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Community Case Management of Malaria and Pneumonia in Children

Exploring use of diagnostics by community health workers in Uganda

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Stockholm 2012

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Printed by Universitetesservise-AB
Nannasvartzväg 4,
SE-17177, Stockholm, Sweden

ISBN 978-91-7457-555-2

ABSTRACT

Background: Malaria and pneumonia are leading causes of under-five mortality in Sub-Saharan Africa. WHO/UNICEF recommend integrated community malaria and pneumonia care in situations where febrile children also have cough and rapid breathing. Presumptive treatment of all fevers as malaria leads to excessive use of anti-malarial drugs and delays the recognition and treatment of non-malaria fevers. Using malaria rapid diagnostic tests (RDTs) and respiratory rate counting could be a potential solution.
Main aim: To assess community acceptability and utilisation, provider competence, and the effectiveness of diagnostic-based integrated community case management of malaria and pneumonia in children in order to inform implementation.
Methods: Four studies (I-IV) were conducted in Iganga district, Uganda with data for Study IV collected at two additional sites in Burkina Faso and Ghana. In Study I, 10 key informant interviews with health workers and community leaders, and 10 focus group discussions with CHWs and caregivers were done. Study II was a prospective case series with 182 child observations. Study III was a cross-sectional study with 423 caregivers of under-fives. Study IV was a cluster randomised controlled trial (cRCT) with 4,216 under-fives. Content analysis was used for qualitative data. Quantitative data was analysed at uni-, bi- and multivariate levels, while analysis of Study IV was by intention to treat.
Results: From the cRCT, the odds of having fever on day 3 was 41% lower in the intervention arm compared to the control arm (OR 0.59, 95% CI 0.38, 0.93; p=0.02). Community acceptability of use of RDTs by CHWs was high (89%; 375/423) (III). Some community members had fears about drawing blood (I), but reports of these were few in Study III (4/423). Most (86%, 365/423) households resided within 1 km of a CHW, compared to 26% (111/423) residing within 1 km of a health facility (p<0.001). CHWs were the first option for care of febrile children (40%, 242/601), and 3-month utilisation was 57% (243/423). CHWs' performance was adequate in taking history, using timers and RDTs, but inadequate in classification of illness. Breath readings (classified as fast or normal) were 85% in agreement with the paediatrician ($\kappa = 0.665$, $p < 0.001$) with a sensitivity and specificity of 81% and 87% respectively (II). In the cRCT, there was good compliance with RDT results in the intervention arm with most (1739/1740) RDT positive children prescribed an anti-malarial, and only 4.9% (17/344) of RDT negative children prescribed an anti-malarial drug. Among children with a high respiratory rate, antibiotics were administered to 86.5% (198/229) in Burkina Faso, 72.5% (103/142) in Ghana, and 98.3% (520/529) in Uganda. Antibiotic overuse was 0.9% (4/446) in Uganda, 38.5% (114/296) in Burkina Faso, and 44.6% (197/442) in Ghana.
Conclusion: Diagnostic-based iCCM improves fever clearance in febrile children compared to presumptive treatment of malaria. RDTs and ARI timers should be introduced into iCCM programmes. CHWs used the two diagnostics to distinguish and treat both malaria and pneumonia; the strategy improves access to treatment for both conditions among under-fives; and communities welcomed the diagnostic-based strategy. While CHW compliance with RDT results was high, compliance to respiratory rate results for pneumonia was lower. Programmes should plan for adequate resources to support CHWs with supplies, logistics and supervision for quality iCCM.

Key words: malaria, pneumonia, case management, community health worker, diagnostics, child, Uganda

LIST OF PUBLICATIONS

I. **Mukanga D**, Tibenderana JK, Kiguli J, Pariyo GW, Waiswa P, Bajunirwe F, Mutamba B, Counihan H, Ojiambo G, Källander K. *Community acceptability of use of rapid diagnostic tests for malaria by community health workers in Uganda.* Malaria Journal 2010, 9:203.

II. **Mukanga D**, Babirye R, Peterson S, Pariyo GW, Ojiambo G, Tibenderana JK, Nsubuga P, Källander K. *Can lay community health workers be trained to use diagnostics to distinguish and treat malaria and pneumonia in children? Lessons from rural Uganda.* Tropical Medicine and International Health 2011, Vol 16 No 10 pp 1234-1242.

III. **Mukanga D**, Tibenderana JK, Peterson S, Pariyo GW, Kiguli J, Waiswa P, Babirye R, Ojiambo G, Kasasa S, Pagnoni F, Källander K. *Access, acceptability and utilisation of community health workers using diagnostics for community case management of fever in Ugandan children.* (Submitted)

IV. **Mukanga D**, Tiono AB, Anyorigiya T, Källander K, Konaté AT, Oduro A, Tibenderana JK, Amenga-Etego L, Sirima SB, Cousens S, Barnish G, Pagnoni F. *Integrated community case management of fever in children under five using rapid diagnostic tests and respiratory rate counting: a multi-country, cluster randomised trial.* (Submitted)

The papers will be referred to by the Roman numbers I - IV.

CONTENTS

LIST OF ACRONYNMS AND ABBREVIATIONS

ACT	Artemisinin-based Combination Therapy
AIDS	Acquired Immuno-deficiency Syndrome
AL	Artemether/Lumefantrine
ARI	Acute Respiratory Infections
CCM	Community Case Management
CDD	Programme for Control of Diarrhoeal Disease
CHW	Community Health Worker
CI	Confidence Interval
C-IMCI	Community IMCI
CQ/SP	Chloroquine/Sulphadoxine-Pyrimethamine
CRF	Case Record Form
DRC	Democratic Republic of Congo
EPI	Expanded Programme on Immunisation
EQA	External Quality Assurance
FGD	Focus Group Discussion
GAPP	Global Action Plan for the Prevention and Control of Pneumonia
GAVI	Global Alliance for Vaccines and Immunisation
GNI	Gross National Income
GoU	Government of Uganda
HBMF	Home Based Management of Fever
HC	Health Centre
Hib	*Haemophilus. influenzae* Type B
HIV	Human Immuno-deficiency Virus
HRP	Histidine-rich Protein
HSD	Health Sub-District
HSSP	Health Sector Strategic Plan
HSSIP	Health Sector Strategic and Investment Plan
iCCM	Integrated Community Case Management
IEC	Information, Education and Communication
IMCI	Integrated Management of Childhood Illnesses
IMR	Infant Mortality Rate
IPTp	Intermittent Presumptive Treatment of Malaria in Pregnancy
KI	Key Informant
KII	Key Informant Interview
LDH	Lactase dehydrogenase
MAFF	Malaria Attributable Fraction
MDG	Millennium Development Goals
MMR	Maternal Mortality Rate
MOH	Ministry of Health
NGO(s)	Non Governmental Organisation(s)
OR	Odds Ratio
ORT	Oral Rehydration Therapy
PCA	Principal Components Analysis

PCV	Pneumococcal Conjugate Vaccine
PDS	Panel Detection Scores
PHP	Private Health Providers
PNFP	Private-Not-for-Profit
PPS	Probability Proportionate to Size Sampling
RDT	Rapid Diagnostic Test
SES	Social Economic Status
SSA	Sub-Saharan Africa
TB	Tuberculosis
TB-DOTS	Tuberculosis Directly Observed Therapy Short Course
TCMP	Traditional and Complimentary Medicine
UCMB	Uganda Catholic Medical Bureau
UMMB	Uganda Muslim Medical Bureau
UN	United Nations
UNDP	United Nations Development Programme
UNICEF	United Nations Children's Fund
UOMB	Uganda Orthodox Medical Bureau
UPMB	Uganda Protestant Medical Bureau
US	United States
VHT	Village Health Team
WHO	World Health Organisation

OPERATIONAL DEFINITIONS

Acceptability: the appropriateness of the social interaction that accompanies care, and how services meet client's cultural values, norms and expectations (Obrist et al., 2007, Etkin, 1991).

Access: how well the system is aligned to meet a client's needs. Is a function of availability, physical accessibility, affordability, adequate supply of services (accommodation), and acceptability (Gulliford et al., 2002, Penchansky and Thomas, 1981).

Accessibility: the geographical relationship between the providers and users of health care (Ricketts and Goldsmith, 2005).

Community case management: a strategy to deliver life-saving curative interventions for common childhood illnesses, in particular where there is little access to facility-based services (CORE et al., 2010).

Community health worker: members of the communities where they work, are selected by the communities, are answerable to the communities for their activities, are supported by the health system, and have shorter training than professional workers (WHO, 2007c).

Diagnostic-based integrated community case management: use of malaria RDTs and respiratory rate counting to target treatment for malaria and pneumonia in children by community health workers practicing community case management.

Fever: elevation of axillary body temperature to 37.5°C or more as measured by a digital thermometer or history of 'hot body' in the last 24 hours as reported by a caregiver.

Household: a group of people at the time of the study that lived together and ate from the same cooking pot.

Malaria: fever and parasitological confirmation with malaria RDT or microscopy.

Pneumonia: severe acute infections of the lungs by viral, bacterial, and other pathogens (Schuchat and Dowell, 2004). Non severe pneumonia is any child with cough or difficult breathing who has fast breathing and no general danger signs (WHO, 2005).

Rapid/fast breathing or high respiratory rate: respiratory rate above IMCI cut-offs for age: 2-12 months > 50 breaths per minute, and 13-59 months > 40 breaths per minute (Redd et al., 1992).

Utilisation: the extent to which a given group uses a particular service in a specified period (Lin et al., 2009).

PREAMBLE

Involving communities in the delivery of primary health care to account for the lack of health infrastructure and skilled manpower as well as enhance community participation in health promotion has regained attention. Many now argue that community-based health service delivery is a key component in strengthening the health system (Task Force on Health Systems Research, 2004, Paul, 2004, Haines et al., 2007).

This thesis was inspired by renewed efforts to improve access to care for febrile children in malarious areas (Kallander, 2006, Nsabagasani et al., 2007, Nsungwa-Sabiiti et al., 2007, Pagnoni et al., 1997, Pagnoni et al., 2005). Highly effective anti-malarial drugs, the artemisinin-based combination therapy (ACTs), became widely available within the last decade. The standard approach of presumptive use of anti-malarial drugs to treat every fever as malaria has raised fears about the efficacy of the ACTs being lost quickly to parasite resistance. Also malaria rapid diagnostics tests (RDTs) have become commercially available over the last few years. There was some evidence that community health workers (CHWs) can be trained to use them effectively. But if they use them in remote rural areas, and determine that a febrile child has no malaria, what does the mother/caregiver do? Could this be pneumonia, the other major cause of fever in this age group? Can CHWs diagnose pneumonia? Interestingly, CHWs in Asia were already doing this, using respiratory rate timers. Can CHWs in Africa do the same? Can they use both RTDs and respiratory rate timers? Would this not be too complex for them? Would we have many false negatives, and instead put the lives of many children at risk? If CHWs in Africa can use these two diagnostics, then we will have moved a notch higher to providing targeted case management in the community to children dying in settings of poverty, poor access to basic health care, and poor care-seeking.

Might we also in the process raise the status of CHWs in their communities, and inspire them and their neighbours to believe in themselves? If they can use these diagnostics, and follow more complex algorithms, then may be communities will be galvanised around these “little doctors” in rural, sometimes forgotten corners of Africa.

1 INTRODUCTION

1.1 CHILD MORTALITY IN SUB-SAHARAN AFRICA

The number of children dying before their fifth birthday is estimated at 7.6 million in 2010 (You et al., 2011). In the poorest households in low income countries, 107 under-fives die for every 1,000 live births, nearly 40 percent higher than in the richest households in those nations (UNICEF, 2007). Figure 1 shows the under-five mortality decline between 1990 and 2010, while figure 2 shows the estimated number of under-five deaths by region in 2010 (You et al., 2011).

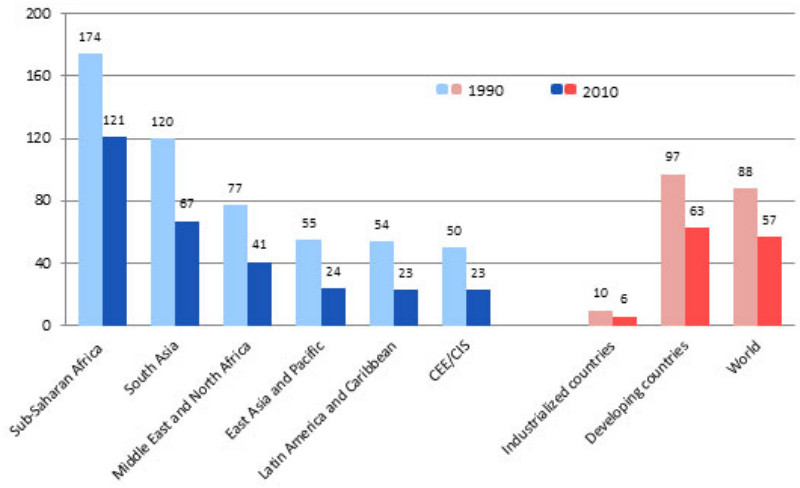


Figure 1: Under-five mortality decline between 1990 and 2010 (You et al., 2011)

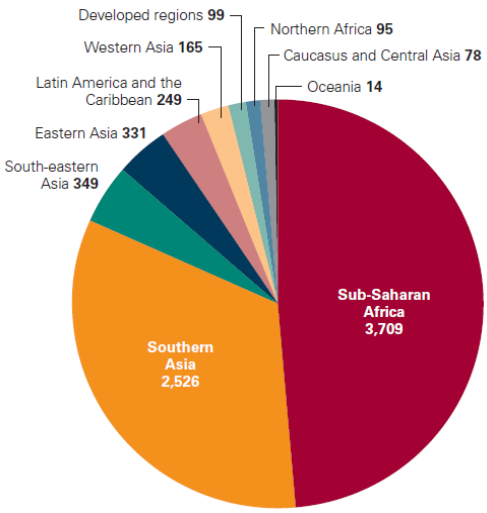


Figure 2: Number of under-five deaths by region (in thousands) (2010) (You et al., 2011)

1.2 CAUSES OF CHILD MORTALITY

In the 1990s, it was estimated that 70% of all global child deaths were due to five conditions: diarrhoea, pneumonia, malaria, measles, and malnutrition (Gove, 1997, Tulloch, 1999). A 2003 review covering 42 developing countries, which account for 90% of all under-five deaths (Black et al., 2003) showed the following distribution of causes: neonatal causes (33% of all deaths), diarrhoea (22%), pneumonia (21%), malaria (9%), AIDS (3%), measles (1%), and other causes (9%). Few conditions, therefore, account for a large proportion of all deaths.

In SSA, the distribution of the main causes of death is estimated to be: neonatal disorders (25%), diarrhoea (19%), pneumonia (18%), malaria (16%), and AIDS (4%) (Black et al., 2010). Most deaths occur in impoverished rural communities where poor access to basic health care results in lack of timely administration of inexpensive treatment. An estimated 60% of these deaths could be prevented by high coverage of simple and cheap interventions such as timely treatment with antibiotics and anti-malarial drugs, oral rehydration therapy (ORT), improved breastfeeding and immunisations (Jones et al., 2003). Weak and inequitable health systems which fail to deliver life-saving interventions – especially to the poor who need them most are a major barrier to improved child survival (Freedman et al., 2005, Gwatkin et al., 2000, Victora et al., 2003).

1.2.1 Fever

Fever or pyrexia is the documented elevation of axillary body temperature to or above 37.5°C. Other literature defines fever as rectal temperature above 38°C (Schmitt, 1980). Fever is more often a response to infection (bacterial, viral, rickettsial, fungal or parasitic), as well as a variety of other causes including neoplasms, vascular, traumatic, immunological, endocrine, metabolic, haematological, and physical agents. Infection is the most common cause of fever in children. Globally, common viral and bacterial illnesses like colds, gastroenteritis, ear infections, croup, bronchiolitis, and urinary tract infections are the most likely illnesses to cause fever (Fruthaler, 1985).

Although fever can be caused by a large number of infections in tropical Africa, the malaria attributable fraction of fever (MAFF) is often high, ranging from 30-60% (Breman, 2001), dropping to 0-20% in urban areas (Wang et al., 2005). Estimates suggest that as high as 43% of paediatric fevers that reach health facilities in Africa to seek care are due to malaria (Gething et al., 2010). With limited laboratory facilities, the aetiology of fever is often difficult to establish. Although diarrhoea is an important condition in many sick children presenting with fever, the focus of this thesis was on malaria and pneumonia, the two conditions with available diagnostics that can be potentially deployed at community level.

1.2.2 Malaria

Malaria is caused by infection of humans with protozoan parasites of the genus *Plasmodium* through bites of infected female Anopheles mosquitoes. Four *Plasmodium* species infect humans, viz: *P. falciparum, P. vivax, P. ovale* and *P. malariae*.

When a susceptible host is bitten by an infected mosquito, sporozoites enter the hepatocytes and develop into exo-erythrocytic schizonts. When these mature, the

infected hepatocytes rupture; asexual parasites reach the bloodstream and invade the erythrocytes where they to grow and multiply cyclically. Most will develop into asexual forms, from trophozoites to mature blood schizonts that rupture the erythrocyte within 48-72 hours, to release 8-30 erythrocytic merozoites (depending on the species) that invade other erythrocytes. At the time of each cycle, rupture of large numbers of erythrocytic schizonts induces clinical symptoms. Within infected erythrocytes, some of the merozoites may develop into male or female forms, gametocytes (Heymann, 2004).

Malaria symptoms on onset include: headache, lassitude, fatigue, abdominal discomfort, and muscle and joint aches, which are usually followed by fever, chills, perspiration, anorexia, vomiting and worsening malaise (WHO, 2010b). If left untreated, the disease may rapidly progress to convulsions, coma, and death within 24 hours of symptom onset. In high-transmission settings, most malaria deaths in children are due to anaemia resulting from repeated untreated malaria infections (Greenwood et al., 1987).Where the transmission of malaria is "stable", partial immunity to the clinical disease and to its severe manifestation is acquired early in childhood. In such situations, which prevail in much of SSA, the acute clinical disease described above is mostly confined to young children, who suffer high parasite densities and acute clinical disease (WHO, 2010b).

For several decades, clinical presentation was the mainstay of malaria diagnosis in Africa. In malaria-endemic regions, all fevers were presumed and treated as malaria. However, due to declining malaria prevalence and rising costs of anti-malarial therapy, the World Health Organisation (WHO) now recommends parasitological confirmation of all malaria cases in all settings before treatment. The first line treatment for uncomplicated *P.falciparum* malaria is the artemisinin-based combination therapy (ACT) (WHO, 2010b)

1.2.3 Pneumonia

The term *pneumonia* is usually used in the broader sense to refer to severe acute infections of the lungs by viral, bacterial, and other pathogens (Schuchat and Dowell, 2004). *Streptococcus pneumonia* (pneumococcus) and *Haemophilus influenzae* (usually type B or *Hib*) are the leading bacterial causes of pneumonia (Schuchat and Dowell, 2004), and respiratory syncytial virus the leading viral cause (Weber et al., 1998). Several studies of the aetiology of childhood pneumonia in developing countries provide similar findings (Shann, 1986, Forgie et al., 1991b, Forgie et al., 1991a, Ghafoor et al., 1990, Greenwood, 1992, Falade et al., 1997, Forgie et al., 1992, Wall et al., 1986).

Pneumonia symptoms include sudden onset of cough, fever, fast and difficult breathing, vomiting, convulsions and chest in-drawing (Chin, 2000). Pneumonia is characterised by inflammation of the alveoli and terminal airspaces in response to invasion by an infectious agent introduced into the lungs. Pneumonia is responsible for stuffing the alveoli with fibrous sticky liquid hindering the exchange of oxygen and carbon dioxide in the blood, resulting in depleted oxygen levels and faster breathing in the affected individual.

The WHO defines non-severe pneumonia as any child with cough or difficult breathing who has fast breathing and no general danger signs, no chest in-drawing and no stridor when calm (WHO, 2005). Currently, the majority of pneumonia in children in countries with high infant mortality is of bacterial origin – mostly *Streptococcus pneumoniae* or *Haemophilus influenzae* - which can be effectively treated using inexpensive antibiotics that can be administered at home.

Effective vaccines against *H. influenza*e b (Hib) are now widely available. The pneumococcal conjugate vaccine, though is in use in some countries, has yet to be introduced into the Expanded Programme on Immunisation (EPI) in Uganda. There are more than 90 serotypes of pneumococcal bacteria, however, the new pneumococcal conjugate vaccine (PCV13) protects against only 13 of them. These serotypes are responsible for most severe pneumococcal infections among children, although scientists argue that the geographical distribution of serotypes may not be the same in Africa as in the US and Europe where the vaccine was tested (Cutts et al., 2005).

Children with respiratory infections requiring antibiotic treatment at home or referral care can be recognised using signs (rapid respiration and lower chest in-drawing) that can be learned and used by health workers with limited clinical training and no capacity for laboratory investigation or radiology (WHO, 2002). For the foreseeable future, presumptive case management of childhood pneumonia will remain an important strategy.

1.2.4 Clinical overlap between malaria and Pneumonia

A number of studies have reported marked symptom overlap, and co-morbidity with malaria and pneumonia among sick children at facility and community levels. About 45% of children admitted to a Kenyan hospital with respiratory signs indicative of severe ARI had malaria as the primary diagnosis (English et al., 1996). Other facility-based studies have reported symptom overlap for malaria and pneumonia in children at 24% in Mozambique (Bassat et al., 2011) and as high as 48% in the Gambia (O'Dempsey et al., 1993). Symptom overlap for malaria and pneumonia has been reported from a community-based study to be as high as 30% (Kallander et al., 2004). However, true co-infection with malaria and pneumonia has been reported to be as low as 1.4% at a hospital in Mozambique (Bassat et al., 2011), and 11.4% at a Kenyan hospital (English et al., 1996).

A study from a Kenyan hospital reports that 62% (8.2-91) of bacteraemia cases in children were attributable to malaria at a community parasite prevalence of 29% (Scott et al., 2011). This suggests that malaria infection strongly predisposes individuals to bacteraemia and can account for more than half of all cases of bacteraemia in malaria-endemic areas.

1.3 GLOBAL TARGETS AND STRATEGIES TO REDUCE CHILD MORTALITY

In 2000 the United Nations (UN) set the goal to reduce under five mortality by two-thirds, from 93 deaths per 1,000 births in 1990 to 31 per 1,000 by 2015 (United Nations, 2000); what is today known as Millennium Development Goal Number 4 (MDG 4).

Progress towards MDG 4

Figure 3 shows progress up to 2010 of the two high-burden regions towards achievement of MDG 4, with SSA being the region with the least progress. There is increasing evidence that MDG 4 can be achieved, but only if countries in SSA and Southern Asia give high priority to scaling up effective health interventions for children, particularly by targeting major killer conditions (including pneumonia, diarrhoea, malaria and under-nutrition) with effective preventative and curative interventions (You et al., 2011).

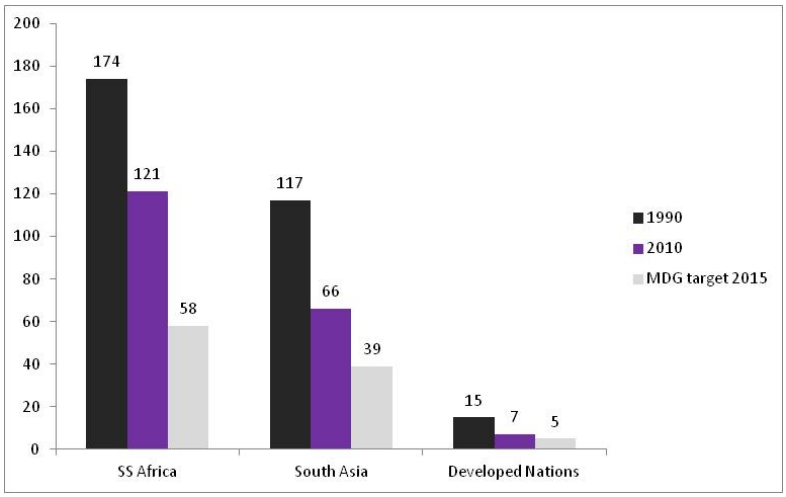


Figure 3: Progress towards achieving MDG 4 in the two high-burden regions (You et al., 2011)

Several global strategies and initiatives have been developed to accelerate achievement of MDG 4 including: the Global Immunisation Vision and Strategy 2006-2015 (WHO/UNICEF, 2005); Global Strategy on Measles Initiative that targets lowering measles mortality in the 45 high burden countries that account for 90% of measles deaths; the Global Action Plan for the Prevention and Control of Pneumonia (GAPP); the Global Alliance for Vaccines and Immunisation (GAVI); the Global strategy for Women's and Children's Health that was launched in 2010 by UN Secretary General Ban Ki-moon to accelerate MDGs 4 and 5 (United Nations, 2010); President Obama's Global Health Initiative that places emphasis on maternal and child health along with HIV/AIDS, tuberculosis, malaria and neglected tropical diseases (US government, 2010); Prime Minister Harper's led Muskoka Initiative launched in 2010 at the G-8 summit focus efforts on helping developing countries deliver key interventions for maternal and child health (Government of Canada, 2010); and several contributing initiatives including the Global Fund to Fight AIDS, Tuberculosis and Malaria. The central theme of all these initiatives is the focus on high-burden countries, with support for delivery of key interventions for maternal, child, newborn health and other key areas.

In Uganda, the Road Map to accelerate Reduction of Maternal and Neonatal Morbidity and Mortality, and the National Child Survival Strategy were formulated in 2007 and

2009, respectively. The National Child Survival Strategy sets out to address the main bottlenecks of child health interventions at household and community level. The goal of the strategy is to reduce the under-five mortality rate from 137 per 1,000 live births in 2009 to 56 per 1,000 live births by 2015 (MOH Uganda, 2010a). One of the components of the strategy is to increase community access to child health commodities such as bed nets, anti-malarial drugs, Oral Rehydration Salt (ORS), Zinc and antibiotics. The Ministry of Health and Ministry of Local Government are responsible for implementation of the Child Survival Strategy as outlined in the Health Sector Strategic and Investment Plan 2010-2015 (HSSIP) (MOH Uganda, 2010a).

Community case management of fever

Countries with weak health systems will require creative approaches to intervention delivery in the short term, while at the same time strengthening the health systems as a long-term strategy. The poorest strata of the population is the group with greatest need in terms of health care and is also the hardest to reach (Victora et al., 2006). Unless equity considerations become a key part of policy making and of monitoring outcomes, interventions may widen instead of narrow inequity gaps (Victora et al., 2003).

Until the mid 1990s, child health programmes were organised as vertical programmes (Nicoll, 2000, Claeson and Waldman, 2000) including the Expanded Programme on Immunisation (EPI), Programmes for Control of Diarrhoeal Disease (CDD) and Control of Acute Respiratory Infections (ARI). Both the CDD and ARI programmes faced the difficult reality of dealing with children with symptoms suggestive of multiple conditions (Nicoll, 2000). Among children who are sick and those who die, a large proportion present with two or more diagnoses (Black et al., 2003).

The reasons for shifting from vertical programmes towards integration have been well articulated by Victora and others (Victora et al., 2006) to include the small number of diseases accounting for a bulk of deaths, achieving managerial efficiency, and improving the quality of case management. In order to address the overall health of a child, WHO and United Nations Children's Fund (UNICEF) launched the Integrated Management of Childhood Illnesses (IMCI) strategy in the mid-1990s (Tulloch, 1999). IMCI has three components, each of which was meant to be adapted at the country level according to local epidemiology, health system characteristics, and culture (Victora et al., 2006), viz: (1) improving case management skills of health workers; (2) improving health system support; and (3) improving household and community practices related to child health, nutrition and development (Community IMCI, or C-IMCI) (Gove, 1997). However, C-IMCI was never fully implemented in most countries that adopted IMCI (Winch et al., 2002, Bessenecker and Walker, 2004). Although the process of integrating C-IMCI into the health system was slow in most low-income countries (Task Force on Health Systems Research, 2004), Bangladesh, Nepal and Nigeria reported successful C-IMCI implementation (IMCI National Working Group, 2004, Brieger et al., 2004, Dawson, 2001). All three countries emphasised treatment of common infections like malaria and pneumonia in the community.

As a result of delayed full-scale implementation of C-IMCI, alternative community based health care delivery strategies have been employed to reach sick children. The most prominent have been the home- and community- based management of fever strategies,

which have shown that safe, timely and appropriate treatment can be provided in communities through the use of community health workers (CHWs) (Kallander, 2006, Nsungwa-Sabiiti et al., 2007). Unfortunately in Africa, home and community management was implemented for malaria with CHWs only trained to refer suspected cases of pneumonia (MOH Uganda, 2005).

While community case management of malaria has been shown to significantly reduce child mortality (Kidane and Morrow, 2000), the impact of case management of pneumonia on child mortality is even stronger (Sazawal and Black, 1992), and is one of the four most cost effective interventions for child survival (Edejer et al., 2005). In 2002, a technical meeting organised in Stockholm, Sweden to review the evidence of community management of pneumonia (WHO, 2002) resulted in the WHO/UNICEF joint statement on integrated malaria and pneumonia care at the community (WHO/UNICEF, 2004). The Global Action Plan for the Prevention and Control of Pneumonia (WHO/UNICEF, 2008) recognises that effective case management at community and health facility levels is an essential part of pneumonia control, and recommends that countries with significant rates of under-five mortality should adopt plans to expand adequate case management of pneumonia.

Implementation of community case management in Uganda is discussed under section 2.2.1 (Community Health Workers in Uganda).

1.4 DIAGNOSTICS IN COMMUNITY CASE MANAGEMENT OF FEVER

1.4.1 Malaria Rapid Diagnostic Tests

Parasitological confirmation before administration of anti-malarial treatment is now recommended by WHO in all cases of suspected malaria at all levels of the health system (WHO, 2010b). Such confirmation is increasingly important in the context of declining malaria transmission, when a decreasing proportion of fever cases is likely to be due to malaria (D'Acremont et al., 2010).

Rapid diagnostic tests (RDTs) are now available with sensitivities comparable with routine microscopy in detecting malaria (Murray et al., 2003, Bell et al., 2006, WHO, 2009). *Plasmodium* parasites produce a number of proteins that are relatively species-specific. RDTs are immunochromatic diagnostic devices that detect these proteins (Drakeley and Reyburn, 2009). There are more than 80 RDTs on the market that are based on the detection of either histidine-rich protein (HRP) (specific to *P. falciparum*) or species-specific isotypes of lactase dehydrogenase (LDH) or aldolase (Murray et al., 2008). The LDH test detects all four species that cause human malaria.

HRP-based tests may detect circulating antigen several days or even weeks after parasites have been eradicated resulting in lower specificity for current infection (WHO, 2006, Tjitra et al., 2001, Singh and Shukla, 2002, Mayxay et al., 2001, Swarthout et al., 2007). Certain conditions such as non-specific fever associated with heterophile antibodies and the presence of rheumatoid factor or anti-mouse antibodies can result in false positive results on some RDTs, although this is probably not common (WHO, 2006).

Persistent antigenemia (antigens persisting in the blood stream after parasite clearance) may limit the usefulness of HRP-based assays in areas of intense malaria transmission, where positive tests may commonly be the result of prior infections that are no longer clinically relevant (Hopkins et al., 2008). LDH-based RDTs appear to be less sensitive than tests that detect HRP, but they are more specific, as LDH is rapidly cleared from the bloodstream and becomes undetectable at about the same time blood smears become negative after anti-malarial therapy (Piper et al., 1999, Moody et al., 2000, Oduola et al., 1997).

The product instructions commonly specify storage between 2°C and ~30°C (WHO, 2006) or to a maximum of 40°C in the case of HRP RDTs (Drakeley and Reyburn, 2009). HRP-based tests have been available in various formats for several years, have shown good sensitivity in a variety of field settings, and they are increasingly recommended for use in settings where reliable microscopy is not available (Bell et al., 2006, Rafael et al., 2006, Drakeley and Reyburn, 2009, WHO, 2009).

Studies from Africa (Premji et al., 1994, Harvey et al., 2008, Elmardi et al., 2009, Hawkes et al., 2009, Yeboah-Antwi et al., 2010) have reported successful use of RDTs by CHWs in community malaria case management programmes. Similar findings have been reported from Asia (Yeung et al., 2008) and South America (Cunha et al., 2001, Pang and Piovesan-Alves, 2001).

1.4.2 Respiratory Rate Counting

Given the symptom and clinical overlap between malaria and pneumonia (O'Dempsey et al., 1993, English et al., 1996, Kallander et al., 2004, Scott et al., 2011), a child presenting with malaria-like symptoms but tests negative for malaria is more likely to have pneumonia.

Increased respiratory rate is one of the most specific symptoms of pneumonia (Berman et al., 1991, Kolstad et al., 1997, Weber et al., 1997). The pneumonia clinical definition has a sensitivity and specificity greater than 60% in distinguishing children with and without radiographic evidence of pneumonia. Children who satisfy the clinical definition for pneumonia are more likely to have radiographic evidence of pneumonia (odds ratio 10.4, 95% confidence interval 5.2-20.7) (Redd et al., 1992).

ARI timers (WHO, 2000b) have been recommended by WHO and UNICEF to aid in the accurate counting of respiratory rates in children. ARI timers were developed by UNICEF Denmark (WHO, 2000a) and provided by UNICEF and WHO. They are simple to use and provide a life span of 8,000 counting cycles of 60 seconds under normal usage. Once the count has been completed, then you classify the count as rapid/fast breathing or not based on IMCI cut-offs for age.

The ARI timer has two main limitations - inaccuracy and a short lifespan. Some ARI timers make ticking sounds every second which users find distracting when counting breaths (they begin to count the ticking sound rather than the breath). Inaccurate results may also be caused by non-registration of the count. To confirm results, the count is repeated two to three times for each child. The current device is unable to record any previous counts made, so that caregivers often forget previous count results. Although the manufacturer indicates the device has a two or three year life span, reports from the field suggest a shorter life span. Philips has developed a new device called the Breath

Counter to address some of the shortcomings of the ARI timer which is currently undergoing field testing (Philips, 2009), and other studies are ongoing using the mobile phone to record the breath rate (UOM, 2009).

1.5 UGANDA COUNTRY PROFILE

Uganda is a landlocked country located in Eastern Africa covering an area of 241,038 sq km. It straddles the Equator and is bordered by Kenya in the East, South Sudan in the North, Tanzania in the South, Rwanda in the South West, and the Democratic Republic of Congo (DRC) to the West. The population is projected to be about 33 million people with 56% of the population below 18 years. Majority (66%) of the population is engaged in agriculture (Population Secretariat, 2011). The GNI per capita is estimated at US$460 (World Bank, 2009). Life expectancy at birth is 54.1 years, and on the basis of the human development index, Uganda is ranked 143 out of 169 countries with comparable data in the world (UNDP, 2010).

1.5.1 Uganda Health Indicators

Uganda belongs to the "high child, very high adult" mortality stratum according to the WHO classification (WHO, 2004). The infant mortality rate in Uganda stands at 76/1000 live births and under-five mortality rate at 137/1,000 (Population Secretariat, 2010). The MDG 4 target for Uganda is 56 deaths per 1,000 live births but with current trends this is unlikely to be achieved (MOH Uganda, 2010a). Some of the child health indicators are presented in table 1 below.

Table 1: Selected Health Indicators for Uganda for the period 1991 – 2010

Indicator	1991	1995	2001	2006	2009	2010[η]
Infant mortality rate (IMR) per 1,000	122	81	88	76	76	63
Under-five mortality rate per 1,000	203	147	152	137	137	99
Maternal mortality rate (MMR) per 100,000	527	506	505	435	435	
Full immunization (%)	31	47	38	38	46	
Stunted children (%)	38	38	39	32	38	

Sources: Population secretariat, 2007, 2010, and η-You et al, 2011

In the Uganda Demographic and Health Survey of 2006, the prevalence of fever and symptoms of acute respiratory infection in the two weeks preceding the survey were 40.9%, and 14.5% respectively (Uganda Bureau of Statistics, 2006).

1.5.2 The Health System in Uganda

WHO defines health systems as "all actors, organisations, institutions and resources whose primary purpose is to promote, restore or maintain health" (WHO, 2000c). Health systems in developing countries are being identified as a key constraint to the implementation of child health programmes (Freedman et al., 2005).

The provision of health services in Uganda has been decentralised (Jeppsson, 2004, Rwabwoogo, 2002) with districts and health sub-districts (HSDs) playing a key role in the delivery and management of health services at district and HSD levels, respectively.

Unlike many other countries, Uganda has no 'intermediate administrative level' between districts and the centre (province, region). The health services are structured into national and regional referral hospitals, general hospitals, health centre (HC): HC IVs, HC IIIs and HC IIs. The HC I has no physical structure but a team of CHWs (the Village Health Team (VHT)) which serves as a link between health facilities and the community (MOH Uganda, 2010a).

Each level provides additional services not available at the lower levels and is aligned to the political structures from the village to the district levels (Table 2). In 2004, only 43% of parishes had a health facility within their boundaries (World Bank, 2004). However, new facilities have been built since this review in 2004, and it is now estimated that about 74% of the population reside within 5 km of some kind of health facility (Government of Uganda, 2007). However, utilisation is limited due to poor infrastructure, lack of medicines and other health supplies. The shortage of human resource in the public sector, low salaries, lack of accommodation at health facilities and other factors further constrain access to quality services (MOH Uganda, 2010a).

Table 2: The Structure of the Uganda National Health System

Health unit	Physical structure	Highest qualified staff	Location	Population
HC I	None	CHW	Village	1,000
HC II	Out-patient services only	Nurse	Parish	5,000
HC III	Out-patient services, maternity, general ward and laboratory	Clinical Officer	Sub-county	20,000
HC IV	Out- and in-patient services, theatre, laboratory and blood transfusion	Medical Officer	County	100,000
General Hospital	Hospital, laboratory, surgery, and medical imaging	Medical Officer	District	500,000
Regional Referral Hospital	Specialist services including pathology	Specialist physician	Region (8-10 districts)	2,000,000
National Referral Hospital	Advanced tertiary care	Specialist physician	National	30,000,000

Adopted from Government of Uganda Health Sector Strategic Plan, 2000/01 – 2004/05 and the National Hospital Policy (2005)

The infrastructure in most peripheral health units is in a deplorable state with non-functional equipment and poorly managed essential drug supplies (World Bank, 2004), as well as grossly under-funded and short on qualified personnel (Rutebemberwa, 2009). The approved posts in government health facilities filled by trained health workers stood at 68% in 2005 (Government of Uganda, 2005). The workforce in rural health facilities mainly consists of clinical officers with 3 years' basic training, nurses with 18 months' training and nurse-aides with 3 months' training. Nurse-aides constitute 56% of the workforce and operate 40% of health units independently, whereas medical officers often are found at district level (World Bank, 2004).

In recent years, external resources from donors have increased, although the greater proportion of the external donor funds are earmarked for HIV/AIDS. This creates pressure on the entire system, especially on human resources, due to increase in activities and changing priorities (MOH Uganda, 2010a).

The public sector includes all Government health facilities under the MoH, health services of the Ministries of Defence (army), of Internal Affairs (Police and Prisons) and of Local Government. The delivery of health services in Uganda is through both public and private sectors with GoU being the owner of most facilities up to HC III level. GoU owns 2242 health centres and 59 hospitals compared to 613 health facilities and 46 hospitals by Private-Not-For-Profit (PNFP) providers, and 269 health centres and 8 hospitals by the Private Health Providers (PHPs) (MOH Uganda, 2008).

The Private Sector

The private sector in the country comprises of the PNFP (which includes the Non-Governmental Organisation (NGO) facilities), and the PHPs which includes drug shops, private clinics, and Traditional and Complimentary Medicine Practitioners (TCMPs) (MOH Uganda, 2010a). The majority of PNFPs are organised under the umbrellas of the Uganda Catholic Medical Bureau (UCMB), Uganda Protestant Medical Bureau (UPMB), the Uganda Muslim Medical Bureau (UMMB) and the Uganda Orthodox Medical Bureau (UOBM). The faith-based PNFPs have provided services since colonial times. The government health system was highly efficient in the 1960s soon after independence in 1962, but collapsed in the 1970s and early 1980s due to political upheaval. This collapse left a gap that was filled by the private sector.

The majority of private clinics and drug shops are located in towns and trading centres and are the first source of treatment for a great proportion of sick children (Konde-Lule et al., 2006, Tawfik et al., 2002). The quality of care is often poor with many outlets manned by unqualified attendants (Tawfik et al., 2006).

2 COMMUNITY HEALTH WORKERS

Based on the current body of evidence, community health workers (CHWs) can play an important role in increasing coverage of essential interventions for child survival (Haines et al., 2007). The use of CHWs has been identified as one strategy to address the growing shortage of health workers, particularly in low-income countries. Using community members to render certain basic health services to their resident communities is a concept that has been around for at least 50 years.

Health systems in many low-income countries face significant pressure, constraints and challenges, and are unable to meet needs of populations especially in hard-to-reach areas. CHW programmes are an important strategy to support health systems to serve the poor living in geographically peripheral areas (Lehmann et al., 2004).

2.1 DEFINITION OF COMMUNITY HEALTH WORKERS

The umbrella term "community health worker" embraces a variety of community health aides selected, trained and working in the communities in which they reside. CHWs are members of the communities where they work, are selected by their communities to provide health services, should be answerable to the communities for their activities, should be supported by the health system but not necessarily a part of its organisation, and have shorter training than professional workers (WHO, 2007c).

The roles and activities of community health workers are enormously diverse throughout their history, within and across countries, and across programmes. While in some cases CHWs perform a wide range of tasks that can be preventive, curative and/or developmental, in other cases CHWs are appointed for very specific interventions (Lehmann et al., 2004). Their training varies from a few days as reported from South Sudan, Niger (WHO, 1975), Uganda (Nsungwa-Sabiiti et al., 2007), and Zambia (Yeboah-Antwi et al., 2010), to several months as reported from Tanzania (WHO, 1975), Malawi, Rwanda and Ethiopia.

2.2 EXPERIENCES WITH CHW PROGRAMMES

There have been innumerable experiences across the world of CHW programmes ranging from large-scale, national programmes to small-scale, community-based initiatives (WHO, 2007a). A WHO-commissioned review found that services offered by CHWs have helped in the decline of maternal and child mortality rates and have also assisted in decreasing the burden and costs of tuberculosis and malaria (WHO, 2010a). The review also found that CHWs provide a critical link between their communities and the health and social services system. Communities across all the countries studied recognised the value of CHWs as members of the health delivery team.

The experiences of CHW programmes have been well described by Lehmann and others (Lehmann et al., 2004) in five important areas:

a. CHWs can improve access to and coverage of communities with basic health services, and in the process lead to improved health outcomes. However, they do not consistently provide services likely to have substantial health impact, and the quality of services they provide is sometimes poor.

b. CHWs must be carefully selected, appropriately trained and adequately and continuously supported in order to be effective.
c. CHW programmes are neither the panacea for weak health systems nor a cheap option to provide access to health care for under-served populations. Numerous programmes have failed in the past because of unrealistic expectations, poor planning and an under-estimation of the effort and input required to make them work. This has unnecessarily undermined and damaged the credibility of the CHW concept.
d. CHW programmes are vulnerable unless they are driven, owned by and firmly embedded in communities. Where this is not the case, they exist on the geographical and organisational periphery of the formal health system, exposed to the moods of policy swings, are fragile and unsustainable.
e. Whether CHWs should be volunteers or remunerated in some form remains controversial. There is limited evidence that volunteerism can be sustained for long periods with the exception of the Nepal volunteering lady health workers (Glenton et al., 2010).

2.2.1 Community health workers in Uganda

CHWs have been used in Uganda to support a variety of initiatives and programmes. Examples include the Safe Motherhood Initiative (Kasolo, 1993); community management of malaria, pneumonia and diarrhoea in Northern Uganda (MOH Uganda, 2009b); promotion of community utilisation of immunisation services, and basic hygiene (Bahai International Community, 1999); and home based management of malaria (MOH Uganda, 2005, Nsungwa-Sabiiti et al., 2007). A 2007 review documents CHWs to have provided services in a variety of areas including, reproductive health, HIV/AIDs, condom and ivermectin distribution, and community TB Directly Observed Therapy (TB-DOTs) (Sekimpi, 2007).

Village Health Teams

CHWs in Uganda are organised around the concept of Village Health Teams (VHT). A network of VHTs has been established in Uganda in order to facilitate health promotion, service delivery, community participation and empowerment in access to and utilisation of health services (MOH Uganda, 2010a). Each Village should have an average of five VHT members/CHWs.

VHTs are responsible for:

- Identifying the community's health needs and taking appropriate measures;
- Mobilising community resources and monitoring utilisation of all resources for their health;
- Mobilising communities for health interventions such as immunisation, malaria control, sanitation and promoting health seeking behaviour;
- Maintaining a register of members of households and their health status;
- Maintaining birth and death registration;
- Serving as the first link between the community and formal health providers; and,
- Community-based management of common childhood illnesses including malaria, diarrhoea, and pneumonia; as well as distribution of any health commodities availed from time to time.

While VHTs are playing an important role in health care promotion and provision, coverage of VHTs is however still limited. VHTs have been established in 75% of the districts in Uganda but only 31% of the districts have trained VHTs in all the villages (MOH Uganda, 2009a). Attrition is quite high among VHTs mainly because of lack of emoluments. The HSSIP 2010-2015 targets increasing the percentage of districts with operational VHTs from 31% to 100% (MOH Uganda, 2010a).

Home Based Management of Fever in Uganda
In Uganda, community case management of fever (better known as Home Based Management of Fever - HBMF) was introduced in 2002 with the distribution of anti-malarial drugs (Chloroquine and Suphadoxine/Pyrimethamine also called HOMAPAK®) by CHWs free of charge (Nsungwa-Sabiiti et al., 2004). Each village had two CHWs trained by health workers. They were under the supervision of the health workers from the health facilities in whose catchment area they worked. They referred children with severe illness or those not presenting with fever. HBMF improved access to prompt and appropriate treatment for malaria by 12% (Nsungwa-Sabiiti et al., 2007).

The programme was faced with a number of challenges. Caregivers' utilisation of CHWs was low because CHWs were using only one drug (HOMAPAK®) while their children had other conditions, and some of the caregivers perceived the HOMAPAK® as ineffective (Nsabagasani et al., 2007, Malimbo et al., 2006). HBMF has not been functional nationally since the change of first line anti-malarial drug from Chloroquine and Suphadoxine/Pyrimethamine (CQ/SP) to artemether/lumefantrine (AL) in 2006.
In 2010, a new policy on integrated community management (iCCM) of malaria, pneumonia and diarrhoea was adopted (MOH Uganda, 2010b). ICCM is currently being implemented in more than 25 of Uganda's 118 districts, although implementation is mainly driven by NGOs.

2.2.2 Access and utilisation of CHW services

Where access to health facilities is a problem, community case management may fill the gap (WHO/UNICEF, 2008). A number of studies in different settings show that CHWs tremendously improve access to and utilisation of health services. CHWs increased the use of curative services by poor children with pneumonia, diarrhoea, or dysentery by five to six-fold in Nicaragua (George et al., 2009). In a CHW programme in Uganda, women accessed intermittent presumptive treatment for malaria in pregnancy (IPTp) two weeks earlier from CHWs compared to those who went to health facilities (Mbonye et al., 2008).

Utilisation of HBMF by caregivers of febrile children in Uganda as the first healthcare option has been reported to range from 15-79%, with 92% (86/94) of caregivers reporting that they knew where to find a CHW (Batega et al., 2004). One study from Uganda during the period after the policy shift from CQ/SP to ACTs (when CHWs had not been provided with ACTs) reports utilisation of HBMF at only 2% (9/456) (Rutebemberwa et al., 2009b). Determinants of care seeking and utilisation of services included: perception of the caregiver regarding the illness and treatment (acceptability); how much the caregiver pays or expects to pay (affordability); geographical location of the

provider in comparison with the caregiver (accessibility) or whether services are actually there for the caregiver (availability) (Rutebemberwa et al., 2009a).

2.3 CHW PROGRAMMES AND THE HEALTH SYSTEM

The health system has been described to have six key components, thus: health services delivery; health workforce; health information; medical products, vaccines and technologies; health financing; and leadership and governance (WHO, 2007b). Health systems in many low income countries are severely constrained by a shortage of the health workforce.

Task shifting has been proposed and adopted in several countries as one method of strengthening and expanding the health workforce to rapidly increase access to health services. Task shifting involves the rational redistribution of tasks among health workforce teams. Specific tasks are moved, where appropriate, from highly qualified health workers to health workers with shorter training and fewer qualifications in order to make more efficient use of the available human resources for health (WHO, 2008) and increase the number of health workers available to deliver quality health services. CHWs represent an important health resource whose potential to provide and extend a reasonable level of health care to under-served populations must be fully tapped (Gilson et al., 1989). Some programmes pay CHWs, while others use volunteers.

The greatest dilemma is that those rural settings with high mortality rates that are most in need of the community-based strategy tend to have the weakest health systems, so that optimal supply, supervision, support and referral options are compromised (WHO/UNICEF, 2008). The CHW should be seen as a part of the health system's approach. They need the health facility as a referral unit and for technical and logistic support. CHWs on the other hand should serve as the anchor for outreach activities of the health facility such as immunisation, Information, Education and Communication (IEC) campaigns and the supply of bed nets. The responsibility of the local health authorities for their supervision and support must be defined and supported with appropriate resources (WHO, 2002).

3 RATIONALE FOR THE STUDIES

Malaria accounts for 21–26% of under-five mortality in Uganda (WHO 2006) with another 17–26% attributed to pneumonia (Black et al. 2003). Children with either condition need to receive prompt treatments, otherwise death can occur rapidly (Greenwood et al., 1987, Jones et al., 2003). In spite of available cost-effective interventions for the two conditions, millions of children in low-income countries remain at risk because of poor access to health care, inadequate quality of health services and inappropriate or delayed care seeking, with most deaths occurring at home (Rutebemberwa et al., 2009a).

Several countries in SSA including Uganda (MOH Uganda, 2002, Nsungwa-Sabiiti et al., 2007) introduced home management of malaria to address the health service access bottlenecks faced by caregivers of febrile children. While home management of malaria has improved access to prompt care for febrile children in Uganda (Nsungwa-Sabiiti et al., 2007, Nsabagasani et al., 2007), at least four concerns have emerged: 1) the overlap in symptoms between malaria and pneumonia (O'Dempsey et al., 1993, Kallander et al., 2004) with the likely outcome that many children with pneumonia receive delayed, or no treatment at all; 2) strong evidence of mortality reduction from community pneumonia programmes (Sazawal and Black, 1992); 3) the declining malaria prevalence observed in several Africa countries, likely resulting into a decreasing malaria attributable fraction of fever cases (D'Acremont et al., 2010); and 4) the shift to ACTs as first line anti-malarial treatment, and the risk of overuse, and drug resistance (D'Alessandro et al., 2005, Staedke et al., 2009).

On the basis of concerns 1 and 2, WHO and UNICEF now recommend integrated community case management of malaria and pneumonia (WHO/UNICEF, 2004). On the basis of concerns 3 and 4, targeted therapy with the aid of malaria RDTs has been proposed for use by CHWs (Chanda et al., 2011, D'Acremont et al., 2011, Drakeley and Reyburn, 2009, Harvey et al., 2008, Msellem et al., 2009, Thomson et al., 2011, Ukwaja et al., 2011, Yasuoka et al., 2010), with WHO recommending parasitological confirmation of all malaria cases before treatment at all levels of the health system (WHO, 2010b).

While it has been demonstrated that CHWs can administer both anti-malarial and antibiotic medicines in the community (though most of the evidence on antibiotics is from Asia), practical experience of using CHWs to implement an integrated diagnostic-based strategy for malaria and pneumonia case management is scanty.

Therefore, this thesis explored the following questions:

a. Can CHWs be trained to follow a more complex diagnostic and treatment algorithm for malaria and pneumonia?
b. What will be the perceptions of community members towards CHWs using RDTs?
c. How accessible are CHWs, and what will be the utilisation of an integrated service by caregivers of febrile children?
d. Will this diagnostic and treatment package be more effective in clearing fever compared to standard presumptive care? Or will there be too many over- or under-treatments (sick child denied care) that the strategy becomes meaningless?

4 CONCEPTUAL FRAMEWORK

In order to describe the interplay of factors between CHW services, and the health of the communities they serve, two models are relevant to this discussion.

CCM Results Framework

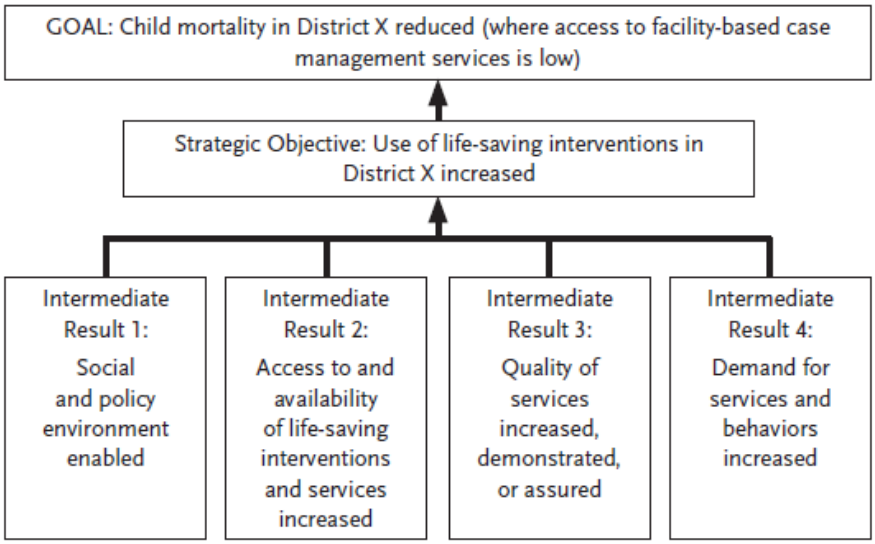


Figure 4: CCM Results Framework (CORE et al., 2010)

The strategic objective is the centre of the results framework (figure 4), the service or commodity with a beneficial impact on health status that the beneficiaries should use. "Use" includes both receiving the intervention and adhering to its administration at home. The goal is the ultimate purpose or "why" for a programme - saving lives (CORE et al., 2010).

The four intermediate results are essential and interrelated steps toward achieving the strategic objective. They are the activities and strategies that lead to increased use. These intermediate results can be described as follows:

- An enabled environment in which social and political factors at all levels (community to national) encourage and support CCM.
- Increased access to interventions and services resulting from reducing barriers (geographic to social) to obtaining treatment services for childhood illnesses.
- Increased quality - the technical quality of services is high and communities perceive the services to be of good quality.
- Increased demand - awareness of CCM services; timely recognition of illness and care-seeking; and effective home management of sick children.

The Access Framework

This framework (figure 5) addresses the interplay of factors that influence access to healthcare once illness has been recognised and a decision made to seek care. Five dimensions of access influence the course of the health-seeking process: Availability, Accessibility, Affordability, Adequacy, and Acceptability. The degree of access reached along the five dimensions depends on the interplay between (a) the health care services and the broader policies, institutions, organisations, and processes that govern the services; and (b) the livelihood assets people can mobilise in particular vulnerability contexts. However, improved access and health care utilisation have to be combined with high quality of care to reach positive outcomes. The outcomes can be measured in terms of health status (as evaluated by patients or by experts), patient satisfaction, and equity (Obrist et al., 2007).

This thesis examines issues of availability, accessibility, and acceptability of CHW services by caregivers of febrile under-five children on the one hand, as well as utilisation of CHW services and the health outcomes resulting from the consumption of these services on the other. While the central theme of my thesis was not access, this framework articulates in a very clear way the inter-linkages between access, utilisation and health outcomes, all important concepts addressed in my four sub-studies.

I found that this framework was the most appropriate in helping me relate the different parts of my work, and helping me to explain them. Therefore, the discussion of my thesis will use the *access framework* to explain how the various parts relate to each other.

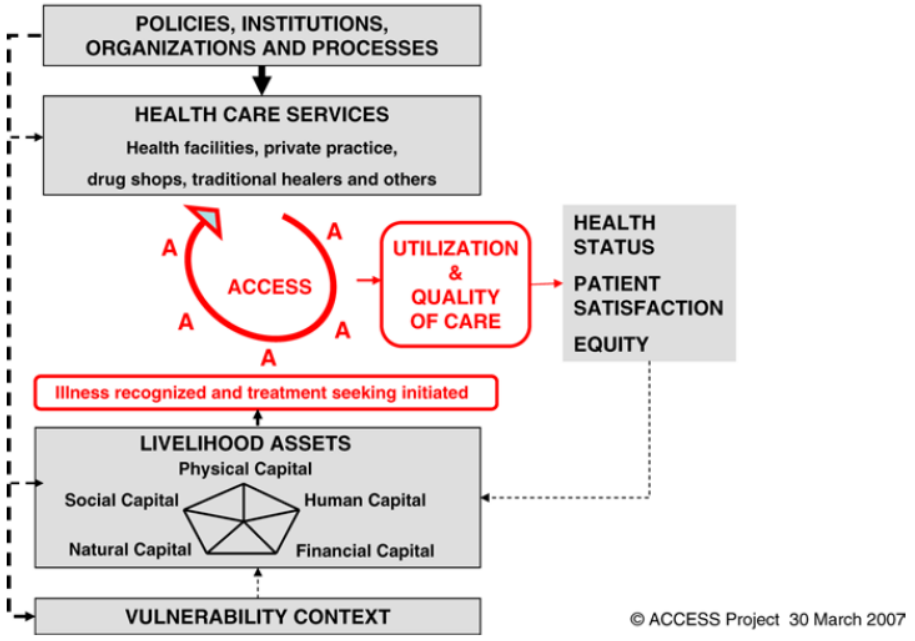


Figure 5: Access Framework (Obrist et al., 2007)

5 AIM AND OBJECTIVES

5.1 GENERAL AIM

To assess community acceptability and utilisation, provider competence, and the effectiveness of diagnostic-based integrated community case management of malaria and pneumonia in children, in order to inform the implementation of this strategy.

5.2 SPECIFIC OBJECTIVES

I. To assess community acceptability of the use of malaria rapid diagnostic tests by community health workers.

II. To assess the competence of community health workers to correctly assess, classify, and treat fever due to malaria and pneumonia following training.

III. To assess household access, acceptability and utilisation of diagnostic-based integrated community case management of fever following implementation.

IV. To determine the effectiveness of diagnostic-based integrated community case management of fever versus standard presumptive case management of fever.

6 METHODS

6.1 STUDY AREA AND POPULATION

The studies were conducted in Iganga district located in south eastern Uganda, approximately 112 km from Kampala, the capital city of Uganda (Figure 6). The information provided here refers to Iganga district in 2008, when study implementation started, before the district was further sub-divided. The district covers a total area of 1680 square kilometres, much of which is land and swamps. Its population of approximately 600,000 consists mainly of subsistence farmers. The leading causes of morbidity and mortality among under-five children are malaria, pneumonia and diarrhoea (Iganga District, 2008).

Iganga district is served by a 200-bed capacity hospital, and 81 health centres at county, sub-county and parish level. The main local language spoken in the district is Lusoga. The study was conducted in the sub-county of Namungalwe, which has a total population of 32,911 in seven parishes and 19 villages.

Figure 6: Map of Uganda showing Iganga district shaded green

Data for Study IV was collected at two additional sites in Burkina Faso and Ghana, in the districts of Saponé, and Kassena Nankana respectively. Saponé and Kassena Nankana are situated in the Sudan-Sahelian eco-climatic zone, with a seasonal malaria transmission pattern peaking during the wet months of May – September, while Iganga has a savannah climate, with all year malaria transmission (MARA/ARMA, 2005).

6.2 STUDY DESIGN AND DATA COLLECTION METHODS

6.2.1 Study Design

Data were collected after the policy shift from CQ/SP to ACTs as first line treatment for malaria. Although nation-wide training of CHWs in use of ACTs had not been undertaken, the study area had been involved in an ACT pilot (Ajayi et al., 2008) during which CHWs in the area were trained and provided with ACTs. During implementation of Study IV, a new policy on integrated community case management of pneumonia, malaria and diarrhoea was adopted by the Uganda Ministry of Health (MOH Uganda, 2010b). Figure 7 shows the study implementation timelines.

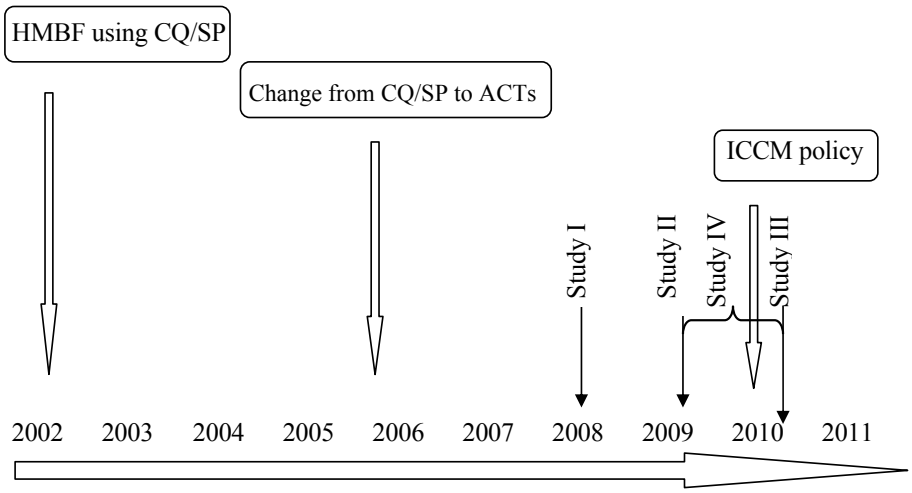


Figure 7: Timeline of the studies in relation to Ugandan national policies

Both qualitative and quantitative methods were used. Focus group discussions (FGDs) and key informant interviews (KIIs) were held to understand community perceptions and acceptability of the introduction of malaria RDTs into iCCM (Study I). A case series design (Carey and Boden, 2003, Kooistra et al., 2009) was used to assess CHW skills and competencies to assess and manage malaria and pneumonia using diagnostics (Study II). To assess household utilisation of the diagnostic-based iCCM package a cross sectional design (Study III) was used, while for estimation of the effectiveness of the integrated package on fever clearance, a cluster randomised design (Study IV) was used.

Description of the Intervention

Training: CHWs were taught how to take history; recognise clinical features of uncomplicated malaria and signs of severe illness requiring referral; prepare thick blood films for malaria microscopy; use of classification and treatment algorithms for malaria and pneumonia (intervention arm only); use of simple dosing guidelines based on age for ACTs and paracetamol; managing drug supplies; obtaining informed consent; and completing CRFs including documentation of reported signs and symptoms, physical examination results, and medications administered to the child. In cases where informed consent was declined, the child received standard presumptive management of fever with an ACT. The training was conducted for a total of five days for control arm CHWs, and eight days for intervention arm CHWs.

In addition, CHWs in the intervention arm were taught the clinical features of non-severe pneumonia; use of malaria RDTs; infection control measures; how to count respiratory rate using an ARI timer; and the use of simple dosing guidelines based on age for antibiotics.

There was interactive training consisting of oral presentations, discussions, role play and supervised hands-on practice for all the study CHWs. At the end of the training, facilitators assessed the competency of the CHWs to follow the algorithm, complete study forms, and for CHWs in the intervention arm the appropriate use of RDTs and ARI timers.

At the health facility level, health personnel were oriented on the treatment strategies in the two arms, and received refresher training on IMCI. These staff provided care to children referred from the study, and provided supportive supervision to the CHWs.

Treatment provided: In the intervention arm, treatment was provided on the basis of the test results. Children with a positive RDT received ACTs for malaria (artemether-lumefantrine in Burkina Faso and Uganda, and artesunate-amodiaquine in Ghana). Children with a high respiratory rate received amoxicillin in Ghana and Uganda, and cotrimoxazole in Burkina Faso. The criterion for antibiotic administration was the presence of a high respiratory rate, regardless of the presence of cough or difficult breathing, in contrast to WHO guidelines (WHO, 2005). All treatments were given for a total of three days. Additionally, paracetamol was provided to all children with a negative RDT and no fast breathing, and/or children with an axillary temperature > 38.5°C for two days.

In the control arm, all febrile children received ACTs presumptively. In Ghana, in line with existing practice, CHWs in the control clusters were also supplied with amoxicillin that they could provide to children with pneumonia based on clinical judgement.

Malaria RDTs used: First Sign® Malaria Pf Card Test (Unimed International, Inc), Paracheck Pf® Rapid test for *P. falciparum* Malaria (Device) (Orchid Biomedical System) and ICT® Malaria Pf Cassette test (ICT Diagnostics SA) were used in Burkina Faso, Ghana and Uganda respectively. First Sign®, Paracheck® and ICT® have panel detection scores (PDS) at parasite densities from 2000 parasites/μL of 86.1%, 97.5% and

97.5% respectively, and PDSs at parasites densities of 200 parasites/μL of 31.7%, 54.4% and 82.3% respectively (WHO, 2009).

Drugs used in the study: ACTs used in Burkina Faso were Coartem® manufactured by Novartis Pharma in Burkina Faso, in Ghana Acumal (artesunate-amodiaquine) manufactured by JCPL Pharma PVT Ltd, India, and in Uganda Coartem® manufactured by Novartis Pharmaceuticals Corporation Suffern, New York. Antibiotics used in the study were cotrimoxazole in Burkina Faso manufactured by Medicamen Biotech Ltd, India, Kinamox™ (amoxicillin) in Ghana manufactured by Kinapharma Ltd and in Uganda amoxicillin manufactured by Zhangjiakou Shengda Pharmaceutical Co Ltd, China (re-packed by Kampala Pharmaceutical Industries, 1996 Ltd). Paracetamol used in the study was manufactured by: Laborate Pharmaceutical (India) for Burkina Faso, Kinapharma Ltd for Ghana, and Kampala Pharmaceutical Industries (1996) Ltd for Uganda.

The first dose of all treatments was administered under the supervision of the CHW, and if the child vomited within 30 minutes they were given another dose. The dosing schedule (table 3) was explained to caregivers who then administered the remaining treatments at home.

Table 3: Drugs used in the Study

Drug	**Age**	**Dose D0**	**Dose D1**	**Dose D2**
Coartem™ 20/120mg Artemether/Lumefantrine	4-35 mo	1x2	1x2	1x2
	36-59 mo	2x2	2x2	2x2
Trimethoprim/Sulphamethoxazole 120mg Tab 3 day regimen*[12]	4-12 mo	2 x 2	2 x 2	2 x 2
	13-59 mo	4 x 2	4 x 2	4 x 2
Amoxycillin 250 mg Tab 25mg/kg/dose twice-daily[13] for 3 days[14,15]	4-12 mo	½ x 2	½ x 2	½ x 2
	13-35 mo	1 x 2	1 x 2	1 x 2
	36-59 mo	1½ x 2	1½ x 2	1½ x 2
Paracetamol 500 mg Tablet	<36 mo	¼ x 4	¼ x 4	
	36-59 mo	½ x 4	½ x 4	

6.2.2 Sampling, sample size, and Data collection methods

Study I – Community perceptions and acceptability of RDTs
Study I employed purely qualitative methods; FGDs and KIIs. A total of 10 FGDs and 10 KIIs were conducted. In FGDs, participants generally are allowed to say anything they would like. Focus groups therefore are considered to be naturalistic (Krueger and Casey, 2000). Focus groups can provide trustworthy naturalistic data that also lead to important insights about human behaviour, but they are not set up to generalise in the same way as survey research (Fern, 2001). The researcher listens not only for the content, but for emotions, ironies, contradictions, and tensions. This allows the researcher to learn or confirm not just the facts but the meaning behind the facts. People feel more relaxed talking when they see others who have similar experiences. Disadvantages include suppression of minority opinions and the researcher's misconceptions driving the group's interaction (Hardon et al., 2001).

FGDs with caregivers were conducted separately for mothers and fathers. Participants were mobilised by community leaders and purposively selected if they had ever cared

for a child with fever. FGDs took place in one of the homes of the participants to provide for privacy. The interviewer and the note taker were social scientists experienced in conducting FGDs, and spoke both English and the vernacular fluently.

Key Informant Interviews are used to discover the subjective meanings and interpretations that people give to their experiences (Rice and Ezzy, 1999). A Key Informant (KI) is an expert source of information. As a result of their personal skills, or position within a society, KIs are able to provide more information and a deeper insight into what is going on around them. An ideal KI should be one whose role in the community has exposed them to the kind of information being sought by the researcher; should have absorbed the information meaningfully; be willing to communicate their knowledge to the interviewer and to cooperate as fully as possible; be able to communicate their knowledge in a manner that is intelligible to the interviewer; and, be objective and unbiased (Marshall, 1996). In our study, KIIs were conducted with health workers and different community leaders. Neither the FGD participants, nor the KIs had seen or been exposed to an RDT, and prior to interviews, the RDT test was described to them.

Study II – Competence of CHWs to assess, classify, and treat malaria and pneumonia

Study II employed a prospective case series design. Case series belong to a group of descriptive studies that do not test the hypothesis of treatment efficacy (Carey and Boden, 2003). Case series serve as a means of initially reporting on novel diagnostic or therapeutic strategies, particularly when the option of waiting for comparative evidence is considered unacceptable. Treatment safety and diagnostic accuracy are the principal outcomes that can be assessed fairly and reliably in a case series (Kooistra et al., 2009). Strengths of case series designs include: high external validity, inexpensiveness, and short study time. The limitations are lack of a comparison group, data collected often incomplete (particularly for retrospective case series), and susceptibility to bias (Kooistra et al., 2009, Grimes and Schulz, 2002).

Two paediatricians and a laboratory scientist served as gold standards in Study II. The paediatricians had specialised post graduate training in paediatrics and had practiced for more than two years as paediatricians, while the laboratory scientist had practiced for more than five years on the bench. Previous studies (Simoes et al., 1997, Weber et al., 1997) have used paediatricians as gold standards in the evaluation of health worker performance in IMCI, as they are considered the clinical experts in child health issues.

All 14 CHWs trained in the use of diagnostics were observed assessing 13 children each, giving a total sample size of 182 child-observations. The inclusion criteria were any child under five years of age with fever or history of fever without danger signs. Under-fives were enrolled as they arrived at the health centre after registration at the outpatient department and after consent being given by their caregivers. Using standardised checklists, two paediatricians observed CHWs' performance on child assessment (history taking, signs and symptoms, temperature reading and rapid breathing), classification and treatment prescription, while a laboratory scientist assessed the use of RDTs. Each CHW was observed by one paediatrician and laboratory scientist, who had been trained in the use of the diagnostics and observation checklists. The ability of CHWs to use RDTs to detect malaria and respiratory timers to

diagnose pneumonia was estimated using a laboratory scientist's RDT repeat reading and a paediatrician's repeat count of the respiratory rate, respectively.
Sixteen indicators were used for history, four for ability to use a respiratory timer, and 14 to assess RDT use. Classification made and treatments prescribed by CHW were compared with those by the paediatrician.

Study III – Access, acceptability and utilisation of CHW services
Study III was a cross-sectional household survey conducted among caregivers of under-fives. The study population consisted of caregivers (parents or guardians of children), and all under-fives within selected households. We defined a caregiver as any person above 18 years of age who at the time of the study was directly responsible for the care of an under-five child eligible for this study, including the seeking of health services for at least three months preceding the survey.

A household was defined as a group of people at the time of the study that lived together and ate from the same cooking pot. Households that had recently (no more than 3 months) moved into the study area, child headed households, and households without under-fives were excluded from the study. A total of 423 households were selected to participate in the survey.

A household register was obtained from the village chairperson, and updated with the help of the chairperson and a village scout. The register was used as the sampling frame. From the sampling frame the required number of households for the survey (as determined by probability proportionate to size sampling (PPS)) (Levy and Lemeshow, 2008) was randomly selected using a table of random numbers.

Within selected households, all under-fives were included in the study. If a selected household was not eligible for the study, or declined the interview, the field team coordinator was contacted by the research assistant(s) via phone to provide a new household. A new household was then selected from the sampling frame. This was repeated for each village until the required sample per village had been enrolled.

A semi-structured questionnaire (English) was used to collect data from the caregivers. Data were collected by research assistants with experience in quantitative data collection. Research assistants were trained for one day in the survey methods for this study, how to replace ineligible households in the field, and completing the study questionnaire. The research assistants participated in the pilot testing of the questionnaire. The pilot was conducted in households that were not part of the pre-selected sample of households, and these did not participate in the final survey. Lessons from the pilot were used to revise the questionnaire to address issues of clarity and the logical flow of questions.

Recall periods of one and three months were used in this study. The one-month recall was used for purposes of eliciting responses to questions about the most recent fever episode in the under-five, and how this was managed. This was done to minimize recall bias because of the details expected from the respondents. We extended the recall period to three months for more general questions around health seeking choices made when under-fives had fever, reasons for choices, acceptability of diagnostics, as well as

estimating utilisation of CHW services, the primary outcome of this study. The extension was also driven by the fact that there had been a recent stock out of drugs among CHWs, that could have affected utilisation, and therefore a shorter recall period could result into an inaccurate estimate of utilisation.

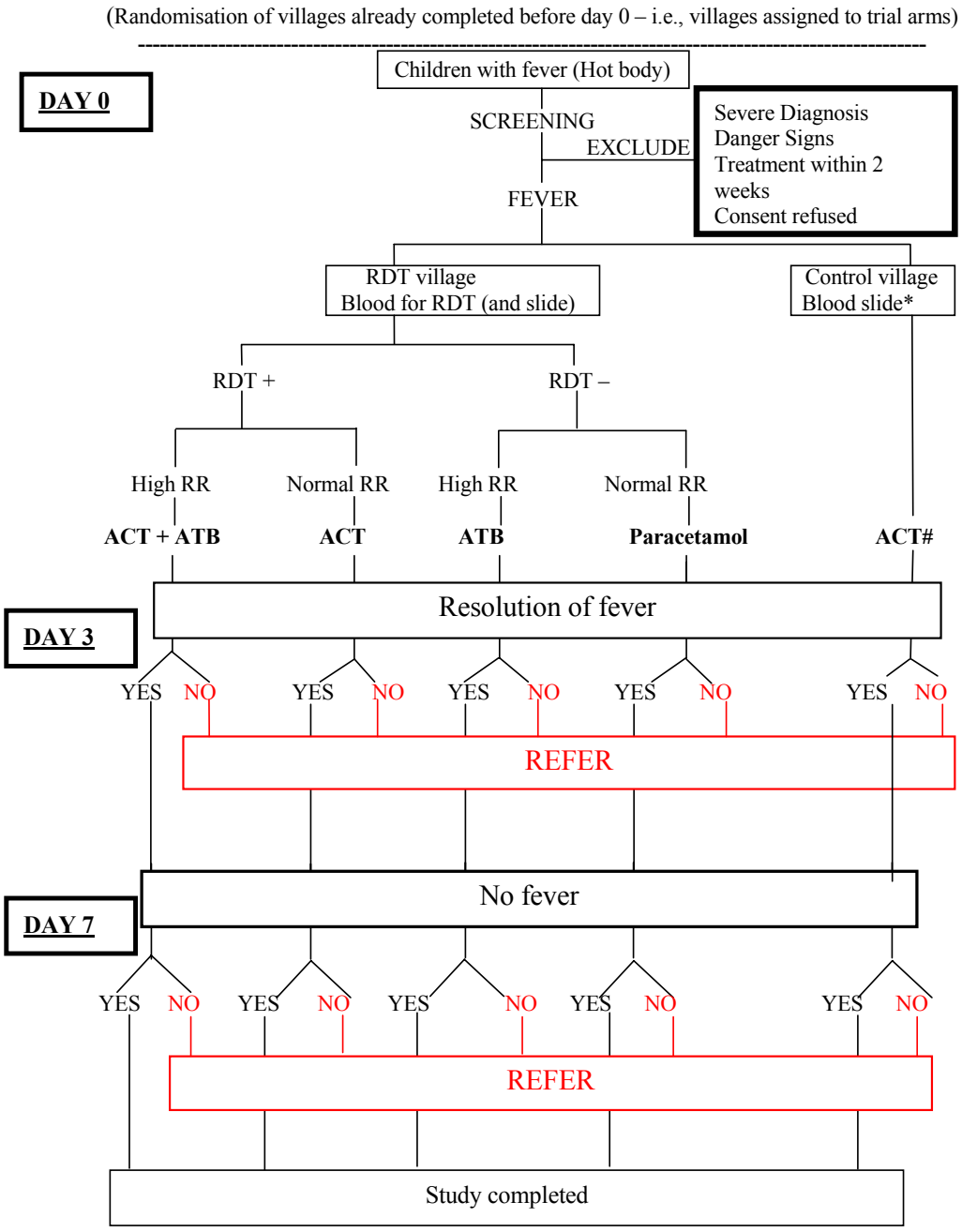
Study IV – Effectiveness of diagnostic-based iCCM
Study IV employed an open, cluster randomised trial (CRT) design (Cochrane Collaboration, 2002). There are a number of advantages of CRTs in the study of infectious diseases whereof one is that - CRTs are able to measure the overall effect of an intervention at the population level (Hayes et al., 2000).

The study was designed to assess the effect of the use of a diagnostic and treatment package for iCCM, comprising RDTs and ACTs for malaria, ARI timers and antibiotics for pneumonia on the clinical fever recovery rate, and the rational use of medicines. Clusters were the villages (catchment populations) of individual CHWs.

The estimated sample size for the study was 4,360 febrile children between 4 and 59 months, with Burkina Faso and Ghana contributing 1,200 each, and Uganda 1,960. The sample size was estimated using the simplified formula by Hayes and Bennett (Hayes and Bennett, 1999) for cluster randomized trials with a power of 80% to detect an absolute difference in fever clearance 72 hours after treatment of 10% (85% against 75%) between the two arms with a two-sided alpha of 0.05. The estimation took seasonality into account, as well as loss to follow up. We assumed a coefficient of variation between clusters of 0.12. Villages outside a 5km radius of a designated health facility used to refer sick children in the study were excluded.

CHWs reviewed children and completed the Case Record Form (CRF) on days 0, 3, 7 and on unscheduled visit days. A review on day 3 determined if a child had fully recovered clinically (resolution of temperature to below 37.5°C as measured by a digital thermometer). Children in either arm who had not recovered were referred to a designated health centre (figure 8). All children not referred at day 3 (clinically recovered) were reviewed on day 7, and any fever relapse cases were referred to the health centre. All children referred (day 3 or 7) were examined by a trained project nurse, and managed according to IMCI guidelines. Children who did not report to CHWs for scheduled visits were traced and assessed at home.

All children who were tested for malaria using the RDT on day 0 also had a thick blood film prepared by the CHWs. The blood films were collected within 24 hours in all the 3 sites. Blood films were stained with 10% Giemsa stain for 10-15 minutes and screened microscopically under X100 oil immersion lens using a light microscope by a microscopist trained by the study teams and based at the reference health centre. The number of parasites present per white blood cell was counted, and the figure multiplied by 8,000 (an average white blood cell count per µl) to give the parasite density (Greenwood and Armstrong, 1991). Slides were double read (by different individuals), and when there was a discrepancy between the two readings the slide was read again by an experienced / senior microscopist who was independent of this study and whose reading was considered final. The microscopy results were used to establish the accuracy of the RDTs when used in the communities.



*only for the sub-sample used for the microscopy comparison

Figure 8: Schematic flow of the Randomised Trial

6.3 DATA MANAGEMENT

For FGDs and KIIs in Study I, notes were written in the field, as well as tape recording done. While notes allowed us to report the non-verbal communication, the tape recording allows us to capture details of the discussions in an accurate way. The recording also frees the moderator from focusing on noting everything said, to noting important non-verbal communication. It also allows more eye contact between the moderator and the respondent (Holstein and Gubrium, 1995). All the KIIs were recorded and transcribed in English. FGDs with health workers were recorded in English, while the rest of the FGDs were recorded and transcribed in Lusoga. Two Lusoga speakers translated the Lusoga material into English.

The observations made during Study II were all recorded on observation checklists by the trained paediatricians and laboratory scientist. The CHWs completed a case report form for each child. The paediatricians abstracted some of the information from the CRFs and reported this on the checklist; for example, the classification made, and the medication prescribed by the CHWs as recorded on the CRFs.

For Study III, the questionnaires were field edited for errors by members of the study team, and corrections made in the field.

During the trial, for each child that was enrolled, the CHW completed a CRF. The CRF had their individual details including unique identifiers, the location of their home, details of assessment, and treatment they received, as well as their follow-up information. A referral form (in triplicate) was used for all children referred to the designate health centre. The CHW maintained a copy, while the caregiver delivered the other two to the health centre. The staff at the designated referral health centres were trained to check the details on the referral forms and to complete a section of the referral form with details of treatment given, and the outcome. The caregiver was given one copy of the completed referral form, which they kept. All the CRFs were kept by the CHW and collected by the study team on a regular basis. The completed referral forms kept at the health centre were collected on a weekly basis by the study team.

6.4 DATA ANALYSIS

Content Analysis: Manifest content analysis was used to categorise key issues out of the data in Study I. Manifest content analysis deals with the content aspect and describes the visible, obvious components (Downe-Wamboldt, 1992, Kondracki et al., 2002). The unit of analysis was the transcripts from FGDs and KIIs. The authors read through the data, identified different issues and debated them, and eventually developed codes. A second review of the material was done that generated more codes, which were discussed and agreed upon. These codes were merged into categories and then into themes reflecting the study objectives and other emerging issues.

In Study II, the proportion of CHWs who complied with the entire algorithm, as well as each part of the algorithm, was calculated. Indicators were measured for each part and given a uniform score of 1 for correct and 0 for incorrect. All indicators used were awarded uniform weight.

The total expected score (n) for each part of the algorithm was computed - the number of indicators multiplied by 13 (the number of children observed by each CHW) multiplied by 14 (number of CHWs). The total score obtained by CHWs (φ) is the sum of the scores obtained by each CHW. The kappa statistic (Cohen 1960) was used to estimate the proficiency of CHWs in reading RDT results, and counting respiratory rates, as well as the sensitivity, specificity and positive predictive value.

Kappa Statistic: is the most commonly used statistic for studies that measure the agreement between two or more observers. A kappa of 1 indicates perfect agreement, whereas a kappa of 0 indicates agreement equivalent to chance. A limitation of kappa is that it is affected by the prevalence of the finding under observation (Viera and Garrett, 2005, Landis and Koch, 1977).

In Study III, a social economic status (SES) index was calculated for all households using materials used for the house's roof, wall and floor. **Principal components analysis (PCA)** was used in constructing the wealth index. Materials used to construct floor, wall, and roof were used as a proxy; these are fewer variables than most often used, for example in the 2006 Uganda Demographic and Health Survey (Uganda Bureau of Statistics, 2006). A total of 8 dummy variables were constructed. STATA version 10 was used to generate weights for each of the variables. These weights were then multiplied with the dummy scores for each individual household and added to generate a score for each household. Households were divided into five wealth quintiles based on their SES score (Vyas and Kumaranayake, 2006). The household quintile was taken as a surrogate indicator for income.

The primary outcome was utilisation of CHWs services as the first healthcare option by caregivers. Secondary outcomes included: access to CHW services; caregiver reported treatment outcomes for CHW services; proportion of caregivers who approved the use of RDTs by CHWs; reasons for non-acceptance of use of RDTs by CHWs; and perceptions about use of ARI timers. Logistic regression analysis was used to explain the relationship between outcomes, and household plus caregiver characteristics. Odds ratios with their corresponding 95% confidence intervals were generated.

Intention to treat analysis: The main approach to the analysis of paper IV was by intention to treat analysis, an approach in which the treatment and comparison groups are analysed with respect to their random allocation, regardless of what happened subsequently. Participants were analysed as allocated regardless of whether or not they accepted and/or adhered to the intervention (Kirkwood and Sterne, 2003). We compared proportions of the study outcomes between the two groups. Odds ratios and 95% confidence intervals (CIs) were calculated using random effects logistic regression analysis with the treatment arm and country as fixed effects, and cluster as a random effect. The significance level was set at p-value ≤ 0.05.

Logistic regression allows for the effect of several independent variables to be estimated while controlling for several confounding factors. Random effect models explicitly model the similarity between individuals in the same cluster allowing for clustering, and are the best approach for analysing clustered data (Kirkwood and Sterne, 2003).

Linear predictor for an individual in cluster j = $\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_p x_p + \mu_j$

The random effect μ_j is assumed to have mean zero, and to vary randomly between clusters. It is assumed that the set of random effects (μ_j) explain the clustering in the data so that, having allowed for the random effects, different observations in the same cluster are independent. Random effects models are also known as multilevel models, because of the hierarchical data structure in which observations at the first level (the individual) are nested within observations at the second level (the cluster) (Kirkwood and Sterne, 2003). Random-effect models are now available in a number of statistical computer packages, and are fairly straightforward to fit.

Sub-group analysis: analysis of groups of individuals within a trial population on the basis of characteristics that may influence the outcome (Wang and Bakhai, 2006). These characteristics may be individual (age, sex, etc) or level of compliance in the trial or occurrence of a specific outcome.

6.5 SUMMARY OF METHODS

Table 4 shows the summary of methods used in this thesis.

Table 4: Summary of Methods

Title of study	Methods	Study population and sample size	Data Analysis	Year of field work
I. Community acceptability (blinded)	Qualitative - FGDs and KIIs	10 FGDs - CHWs & caregivers 10 KIIs - health workers & community leaders	Manifest content analysis. Generated codes and themes.	2008
II. Competence of CHWs	Prospective case series	14 CHWs, 182 observations	Univariate and bivariate. Total score for each part of the algorithm vs a *gold standard.* Generated frequencies proportions, kappa-statistic & chi-square values.	2009
III. Access, acceptability (unblinded) and utilisation	Cross sectional	Caregivers of under-fives in 423 households	Uni-, bi- and multivariate (logistic regression) Principal components analysis (PCA). Generated frequencies proportions, odds ratios	2010
IV. Effectiveness of diagnostic-based ICCM	Cluster Randomized Trial	4216 children 4-59 months old	Intention to treat, multivariate logistic regression generating odds ratios. Proportions	2009-2010

6.6 ETHICAL ISSUES

Ethical approval for the studies was obtained from the World Health Organisation Ethical Review Committee (WHO TDR project numbers are A60486 for Burkina Faso, A60490 for Ghana and A60487 for Uganda), Makerere University School of Public Health Institutional Review Board (4/36/2006), and the Uganda National Council for Science and Technology (Number: HS230). Approval was obtained from district, local, and community leaders as well as household heads. Informed consent was obtained from caregivers of children and other respondents who participated in the studies. Confidentiality was maintained throughout data collection, management, analysis, and reporting. The trial was registered online at http://register.clinicaltrials.gov with the registration number NCT00720811.

Drawing of blood from under-fives by CHWs was a key ethical concern. To address this problem, we ensured CHWs were adequately trained and examined before being allowed to practice. CHWs were also provided with protective material such as gloves, and waste disposal boxes. The research teams collected the waste materials on a regular basis. To protect the CHW families, the waste disposal boxes were placed at points beyond the reach of children in the CHW homes.

The risk of denying anti-malarial treatment to children with false negative RDT results was another ethical concern. To address this potential problem, all children in the intervention arm had a thick blood smear done at the time of preparing the RDT. These smears were collected daily by the study teams from the CHWs, and taken to the health facility for microscopy. All children with RDT negative results, who had a positive blood smear had the results returned to the CHW within 24 hours by the study team. These children were traced and treated at home. Caregivers were encouraged to return to the CHW at anytime they felt the child was not improving or getting worse.

Records for all children enrolled into the study were maintained on a CFR that identified the child's home for ease of tracing by the CHW.

7 RESULTS

7.1 COMMUNITY PERCEPTIONS AND ACCEPTABILITY (I)

Study I investigated how communities in Iganga district Uganda perceive the role of CHWs. The study also investigates how RDTs handled by CHWs would be accepted by communities in Iganga district. The utility of RDTs within the frame of community case management of malaria is dependent on their acceptability by communities. The study also provides information about problems associated with drawing blood from children, and challenges anticipated to be faced by CHWs.

This paper had four key findings: (1) CHWs (called community medicine distributors under HBMF in Uganda) are trusted by their communities because of their spirit of volunteerism, accessibility, and the community's perception of the effectiveness of the anti-malarial drugs they distribute; (2) community members, health workers and CHWs welcomed the use of RDTs by CHWs who have some formal education and have been well trained to use RDTs; (3) some community members had fears that the finger-pick to draw blood for the RDT could expose children to HIV, that the blood could be used to test their children for HIV, or that the blood could be used for witchcraft; (4) CHWs may face challenges with transport for follow up of patients and re-stocking of supplies, adults may demand to be tested as well, and in instances where children will require referral, caregivers may insist they be treated rather than be referred.

The commitment demonstrated by CHWs through volunteering time to serve their communities endeared them to their community members. The community trusts them because they are not 'trying to make money'. On the other hand, although CHWs are not paid for their services, their standing and respect in the community motivates them to serve. Their previous experience with distribution of HOMAPAK® and Coartem®, and the perceived effectiveness of the drugs reassured the community.

> "According to me, they [CHWs] have done commendable work. They have a good relationship with the people and they have helped them a lot. They have been effective in distributing HOMAPAK® and Coartem®. I heard that the tablets are to be distributed freely and they are doing it - they fulfilled the intention. My twins are making 3 years and I've never taken them to hospital. They are treated at home and given Coartem®. They [CHWs] have never asked for money for treatment." (KI, community leader)

CHWs are accessible physically and socially as expressed by this health worker:

> "They [CHWs] carry out health education among community members like recently they gave out mosquito nets. They go and train people on how to use those mosquito nets. They also check the child's temperature using their palms and when they suspect malaria, they give them treatment. In the communities, they are seen as extending services nearer to the people instead

> of coming to the health centre every time a child falls sick. It is an advantage to them." (KI, health workers)

The CHWs expressed willingness to use the RDTs, and health workers and the community supported the idea provided they are well trained.

> "I would second it provided they are trained to do it safely. It is very important. I recommend them to people who are very lazy [with poor health-seeking behaviour] in taking children to hospitals. If it is done from there, you will be bringing services nearer to the people. Secondly, our people have a tendency of thinking that if one has malaria, it is cheap to buy drugs from the clinics, yet not sure of the type [or severity] of malaria s/he is treating. So, if those people [CHWs] start testing blood, it will help them a lot." (KI, community leader)

> "If they know that we have been trained, they will accept [the use of RDTs]. Even for the giving out drugs they first resisted but later accepted." (FGD, CHWs)

Even though most community members were positive towards the use of RDTs by CHWs, many had mixed feelings about the taking of blood from children. The fear included concerns that their children could get infected with HIV in the process of undertaking an RDT and that the blood could be used to test children for HIV rather than malaria.

> "People have fears about blood and that it can lead to contracting HIV. It would also imply to some people that when they prick to test the blood, they think you are testing for HIV but not malaria. They believe you can prove malaria by mere looking at signs like vomiting, shivering, diarrhoea and other basic signs." (KI, community leader)

Given the tasks that the CHWs are given, views regarding the challenges that CHWs are likely to face were solicited. The reported challenges that were foreseen included that CHWs will lack transport for follow up of patients and for replenishment of supplies from the health facilities; that adults will try to force CHWs to also test them for malaria; that caregivers will insist that CHWs treat their children even when the child needs referral; and that some leaders will try to seek for favours for themselves and their relatives.

> "I have seen some of them [CHWs] walking all the way to the health centre to get drugs, and when following up children. They need to be assisted with transport for drugs". (FGD, male caregivers)

> "These tests [RDTs] will create a lot of interest. I am concerned that adults will also demand to be tested. I think also some of our people will insist that their children are treated when they should be referred as now CHWs will be seen as "little doctors" who can take blood and examine it". (KI, community leader)

Findings from Study I were used to develop appropriate communication messages for a community engagement campaign prior to the intervention (IV). We used village and opinion leaders, health workers and CHWs themselves to address community concerns expressed in Study I, and educate the community about the intervention**.**

7.2 CHW COMPETENCE IN USING DIAGNOSTICS (II)

In Study I, one of the main caveats to community acceptability of CHWs' use of RDTs was that they must be well trained. Study II examines the competency of CHWs to use an integrated algorithm for malaria and pneumonia case management to assess, classify and prescribe treatment to febrile children. The assessment of children included use of malaria RDTs and respiratory rate timers.

Using timers for measuring respiratory rate
When comparing classification of respiratory rates (normal and fast breathing) between CHWs and paediatricians for each child, six of the 14 CHWs had 12 or more readings in concordance, while the others had concordances ranging from 7 to 11. No CHW repeated a respiratory rate count as per training guidelines. As shown in table 5, CHW readings (classified as fast breathing or not) were 84.6% (154/182) in agreement with the paediatrician ($\kappa = 0.665$ and $p < 0.001$); 64% (116/182) of CHW respiratory rates were within ±2 breaths/minute of the paediatrician's. Differences in CHWs respiratory rates were due to child changing posture during counting (most common), breastfeeding, crying or restlessness.

Table 5: Classification of children by CHW with and without fast breathing against gold standard

	Gold Standard		Totals (row)
CHW	Fast Breathing	Normal Breathing	
Fast Breathing	51	16	67
Normal Breathing	12	103	115
Totals (column)	63	119	182

CHW, community health worker
$\kappa = 0.665$, $p < 0.001$

The sensitivity and specificity of the CHW classification was 81% (51/63) and 86.6% (103/119) respectively. The positive predictive value was 76.1% (51/67).

Using a rapid diagnostic test for malaria
CHWs' RDT readings were all (182/182) in agreement with the laboratory scientist – 138 were positive, 40 were negative and four were invalid. The four invalid results were repeated and found to be positive. Malaria prevalence in this population of children was therefore 78% (142/182).

Table 6 summarises the performance of CHWs in assessing, classifying (as having malaria or pneumonia), and treating children. Overall CHWs' performance was adequate in taking history, use (following procedures prior to reading result) of timers and use of RDTs. Overall CHW performance was however inadequate in classification of children as having malaria or pneumonia on the basis of the gold standards' (paediatrician and laboratory scientist) measurements using the two tests.

Table 6: Performance of CHWs in assessing, classifying and treating children with malaria and pneumonia

Area of performance	**Overall performance (total score (φ) ÷ Maximun score (n))**	**Percentage**
Taking history	2816/(208*14)	97%
Use of timers	699/(52*14)	96%
Use of RDTs	2453/(182*14)	96%
Classification	158/(13*14)	87%
RDT reading	182/182	100%
Child with +RDT test prescribed an ACT	85/86	96%
Children with fast-breathing prescribed an antibiotic	4/10	40%
Children with +RDT test & fast-breathing prescribed ACT and antibiotic	48/53	91%
Children with -RDT test & normal breathing prescribed ACT or antibiotic	3/30	10%

φ – sum of the scores for each CHW (i.e., sum of scores of each of 13 children observed by CHW, for all 14 CHWs).
n – total expected score i.e., the number of indicators multiplied by 13 (the number of children observed by each CHW) multiplied by 14 (total number of CHWs).

Over 90% of RDT positive children, as well as those who had an RDT+ result and fast breathing were prescribed appropriate treatment. However, only 40% of children with fast breathing were prescribed an antibiotic.

On the basis of CHW classification of the children as having malaria, pneumonia or neither of the two, 99% (82⁄83) of children classified as having malaria only by the CHW were prescribed an anti-malarial drug; all (7⁄7) children classified as having pneumonia only an antibiotic; and 94.7% (54⁄57) classified as having both conditions were prescribed both medicines.

A total of 20 children were excluded from the study for being too ill. Table 7 shows how CHWs performed in managing referral for these 20 children.

Table 7: CHW Performance in managing referral cases

Variable	**Frequency (n=20)**	**Percentage**
CHW provided appropriate referral advise Yes	18	90
CHW provided referral note Yes	19	95
Caregiver accepted referral Yes	19	95

Under-performing CHWs (score below 80% for any part of the algorithm) were retrained at end of Study II before they were provided with suppliers and sent home to start practicing (IV). The training emphasised individual CHW areas of inadequate performance.

7.3 COMMUNITY ACCESS, ACCEPTABILITY AND UTILISATION (III)

In Study III, a household survey was undertaken to investigate household access, utilisation and acceptability of diagnostic-based iCCM. Study III was conducted in the areas where the 14 CHWs evaluated in Study II (intervention arm) practised diagnostic-based iCCM.

Using the type of material used to build the main family house as a proxy for income, grass roofs, mud walls and mud floors were common at the lower end of the index, while iron sheets, plastered walls and cemented floors were common at the upper end of the distribution (table 8). The distribution of households across different quintiles was as follows: Q1 (21.3%), Q2 (24.1), Q3 (26.7%), Q4 (18.7%), and Q5 (9.2%).

Table 8: Composition of unique assets values

		Type of materials used on the main house		
Closest to	Index value (score)	Roof	Wall	Floor
Lowest value	-4.275	Grass	Mud	Mud
25th pecentile	-0.648	Iron sheets	Bricks/Mud	Mud
Median	0.150	Iron sheets	Bricks/cement	Mud
75th pecentile	1.417	Iron sheets	Bricks/Mud	Cement
Highest value	2.539	Iron sheets	Plastered cement	Cement

Access: Most (86%, 365/423) households resided within 1 km of a CHW's home, compared to 26% (111/423) residing within 1 km of a health facility ($p<0.001$) (figure 9). The median reported walking time by caregivers to a CHW was 10 minutes (IQR 5-20).

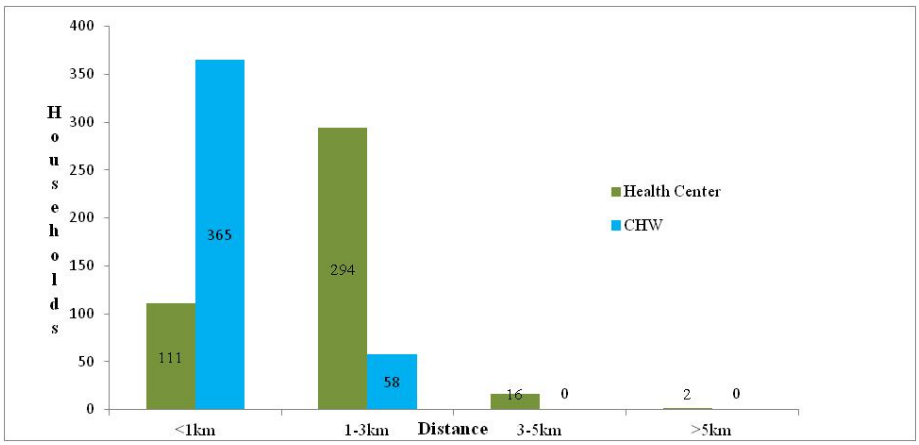


Figure 9: Household access to health facilities and CHWs

Demand for and satisfaction with CHW services: Forty percent (242/601) of caregivers with febrile children chose the CHW as their first option for care in the month preceding the survey, followed by drug shops (33%; 196/601). Convenient location (50.8%; 305/601) was the most important reason for choice of provider.

Among the caregivers whose first option for care was a CHW, 97.9% (237/242) reported that they were satisfied with the service they received. The main reasons for satisfaction were: availability of drugs (89.5%; 212/237), use of RDT (73.4%, 175/237), and use of ARI timers (60.8%, 144/237).

Household utilisation of CHW services: Household utilisation of CHW services was estimated at 57% (243/423) for the three month period preceding the survey. Table 9 shows the association between household characteristics and utilisation of CHW services. Households located at least 1 km from a health facility were 60% (OR 1.60; 95% CI 1.04-2.49) more likely to utilise CHW services compared to households within 1 km of a health facility. Households located 1-3 km from a CHW were 80% (OR 0.19; 95% CI 0.10-0.36) less likely to utilise CHW services compared to those households residing within 1 km of a CHW.

Table 9: Association between household characteristics and utilisation of CHWs

Variable	**Utilised CHW**		**OR (95% CI)**	**p-value**
	Yes n=243	**No n=181**		
Distance to nearest Health Centre				
< 1 km	54	57	1.00	
≥ 1 km	189	124	1.60 (1.04-2.49)	0.032*
Distance to nearest CHW				
<1 km	229	137	1.00	
1-3 km	14	44	0.19 (0.10-0.36)	<0.001*
Education of head of household				
Never	25	20	1.00	
Primary	165	128	1.03 (0.54-1.94)	0.924
Secondary above	53	83	1.28 (0.62-2.67)	0.502
Occupation of head of household				
Employed/self employed	21	9	1.00	
Farmer	199	162	0.53 (0.23-1.18)	0.120
Other/Casual	23	10	0.99 (0.34-2.90)	0.979
Indicator for SES				
Poorest (quartile 1)	49	41	1.00	
Second (quartile 2)	55	48	0.96 (0.54-1.69)	0.884
Middle (quartile 3)	73	40	1.53 (0.87-2.69)	0.143
Fourth (quartile 4)	44	35	1.05 (0.57-1.93)	0.870
Richest (quartile 5)	22	17	1.08 (0.51-2.31)	0.837

Adherence to test results by CHWs and caregiver trust in test results
Of the 243 respondents who took a child to a CHW in the three months preceding the survey, 88.9% (216/243) said CHWs administered drugs based on test results, 7.8% (19/243) said "No, they did not" while 3.3% (8/243) did not know.

Ninety-five percent (230/243) of respondents said they trust the tests. Among those who said "No", the most commonly mentioned reasons were: CHW did not do the test (6/13); CHW did not explain results (3/13); and, "my child did not improve" (2/13).

Acceptability of diagnostics: 88.6% (375/423) of all caregivers interviewed, and 98.8% (240/243) of caregivers that had visited a CHW would like CHWs to continue using malaria RDTs. A majority (99.1%; 419/423) of respondents said they had no fears or concerns regarding drawing of blood from children by CHWs. Among the four respondents who had fears, the reasons were: the agony of pain suffered by the child and concerns about CHWs' safe use of RDTs without causing infections. Safety was an issue that emerged in Study I and although reported by a very small number of caregivers, it recurs in Study III.

7.4 EFFECTIVENESS OF INTEGRATED STRATEGY (IV)

Following the training and evaluation of CHWs in Study II, the 14 CHWs were equipped to implement diagnostic-based iCCM in Study IV. Another 14 CHWs were trained to provide standard presumptive case management of malaria with ACTs. In Study IV, the diagnostic-based iCCM was compared with standard care using fever clearance as the primary outcome, and rational use of drugs as a secondary outcome. Study IV includes data from two additional sites in Burkina Faso and Ghana (using same protocol), all funded by WHO/TDR. A total of 2,084, and 2,132 under-fives were enrolled (figure 10) into the intervention and control arms of the study respectively.

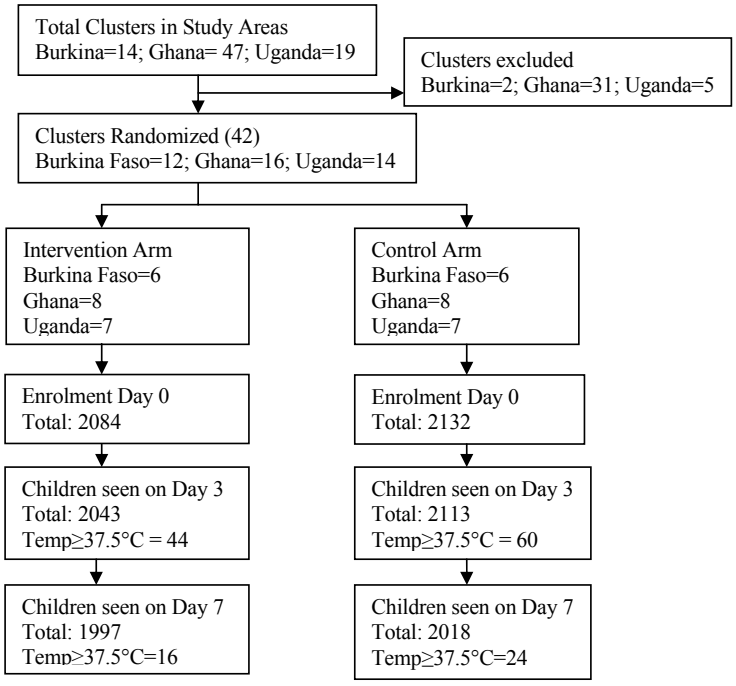


Figure 10: Study Profile

Impact of diagnostic-based iCCM on fever clearance

Fever clearance was better in the intervention arm (31% reduction in odds of having fever at Day 3) compared to the control arm. This difference was however not statistically significant (table 10). Results were generally similar at Day 7 between the two arms.

Table 10: Fever persistence on study day 3 after onset of treatment

Arm	Children with temp ≥ 37.5°C or history of hot body on day 0	# of children seen at day 3	Temp ≥ 37.5°C on day 3 (% of children seen at day 3)	OR, 95% CI	P-value
Intervention	2084	2043	44 (2.2)	0.69, 0.41-1.16	0.17
Control	2132	2113	66 (3.1)		

Due to concerns about the use of antibiotics in the control arm in Ghana diluting the effect of the intervention, we conducted a sub-group analysis with Ghana data excluded (table 11). Fever clearance was significant higher in the intervention arm with a 41% reduction in odds of having fever at Day 3 compared to the control arm (OR 0.59, 95% CI 0.38-0.93).

Table 11: Fever persistence on study day 3 after onset of treatment (Burkina Faso and Uganda data only)

Arm	Children with temp ≥ 37.5°C or history of hot body on day 0	# of children seen at day 3	Temp ≥ 37.5°C on day 3 (% of children seen at day 3)	OR, 95% CI	P-value
Intervention	1500	1465	34 (2.3)	0.59, 0.38-0.93	0.02
Control	1541	1522	58 (3.8)		

Use of medicines by CHWs

There was good compliance with RDT results in the intervention arm across the three sites. Only 1 case out of 1,740 RDT positive children did not receive an ACT, while only 4.9% (17/344) of RDT negative children were prescribed an ACT. In the control clusters, ACTs were given to all children in all countries, leading to potential unnecessary prescription of ACTs in 25.6%, 15.8% and 12.1% of cases in Burkina Faso, Ghana and Uganda respectively (assuming a similar proportion of RDT negative cases in the control and intervention clusters). Considering actual use of ACTs in the intervention arm, the intervention saved ACTs in 16% (334/2084) of cases.

Among children with a high respiratory rate, antibiotics were administrated to 86.5% (198/229) in Burkina Faso, 72.5% (103/142) in Ghana, and 98.3% (520/529) in Uganda.

Among children with high respiratory rates, we analysed data within the subgroup that also had a cough; 84% (105/125) in Burkina Faso, 82.1% (32/39) in Ghana, and 99.1% (334/337) in Uganda of these children received an antibiotic. The overall rate of antibiotic underuse in this subgroup was only 6.0% (30/501).

There were varying degrees of antibiotic overuse (prescription to a child with a normal respiratory rate) in Burkina Faso, Ghana and Uganda, with 38.5% (114/296), 44.6% (197/442), and 0.9% (4/446) of children with normal respiratory rate receiving an antibiotic respectively.

In Ghana, where CHWs could prescribe antibiotics in control clusters based on their clinical judgement, 64.3% (380/591) of children were treated with antibiotics in control clusters compared to 51.4% (300/584) in intervention clusters (OR 1.7, 1.34-2.17; $p<0.001$).

8 DISCUSSION

8.1 MAIN FINDINGS

This thesis assessed community acceptability and utilisation, provider competence, and the effectiveness of diagnostic-based integrated community case management of malaria and pneumonia in children in order to inform the implementation of this strategy. The key findings of the studies were:

1) Community members' acceptability and approval of use of malaria RDTs and respiratory rate counting by CHWs was high. Accessibility to CHWs was also high, with most households residing within 1 km of a CHW, and 10 minutes walking distance from a CHW home.
2) CHWs were the first option for care of febrile children, followed by drug shops, and their 3-month utilisation was over 50%. Residing close to a CHW and residing further away from a health facility were associated with utilisation.
3) CHWs' performance in taking history, using timers and RDTs was adequate, but inadequate in classification of illness. CHWs compliance with RDT results was very high with only one RDT positive child not receiving an anti-malarial drug, and very few RDT negative children were prescribed an anti-malarial drug across the three study sites. The intervention saved ACTs in 16% (334/2084) of cases in the intervention arm. Majority of children with a high respiratory rate received antibiotics; however, antibiotic overuse was high in Burkina Faso, and Ghana.
4) There was better fever clearance in the intervention arm compared to the control arm, with a 41% reduction in odds of having fever at Day 3 compared to the control arm.

In this chapter, the key findings are presented and discussed in relation to the access framework (Obrist et al., 2007) presented in Chapter four.

Acceptability: Acceptability and approval of use of malaria RDTs and respiratory rate counting by CHWs by community members was high. CHWs were trusted by communities because of their commitment, volunteerism, accessibility and perceived effectiveness of the drugs they provide. A multi-country study on the acceptability of ACTs in community management showed high community acceptability of CHWs (Ajayi et al., 2008). High acceptability of anti-malarial drug distribution through CHWs has also been reported from western Uganda (Kilian et al., 2003) and Ghana (Chinbuah et al., 2006). This high level of community acceptability of community management of fever programmes is likely a result of its convenience and low cost, given the fact that malaria risk is often highest in remote rural areas where the quality and coverage of health services is lowest (Bhasin and Nair, 2003).

The commitment demonstrated by the CHWs through volunteering time to serve their communities endeared them to their community members. In South Africa, volunteer caregivers derived intrinsic rewards related to self-growth and personal (emotional and psychological) development on the job; they also derived satisfaction from community members taking a liking for them and expressing a need for their services. Volunteers felt gratified by the improvements in their health behaviours, which were a direct consequence of the experiences of caring for terminally ill patients with AIDS. Extrinsic rewards came from appreciation and recognition shown by patients and community

members. Extrinsic rewards also accrued to volunteers when the services they rendered made their patients happy. Perhaps the greatest sources of extrinsic rewards are skills and competencies acquired from training and experience while caring for their patients, and volunteers' ability to make a difference in the community (Akintola, 2010). In Nepal, stakeholders saw volunteers as motivated primarily by social respect, religious and moral duty (Glenton et al., 2010).

Communities welcomed the use of RDTs by CHWs, emphasising the need for training and health system support to CHWs. Communities would like to see CHWs with some education at a minimum, trained to use RDTs. A study in Sudan found community acceptability of ACTs and RDTs in community management of fever to be high, with a marked increase in treatment-seeking behaviour following implementation (Elmardi et al., 2009). High caregiver acceptance and satisfaction with RDTs has also been reported from Tanzania (Williams et al., 2008), and the DRC (Hawkes et al., 2009).

Some community members expressed fears about CHWs using RDTs including, their children being infected with HIV, the blood used to test their children for HIV, and the blood being used for witchcraft. In Tanzania, though there was a high degree of provider and caregiver acceptance and satisfaction with RDTs, some caregivers had reservations about RDTs, with some thinking they were HIV test kits (Williams et al., 2008).

In order to address fears about CHWs drawing blood, findings from Study I were used to develop appropriate communication messages for a community engagement campaign. Village and opinion leaders, health workers and CHWs were used to address concerns of community members expressed about use of RDTs by CHWs ahead of Study IV.

In Study III, over 99% of caregivers interviewed had no fears or concerns regarding drawing of blood from children by CHWs. Similar findings have been reported from Zambia (Chanda et al., 2011). Concerns about CHWs' safe use of RDTs without causing infections emerged in this study as they did in Study I, but in less than 1% of respondents. It would appear that the community engagement campaign, as well as the contact by the community with CHWs using RDTs over the implementation period diminished community concerns and fears. The CHWs' safe handling of sharp instruments, use of protective gloves, use of hazard disposal bags, and the regular collection of the waste by the research team may have reassured the community about the safety of the process. This was possible in a research setting, and may be more difficult to implement in a real programme setting.

From Study III, most caregivers who visited a CHW trusted the test results. However, a study from the Solomon Islands on acceptability of RDTs reports a general distrust by the community of the accuracy of RDTs, resulting in continued presumptive treatment of malaria (Wijesinghe et al., 2011). From Study III, most of the respondents thought CHWs services were better with RDTs, and most approved CHWs' continued use of RDTs.

Accessibility to CHW services: Geographical accessibility to CHWs was high. Nearly 90% of households resided within 1 km of a CHW's home, compared with only 26% residing within 1 km of a health facility. It takes about 10 minutes for most caregivers to

walk to the CHW's home. The high geographical accessibility by households to CHWs suggests that the programme is meeting its goal of bringing services for febrile children as close as possible to their homes. CHW programmes have been reported to improve access to prompt treatment for febrile children (Pagnoni, 2009, Elmardi et al., 2009, Ajayi et al., 2008, Zuvekas et al., 1999).

CHWs (40%), followed closely by drug shops (33%) were the first option for care for febrile children in the month preceding the survey (Study III). Convenient location was the main reason for choice of first healthcare option. A spatial analysis conducted in Iganga district showed greater preference for treatment at home or at drug shops among caregivers living more than 3 km from health facilities (Ettarh et al., 2011). Similar findings have been reported by other authors from Uganda (Rutebemberwa et al., 2009b, Konde-Lule et al., 2006).

Utilisation of CHW services: Household utilisation of CHWs was high and more than half of caregivers took a febrile child to a CHW at least once in the three month period preceding the survey. Households located at least 1 km from a health facility were 60% more likely to utilise CHW services compared to households within 1 km of a health facility. Since programmes are designed to provide access to care for under-served, hard-to-reach communities, the CHW selection criteria will need to be carefully designed, so that under-served communities are selectively included. In well-served communities, CHWs could provide complementary services to the nearby facility, including health education, health promotion and referral services.

Households located 1-3 km from a CHW were 80% less likely to utilise CHW services compared to those households residing within 1 km of a CHW. These results strengthen the case for closing the geographical gap between healthcare provider and consumer. A systematic review of access and utilisation of health services shows that availability of drugs, distance to health facilities, and perceived quality of care are the key determinants influencing health service utilisation (Kiwanuka et al., 2008).

In the month preceding the survey (Study III), 40% of caregivers of febrile children went to the CHW as their first option, followed by drug shops at 33%. This is in contrast to findings by Rutebemberwa and colleagues (Rutebemberwa et al., 2009b) that showed the main providers of treatment for febrile children as drug shops/private clinics, and government health facilities, with very few caregivers going to CHWs. Although this study was conducted in the same district (Iganga), their data was collected during the period of policy transition from CQ/SP to ACTs at community level, and CHWs had limited supplies of at drugs. Study III followed a period of one year of full-scale implementation with only limited drug stock-outs. These scenarios are likely to explain the different utilisation rates.

Drug shops and private clinics continue to serve as a key source of treatment for febrile children. There is extensive literature from Tanzania (Alba et al., 2010a, Alba et al., 2010b, Sabot et al., 2009, Cohen et al., 2010), Kenya (Snow et al., 1992, Marsh et al., 1999), Uganda (Ndyomugyenyi et al., 2007, Rutebemberwa et al., 2009b) and elsewhere showing the important role that drug shops play as a source of care, especially for

malaria. It is important that providers in these outlets are well trained and supported to provide appropriate treatments. A study from Tanzania reports that surveyed drug shops illicitly sold SP and quinine, with very low sales of ACT (Ringsted et al., 2011). Some recent literature on the feasibility of introducing RDTs into drug shops reports mixed results (Chandler et al., 2011, Mbonye et al., 2010).

Satisfaction with CHW services: Community satisfaction with CHW services was high. In Study III, over 60% of all respondents interviewed thought CHW services were better than other health services for febrile children. Among those who visited a CHW in the 3 months preceding the survey, about 90% thought CHW services were better than other health services. Most caregivers who went to a CHW as their first point of care were satisfied with the service they received. The main reasons for satisfaction were: availability of drugs, use of RDT and ARI timers, the way the child was examined, and the way history was taken. Availability of drugs and use of diagnostics in this setting were key drivers of satisfaction. This is consistent with findings of a study from western Uganda (Nsabagasani et al., 2007) where both CHWs and caregivers agreed that diagnostic equipment at community level would improve diagnosis and attract more caregivers of febrile children. Caregivers do not want to go where there are no drugs, as they feel they are wasting time and will have to go to the next provider.

Quality of care: In Study II, CHW performance was adequate in taking history, use of ARI timers and RDTs, and reading RDT results but inadequate in classification of under-fives as having malaria or pneumonia. With regard to classification of children with and without fast breathing, CHWs were 85% in agreement with the paediatrician. Therefore, only 15% of paired breath count observations between the CHW and paediatrician fell on opposite sides of the cutoffs for age. In some situations, this was a result of borderline counts. A kappa of 0.67 reported in this study denotes good agreement between CHWs and paediatricians (Landis and Koch, 1977). There were however challenges with accurate breath counting. Similar findings are reported from a study from Western Uganda where 71% CHWs were within ±5 breaths/min from the gold standard and 79% classified the breathing rate correctly (Kallander et al., 2006a), as well as from Bolivia where the need for CHW training to emphasize counting respiratory was reported (Zeitz et al., 1993). Emphasis needs to be made regarding counting respiratory rates when the child is settled and not breastfeeding. Regular supervision of CHWs helps identify problem areas, and strengthen their skills through on-job retraining. Supportive supervision has been reported to impact positively on performance (Hill and Benton, 2010). Evidence from China and Sudan showed that with suitable supervision and provision of medicine, CHWs could manage ARI effectively including counting breathing rate, assessing chest in-drawing and giving antibiotics correctly to children with pneumonia (WHO, 2002).

Some CHWs had difficulty moving from classification of an under-five with or without fast breathing to assigning them as having pneumonia or not respectively. Wrong assignment to disease category invariably leads to wrong prescriptions. CHWs prescribed an anti-malarial drug to 96% of children with an RDT positive result, an antibiotic to 40% of children with fast-breathing, and both medicines to 91% of children with both an RDT positive result and fast-breathing. However, based on CHW classification of children, a reasonably high proportion of children with malaria and/or pneumonia were prescribed the correct treatment. This demonstrates the potential for improved treatment

if CHWs can be enabled to become more accurate in their classification. An IMCI evaluation found that incorrect diagnosis was a key problem which preceded two-thirds of all treatment errors (Osterholt et al., 2009). Once pneumonia was correctly diagnosed, failure to prescribe an antibiotic was unusual. Other studies from Tanzania (Nsimba et al., 2002), Bangladesh (Arifeen et al., 2005) and Burkina Faso (Krause et al., 1998) show poor health worker performance in history taking, physical examination and consultation time at primary healthcare facilities. Putting our results into context, performance of CHWs was satisfactory.

CHWs demonstrated a high degree of competence in preparation and reading of RDT results. Similar results have been reported from South America (Cunha et al., 2001, Pang and Piovesan-Alves, 2001), Asia (Yeung et al., 2008), and Africa (Premji et al., 1994, Harvey et al., 2008, Elmardi et al., 2009, Hawkes et al., 2009) where CHWs diagnosed and treated malaria in remote villages using RDTs. In our studies, the use of dummy fingers during the training helped CHWs in building confidence when practicing finger pricking. This was followed by CHWs working in pairs and pricking and drawing blood from each other to prepare an RDT and a blood slide.

CHW classification of under-fives into disease categories was 87% in agreement with the paediatrician (II). Some CHWs appeared to have difficulty linking diagnostic results to classification, in particular to relate assessment results with classification alternatives. Interpretation of thermometer readings in relation to the RDT might have confused some CHWs, particularly what classification to make of a child with a positive RDT with temperature below 37.5 °C (no fever) or a negative RDT with fever. Traditionally, CHWs are trained to use fever as a proxy for malaria.

Use of medicines: CHW compliance with prescription guidelines was reportedly high. From Study III, about 90% of caregivers who visited a CHW with a febrile child in the three months preceding the survey said CHWs administered drugs based on RDT test results and respiratory rate count. This was confirmed from Study IV, where good compliance with RDT results was documented in the intervention arm across the three sites, with only 5% of RDT negative children prescribed an anti-malarial drug. Considering actual use of ACTs in the intervention arm, the intervention saved ACTs in 16% of cases. In spite of concerns over inappropriate use of ACTs at community level (Maude et al., 2010, D'Alessandro et al., 2005, Charlwood, 2004), the results here point in a different direction which is in line with study findings from other settings where RDTs have been used at the community level, including Zambia (Yeboah-Antwi et al., 2010), Cambodia (Yasuoka et al., 2010), Tanzania mainland (D'Acremont et al., 2011, Ishengoma et al., 2011) and Zanzibar (Msellem et al., 2009). This may be explained by the availability of alternative treatment at community level, as well as the high likelihood for CHWs and similar types of health workers to better adherence to guidelines than formally trained health workers. In contrast, incomplete adherence to RDT results is lower at health facilities, and leads to substantial proportions of patients with negative tests receiving ACTs as has been frequently reported (Hamer et al., 2007, Chandler et al., 2010, Reyburn et al., 2007, Lubell et al., 2008, Chinkhumba et al., 2010).

Inappropriate use (non-compliance with treatment guidelines) of antibiotics was high in two of the three study sites. More than a third of children with a normal respiratory rate

received antibiotic treatment in Ghana and Burkina Faso, while 27% and 14% of children with high respiratory rate in Ghana and Burkina Faso respectively did not receive any antibiotics. However in Ghana, where CHWs could prescribe antibiotics in control clusters based on their clinical judgement, 64.3% of children were treated with antibiotics in control clusters compared to 51.4% in intervention clusters.

Overuse of antibiotics is a well-known phenomenon at all levels of the health system in low, middle and high income countries (WHO, 2011) and has been recently reported to be aggravated by the introduction of RDTs in the decision algorithm in health facility settings (D'Acremont et al., 2011). In Uganda, over- or under-prescription of antibiotics was rare, occurring only in 0.9% and 1.7% of cases. This difference between Uganda and the other sites may be explained by differences in the more intensive supervision of the CHWs. It is also possible that local antibiotic prescription practices influenced CHW behaviour. Vialle-Valentin and colleagues have reported higher antibiotic use among under-fives in Ghana compared to other countries, including Uganda (Vialle-Valentin et al., 2011). Several strategies have been shown to improve rational drug prescribing including: prescriber education (Avorn and Soumerai, 1983), and empowerment of consumers (Homedes and Ugalde, 2001). It will therefore be important for iCCM programmes to continually educate CHWs about rational use of medicines, as well as empower caregivers on issues of rational use of medicines so that they can demand for appropriate medicines from CHWs, and avoid putting pressure on CHWs to prescribe irrationally.

It is probable that the use of medicines may be different in settings with lower malaria prevalence, in which most of the RDTs would be negative. It will be important to explore this issue further across areas with varying transmission levels. The variation in use of medicines across the three sites suggests that unless strong and effective supervision is put in place, as was the case in Uganda, irrational use of antibiotics will compromise the viability of iCCM. Experience from the Ugandan study arm showed that regular supportive supervision by health facility and study staff; monthly meetings with health facility and study staff; and CHW peer supervision were extremely powerful in keeping CHWs motivated, focused, and performing well. In addition, the provision of mobile phones to CHWs and the set-up of 'a closed-user group' which enabled a real time communication line between CHWs, and between CHWs and study staff was effective in enhancing performance. A range of methods of supportive supervision, including the use of mobile phone communication, needs to be developed and evaluated, focusing on achieving defined supervisory functions (contact with staff, problem solving, training and follow up, outcome monitoring, coordination (WHO, 2002, Hill and Benton, 2010).

Performance of RDTs during the trial: The positivity rates for microscopy were consistently lower than those for RDTs across the three sites (Study IV), which means that there were false positives across the sites. This may be explained by the fact that all three RDTs used HRP2 as the target antigen which can persist in the blood stream for several days or even weeks after parasite clearance (Tjitra et al., 2001, Singh and Shukla, 2002, Mayxay et al., 2001, Swarthout et al., 2007), suggesting that some positive RDTs were indicative of past rather than current infection. The choice of which RDT to use was made for one of the following reasons: availability, resistance to high storage temperature (40^{o}C), delivery time, and national policy. The RDTs used were: FirstSign® in Burkina

Faso, Paracheck pf® in Ghana and ICT® in Uganda. It should also be noted that the RDTs used in the study sites were selected prior to the publication of a WHO document reporting on the performance of 67 different RDTs (WHO, 2009). The ranking of the panel detection scores (PDS) for the RDTs were 28 for ICT®, 49 for Paracheck® and 59 for First Sign® (WHO, 2009) indicating that none really achieved a high combined measure of positivity rate, along with inter-test and inter-lot consistency, although their PDS's were above 70/100.

A study conducted in Tanzania reports that the risk of a false negative RDT test was significantly lower among cases with fever (axillary temperature ≥37.5 °C). In this study, the risk of false positive RDT was significantly higher in cases with fever compared to afebrile cases (Ishengoma et al., 2011).

Impact of intervention on fever clearance: There was high fever clearance in both the intervention and control arms, with clearance slightly higher in the intervention arm. Consistently across the three study sites, over 96% of the children were afebrile at the follow up visits, with no detectable difference between intervention and control clusters. While a smaller proportion of children in the intervention arm remained febrile at days 3 and 7 compared to the control arm, the difference was not statistically significant.

There are several possible reasons of this result, the most likely being the use of antibiotics in the control arm in Ghana that could have diluted the effect of the intervention. The subgroup analysis that was conducted strongly suggested that the use of antibiotics in the control arm in Ghana is likely to have diluted the effect of the intervention, as there was a significant effect of the intervention on fever clearance when data from only Burkina Faso and Uganda were used, with a 41% reduction in odds of having fever at Day 3 compared to the control arm. This result means that diagnostic-based iCCM is better than presumptive management of all fevers as malaria. This evidence supports the introduction of diagnostic-based iCCM.

Other possible reasons for the absence of an effect seen when data from all three sites was analysed include the possibility of a high frequency of minor, self-limiting viral infections as the cause of fevers, that could have diluted the effect of specific anti-malarial and antibacterial treatment. Furthermore, in a context of high parasitaemia, it is possible that antibiotics might not have a substantial measurable effect on fever clearance. Similar results have been reported from a study in Zambia (Yeboah-Antwi et al., 2010) which found no evidence that the risk of persistence of fever differed in intervention and control clusters after 5 and 7 days of treatment. The Zambia study was however not design to measure the effect of the intervention on fever clearance as a primary outcome, but rather the effect of the intervention on use of medicines. Adding cough/difficulty breathing to our treatment algorithm would not have altered this since most under-fives who needed an antibiotic received one in the intervention arm, with under-use of antibiotics at only 6%.

8.2 CONSIDERATIONS IN RELATION TO MAIN FINDINGS

Cost effectiveness and potential role of RDTs
As parasite prevalence increases, it becomes relatively less cost effective to conduct a malaria diagnostic test before deciding on treatment. At some point - depending on the relative costs of the test and treatment - presumptive treatment becomes more cost effective (Drakeley and Reyburn, 2009).

Shillcut et al. have concluded that RDTs are cost-effective compared with presumptive treatment with at least 50% confidence when prevalence of malaria is below 81% and with 95% confidence when prevalence is below 62% (Shillcutt et al., 2008). Relative to microscopy, RDTs were more than 85% likely to be cost-effective across all prevalence levels. The cost-effectiveness of RDTs mainly reflected improved treatment and health outcomes for non-malarial febrile illness, plus savings in anti-malarial drug costs. Results were dependent on the assumption that prescribers used test results to guide treatment decisions (Shillcutt et al., 2008). In this setting RDT positivity was in the region of 70-80%, which means RDTs are cost-effective with at least 50% confidence based on the work by Shillcutt and colleagues.

One would also argue that the cost effectiveness models currently used do not take into account the benefits of targeted treatment resulting into reduced drug pressure with subsequent slowed drug resistance development. With treatment failure, the costs of second line regimes are often much higher. Taking these considerations into account could greatly increase the projected cost-effectiveness of RDTs. This is an area that requires future study.

Use of RDTs in iCCM will require some form of external quality assurance scheme. Facility-based microscopy may play an important role in this process. There will be need to transform malaria microscopy from a ‘low quality, high volume’ to a ‘high quality, low volume’ service that can direct and monitor treatment in severely ill patients and contribute to quality control of RDTs (Drakeley and Reyburn, 2009).

With the high overuse of antibiotics at two sites, it does appear that RDT use may shift unnecessary overuse of medicines from anti-malarial drugs to antibiotics. This has been observed at health facilities in Tanzania and Zanzibar were RDT use resulted in reduced anti-malarial drug use, but an increase in antibiotic use (D'Acremont et al., 2011, Msellem et al., 2009). However, the appropriate use of antibiotics in Uganda presents a different picture, and this issue will require further inquiry at community level as the Tanzania and Zanzibar studies were facility-based. The discussion around use of antibiotics at community level needs to take into account equity considerations, as well as the fact that when children with respiratory symptoms are not treated but instead referred from CHWs to health facilities, they take long to go and some children do not reach at all (Kallander et al., 2006b). Delayed care-seeking and use of anti-malarial medicines for ARI symptoms have been shown to be main risk factors for children dying of pneumonia (Kallander et al., 2008).

Motivation of CHWs
Motivation of CHWs is an important but complex subject. Countries need to make the investment in CHW programmes, understanding that CHWs are not a cheap alternative form of primary health care, but are an integral part of the health system. They add

value to basic medical services extending service coverage in an equitable and cost-effective way (WHO 1990).

Some authors have argued that intrinsic motivation (encompassing such feelings as empathy and altruism, and factors such as religious and cultural conviction) alone may be inadequate to provide continued motivation for CHWs (Kironde and Bajunirwe, 2002), and that extrinsic motivators, such as money, are required to keep sustained interest, particularly in resource-limited settings. In some settings, TB volunteers have initially offered their assistance without monetary incentives hoping that there will eventually be remuneration, and when this does not materialise, attrition rates are high (22%), with three quarters leaving for this reason (Kironde and Klaasen, 2002).
In a community HIV care project using volunteers in South Africa, community members indicated that it was unlikely that efforts would be sustainable in the long term, due to lack of support for volunteers both within and outside of the community. The authors argue that those seeking to increase the role and capacity of community volunteers in AIDS care need to make substantial efforts to ensure that appropriate support structures are in place including sustainable stipends for volunteers (Campbell et al., 2008). In a home management of malaria programme in Uganda, CHWs expressed concerns about lack of incentives and facilitation such as torches, gumboots and diagnostic equipment to improve their performance (Nsabagasani et al., 2007).

There are successful programmes that have employed volunteers, most notably being the lay health worker programme in Nepal that was established in 1988 with a reported annual attrition rate of about 4% (JSI, 2010). In Nepal stakeholders saw volunteers as motivated primarily by social respect, religious and moral duty. Regular wages were regarded not only as financially unfeasible, but as a potential threat to the volunteers' social respect, and thereby to their motivation. Some of these views appear to be influenced by a tradition of volunteering as moral behaviour, and a lack of respect for paid government workers. It may not be useful to promote a generic range of incentives, such as wages, to improve the sustainability of CHW programmes. Context-specific expectations of CHWs, programme managers, and policy makers should be in alignment if low attrition and high performance are to be achieved (Glenton et al., 2010).

8.3 CONSIDERATION OF THE ACCESS FRAMEWORK

In Studies I and III, the issues of availability of diagnostic-based iCCM through CHWs, accessibility and acceptability were examined. The concepts of affordability and adequacy were not examined in these studies. In this context, CHWs do not charge for their services and therefore we can assume that their services are free and affordable. These five components explore the issues around access as articulated by Obrist and others (Obrist et al., 2007), and provide a very useful way to frame the issues.

Study III assessed utilisation of diagnostic-based iCCM through CHWs, as well as issues of quality of care. In Study III, quality of care was measured through caregiver reports of CHW compliance to diagnostic test results, as well as reported patient satisfaction (perceived quality). Study II measured the technical skills (technical quality) of CHWs whereas Study IV also measured the quality of services through CHW compliance to diagnostic test results as evidenced in the appropriate use of medicines. Utilisation of

quality health services should result in improved health status, and patient satisfaction. Based on the quality outcomes, it can be postulated that the services provided by CHWs were of high quality and resulted in improved health status of under-five children as measured by fever clearance at days 3 and 7 (IV).

Issues of livelihood assets are addressed in Study II where a wealth index using principal components analysis was developed. In a logistic model with other variables, wealth did not influence utilisation of CHWs services in this study. Other livelihood assets (social, natural, financial capital) as proposed by Obrist et al were not explored in these studies.

I propose the addition of technologies and diagnostics into the health services component of the access framework. They could be embedded into the health services component, or directed at the "5 A's" as contributing factors to availability, accessibility, acceptability, affordability, and adequacy. This thesis shows that use of diagnostics has an influence on the perception, and acceptability of health services. Diagnostics and other technologies could also have an influence of availability, accessibility, affordability and the adequacy of health services, although that was not explored in this thesis.

8.4 METHODOLOGICAL CONSIDERATIONS

Triangulation
Triangulation usually refers to employing multiple methods to examine a single problem, often through the combination of qualitative and quantitative approaches. In addition to *methods triangulation*, *data triangulation* (the use of more than one source of data in a study), *investigator triangulation* (the use of several different researchers' perspectives), and *theoretical triangulation* (the use of more than one theoretical perspective to interpret data) can be used (Patton, 2002). Study I triangulated information from caregivers, health providers, CHWs and community and opinion leaders using both FGDs and KIIs. This was a useful strategy for checking consistency and contradictions across and within groups (Flick, 1992, Berg, 2001). Investigator triangulation (social scientist, anthropology, medicine) was used in Study I. Information was also triangulated between Studies I and III (methods triangulation), greatly enhancing the scientific rigour.

Cluster analysis
This is a statistical technique in which the unit of analysis is the cluster (Wang and Bakhai, 2006). The study units sampled in Study III and IV were clustered. Not adjusting for clustering of households in Study III or CHWs in Study IV could result into narrowed confidence intervals. In the studies included in the thesis, the analysis adjusted for the cluster effect.

Principal components analysis
Principal components analysis was used to generate a socio-economic status (SES) index. We used fewer variables than most often used, for example in the 2006 Uganda Demographic and Health Survey (Uganda Bureau of Statistics, 2006). However, the index does portray the actual picture on the ground in terms of the components used and what is generally understood as what these components represent in terms of SES in the community. While asset-based measures are increasingly being used, there continues to be some debate about their use. These measures are more reflective of longer-run household wealth or living standards, failing to take account of short-run or temporary interruptions, or shocks to the household (Filmer and Pritchett, 2001). Therefore, if the

outcome of interest is associated with current resources available to the household (*as health services utilisation might be*), then an index based on assets may not be the appropriate measure (Vyas and Kumaranayake, 2006). However, under the circumstance, with no other source of information on household income and expenditure in this rural community with a large informal sector, the approach used was considered a reasonable alternative.

Subgroup analysis
The immediate problem with subgroup analyses is that the individual subgroups of interest are usually small compared with the trial population, which can therefore reduce the statistical power for determining an estimate of the true treatment effect within the subgroup. Secondly, when many subgroup analyses are undertaken in a clinical trial, the chance of finding a false-positive result (Type I error) by random chance alone increases if the significance level or threshold is kept the same (Wang and Bakhai, 2006).

Reporting bias
Reporting bias occurs when a subject is reluctant to report on exposure he is aware of because of attitudes, beliefs and perceptions (Gordis, 2000). Information obtained in Study III was based on caregivers' reports on health and care seeking practices. Some caregivers, for example, may have declined to report on where they actually sought care if they felt the source was not perceived by others to be appropriate for instance traditional healers. When face-to-face interviews are conducted, there is often over-reporting and under-reporting of some events (Lilienfeld and Stolley, 1994). This was minimised by using experienced research assistants who tried to ensure that respondents were as comfortable and as free as possible to share information without feeling that some of their answers could be wrong.

Recall bias
Caregivers of children with more severe illness are often more likely to recall events than those with less serious illness; a type of bias known as recall bias (Gordis, 2000). In Study III, bias in recall was a potential problem with caregivers being asked to remember things that happened in the past about an event that may not have been a major event in the home. Poor recall by caregivers of children who experienced a 'mild' fever episode may have resulted in under-reporting of associated events of interest to the study. We attempted to minimise this by limiting the recall period to one month for key details, and three months for more general questions about a most recent fever episode in the child. We also interviewed caregivers that were responsible for the under-five and not anyone in the household.

Interviewer bias
Bias introduced into a study as a result of the way information is abstracted from records, or the manner in which interviewers ask questions is referred to as interviewer bias (Wynder, 1994, Gordis, 2000, Salazar, 1990). Interviewer bias could have occurred in Studies I and III, if interviewers, for example had posed leading questions that made responders provide answers they thought the interviewers wanted to hear. We attempted to minimise this bias by using experienced research assistants and standardised questions. For Study III, we used research assistants who were not involved in the intervention and were blinded to the hypothesis.

Observer bias
When knowledge of the treatment assignment by participants, investigators or persons involved in the analysis leads to a systematic distortion of the trial conclusion, observer bias is said to have occurred (Wang and Bakhai, 2006). In Study II, observation of consultations could have influenced CHW practices, perhaps overestimating their performance. However, the intent of this study was to measure CHW competence (efficacy) after training, although this may not be replicated in real life. Also the observers were not blinded to the results of the CHWs before they undertook their own readings, which could have influenced their own readings. We tried to minimise this by using highly qualified observers and training them prior to the observations. The observers were also closely supervised by the study team.

Generalisability
The ability for the results of a study to be applicable to a wider audience or population is referred to as external validity or generalisability (Wang and Bakhai, 2006). In Study II, a small number of CHWs was used, which is a limitation in this study, as it did not provide sufficient power to allow detection of associations between performance and CHW attributes. The ability of CHWs to correctly interpret RDTs in a low-prevalence area, when many tests are negative may be quite different from what was observed in this study. We recommend that similar studies be replicated in low-prevalence settings with larger numbers of CHWs.

In Study IV, we used only high respiratory rate as the criterion for pneumonia classification and subsequent antibiotic use while the WHO recommends the presence of cough or difficulty breathing together with high respiratory rate as the classification of pneumonia (WHO, 2005). This is a limitation of this study, and fewer children would have been treated with antibiotics under WHO guidelines than were treated using a criterion of rapid breathing alone. We conducted a sub-group analysis of children with cough among those with high respiratory rate and found 6% (30/501) of children in this sub-group were under-treated with antibiotics (children with pneumonia symptoms who did not receive an antibiotic). As this is a low proportion it is unlikely to have changed the effect of the intervention as reported.

9 CONCLUSIONS AND POLICY IMPLICATIONS

The main conclusions from this thesis are:

1. Use of malaria rapid diagnostic tests (RDTs) by community health workers (CHWs) is acceptable to community members and health workers (I).

2. CHWs can be trained to use RDTs and respiratory rate counting to assess, classify, and treat malaria and pneumonia in children (II).

3. CHWs practicing diagnostic-based integrated community case management (iCCM) are highly accessible, accepted, and are often the first choice of care for caregivers of febrile children (III).

4. Diagnostic-based iCCM improves access to appropriate treatment for malaria and pneumonia, and reduces unnecessary use of anti-malarials and antibiotics at community level (IV).

5. Diagnostic-based iCCM is more effective compared to presumptive home management of malaria in clearing fever in settings of high malaria prevalence, and improves rational use of medicines (IV).

Policy Implications

The results have the following policy implications:

a. **Strategy:** the evidence from this thesis shows that diagnostic-based iCCM is more effective at clearing fever in febrile under-fives compared to the presumptive management of malaria.

b. **Community Health Workers:** The evidence from the thesis shows that CHWs can use these two diagnostics (RDTs and ARI timers) to distinguish and treat both malaria and pneumonia, and communities welcome this diagnostic-based strategy. While it is clear that CHW compliance with malaria RDT results was high, compliance to pneumonia diagnostics was much lower with overuse of antibiotics at two of the study sites. Some CHWs had difficulty using the ARI timer to count respiratory rates correctly. Also, some CHWs had difficulty moving from classification of an under-five with or without fast breathing to assigning them as having pneumonia or not respectively. Without adequate supervision by the health system, it will be difficult for CHWs to practice diagnostic-based iCCM. Therefore, programmes that seek to introduce diagnostics need to plan for adequate resources to support CHWs with supplies and logistics, and the supportive supervision needed to deliver quality iCCM.

c. **Malaria RDTs:** The results support the introduction of malaria RDTs into iCCM. RDT use by CHWs reduced ACT use in the intervention arm with high prescriber compliance with test results. CHWs were found to be competent in the use of RDTs, and their use by CHWs was highly acceptable to community members.

d. **Use of antibiotics:** The results are less convincing regarding use of ARI timers and the appropriate use of antibiotics. Programmes introducing antibiotics into community based treatment, need to plan for adequate on the job training, supportive supervision, and continuous refresher training of CHWs to be able to correctly count, classify and treat children with pneumonia.

e. **Child management** – iCCM with RDTs and respiratory rate counting provide a simple but effective way to distinguish and treat the two leading infections in children, and can help countries meet their MDG 4 targets in reducing under-five mortality rates, especially in malaria endemic settings. The results show that diagnostic-based iCCM improved fever clearance, and access to appropriate treatment for both conditions among under-fives. We therefore recommend scaling up diagnostic-based iCCM in rural, hard-to-reach areas, where under five mortality is high.

Reflections for the Future

Several issues important for achieving effective diagnostic-based iCCM in different settings need to be better understood, including:

1. The implications of RDT use on the rational use of antibiotics by CHWs. Will CHWs appropriately use anti-malarial drugs at the expense of antibiotics?
2. How do programmes in which CHWs are provided with ARI timers and antibiotics and managing children with pneumonia affect community drug use patterns?
3. CHWs' anti-malarial drug prescription behaviour in low malaria transmission settings in the context of diagnostic-based iCCM. Will low RDT positivity affect compliance?
4. An External Quality Assurance (EQA) scheme that would be appropriate for RDTs in iCCM, and the practicalities of organising such an EQA scheme. The EQA scheme may include facility-based malaria microscopy.
5. How best to coordinate, provide, and facilitate supportive supervision to CHWs using diagnostics in iCCM.
6. The role of the private sector (drug shops and private clinics) in providing and/or supporting diagnostic-based iCCM.
7. Ways to improve or develop new point of care diagnostics for ARI/pneumonia, as respiratory rate counting is difficult for some CHWs.

10 ACKNOWLEDGEMENTS

Several individuals have contributed to my PhD project and to them all I am deeply grateful. I may not be able to mention everyone that has supported me in this limited space, but I wish to thank in a very special way the following:

Caregivers, health workers, children and community members who participated in the studies, and shared their experiences with the research team.

My main supervisor, Dr. Karin Källander for your dedication, insightful comments, and advice. You have been an inspiration to me! Thank you for all the literature that you shared with me, and being very patient and understanding; without this, it would have been impossible for me to complete this journey. Thank you for the visa letters, and all the non-academic support.

My co-supervisors: Prof. Stefan Peterson for the critical questions, keeping me in focus, and all the support. Your advice has been invaluable on many fronts. Thank you for the visa letters, and numerous tips on how to navigate around Stockholm. Assoc. Prof George Pariyo for getting me onto this journey when you tasked me to draw up that letter of intent to WHO/TDR in 2006, that became the centre of my PhD project. You have consistently provided comments to my work, and raised those provocative critical questions, even when you moved to Geneva. I truly value this, and say thank you.

My Mentor: Assoc Prof Fred Nuwaha for his availability to support. Thank you for your support during the pre-disputation, and making me aware of the important issues I needed to take into account.

Dr. Lynn Atuyambe, thank you for the critique during my pre-disputation, and sharpening my thinking.

My colleague and dear friend Simon Kasasa, thank you for all the help with the statistical analysis. You were always willing to spare time away from your own PhD studies in Basel to help me out.

Dr. Peter Nsubuga from the U.S. Centres for Disease Control and Prevention, Atlanta, I thank you for supporting and encouraging me to stay the course. Your advice and support has kept me going through this journey. Thank you too for your critique of my statistical methods.

Dr. Franco Pagnoni at the WHO/TDR, Dr. Guy Burnish formerly at the Liverpool School of Tropical Medicine and Hygiene (happily retired in France), and Prof. Simon Cousens at the London School of Hygiene and Tropical Medicine, I thank you all for being willing to work with me through the analysis and manuscript writing for paper IV, and teaching me how to deal with multi-country data. You all were an inspiration.

UNICEF/UNDP/World Bank/WHO/TDR and DELPHE/British council/DfID for supporting the field work.

All the co-authors for the various papers, thank you for your cooperation and support. Special thanks to Dr. James Tibenderana for leading the Uganda team (for which I was a part) of this multi-country study and for your support and cooperation.

Anna-Berit Ransjö-Ardidsson, thank you for welcoming me to your home and making me enjoy my study in Sweden. You are so gracious!

Mr. Moses Matovu, Mr. Godfrey Ojiambo and Dr. Rebecca Babirye for your dedication to coordinating the field activities over the duration of the studies in Iganga. You were a great and dependable team. All the staff at Namungalwe health centre, thank you for the support and cooperation you accorded us. The CHWs that participated in these studies, I thank you for your unwavering dedication to service. You that made this project possible!

Makerere University School of Public Health staff: Prof. Fred Wabwire-Mangen, Assoc. Prof David Guwatudde, Dr. Fred Makumbi, and all the colleagues in the department of Epidemiology and Biostatistics. Thank you for your support, and understanding during this period, and taking over my teaching and other assignments.

AFENET Board of Directors, thank you for your understanding and support and allowing me time to carry this project to completion. Special thanks go to the Board Chair Prof. Mufuta Tshimanga.

AFENET staff: I thank you for taking on extra tasks while I was away. Special thanks go to Drs. Olivia Namusisi and Sheba Gitta for standing in for me while I was away.

The health systems research group at IHCAR, thank you for your support, advice and mentorship. Special thanks to Prof. Göran Tomson, and Assoc. Prof Rolf Wahlström for your critique of my work at various stages, and Dr. Andreas Mårtensson for your invaluable comments during the presentation of my project to the research group.

Faculty at IHCAR: Thanks to Prof. Vinod Diwan, Prof Lucie Laflamme, Assoc. Prof. Marie Hasselberg, Prof. Hans Rosling, Dr. Asli Kulane, Dr. Birger Forsberg, Dr. Johan von Schreeb, Gun-Britt Eriksson, Gunilla Risberg, Kersti Rädmark, Birgitta Rubenson, Bo Planstedt.

Colleagues at IHCAR: Gorrette Nalwadda, Anastasia Pharris-Ciurej, Elin Larsson, Anna Bergström, Amanda Haggblom, Patricia Awiti, Christine Nalwadda, Roy Mayega, Agnes Nanyonjo, Joan Nakayaga-Kalyango, Netta Beer, Sandeep Nerkar for sharing your experience during this journey. Special thanks go to Dr. Elizeus Rutebemberwa with whom I worked to secure clearance to import study drugs for both our projects, and also for his editorial support to this thesis.

My family: my wife Jolly, daughters Larissa and Ruth, and son Jonathan. Thank you for bearing with my absence while I was away in Stockholm, and for all your support and encouragement. You are all very special, and you make my life the great joy that it is.

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Mukanga et al. Malaria Journal 2010, 9:203
http://www.malariajournal.com/content/9/1/203

MALARIA JOURNAL

RESEARCH Open Access

Community acceptability of use of rapid diagnostic tests for malaria by community health workers in Uganda

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Abstract

Background: Many malarious countries plan to introduce artemisinin combination therapy (ACT) at community level using community health workers (CHWs) for treatment of uncomplicated malaria. Use of ACT with reliance on presumptive diagnosis may lead to excessive use, increased costs and rise of drug resistance. Use of rapid diagnostic tests (RDTs) could address these challenges but only if the communities will accept their use by CHWs. This study assessed community acceptability of the use of RDTs by Ugandan CHWs, locally referred to as community medicine distributors (CMDs).

Methods: The study was conducted in Iganga district using 10 focus group discussions (FGDs) with CMDs and caregivers of children under five years, and 10 key informant interviews (KIIs) with health workers and community leaders. Pre-designed FGD and KII guides were used to collect data. Manifest content analysis was used to explore issues of trust and confidence in CMDs, stigma associated with drawing blood from children, community willingness for CMDs to use RDTs, and challenges anticipated to be faced by the CMDs.

Results: CMDs are trusted by their communities because of their commitment to voluntary service, access, and the perceived effectiveness of anti-malarial drugs they provide. Some community members expressed fear that the blood collected could be used for HIV testing, the procedure could infect children with HIV, and the blood samples could be used for witchcraft. Education level of CMDs is important in their acceptability by the community, who welcome the use of RDTs given that the CMDs are trained and supported. Anticipated challenges for CMDs included transport for patient follow-up and picking supplies, adults demanding to be tested, and caregivers insisting their children be treated instead of being referred.

Conclusion: Use of RDTs by CMDs is likely to be acceptable by community members given that CMDs are properly trained, and receive regular technical supervision and logistical support. A well-designed behaviour change communication strategy is needed to address the anticipated programmatic challenges as well as community fears and stigma about drawing blood. Level of formal education may have to be a criterion for CMD selection into programmes deploying RDTs.

Background

Globally 3.2 billion people remain at risk of malaria and nearly one million malaria deaths occur each year, mostly in children under five years of age in sub-Saharan Africa [1]. Besides neonatal-related causes, malaria is the second leading cause of morbidity and mortality in Africa, and accounts for 21-26% of all under-five mortality in Uganda [2,3]. Many of these deaths occur at home due to poor access to health care, inappropriate or delayed care seeking and inadequate quality of health services [2,4]. Based on the current body of evidence, community health workers (CHWs) can play an important role in increasing coverage of essential interventions for child survival [5]. One such strategy recommended by WHO and UNICEF is Home

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Management of Malaria (HMM) which has been shown to be effective in reducing malaria mortality and morbidity in under-five children in a number of malaria endemic countries [6-8].

Since 2002, Uganda has adopted and implemented HMM at scale, locally referred to as Home Based Management of Fever (HBMF) strategy [9-11]. Under HBMF, community medicine distributors (CMDs) provided unit-dosed prepackaged Homapak™ (chloroquine and sulphadoxine/pyrimethamine - CQ + SP) presumptively to children that presented with, or had a history of fever [9]. More than 45% of first care contact for under-five children with fever was obtained through HBMF in program areas [12], and Kilian *et al* [13] found that caregivers of children had high acceptability towards Homapak™.

Due to increase in resistance to CQ and SP, in 2006 the National Malaria Control Programme (NMCP) made a policy change to cost-free artemisinin-based combination therapy (ACT) at all levels of the health system - including community level. Coartem®, the ACT that is in use Uganda is composed of a fixed combination of 20 mg of artemether and 120 mg of lumefantrine and is supplied in prepacked weight- and age-specific forms. There are concerns that the introduction of such a highly efficacious but expensive new treatment at community level, with reliance on presumptive diagnosis alone, may lead to excessive use, increased costs and risk of development of resistance [14,15].

The encouraging decline in malaria prevalence that has been observed in several African countries where integrated malaria control strategies have been implemented on a large scale [16-20] may also amplify the risk of misdiagnosis of fever episodes in absence of malaria diagnostic tools [21]. With policies that recommend presumptive treatment of fever, health workers and caretakers are less likely to look for other causes of fever, leading to delay in appropriate treatment and higher case fatality rates among non-malaria fevers than in malaria fevers [22]. There is limited evidence that shows change in malaria prevalence in the recent past in Uganda [23].

Given that rapid diagnostic tests (RDTs) are now available with sensitivities comparable to routine microscopy in detecting malaria [24-27] these tests are now increasingly being seen as an alternative to improve diagnosis and quality of care of febrile children in malarious areas [10,28]. RDTs are now being rolled out in many countries to all tiers of the formal health care system to guide malaria treatment decisions in routine care [29]. The potential role of RDTs in HMM is still highly debated; a facility based study in Tanzania found some caregivers with reservations about RDTs for malaria, thinking they were HIV test kits [30]. Studies from sub-Saharan Africa [31-33] document community stigma about drawing blood that may impede acceptability of RDTs. In addition, English *et al* [34] argue that there is inadequate evidence to support abandoning presumptive treatment and that African health systems have yet to demonstrate the capacity to support a shift toward laboratory-confirmed diagnosis rather than presumptive treatment of malaria in children under five. Some of these concerns include the implications of not providing treatment to childern with false-negative test results. Finally, diffusion of innovations in the health system depend on individuals' perceptions of the innovation, characteristics of the individual who may adopt the change, and contextual factors within the community [35]. It is still unclear what role RDTs will play in a situation where HBMF recommendations are blended with local and biomedical knowledge, and little is known about whether the community will accept the use of RDTs in the hands of CMDs with low education level and no formal health care background. The aim of this study was, therefore, to explore community acceptability of the use of RDTs for malaria diagnosis by CMDs within the context of community case management of fever in children under five in Uganda.

Methods

Study area

The study was conducted in the rural Ugandan district of Iganga as part of a larger study on the feasibility of deploying RDTs at community level in Uganda (Clinical Trials.gov Identifier NCT00720811). Uganda has an estimated population of 34 million inhabitants of whom about 80% live in rural areas. The economy is predominantly agricultural with the majority of the population dependent on subsistence farming.

Iganga District is located in South Eastern Uganda, approximately 112 km from Kampala, the capital city of Uganda. Iganga district is served by a 200-bed capacity hospital, and 81 health centres at county, sub-county and parish level. The main local language spoken in the district is Lusoga. Iganga has high transmission rates (holoendemic) for malaria [36]. HBMF was started in Iganga district in 2003 with district-wide 3-day training of CMDs in use of Homapak®. All the CMDs were retrained over 3 days in using Coartem® in 2006, but due to inadequate stocks of ACT at national level the medicines were limited to facility-based deployment and were not deployed through CMDs during this study period. The study was conducted in August 2008 in the sub-county of Namungalwe, which has a total population of 32,911 in seven parishes and 19 villages. There are a total of 48 CMDs in the sub-county, majority of who are female and have attained some secondary school education. The sub-county of Namungalwe was

selected because of a planned intervention study that will introduce the use of RDTs by CMDs.

Data collection

A qualitative research approach using Focus Group Discussions (FGDs) and Key Informant (KI) interviews was deemed appropriate for the study aim. Ten FGDs with 6-10 participants in each group were conducted with caregivers of under-five children and CMDs (Table 1). Whereas most fevers are managed by mothers, FGDs were also conducted separately with fathers, as they play a significant role in the health care seeking of sick children, especially when costs are incurred [37].

FGD participants were mobilized by the community leaders and purposively selected if they had ever cared for a child with fever. FGDs were conducted in different parishes, and took place in one of the homes of the participants to provide for privacy. Pre-designed interview guides were piloted and used to collect information on trust and confidence in CMDs, community willingness and acceptability of CMDs to use RDTs, anticipated challenges that CMDs could be faced with using RDTs, and stigma associated with taking blood from children in the community. Both the interviewer and the note taker were social scientists, spoke both English and the vernacular fluently and were experienced in conducting FGDs. The first FGDs were attended by two of the research team members who reviewed the notes afterwards. They also discussed with the interviewer and the note taker their experiences of the emerging issues and whether questions were being understood.

Key informant interviews were conducted with health workers and different community leaders (Table 1) to capture their experiences of CMD management of sick children, their perceptions of CMDs' abilities in using RDTs as part of the treatment of children with fever, anticipated challenges that CMDs could face with using RDTs and stigma associated with taking blood from children in the community. The research assistants were trained by the investigators on how to use the KI interview guide.

All the FGDs and KI interviews were conducted in the local language, transcribed and later translated into English by the interviewers. The participants had never seen nor had an RDT used on them, and during interviews the RDT test was described to the interviewees.

Data analysis

Manifest content analysis [38] was used to categorize key issues out of the data. The unit of analysis was the transcripts from FGDs and KIIs. The authors (DM, JT, JK, BM, GO and KK) read through the data, identified different issues and debated them, and eventually developed codes. A second review of the material was done that generated more codes, which were discussed and agreed upon. These codes were merged into categories and then into themes reflecting the study objectives and other emerging issues.

Ethical clearance

Ethical approval for the study was obtained from the WHO Ethical Review Committee, the Makerere University School of Public Health Institutional Review Board, and the Uganda National Council for Science and Technology. Presentations to the district health team for Iganga district, as well as to the local area authorities at the sub-county were made and permission obtained from them to conduct the study. Individual written (signed or thumb print) informed consent was obtained from each of the study participants for both key informant interviews and focus group discussions.

Results

There were four key findings of the study: (1) CMDs are trusted by their communities because of their commitment to voluntarism, accessibility, and the perceived effectiveness of the anti-malarial drugs used, and their activities have led to a perception of reduced workload among health workers in health facilities; (2) community members, health workers and CMDs welcomed the use of RDTs by CMDs provided they have sufficient education level, are trained in their use, and supported to follow up children; (3) fears were expressed that CMDs who collect blood using RDTs could expose the children to HIV, that the tests could be used to test children for HIV, or that the blood could be used for witchcraft; (4) CMDs were anticipated to face challenges with transport for follow up of patients and re-stocking of supplies,

Table 1 Number and mix of key informants and focus groups conducted

Key Informant Interviews (KIIs)	Number	Focus Group Discussions (FGDs)	Number
Health workers at local Health centre III	2	Female caregivers/mothers of children under five years	4
Civil society leaders/teachers	2	Male caregivers/fathers of children under five years	4
Local political leaders	2	Community medicine distributors (CMDs)	2
Health unit management committee members	2		
Religious leaders	2		

adults demanding to be tested, and caregivers insisting their children be treated instead of being referred.

Trust in and acceptability of CMDs managing children with fever

The role of CMDs in malaria management was well appreciated by the community since the CMDs were perceived to be accessible both physically and socially. Many community members reported trust and confidence in CMDs ability to handle sick children given their past experiences of helpful available CMDs.

> *"She [the CMD] even asks us to take our children when they are sick to give us drugs. She has been very good because even if I go to her place at night she opens and gives me drugs. Even if I find her in the garden digging she comes back home to give me medicine. I trust her."* (FGD, female caregivers)

The spirit of volunteerism as demonstrated by CMDs not demanding to be paid for their services was greatly appreciated by community members, and their trust and confidence in the CMD services was often the main motivating factor for the CMDs to do voluntary work. The community members who had used the CMDs perceived the medicines provided to them as effective in treating children with malaria, and the recovery of sick children after treatment by CMDs was said to enhance the reputation of the CMDs amongst their neighbours and community.

> *"According to me, they [CMDs] have done commendable work. They have a good relationship with the people and they have helped them a lot. They have been effective in distributing Homapak® and Coartem®. I heard that the tablets are to be distributed freely and they are doing it - they fulfilled the intention. My twins are making 3 years and I've never taken them to hospital. They are treated at home and given Coartem®. They [CMDs] have never asked for money for treatment."* (KI, community leader)

Health workers reported to have observed a reduced workload at the health facilities as a result of CMD management of children with fever in the communities.

> *"We have trained CMDs in many workshops. We taught them about the danger signs, so in case of such they refer them to the health centre immediately. The CMDs also sensitize the communities where they stay on malaria prevention. They have really helped us health workers. The work load has reduced. We appreciate [their contribution]".* (KI, health worker)

> *"There is a good relationship with us because they know where they stop. They know that they can't manage [everything] according to how they were trained. [For complicated cases] they immediately refer them to the health facilities. These people have really helped very much in the areas where they operate. We have not heard cases that a child has died at the CMDs level."* (KI, health worker)

However, there were also some reservations about CMDs performance in the management of malaria at community level. Some informants reported that CMDs are sometimes difficult to find and in some instances they are looked down upon by caregivers because they are not trained professionals. Others reported that medicine distribution is a difficult task and that CMDs can easily give medicines without understanding what the underlying problem is. Some KIs indicated that CMDs are not trusted because of their low level of education.

> *"In some cases [instances] they are minimized because they are not trained professionals. Medicine distribution [prescription] is very hard and they can easily give you medicine without understanding what you are suffering from. If you explain to him that you have malaria or that you are not feeling well, of cause; for him he has the medicine he just gives you".* (FGD, male caregivers)

Opinions, concerns and acceptability of the use of RDTs by CMDs

Although it emerged that community members had some doubts about CMD skills, there was consistency across the FGDs and KIIs a high degree of confidence that CMDs can perform the test once they are provided with adequate training. This trust and confidence was based on the education level of the CMDs, their experience, as well as perceptions about their commitment to work.

> *"If a person is trustworthy in a small thing they can work equally well even in a bigger one. These people have worked well and we never got problems with them. If my child falls sick, I just cross the road to him instead of going to Namungalwe where a person from Marina [name of place outside Iganga] knows nothing about me."* (FGD, male caregivers)

Community members also echoed the need for refresher training for CMDs in addition to training on RDTs.

> *"That will be very good [introducing RDTs] only that they will need to be trained like how they were*

trained before starting to give out coartem."(KI, health worker)
"I would second it [introducing RDTs] provided they are trained to do it safely. It is very important." (KI, community leader)

CMDs expressed willingness to use RDTs as part of the services they provide, and are confident they can perform it if they receive adequate training. CMDs contended that they have been voluntarily distributing drugs and would now volunteer also for this new task. CMDs were optimistic that the community would welcome their use of RDTs.

"If they know that we have been trained, they will accept [the use of RDTs]. Even for the giving out drugs they first resisted but later accepted." (FGD, CMDs)

Also the majority of health workers supported the idea of CMDs conducting RDTs as long as they are given practical training to acquire additional skills, accurate information, and guidelines to ensure safety. They asserted that this is one way of taking services nearer to people, encourage early treatment seeking behaviour, and is one way of providing CMDs with additional skills crucial for managing malaria. They also appreciated the fact that the CMD treatment of malaria could be performed more effectively if an RDT was introduced, so as to distinguish between malaria and other types of fever.

"That is a good thing [the use of RDTs], and it will work because people have been coming here a lot because of malaria. So if it [RDT and malaria treatment] is taken near them it will help them so that a person knows what is required and will help them get early treatment. But these CMDs need to be given additional skills because they need to have enough information to avoid questions like why they are taking blood." (KI, health worker)

Fears and stigma associated with taking blood from children in the community

Even though most community members were positive towards the use of RDTs by CMDs, many had mixed feelings about the taking of blood from children. The fear included concerns that their children could get infected with HIV in the process of undertaking an RDT and that the blood could be used to test children for HIV rather than malaria.

"People have fears about blood and that it can lead to contracting HIV. It would also imply to some people that when they prick to test the blood, they think you are testing for HIV but not malaria. They believe you can prove malaria by mere looking at signs like vomiting, shivering, diarrhea and other basic signs." (KI, community leader)

Another frequently mentioned concern was that the blood could end up in the wrong hands and be used for witchcraft.

"Since people use it [blood] for bewitching, someone can draw it from you without you being aware that it will be used for other things. If you have a co-wife she can use it to bewitch you to death or stop producing children. Some say that they use it as sacrifice." (FGD, female caregivers)

Challenges anticipated to hamper the success of CMD management of fever using RDTs

Given the tasks that the CMDs are given, views regarding the challenges that CMDs are likely to face were solicited. The reported challenges that were foreseen included that CMDs will lack transport for follow up of patients and for replenishment of supplies from the health facilities, that adults will try to force CMDs to also test them for malaria, that caregivers will insist that CMDs treat their children even when the child needs referral, and that some leaders will try to seek for favours for themselves and their relatives.

"I have seen some of them [CMDs] walking all the way to the health center to get drugs, and when following up children. They need to be assisted with transport for drugs". (FGD, male caregivers)
"These tests [RDTs] will create a lot of interest. I am concerned that adults will also demand to be tested. I think also some of our people will insist that their children are treated when they should be referred as now CMDs will be seen as "little doctors" who can take blood and examine it". (KI, community leader)

Discussion

The study found that community medicine distributors (CMDs) were trusted by their communities because of their voluntary services, ease of access, and perceived effectiveness of the anti-malarial drugs they use. This is in line with the findings from a multi-country study (including Uganda) which showed high community acceptability of CMD management of sick children, with most children receiving treatment on the same day or within one day of onset of symptoms [39]. Kilian *et al* [13] found similar results in western Uganda, where

women showed high acceptability of pre-packaged anti-malarial drugs in the hands of CMDs. However, while Ajayi *et al* [39] also concluded that most caregivers perceived the anti-malarials used by CMDs to be effective, Nsabagasani *et al* [40] demonstrated that although caregivers concurred that they were benefiting from the CMD programme, the treatment was perceived as a drug of lower quality. The contradicting finding is likely to be a result of the type of medicine used, as Ajayi *et al* [39] evaluated the use of highly efficacious pre-packed ACT, whereas Nsabagasani *et al* [40] evaluated the use of Homapak® (chloroquine and sulphadoxine/pyrimethamine) - a combination drug known to have low clinical efficacy due to parasite resistance.

CMDs were trusted by health workers who recognized that the CMDs have contributed to a reduced workload in the health facilities. This concurs with what was found in a rural district in Burkina Faso, where a reduction in workload at peripheral health facilities was observed after HMM was implemented [41]. Similarly, HMM with ACT using community health workers who are supervised regularly was found to be feasible and acceptable by health workers in Ghana [42]. In resource constrained rural communities with geographically sparse health services, CMDs could fill a major gap in access to health care for under-five children [43]. The high level of community acceptability for HMM is likely a result of its convenience, given the fact that malaria risk is often highest in remote rural areas where the quality and coverage of health services is lowest [44].

In this study, the formal education level of CMDs appeared to be a key factor in their acceptability by the community, with CMDs with low education being viewed less positively. This finding needs to be explored further, as it could have major implications on what criteria should be used to select CMDs under home management of malaria (HMM) programmes. Current selection criteria for the community to consider when they choose their CMDs include: age, literacy levels, and gender but different districts and sub-districts may however, choose different criteria for nominating CMDs and ability to read and write may not be prioritized in certain areas [45]. If shown to be consistent across countries and programmes, this could have negative implications if RDTs are to be deployed. Alternatively, programs that want to scale up CMD use of RDTs would need to demonstrate that CMDs are able to use the test and that communities accept their services, regardless of education level.

A majority of community members, health workers and CMDs welcomed the use of RDTs by CMDs, provided that they are properly trained in their use. A similar study in Sudan also found community acceptability of Coartem® and RDTs in HMM to be high, with a marked increase in treatment-seeking behaviour following the implementation [46]. In the present study, the high community acceptability of RDTs was partly due to the appreciation that CMDs would be able to offer treatment which was based on test results rather than just presence of symptoms and signs.

While RDTs have the potential to greatly enhance the management of febrile illness [47] the success of their use in the hands of CMDs is highly dependent on how the community will accept the services provided. Health care policies such as HMM are often formulated at national level and need to take into account local cultural context; sometimes assumptions are made based on what can be communicated through simplified biomedical terms, and how this will result in behaviour change [48]. However, acceptability of medical care by different ethnic groups is associated with the degree to which the services meet cultural values, norms, and expectations [49]. These factors need to be taken into account to ensure successful uptake of community programs [50]. While a desirable, participatory process in every village is not compatible with rapid national scale-up - a balance needs to be reached [40]. Having CMDs of the same ethnic group, who speak the same language, and are familiar with the culture and its traditions and values are factors that can increase acceptability [51]. The findings of this study also show that the community demands for well trained CMDs to handle and interpret the tests - some critical characteristics also identified by Din and Bell [52]. Equally, programmes will need to address concerns about children with false negative results, as now CMDs will be required to without the ACT. If, however, the child is not followed closely and gets worse or even dies, this could potentially undermine the credibility of the entire programme. In the trial that followed this study, blood slides for microscopy were collected from each child on the same day; microscopy results for all RDT negative children were returned to the CMD within 24 hours to try and address this problem. This approach will not be possible in non-research settings.

Fears and stigma of taking blood of children in the community were common, relating both to risk of exposure to HIV and witchcraft. Myths about blood could have serious consequences to the HMM programme, especially if there is a bad outcome for a child. In Tanzania, though there was a high degree of provider and caregiver acceptance and satisfaction with RDTs, some caregivers had reservations about RDTs, with some thinking they were HIV test kits [30]. To counter for this potential threat to the programme, a well-designed behaviour change communication strategy will be required, since a successful HMM strategy relies not only on adequately trained CMDs and the availability of drugs, but also on a well informed community [53,43].

In this study, community members anticipated that CMDs would face difficulties with adults demanding to be tested and caregivers insisting that their children should be treated instead of being referred. Compliance to guidelines is often a major challenge and a study in Burkina Faso found very low health worker compliance to negative RDT results, as they still went on to prescribe anti-malarial drugs for patients who tested negative [54]. This was also observed in another study in Sudan [46]. These issues will require special attention through frequent supportive supervision meetings to monitor and assess performance, and during regular CMD mentoring sessions. It has been observed that lower level health workers are more likely to comply with guidelines as compared to more experienced or high cadre health workers [55]. A follow up study is planned to assess community acceptability of RDT use by CMDs following RDT deployment in HMM.

Methodological considerations

One of the limitations of qualitative methods is that the magnitude of a variable of interest across different categories of respondents cannot be measured. However, it was not the intent of this study to quantify the issues under study as a household survey is planned for this purpose. Triangulation of information from caregivers, health providers, CMDs and community and opinion leaders using both FGDs and KIIs, was a useful strategy for checking consistency and contradictions across and within groups [56,57]. The geographical spread of the FGDs allowed us to interview participants from across the study area, getting as close to representative views of the study population as practically possible. Separating women from men in the FGDs and focused questions to the research issues could have promoted free expression of the participants and also reduced answers given to please the researcher.

Conclusion

Use of rapid diagnostic tests (RDTs) by community medicine distributors (CMDs) is likely to be acceptable by community members given that CMDs are properly trained, supported and provided logistical support. A well-designed behaviour change communication strategy is needed to address the anticipated programmatic challenges as well as community fears and stigma about drawing blood. Level of formal education may have to be a criterion for CHW selection into programmes deploying RDTs.

Acknowledgements

We are grateful to the study participants, research assistants, sociologists Charles Mucunguzi and Collins Agaba for their support during data collection and analysis, Iganga district local council officials, and Ministry of Health Uganda. Stella Nyanzi gave useful input in the final stage of writing up the manuscript. This study received financial support from UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, and from two separate grants from the Division for International Development DfID to the Makerere University School of Public Health (DeLPHE) and the Malaria Consortium (COMDIS RPC). Its contents are solely the responsibility of the authors and do not reflect the views of UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases nor DfID nor the authors' institutions of affiliation.

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Authors' contributions

DM, JT, JK, GP, PW, FB, BM, HC, GO and KK took part in designing the study, in tools development, in data analysis and in manuscript writing. DM, JK, FB, BM, GO and KK did field work. All authors approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Received: 6 April 2010 Accepted: 13 July 2010 Published: 13 July 2010

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doi:10.1186/1475-2875-9-203
Cite this article as: Mukanga *et al.*: Community acceptability of use of rapid diagnostic tests for malaria by community health workers in Uganda. *Malaria Journal* 2010 **9**:203.

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Tropical Medicine and International Health doi:10.1111/j.1365-3156.2011.02831.x

VOLUME 16 NO 10 PP 1234–1242 OCTOBER 2011

Can lay community health workers be trained to use diagnostics to distinguish and treat malaria and pneumonia in children? Lessons from rural Uganda

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Summary

OBJECTIVE To determine the competence of community health workers (CHWs) to correctly assess, classify and treat malaria and pneumonia among under-five children after training.

METHODS Consultations of 182 under-fives by 14 CHWs in Iganga district, Uganda, were observed using standardised checklists. Each CHW saw 13 febrile children. Two paediatricians observed CHWs' assessment, classification and prescription of treatment, while a laboratory scientist assessed CHW use of malaria rapid diagnostic tests (RDTs). The validity of CHWs' use of RDTs to detect malaria and respiratory timers to diagnose pneumonia was estimated using a laboratory scientist's RDT repeat reading and a paediatrician's repeat count of the respiratory rate, respectively.

RESULTS From the 182 consultations, overall CHWs' performance was adequate in taking history (97%), use (following procedures prior to reading result) of timers (96%) and use of RDTs (96%), but inadequate in classification (87%). Breath readings (classified as fast or normal) were 85% in agreement with the paediatrician ($\kappa = 0.665$, $P < 0.001$). All RDT readings were in agreement with those obtained by the laboratory scientist. Ninety-six per cent (85/89) of children with a positive RDT were prescribed an antimalarial drug, 40% (4/10) with fast breathing (gold standard) were prescribed an antibiotic and 91% (48/53) with both were prescribed both medicines.

CONCLUSION Community health workers can be trained to use RDTs and timers to assess and manage malaria and pneumonia in children. We recommend integration of these diagnostics into community case management of fever. CHWs require enhanced practice in counting respiratory rates and simple job aides to enable them make a classification without thinking deeply about several assessment results.

keywords community health worker, performance, integrated community case management for malaria and pneumonia, diagnostics, rapid diagnostic test, respiratory rate timer, Uganda

Introduction

Malaria and pneunomia are leading causes of morbidity and mortality among under-five children in Africa (Black *et al.* 2003, 2010; Kinney *et al.* 2010). Malaria alone accounts for 21–26% of under-five mortality in Uganda (WHO 2006) with another 17–26% attributed to pneumonia (Black *et al.* 2003).

In spite of available cost-effective interventions for the two conditions, millions of children in low-income countries remain at risk because of poor access to health care, inadequate quality of health services and inappropriate or delayed care seeking, with most deaths occurring at home (Black *et al.* 2003; Rutebemberwa *et al.* 2009). Community health workers (CHWs) (WHO 2007) can play an important role in increasing coverage of essential interventions for child survival (Lewin *et al.* 2005; Haines *et al.* 2007). Community case management (CCM) is effective in reducing malaria and pneumonia mortality and morbidity among under-fives (Kidane & Morrow 2000; Sazawal & Black 2003; Sirima *et al.* 2003; Winch *et al.* 2005). CCM has been in place in Uganda since 2002 (MOH Uganda

2002). Through CCM, CHWs provide pre-packaged antimalarial drugs presumptively to children with fever, initially chloroquine and sulfadoxine/pyrimethamine and since 2006, cost-free artemisinin-based combination therapy (ACT).

Introduction of this highly efficacious but expensive treatment at community level, with reliance on presumptive diagnosis, may lead to excessive use, increased costs and risk of development of resistance (D'Alessandro *et al.* 2005; Staedke *et al.* 2009). With presumptive treatment of fever, health workers and caregivers are less likely to look for other causes of fever, leading to delay in appropriate treatment and higher case fatality rates among non-malaria fevers (Kallander *et al.* 2004; Reyburn *et al.* 2004). Rapid diagnostic tests (RDTs) or dipsticks are now available with sensitivities comparable with routine microscopy in detecting malaria (Murray *et al.* 2003; Bell *et al.* 2006) and could be used to improve diagnosis and quality of care (Young 2003; Drakeley & Reyburn 2009).

Malaria and pneumonia share several characteristics including both initial symptoms and signs of severe illness (O'Dempsey *et al.* 1993). In the absence of laboratory investigations, it is difficult to distinguish between the two conditions (Kallander *et al.* 2004). Pneumonia has not been integrated into CCM, yet the strongest evidence of mortality reduction has been reported from community-based pneumonia case management in Asia where oral antibiotics are delivered by CHWs (Sazawal & Black 2003). In situations where febrile children also have cough and rapid breathing, WHO/UNICEF now recommend integrating malaria and pneumonia care in the community (WHO/UNICEF 2004).

Practical experience of using CHWs to implement the WHO/UNICEF recommendation on integrated malaria and pneumonia CCM is lacking. It is not clear whether CHWs can be trained to acquire competence in the full range of more complex integrated guidelines that include use of diagnostics. We assessed the competences of CHWs to use diagnostics to assess, classify and prescribe treatment for malaria and pneumonia immediately after an 8-day training in CCM.

Materials and methods

Study area

The study was conducted in the rural Ugandan district of Iganga as part of a larger study on the feasibility of deploying RDTs at the community level (Clinical Trials.gov Identifier NCT00720811). Uganda has an estimated population of 34 million, about 80% of whom live in rural areas. Iganga district is located in south-eastern Uganda, approximately 112 km from Kampala. Its population of approximately 600 000 consists mainly of subsistence farmers. Iganga has high transmission rates for malaria (MARA/ARMA 2001). CHWs in this study were drawn from Namungalwe subcounty, which is comprised of seven parishes and 19 villages with a population of 32 911. Namungalwe subcounty was selected as the site for the intervention study that introduced RDTs and respiratory timers for management of malaria and pneumonia by CHWs. Three health centres were used: Namungalwe HC III, Busesa HC IV and Bugono HC IV.

Study population

We enrolled all 14 CHWs of Namungalwe subcounty that participated in the intervention arm of the trial.

Study design and data collection

Training was conducted in September 2009 for 8 days, by three experienced national CCM trainers and one laboratory scientist. Topics covered are shown in Figure 1. After the training, CHWs were provided with supplies and materials including job aides.

Several studies have conducted observations of patient–provider interactions. Some observe care at facilities for a certain time period, with a wide range from 3 days (Arifeen *et al.* 2005) to 14 days (Krause *et al.* 1998). Others use a certain number of consultations per facility, ranging from two to six per condition per facility (Armstrong Schellenberg *et al.* 2004; Ehiri *et al.* 2005). CHW performance evaluations using lot quality assurance (LQA) technique have used consultations as small as 6 (Valadez *et al.* 1995). A total of 13 consultations for each CHW was considered adequate to measure CHW performance, giving a total of 182 consultations.

Tools were pretested and any ambiguities addressed in developing the final version. Evaluation started 3 days after training and lasted for 2 weeks. Any under-five with fever or history of fever without danger signs was enrolled into the study. Under-fives were enrolled as they arrived at the health centres after registration at the outpatient department and consent by their caregivers. Enrolled children were managed by the study paediatricians at the end of their participation.

Using standardised checklists[1] two paediatricians observed CHWs' performance on child assessment (history

[1]Available at www.afenet.net/english/publications/Peadiatrician_evaluation_toolv09-10-09.doc and www.afenet.net/english/publications/Laboratory_scientist_evaluation_toolv09-10-09.doc or upon request from the corresponding author.

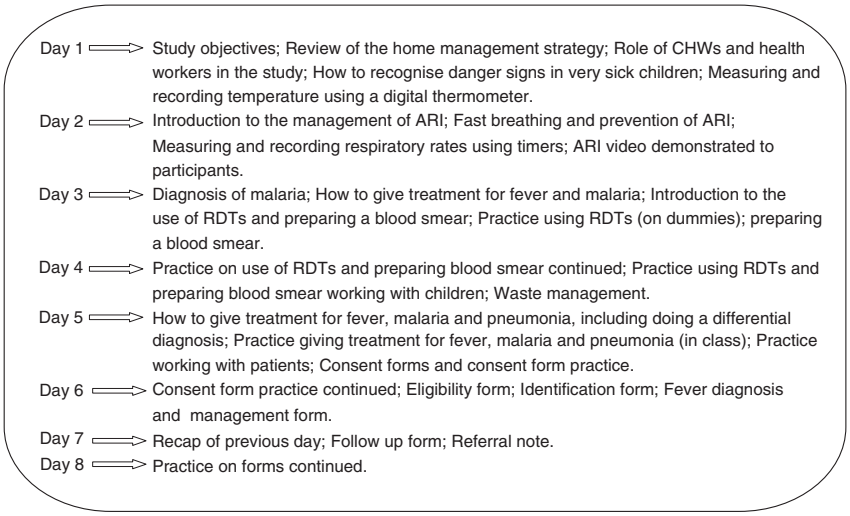

Figure 1 Content of training provided to community health workers on integrated malaria and pneumonia community case management.

taking, signs and symptoms, temperature reading and rapid breathing), classification and treatment prescription, while a laboratory scientist assessed the use of RDTs. Each CHW was observed by one paediatrician and laboratory scientist, who had been trained in the use of the diagnostics and observation checklists. One CHW was observed at a time. CHWs with a score of <90% (cut-off for adequate performance) on any part of the algorithm were retrained on that part before deployment into the field. The ability of CHWs to use RDTs to detect malaria and respiratory timers to diagnose pneumonia was estimated using a laboratory scientist's RDT repeat reading and a paediatrician's repeat count of the respiratory rate, respectively.

Definition of indicators and variables

Sixteen indicators were used for history including the following: CHW asked and recorded age and location of child's home; asked whether child had fever, cough, cold and danger signs (convulsions, difficulty drinking or feeding, and vomiting everything); looked for signs of dehydration, severe anaemia, chest in-drawing, prostration and altered mental state; and he/she asked whether child has received any treatment in past 7 days. CHW temperature reading was compared with paediatrician's.

Four indicators were used to assess ability to use a respiratory timer including counting rate before taking off blood, ensuring child is settled before beginning to count, following instructions (looks at child's lower part of the chest, start the timer by pressing centre circle, start counting at the beep and stop counting after two beeps indicating a minute) on how to take the count and recording rate.

Fourteen indicators were used to assess RDT use: ensuring all inputs required are available before start, correctly wearing gloves, selecting correct finger to puncture, cleaning finger with alcohol swab, allowing finger to dry, puncturing finger correctly, drawing blood at this point using a pipette, wiping finger with cotton after collecting blood, labelling child's ID number on cassette, putting five drops of buffer into appropriate hole, recording time after adding buffer, waiting 15 min after adding buffer to read results and recording test results. Classification/diagnosis made by CHW, and treatment prescribed were compared with that by the paediatrician.

Data analysis

Data were entered into EpiData (EpiData Association, Odense, Denmark) statistical software and analysed using Stata version 10 (Stata Corp., College Station, TX, USA). The proportion of CHWs who complied with the entire algorithm, as well as each part of the algorithm, was

calculated. Indicators were measured for each part and given a uniform score of 1 for correct and 0 for incorrect. The total score for each part of the algorithm was computed. A cut-off of 90% was set as adequate performance based on lessons from LQA techniques that use thresholds of 80%.The kappa statistic (Cohen 1960) was used to estimate the proficiency of CHWs in reading RDT results, as well as counting respiratory rates. Bivariate analysis was used to assess the association between overall performance of CHWs and CHW social demographic characteristics.

Ethical clearance

Ethical approval for the study was obtained from Institutional Review Boards of WHO, the Makerere University School of Public Health, and the Uganda National Council for Science and Technology. Permission was obtained from the Iganga District Health Office, the health centre incharges and from local authorities to conduct the study. Individual (signed or thumb print) informed consent was obtained from each caregiver.

Results

Socio-demographic characteristics of community health workers and children

Median age of the 14 CHWs was 42.5 years (range 28–50), and their mean duration in service was 3 years (SD 1.14). Eight of the 14 were women; 11 had attained at least primary education (1st 7 years of school), while the other three had not gone beyond primary school; 13 were married; 11 were self-employed (business and farming); two were teachers; and one was a nursing assistant. Mean age of the children was 21.3 months (SD 13.9); 51.5% (104/202) were girls. Of 202 children, 20 were excluded as they were too ill to participate in the study.

Overall performance of community health workers in assessing, classifying and treating children with malaria and pneumonia

Overall performance of CHWs in taking history was 96.7% (Table 1). Three CHWs scored <90% in temperature reading. All CHWs scored above 90% in using timers

Table 1 Performance of CHWs in assessing, classifying and treating children with malaria and pneumonia

CHW no. (Each saw 13 children) *n* = 182	Paediatrician (Assessor)	History* (score and %) *n* = 208	Actual temp reading Vs gold standard (score and %) *n* = 13	Using timer for Resp. Rate* (score and %) *n* = 52)	RDT preparation† (*n* = 182)	Classification *vs.* gold standard* (score and %) *n* = 13	Prescribing treatment *vs.* gold standard diagnosis (score and %) *n* = 26
1	1	206 (99)	12 (92)	48 (92)	177 (97)	11 (85)	24 (92)
2	1	201 (97)	12 (92)	52 (100)	178 (98)	11 (85)	24 (92)
3	2	204 (98)	12 (92)	49 (94)	180 (99)	12 (92)	25 (96)
4	2	200 (96)	12 (92)	47 (90)	180 (99)	12 (92)	25 (96)
5	2	201 (97)	12 (92)	48 (92)	178 (98)	12 (92)	25 (96)
6	1	200 (96)	12 (92)	51 (98)	176 (97)	6 (46)	22 (85)
7	2	198 (95)	11 (85)	52 (100)	178 (98)	13 (100)	25 (96)
8	2	208 (100)	11 (85)	51 (98)	179 (98)	11 (85)	24 (92)
9	2	187 (90)	10 (77)	48 (92)	158 (87)	12 (92)	24 (92)
10	1	199 (96)	13 (100)	51 (98)	180 (99)	12 (92)	24 (92)
11	1	200 (96)	12 (92)	51 (98)	159 (87)	12 (92)	24 (92)
12	1	201 (97)	13 (100)	48 (92)	175 (96)	10 (77)	23 (88)
13	1	206 (99)	12 (92)	51 (98)	175 (96)	11 (85)	24 (92)
14	2	205 (99)	13 (100)	52 (100)	180 (99)	13 (100)	26 (100)
Overall by area		96.7%	91.8%	96.0%	96.3%	86.8%	93.1%

CHW, community health worker; RDT, rapid diagnostic test.
n, number of observations for each CHW (=number of indicators multiplied by 13 children for each CHW). We used the following indicators for the different variables: history, a total of 16 indicators (A3–7, 9, 11, 13, 14, 16 and 18–23); temperature reading, 1 indicator (A32) *vs.* A35 (gold standard); using timer, 4 indicators (A36–39); RDT preparation, 14 indicators (P3–8, P12, P14, R4–5, R7–10); Classification, 1 indicators (C13) *vs.* C14 (gold standard); Prescribing, 2 indicators (T2 Coartem, T2 Amoxyl – CMD) *vs.* (T2 Coartem, T2 Amoxyl – gold standard).
*Refer to checklist at http://www.afenet.net/english/publications/Peadiatrician_evaluation_toolv09-10-09.doc
†Refer to checklist at http://www.afenet.net/english/publications/Laboratory_scientist_evaluation_toolv09-10-09.doc

and RDT preparation. Overall CHW performance in classification was 86.2%, with 6 scoring <90%. Regarding prescribing treatment against gold standard classification of child's illness, we analysed CHW decision in giving correct treatment for malaria and pneumonia for each child. Expected total score was 26 (13 for ACT and 13 for antibiotic). Overall performance was 93% with only two CHWs below 90%. There was no significant correlation between the paediatricians and overall performance of CHWs (pairwise coefficient = 0.408 and $P = 0.147$), which means performance was not a function of the paediatrician.

Community health worker assessment and diagnosis

Community health workers took axillary temperature for all 182 children not referred and used the thermometer correctly as per instructions in 179 instances (98%). Only six CHWs repeated the temperature reading as per training. The mean temperature reading for the CHWs was 37.25 °C, while that for the paediatricians was 37.31 °C with a mean difference in paired observations of −0.060 °C ($t = -1.834$, $P = 0.068$). The categorical classification of temperature readings (below 37.5, or 37.5 and above) between CHWs and paediatricians for each child was strongly correlated (concordance in 167 of 182 readings; pairwise coefficient = 0.803 and $P < 0.001$).

Using timers for measuring respiratory rate

When comparing classification of respiratory rates (normal and fast breathing) between CHWs and paediatricians for each child, six of the 14 CHWs had 12 or more readings in concordance, while the others had concordances ranging from 7 to 11.

No CHW repeated a respiratory rate count as per training guidelines. As shown in Table 2, CHW readings (classified as fast breathing or not) were 84.6% (154/182) in agreement with the paediatrician ($\kappa = 0.665$ and $P < 0.001$); 64% (116/182) of CHW respiratory rates were within ±2 breaths/minute of the paediatrician's. Differences in CHWs respiratory rates were because of child changing posture during counting (most common), breastfeeding, crying or restlessness.

Table 2 Classification of children by CHW with or without fast breathing against gold standard

	Gold Standard	
CHW	Fast Breathing	Normal Breathing
Fast Breathing	51	16
Normal Breathing	12	103

CHW, community health worker.
$\kappa = 0.665$, $P < 0.001$.

Using a rapid diagnostic test for malaria

Community health workers RDT readings were all (182/182; 100%) in agreement with the laboratory scientist – 138 were positive, 40 were negative and four were invalid. The four invalid results were repeated and found to be positive. Malaria prevalence in this population of children was therefore 78% (142/182).

Community health worker performance in classifying children with fever

Results in Table 3 show that agreement between CHWs and paediatrician classification was 86.8% (158/182) ($\chi^2 = 303.3$, df 9 and $P < 0.001$). CHWs correctly classified 88 of 89 children as being infected with malaria, five of 10 children as having pneumonia and 47 of 53 children as having both malaria and pneumonia.

Association between CHW characteristics and performance in classification of children with fever

At bivariate analysis using performance cut-off scores at 80% and 90% as the dependent variable, there was no association between socio-demographic characteristics and CHW performance in classification of children. The small number of CHWs (14) inhibited meaningful analysis at bivariate level.

Table 3 CHW performance in classifying children with fever compared with a paediatrician

	Gold standard (RDT and paediatrician)			
CHW (Row)	Malaria only	Pneumonia only	Both malaria and pneumonia	Neither malaria nor pneumonia
Malaria only	79	0	4	0
Pneumonia only	0	4	1	2
Both malaria and pneumonia	9	1	47	0
Neither malaria nor pneumonia	1	5	1	28

CHW, community health worker; RDT, Rapid diagnostic test.
$\chi^2 = 303.3$, $df^2 = 9$, $P < 0.001$.

Table 4 Treatment prescribed by CHWs to children as per paediatrician and CHW classification

	Gold standard classification (RDT and paediatrician)			
Treatment prescribed by the CHW	Malaria only (n = 89)	Pneumonia only (n = 10)	Both malaria and pneumonia (n = 53)	Neither malaria nor pneumonia (n = 30)
Antimalarial drugs only	77	0	4	1
Antibiotic only	0	4	1	2
Both medicines	8	0	48	0
Neither of the medicines	4	6	0	27
	Classification by CHW			
Treatment prescribed by the CHW	Malaria only (n = 83)	Pneumonia only (n = 7)	Both malaria and pneumonia (n = 57)	Neither malaria nor pneumonia (n = 35)
Antimalarial drugs only	80	0	2	2
Antibiotic only	0	7	0	0
Both medicines	2	0	54	0
Neither of the medicines	1	0	1	33

CHW, community health worker; RDT, Rapid diagnostic test.

Community health worker performance in prescribing treatment

Based on gold standard diagnosis (RDT and paediatrician), 95.5% (85/89) of children with malaria only were prescribed an antimalarial drug by the CHW, 40% (4/10) with pneumonia only prescribed an antibiotic, while 90.6% (48/53) with both conditions were prescribed both medicines (Table 4). Among those with neither condition, 10% (3/30) were prescribed one of the two medicines.

Based on CHW classification of the children, 99% (82/83) with malaria only were prescribed an antimalarial drug, 100% (7/7) with pneumonia only an antibiotic and 94.7% (54/57) with both conditions were prescribed both medicines.

Discussion

For remote and poor communities without access to health services, CHWs often are the only option for the survival of febrile children. Little has been reported on the implementation of the WHO/UNICEF recommendation on iCCM for malaria and pneumonia. Our results provide evidence that it is possible to train CHWs to provide diagnostic-based iCCM for malaria and pneumonia.

Community health worker performance in taking history, and using RDTs and timers

The performance of CHWs was adequate in history taking, following correct procedures prior to reading off result of RDT and using a timer. The need for CHWs to repeat their temperature and respiratory count measurement needs to be emphasized in training, as this point was often forgotten. Although only 64% of CHW respiratory rate counts were within two breaths of the paediatrician's, classification of children as having fast or normal breathing was 85% in agreement with the paediatrician. Therefore, only 15% of paired breath count observations between the CHW and paediatrician fell on opposite sides of the cut-offs for age. In some situations, this was a result of borderline counts. A kappa of 0.67 reported in this study denotes good agreement between CHWs and paediatricians (Landis & Koch 1977). Emphasis needs to be made regarding counting respiratory rates when the child is settled and not breastfeeding. A study from Western Uganda evaluated the ability of CHWs to assess rapid breathing among under-fives and found that 71% of 96 CHWs were within ±5 breaths/min from the gold standard and 79% classified the breathing rate correctly (Kallander *et al.* 2006).

Community health workers were excellent in interpreting RDT results as all readings were in agreement with those obtained by the laboratory scientist. This is likely a result of intensive practice during training. Reports from South America (Cunha *et al.* 2001; Pang & Piovesan-Alves 2001), Asia (Yeung *et al.* 2008) and Africa (Premji *et al.* 1994; Harvey *et al.* 2008; Elmardi *et al.* 2009; Hawkes *et al.* 2009) describe successful use of CHWs to diagnose and treat malaria in remote villages using RDTs. In Cambodia, village malaria workers have provided acces-

sible malaria diagnostic and treatment services in remote communities since 2001 (Yeung *et al.* 2008). There is a growing body of evidence that suggests use of RDTs by CHWs is likely to be acceptable by community members in other countries, including Democratic Republic of Congo (Hawkes *et al.* 2009), Zambia (Yeboah-Antwi *et al.* 2010) and Uganda (Mukanga *et al.* 2010).

Lessons from this study also show that CHW vision (optics) needs to be assessed to ensure that those with poor vision are assisted. In practice sessions with RDTs during training, two CHWs were unable to differentiate between a positive and negative RDT result because of visual problems. The study supported (on the recommendation of trainers) them to take optical examinations, and they were provided with free reading glasses.

Performance in classification

Community health workers performance in classification was 86%. Some CHWs appeared to have difficulty linking diagnostic results to classification. They had difficulty relating assessment results and classification alternatives. Interpretation of thermometer readings in relation to the RDT might have confused some CHWs, particularly what classification to make of a child with a positive RDT with temperature below 37.5 °C (no fever). Traditionally, CHWs are trained to use fever as a proxy for malaria. How can a child with malaria not have fever? The job aide needs to clearly indicate that the RDT is the only guide to deciding whether a child has malaria or not. The importance of making a correct classification needs to be conveyed to CHWs using examples that highlight the risk to children of wrong classification.

This session requires more time and practice during training, and an improved and simplified job aide that allows CHWs to follow through from assessment to classification. Similar experiences with job aides have been reported from Integrated Management of Childhood Illness (IMCI) programmes (Osterholt *et al.* 2009). A study in Bolivia showed that CHWs are capable of acquiring skills needed to effectively manage acute respiratory illness, but highlighted the importance of training emphasis on how to count the respirations of children with fast breathing (Zeitz *et al.* 1993).

Performance in prescribing treatment

In spite of misclassification problems, a high proportion of children with a positive RDT were prescribed appropriate treatment, whereas a substantial proportion of children with pneumonia (paediatrician) were not. However, based on CHW classification of children, a reasonably high proportion of children with malaria and/or pneumonia were prescribed the correct treatment. This demonstrates the potential for improved treatment if CHWs can be enabled to become more accurate in their classification.

Osterholt *et al.* 2009 in IMCI evaluation found that incorrect diagnosis was a key problem which preceded two-thirds of all treatment errors. However, once pneumonia was correctly diagnosed, failure to prescribe an antibiotic was unusual. Other studies from Tanzania, Bangladesh and Burkina Faso show poor health worker performance in history taking, physical examination and consultation time at primary healthcare facilities (Krause *et al.* 1998; Nsimba *et al.* 2002; Arifeen *et al.* 2005). Putting our results into context, performance of CHWs was very satisfactory.

Pariyo *et al.* 2005 show that while high-quality training can lead to improved performance and quality of care, it is not enough and other factors such as supervision play a key role. Therefore, programmes need to invest into support structures for community programmes such as these to be effective. If appropriately used, these diagnostic tools will greatly improve access to and use of medicines, lower the risk of development of microbial resistance and improve the quality of care for febrile children.

Methodological limitations

The entire evaluation lasted 2 weeks. It is possible that CHWs' performance could be influenced by this longitudinal approach with those evaluated later not performing as well, having lost some of the skills or forgotten issues. On testing this relationship, there was no correlation (coefficient = −0.091 and $P = 0.756$). The observation of consultations could have influenced CHW practices, perhaps overestimating performance in real life. However, the intent of this study was to measure CHW competence after training, although this may not be replicated in real life.

This was a facility-based study with an environment different from the CHWs' home where they practice, and this could have influenced CHW performance. At home, they have other pressures from work and family that could affect performance. Results may seem promising but need confirmation in a real-world setting. The small number of CHWs is a limitation in this study, and because of this, we did not have sufficient power to detect associations between performance and CHW attributes. The ability of CHWs to correctly interpret RDTs in a low-prevalence area, when many tests are negative, may be quite different from what we saw in this study. We recommend that similar studies be replicated in these settings with larger numbers of CHWs.

The observers were not blinded to the results of the CHWs before they undertook their own readings. This may have influenced their own readings. We tried to minimise this by using highly qualified observers and training them prior to the observations. The observers were also closely supervised by the study team. All indicators used were awarded uniform weight. Although desirable, weighting of indicators could have made this analysis much more complex than it already is, and difficult to explain.

Conclusion

Findings of this study show that it is possible to train lay CHWs to use RDTs and timers to assess and manage malaria and pneumonia in children. The integration of these diagnostics into CCM is therefore recommended. CHWs need more practice on use of timers to count respiratory rates. In addition, provision of simple job aides will enable CHWs to make a classsification based on diagnostic results without having to think about several assessment results, minimising misdiagnosis.

Acknowledgements

This study received financial support from UNICEF/UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases (TDR), and two separate grants from the Division for International Development DfID to the Makerere University School of Public Health (DeLPHE) and the Malaria Consortium. Its contents are solely the responsibility of the authors and do not reflect the views of TDR, DfID or the authors' institutions of affiliation. We thank in a special way Dr Franco Pagnoni of TDR for his invaluable support and guidance. The study participants, the community health workers, the three trainers, two paediatricians, laboratory scientists, health workers at the three health facilities used for this study, the health facility incharges, Iganga district, local council officials and Ministry of Health Uganda are all acknowledged for their support and contribution.

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III

Access, acceptability, and utilisation of community health workers using diagnostics for case management of fever in Ugandan children: a cross-sectional study

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Submitted: Malaria Journal

Abstract

Background: Use of diagnostics in integrated community case management (iCCM) of fever is recognised as an important step in improving rational use of drugs and quality of care for febrile under-5 children. This study assessed household access, acceptability and utilisation of community health workers (CHWs) trained and provided with malaria rapid diagnostic tests (RDTs) and respiratory rate timers (RRTs) to practice iCCM.

Methods: A total of 423 households with under-5 children were enrolled into the study in Iganga district, Uganda. Households were selected from seven villages in Namungalwe sub-county using probability proportionate to size sampling. A semi-structured questionnaire was administered to caregivers in selected households. Data were entered into Epidata statistical software, and analysed using SPSS Statistics 17.0, and STATA version 10.

Results: Most (86%, 365/423) households resided within a kilometre of a CHW's home, compared to 26% (111/423) residing within 1 km of a health facility ($p<0.001$). The median walking time by caregivers to a CHW was 10 minutes (IQR 5-20). The first option for care for febrile children in the month preceding the survey was CHWs (40%, 242/601), followed by drug shops (33%, 196/601).

Fifty-seven percent (243/423) of caregivers took their febrile children to a CHW atleast once in the three month period preceding the survey. Households located 1 km or more from a health facility were 60% (OR 1.60; 95% CI 1.04-2.49) more likely to utilise CHW services compared to households within 1km of a health facility. Households located 1-3

km from a CHW were 80% (OR 0.19; 95% CI 0.10-0.36) less likely to utilise CHW services compared to those households residing within 1 km of a CHW.

Majority (79%, 336/423) of respondents thought CHWs services were better with RDTs, and 89% (375/423) approved CHWs' continued use of RDTs. Eighty-six percent (209/243) of respondents who visited a CHW thought RRTs were useful.

Conclusion: ICCM with diagnostics is acceptable, increases access, and is the first choice for caregivers of febrile children. More than half of caregivers of febrile children utilised CHW services over a 3-month period. However, one-third of caregivers used drug shops in spite of the presence of CHWs.

Keywords: community health worker; case management; malaria; pneumonia; febrile children; diagnostics; access; acceptability; utilisation; Uganda.

Background

Malaria and pneumonia are leading causes of morbidity and mortality among under-fives in sub-Saharan Africa [1-3]. Many of these deaths occur at home due to poor access to health care [1, 4]. Community case management (CCM) of malaria and pneumonia have both been shown to reduce under-five mortality [5, 6], and are recommended by the WHO [7-9]. Since 2002, Uganda has adopted and implemented CCM for malaria (locally referred to as home-based management of fever, HBMF). Under CCM, Community Health Workers (CHWs) provide pre-packaged anti-malarial drugs (initially chloroquine and sulphadoxine/pyrimethamine, and later Artemisinin-based Combination Therapy - ACT) presumptively to children that present with, or have a history of fever [10]. In mid 2010 (after this study had commenced), Uganda adopted a national policy on integrated community case management (iCCM) for malaria, pneumonia and diarrhoea [11].

Parasitological confirmation in all patients presenting with symptoms compatible with malaria at all levels of the health system before administration of anti-malarial treatment has been recently recommended by WHO [12]. Parasitological confirmation improves quality of care and is particularly important in the context of declining malaria transmission, when malaria will be responsible for a decreasing proportion of fever cases [13].

Given that rapid diagnostic tests (RDTs) are now available with sensitivities comparable to routine microscopy in detecting malaria [14-17] these tests could improve diagnosis and quality of care of febrile children in malarious areas [18]. Use of diagnostic tools for malaria has the potential to reduction waste and cost of anti-malarial medication [19], potentially delay the development of parasite resistance to drugs, and improve

treatment of alternative causes of fever such as pneumonia [20-22]. Indeed studies from Tanzania [23] and Zambia [24] have demonstrated decreased ACT prescription following use of RDTs by CHWs.

Respiratory rate timers (RRTs) [25] have been recommended by WHO and UNICEF as a diagnostic tool for pneumonia. The use of RRTs by CHWs in sub-Saharan Africa has been reported elsewhere [24, 26].

A multi-country study [27] that included Uganda deployed and evaluated the feasibility of introducing RDTs and RRTs as diagnostic tools in iCCM. Prior to the study, a qualitative assessment of community acceptability of RDT use by CHWs was conducted in Uganda [28]. There is limited evidence of community access to, acceptability and utilisation of programmes deploying diagnostics into iCCM. Following one year of use of RDTs and RRTs by CHWs in iCCM, a follow up quantitative household survey was conducted to assess household access, utilisation and acceptability of the use of RDTs and RRTs by CHWs. Questions about acceptability were informed by the findings of the qualitative study [28]. This paper reports key findings from this survey.

Methods

Study Area

The study was conducted in the rural Ugandan district of Iganga as part of a larger study on the feasibility of deploying RDTs and RRTs at community level (Clinical Trials.gov Identifier NCT00720811). Uganda has an estimated population of 34 million inhabitants of whom about 80% live in rural areas. The district is located in South Eastern Uganda,

approximately 112 km from Kampala, the capital city. It borders Mayuge district to the south, Bugiri to the southeast, Kaliro and Namutumba to the North and Jinja District to the West. The district is divided into 3 counties with a total of 19 sub-counties [29]. The district has a total population of approximately 600,000 that is mainly rural and engaged in subsistence agriculture. The district has one hospital, 23 HC IIIs, and 52 facilities providing only outpatient care. Iganga has high transmission rates (holoendemic) for malaria [30]. The study was conducted in Namungalwe sub-county which is comprised of 7 parishes and 19 villages with a projected total population of 32,911. A total of 14 villages were selected to participate in the larger trial with half of them randomised into the intervention arm. This study was conducted in the seven intervention villages.

Brief Description of the intervention

In the intervention arm, CHWs were trained to use RRTs and RDTs to assess and manage febrile children as reported elsewhere [26]. Children with a positive RDT were treated with Artemether-Lumefantrine (AL), while those with fast breathing (above IMCI cut offs for age: 2-12 months > 50 breaths per minute, 13-59 months > 40 breaths per minute) with the aid of a RRT were treated with amoxicillin. AL and amoxicillin dosages were administered for age, and for a total duration of 3 days according to WHO guidelines [12, 31]. Paracetamol was given to children with temperature measuring 38.5°C and above, as well as all children with a negative RDT, and no fast breathing.

Study design and Population

A cross-sectional household survey was conducted among caregivers of children 4-59 months old (under-5s). The study population consisted of caregivers (parents or guardians of children), and all under-5 year old children within selected households. We defined a caregiver as any person above 18 years of age who at the time of the study was directly responsible for the care of an under-5 eligible for this study, including seeking health services. They should have been responsible for the under-5 for at least the preceding 3 months to the survey.

We defined a household as a group of people at the time of the study that lived together and ate from the same cooking pot. Polygamy is a common practice in the area, and for avoidance of doubt, in homesteads where different groups of people prepared and ate meals separately, we considered each of these groups as separate households.

Households that had recently (no older than 3 months) moved into the study area, child headed households, and households without under-5s were excluded from the study.

Sample Size Consideration

A total of 423 households were selected to participate in the survey. The sample size was estimated using the formula for a single proportion by Kish [32], allowing for a sampling error of 6%, 95% confidence level, utilisation of CHW services of 50% and a design effect of 1.5. A non-response rate of 5% was allowed for.

Sampling Strategy

A household register was obtained from the Local Council I (village) chairperson, and updated with the help of the chairperson and a village scout. The updated total number of households in the area was 857 with Bufuntula village having 305, Nabikoote 154, Bubogo A 122, Namunkesu 114, Bubogo B 63, Namufuma 55, and Namunsala 44. The register was used as the sampling frame. From the sampling frame the required number of households for the survey (as determined by probability proportionate to size sampling (PPS)) [33] was selected using a table of random numbers. Using PPS, villages contributed households to the sample relative to the number of households in the village. The field team coordinator (GO) who was trained in use of PPS and the table of random numbers, was responsible for the selection of households.

The household register(s) maintained by the chairperson record households using the name of head of household. In certain homesteads under a single head of household, there were more than one eligible household per operational definition. Within these eligible homesteads one household (per operational definition) was randomly selected using the ballot method.

Within selected households, all under-5s were included in the study. If a selected household was not eligible for the study, or declined the interview, the field team coordinator was contacted by the research assistant(s) via phone to provide a new household. A new household was selected from the sampling frame. This was repeated for each village until the required sample per village had been enrolled. The non-response rate in this study was 3% (14 households).

Data Collection Methods

A semi-structure questionnaire was used to collect data from the caregivers. Data were collected by a team of seven research assistants with experience in quantitative data collection drawn from the Makerere University Iganga/Mayuge Demographic Surveillance Site. Research assistants were trained for one day in the survey methods for this study, how to replace ineligible households in the field, and completing the study questionnaire. The research assistants participated in the pilot testing of the questionnaire. The pilot was conducted in households that were not part of the pre-selected sample of households, and these did not participate in the final survey. Lessons from the pilot were used to revise the questionnaire to address issues of clarity and the logical flow of questions.

Data collection was conducted over a 10-day period in the month of October 2010. Questions asked (or observations made) included: distance of the household from nearest health facility and CHW, socio-demographic characteristics of the head of household, type of housing (as a proxy to socio-economic status), history of fever among under-5, health seeking behaviour, perceptions of quality of services, utilisation of CHW services, and perceptions of CHW services. The questionnaire can be obtained from the authors upon request.

Recall periods of one and three months were used in this study. The one-month recall was used for purposes of eliciting responses to questions about the management of the most recent fever episode in the under-5. This was done to minimize recall bias because of the details expected from the respondents. We extended the recall period to three months for more general questions around health seeking choices made when under-5

had fever, reasons for choices, acceptability of diagnostics, as well as estimating utilisation of CHW services, the primary outcome of this study. The extension was also driven by the fact that there had been a recent stock out of drugs among CHWs, that could have affected utilisation, and therefore a shorter recall period could result into an inaccurate estimate of utilisation.

Data Management and Analysis

Data was field edited for completeness and consistency by members of the study team, and changes were made in the field. Data were double entered into EpiData (EpiData Association, Odense, Denmark - www.epidata.dk) statistical software, and analysed using a combination of SPSS Statistics 17.0 (SPSS Inc - www.spss.com) and Stata version 10 (College Station, Texas, USA). Data was checked for consistency, and cleaned.

The primary outcome (utilisation of CHWs services) was estimated using the first healthcare option by caregivers of febrile children. Secondary outcomes included: access to CHW services, caregiver reported treatment outcomes for CHW services, proportion of caregivers who approved the use of RDTs by CHWs, reasons for non-acceptance of use of RDTs by CHWs, and perceptions about RRTs. Multivariate logistic regression analysis was used to explain the relationship between outcomes, and household as well as caregiver characteristics. A social economic status (SES) index was calculated for all households using materials used for the house roof, wall and floor. Principal components analysis (PCA) was used in constructing the index. Households were divided into five wealth quintiles based on their SES score [34]. The household quintile was taken as

surrogate indicator for income. Odds Ratios with their corresponding 95% confidence intervals were generated.

The SES index was constructed as described by Vyas and Kumaranayake [34]. Materials used to construct floor, wall, and roof were used as a proxy. A total of 8 dummy variables were constructed. STATA version 10 was used to generate weights for each of the variables. These weights were then multiplied with the dummy scores for each individual household and added to generate a score for each household.

Ethical Approval

Ethical approval for the study was obtained from the World Health Organisation Ethical Review Committee, Makerere University School of Public Health Institutional Review Board, and the Uganda National Council for Science and Technology.

Permission was obtained from the Iganga District Health Office, and from the local authorities to conduct the study. Individual written informed consent was obtained from each of the caregivers. Confidentiality was maintained throughout data collection, management, analysis, and reporting.

Results

Background Characteristics of Households

Most heads of household were male (89.8%; 380/423), married (91.3%; 386/423), farmers (49.2%; 208/423) and had attained at least primary education (93.4%; 395/423) (Table 1). Median age of head of households was 39 years (IQR 32-47).

There was slight female predominance (52.7%, 401/761) among the under-fives. Most

(63.6%, 484/761) respondents were mothers of the under-fives.

Most main family houses were built with iron sheets roofs (68.8%, 291/423), were made of brick and cement walls (33.3%, 141/423), and had a mud floor (53%, 224/432). Using the type of material used to build the main family house as a proxy for income, grass roofs, mud walls and mud floors were common at the lower end of the index, while iron sheets, plastered walls and cemented floors were common at the upper end of the distribution (table 2). The distribution of households across different quintiles was as follows: Q1 (21.3%), Q2 (24.1), Q3 (26.7%), Q4 (18.7%), and Q5 (9.2).

Geographical access to services provided by community health workers

Eighty-six percent (365/423) of households reported to reside within a kilometre of a CHW's home, compared with only 26.2% (111/423) residing within 1 km of a health facility ($p<0.001$). Most (69.5%; 294/423) households reported to reside 1-3km of a health facility. The median time it takes for households to walk to a CHW was 10 minutes (IQR 5-20).

Utilisation of services provided by community health workers

Fever in the last one month was reported in 79% (601/761) of all the children. More than half of children (380/601) were reported to have had more than one fever episode in the month preceding the survey. Respondents were asked about their first action for the most recent fever episode for each child in the month preceding the survey. Forty percent (242/601) sought care from a CHW, 32.7% (196/601) from a drug shop, 19.1% (115/601)

from a health centre, 2.5% (15/601) from a hospital, 2.0% (12/601) gave drugs available at home, 0.3% (2/601) did nothing, while 3.2% (19/601) used other alternatives.

Respondents were asked about reasons for choice of first healthcare option. Fifty-one percent (305/601) mentioned convenient location, 30.3% (182/601) mentioned technical skills of personnel, 25.8% (155/601) were recommended by a friend/family, 10.5% (63/601) mentioned relatively low cost, 9.3% (56/601) mentioned courtesy of personnel, and 20.3% (122/601) had other reasons. The key "other" reasons were: CHW has drugs (62/122), and CHW was absent when I went there (29/122).

Perceived quality of service

Ninety five percent (568/601) of respondents reported that they were satisfied with the services provided by the first option of care for the most recent fever episode. The aspects of services respondents were satisfied with were: drugs given (89.4%; 508/568), RDTs (33.5%; 190/568), RRTs (27.6%, 157/568), physical examination (18.5%, 105/568), laboratory tests (14.8%, 84/568), taking history (14.6%, 83/568), and others (2.6%; 15/568).

Of the 242 respondents whose first point of care was a CHW, 97.9% (237/242) reported that they were satisfied with the service they received. The main reasons for satisfaction were: availability of drugs (89.5%; 212/237), use of RDT (73.4%, 175/237), and use of RRT (60.8%, 144/237). Others were: the way the child was examined (20.3%, 48/237) and the way history was taken (9.3%, 22/237). Multiple responses were allowed for these questions on perceived quality.

Utilisation of CHW services in the three months preceding the survey and RDT acceptability

Table 3 shows the utilisation of CHW services in the three months preceding the survey, as well as caregiver perceptions regarding use of malaria RDTs by CHWs. Fifty-seven percent (243/423) of respondents took an under-5 to a CHW in the 3 month period preceding the survey. Reasons for not going to a CHW were: CHW had no drugs or was told they had no drugs (27.2%, 49/180); no child had been sick (21.7%; 39/180); do not like CHW services (12.7%; 23/180); did not know CHWs existed or where to find them (8.3% 15/119); CHWs was unavailable when they went there (7.2%; 13/180); CHWs are far compared to health centre (5.5%, 10/119), and a variety of other reasons (31/180).

Of the respondents reporting to have visited a CHW in the 3 months preceding the survey, 87.2% (212/243) reported CHW was using RDTs. Sixty-six percent (280/423) of respondents thought CHW services were better than other health services for febrile children. Among those who visited a CHW in the 3 months preceding the survey 88.1% (214/243) thought CHW services were better than other health services.

Respondents were asked to compare CHWs services before and after introduction of RDTs. Seventy-nine percent (336/423) of all respondents, and 97.1% (236/243) of those who visited a CHW thought they are now better. Eighty-nine percent (375/423) of all respondents and 98.8% (240/243) would had visited a CHW would like CHWs to continue using RDTs.

Majority (99.1%; 419/423) of respondents said they had no fears or concerns regarding drawing of blood from children by CHWs. Among the 4 respondents who had fears, the

reasons were: the agony of pain suffered by the child, and concerns about CHWs' safe use of RDTs without causing infections.

Adherence to test results for prescription of medicines

Of the 243 respondents who took a child to a CHW in the three months preceding the survey, 88.9% (216/243) said CHWs administered drugs based on test results, 7.8% (19/243) said "No", while 3.3% (8/243) did not know. Among those who said "No", the most commonly mentioned reason was that the CHW did not do the test, but gave the drugs anyway.

Respondents were asked if they trusted the test results, and 94.7% (230/243) said they did, while 5.3% (13/243) did not. Among those who said "No", the most commonly mentioned reasons were: CHW did not do the test (6/13); CHW did not explain results (3/13); and, "my child did not improve" (2/13).

Do caregivers influence CHW to administer drugs even when tests are negative?

A total of 41 respondents who visited the CHW in the 3 months preceding the survey reported to have recognised that one of the test results was negative. Of these, 12.2% (5/41) said they asked the CHW to administer medicines even when the result was negative. The reasons given for this were: "I saw my child was very sick", and "I needed the medicine for protection" (precaution, just in case the test was wrong).

Relationship between household characteristics and utilisation of CHW services

Table 4 shows the relationship between household characteristics and utilisation of CHW services. Utilisation of CHW services was associated with distance of household to the nearest health facility. Households residing 1 km or more from a health facility were 60% (OR 1.60; 95% CI 1.04-2.49) more likely to utilise CHW services compared to households residing within 1 km of a health facility.

Utilisation of CHW services was also associated with distance of the household to the nearest CHW. Households residing within 1-3 km from a CHW were 80% (OR 0.19; 95% CI 0.10-0.36) less likely to utilise CHW services compared to households residing within 1 km of a CHW. Other relationships were not statistically significant.

Discussion

This study assessed community access, utilisation and acceptability of the use of malaria rapid diagnostic tests (RDTs) and respiratory rate timers (RRTs) by CHWs following one year of implementation. Accessibility to CHWs was high, with majority of the households residing within one kilometer of a CHW's home. Most respondents reported taking 10 minutes to walk to a CHW's home. Utilisation of CHW services for febrile children was high, with more than half of respondents reporting to have taken an under-5 to a CHW in the three-month period preceding the survey. About 80% of all respondents reported CHWs services as better after introduction of RDTs, while among respondents that utilised CHWs services in the three months to the survey, nearly all reported services as having improved following introduction of RDTs. Majority of respondents reported that RRTs were useful. Utilisation of CHW services was associated with, distance of

household to the nearest health facility, and distance of household to nearest CHW. Households residing at least 1 km from a health facility were 60% more likely to utilise CHW services compared to households residing within 1km of a health facility. Households residing within 1-3km from a CHW were 80% less likely to utilise CHW services compared to those households residing within 1km of a CHW.

The high accessibility by households to CHWs suggests that the programme is meeting its goal of bringing curative services for febrile children as close as possible to their homes. CHW programmes have been reported to improve access to prompt treatment for febrile children [35-38].

CHWs were the preferred choice for care for febrile children with drug shops a close second at over 30%. Drug shops remain very popular in spite of available free services for febrile children through CHWs. There is extensive literature from Tanzania [39-42], Kenya [43, 44], Uganda [45, 46] and elsewhere showing the important role that drug shops play as a source of care especially for malaria. Some of the reasons why caregivers did not utilise CHW services were lack of drugs, dislike of CHW services, not being aware of the CHWs services in the community, missing CHW in their homes on a visit, or being closer to a health facility. The programme indeed experienced drug stock-outs from time to time, and this appears to have had a significant impact on caregiver choices. In many cases, caregivers continued to bypass CHWs and go elsewhere even when drug stocks had been replenished. CHW programmes need to take measures to ensure stockouts do not occur or are kept at a minimum. In case it becomes unavoidable, there should be clear and timely information regarding when drugs are expected. Distance to the provider, and perceived skills of the provider were also found to be key drivers of

choice of service provider. CHW programmes need to ensure that the majority of community members have easy reach to CHWs, especially those in rural and hard to reach areas. A systematic review of access and utilisation of health services shows that availability of drugs, distance to health facilities, and perceived quality of care are the key determinants influencing health service utilisation [47].

Geographical factors influenced utilisation of CHW's services. The closer caregivers were to CHWs the more likely they were to use them. This is consistent with the programme objectives. However, caregivers who were close (within a kilometer) to a health facility were less likely to utilise CHWs compared to those who resided farther way from a health facility. This finding has policy implications for CHW programmes such as this. Since programmes are designed to provide access to care for under-served, hard-to-reach communities, CHWs will need to be located carefully, so that only under-served communities are selectively included. In well-served communities where CHWs exist, they could provide services that complement what a nearby facility provide, including health education, health promotion, and referral services. Programmes in these areas will also need to take into account the other contextual factors such as buy-in from medicine sellers as proposed by Goodman et al [48]. Lehmann et al [49] have made the case that CHWs are neither a panacea, nor cheap option for weak health services. As health services increasingly get strengthened and coverage improves, the roles of CHW will need to be carefully defined and refocused. Equally important is the fact that even when services are available they may not be accessible to the poorest in a community and in turn enhance inequities [50]. CHWs have a role in bringing these services closer to the poorest and excluded segments of communities.

Majority of caregivers that visited a CHW were satisfied with the service they received. Availability of drugs, use of RDT and use of RRT were main reasons for satisfaction. Availability of drugs and use of diagnostics in this setting were key drivers of satisfaction. This is consistent with findings reported by Nsabagasani et al [51] from western Uganda where both CHWs and caregivers agreed that diagnostic equipment at community level would improve diagnosis and attract more caregivers of febrile children. Caregivers do not want to go where there are no drugs, as they feel they are wasting time and will have to go to the next provider.

Almost all caregivers had no fears about drawing of blood from under-5s by CHWs for the RDT test. Similar results have been reported from Zambia in a study where CHWs used RDTs in home management of childhood fever [52]. An earlier qualitative study from this area reported that some caregivers expressed fear that the blood collected could be used for HIV testing, the procedure could infect children with HIV, and the blood could be used for witchcraft [28]. This study was conducted prior to the introduction of RDTs in the community. It appears that the direct interaction of caregivers with competent CHWs [26] using the RDTs, and the community engagement that was undertaken prior to the intervention may have changed some of the negative perceptions. Majority of caregivers thought CHW services were better after introduction of RDTs, and nearly 90% of all caregivers interviewed approved of CHWs continued use of RDTs and RRTs.

The overall RDT positivity rate in the intervention study preceding this study was 88% (857/975) [27]. Acceptability of RDTs by caregivers might be different in settings were the positivity rate is much lower. In situations where caregivers of children feel that their

children are “ill enough” to warrant prescription of an anti-malarial drug, with or without a positive test result, and where CHWs strictly adhere to RDT test results to guide prescription practices, it is plausible that popularity of tests and CHWs will be lower. The importance of identifying alternative causes of fever will be even more critical in these settings, as well as ensuring that CHWs are equipped to manage conditions such as non-severe pneumonia as has been reported elsewhere [24, 27]. A study from the Solomon Islands, on acceptability of RDTs reports a general distrust by the community of the accuracy of RDTs, resulting in continued presumptive treatment of malaria [53]. Also, a study from Sudan reports that although the use of RDTs seemed to have improved the level of accuracy and trust in the diagnosis, 30% of volunteers did not rely on the negative RDT results when treating fever cases [36]. These mistrusts may be a result of the lack of intensive CHW training and supervision, as well as absence of services for alternative causes of fever at the CHW’s post.

Respondents reported that the majority of CHWs adhered to test results for prescription of drugs to patients. A small portion of CHWs were reported to have been coerced into providing medication to children with a negative RDT or RRT. This is in contrast to a study from Zambia that found adherence to test results to be high with over 99% of patients with a negative RDT result not prescribed an anti-malarial [52].

Methodological considerations

Bias in recall was a potential problem in this study with caregivers being asked to remember things that happened in the past about an event that may not have been a major event in the home. We attempted to minimise this by limiting the recall period to 1 month

for key details, and 3 months for more general questions about a most recent fever episode in the child. We also interviewed caregivers that were responsible for the under-5 and not anyone in the household.

We asked respondents to compare current CHW services with those before introduction of RDTs. We did not establish who had utilised CHWs before introduction of RDTs and it is likely that some respondents had never used CHWs in the areas before RDT introduction, but nevertheless responded to the question. This could lead to over or under estimation of the true positive or negative responses.

Interviewer bias is always a possibility in these kinds of studies. We attempted to minimise this bias by using research assistants who had not been involved in the intervention and were blinded to the hypothesis the data collection was based on.

Principal components analysis was used to generate a socio-economic status (SES) index. We used fewer variables than most often used, for example in the 2006 Uganda Demographic and Health Survey [54]. However, the index does portray the actual picture on the ground in terms of the components used and what is generally understood as what these components represent in terms of SES in the community. While asset-based measures are increasingly being used, there continues to be some debate about their use. These measures are more reflective of longer-run household wealth or living standards, failing to take account of short-run or temporary interruptions, or shocks to the household [55]. Therefore, if the outcome of interest is associated with current resources available to the household (*as health services utilisation might be*), then an index based on assets may not be the appropriate measure [34]. However, under the circumstance, with no other

source of information on household income and expenditure in this rural community with a large informal sector, the approach used was considered a reasonable alternative.

Conclusion

ICCM with diagnostics is acceptable, increases access, and is the first choice for caregivers of febrile children. However, one-third of caregivers used drug shops in spite of the presence of CHWs. This implies that the service still needs to be better known, and better accepted, and CHWs need to have a constant supply of commodities. It also underscores the significant role played by drug shops and the need to involve them during programming. More than half of caregivers of febrile children utilised CHW services over a 3-month period. It appears that the use of RDTs and RRTs may have improved the utilisation of CHWs services.

Competing Interests

The authors declare that they have no competing interests.

Authors' contributions

DM, JKT, SP, GP, JK, PW, FB, RB, GO, FP and KK took part in designing the study, in tools development, in data analysis and in manuscript writing. SK participated in data analysis and manuscript writing. DM, RB, and GO participated in data collection. All authors approved the final manuscript.

Acknowledgements

We are grateful to the study participants, and research assistants for their support during data collection, Iganga district local council officials, Makerere University Iganga demographic surveillance site, and Ministry of Health Uganda. This study received financial support from UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases. Its contents are solely the responsibility of the authors and do not reflect the views of UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases nor the authors' institutions of affiliation.

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Table 1: Background characteristics of households and under-fives

Variable	Frequency (n=423)	Percentage
Location of households by village		
Bufutula	151	35.7
Nabikoote	76	18.0
Bobogo A	60	14.2
Namunkesu	56	13.2
Bubogo B	31	7.3
Namufuma	27	6.4
Namunsala	22	5.2
Head of household		
Sex		
Male	380	89.8
Female	43	10.2
Marital status		
Married/cohabiting	386	91.3
Widowed	23	5.4
Divorced/separated	11	2.6
Single	3	0.7
Religion		
Muslim	216	51.1
Protestant/Evangelical	172	40.7
Catholic	26	6.1
Other	4	0.9
Missing	5	1.2
Occupation		
Employed	34	8.0
Trader/self employed	176	41.6
Farmer	208	49.2
Does not work	5	1.2
Highest education level attained		
Never been to school	28	6.6
Primary	271	64.1
Secondary and above	124	29.3
Under-fives	(n=761)	
Median age	36 months	IQR 19-48
Sex		
Male	360	47.3
Female	401	52.7
Relationship of respondent with under-5		
Father	138	18.1
Mother	484	63.6
Grandparent	90	11.8
Other	49	6.4
Fever in last 1 month		
Yes	601	79.0
No	160	21.0

Table 2: Composition of unique assets values

		Type of materials used on the main house		
Closest to	Index value (score)	Roof	Wall	Floor
Lowest value	-4.275	Grass	Mud	Mud
25th pecentile	-0.648	Iron sheets	Bricks/Mud	Mud
Median	0.150	Iron sheets	Bricks/cement	Mud
75th pecentile	1.417	Iron sheets	Bricks/Mud	Cement
Highest value	2.539	Iron sheets	Plastered cement	Cement

Table 3: Utilisation of CHW services and caregiver perceptions about CHW use of RDTs

Variable	Frequency (n=423)	Percentage
Respondent visited CHW in past 3 months to seek care for under-five with fever		
Yes	243	57.4
No	180	42.6
Those who visited CHW	n=243	
Was CHW using RDT		
Yes	212	87.2
No	28	11.5
Missing	3	1.2
Was CHW using RRT		
Yes	207	85.2
No	36	14.8
Was RRT useful		
Yes	209	86.0
No	29	11.9
Missing	5	2.1
Acceptability of RDTs (all respondents asked question regardless of visit to CHW in 3 months)	n=423	
CHW services compared with other health services for children with fever		
Better	280	66.2
No difference	57	13.4
Worse	5	1.2
I don't know	75	17.7
Other	4	0.9
Missing	2	0.5
CHW services before and after RDTs were introduced		
Now better	336	79.4
No difference	5	1.2
Worse	5	1.2
I don't know	77	18.2
Should CHWs continue using RDTs		
Yes	375	88.7
No	1	0.2
Can't answer the question	47	11.1

Table 4: Association between household characteristics and utilization of CHW services

Variable	Utilised CHW services		OR (95% CI)	p-value
	Yes n=243	No n=181		
Distance to nearest Health Centre				
< 1 km	54	57	1.00	
≥ 1 km	189	124	1.60 (1.04-2.49)	0.0325*
Distance to nearest CHW				
<1km	229	137	1.00	
1-3km	14	44	0.19 (0.10-0.36)	<0.001*
Education of head of household				
Never	25	20	1.00	
Primary	165	128	1.03 (0.54-1.94)	0.924
Secondary above	53	83	1.28 (0.62-2.67)	0.502
Occupation of head of household				
Employed/self employed	21	9	1.00	
Farmer	199	162	0.53 (0.23-1.18)	0.120
Other/Casual	23	10	0.99 (0.34-2.90)	0.979
Indicator for SES				
Poorest (quartile 1)	49	41	1.00	
Second (quartile 2)	55	48	0.96 (0.54-1.69)	0.884
Middle (quartile 3)	73	40	1.53 (0.87-2.69)	0.143
Fourth (quartile 4)	44	35	1.05 (0.57-1.93)	0.870
Richest (quartile 5)	22	17	1.08 (0.51-2.31)	0.837

IV

Integrated Community Case Management of Fever in Children Under Five using Rapid Diagnostic Tests and Respiratory Rate Counting: a Multi-country Cluster Randomized Trial

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Abstract. Evidence on the feasibility of using diagnostic tests in integrated community case management of febrile children is limited. This multi-country cluster randomised trial enrolled a total of 4216 febrile children between 4 and 59 months in Burkina Faso, Ghana, and Uganda to evaluate an integrated diagnostic and treatment package for malaria and pneumonia. The package was compared with standard presumptive treatment with anti-malarial drugs without diagnostic tests. There was high compliance with malaria rapid diagnostic test (RDT) results in the intervention arm across the 3 sites with only 4.9% (17/344) of RDT negative children prescribed an anti-malarial drug. Antibiotic overuse was 0.9% (4/446) in Uganda, 38.5% (114/296) in Burkina Faso, and 44.6% (197/442) in Ghana. Fever clearance tended to be higher in the intervention arm at both Day 3 and Day 7 compared to the control arm, but this may be a chance finding (p=0.17).

Running head:

MUKANGA AND OTHERS

DIAGNOSTIC-BASED INTEGRATED COMMUNITY CASE MANAGEMENT

Trial registration: http://register.clinicaltrials.gov NCT00720811

INTRODUCTION

Malaria and pneumonia are leading causes of morbidity and mortality among under-fives in sub-Saharan Africa,[1, 2, 3] despite the availability of cost-effective interventions for both conditions. Community case management of malaria and pneumonia have both been shown to reduce under-five mortality,[4, 5] and both strategies are recommended by the World Health Organization (WHO).[6, 7, 8]

Parasitological confirmation before administration of antimalarial treatment has recently been recommended by WHO for everyone presenting with symptoms compatible with malaria at all levels of the health system.[9] Such confirmation is increasingly important in the context of declining malaria transmission, when a decreasing proportion of fever cases is likely to be due to malaria.[10] Furthermore, given the overlap in symptoms between malaria and pneumonia,[11] the World Health Organization (WHO) and the United Nations Children Fund (UNICEF) now recommend integrated community case management (iCCM) of malaria and pneumonia in endemic areas in low and middle income countries.[8]

Rapid diagnostic tests (RDTs) for malaria are now available with sensitivities comparable to routine microscopy in detecting malaria[12, 13, 14] and offer a practical means[15, 16] to improve diagnosis and quality of care of febrile children in malarious areas. Several studies have shown that community health workers (CHWs) can use RDTs safely and effectively.[14, 17, 18, 19, 20]

Increased respiratory rate is one of the most specific symptoms of pneumonia[21, 22, 23] and respiratory rate timers (RRTs)[24] have been recommended by WHO and UNICEF as a diagnostic tool for pneumonia, with studies[19, 25, 26] showing that CHWs can be successfully trained to use them.

We designed an integrated diagnostic and treatment package for malaria and pneumonia,

which involves trained CHWs, equipped with RDTs and RRTs and supplied with ACTs and antibiotics, administering treatments based on the results of the two tests. We report here an evaluation in three African countries, Burkina Faso, Ghana and Uganda, of the effect of this package on the clinical outcome of febrile episodes in children and on the use of anti-malarial and antibiotic drugs.

MATERIALS AND METHODS

Study areas and populations. We report this evaluation using the Consort statement extension to cluster randomised trials.[27] The evaluation was conducted in Burkina Faso, Ghana and Uganda, in the districts of Saponé, Kassena Nankana and Iganga respectively. Saponé and Kassena Nankana are situated in the Sudan-Sahelian eco-climatic zone, with a seasonal malaria transmission pattern peaking during the wet months of May – September. Iganga is situated in South Eastern Uganda and has minimal seasonal variation in malaria transmission.[28] Data were collected in Burkina Faso from August 2009 to June 2010, in Ghana from May 2008 to December 2008, and in Uganda from October 2009 to October 2010.

Twelve villages participated in the study in Burkina Faso, 16 in Ghana, and 14 in Uganda. In Burkina Faso, the 12 villages were selected from two community clinic catchment areas within the Saponé Health District with an estimated total population of 9,000. The 16 villages selected in the Kassena-Nankana districts were drawn from 47 villages with a total population of 150,000 under continuous demographic surveillance. The 14 villages in Iganga were all drawn from Namungalwe sub-county which has a population of approximately 38,100 in 19 villages. Malaria, pneumonia, and diarrhoeal diseases are the leading causes of ill-health amongst children aged 1-59 months in the three study areas.

The study population comprised children aged 6 - 59 months (with the exception of Uganda where the lower limit was 4 months in line with national guidelines on use of ACTs in children[29, 30]) with fever or history of fever in the previous 24 hours, who presented to a CHW. Exclusion criteria included severe illness according to IMCI guidelines, known chronic disease, reported anti-malarial or antibiotic treatment in the previous two weeks, or known sensitivity to the study medications.

Study design. The study was designed to assess the effect of the use of a diagnostic and treatment package for iCCM, comprising RDTs and ACTs for malaria, RRTs and antibiotics for pneumonia, on recovery from fever, and the rational use of medicines.

We performed an open, cluster randomised two arm trial in the three countries. Clusters were the villages (catchment populations) of individual CHWs. Within the study areas, we excluded for ethical reasons clusters that were more than 5 km from a designated health facility where CHWs referred cases for special care in order to minimize non-referral completion due to distance. A cluster randomized design was chosen over an individually randomized design to reduce contamination, facilitate supervision, reduce costs, and to ensure that the CHWs maintained the correct treatments based on the tests in the intervention arm and the presumptive treatment in the control arm.

In the intervention arm, CHWs assessed children with acute febrile illness for malaria using RDTs, and for pneumonia by counting their respiratory rate with RRTs. Treatment was then provided on the basis of the test results. Children with a positive RDT received artemether-lumefantrine in Burkina Faso and Uganda, and artesunate-amodiaquine in Ghana. Children with a high respiratory rate received amoxicillin in Ghana and Uganda, and cotrimoxazole in Burkina Faso. The criterion for antibiotic administration was the presence of a high respiratory rate,

regardless of the presence of cough or difficult breathing, in contrast to WHO guidelines[31]. Additionally, paracetamol (PCT) was provided to all children in whom both RDT and RRT were negative, and/or children with an axillary temperature > 38.5°C.

In the control arm, all febrile children received ACTs based on a presumptive diagnosis of malaria as provided for in the current IMCI guidelines. CHWs in Burkina Faso and Uganda had no antibiotics. In Ghana, in line with existing practice, CHWs in the control clusters were also supplied with amoxicillin that they could provide to children based on clinical judgement. Antibiotics and anti-malarial drugs were provided as three-day treatment courses, while paracetamol was provided for two days, so that it did not interfere with the fever assessment on Day 3. The first dose of all treatments was administered under the supervision of the CHW, and if the child vomited within 30 minutes they were given another dose. The dosing schedule was explained to caregivers who then administered the remaining treatments at home.

Malaria RDTs used. First Sign® Malaria Pf Card Test (Unimed International, Inc), Paracheck Pf® Rapid test for *P. falciparum* Malaria (Device) (Orchid Biomedical System) and ICT® Malaria Pf Cassette test (ICT Diagnostics SA) were used in Burkina Faso, Ghana and Uganda respectively. First Sign®, Paracheck® and ICT® have panel detection scores (PDS) at parasite densities from 2000 parasites/μL of 86.1%, 97.5% and 97.5% respectively, and PDSs at parasites densities of 200 parasites/μL of 31.7%, 54.4% and 82.3% respectively.[32]

Drugs used in the study. ACTs used in the study were Coartem® manufactured by Novartis Pharma in Burkina Faso, Acumal (artesunate-amodiaquine) manufactured by JCPL Pharma PVT Ltd, India in Ghana, and Coartem® manufactured by Novartis Pharmaceuticals Corporation Suffern, New York in Uganda. Antibiotics used in the study were cotrimoxazole in Burkina Faso manufactured by Medicamen Biotech Ltd, India, Kinamox™ (amoxicillin) in Ghana

manufactured by Kinapharma Ltd and in Uganda amoxicillin manufactured by Zhangjiakou Shengda Pharmaceutical Co Ltd, China (re-packed by Kampala Pharmaceutical Industries, 1996 Ltd).

Paracetamol used in the study was manufactured by: Laborate Pharmaceutical (India) for Burkina Faso, Kinapharma Ltd for Ghana, and Kampala Pharmaceutical Industries (1996) Ltd for Uganda.

Community Health Workers. A total of 57 CHWs were recruited (13 in Burkina Faso; 16 in Ghana, and 28 in Uganda), half of whom were randomised to the intervention arm. CHWs were selected by their respective community, based on minimum criteria that included the ability to read and write clearly so that they would be able to complete the study Case Report form (CRF). In Ghana existing community health nurses (living within the community and hired and trained by the Ghana Health Service to provide basic services) were used.

Sample size. The estimated sample size for the study was 4360 febrile children between 4 and 59 months, with Burkina Faso and Ghana contributing 1200 each, and Uganda 1960. The sample size was estimated using the simplified formula by Hayes and Bennett[33] for cluster randomized trials with a power of 80% to detect an absolute difference in fever clearance 72 hours after treatment of 10% (85% against 75%) between the two arms with a two-sided alpha of 0.05. The estimation took seasonality into account, as well as accounted for loss to follow up. We assumed a coefficient of variation between clusters of 0.12.

Training. CHWs were taught how to take a history, recognise clinical features of uncomplicated malaria and signs of severe illness requiring referral; preparation of thick blood films for malaria microscopy; the use of classification and treatment algorithms for malaria and pneumonia (intervention arm only); use of simple dosing guidelines based on age for ACTs and

PCT; managing drug supplies; obtaining informed consent; and completing CRFs including documentation of reported signs and symptoms, physical examination results, and medications administered to the child. In cases where informed consent was declined, the child received standard presumptive management of fever with an ACT.

In addition, CHWs in the intervention arm were taught the clinical features of non-severe pneumonia; use of malaria RDTs; infection control measures; how to count respiratory rate; and the use of simple dosing guidelines based on age for antibiotics.

There was interactive training consisting of oral presentations, discussions, role play and supervised hands-on practice for all the study CHWs. At the end of the training, facilitators assessed the competency of the CHWs to follow the algorithm, complete study forms, and for CHWs in the intervention arm the appropriate use of RDTs and RRTs, as reported elsewhere.[19]

At the health facility level, health personnel were oriented on the treatment strategies in the two arms, and received refresher training on Integrated Management of Childhood Illnesses (IMCI). These staff provided care to children referred from the study, and provided supportive supervision to the CHWs.

Quality assurance plan. The CHWs were supervised weekly by field supervisors to detect and correct any deviations from the protocol. During these visits, the following were monitored: completeness of data captured in the CRFs, respect of inclusion/exclusion criteria, drug administration, drug and RDT storage conditions, and assessment and follow-up of enrolled children.

At each supervisory visit three samples of RDTs were collected from the batch in use. The RDT samples were tested against a sample of blood confirmed positive by microscopy to ensure the RDTs were still functioning with adequate sensitivity.[34]

At the end of each month all CHWs attended a review meeting at the health center at which the assessment, treatment and follow up algorithms were reviewed, and problem areas were identified and discussed. CHWs brought their registers and CRFs. CHWs identified as having problems with a particular part of the algorithm were followed up and were provided with support and re-training by the study team. The accuracy of CHWs in performing the RDTs was assessed as part of each supervisory visit. When there were no patients at the time of the visit, CHWs were asked to demonstrate how they perform the procedure, including how they do the finger-prick and how they read the RDT result. CHWs were observed and reminded to perform the RDT in a well-lit place.

Refresher training was provided to the health facility microscopists on malaria microscopy before enrolment started. Ten slides per month were selected for quality control (5 low density, and 5 negative slides) using a random number system recommended by WHO[35] and sent to a reference laboratory for re-reading on a "blinded" basis.

Data collection methods. All children who were tested for malaria on day 0 also had a thick blood film prepared by the CHWs. The blood films were collected within 24 hours in all the 3 sites by a field work supervisor with a motorbike. Blood films were stained with 10% Giemsa stain for 10-15 minutes and screened microscopically under X100 oil immersion lens using a light microscope by a microscopist trained by the study teams and based at the referral centre.

The number of parasites present per white blood cell was counted, and the figure multiplied by 8000 (an average white blood cell count per µl) to give the parasite density.[36] Slides were double read, and when there was a discrepancy between the two readings the slide was read again by an experienced / senior microscopist who was independent of this study and whose reading was considered final. The microscopy results were used to establish the accuracy of the RDTs when

used in the communities. Children with a negative RDT, but with a positive slide reading were traced at home and treated with ACTs. All patient data were recorded on CRFs at all three sites.

Patient management and follow-up. CHWs reviewed children and completed the CRF on days 0, 3, 7 and on unscheduled visit days. A review on day 3 determined if a child had recovered from fever (temperature below 37.5°C as measured by a digital thermometer). Children in either arm who had not recovered were referred to a designated health centre. All children not referred at day 3 (clinically recovered) were reviewed on day 7, and any fever relapse cases were referred to the health centre. All children referred (day 3 or 7) were examined by a trained project nurse, and managed according to IMCI guidelines. Children who did not come for scheduled visits were traced and assessed at home.

Study Outcomes. The study outcomes measured were resolution of fever at Day 3 and Day 7 in febrile children, and the use of anti-malarial and antibiotic drugs. Outcomes were measured and analysed at the individual level.

Data analyses. Data were entered into microcomputers and analysed using Epi-Info 6.0 and STATA 9.0. We compared proportions of the study outcomes between the two groups. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using random effects logistic regression analysis with the treatment arm and country as fixed effects, and cluster as a random effect. Analysis was by intention-to-treat.

Ethical approval. Ethical approval for these studies was granted by the WHO Ethics Review Committee and by the appropriate national and Institutional Ethical Review Boards of each participating country. Approval was obtained from district, local, and community leaders as well as household heads. Informed consent was obtained from caregivers of children who participated in the studies. The WHO TDR project numbers are A60486 for Burkina Faso, A60490 for Ghana

and A60487 for Uganda. The trial was registered online at http://register.clinicaltrials.gov with the registration number NCT00720811.

RESULTS

Baseline characteristics. Overall, 4216 children aged between 4 and 59 months were enrolled in Burkina Faso, Ghana, and Uganda. The number of children enrolled in intervention and control arms respectively were: 525 and 576 in Burkina Faso, 584 and 591 in Ghana, and 975 and 965 in Uganda (Figure 1). With the exception of reported cough, baseline characteristics were comparable across the two arms (Table 1). In total, 64.5% (2691/4216) had temperatures ≥ 37.5°C at enrolment and 69.5% (2729/3925[1]) had microscopically confirmed malaria.

Use of medicines. Use of medicines by assessment classification is summarized in tables 2a, 2b and 2c. In the intervention clusters, there was good compliance with RDT results by CHWs across the 3 sites with minimal overuse of ACTs. Only 1 case out of 1740 RDT positive children did not receive an ACT, while only 4.9% (17/344) of RDT negative children were prescribed an ACT.

With regard to antibiotics, there were varying degrees of overuse (prescription to a child with a normal respiratory rate) in Burkina Faso, Ghana and Uganda, with 38.5% (114/296), 44.6% (197/442), and 0.9% (4/446) of children with normal respiratory rate receiving an antibiotic respectively. Conversely, some children with high respiratory rates did not receive an antibiotic: 13.5% (31/229) in Burkina Faso, 27.5% (39/142) in Ghana, and 1.7% (9/529) in Uganda. Among children with high respiratory rates, we analysed data within the subgroup who also had a cough; 16% (20/125) in Burkina Faso, 17.9% (7/39) in Ghana, and 0.9% (3/337) in Uganda of these

[1] Blood smear for microscopy done in only a sub-sample of children in the control arm in Uganda

children did not receive an antibiotic. The overall rate of antibiotic underuse in this subgroup was 6.0% (30/501).

In the control clusters, ACTs were given to all children in all countries, leading to potential unnecessary prescription of ACTs in 25.6% , 15.8% and 12.1% of cases in Burkina Faso, Ghana and Uganda respectively (assuming a similar proportion of RDT negative cases in the control and intervention clusters). In Ghana (where antibiotics were used in control clusters as well) 51.4% of all children were prescribed antibiotics in the intervention clusters compared to 64.3% in the control clusters, suggesting less over-prescription of antibiotics in the intervention arm.

Impact on fever clearance. Fever clearance results are summarized in table 3. There were high fever clearance rates overall across sites and arms. Fever clearance rates at Day 3 and Day 7 were 97.8% and 99.2% in intervention clusters, and 96.9% and 98.8% in control clusters. The estimated odds ratios for failure to clear fever (intervention vs control) were 0.69 (95% CI 0.41, 1.16; p=0.17) at day 3 and 0.62 (95% CI 0.32, 1.22; p=0.17) at Day 7, compatible with improved fever clearance in the intervention arm, but also compatible with no effect of the intervention.

While no formal pharmacovigilance system had been put in place, there were no passive reports of severe adverse events or deaths at any of the three sites.

DISCUSSION

This cluster randomized trial evaluated the effect of a diagnostic and treatment package, comprising RDTs and ACTs for malaria, RR timers and antibiotics for pneumonia, implemented at the community level to treat children under the age of 5 years with fever episodes. The package led to a clear improvement in the appropriate use of ACTs, and in Ghana, the only site in which antibiotics were available in the control arm, to fewer prescriptions of antibiotics. The

vast majority of children recovered from fever in both the intervention and control groups, and no effect of the intervention on the clinical outcome (recovery from fever) was detected.

Inappropriate use of ACTs is a major concern, as it may lead to the development of resistance to these highly effective drugs.[37] The potential for misuse of ACTs could be particularly high at the community level, where ACTs are distributed by non-professional staff.[38, 39] The latest WHO malaria treatment guidelines[9] recommend parasitological confirmation before administering anti-malarial drugs to a patient presenting with fever in all areas, including highly malaria-endemic settings. The shift from symptom-based to RDT-based treatment with ACTs has major implications. It limits the over-diagnosis of malaria and thus the inappropriate use of ACTs and expenditure,[40] and reduces missed diagnosis of other causes of fever[41, 42] at a time when a declining proportion of fevers in Africa are attributable to malaria.[10] Administering ACTs only to patients with a positive RDT has led to dramatic reductions in the use of ACTs in Cambodia,[18] mainlandTanzania,[43] and Zanzibar.[44] Nevertheless, in some settings incomplete adherence to RDT results leads to substantial proportions of patients with negative tests receiving ACTs as has been frequently reported from health facilities,[45, 46, 47, 48] although improvements in adherence have been achieved after intensive training in some cases.[43, 49]

Poor adherence to RDT results has also been reported when febrile episodes are managed at the community level by CHWs, with up to 58% of patients with a negative RDT result being treated with an antimalarial.[50] Poor compliance with referral advice by patients with fever but with a negative RDT result has also been reported.[51] It is noteworthy that in both these studies there was no alternative diagnostic test, nor treatment for RDT negative patients. However, very high levels of appropriate prescription of ACTs after rapid malaria testing were achieved in Chikankata, Zambia in a program in which febrile children were assessed for pneumonia, and

antibiotic treatment was provided as appropriate.[25] Similar findings were reported more recently in another study in Zambia that used an intensive training and supervision model.[52]

The results of our study in three sub-Saharan African countries, conducted with a similar design to the one in Chikankata, confirm that inappropriate use of ACTs is extremely rare (less than 5% of cases) when alternative diagnostic tests and treatment for other conditions are provided to patients with negative RDT results (in our study children with fever and a negative RDT were prescribed antibiotic treatment if there were signs of pneumonia, and paracetamol if there were none). On the contrary, when anti-malarial treatment is administered to all febrile children, without prior parasitological confirmation, as in the control clusters of our study, an important proportion of cases are treated with ACTs unnecessarily. This study was conducted in areas of high malaria prevalence, confirmed both by microscopic examination and rapid diagnostic testing (tables 1 and 2). Nonetheless, based on the proportion of negative RDT results in the intervention clusters of the study sites, the proportion of unnecessary use of ACTs can be estimated to vary between 12% and 26% across the 3 sites. This is a significant finding with public health implications, suggesting that a disease management approach based on a diagnostic and treatment package improves the appropriate use of ACTs, and provides alternative treatment for other causes of febrile illness.

Inappropriate use (non-compliance with study guidelines) of antibiotics was high in two study sites. More than a third of children with a normal RR received antibiotic treatment in Ghana and Burkina Faso, while 27% and 14% of children with high RR did not receive any antibiotics in the two countries respectively. In Ghana, however, where CHWs could prescribe antibiotics in control clusters based on their clinical judgement, 64.3% of children were treated with antibiotics in control clusters compared to 51.4% in intervention clusters. In this study, we used only high

respiratory rate as the criterion for antibiotic use, while the WHO[31] recommends the presence of cough or difficulty breathing together with high respiratory rate as the criteria. This is a limitation of this study, and fewer children would have been treated with antibiotics under WHO guidelines than were treated using a criterion of rapid breathing alone. Overuse of antibiotics is a well-known phenomenon at all levels of the health system in low, middle and high income countries, as reported by the WHO[53], and has been recently reported to be aggravated by the introduction of RDT in the decision algorithm.[43] In Uganda, over- or under-prescription of antibiotics was rare, accounting for only 0.9% and 1.7% of cases. This difference between Uganda and the other sites may be explained by differences in the more intensive supervision program of the CHWs, as well as by local treatment practices. It is possible that local antibiotic prescription practices influenced behaviour in the intervention clusters. Vialle-Valentin and colleagues[54] have reported higher antibiotic use among under-5s in Ghana compared to other countries including Uganda.

The second endpoint of our study was fever clearance after three and seven days from onset of symptoms. One might expect a higher proportion of children with fever to be afebrile after a few days if treated more rationally, with different drugs based on the results of diagnostic tests. Consistently across the study sites, over 96% of the children were afebrile at the follow up visits in both intervention and control arms. While a smaller proportion of children in the intervention arm remained febrile at Days 3 and 7 compared to the control arm, the numbers of such children were small and the difference observed could be due to chance. This result is not easy to interpret. One possibility is that the frequency of minor, self-limiting viral infections as the cause of fevers was high, and diluted the effect of specific anti-malarial and antibacterial treatment. Furthermore, in a context of high parasitaemia, it is possible that antibiotics might not have a

substantial measurable effect on fever clearance. Our findings are consistent with those from a study in Zambia[25] which found no evidence that the risk of persistence of fever differed in intervention and control clusters after 5 and 7 days of treatment. Adding cough/difficulty breathing to our treatment algorithm would not have altered this since most under-fives who needed an antibiotic received one in the intervention arm.

Other aspects of feasibility, and acceptability of the approach based on the diagnostic and treatment package was assessed in all sites and will be reported in detail elsewhere. Overall, the CHWs were found to be able to perform their tasks satisfactorily, including rapid diagnostic testing for malaria and respiratory rate counting. A study in Uganda showed that when RDT results and RR were double-checked by laboratory technicians and paediatricians there was a concordance rate of 100% for RDTs and 93% for RR.[19] The acceptability of CHWs performing RDTs and RR counting was also high among communities, CHWs and health staff. The majority of interviewed community members were satisfied with CHWs treating children according to the package.

Though the study was not designed to evaluate RDT performance, the positivity rates for microscopy were consistently lower than those for RDTs across the three sites. This may be explained by the fact that all three RDTs used HRP2 as the target antigen which can persist in the blood stream after parasite clearance suggesting that some positive RDTs were indicative of past rather than current infection. The choice of which RDT to use was made for one of the following reasons: availability, resistance to high storage temperature (40^{o}C), delivery time, and national policy. Burkina Faso received their supply from TDR as their original supplier failed to deliver. The RDTs used were: FirstSign in Burkina Faso, Paracheck pf in Ghana and ICT in Uganda. It should also be noted that the RDTs were selected prior to the publication of "Malaria Rapid

Diagnostic Test Performance – Results of WHO product testing of malaria RDTs Round 2 (2009)"[32] in which RDT performance was recorded for 67 RDTs. The ranking of the panel detection scores (PDS) for the RDTs was 28 for ICT, 49 for Paracheck and 59 for First Sign,[32] indicating that that none really achieved a high combined measure of positivity rate, along with inter-test and inter-lot consistency, although their PDS's were above 70/100.

The study shows that an integrated community case management approach based on the use of diagnostics and medicines for malaria and pneumonia by CHWs improves the rational use of anti-malarial drugs, and may reduce the inappropriate use of antibiotics at the community level in settings where they are already available, thus adding to the evidence base for iCCM as a public health strategy. Fever clearance tended to be higher in the intervention arm at both Day 3 and Day 7 compared to the control arm, but this may be a chance finding.

Acknowledgements: We thank the community members, opinion leaders, CHOs, the health workers, research assistants, field supervisors and workers in the districts of Sapone in Burkina Faso, Kassena Nankana in Ghana, and Iganga in Uganda without whose co-operation and help this study would not have been possible. We also acknowledge the technical and financial support from the UNICEF/UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases.

Financial support: This study was funded by UNICEF/UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases (TDR) through project numbers A60486 for Burkina Faso, A60490 for Ghana and A60487 for Uganda.

Competing interests: The authors declare that they have no competing interests.

Author contributions: ICMJE criteria for authorship read and met: DM, AT, TA, KK, ATK, ARO, JKT, LA, SBS, SC, GB, and FP. All the authors except GB conceived the study; DM, AT, TA were the principal investigators for their respective country's study site and together with KK, ATK, ARO, JKT, LA participated in the research design and supervised data collection from the field. SC performed most of the quantitative data analysis. FP, the WHO/TDR CCMm research program manager supervised all the field sites. FP, SBS, and SC facilitated the proposal development workshop. FP, SC and GB facilitated the data analysis workshop. GB and FP co-ordinated the final reports and developed the final manuscript together with DM. All authors read and approved the final manuscript.

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Annex: Figures and Tables

Figure 1. Study Profile

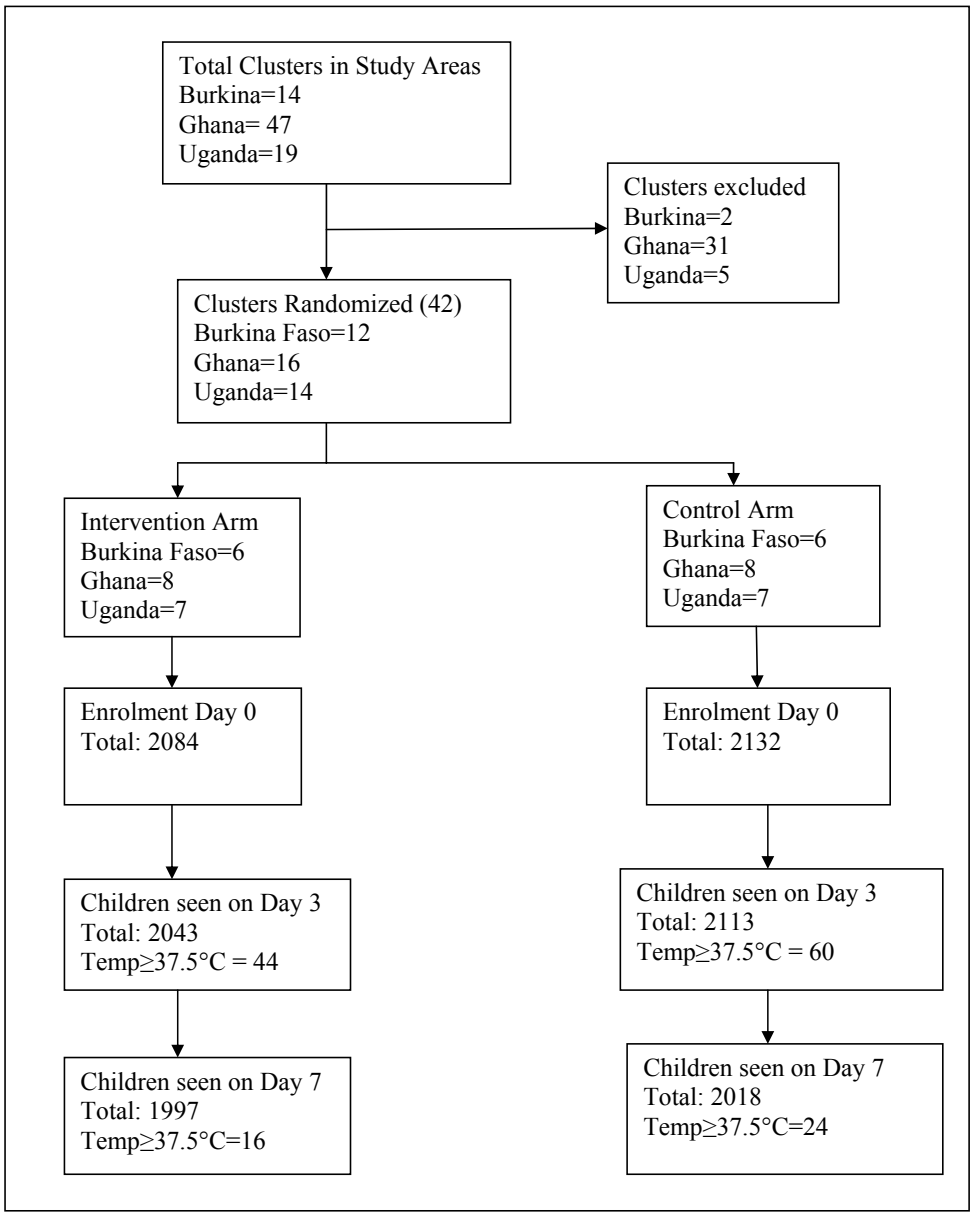

Table 1. **Baseline characteristics of children at enrolment**

	Burkina Faso		Ghana		Uganda	
	Intervention	**Control**	**Intervention**	**Control**	**Intervention**	**Control**
Number of children enrolled	525	576	584	591	975	965
Number (%) with measured temperature ≥ 37.5	436 (83.0%)	457 (79.3%)	351 (60.1%)	372 (62.9%)	563 (57.7%)	512 (53.1%)
Mean age (in months)	28.7	30.3	24.6	26.0	27.8	27.3
Number (%) of females	277 (52.8%)	276 (47.9%)	277 (47.4%)	317 (53.6%)	451 (46.3%)	478 (49.5%)
P.f. asexual parasitaemia prevalence (by microscopy)	284 (54.1%)	313 (54.3%)	439 (75.2%)	435 (73.6%)	783 (80.3%)	475/674[2] (70.5%)
Geometric mean parasite density in positives	11,841	10,505	15,320	12,350	7,663	7,318
Number (%) of children with cough	252 (48.0%)	241 (41.8%)	123 (21.1%)	226 (38.2%)	555 (56.9%)	-
Number (%) of children with diarrhoea	134 (25.5%)	154 (26.7%)	208 (35.6%)	208 (35.2%)	-	-

[2] Blood smear for microscopy done in only a sub-sample of children in the control arm in Uganda

Table 2a. Assessment classification and treatment in Burkina Faso

		Number (%) of children treated with			
	Number (%) of children by assessment classification	ACT+; AB+; PCT+/- (A)	ACT+; AB-; PCT+/- (B)	ACT-; AB+; PCT+/- (C)	ACT-; AB-; PCT+ (D)
Intervention clusters					
Children with positive RDT and high RR (1)	173* (32.9)	141 (81.5)	31 (17.9)	0 (0.0)	0 (0.0)
Children with positive RDT, high RR and Coughφ (2)	90 (17.1)	70 (77.8)	20 (22.2)	0 (0.0)	0 (0.0)
Children [3]with positive RDT and normal RR (3)	218* (41.5)	75 (34.4)	141 (64.7)	0 (0.0)	0 (0.0)
Children with negative RDT and high RR (4)	56* (10.7)	3 (5.4)	0 (0.0)	37 (66)	0 (0.0)
Children with negative RDT, high RR and Coughφ (5)	35 (6.7)	2 (5.7)	0 (0.0)	33 (94.3)	0 (0.0)
Children with negative RDT and normal RR (6)	78* (14.9)	2 (2.6)	0 (0.0)	37 (56.4)	26 (33.3)
Total	525	221 (42.1)	172 (32.8)	74 (14.1)	26 (5.0)
Control clusters					
Total	576	0	575 (99.8)	0	0

N.B: Cells shaded gray represent correct treatment for the row.
The rows with the symbol φ at the end of the row title are a subset of the row just above them. The numbers in the row cells do not count in the respective column totals.

[3] *Row data has missing records on treatment given.

Table 2b. Assessment classification and treatment in Ghana

		Number (%) of children treated with			
	Number (%) of children by assessment classification	ACT+; AB+; PCT+/- (A)	ACT+; AB-; PCT+/- (B)	ACT-; AB+; PCT+/- (C)	ACT-; AB-; PCT+ (D)
Intervention clusters					
Children with positive RDT and high RR (1)	130 (22.3)	92 (70.8)	38 (29.2)	0 (0.0)	0 (0.0)
Children with positive RDT, high RR and Coughφ (2)	32 (5.5)	25 (78.1)	7 (21.9)	0 (0.0)	0 (0.0)
Children with positive RDT and normal RR (3)	362 (62)	144 (39.8)	218 (60.2)	0 (0.0)	0 (0.0)
Children with negative RDT and high RR (4)	12 (2.1)	0 (0.0)	1 (8.3)	11 (91.7)	0 (0.0)
Children with negative RDT, high RR and Coughφ (5)	7 (1.2)	0 (0.0)	0 (0.0)	7 (100)	0 (0.0)
Children with negative RDT and normal RR (6)	80 (13.4)	0 (0.0)	2 (2.5)	53 (66.3)	25 (31.3)
Total	584	236 (40.4)	259 (44.3)	64 (11)	25 (4.3)
Control clusters					
Total	591	360 (60.9)	203 (34.4)	20 (3.4)	8 (1.4)

N.B: Cells shaded gray represent correct treatment for the row.
The rows with the symbol φ at the end of the row title are a subset of the row just above them. The numbers in the row cells do not count in the respective column totals.

Table 2c. Assessment classification and treatment in Uganda

		Number (%) of children treated with			
	Number (%) of children by assessment classification	ACT+; AB+; PCT+/- (A)	ACT+; AB-; PCT+/- (B)	ACT-; AB+; PCT+/- (C)	ACT-; AB-; PCT+ (D)
Intervention clusters					
Children with positive RDT and high RR (1)	459 (47.1)	449 (97.8)	9 (2.0)	1 (0.2)	0 (0.0)
Children with positive RDT, high RR and Coughφ (2)	286 (29.3)	282 (98.6)	3 (1.0)	1 (0.3)	0 (0.0)
Children with positive RDT and normal RR (3)	398 (40.9)	4 (1.0)	394 (99.0)	0 (0.0)	0 (0.0)
Children with negative RDT and high RR (4)	70 (7.2)	2 (2.9)	0 (0.0)	68 (97.1)	0 (0.0)
Children with negative RDT, high RR and Coughφ (5)	51 (5.2)	2 (3.9)	0 (0.0)	49 (96.1)	0 (0.0)
Children with negative RDT and normal RR (6)	48 (4.9)	0 (0.0)	7 (14.6)	0 (0.0)	41 (85.4)
Total	975	455 (46.7)	410 (42.1)	69 (7.1)	41 (4.2)
Control clusters					
Total	965	0 (0.0)	965 (100.0)	0 (0.0)	0 (0.0)

N.B: Cells shaded gray represent correct treatment for the row.
The rows with the symbol φ at the end of the row title are a subset of the row just above them. The numbers in the row cells do not count in the respective column totals.

Table 3. Fever persistence on study days 3 and 7 after the onset of treatment

Cluster	# of ch. with Temp ≥37.5 and/or reported hot body at D0	# of ch. seen at D3	# of ch. with Temp ≥37.5 at D3 (% of ch. Seen at D3)	#. of ch. seen at D7	# of ch. with Temp ≥37.5 at D7 (% of ch. Seen at D7)
Intervention clusters					
Burkina Faso	525 (436)	507	11 (2.2)	485	2 (0.4)
Ghana	584 (351)	578	10 (1.7)	561	6 (1.1)
Uganda	975 (563)	958	23 (2.4)	951	8 (0.8)
Total	2084	2043	44 (2.2)	1997	16 (0.8)
Control clusters					
Burkina Faso	576 (457)	563	21 (3.7)	527	5 (0.9)
Ghana	591 (372)	591	8 (1.4)	573	10 (1.7)
Uganda	965 (512)	959	37 (3.9)	918	9 (1.0)
Total	2132	2113	66 (3.1)	2018	24 (1.2)

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Printed in Sweden 2012, www.us-ab.com