literature.

First, our systematic review could be updated to include new research, such as this trial, and/or to include other population groups, conditions, or outcomes. Including proactive case detection of pregnancy could help to contextualise our trial's results on maternal health care utilisation. Second, we could conduct further analyses of trial data to better understand which children did not receive health sector treatment or died during the implementation period. While we did conduct heterogeneous treatment effect analyses, which assessed effect modification of the effects of home visits by cluster population size, distance to PHC, and household wealth, we could also assess modification of the pre-post effects by these characteristics. This would allow us to determine if the overall improvements in both arms relative to baseline were modified by these equity dimensions. Our baseline analyses showed that, prior to any intervention in the trial area, distance to PHC even within five kilometres was associated with higher under-five mortality (Boettiger *et al.*, 2021), lower health care utilisation among sick children (Treleaven *et al.*, 2021), and lower contraceptive use among women (Whidden *et al.*, 2021). It could be important to see whether this relationship with distance changed after implementation of the co-interventions in both trial arms. We considered conducting social and verbal autopsies to better understand why children died during the trial, including comparing causes of death between the two trial arms. This would help us to know how to prevent future deaths in the implementation area beyond the end of the trial. However, we were unsuccessful in securing funding and the trial team also had limited bandwidth to design,

plan, and implement this new study during a reasonable recall window whilst delivering on the planned analyses for the trial.

The process evaluation covered much terrain and several further analyses could explore certain themes in greater depth, such the impact and process of ProCCM's model of dedicated, 360-degree CHW supervision. While global CHW guidelines recommend supportive supervision, there is insufficient evidence to recommend which supervisory strategies are most effective, how or in what contexts, in combination with what other health system support, and the role of human interactions involved in supervision (Cometto *et al.*, 2018; Kok *et al.*, 2018; Agarwal *et al.*, 2019; Westgate *et al.*, 2021). Our RCT in Yirimadio, Mali that evaluated the CHW performance dashboard also found that the quantity, speed, and quality of care by CHWs improved over the six months of study in both arms, which received individual monthly CHW supervision by dedicated supervisors (Whidden *et al.*, 2018). This model of dedicated CHW supervision was used in the Bankass trial in both arms. A mixed method analysis, that brings together IDI data with CHWs and supervisors and programmatic data collected on CHW and supervisor mobile-phone applications, could help elucidate the effects and processes related to CHW supervision in our trial context.

Conclusion

The addition of proactive case-finding home visits by CHWs to reinforced iCCM did not reduce under-five mortality or the prevalence of common childhood illnesses in rural Mali, and increased the timeliness of treatment only within the first year of the three-year period. Proactive CHW home visits can be recommended to reinforce community embeddedness, improve acceptability and uptake of health system reforms, and increase overall health service coverage and equity, especially of interventions requiring preventive actions or repeat visits. However, proactive CHW service delivery cannot replace health system support that enables providers and patients to work together to

improve the health of their communities. A foundation of user fee removal, professional CHWs, and upgraded PHCs leads to an accessible, acceptable, high-quality health system. In our study, actors within this health system context doubled children's health care utilisation and cut the under-five mortality rate in half during the implementation period, even while faced with an escalating security crisis.

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