Drug shops in integrated community case management of malaria, pneumonia and diarrhoea in Uganda

Appropriateness of care and adherence to treatment guidelines

Phyllis Awor

Dissertation for the degree of philosophiae doctor (PhD)

at the University of Bergen

2016

Dissertation date: February 2016

Contributors

This thesis is the result of Afro-Scandinavian collaboration between Makerere University College of Health Sciences, School of Public Health, Uganda; the Centre for International Health, University of Bergen, Norway; Division of Global Health, Karolinska Institutet, Sweden; and the International Maternal and Child Health Unit, Department of Women's and Children's Health, Uppsala University, Sweden.

The research was conducted in two rural districts of Eastern Uganda, Kaliro and Kamuli.

Acknowledgements

I feel privileged to have had the opportunity to carry out this work to completion, not only for the doctoral degree and scientific growth, but also for the huge personal growth that the entire process allowed me to achieve. However, this work would not have been conceivable without the full support, commitment and sustained interest of many people. While I am grateful to everyone who has contributed towards making this work possible, I would like to particularly thank the following people:

Professor Stefan Peterson: Thank you very much for your excellent supervision and guidance. You have always focused on the big picture; ensured that I led every aspect of the studies, writing and dissemination of results; and you have responded to every question that I asked and email that I wrote. Thank you for walking with me every step of the way.

Professor Thorkild Tylleskar: Thank you for being my main supervisor at the University of Bergen, which allowed me return to Norway, where I had also undertaken my MSc. degree. Thank you also for allowing me the flexibility that I needed, in order to undertake both studies and childcare.

Dr. Henry Wamani: Thank you very much for your guidance throughout the project work in Uganda; for introducing me to your network of health systems researchers who also became my supervisors and mentors; and for you friendship.

Professor Jan Helge Solbakk: You were the first person to introduce the idea of pursuing a PhD to me, when you offered to be my supervisor, way before I even thought a PhD could be relevant in my life. Thank you for allowing me to open up my mind to taking on a PhD.

Professor Stefan Einhorn: I am very grateful to you for funding this work, and for your family and foundation's personal interest in the work in Uganda. We are privileged to have had your full support though out the years.

Faculty and administrative staff at UiB: Thank you for making my stay in Bergen very productive and smooth. Special thanks to Borgny, Ingvild Hope and Oyvind for your timely administrative and logistical support, whenever I needed any assistance.

Faculty at Makerere University, School of Public Health and the department of Community Health and Behavioural Sciences (CH&BS): I am grateful for all the support and understanding provided to me, while I undertook the PhD studies. I specifically thank the head of department, Professor C.G. Orach and the entire department of CH&BS for warmly welcoming me.

Colleagues in Bergen and members of the Makerere School of Public Health (MakSPH) PhD forum: I have learned so much from every one of you during this PhD journey. In our office "the palace" in Bergen, we have encouraged and supported each other. I wish you all a very successful future. At MakSPH, we have the PhD forum. This is a group of nearly 50 current PhD students and recent PhD graduates who support each other scientifically, socially and psychologically. It is not possible to list everyone's name, but thank you all for your tremendous generosity.

The data collection teams and field supervisor: To Joy Kwikiriza and the nearly 40 data collectors we worked with: thank you for all your hard work during these studies! I enjoyed very much all the time we spent, trying to ensure that we got good quality data.

Finally, I would like to thank my family for always taking care of our children whenever I had to be away, either abroad or in the field in Uganda. I thank my parents for supporting the children, encouraging me and for always being available. I also thank Jonathan, Jason and Esther for turning into very well behaved and understanding little people.

Table of Contents

Operational definitions

Appropriate management/care: Providing care for malaria, pneumonia or diarrhoea in children, according to the Ministry of Health and community case management guidelines, including utilization of the relevant diagnostic test for malaria and pneumonia, prior to treatment with the recommended drug

Appropriate treatment: Dispensing/receiving the recommended drug in the recommended dose, for the recommended frequency and duration, (Nsungwa-Sabiiti et al. 2005) according to the Ministry of Health community health worker national guidelines

Community Health Workers (CHWs): This term embraces a variety of community health aides, selected, trained and working in the communities from which they come. "CHWs should be members of the communities where they work, should be selected by the communities, should be answerable to the communities for their activities, should be supported by the health system but not necessarily be part of its organization and they normally have shorter training than professional health workers." (Lehmann U & Sanders D, Report to WHO, 2007)

Drug shops: Shops selling medicines on retail basis for profit

Drug shop attendant: A person selling medicines or providing medical services at a drug shops. This person may or may not possess prior medical training.

Fever: Febrile to touch or having a history of "hot body" in the last 24 hours, as reported by a caregiver; or temperature $>= 37.5^oC$ (axillary).

Franchise: It comprises a contractual relationship between a franchisee (usually a small business) and a franchisor (usually a larger business) in which the former agrees to produce or market a product or service, in accordance with an overall blue print devised by the franchisor. Franchising is a business strategy targeting market growth through

grouping existing providers under a specific brand supported by training, advertising and supplies. (Montagu 2002)

Social franchise: A franchise system that is usually run by a non-governmental organization, and uses the structure of a commercial franchise to achieve social goals.

Informal private health care providers (IPPs): Those health providers who practice allopathic medicine but have no formally recognized training, and they are not legally recognized, typically functioning outside the realm of government regulation. These may include traditional healers who use both allopathic and traditional systems of medicine, lay community health workers, and drug shop owners/attendants who make diagnosis, give advice and sell medicine. (Shah, 2010)

Malaria: An acute infection presenting with fever, chills and rigors, joint pains and general malaise, caused by a parasite of the plasmodium species, and confirmed by parasitological diagnosis using a malaria rapid diagnostic test or microscopy.

Pneumonia: A viral, bacterial or fungal acute lung infection presenting with cough and/or difficult breathing with or without fever, with either fast breathing or lower chest in-drawing or noisy breathing in a calm child.

ICCM classification of pneumonia: Non-severe pneumonia was taken as the presence of cough with fast or difficult breathing

Quality: Quality is – doing the right thing the right way. Quality in health care is defined as the proper performance (according to standards) of interventions that are known to be safe, that are affordable to the society in question, and that have the ability to produce an impact on mortality, morbidity, disability and malnutrition. (M.I Roemer and C. Montoya Aguilar, WHO, 1988)

Rapid/fast breathing: Having 50 or more breaths per minute in a child aged 2 - 11 months and 40 or more breaths per minute in a child aged 1-5 years. (ICCM guidelines)

Abbreviations

ACT	Artemisinin Combination Therapy
CCM	Community Case Management
CHWs	Community Health Workers
CI	Confidence Interval
FGDs	Focus Group Discussions
HBMF	Home Based Management of Fever
HSSIP	Health Sector Strategic and Investment Plan
ICCM	Integrated Community Case Management
IMCI	Integrated Management of Childhood Illnesses
IDIs	In-depth Interviews
MDGs	Millennium Development Goals
MoH	Ministry of Health
ORS	Oral Rehydration Salts
PR	Prevalence Ratio
PFP	Private for Profit
PNFP	Private Not for Profit
PPPH	Public-Private Partnerships in Health
RDT	Rapid Diagnostic Test
SSA	Sub-Saharan Africa
UN	United Nations
UNICEF	United Nations Children's Fund
VHT	Village Health Team
WHO	World Health Organization

Abstract

Introduction. Private drug shops are an important source of care for children in sub-Saharan Africa, with about half of sick children seeking care at this level. However, these drug shops receive minimal regulation and government oversight and little is documented about the quality of care they provide, although it is generally known to be poor. A strategy recommended by WHO and UNICEF for integrated community based management of childhood illnesses through community health workers exists, within the public sector. This is the integrated community case management (iCCM) of malaria, pneumonia and diarrhoea intervention. However, this iCCM intervention is not available at the level of drug shops, which see the majority of sick children in Uganda.

Aim. To determine the feasibility and effect on appropriateness of care of introducing the iCCM intervention (diagnostic tests; pre-packaged paediatric dosage drugs for malaria, pneumonia and diarrhoea; training and community awareness) within private sector registered drug shops in eastern Uganda.

Methods. Three studies (1-III) were conducted using a quasi experimental design in one intervention and one comparison district between May 2011 and June 2012. Household surveys, exit interviews, focus group discussions and in-depth interviews were conducted before (at baseline) and after the intervention (at end-line) in both areas. The baseline sample size was calculated for cross sectional studies, to determine the proportion of appropriate treatment for malaria, pneumonia and diarrhoea respectively, as these were unknown. The end-line sample size was increased based on the baseline proportion of appropriate treatment and assuming 50% improvement in appropriateness of treatment for household survey and 100% improvement for exit interviews. A total of 3759 (1604 before/2155 after) households interviews and 943 (163 before/780 after) exit interviews were conducted with caretakers of children under five years of age. The role and appropriateness of care provided by drug shops in treating childhood illnesses (study I) was determined from the baseline data by computation of proportions. The effect of the iCCM intervention on appropriateness

of care at drug shops was determined using generalized linear regression models and difference-in-difference analysis, comparing baseline and end-line data (study II). For study III, the proportion of adherence to treatment protocols was determined from a review of the drug shop treatment registers, which included 7,667 child visits.

Results. From the baseline assessment, the majority of children with a recent illness sought care in the private sector 496 (53%) compared to the public sector (154, 16.5%). However, at the level of drug shops, only 15 (10%) received appropriate treatment for malaria and almost none for pneumonia symptoms or diarrhoea. With the introduction of the iCCM intervention at drug shops in the intervention area, 88% (95% CI 79.0 – 96.4) of children with fever received parasite diagnosis of malaria prior to treatment with appropriate drugs. Further, children with pneumonia symptoms or diarrhoea in the intervention area were 3 (2.8; 95% CI 2.0 – 3.9) and 13 times (12.8; 95% CI 4.2 – 38.6) more likely to receive appropriate treatment with amoxicillin and oral rehydration salts + Zinc, respectively. Finally, from the review of registers, 90% of children categorized as having either malaria, pneumonia or diarrhoea or a mix of these classifications were treated according to the iCCM guidelines.

Conclusion. Introduction of the iCCM intervention at drug shops in rural Uganda resulted in high levels of appropriateness of care for malaria, pneumonia and diarrhoea in children and high adherence to treatment protocols by drug shop attendants.

Original papers

The thesis is based on the following papers:

I.   **Awor P**, Wamani H, Bwire G, Jagoe G, Peterson S. (2012) Private sector drug shops in integrated community case management of malaria, pneumonia and diarrhoea in children in Uganda. American Journal of Tropical Medicine and Hygiene. 87:92-96

II. **Awor P**, Wamani H, Tylleskar T, Jagoe G, Peterson S. (2014) Increased access to care and appropriateness of treatment at private sector drug shops with integrated management of malaria, pneumonia and diarrhoea: a quasi-experimental study in Uganda. PLoS ONE 9(12): e115440.

III. **Awor P**, Wamani H, Tylleskar T, Peterson S. (2015) Drug seller adherence to clinical protocols with integrated management of malaria, pneumonia and diarrhoea at drug shops in Uganda. Malaria Journal. 2015, 14: 277.

The original paper in the American Journal of Tropical Medicine and Hygiene is reproduced with the permission of the publisher. The author has the copyright to the other two papers.

Introduction

In 2014, more than 6 million children under five years of age died worldwide. Over 95% of these deaths were in low and middle income countries and most of these deaths could have been prevented [1-2].

After the first year of life, over 50% of deaths in children less than 5 years of age in Sub-Saharan Africa are caused by malaria, pneumonia and diarrhoea [3]. Access to preventive care and timely treatment for these illnesses is paramount to preventing the unnecessary deaths.

We already know several simple life saving interventions that should be scaled up in order to reduce child mortality. These include: promotion of exclusive breast feeding, complementary feeding, insecticide treated bed nets to prevent malaria as well as timely access to treatment when ill including: anti malaria drugs, antibiotics for pneumonia and sepsis, zinc and Vitamin A supplementation and oral rehydration salts and zinc for diarrhoea [4]. The problem is that children who need these lifesaving interventions are not able to access them, leading to the excess mortality in low income countries [4-5]. There is thus an urgent need for innovative and sustainable delivery strategies to get the known interventions to children who need them.

Meanwhile, the majority of children in low income countries first seek care at a private drug shop when ill [6-8]. Unfortunately the quality of care in these facilities is generally low and poorly documented.

Using a quasi-experimental design in two districts - Kaliro and Kamuli - in Eastern Uganda, this thesis aims to address the following research questions:

1. What are the current community treatment practices for childhood fever, respiratory symptoms and diarrhoea? How appropriate is the care provided?

2. What is the effect of introducing diagnostics and subsidized recommended treatment for malaria, pneumonia and diarrhoea at drug shops on appropriateness of care?

3. What is the level of adherence to treatment protocols by drug shop attendants?

To answer these questions, three studies (I, II & III) were conducted: first a baseline study to understand the community health care seeking behaviour as well as the quality of care children received at drug shops, a predominant source of care. Secondly, an innovative introduction of a tested public sector intervention – the integrated community case management of malaria, pneumonia and diarrhoea intervention – within private sector drug shops, with an evaluation of the effect of the intervention on appropriateness of care. Finally, a cross-sectional review of the routine treatment records from the drug shops was conducted, in order to determine their level of adherence to treatment protocols.

In the next section, I review the relevant literature around child mortality and access to care; global interventions to reduce child mortality; the role of the private sector in child care; the importance of integration of care of common childhood illnesses; and the importance of strong health systems. I also present a conceptual model which shows how the studies making up this thesis are linked and guides the discussion of the results.

Mortality in children under 5 years

As we conclude the Millennium Development Goals (MDG) era in 2015, we take-stock of the gains made through the concerted effort of the world to end poverty, hunger and avoidable death. The MDG 4 pledged to reduce by two thirds, between 1990 and 2015, the under-5 mortality rate. This corresponds to an annual rate of reduction of 4.4%.

Globally, there has been steady progress in reduction in mortality in children below 5 years of age over this period from 12.7 million deaths in 1990 to 6.3 million deaths in 2013 [1-2]. While the progress is commendable, halving under-5 mortality within this period, the actual MDG target – reducing the under-5 mortality rate by two thirds – will not be met by the majority of low income countries.

Even though there is global progress in reduction of under-5 mortality, the reduction is not uniform worldwide. The progress is slowest in Sub-Saharan Africa (SSA) and Southern Asia where the burden of death remains highest. Unfortunately four out of five deaths in children under-5 years now occurs in these 2 regions [9-10]. In sub-Saharan Africa, about 1 out of every 10 children dies before reaching their 5th birthday (92/1000 live births) compared to 1 out of 100 children in the European region (12/1000 live births) representing almost 10 times higher mortality [10].

Nonetheless, there are some success stories within Sub-Saharan Africa and southern Asia. There have been huge reductions in under-5 mortality in Rwanda and Ethiopia as well as Laos, Cambodia and Vietnam. All these countries have an annual rate of reduction in under-5 mortality of 4.0 – 4.3% [2].

In Uganda, there has also been a high reduction in under-5 mortality. Between 1990 and 2013, the under-5 mortality rate in Uganda reduced from 179/1000 live births to 66/1000 live births with an annual rate of reduction of 4.3%. The MDG target for reduction in under-5 mortality in Uganda is 60 deaths per 1000 live births by 2015,

putting Uganda currently on track to achieve MDG 4 [1, 11]. However, this is just the first step in the drive to eliminate all preventable child deaths in Uganda and SSA, since a lot of the deaths are still preventable and the high under-5 mortality in Uganda is unacceptable. In comparison, high income countries have eliminated most preventable child deaths and have reached an under- mortality of 6/1000 live births.

Further, the currently available projections for reduction in under-5 mortality beyond 2015 through to 2035 show insufficient progress. Even with the current momentum in worldwide reduction in child deaths, about 4 million children will still die in 2030 and Sub-Saharan Africa is projected to contribute 60% to this mortality, from 50% in 2013 [2, 12]. This shows that even more effort is necessary for further reduction in under-5 mortality, beyond the current achievements of the MDG era.

Causes of under-5 mortality

Worldwide, 50% of all child deaths in 2013 were caused by infectious causes. In addition, 44% of all deaths occurred in the neonatal period. Pneumonia (15%) and prematurity (15%) were the leading individual causes of death in children under-5, followed by intrapartum-related complications including birth asphyxia (11%) and then diarrhoea (9%) – Figure 1 [12-13].
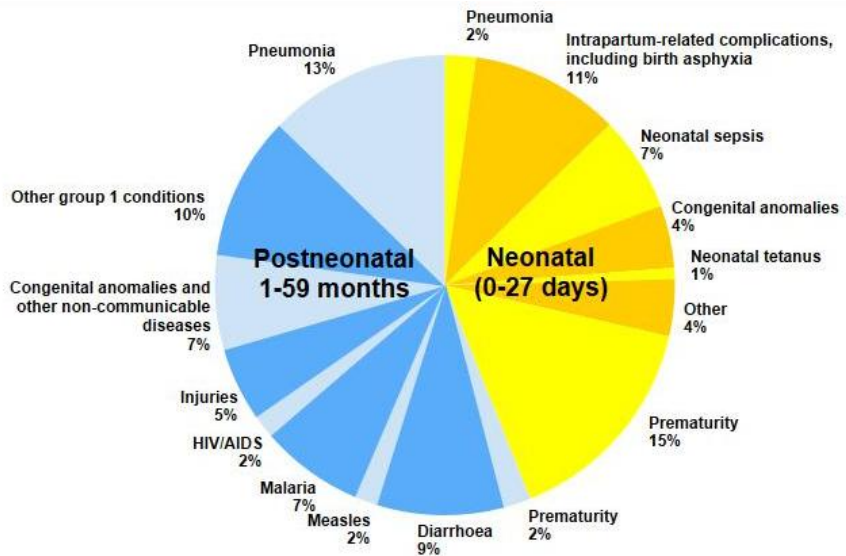
Figure 1 - Global causes of under-5 mortality in 2013.
Source: CHERG – WHO methods and data sources for child causes of death 2000 – 2013
(Global Health estimates technical paper WHO/HSI/GHE/2014.6.2)

Meanwhile, causes of child deaths are different in the various regions of the world. While infectious causes account for 50% of global child deaths, they account for nearly 70% of child deaths in Sub-Saharan Africa [14]. Within the age group of 1-59 months, malaria, pneumonia and diarrhoea accounted for nearly 60% of child deaths in sub-Saharan Africa (figure 2) and about 55% of deaths in Uganda (figure 3) [14].
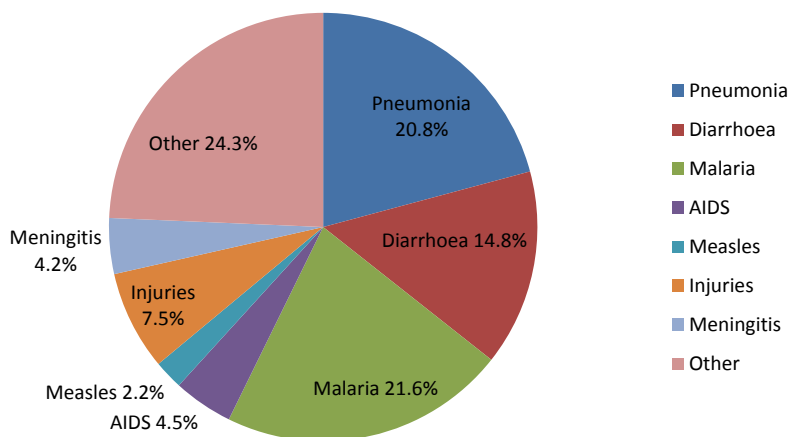
Figure 2 - Causes of death in children 1- 59 months in Sub-Saharan Africa in 2013. Drawn using data from: UNICEF global data bases. Child mortality estimates: Regional child deaths by cause. http://data.unicef.org
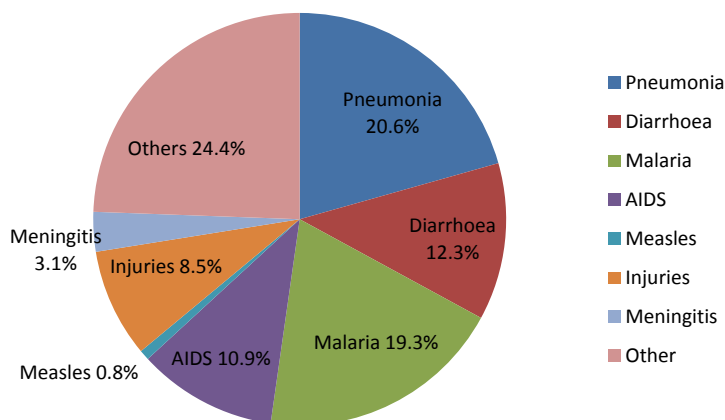
Figure 3 - Causes of death in children 1-59 months in Uganda in 2013. Drawn using data from: UNICEF global data bases. Child mortality estimates:Country specific child deaths by cause. http://data.unicef.org

Global and national action for reduced child mortality

Both globally and at country level, many initiatives are in place, with the aim of improving maternal and child health. Some of these initiatives have been recently instituted, with targets set to maintain the momentum of progress gained in reducing maternal and child deaths, during the MDG era. Here I summarize the key initiatives.

The first initiative is commonly referred to as simply, "a promise renewed." Since 2012, about 200 countries have signed on to an initiative called "Committing to Child Survival: A promise renewed." This is a global call to accelerate declines in preventable maternal, newborn and child deaths that were achieved by the MDG agenda. This action was led by the governments of Ethiopia, India and USA, in partnership with UNICEF. The promise here is to end preventable child deaths within a generation and the new target is of 20 or fewer under-5 deaths per 1000 live births by 2035 [11]. Second is the "Every newborn action plan." This initiative has a target of 10 or fewer neonatal deaths per 1000 live births by 2035 and stipulates actions that should be scaled up to enhance newborn survival [15]. Third, the "Global Vaccine Action Plan 2011 - 2020" was endorsed by the 194 member states at the World Health Assembly in 2012. This initiative targets universal access to existing vaccines by 2020, as vaccination against preventable diseases can be one of the most effective strategies for reduction of child mortality [16].

The United Nations Commission on Life-Saving Commodities for women and children identified and endorsed 13 lifesaving commodities along the continuum of care from pre-pregnancy, pregnancy, delivery and childhood [17]. If widely accessed, these 13 commodities could save the lives of more than 6 million women and children. In terms of child health, this initiative supports countries to access priority medicines including antibiotics like amoxicillin for pneumonia and oral rehydration salts with zinc tables for management of acute diarrhoea. Further, the "integrated Global action plan for pneumonia and diarrhoea (GAPPD)" is being led by WHO and UNICEF and aims to end preventable deaths from these 2 illnesses by 2025. The

GAPPD acts by advocating for and engaging all sectors and actors to protect children from birth; prevent children from contracting pneumonia and diarrhoea; and treat children with these illnesses using appropriate drugs [18]. Finally, the "Scaling up Nutrition" initiative is a partnership between UNICEF, WHO, World Bank and 55 countries, focusing on programs to scale up nutrition interventions and women empowerment [19].

Clearly, global partnerships to help achieve further reduction in under-5 deaths beyond 2015 are essential in Sub-Saharan Africa and other low income settings. Renewed commitment by governments and the international community is paramount and should be sustained. Focus should be on improving access, quality of care and maintaining high coverage of proven preventive, promotive and curative interventions to reduce under-5 mortality [4-5, 12, 20].

Health systems

To achieve sustained reductions in under-5 mortality and better health, strong health systems are essential. Health systems play a key role in the growth and development of individuals and communities worldwide, and progress towards universal health coverage depends on how well health systems carry out their core functions.

It is easy to think that a health system is simply those providers and organizations which deliver personal medical services. However there is much more to a health system than the frontline delivery of medical care. In order for health workers to deliver health care to the population effectively, they must be well trained, financed, supplied, and led. The population they serve should also be empowered to make good health decisions and to contribute towards the financing of their health care [21].

Health systems are thus defined by the WHO as consisting of all the organizations, people and actions whose primary purpose is to promote, restore or maintain health [22]. Health systems have a responsibility not just to improve people's health but to

also protect people against the financial cost of illness and to treat them with dignity. The fundamental goals of health systems are thus to ensure better health for the populations they serve; fairness in financial contributions; and responsiveness to peoples' expectations including dignity, autonomy and confidentiality. In order to achieve their goals, health systems performs various functions which have been described in the WHO health systems framework as building blocks and include: service delivery, generation of well trained and motivated health workers; collecting and utilization of health information; availing medical products, vaccines and technologies; financing; and leadership or governance [21-22].

These health system building blocks are interconnected like a wheel and weakness in any one block (for example shortage of human resources) can impact negatively on the entire system – Figure 4. Further, people are at the centre of the health system both as providers and consumers of health care [23].

Figure 4 – the dynamic nature and interconnectedness of the health system building blocks. (Source de Savigny and Adams 2009)

Health systems reform and universal health coverage

In a bid to ensure better efficiency, fairness and responsiveness of health systems, there have been at least 3 generations of health system reforms over the last 100 years. These include the adoption of national health care systems in the 1940s and 50s in Europe; followed by the Primary Health Care revolution initiated by the Alma Ata declaration in 1979; and finally more recently, starting with the world health assembly resolution in 2005, the Universal Health Coverage drive [24-25].

Universal Health Coverage is defined as "ensuring that all people have access to the needed promotive, preventive, curative and rehabilitative health services of sufficient quality to be effective, while also ensuring that people do not suffer financial hardship when paying for these services" [26]. However, the world today is still very far away from Universal Health Coverage. Particularly in low income countries, access to health care is usually a privilege of the rich who can afford private health care. Health systems in Sub-Saharan Africa are severely strained with shortages of health workers, lack of health infrastructure, irregular supply of medicines and vaccines, severe shortage of funding for the health sector and poor leadership [25, 27]. This directly translates into high morbidity and mortality from preventable illnesses, both communicable and non-communicable.

Pluralistic health systems

Many low income countries, have established a government led health service delivery system and tend to ignore the mixed or pluralistic nature of health care delivery that actually exists [28]. When people are ill, they do not necessarily go to a government health facility but prefer to utilize private providers [29], self medicate or forego treatment altogether [30].

Pluralism in health thus refers to "the many stakeholders or agents who are present in a health system and working in different ways – e.g. through the co-existence of different medical traditions" [31]. Pluralism recognizes the existence of different

stakeholders and the definition of their respective roles [22], and challenges the conventional state-centred view of the health sector and embraces a mixed character where many non-state stakeholders define the structure and functioning of the health system [30-32].

Today, the private sector provides more than half of all health care services in low income countries [33-34]. In sub-Saharan Africa in particular, drug shops (which sell drugs on a retail basis for profit) provide up to 40% of health care within this private sector [35-36]. In India, 80% of all outpatient care is provided by the private sector [33, 35, 37] and informal providers account for 51-55% of all providers [38]. In Bangladesh, the majority of health care (65%) is through informal private providers [39-40]. This high proportion of health care services through the private sector is largely attributed to huge gaps in the public health sector in low income countries that the private sector proliferates to fill up.

The important role of the private sector in health care delivery in low income countries is well accepted today. Health systems research is now moving towards policy options [29, 41] and interventions for engagement of the private sector [42-43] to achieve better public health outcomes. In this regards, in 2010 the World Health Assembly passed a resolution calling on countries to "constructively engage the private sector in providing essential health-care services" [44].

Experiences from Bangladesh's successful reduction in maternal and child morbidity and mortality show that pluralism in health may have positive effects but "requires active management that acknowledges and works with its polycentric nature" [31]. Ahmed et al. in 2013 proposed four key areas where management of pluralism in health systems is crucial, including: participatory governance, accountability and regulation, information systems and capacity development [31, 45].

Uganda country profile

Uganda is a landlocked country in the east of Africa, 241,000 square kms, and is approximately the size of Norway. The total population is nearly 36 million people with 80% living in the rural areas. The main economic activity in Uganda is subsistence agriculture. The gross national income per capita in 2013 was US$1,370 and the life expectancy at birth in 2012 was 56 years. The total expenditure on health per capita was US$ 108 and the total expenditure on health as a percentage of the GDP was 8% in 2012 [46].

Uganda health indicators

The maternal mortality ratio in Uganda has stagnated around 400/1000 live births over the last 10 years. The under-five morality rate has reduced tremendously from 179 to 66 deaths per 1000 live births, between 1990 and 2013. Immunization coverage with DPT3 vaccine is 90% in three quarters of the country and 38% of Ugandan children are stunted. As shown previously, malaria, pneumonia and diarrhoea are the leading causes of death in children in Uganda.

Ugandan health care system

The health system in Uganda is made up of both the public and private sector, each contributing about 50% of the health service delivery. The Ministry of Health (MoH) provides overall leadership for the health sector in terms of curative, preventive, promotive and rehabilitative services. Health service delivery is through a decentralized process with the health sub district playing a key role in service delivery and management. There is a tiered system starting from the grass root level where community health workers provide mainly promotive and basic care (also called health centre I); to an out-patient unit (health centre II); the health centre III provides first level inpatient care including a maternity unit; and the health sub-district or health centre IV includes an operation theatre and blood transfusion services in addition to outpatient, curative and promotive care. Finally, the three highest levels

include the general hospitals, regional hospitals and finally the national referral hospitals, with systematically advancing levels of care for example medical imaging, specialist care and advanced tertiary care [47].

Numerous challenges exist within the health system. While Uganda has excellent policies, financial constraints are huge, with low per capita expenditure on health, high out of pocket contribution (54%) and no national health insurance scheme to protect people against catastrophic health expenditures. There are also few health workers especially in the rural areas, where it is difficult to attract and retain staff. The referral system does not function effectively, with patients bypassing lower level health facilities in the urban areas or ignoring the referral system entirely, due to high individual costs incurred during care seeking [48].

A recent health system assessment report recommended that the Uganda health system needs to prioritize: focusing resources on the poor; improving efficiency to maximize the available resources; focus on improving quality at all levels; improve coordination of stakeholders; and harness the potential of other sectors including the private sector to improve access to health care [47-48].

Public-private partnership in health in Uganda

Given the above health system challenges, it is not surprising that the private sector in Uganda is large and dynamic. Half of all health services and products are provided by the private sector [47]. A draft policy document on the public-private-partnership in health (PPPH) was developed in 2012 and is being utilized as a framework guiding partnership with the private sector, in order to improve access to quality health care [49]. The private sector is recognized as complementary to the public health sector.

The PPPH policy document categorizes the private sector into three diverse groups: private-not-for-profit (PNFP) health providers; private health practitioners (PHP); and traditional and complementary medicine practitioners (TCMP). The PNFP providers

are 75% faith-based (catholic, protestant, orthodox and muslim); are concerned for the welfare of the population; operate about 30% of the health care facilities in Uganda; own many large hospitals and health centres; and train health workers. The private health practitioners include all health professional cadres who provide private health services beyond the PNFP umbrella. Within this category, registered drug shops are recognized players in health service delivery. In order to receive an operating licence, to sell over the counter medication, drug shops must be registered by trained medical personnel (nurse or clinical officer) who should provide supervision of the drug shop. Finally, the TCMP include all types of traditional healers including herbalists, traditional birth attendants and bone setters amongst others. The complementary medicine providers include reflexology, chiropractics, Chinese and ayurvedic medicine.

The Ugandan government recognizes the pivotal role of the private sector in health and national development and is committed to working with this sector in improving equity, access, efficiency, quality and sustainability of health services. In this regard, the government subsidizes care within the PNFP health facilities although the level of this subsidy is small and has been reducing over the years.

While the private sector is recognized and actively participates in various policy and regulatory fora, the public and private sector merely coexist and do not function in a coordinated nor integrated manner [48]. For example, over one third of health workers have dual practice in both the public and the private sector. Further, regulation of the private sector is weak, allowing it to function almost independently with varying levels of quality, competences and service availability. Better coordination at this level is needed as in other pluralistic health systems in low income countries [8, 47-48].

Care-seeking and the role of the drug shops in health service delivery

With the high burden of infectious diseases, the severe shortages of human resources for health, and widespread poverty, drug stores and private pharmacies play a pivotal role in the provision of health care in low income countries [34-35, 50]. They are often the first and sometimes only contact that people ever have with the health system [6, 8, 51].

In sub-Saharan Africa, nearly half of all outpatient care is at drug shops [35]. The majority of fevers around Africa are treated using medicines purchased from a shop, based on advice of shop keepers or pharmacists [36, 52-54]. In Nigeria alone, 64% of people treated their last episode of malaria either by obtaining medicines from a patent medicine vendor directly or using medicines previously purchased from a drug shop [28, 36, 55].

In Uganda, the role of drug shops and the private sector in management of children and adults is beginning to be understood. One study mapped all health care providers in 3 rural districts in Uganda and found that 96% of 445 health facilities surveyed were private while 4.3% were public. The majority of these private health facilities were drug shops [8]. Another study in eastern Uganda found that 63% of children with fever within 2 weeks prior to the survey first sought care in the private sector/drug shops compared to 33% in the public sector [6].

People seek care at drug shops and private pharmacies for both simple and complicated illnesses because they are easily accessible, the cost of care is perceived to be affordable, payment can be deferred, drugs are available and quality of care as well as health worker attitudes are perceived to be better at this level than within public health centres [6, 8, 28, 51, 56]. Also, where it is perceived that stigmatizing illnesses like sexually transmitted diseases may not be treated with confidentiality and

respect, people shy away from public health facilities and prefer to seek care at private drug stores [57-58].

The Affordable Medicines Facility – Malaria (AMFm)

Recognizing the high utilization of the private sector and drug shops in provision of health care in low income countries, the Global fund to fight HIV/AIDS, TB and malaria hosted and managed a program called the Affordable Medicines Facility – Malaria from 2010 to 2013 [59]. This was an innovative financial mechanism that was focused on increasing access to artemisinin combination therapy (ACT), currently the most effective treatment for malaria, through both the public and private sector in 8 African countries.

The AMFm's main objectives were: to increase ACT affordability, availability, use and to crowd out oral artemisinin monotherapies, choloroquine and sulphadoxine-pyremethamine through gaining market share. The AMFm intervention was piloted in eight countries: Cambodia, Ghana, Kenya, Madagascar, Niger, Nigeria, Tanzania and Uganda. An independent evaluation of the AMFm initiative found that success benchmarks were clearly met in 5 countries for availability and affordability; 4 countries for market share and all countries for crowding out of artemisinin monotherapies [51]. After the 1st phase of the AMFm pilot, the Global Fund board in 2012 recommended the integration of AMFm into its core grant management and financial processes. This means that countries should apply for funding to subsidize ACTs through their usual Global Fund applications [60].

However, this implies that funding for malaria and possibly malaria rapid diagnostic tests may be available to countries through the Global Fund, but not funding for diagnosis and treatment of non-malaria fevers including pneumonia. It is thus important not to leave out correct management of febrile children including differential diagnosis and treatment for non-malaria fevers even within the private sector and drug shops.

Ensuring quality of care in the private sector

While utilization of drug shops and informal health providers is high, the quality of care provided at this level is poorly documented, even though there is a general acceptance that quality of care is poor [61-62]. Provider knowledge can be used as an indicator for quality of care, but many other factors affect private provider practice including patient demand for specific drugs, as well as profit motivation. Regardless, compared to the formal health sector, informal providers (even by their definition) generally lack the necessary training and skills to provide basic curative services [39, 57]. Measurement of actual practice of private providers for example using adherence to clinical guidelines as an indicator would thus provide a more objective assessment of quality of care [61].

The scarce literature available on quality of care at drug shops also points to substandard care. One study in Uganda found up to 17 different brands of antimalarial drugs stocked in drug shops, with multiple dosages and combinations of these drugs being used to treat malaria. The shop keepers in this study did not feel that they had enough knowledge to even prescribe all the drugs they stocked [56]. Another study in Uganda found low levels of knowledge on symptoms, signs and management of acute respiratory infections amongst drug shop attendants in Kampala [63]. Studies on sexually transmitted infections (STIs) in Asia have also shown inappropriate management of STIs at drug shops [57-58].

In Bangladesh the professional knowledge of informal private providers has been documented to be below the minimum level necessary for providing basic curative services [39]. Similar results have been found amongst informal private providers treating children in India. However, when private practitioners in 110 villages in Bihar state in India received: training on integrated management of acute respiratory infections, diarrhoea and fever; support supervision; and contractual support, improvements in history taking, examination and counselling were observed [64].

A variety of strategies exist for ensuring quality of care and expanded access to care through the private sector, in order to improve health outcomes in the population [65]. The most common is regulation, the process of setting and enforcing standards in the private sector, including: licensing, certification and accreditation. Regulation is primarily directed at improving quality of care and is a standard government strategy, although its enforcement is very weak in low income countries, allowing the private sector to largely operate independently, with potential adverse consequences. Another strategy is contracting. This is the purchase of services (both health and non-health services) from the private sector. Contracting also addresses quality of care in addition to expansion of services and rationalization of coverage [65]. In addition, other key operational strategies are often employed to reinforce regulation and contracting. These include: financing and social marketing – the provision of financial incentives for private services for public good; training which includes educating and supporting private service providers; coordinating, which is the organization and creation of alliances between private and public providers; and finally, community awareness/information – the education of consumers about healthy behaviour and the role of private sector [65].

A recent review on interventions to improve health services from informal private providers in low income countries concluded that although training was the most common intervention, it was ineffective on its own [66]. Strategies which focused only on building individual capacities of informal private providers were less likely to succeed [67] compared to those which changed market conditions, and institutional relationships including incentives and accountability [66]. Thus, the above strategies should be applied in combination and not individually. For example in Uganda, when drug shop attendants received training on management of acute respiratory infections (ARI) in children, there was no improvement in actual practice and attendants who received training remained with similarly poor ARI management practices like those who did not receive training [67]. However, when training was combined with negotiation sessions and contractual obligations which sought to satisfy both public

health interest and private provider incentives, there was significant improvement in drug seller practices [68].

Integrated Community Case Management (iCCM) of malaria, pneumonia and diarrhoea

Improving access to treatment for the febrile child has been a priority in low income countries for a long time, with the strategies used evolving over time. In 1996, the integrated management of childhood illnesses (IMCI) strategy was initiated with the following objectives: to reduce infant mortality; to reduce the incidence and severity of childhood illnesses; and to improve growth and development during childhood. The objectives were to be achieved through improving health worker skills, strengthening the health system and improving family and community care practices (community IMCI). While IMCI was shown to improve health worker performance and quality of care [69-70], it did not achieve the expected impact on mortality mainly due to delayed care seeking [71].

In order to improve the treatment seeking practices for sick children under IMCI, community case management (CCM) was recommended, to complement the health facility based services. CCM includes treatment of sick children at the community level and promotes timely care seeking and referral to health facilities. From 2002 the Home Based Management of Fever (HBMF) strategy promoted presumptive treatment of all fever with antimalarial drugs in the community, with support from WHO and UNICEF. However, due to the finding of multiple illnesses in children, delayed care seeking for non-malaria fevers and symptomatic overlap of malaria, pneumonia and diarrhoea, WHO and UNICEF now recommend integrated community case management of malaria, pneumonia and diarrhoea in children (iCCM).

In 2012, WHO and UNICEF released a joint statement supporting iCCM as an equity-focused strategy to increase access to care for malaria, pneumonia and diarrhoea in children under-5 years of age [72]. Consequently, 28 low income countries including

Uganda now have a policy for integrated community case management (iCCM) of malaria, pneumonia and diarrhoea in children less than five years old, through community health workers [73]. In addition, WHO now recommends parasitological diagnosis of malaria before treatment with artemisinin combination therapy (ACT), [74] which has been incorporated into the iCCM strategy.

In 2010 the iCCM policy was adopted in Uganda for community level integrated management of malaria, pneumonia and diarrhoea in children less than 5 years old. The iCCM policy in Uganda is implemented through volunteer community health workers in the public sector and is part of the village health team (VHT) strategy for promoting health and preventing deaths [75]. The VHT strategy aims to deploy about five volunteer health workers called VHT members in each village. These CHWs are trained and supported to deliver or promote the use of many preventive interventions, particularly immunization, hand washing, optimal complementary feeding, insecticide treated nets and intermitted preventive treatment of malaria during pregnancy. ICCM adds treatment to the VHT preventive platform.

The main components of the iCCM strategy include: supplying CHWs with a kit of pre-packaged medicines and commodities including diagnostic tools; CHWs mobilizing communities to demand, support and use the iCCM intervention; CHWs treating children under five with fever, cough and diarrhoea and counselling mothers on home care and care seeking; CHWs referring immediately newborns with danger signs and severely ill children and giving pre-referral rectal artesunate for severe malaria; CHW collecting iCCM data and reporting timely; peer supervision amongst the CHWs; and trained health facility staff managing referred cases and supervising CHWs in their catchment area and monitoring program progress. The contents of the VHT kit for iCCM include: Pre-packaged medicines for malaria, pneumonia and diarrhoea including amoxicillin for non-severe pneumonia, ACT for uncomplicated malaria, low-osmolarity ORS for diarrhoea, Zinc for diarrhoea and rectal artesunate for pre-referral treatment of patients with severe malaria; diagnostic commodities e.g. respiratory timers, MUAC tape; and user items e.g. job aid cards.

Experiences from community case management of childhood malaria, pneumonia and diarrhoea in the context of home based management of fever and more recently with CHWs show that while communities value, use and comply with treatment, motivation of the CHW is very critical. Also, for sustainability, overloading VHTs with treatment of several diseases beyond their capacity should be avoided.

Utilization of the private sector for integrated management of childhood illnesses – a systematic review of the evidence

In 2014, we reviewed the available literature, for iCCM-related experiences within both the public and private sector. We wanted to understand the degree to which the private sector was utilized for integrated management of childhood illnesses. We searched for evaluation studies investigating the effect of introducing any intervention with drugs or diagnostics, for malaria, pneumonia or diarrhoea, within both the public and the private sector [76]. We found four times as many evaluation studies referring to malaria, pneumonia and or diarrhoea in the public sector (49 studies), as compared to similar studies within the private sector (13 studies). Most public sector iCCM-related studies evaluated the introduction of drugs and/or diagnostics for 2 or more illnesses (malaria, pneumonia and diarrhoea), while almost all studies in the private sector were related to interventions for one disease only, malaria [76]. These results indicate that private sector involvement has focused more on single disease interventions and not integrated care. Clearly, the private sector has not been effectively utilized for integrated child care.

A summary of the studies found within the private sector is included in table 1. The studies all happen to be within drug shops. This table includes the intervention, study design, outcome measured and results of impact evaluation studies related to iCCM within the private sector.

Table 1: Degree of utilization of the private sector in Africa, for integrated management of malaria, pneumonia and diarrhoea - a systematic review of the evidence [76].

	Author	Study design and outcome measure	Results
Malaria	Thomson et al. 2014 [77]	Pre-post study without a control. Community use of ACT in Tanzania	Mixed results: No change in population level utilization of ACTs despite increased availability, affordability and market share of ACTs in private sector
	Ikwuobe et al. 2013 [78]	Pre-post study with a control (2 pharmacies only). Change in ACT purchase from pharmacies in Nigeria	Positive results: 40% reduction in ACT purchase with introduction of RDTs
	Kangwana et al. 2013 [79]	A cluster randomized controlled trial. ACT stocking and prescription practices in Kenya	Positive results – increased ACT stocking and better prescription practices in intervention area
	Tougher et al. 2012 [51]	A before-and-after analysis of outlet survey data. Effect of AMFm on ACT availability, price, market share in 8 African countries	Mixed results – increased availability, and market share of ACTs in some countries; and reduced price of ACTs in some countries
	Talisuna et al. 2012 [80]	Pre-post study with a control. Effect of private sector subsidy on community access to ACT in Uganda	Positive results – 6 times better odds of access to ACT within 24 hours in intervention areas compared to control areas
	Yeung et al. 2011 [81]	Pre-post without a control – multiple rounds of household and outlet surveys. Uptake and utilization of ACT and RDT over 10 years of implementation in Cambodia	Mixed results: improvements in ACT and RDT availability and uptake were relatively slow especially in rural areas
	Rutta et al. 2011	Pre-post study with no control. Review of drug shop registers for ACT dispensing practice and market share at accredited drug dispensing outlets in Tanzania [82]	Positive results: increased ACT dispensing from 3% -26%

	Kangwana et al. 2011 [42]	A cluster randomized controlled trial. Proportion of children with fever getting ACT within 24 hours of fever onset in Kenya	Positive: Increased coverage of ACT treatment for fever in children (25% difference between intervention and control at follow up)
	Alba et al. 2010 [83]	Three repeat household surveys 2004 – 2008. Community awareness and use of malaria treatment for malaria in Tanzania	Mixed results – increased community awareness (62% - 84%) but decreased utilization of recommended treatment (85%-53%), attributed to policy change for 1st line anti malaria drug
	Abuya et al. 2010 [84]	Pre-post study without a control. Drug seller knowledge and prescription practices for malaria in Kenya	Positive: high drug seller knowledge and higher prescription of the recommended amodiaquine in intervention (61%) compared to control areas (2.8%)
Pneumonia		No articles	
Diarrhoea	Larson et al. 2012 [85]	National scale up of zinc treatment for diarrhoea in Bangladesh. Repeat surveys to determine caretaker awareness and actual use of zinc and ORS for diarrhoea	Mixed results: Rapid increase in community awareness on use of zinc for diarrhoea to 90% but lower actual utilization of zinc (10-30%)
Integrated care for malaria, pneumonia and diarrhoea	Awor et al. 2014 (Paper II)	No studies except paper II in this thesis.	

Justification for the studies

Following the iCCM policy, community health workers with minimal training have been empowered to provide integrated management of malaria, pneumonia and diarrhoea using pre-packaged drugs and diagnostics, in the community [72, 75, 86]. However, as the majority of febrile children in Uganda are treated at drug shops, where the quality of care is poor, it is important to similarly improve the quality of care that children receive within this sector.

Despite the ubiquitous utilization of the private sector in Africa, little has been done to harness its potential for integrated management of childhood illnesses. Utilizing the private sector for integrated child care has the potential to increase prompt access to appropriate care, also for non-malaria fevers, which would reduce morbidity from these illnesses. There is also need to test and implement appropriate interventions which improve quality of care and rational drug use at private sector drug shops in order to slow development of antimicrobial resistance and reduce the cost of care. This includes exploring the feasibility and effectiveness of introducing malaria RDT in the private sector, along with appropriate alternative treatment for the "RDT negative" child.

Conceptual framework

We considered different conceptual frameworks in an attempt to show the links between the various studies in this thesis and to focus the discussion of the results. All studies I, II and III are looking at one or more dimensions of quality in health care including: the technical competence of drug shop attendants in terms of the appropriateness of care they give and adherence to clinical protocols; the effectiveness of the iCCM intervention on appropriateness of care; and issues of access to care and choice of health care providers.

Different models explaining quality of health care exist and were considered. One is the Donabedian model for assessing the quality of care. This is a pioneer and simple model for assessing quality and considers three categories: the structure, process and outcome. It considers the structural dimensions and process factors that lead to a particular health outcome [87]. Such a model is well suited for assessing quality in an individual health facility but can also be used when evaluating quality in an entire health system.

Quality in health care can also be examined through categorically looking at various areas or dimensions where improvements in outcome are relevant, for both individual service users and communities [88-89]. Brown et al in 1989 presented 8 dimensions of quality that are important in quality assurance of health care in developing countries [89]. The World Health organization in a 2006 quality-of-care report also presented six dimensions of quality where improvements in the health system should be focused [88]. Within both frameworks, 4 dimensions of quality are the same and there is some variation in the remaining dimensions. The dimensions include: 1) effectiveness of health care, implying that it is based on an evidence base and results in improvement in health outcomes based on need; 2) efficiency in health care, maximizing resources and avoiding wastage; 3) accessibility of health care in terms of timeliness, geographical proximity and skills base; 4) technical competence, referring to skills,

knowledge/capability, actual performance; 5) acceptable/patient-centred health care; 6) continuity of health care; 7) amenities which are not related to effectiveness but enhance client satisfaction and return; 8) safety – minimal risk or harm to users; 9) acceptability and patient-centeredness and finally 10) equitable health care, which does not vary in quality for different gender, race, ethnicity or social economic status.

These dimensions of quality are a useful framework to help define and analyze health problems and to measure the extent to which programs are achieving standards/goals [89]. The dimensions are as appropriate for clinical care as for management services that support service delivery. However, they do not necessarily carry equal weight.

In order to illustrate the linkages between our studies, we present a modified dimensions-of-quality-of-health care frame work, which incorporates dimensions of quality from both Brown's and the WHO framework described above. Using this modified framework, figure 5 shows which dimension of quality in health care are assessed within this thesis. While numerous dimension of quality are well explored within this thesis, including technical competence, effectiveness and access to services, some dimensions like continuity (for example referral of sick children from drug shops) and efficiency have not been studied in this thesis.

Figure 5: Conceptual framework showing the dimension of quality in health care and the studies in this thesis

Finally, this is an intervention within the Ugandan health system and cannot be looked at in isolation. The studies and intervention should be looked at with a health systems lens. The system thinking approach emphasizes the interconnectedness of the components of a health system and allows us to consider both the expected and unexpected effects of an intervention within any of the WHO building blocks – Figure 4 [23]. Thus the discussion of this thesis will include a section on health system strengthening, and the potential positive and negative effects of our intervention on the entire health system.

Study objectives

General aim

The aim of this thesis was to determine the feasibility and effect on quality of care after introducing diagnostics (RDTs and respiratory timers) and promoting paediatric-dosage pre-packed drugs for malaria, pneumonia and diarrhoea in private sector registered drug shops in Eastern Uganda, in order to contribute to rational use of drugs and child survival.

Specific objectives

1. To determine the role and appropriateness of care provided by private sector drug shops when treating childhood fever, respiratory symptoms and diarrhoea in Uganda (Paper I)

2. To determine the feasibility and effect on appropriateness of care of introducing diagnostics (RDT and respiratory timers) and pre-packaged paediatric-dosage drugs for malaria, pneumonia and diarrhoea at private sector drug shops in Eastern Uganda (Paper II)

3. To determine the level of adherence by drug shop attendants in Eastern Uganda, to the integrated community case management (iCCM) of malaria, pneumonia and diarrhoea treatment protocol (Paper III)

Study subjects and methods

Study area

All three studies were conducted in eastern Uganda, in the two nearby rural districts of Kaliro and Kamuli located around 160 km and 140 km respectively, north east of the capital Kampala. From the 2014 national population census the total population in these districts is currently 237,000 and 490,000, respectively. Kaliro district was carved out of Kamuli district in 2006 and the people in both districts speak the same language – Lusoga with slight variation in the dialect in different areas.

Kaliro and Kamuli districts lie at an altitude of about 1000 metres above sea level. The districts experience an equator-near climate with two rainy seasons a year, when the zenith of the sun passes the equator, March – June and August – November with an annual average annual rainfall of 1350 mm. Subsistence farming is the main economic activity in the area. Malaria is holo-endemic in this area, with an estimated parasite prevalence of over 60% in school-age children. Malaria is mainly caused by the *plasmodium falciparum* species.

While Kaliro district has 6 sub-divisions (sub-counties), Kamuli district, which is larger, has 13 sub-divisions. All registered drug shops in all sub-divisions in both districts were included in the intervention study and child caretakers in villages from all subdivisions in both districts were included in the household surveys.
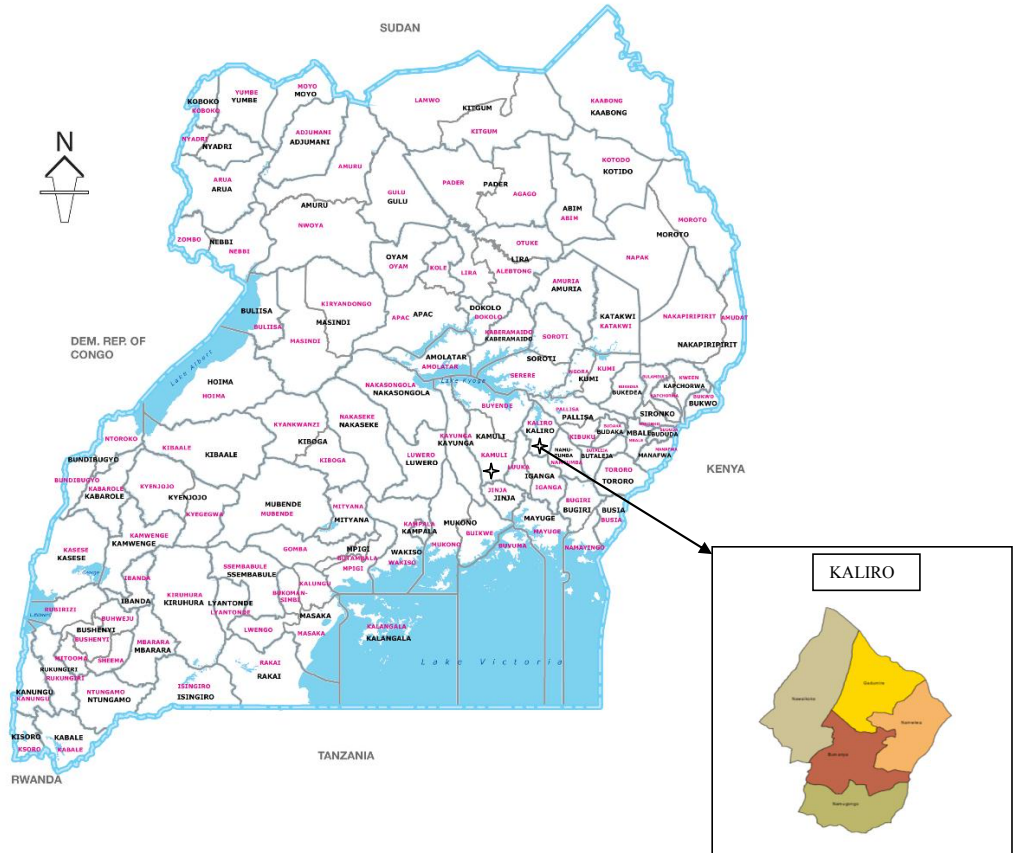
Figure 6. The study districts, Kaliro and Kamuli, located in Eastern Uganda

Study population

The study population included all children less than five years of age, living within both study districts. It also included their parents, guardians or caretakers and the drug shop attendants within both study districts.

Study design

The overall study design was a quasi-experimental study using one intervention district (Kaliro) and one comparison district (Kamuli). We collected data in the intervention and comparison districts twice, both before and after introducing the intervention (iCCM) in Kaliro, in order to determine its effect on quality of care. Such studies are sometimes called non-randomised, pre-post-intervention studies [90] and more recently have been classified as plausibility studies [23, 91]. This quasi experimental design is often used when it is not logistically possible or ethical to conduct a randomized controlled trial, which is accepted as the gold standard, to show a causal relationship between exposure and outcome in research studies.

We chose a plausibility design, a quasi experimental study in one intervention and one control district with before-and-after assessment in both areas, for three reasons. First, given that there was no previous evidence on the use of the iCCM intervention at drug shops, a reasonable (plausible) statement of truth would be good initial evidence on the feasibility and effectiveness of the utilization of this intervention at drug shops [91]. We also found the quasi experimental design comparing two entire districts most suitable, for logistical and pragmatic reasons. Given that supervision of the registered drugs shops is arranged from district level, and both supervisors and patients would likely have contaminated the study, if individual drug shops had been randomized in a probability design (randomized controlled trial). As advised by the WHO Alliance for Health Policy and Systems Research, a plausibility design comparing areas before-and-after, coupled with process and context evaluation was therefore chosen [23, 91-92]. This is because while randomized controlled trials have high internal validity when determining efficacy of an intervention, they are often not

feasible or acceptable and their results are rarely enough without additional contextual information and economic evaluation [23]. Finally, a cluster randomized controlled study design, taking for example villages as clusters which in turn are randomized to either intervention or control, could have been attempted at a much higher cost. However, due to the fact that we included social marketing and a community awareness campaign, contamination of the study would likely have occurred.

The intervention

There were 3 main components of the intervention. These included 1) availing subsidized, dose specific, pre-packaged drugs and free diagnostics for malaria, pneumonia and diarrhoea through drug shops; 2) training of drug shop attendants in the iCCM intervention and 3) a community awareness campaign. We used a social franchise model where drug shops were grouped under a known local brand. They were also supported by training, supervision and access to quality drugs and diagnostics for management of common childhood illnesses [43].

Only registered drug shops in the intervention district (Kaliro) received the following: **Subsidized Drugs:** artemisinin combination therapy (dispersible); amoxicillin tablets (dispersible); low osmolar oral rehydration solution (ORS); zinc Sulphate tablets. **Free Diagnostics:** malaria rapid diagnostic tests (RDTs); respiratory timers and diagnostic algorithms/charts. **Training:** two drug shop attendants per drug shop received 5-day training on how to use the above diagnostics and to dispense pre-packaged drugs. The training was based on the Uganda Ministry of Health training material for integrated Community Case Management with community health workers. **A community awareness campaign**: including inter personal communication and radio messages/public announcements at gatherings like markets. Meanwhile, the comparison district continued current practice of distributing subsidized ACTs only.

All registered drug shops in the intervention district were recruited to participate in the study and received iCCM training. Drug shop attendants were trained to perform a malaria rapid diagnostic test on each child with fever and to count the respiratory rate of each child with cough and fast/difficult breathing, before treating them with the recommended drugs. The training was conducted by the Uganda Ministry of Health iCCM trainers. The community was made aware of the availability of subsidized drugs and free diagnostics at drug shops and was also informed about the availability of these drugs and diagnostics free-of-charge at the public health centres. All drugs distributed were dispersible (able to dissolve in water) for easy administration to children. A minimum recommended price was written on the packaging material of the drugs. The drugs were purchased by the drug shop attendants from a drug distribution company, contracted by the study team to deliver the drugs and diagnostics directly to the drug shops.

Supervision and quality control of diagnostic testing and treatment

A full time study nurse was employed for support supervision and quality control. At each support supervision visit, the study nurse observed the management of sick children by drug shop attendants, recorded this, and discussed the positive and negative aspects observed with the respective person. The study nurse also reviewed all patient records since her last visit and discussed any arising issues with the drug shop attendant. The district drug inspector also carried out monthly supervision visits to the drug shops where he combined routine regulatory functions with support supervision.

Timing of data collection

The study was conducted from May 2011 – August 2012. Baseline data collection was done in May and June 2011 and end-line data collection in May and June 2012. The actual intervention at drug shops started in September 2011 after the training of drug shop attendants and went on for 8 months before the end-line assessment. Refer to

paper II, figure 1 (page 5), for a schematic diagram showing the study design and timing of the interventions and data collection.

Sample size calculation

The sample size was determined in 2 phases, at baseline and then at end-line. At baseline, the sample size was calculated to determine the prevalence of appropriate treatment of children with malaria, pneumonia or diarrhoea respectively, as this was unknown. We used the 95% CI, 5% error and design effect of 2, giving a sample size of 800 children in the intervention district and 800 children in the comparison district. The prevalence of appropriate treatment determined at baseline informed the calculation of the end-line sample sizes.

The end-line sample size for household survey was calculated based on: 30% appropriate treatment of cough with fast breathing at baseline; 50% increase in appropriate treatment between baseline and end-line; 5% error and design effect of 2. This gave a sample size of 200 children with cough and fast breathing in the intervention district and 200 children in the comparison district, at end-line. In order to achieve this sample size, we needed to visit around 1100 households per district, based on a prevalence of pneumonia symptoms of 30% amongst children with an illness 2 weeks prior to the interview and 58% prevalence of any illness within 2 weeks.

The end-line sample size for exit interviews was also calculated based on an increase in appropriate treatment of children from 10% to 20% (100% improvement), giving 250 children in each of the intervention and comparison districts, respectively. In order to answer an additional objective on child adherence to purchased medicines, the end-line sample size for exit interviews in the intervention area was increased and is more than that in the comparison area.

Finally, for study III, we utilized all the records of children who sought care at drug shops during the study period (N=7667).

Inclusion and exclusion criteria

The inclusion criteria included: all registered drug shops in both the intervention and comparison districts; all caretakers and children under 5 years seeking care at drug shops; and all households in both districts which had at least one child who was under 5 years of age. The exclusion criteria included any child who was considered to be very sick, based on the iCCM classification, found either at home or at the drug shop.

Data collection methods

The same data collection methods and tools were used both at baseline and at end-line, in both districts. These were both qualitative and quantitative data collection methods, as summarized in table 2.

At baseline (Paper I), we conducted community household surveys and exit interviews at drug shops in both districts, using paper based questionnaires. We also conducted in-depth interviews with drug shop attendants in both districts. The objective of the baseline data collection was to determine household treatment seeking practices, including the role that drug shops play in the management of sick children. We were also interested in determining the appropriateness of care provided to children at the level of drug shops.

For paper II we utilized data from both the baseline and end-line data collection rounds from both districts. Again, this included data from community household surveys and drug shop exit interviews. We also utilized direct observation of drug shop attendants, to document the quality of care they provided. The objective of paper II was to determine the effect of the iCCM intervention on appropriateness of care for children at drug shops.

Table 2: Summary of the methods used in the different papers

Paper	Design	Data collection method and sample size	Data analysis method
Paper I (baseline data)	Cross-sectional analysis of survey data (combined for both districts)	Household survey (n = 1604) Exit interviews (n = 163)	- Descriptive statistics - Proportions of appropriate treatment
Paper II (both baseline and end line data)	Quasi experimental design Before and after assessment in both intervention and comparison areas	Household surveys (n = 3759; 1604 before/2155 after) Exit interviews (n = 943; 163 before/780 after)	- Multivariate analysis - Survey adjusted generalized linear regression models - difference in difference analysis
Paper III	Review of records	Review of records from drug shop patient registers (n = 7667)	- Descriptive statistics - Proportions of appropriate treatment
Additional analysis – Equity of access to care	Cross sectional analysis of household survey data	N = 3759	- Principal component analysis - Descriptive statistics
Additional data	Qualitative data	In-depth interviews with drug shop attendants (n = 25 before/14 after) Focus group discussion (n=4 before)	- Manifest content analysis

In order to assess equity in access to care, we created a five quintile wealth index using principal component analysis. We utilized the following household assets information to create the wealth index: ownership of a radio, radio cassette player, television, bicycle, motorbike, car, mobile phone, and the type of floor of the respondent's house (mud, wood, cement or tiled). We utilized all complete data from both the baseline and end line data collection rounds, in both districts (n = 3641).

For paper III, we reviewed data from the drug shop registers where all child visits to all drug shops were routinely recorded. A total of 7667 child visits to drug shops occurred during the study period. The purpose of this review of data in the registers was to determine the level of adherence by drug shop attendants to the iCCM treatment guidelines.

In terms of the qualitative methods, we conducted both in-depth interviews (IDIs) and focus group discussions (FGDs). The IDIs with drug shop attendants were conducted both at baseline and end-line and the results, while not included in any of the papers, are presented separately within this thesis. The purpose of the IDIs was to understand the role played by drug shops in the care of sick children in the community, from the perspective of the drug shop attendants. At end-line, IDIs were also used to explore drug shop attendants' experiences with the iCCM intervention. FGDs were also conducted with child caretakers at baseline, to understand their treatment seeking practices and child health care preferences.

Data management and analysis

All data collected from household interviews and exit interviews were cross-checked for errors immediately after the data collection and corrected in the field. The principal investigator and field supervisors also cross-checked all data at the end of each day and any errors discovered were corrected by the data collector the next morning. Quantitative data was entered into Epi Data, and was exported and analyzed in stata version 12. Descriptive statistics were computed in all the studies.

Multivariable analysis:

In paper II, for both household survey and exit interview data, we used survey-adjusted generalized linear regression models (with log transformation and binomial distribution) and difference-in-difference analysis to derive prevalence ratios of the effect of the iCCM intervention on appropriateness of care. Un-adjusted and adjusted results are presented. Covariates which had a p-value less than 0.1 at unadjusted

analysis were included in the multivariable analysis. All analysis of household survey and exit interview data were adjusted for clustering.

Manifest content analysis

In-depth interviews were conducted in English by the principal investigator and one field supervisor and detailed notes were taken in the field. The interviews were then transcribed and analysed using manifest content analysis. The analysis focused on the actual visible and obvious content of the text, which was grouped into codes and emerging themes were derived as described by Graneheim, 2004 [93]. FGDs were conducted in the Lusoga language, translated into English, transcribed and also analyzed using manifest content analysis.

Ethical considerations

Ethical approval for this study was obtained from Uganda National Council of Science and Technology (Number: HS 1184 & HS 750), the Uganda National Drug Authority (Number: 0456/ID/NDA) and Makerere University School of Public Health's, Higher Degrees Research and Ethics Committee (Number 166). Informed written consent was obtained from all child caretakers interviewed in these studies, as well as the participating drug shop attendants. Permission to conduct the studies was also obtained from the district community leaders. Participant confidentiality was maintained throughout recruitment, data collection, management, analysis and dissemination of results.

Potential ethical risks from this study included: the possibility that drug shop attendants would not be able to perform the diagnostic tests properly despite training; that disposal of sharp instruments, gloves and blood-stained materials at the drug shops may be substandard; and that this study at drug shops may promote the utilization of the private sector at the expense of the public sector and yet quality of care in the private sector was substandard. These risks were mitigated through intensive training of drug shop attendants; support supervision; demonstration

exercises to ensure disposal of medical waste material followed standard procedures; and a community awareness component where communities were informed about the availability of the same iCCM drugs and commodities free of charge at public health centres and at a subsidized price at drug shops.

Results

Here I include a summary of the main results from papers I-III and from the qualitative data analysis not presented in the papers.

Role of drug shops and appropriateness of care provided to children – Paper I

An important result from this paper is that the first point of care for sick children in the community is commonly at drug shops. Of 934 children with an illness within 2 weeks of the household survey, 53% first sought care from a private provider (30% from drug shops and 23% from other private sector) compared to 17% at a government health facility – see paper I, table 2. The main reasons given for choosing to seek care at a drug shop were good services/customer care (62%); proximity (21%); good trained staff (20%); a regular supply of drugs (14%) and that the drug seller was a friend to the child caretaker (14%) – see paper I, table 5. Management of children at home when ill was also high with 228/934 (24%) sick children first receiving some sort of care at home only.

However, from the exit interviews, management of malaria, pneumonia and diarrhoea at drug shops was poor. Only 19% of children treated as having malaria received appropriate treatment with the recommended drug, in the recommended dosage, and for the recommended frequency and duration. Meanwhile none of the children treated for pneumonia and diarrhoea received the full recommended treatment, according to the current national guidelines, Paper I, table 4.

But how did the community and the drug shop attendants view the role of drug shops in the management of sick children? From the baseline focus group discussions, we found that the community had confidence in the ability of drug shop attendants to manage their illnesses and thought them to be competent, as in the quotations below:

"We first use traditional herbs to treat our children at home, when they have fever. If the condition requires additional treatment, we buy drugs at a drug shop....if the child does not improve, then we take to a health centre/hospital" Mother, FGD 4.

"we have no private clinics in this area, only drug shops.....the drug shop attendants are very welcoming, they look at the child [examine child] and then give you treatment.... the government health centre has no drugs, they just write a prescription. So it is better to go directly to a drug shop" Mother, FGD 3.

While some people thought they could get health care on credit at drug shops, some people felt that having to pay for care was a problem with use of the private sector as below.

"At a drug shop, you can get [treatment on] credit if the child is very sick, but in a clinic, if they do not know you, no credit." Caretaker, FGD 1

"Drug shops are mainly interested in profit. Some of them think that if you go there with your child, you do not have money and you want them to help you." Caretaker, FGD 2

"However, some drug shops are good. They check the children and give you good medication. One particular shop insists that you take the full dose....but you have to pay the full price." Mother, FGD 2

Meanwhile, drug shops attendants unanimously reported that their role included: taking history of the child's illness from the caretakers; assessing sick children, usually using thermometers or their palm to determine the temperature of a child; making a diagnosis; treating the sick child; and finally giving advice on how to administer the medication and on additional care for the child at home. They also

reported providing referral to the next level health facility, if they could not manage the child's illness. Related quotations from drug shop attendants are below.

"I see myself as a good servant of the community.... I help to treat people, even when the customer has no money." Baseline, IDI 19

"I welcome the customer and show them a seat. If they have a child I take the child from them and start examining thoroughly e.g. body temperature, skin colour and appearance of the eyes... at the same time I ask many questions from the care taker to find out the profile of the illness. After zeroing in on a particular sickness depending on the signs observed, I treat accordingly. Then if I find out the sickness is beyond my control, I advise the customer to go elsewhere [oral referral], possibly to the main hospital." Baseline, IDI 24

"The parents usually come when they have left back their sick children. They just tell me the signs that the sick child is showing and with that I discover that such a child is suffering from a particular disease. I give them the treatment depending on the signs the parent has told me." Baseline, IDI 2

"As a professional drug seller, I make sure that at least drugs for malaria are available all the time. I make sure that the drugs I sell are not expensive and that prices are within the customers' reach" Baseline, IDI 20

Effect of the iCCM intervention on appropriateness of care at drug shops – Paper II

The children in both the intervention and comparison districts were generally similar in most of their characteristics including: their age and sex as well as the caretakers' age, education and employment. There were some differences in terms of their household head and main source of water – Paper II table 1.

The main result in this paper is that with the introduction of the iCCM intervention at all registered drug shops in Kaliro district (n=44), appropriateness of care for malaria, pneumonia and diarrhoea improved greatly. First, the utilization of diagnostics for malaria and pneumonia in the intervention district improved from 0% to 88% and 55% respectively, between baseline and end-line. Meanwhile, the utilization of diagnostic testing in the comparison district drug shops remained 0%. Also, the correct treatment of diarrhoea using the recommended drug ORS/Zinc increased from 0% to 77% in the intervention area between baseline and end-line, compared to only 0% - 5% at end-line in the comparison district drug shops.

Further, the prevalence ratios of the effect of the intervention on treatment of cough and fast breathing with amoxicillin and diarrhoea with ORS/zinc at the drug shop were 2.8 (2.0-3.9), and 12.8 (4.2 – 38.6) respectively – Table 3. This means there was 3 times better management of cough and fast breathing at intervention drug shops compared to non-intervention drug shops and thirteen times better management of diarrhoea at intervention drug shops as compared to non-intervention drug shops.

Table 3. The effect of the iCCM intervention on treatment using antibiotics, ACTs and ORS/zinc at drug shops, from exit interviews – survey adjusted prevalence ratios using difference in difference analysis and generalized linear models

Management	Prevalence ratios (95% CI)
Children with pneumonia treated with amoxicillin (5-7 days)	2.8 (2.0 – 3.9)
Children with pneumonia treated with cotrimoxazole	0.07 (0.01 – 0.39)
Overall antibiotic use	0.82(0.69 – 0.97)
Children with fever treated with ACT	4.2 (1.9 – 9.4)
Children with diarrhoea treated with ORS/zinc	12.8 (4.2 – 38.6)

The prevalence ratios provided are in reference to the control area

Finally, from the household survey, the prevalence ratio of the intervention effect on use of RDTs was 3.2 (1.9 – 5.4); Artemisinin Combination Therapy (ACTs) for malaria was 0.74 (0.65 -0.84), and ORS/zinc for diarrhoea was 2.3 (1.2 – 4.7). This also means that there was three times higher utilization of RDTs in the intervention district compared to the comparison district, and 26% lower utilization of ACTs for malaria in the intervention district. There was also twice as much use of ORS/Zinc for diarrhoea in the intervention district as compared to the comparison district.

Care seeking at drug shops – papers I, II and III

At both baseline and end line, we determined the level of careseeking at drug shops. At baseline we found care seeking at drug shops to be 30% while at end-line, the utilization of drug shops in the comparision district remained 35%, but in the intervention district it increased to 55%, mainly from people already utilizing the informal private sector for child care – Paper II, table 6.

In paper III, we found that care seeking concentrated within particular drug shops. While 22 of 40 drug shop saw nearly 90% of the children in the study, just 5 of these drug shops treated almost half of all the children.

Adherence by drug shop attendants to the iCCM treatment protocol – Paper III

In this paper, we reviewed the treatment registers of all drug shops in the intervention district and included all child visits to drug shops (N=7667). We found that 80% of children presenting to drug shops had fever, and almost 100% of the children with fever received diagnostic testing with malaria RDT. While the RDT positivity rate was high 78% (95% CI 77-79), of those with positive malaria RDT, 94% received the correct treatment with ACTs, figure 7.

Similarly, drug shop attendants largely adhered to the treatment protocol for pneumonia and diarrhoea. While 68% of children presenting to the drug shops had some sort of respiratory symptoms, 3437 were categorized as having pneumonia after assessment and 91% of these received the recommended treatment, amoxicillin – figure 8. Finally, figure 9 also shows that nearly all children presenting with diarrhoea at the drug shop received the recommended treatment, ORS/zinc.
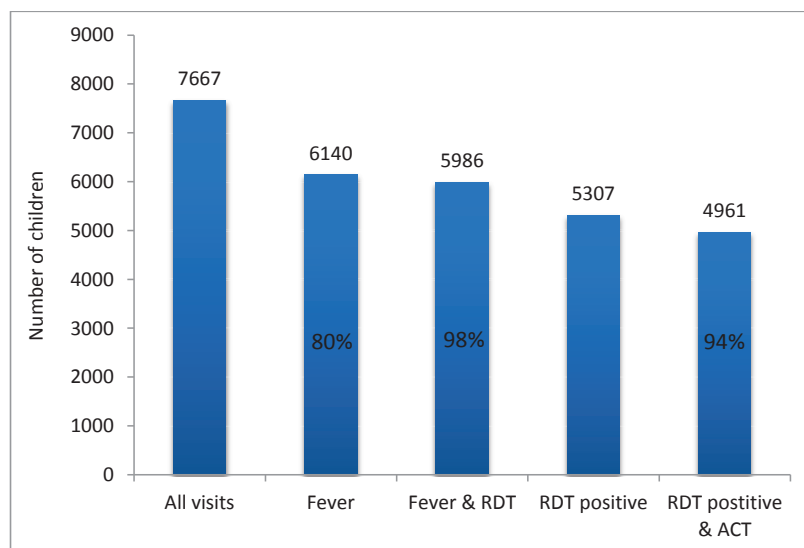

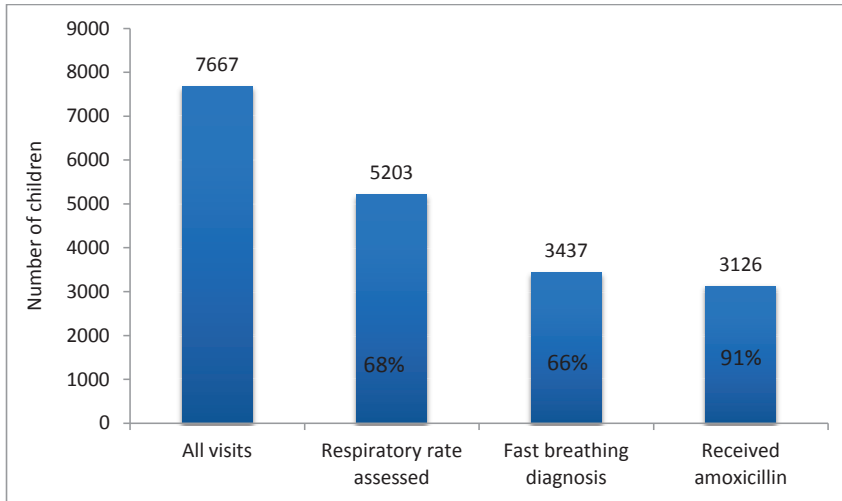Figure 7. Adherence to malaria treatment guidelines, from treatment registers

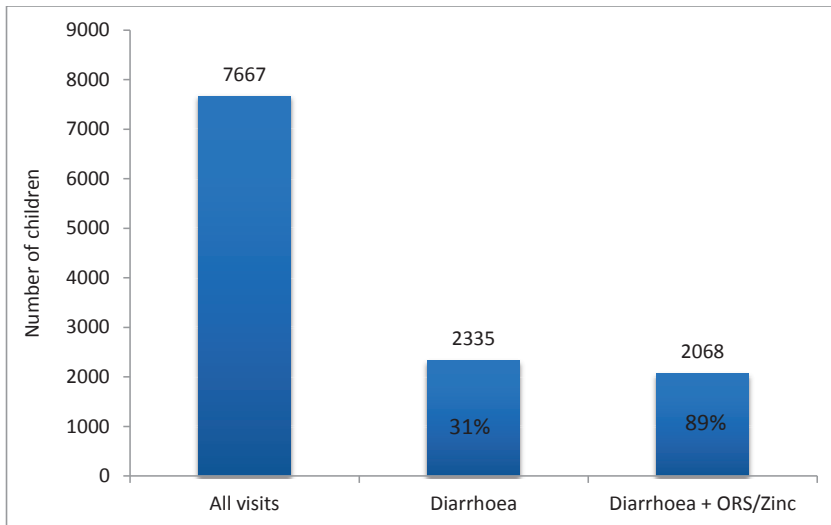Figure 8. Adherence to pneumonia treatment guidelines, from treatment registers

Figure 9. Adherence to diarrhoea treatment guidelines, from treatment registers

At the end of the intervention, we also explored the experiences of drug shop attendants around utilization of the pre-packaged drugs and diagnostics, using in-depth interviews. Their experiences were mainly positive and they all appreciated the new knowledge and skills, which brought self-confidence and community trust in them, as quoted below.

"I did not know how to examine for malaria before. I did not know that ORS/Zinc can treat diarrhoea very effectively. Now I know..... My name is up [(popular] because I am able to examine and diagnose sick children......tablets are already pre-packaged and now people are forced to buy a full dose." End line, IDI 10

"It has been a learning process, especially that not all fever is malaria....I am now sure that amoxicillin tablets are a good treatment for curing pneumonia." End line, IDI 14

The majority of the drug shop attendants interviewed reported that their profit margin increased by about one half of their previous profit, and was dependent up on the number of children they saw. The patient load was perceived to have increased but was alright and manageable as the more children they saw, the more money they made. For example one drug shop attendant said: *"patient load is not an issue as the more patients, the more money and happiness"* End line, IDI 2.

The most important factor perceived to have improved their business was the use of diagnostics, particularly the malaria RDT. All of them reported that the use of diagnostics improved their perceived professionalism and patient trust. Some relevant quotations from drug shop attendants are included below.

"It [the use of diagnostics] has made our name popular. People come from far away to the drug shop because they want to test their children for malaria." IDI 1

"The [availability of] RDT has encouraged patients to come. The patients get confidence in you when you use the RDT and respiratory timer." IDI2

"The use of the pre-packaged drugs and diagnostics has made me gain confidence because I treat what I know!" IDI 6

"When you give amoxicillin, the mother comes back saying, "these tablets work very well." They are happy and so are we." IDI 1

"Whenever you give a child amoxicillin tablets, they [the care taker] just come back to say thank you..." IDI 2

The use of the treatment algorithms, the laminated sick child job aid, was also lauded. For example one attendant reported that *"sometimes I forget what treatment to give but when I look at the chart, I know what to give. The chart is very useful."* IDI 1

On whether they would be able to purchase RDT on their own and continue to offer diagnostics in the community, the majority said that if the RDT were available in the big district nearby (Iganga), they would continue to purchase and offer them to their clients. The retail price which they thought their patients could afford was between 500-1000 UGX (0.2 - 0.4 USD).

"There will be no problem with buying RDTs and drugs. Since we refill our stocks, we will definitely buy the RDTs....we knew this was a study period and the time will come when we have to buy these things." IDI2

"When the program stops, the business will not be affected provided the RDTs are available in Iguana. If they are in Kampala or Jinja, the transport costs will affect the purchase prices and customers may fail to buy." IDI 4

Equity of access to care at drug shops

While not included within the publications, I also explored the issue of equity in access to care at drug shop. In table 4 below, I present the results from the five quintile wealth index, cross tabulated with the first source of care for children with symptoms of malaria, pneumonia or diarrhoea (either 2 weeks prior to the household survey or longer). When this analysis was repeated within each district, at the different data collection time points, the results are very similar (not presented). For comparison, I also present equity in access to care from other prominent sources of child care including: government health facilities, the other private sector and home management.

Table 4 shows that the majority of children received care at a drug shop, when they were ill (1412/3641). Further, more children from the poorest two quintiles utilized drug shops, compared to those from the least poor households. Utilization of home management and rural health centres was also higher in the poorest 2 quintiles than in the less poor ones.

Table 4. Equity of access to care, from household survey data

First source of care	Five quintile asset index n (%), row percentages					Total
	1 – poorest	2	3	4	5 – least poor	
Drug shops	306 (22)	318(23)	418(30)	117(8)	253(18)	**1412**
Other private sector	71 (16)	92 (21)	124 (29)	43 (10)	102 (24)	**432**
Managed at home	212 (22)	198 (20)	263 (27)	104 (11)	201 (21)	**978**
Rural health centre	124 (22)	128 (23)	177 (31)	51 (9)	82 (15)	**562**
Hospital	24 (16)	22 (14)	36 (24)	18 (12)	52 (34)	**152**
others	30 (29)	15 (14)	28 (27)	17 (16)	15 (14)	**105**
Total	**767 (21)**	**773 (21)**	**1046 (29)**	**350 (10)**	**705 (19)**	**3641 (100)**

Note: There is some variation in the quintile sizes due to clustering of regression coefficients.
All percentages are row percentages.

Discussion

The results in this thesis confirm that drug shops were the first source of health care for almost half of the sick children in rural Uganda, but the quality of care they provided was poor. However, with the introduction of the iCCM intervention at registered drug shops, it was possible to greatly improve the quality of care that children received. There was high uptake and utilization of diagnostic tests for malaria and pneumonia by drug shop attendants; large improvement in appropriateness of care for malaria, pneumonia and diarrhoea in children both at the drug shop level and at population level; and high drug seller adherence to treatment protocols. The results provide good evidence that drug shops can be utilized to expand access to point-of-care diagnostics and appropriate treatment for malaria, pneumonia and diarrhoea in children. This could contribute to reduced morbidity and mortality in children, from these illnesses.

In the next sections, I discuss the strengths and weaknesses of these results; reflect further upon the meaning of the results; discuss relevant policy options; next steps in research; and I provide recommendations for both policy and research.

Methodological considerations

There are two main strengths of this thesis. First, we used various data collection methods throughout these studies including: household surveys, exit interviews, direct observation, review of treatment registers, in-depth interviews and focus group discussions. All these methods converged in producing similar results, a form of triangulation, adding credibility to the results in this thesis.

The second strength is the large magnitude of the effect size (strength of association) obtained, in terms of improvement in appropriateness of care, after introduction of the iCCM intervention at drug shops. The large improvement in appropriateness of care leaves little doubt of the direction of the results and the positive effect of the

intervention. In relation to consistency of results, and adding credibility to the results in this thesis, a recent publication from the Uganda Ministry of Health also found large improvements in appropriateness of care for malaria, with introduction of the RDT at drug shops [94]. That study found 73% appropriate treatment of malaria (confirmed diagnosis and ACT dispensed) in the intervention clusters compared to 34% in the control clusters.

Consistency of results and the strength of association are important parameters when assessing causal relationships in epidemiology, as suggested by Bradford Hill in 1965 [95]. The full Bradford Hill criteria, most of which are met in this thesis, include: the strength of an association – a strong association is more likely to have a causal component than a modest association; consistency or reproducibility – that a relationship is observed repeatedly, using different methods or sources; temporality – that the causal factor precedes the outcome it is associated; biological gradient or does-effect; plausibility; specificity; coherence with existing knowledge; utilization of experimental designs; and the use of analogy in judgement.

Study design
The chosen quasi-experimental design, a non-randomized pre-post intervention study with a control group, may be considered a weakness in this thesis, as it is not the gold standard design, when trying to determine causality in epidemiology – that a specific exposure causes a specific outcome. Rather, randomized controlled trials (RCT) are considered the gold standard when determining causality, and non-randomized studies with a control group come second in the strength of study designs. Other study designs then follow in the hierarchy, including: cohort studies, case-control studies, cross sectional studies and case series, respectively. In the RCT study design, every individual or cluster has an equal chance of being recruited into the study, unlike with other study designs. With random allocation of subjects into study groups, any difference in individuals is assumed to be equally distributed between the study groups, thus minimizing the risk of bias (systematic error) which would cause obtained results to be systematically different from the truth. This is not the case with

other study designs, including the one chosen in this thesis, and so alternative explanations (for example confounders) for the results obtained may continue to exist. As one cannot completely rule out every alternative explanation for observed differences obtained from a plausibility design, for academic purposes, the next logical step in evidence generation could be to conduct a randomized controlled trial. However, given the large magnitude of effect size obtained in the improvement in appropriateness of care of children at the level of drug shops, there is little doubt of the causal relationship and therefore, there may be little additional value of conducting an RCT. In addition, many techniques were utilized to eliminate or reduce bias and confounding in our studies and these are further described below.

Information bias

One data collection method used, the household survey, is prone to recall bias – a situation where parents may not remember relevant aspects of their child's illness, especially if it was not a recent illness. Recall bias was reduced by restricting the analysis to only illnesses that had occurred within 2 weeks prior to the interview. The 2 week recall period is now commonly used and most literature reporting on child illness from cross-sectional studies utilize this recall period. Also, exit interviews were used at the drug shop, as parents were just leaving after seeking care for their child, to reduce recall bias and to collect real time data to assess the appropriateness of care provided by drug shop attendants.

The use of records data from drug shop registers for study III is a weakness of this study, as the data could not be validated. However, the strength of this study is that we used all the data and all records of children seen at the drug shops during the study period and the results obtained are very similar to those obtained from the other data collection methods including household surveys, exit interviews and direct observation.

Selection bias

Both the selection of respondents into the study and loss to follow up of participants are potential sources of selection bias. Loss to follow up is not an issue in this thesis as we utilized repeated cross sectional studies and did not follow up any individual participants. However, in order to eliminate selection bias, we recruited all registered drug shops within both the intervention and control districts and included all the drug shop attendants into the study. Further, we interviewed all caretakers of children under five years old who were exiting the drug shops for papers I and II and we also utilized all records of children within the drug shop registers, for paper III.

For the household surveys in papers I and II, selection bias was minimized by using a two stage cluster sampling technique, with probability proportional to the size of the population. At the first stage, a fixed number of villages/clusters were sampled and at the second stage the individual households were systematically sampled, based on the predetermined sample size and number of individuals per cluster. The study team randomly identified a starting point from the list of households and there after sampled every fifth house. From the baseline results of the household survey, we see that we were able to minimize selection bias as both the intervention and control groups appeared to have been similar – see Paper II, table 1.

Confounding and interactions

Confounding could provide an alternative explanation for results obtained and should be carefully considered within observational studies. A Confounder has three key characteristics: it is a risk factor for the outcome, associated with the exposure and is not an intermediate factor in the causal pathway. To control for confounding, I utilized multivariate regression analysis. I considered multiple sets of confounders and the results were largely robust.

Clustering

Clustering was expected at the drug shop level, with children treated at a particular drug shop receiving similar care, thus affecting treatment outcomes. Clustering was also expected at the village level in the household surveys, with children in the same village having similar treatment seeking practices. When not adjusted for, clustering causes narrow confidence intervals and may cause wrong conclusion of statistical significance where it does not exist [96]. Clustering was adjusted for both during sample size estimation and analysis of the exit interview and household survey data.

Generalisability/external validity

The findings in this thesis may be extrapolated to regions with similar utilization of drug shops for childhood care; similar socio-demographic characteristics; and similarly high malaria prevalence. This is because all drug shops were utilized and entire districts were utilized for data collection. The study design and conduct was also closer to the real-life situation than a randomized controlled study. However, additional studies are necessary where malaria prevalence is low (and we are now conducting one such study), in order to better understand drug seller practices in these settings, where less profitable drugs than anti malaria treatment, for example paracetamol, may have to be sold to febrile children.

Discussion of the results

The existence of and high utilization of drug shops in sub-Saharan Africa and beyond is a reality that cannot be ignored. With nearly half of all outpatient health care occurring at drug shops, albeit with poor quality care, choosing to ignore them would leave many children at risk of receiving sub-optimal care. On the contrary, it would be wise to prioritize options for integrating drug shops within the wider health system and harnessing their potential to provide good quality health care for children, as within this thesis. This would be in line with the task shifting strategies currently on going through community health workers, to expand the health workforce for primary health.

Looking at the conceptual framework in figure 5, we see that many dimensions of quality of health care are well studied within this thesis. Technical competence (knowledge, skills, capability and actual practice), effectiveness of care (based on an evidence base/the existing guidelines) and access to care are assessed within studies I, II and III and the results are discussed below. Patient centeredness including the reasons for choice of a particular care provider and equity in access to care is also assessed within the studies and discussed. However, some dimensions of quality of health care were beyond the scope of these studies, including: efficiency, continuity of care and safety. In terms of efficiency, there are no previous studies on cost effectiveness of the iCCM intervention at drug shops so this will need to be studied. There is also limited literature on continuity of care, for example in relation to referral from drug shops to higher levels in the health system, supervision of drug shops and the flow of patient data. While we did not directly study safety of the intervention, we relied on the fact that the iCCM strategy can be safely implemented through public sector CHWs, when deciding to introduce the strategy at drug shops.

Our results in paper I, on poor quality of care at the drug shops, add to the evidence confirming the general perception that quality of care from informal private providers, including drug shops, is low. For example, Jacobs et al. also found poor adherence to national clinical guidelines, with only 7% of clients with urethral discharge who went

to private clinics and drug shops in Uganda, receiving management according to the guidelines [97]. Further, a recent systematic review on the role of informal health providers in low income countries found only 17 of 122 included articles reporting a clinical quality outcome [61]. From this review, compared to the formal health sector, knowledge and practice of informal private health providers was poorer due to lack of training and capacity (or technical competence) to provide basic curative services [39, 98-99].

We also showed high adherence by drug shop attendants to the iCCM treatment guidelines. This high adherence to protocols is impressive, given that health workers are notorious for poor adherence to protocols [100-101]. However, the finding is in line with other research that shows that lower level health workers, like CHWs, are more likely to adhere to the treatment protocols than more highly trained health workers like nurses or doctors [102-103].

The effect of the iCCM intervention on access, quality of care and morbidity, are well documented within the public sector [86, 104]. Where community health workers are well trained; supervised; and supplied with the drugs and commodities, the iCCM intervention may reduce mortality in children [105-106]. However, in the private sector, there is very little evidence on the use of diagnostics and alternative appropriate treatment for non-malaria fevers. One recent publication from the Ministry of Health in Uganda also confirms large improvements in correct treatment of patients with malaria, after introduction of RDTs at drug shops. That study used a cluster randomized controlled design and found 73% appropriate treatment of malaria (confirmed diagnosis and ACT dispensed) in the intervention clusters compared to 34% in the control clusters [94]. However, the abovementioned study did not provide alternative appropriate treatment for non-malaria fevers, at drug shops, when the malaria test result was negative. Also, our recent systematic review found no evidence on the use of diagnostics with alternative appropriate treatment for non-malaria fevers at drug shops in Africa [76]. Thus, to my knowledge, the studies in this thesis present the first set of evidence on the utilization of the iCCM intervention at drug shops. The

positive results are encouraging, as countries look for ways to engage with the private sector, in pluralistic health systems. I argue that given the high care seeking at drug shops, and the great improvement in appropriateness of care for children with introduction of the iCCM intervention, it is logical to provide diagnostic testing and treatment for both malaria and non-malaria fevers, also at drug shops. This will ensure that children have timely access to life saving treatment, at their first source of care. This implies delivering the iCCM intervention also through private sector drug shops.

However, several issues need to be taken into account. First, drug shops in Uganda and most of SSA are not yet authorized to utilize diagnostics like the malaria RDT, unlike their counterparts, the CHWs, who are authorized to use diagnostic tests. Drug shop attendants generally have similar characteristics to CHWs, including their level of education. There is thus an opportunity to expand the iCCM strategy to include drug shops. This will require policy changes, both at the national and international level, although this is usually a slow process.

Secondly, drug shops are a diverse group, including those registered by the national drug authority to sell over the counter medication (as within my studies), as well as unregistered drug shops also selling similar medicines to the population. In Uganda, unregistered drug shops are considered illegal, although from my experience in the field, there are as many unregistered drug shops as there are registered ones. While I recommend working with registered drug shops, the problem of unregistered, shops remains unresolved, and additional research needs to be done, in order to understand whether or not to engage with this group. Within our studies we found that there was concentration of care seeking at a few registered drug shops. This may be useful for crowding out less skilled drug shops including the unregistered ones. The concentration of care seeking at few drug shops could simplify implementation during a scale-up phase, as it is easier to supervise fewer drug shops.

Incentives, profit motivation and equity in the private sector

Our results are in contrast to one study in Kampala in 2004, which utilized only training of drug shops attendants and pharmacists in an attempt to improve their knowledge and management of acute respiratory infection [67]. In that study, Tumwikirize et al. utilized three sessions of face-to-face training of pharmacists and drug shops attendants in a quasi experimental design with a comparison group. Despite the training, assessment of the children remained inadequate in both comparison groups and dispensing practices also remained inappropriate [67]. This is similar to findings from studies which highlight that training alone is seldom sufficient to change provider practice and any improvements may be short-lived [107]. Rather, a combination of strategies is recommended including addressing financial incentives and market conditions [61, 66]. In introducing the iCCM at drug shops in study II, we incorporated drug shop incentives (branding, in-built profit mark-ups, involvement of the district drug inspector for regulation) and community awareness which could have contributed to the positive results.

The issue of financial incentives and the inherent profit motivation within the private health sector is extremely important and needs further discussion. Private health providers may have a tendency of inducing demand unnecessarily, in order to maximize collection of fees from patients, because their profit comes directly from health facility returns, unlike their counterparts in the public sector. This is described as the principal-agent problem in health care, which asserts that private providers, being the imperfect agents of patients (the principal), will act to maximize their profits at the expense of the patients' interest [108]. While the principal-agent problem in health care is well documented in high income settings, [109-110] there is less evidence from low income countries, but points toward the existence of financial incentives leading to over-prescription of antibiotics, injections, brand names and even surgical procedures like caesarean section, in the private health sector [108, 111-112]. This problem in health care is of particularly great concern in health systems where out-of-pocket expenditure is high, provider regulation is weak and there are no

consumer organizations or structures to protect patient interests. This is the situation in Uganda and most other low income countries.

Our studies did not directly investigate provider-induced demand at the level of the drug shops but were designed to mitigate the issue of perverse incentives at the expense of patients in the following ways. First, we had a community awareness campaign during the entire study period where thousands of people were informed about the existence of drugs and diagnostics both at drug shops (subsidized) and in the public health facilities (free-of-charge) and good health seeking behaviour for sick children among other things. Secondly, the prices of drugs were also communicated to people and the minimum recommended price was printed on the packaging of drugs provided at drug shops. Diagnostics were provided free-of-charge to drug shops and patients paid very little for the drugs they purchased. The high RDT positivity rate of 77% could also have ensured profitability, since the majority of patients seen purchased malaria medicine. Finally, there was high patient turn over at drug shops ensuring that even though drugs were sold at low prices, the volume of sales was high, ensuring a profit to drug sellers.

However, the question of equity – whether the poor benefit – of interventions within the private-for-profit sector remains unresolved, due to a paucity of data from impact evaluations of interventions in this sector [113]. Our analysis exploring equity of access to care for children in this rural area adds to the little evidence available. While such a drug shop intervention may be considered a priori to be pro-rich, as it requires out-of-pocket payment [114], we found that more children from the poorest 2 quintiles sought care at the drug shop, when compared to those from the least poor households. The total direct cost of the consultation and purchase of the cheapest drugs at the drug shops in these studies was less than 0.3 USD before the intervention, and this is the cost price that was maintained through the provision of subsidized drugs and free diagnostics. This price seems to have been affordable for even the poorest families.

Further, even with free health care at public health facilities, indirect costs including transport, time away from work, and unofficial payments etc. may still need to be met. These indirect costs are sometimes higher than the cost of seeking care at a drug shop, hence the high care seeking in the private sector [61]. Finally, if you use the "average" as opposed to "relative" (wealth quintiles) social economic status measure, this study implemented within drug shops in a rural district in a poor country, can be seen as having successfully improved quality of care within all social economic groups, because most of the population is disadvantaged [113].

Nonetheless, while we provided the diagnostic tests free of charge to drug shop attendants, studies have shown a lower willingness-to-pay for malaria diagnostic tests and treatment than the cost price of the test and drugs [115]. This confirms that in order to ensure access to diagnostic testing and treatment for febrile illness through drug shops in Uganda and other poor countries, subsidies as included within the studies in this thesis would be necessary.

Finally, some additional ethical considerations within these studies are worth discussing. Potential risks included: fears that drug shop attendants may not be able to utilize the diagnostic tests and treatment algorithms effectively; that disposal of medical waste may be sub-optimal; and that the study may promote the utilization of drug shops at the expense of the public sector. The study results confirm that drug shop attendants were able to utilize the diagnostic tests and algorithms effectively and that utilization of the public health facilities remained constant throughout the studies (see paper II, table 6). This implies that care seeking did not shift from the public health facilities to the private sector. However, an increase in care seeking at intervention district drug shops occurred, mainly coming from the rest of the informal private sector, including un-registered (hence non-participating) drug shops. This implies that care seeking shifted from possibly poor quality private providers to better quality ones at the study drug shops. Finally, from the supervisory reports, the disposal of medical waste was optimal, in the form of burning and disposal of any remains into pit latrines, as per training.

Health systems strengthening

The scope and practice of informal health providers is modified by many contextual factors including: the strength of the regulatory framework; the strength of enforcement mechanisms; the condition of the formal health infrastructure; cultural influences and the demand for services from the informal sector [61]. With the weak public health system, lack of regulation and high demand for services from the private sector, drug shops will continue to be a major source of health care in Uganda and SSA for the foreseeable future.

By recognizing the important role played by drug shops and the private sector in health care delivery, the public sector has an even greater role to play within the health system. The stewardship over both the public and private health sector needs to be strengthened. The lack of regulation or its poor implementation is one of the biggest weakness in the health system in Uganda and sub-Saharan Africa [116] and this has contributed substantially to the proliferation of the informal private sector in the region [117]. The public health sector itself is also poorly regulated, poorly managed and does not serve the public interest adequately. Governments and health ministries in SSA need to critically assess the status of the health sector and take necessary action.

In order to achieve universal health coverage, major health system restructuring will be necessary. In terms of financing, important considerations include higher budgetary expenditure on health as per the Abuja declaration; and a national health insurance scheme which will serve to ensure equitable access to health care and to protect people from catastrophic health expenditures. Contracting out to the private sector both non-clinical services and some clinical services, can also serve to improve efficiency and quality of health care [117]. In terms of human resources for health, maintaining a well remunerated and motivated health workforce is crucial. Decent salaries, defined career paths for health workers and sufficient supervision and mentoring are important for recruiting and maintaining the health workforce.

However, achieving strong health systems that can ensure universal access to health care in SSA is a long term aspiration. In the meantime, the use of frontline health workers like CHWs and strategies to improve community access and quality of care, like iCCM, will remain important in health service provision. In this thesis, I show that drug shop attendants, when trained and supported using the iCCM intervention, can provide highly appropriate care to children at their first source of care. I also provide pioneer evidence on what can be done to operationalise the WHO global action plan on antimicrobial resistance within the private sector, using low cost diagnostic tools, to ensure evidence based prescribing and dispensing as the standard of care. I thus recommend the scale up of diagnostics and treatment for alternative febrile illnesses, also within drug shops. During scale up, a stepped wedge cluster randomized evaluation design could be used, with some districts receiving the intervention earlier than others, in a randomised order. This would provide a strong evaluation design and robust data on the effect of the intervention, which could be compared with those within this thesis.

However, there will be challenges in moving from a small intervention to a wider scale up. Costs of training, supervising and drug distribution will rise sharply, with the size of the scale up. This has been the challenge with the public sector community health worker iCCM programs, which have largely remained donor funded in Uganda and other countries with little local ownership. A level of subsidy will also be required with the drug shop iCCM intervention, in order to ensure that the entire cost of treatment is not transferred to the child. However, overall start up costs and drug distribution costs may be lower, with utilization of the private sector.

Finally, our intervention at drug shops is a pragmatic, intermediate solution to improving access and quality of care for children. For the long term, the focus should be on concurrent strengthening within the entire health system, in order to meet the health needs of Ugandans. This will require concurrent interventions within all the health system building blocks including governance, financing, and human resources for health and service delivery among others.

Conclusions

- The majority of parents seek care for febrile children in the private sector, mainly comprising of drug shops, where the management of malaria, pneumonia and diarrhoea is largely inappropriate - Paper I

- Introduction of the iCCM intervention at drug shops in rural Uganda resulted in high levels of appropriateness of care for malaria, pneumonia and diarrhoea in children - Paper II

- There was also high adherence to the iCCM treatment protocols by the drug shop attendants - Paper III

Recommendations to policy makers

- The quality of care for children with malaria, pneumonia and diarrhoea can be considerably improved by extending the iCCM strategy to drug shops in Uganda

- As with the public sector iCCM intervention, a subsidy is also necessary in the private sector in order to ensure affordability for the majority of patients

- For ease of implementation, one may consider to include a limited number of dedicated drug shops per village

- Scale up could be done in a step-wise fashion to allow for proper assessment of the effect of the intervention

Recommendations to researchers

- If a stepped wedge cluster randomized evaluation design is used during scale up, solid data on the effect of the intervention can be collected

- Further studies are also necessary within a low malaria endemic area, for comparison purposes

- Studies on how to engage with unregistered drug shops are also necessary

- Finally, studies around the following additional areas are necessary: continuity of care; cost effectiveness of the intervention; the effect of the intervention on mortality; and studies on antimicrobial resistance

References

1. UN, *The UN Inter-Agency Group for Child Mortality Estimation - Levels and trends in child mortality*, in *Report 2014*. 2014, UNICEF: New York.
2. Wang, H., et al., *Global, regional, and national levels of neonatal, infant, and under-5 mortality during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013.* Lancet, 2014. **384**(9947): p. 957-79.
3. Lozano, R., et al., *Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010.* Lancet, 2012. **380**(9859): p. 2095-128.
4. Jones, G., et al., *How many child deaths can we prevent this year?* Lancet, 2003. **362**(9377): p. 65-71.
5. Bryce, J., et al., *Reducing child mortality: can public health deliver?* Lancet, 2003. **362**(9378): p. 159-64.
6. Rutebemberwa, E., et al., *Utilization of public or private health care providers by febrile children after user fee removal in Uganda.* Malar J, 2009. **8**: p. 45.
7. Littrell, M., et al., *Monitoring fever treatment behaviour and equitable access to effective medicines in the context of initiatives to improve ACT access: baseline results and implications for programming in six African countries.* Malar J, 2011. **10**: p. 327.
8. Konde-Lule, J., et al., *Private and public health care in rural areas of Uganda.* BMC Int Health Hum Rights, 2010. **10**: p. 29.
9. U.N. *Millennium Development Goals and Beyoned 2015*. Goal 4: Reduce Child Mortality 2015 [cited 2015 15-04-2015]; Available from: http://www.un.org/millenniumgoals/childhealth.shtml.
10. WHO. *Global Health Observatory*. Under-5 Mortality 2014 [cited 2015 15-04-2015]; Available from: http://www.who.int/gho/child_health/mortality/mortality_under_five/en/index1.html.
11. UNICEF, *Committing to Child Survival: A promise Renewed. Progress Report 2014*. 2014, United Nations Children's Fund: New York.
12. Liu, L., et al., *Global, regional, and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: an updated systematic analysis.* Lancet, 2015. **385**(9966): p. 430-40.
13. WHO, *Global Health Observatory: Causes of Child Mortality, 2013*. 2014, World Health Organization.
14. UNICEF, *UNICEF Global databases: Child mortality estimates*. 2014, United Nations Children's Fund.
15. WHO, U., *Every Newborn: an action plan to end preventable deaths. Executive summary*. 2014, World Health organization: Geneva.
16. WHO, *Global Vaccine Action Plan 2011-2020*. 2013, World Health Organization: Geneva.
17. U.N., *UN commission on life saving commodities for women and children: commissioners' report*. 2012, United Nations: New York.

18. UNICEF, *Ending preventable child deaths from pneumonia and diarrhoea by 2025:the integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD)*. 2013, United Nations Childrens' Fund/World Health Organization: New York.

19. SUN. *Sacling Up Nutrition Movement*. 2012; Available from: scalingupnutrition.org.

20. Black, R.E., S.S. Morris, and J. Bryce, *Where and why are 10 million children dying every year?* Lancet, 2003. **361**(9376): p. 2226-34.

21. WHO, *World Health Report 2000*, in *Health Systems: Improving Performance*. 2000, World Health Organization: Geneva.

22. WHO, *Everybody's bussiness: Strengthening health systems to improve health outcomes. WHO's framework for action*. 2007, World Health Organization: Geneva.

23. de Savigny, D. and T. Adams, *Systems Thinking for Health Systems Strengthening*. 2009: Alliance for Health Policy and Systems Research, WHO.

24. Resolution WHA 58.33, *Sustainable health financing, universal coverage and social health insurance*, in *Fifty eighth World Health Assembly, Geneva, 16–25 May 2005*. 2005, World Health Organization: Geneva.

25. WHO, *World Health Report 2008 - primary health care, now more than ever*. 2008, World Health Organization: Geneva.

26. WHO, *World Health Report 2010 - Health systems financing: the path to universal coverage*. 2010, World Health Organization: Geneva.

27. WHO, *World Health Report 2006 - working together for health*. 2006, World Health Organization: Geneva.

28. Bloom, G., et al., *Making health markets work better for poor people: the case of informal providers*. Health Policy Plan, 2011. **26 Suppl 1**: p. i45-52.

29. Forsberg, B.C., D. Montagu, and J. Sundewall, *Moving towards in-depth knowledge on the private health sector in low- and middle-income countries*. Health Policy Plan, 2011. **26 Suppl 1**: p. i1-3.

30. Meessen, B., et al., *Composition of pluralistic health systems: how much can we learn from household surveys? An exploration in Cambodia.* Health Policy Plan, 2011. **26 Suppl 1**: p. i30-44.

31. Ahmed, S.M., et al., *Harnessing pluralism for better health in Bangladesh*. Lancet, 2013. **382**(9906): p. 1746-55.

32. Lagomarsino, G., et al., *Public stewardship of mixed health systems.* Lancet, 2009. **374**(9701): p. 1577-8.

33. Marek, T., O'Farell, C. , Yamamoto, C. , Zabel, L., *Trends and opportunities in public-private partnerships to improve health service delivery*. 2005, WorldBank: Washington, D.C.

34. Bustreo, F., A. Harding, and H. Axelsson, *Can developing countries achieve adequate improvements in child health outcomes without engaging the private sector?* Bull World Health Organ, 2003. **81**(12): p. 886-95.

35. Marriot, A., *Blind optimisim: challenging the myths about private health care in poor countries*, in *Oxfam briefing paper*. 2009, Oxfam international.

36. Enato, E.F. and A.O. Okhamafe, *A survey of anti-malarial activity during pregnancy, and children's malaria care-seeking behaviour in two Nigerian rural communities.* Scand J Infect Dis, 2006. **38**(6-7): p. 474-8.

37. Peters, D.H., Yazbeck, A. , Sharma, R., *Better health systems for India's poor: findings, analysis and options*. 2002, World Bank: Washington D.C.

38. De Costa, A., et al., *Where are healthcare providers? Exploring relationships between context and human resources for health Madhya Pradesh province, India.* Health Policy, 2009. **93**(1): p. 41-7.

39. Ahmed, S.M., M.A. Hossain, and M.R. Chowdhury, *Informal sector providers in Bangladesh: how equipped are they to provide rational health care?* Health Policy Plan, 2009. **24**(6): p. 467-78.

40. Levin, A., et al., *The demand for child curative care in two rural thanas of Bangladesh: effect of income and women's employment.* Int J Health Plann Manage, 2001. **16**(3): p. 179-94.

41. Lagomarsino, G., Nachuk, S. , Kundra, S.S. (eds), *Public Stewardship of private providers in mixed health systems*. 2009, Rockerfeller foundation/Results for Development Institute: Washington, D.C.

42. Kangwana, B.P., et al., *The impact of retail-sector delivery of artemether-lumefantrine on malaria treatment of children under five in Kenya: a cluster randomized controlled trial.* PLoS Med, 2011. **8**(5): p. e1000437.

43. Montagu, D., *Franchising of health services in low-income countries.* Health Policy Plan, 2002. **17**(2): p. 121-30.

44. WHO, *World Health Assembly Resolution: Strengthening the capacity of governments to constructively engage the private sector in providing essential health-care services*, in *63rd World Health Assembly, A63/25*. 2010, World Health Organization: Geneva.

45. Chowdhury, A.M., et al., *The Bangladesh paradox: exceptional health achievement despite economic poverty.* Lancet, 2013. **382**(9906): p. 1734-45.

46. WHO. *Uganda country profile*. 2012 [cited 2015 04-05]; Available from: http://who.int/countries/uga/en/.

47. Government of Uganda, *Health sector strategic plan III, 2010/11 - 2014/15* Ministry of Health, Editor. 2010, Ministry of Health: Kampala.

48. Uganda Ministry of Health, *Uganda health system assessment 2011*. 2011, Ministry of Health, Health Systems 20/20, and Makerere University School of Public Health: Kampala.

49. Government of Uganda, *National Policy on Public Private Partnership in Health* 2012, Government of Uganda: Kampala.

50. Berman, P. and R. Laura, *The role of private providers in maternal and child health and family planning services in developing countries.* Health Policy Plan, 1996. **11**(2): p. 142-55.

51. Tougher, S., et al., *Effect of the Affordable Medicines Facility--malaria (AMFm) on the availability, price, and market share of quality-assured artemisinin-based combination therapies in seven countries: a before-and-after analysis of outlet survey data.* Lancet, 2012. **380**(9857): p. 1916-26.

52. Deming, M.S., et al., *Home treatment of febrile children with antimalarial drugs in Togo.* Bull World Health Organ, 1989. **67**(6): p. 695-700.

53. Foster, S., *Treatment of malaria outside the formal health services.* J Trop Med Hyg, 1995. **98**(1): p. 29-34.

54. Mnyika, K.S., J.Z. Killewo, and T.K. Kabalimu, *Self-medication with antimalarial drugs in Dar es Salaam, Tanzania.* Trop Geogr Med, 1995. **47**(1): p. 32-4.

55. Oladepo, O., Salami, K.K. , Adeoye, B.W. , Oashiname, F. Ofie, B., *Malaria treatment and policy in 3 regions in Nigeria: The role of patent medicine vendors.* 2007, Future Health Systems.

56. Ongore, D. and L. Nyabola, *Role of shops and shopkeepers in malaria control.* East Afr Med J, 1996. **73**(6): p. 390-4.

57. Chalker, J., et al., *STD management by private pharmacies in Hanoi: practice and knowledge of drug sellers.* Sex Transm Infect, 2000. **76**(4): p. 299-302.

58. Chalker, J., et al., *Private pharmacies in Hanoi, Vietnam: a randomized trial of a 2-year multi-component intervention on knowledge and stated practice regarding ARI, STD and antibiotic/steroid requests.* Trop Med Int Health, 2002. **7**(9): p. 803-10.

59. Global-Fund. *Affordable Medicines Facility - malaria.* 2011 [cited 2013 13 - Feb]; Available from: http://www.theglobalfund.org/en/amfm/.

60. Global-Fund. *Board approves integration of AMFM into core global fund grant processes.* 2012 [cited 2013 15-Feb-2013]; Available from: http://www.theglobalfund.org/en/mediacenter/newsreleases/2012-11-15_Board_Approves_Integration_of_AMFm_into_Core_Global_Fund_Grant_Processes/.

61. Sudhinaraset, M., et al., *What is the role of informal healthcare providers in developing countries? A systematic review.* PLoS One, 2013. **8**(2): p. e54978.

62. Cross, J. and H.N. MacGregor, *Knowledge, legitimacy and economic practice in informal markets for medicine: a critical review of research.* Soc Sci Med, 2010. **71**(9): p. 1593-600.

63. Tumwikirize, W.A., et al., *Management of acute respiratory infections in drug shops and private pharmacies in Uganda: a study of counter attendants' knowledge and reported behaviour.* East Afr Med J, 2004. **Suppl**: p. S33-40.

64. Chakraborty, S., S.A. D'Souza, and R.S. Northrup, *Improving private practitioner care of sick children: testing new approaches in rural Bihar.* Health Policy Plan, 2000. **15**(4): p. 400-7.

65. Waters, H., L. Hatt, and D. Peters, *Working with the private sector for child health.* Health Policy Plan, 2003. **18**(2): p. 127-37.

66. Shah, N.M., W.R. Brieger, and D.H. Peters, *Can interventions improve health services from informal private providers in low and middle-income countries?: a comprehensive review of the literature.* Health Policy Plan, 2011. **26**(4): p. 275-87.

67. Tumwikirize, W.A., et al., *Impact of a face-to-face educational intervention on improving the management of acute respiratory infections in private pharmacies and drug shops in Uganda.* East Afr Med J, 2004. **Suppl**: p. S25-32.

68. Tawfik, Y., et al., *Negotiating improved case management of childhood illness with formal and informal private practitioners in Uganda.* Trop Med Int Health, 2006. **11**(6): p. 967-73.

69. Nguyen, D.T., et al., *Does integrated management of childhood illness (IMCI) training improve the skills of health workers? A systematic review and meta-analysis.* PLoS One, 2013. **8**(6): p. e66030.

70. Gouws, E., et al., *Improving antimicrobial use among health workers in first-level facilities: results from the multi-country evaluation of the Integrated Management of Childhood Illness strategy.* Bull World Health Organ, 2004. **82**(7): p. 509-15.

71. Chopra, M., et al., *Integrated management of childhood illness: what have we learned and how can it be improved?* Arch Dis Child, 2012. **97**(4): p. 350-4.

72. Young, M., et al., *World Health Organization/United Nations Children's Fund Joint Statement on Integrated Community Case Management: An Equity-Focused Strategy to Improve Access to Essential Treatment Services for Children.* Am J Trop Med Hyg, 2012. **87**(5 Suppl): p. 6-10.

73. Rasanathan, K., et al., *Community case management of childhood illness in sub-Saharan Africa - findings from a cross-sectional survey on policy and implementation.* J Glob Health, 2014. **4**(2): p. 020401.

74. WHO, *Guidelines for the Treatment Malaria. Second Edition.* 2010: Geneva.

75. MoH, *Intergrated Community Case Management of Childhood Malaria, Pneumonia and Diarrhoea: Implementation Guide*, C.H.D. Ministry of Health, Editor. 2010: Kampala.

76. Awor, P., J. Miller, and S. Peterson, *Systematic literature review of integrated community case management and the private sector in Africa: Relevant experiences and potential next steps.* J Glob Health, 2014. **4**(2): p. 020414.

77. Thomson, R., et al., *Has Tanzania embraced the green leaf? Results from outlet and household surveys before and after implementation of the Affordable Medicines Facility-malaria.* PLoS One, 2014. **9**(5): p. e95607.

78. Ikwuobe, J.O., et al., *The impact of rapid malaria diagnostic tests upon anti-malarial sales in community pharmacies in Gwagwalada, Nigeria.* Malar J, 2013. **12**: p. 380.

79. Kangwana, B.P., et al., *The effect of an anti-malarial subsidy programme on the quality of service provision of artemisinin-based combination therapy in Kenya: a cluster-randomized, controlled trial.* Malar J, 2013. **12**: p. 81.

80. Talisuna, A.O., et al., *Closing the access barrier for effective anti-malarials in the private sector in rural Uganda: consortium for ACT private sector subsidy (CAPSS) pilot study.* Malar J, 2012. **11**: p. 356.

81. Yeung, S., et al., *Socially-marketed rapid diagnostic tests and ACT in the private sector: ten years of experience in Cambodia.* Malar J, 2011. **10**: p. 243.

82. Rutta, E., et al., *Increasing Access to Subsidized Artemisinin-based Combination Therapy through Accredited Drug Dispensing Outlets in Tanzania.* Health Res Policy Syst, 2011. **9**: p. 22.

83. Alba, S., et al., *Improvements in access to malaria treatment in Tanzania following community, retail sector and health facility interventions -- a user perspective.* Malar J, 2010. **9**: p. 163.

84. Abuya, T.O., et al., *Evaluating different dimensions of programme effectiveness for private medicine retailer malaria control interventions in Kenya.* PLoS One, 2010. **5**(1): p. e8937.

85. Larson, C.P., T.P. Koehlmoos, and D.A. Sack, *Scaling up zinc treatment of childhood diarrhoea in Bangladesh: theoretical and practical considerations guiding the SUZY Project.* Health Policy Plan, 2012. **27**(2): p. 102-14.

86. Diaz, T., S. Aboubaker, and M. Young, *Current scientific evidence for integrated community case management (iCCM) in Africa: Findings from the iCCM Evidence Symposium.* J Glob Health, 2014. **4**(2): p. 020101.

87. Donabedian, A., *The quality of care. How can it be assessed?* JAMA, 1988. **260**(12): p. 1743-8.

88. WHO, *Quality of care. A process for making strategic choices in health systems.* 2006, World Health Organization: Geneva.

89. Brown, L.D., Franco, L.M., Rafeh, N., Hatzell, T., *Quality assuranceof health care in developing countires.* 1998, Quality Assurance Project: Bethesda.

90. Harris, A.D., et al., *The use and interpretation of quasi-experimental studies in infectious diseases.* Antimicrobial resistance, 2004.

91. Habicht, J.P., C.G. Victora, and J.P. Vaughan, *Evaluation designs for adequacy, plausibility and probability of public health programme performance and impact.* Int J Epidemiol, 1999. **28**(1): p. 10-8.

92. Bonell, C.P., et al., *Alternatives to randomisation in the evaluation of public-health interventions: design challenges and solutions.* J Epidemiol Community Health, 2009.

93. Graneheim, U.H. and B. Lundman, *Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness.* Nurse Educ Today, 2004. **24**(2): p. 105-12.

94. Mbonye, A.K., et al., *A Cluster Randomised Trial Introducing Rapid Diagnostic Tests into Registered Drug Shops in Uganda: Impact on Appropriate Treatment of Malaria.* PLoS One, 2015. **10**(7): p. e0129545.

95. Hill, A.B., *The Environment and Disease: Association or Causation?* Proc R Soc Med, 1965. **58**: p. 295-300.

96. Wears, R.L., *Advanced statistics: statistical methods for analyzing cluster and cluster-randomized data.* Acad Emerg Med, 2002. **9**(4): p. 330-41.

97. Jacobs, B., et al., *Sexually transmitted disease management in Uganda's private-for-profit formal and informal sector and compliance with treatment.* Sex Transm Dis, 2004. **31**(11): p. 650-4.

98. Mignone, J., et al., *Formal and informal sector health providers in southern India: role in the prevention and care of sexually transmitted infections, including HIV/AIDS.* AIDS Care, 2007. **19**(2): p. 152-8.

99. Bryant, J. and A. Prohmmo, *Use of drug sellers by old people in northeast Thailand.* Asia Pac J Public Health, 2001. **13**(2): p. 91-5.

100. Ansah, E.K., et al., *Rapid testing for malaria in settings where microscopy is available and peripheral clinics where only presumptive treatment is available: a randomised controlled trial in Ghana.* BMJ, 2010. **340**: p. c930.

101. Bastiaens, G.J., T. Bousema, and T. Leslie, *Scale-up of malaria rapid diagnostic tests and artemisinin-based combination therapy: challenges and perspectives in sub-Saharan Africa.* PLoS Med, 2014. **11**(1): p. e1001590.

102. Mukanga, D., et al., *Can lay community health workers be trained to use diagnostics to distinguish and treat malaria and pneumonia in children? Lessons from rural Uganda.* Trop Med Int Health, 2011. **16**(10): p. 1234-42.

103. Kalyango, J.N., et al., *Performance of community health workers under integrated community case management of childhood illnesses in eastern Uganda.* Malar J, 2012. **11**: p. 282.

104. Marsh, D.R., et al., *Introduction to a special supplement: Evidence for the implementation, effects, and impact of the integrated community case management strategy to treat childhood infection.* Am J Trop Med Hyg, 2012. **87**(5 Suppl): p. 2-5.

105. Chinbuah, M.A., et al., *Impact of community management of fever (using antimalarials with or without antibiotics) on childhood mortality: a cluster-randomized controlled trial in Ghana.* Am J Trop Med Hyg, 2012. **87**(5 Suppl): p. 11-20.

106. Theodoratou, E., et al., *The effect of case management on childhood pneumonia mortality in developing countries.* Int J Epidemiol, 2010. **39 Suppl 1**: p. i155-71.

107. Ofori-Adjei, D. and D.K. Arhinful, *Effect of training on the clinical management of malaria by medical assistants in Ghana.* Soc Sci Med, 1996. **42**(8): p. 1169-76.

108. Nguyen, H., *The principal-agent problems in health care: evidence from prescribing patterns of private providers in Vietnam.* Health Policy Plan, 2011. **26 Suppl 1**: p. i53-62.

109. Birch, S., *The identification of supplier-inducement in a fixed price system of health care provision. The case of dentistry in the United Kingdom.* J Health Econ, 1988. **7**(2): p. 129-50.

110. Cromwell, J. and J.B. Mitchell, *Physician-induced demand for surgery.* J Health Econ, 1986. **5**(4): p. 293-313.

111. Trap, B., E.H. Hansen, and H.V. Hogerzeil, *Prescription habits of dispensing and non-dispensing doctors in Zimbabwe.* Health Policy Plan, 2002. **17**(3): p. 288-95.

112. James, C.D., et al., *An unhealthy public-private tension: pharmacy ownership, prescribing, and spending in the Philippines.* Health Aff (Millwood), 2009. **28**(4): p. 1022-33.

113. Patouillard, E., et al., *Can working with the private for-profit sector improve utilization of quality health services by the poor? A systematic review of the literature.* Int J Equity Health, 2007. **6**: p. 17.

114. Kamal-Yanni, M.M., J. Potet, and P.M. Saunders, *Scaling-up malaria treatment: a review of the performance of different providers.* Malar J, 2012. **11**: p. 414.

115. Hansen, K.S., et al., *Willingness-to-pay for a rapid malaria diagnostic test and artemisinin-based combination therapy from private drug shops in Mukono District, Uganda.* Health Policy Plan, 2013. **28**(2): p. 185-96.

116. Wafula, F., et al., *Protecting the public or setting the bar too high? Understanding the causes and consequences of regulatory actions of front-line regulators and specialized drug shop operators in Kenya.* Soc Sci Med, 2013. **97**: p. 220-7.

117. Mills, A., et al., *What can be done about the private health sector in low-income countries?* Bull World Health Organ, 2002. **80**(4): p. 325-30.

Errata list

	Now reads	**Was:**
Page 10, Quality	Quality is....	Simply, quality is...
Page 42, General aim	...effect on quality of care after introducing...	...effect on quality of care of introducing...
Page 57, table III & Paper II, table 3: Overall antibiotic use	Note: The result for overall antibiotic use (prevalence ratio = 0.82) was obtained from end-line data only.	

Paper I

Private Sector Drug Shops in Integrated Community Case Management of Malaria, Pneumonia, and Diarrhea in Children in Uganda

Phyllis Awor,* Henry Wamani, Godfrey Bwire, George Jagoe, and Stefan Peterson

*Department of Community Health and Behavioral Sciences, School of Public Health,
Makerere University College of Health Sciences, Kampala, Uganda; Medicines for Malaria Venture, Kampala, Uganda;
Medicines for Malaria Venture, Geneva, Switzerland; Division of Global Health, Karolinska Institute, Stockholm, Sweden;
International Maternal and Child Health Unit, Uppsala University, Uppsala, Sweden*

Abstract. We conducted a survey involving 1,604 households to determine community care-seeking patterns and 163 exit interviews to determine appropriateness of treatment of common childhood illnesses at private sector drug shops in two rural districts of Uganda. Of children sick within the last 2 weeks, 496 (53.1%) children first sought treatment in the private sector versus 154 (16.5%) children first sought treatment in a government health facility. Only 15 (10.3%) febrile children treated at drug shops received appropriate treatment for malaria. Five (15.6%) children with both cough and fast breathing received amoxicillin, although no children received treatment for 5–7 days. Similarly, only 8 (14.3%) children with diarrhea received oral rehydration salts, but none received zinc tablets. Management of common childhood illness at private sector drug shops in rural Uganda is largely inappropriate. There is urgent need to improve the standard of care at drug shops for common childhood illness through public–private partnerships.

INTRODUCTION

Fever-related conditions, including malaria, pneumonia, and diarrhea, are the major causes of mortality among children less than 5 years old in low-income countries.[1] In Uganda, the Home-Based Management of Fever (HBMF) strategy was initiated in 2002 to treat all febrile children with antimalarials. The HBMF strategy was promoted through public and community health worker systems. As a result, the community health workers' mandate has been broadened to use diagnostics such as rapid diagnostic tests (RDTs) for malaria and respiratory timers for pneumonia and treat febrile children with antimalarials, antibiotics, and oral rehydration salt with zinc tablets (ORS/Zinc) accordingly. This new approach is called the integrated community case management (iCCM) of malaria, pneumonia, and diarrhea in children, which is now national policy in Uganda.[2]

Whereas the iCCM strategy is implemented through volunteer community health workers, the majority of parents in Uganda seek care for their febrile children from private clinics and drug shops.[3,4] Unfortunately, the standard of care in private health facilities, including drug shops, is not well-documented, although it is known to be wanting. There is need to study interventions aimed at improving the standard of care provided by the private sector in the management of common childhood illnesses.[4,5]

In 2011, the Global Fund, through the Affordable Medicines Facility−Malaria (AMFm), began to subsidize and promote artemisinin combination therapy (ACT) for the treatment of fever through the private sector in eight low-income countries, including Uganda.[6] Studies have shown that subsidizing ACT through private drug shops in rural areas can greatly increase ACT coverage for reported fevers.[7,8] Unfortunately, there is no similar strategy to improve treatment of pneumonia and diarrhea in the private sector, where many sick children are first seen.

In addition, studies are exploring the feasibility of introducing malaria RDT in the private sector. However, there is extremely limited understanding of how to offer appropriate alternative treatment to those children with RDT-negative fever with or without signs of other illnesses.[9] This lack of understanding limits the adherence to RDT results and leads to continued inappropriate use of ACT, with adverse consequences for cost, resistance development, and children suffering from other illnesses than malaria.[10,11] Furthermore, there is also indication of increased likely inappropriate use of antibiotics to treat RDT negative fever.[9]

The private sector plays an important role for care of febrile children in Uganda. Through the AMFm, the role of the private sector may further be expanded for care of malaria. The objective of this study was to determine the role and appropriateness of care provided by private sector drug shops in treating childhood fever, respiratory symptoms, and diarrhea in Uganda.

METHODS

The study was conducted in two rural districts of Kaliro and Kamuli in eastern Uganda as part of a baseline assessment for a larger study determining the effectiveness of introducing and promoting pre-packaged drugs and diagnostics for treatment of childhood fever and diarrhea within drug shops in Uganda.

The two districts were purposively selected as representative of a typical rural setting with a high burden of febrile illness and diarrhea in children. The research strategy included a community household survey and exit interviews at drug shops to determine care-seeking patterns and the appropriateness of treatment provided at drug shops for febrile children less than 5 years of age in Uganda. All data were collected in May of 2011.

Household survey. A two-stage cluster sampling using probability proportional to population size was used to select 1,604 households with children less than 5 years of age in both study districts. At the first stage, a probability sample of 30 villages/clusters was sampled. At the second stage, 26 target households were sampled from each cluster. Because of

* Address correspondence to Phyllis Awor, Department of Community Health and Behavioral Sciences, School of Public Health, Makerere University College of Health Sciences, 7072 Kampala, Uganda. E-mail: pawor@musph.ac.ug

the lack of an updated village list of households, it was not possible to have a random sample within a cluster. The study team, therefore, randomly identified a starting point from a list of households obtained from the local leaders and thereafter, sampled every fifth household with children less than 5 years of age. The main caretaker (usually the mother) aged 15 years and above was interviewed face to face using a semistructured questionnaire. If a sampled house was empty or the caregiver was absent, it was replaced by the neighboring house. The questionnaire was designed to elicit care-seeking practice for the most recent illness (less than 2 weeks before the interview).

Five-day training was conducted for data collectors, and it included a pilot within a cluster that was not included in the survey. Five field teams collected the data, and a team was comprised of four data collectors and one supervisor.

Exit interviews at drug shops. One-half of all the licensed/registered drug shops in the two study districts were randomly selected for exit interviews ($N = 40$). All clients exiting the drug shops were approached and requested to be interviewed if they had come to the drug shop seeking treatment of a child less than 5 years of age. Data collectors were at the drug shop all day (from 8:30 AM to 7:00 PM) during the study period, and 163 interviews were conducted.

A semistructured questionnaire was used. The questions asked included what the child's symptoms were, when the current illness was noticed, and any care sought before coming to the drug shop. We asked for all the medicines purchased and noted down information, including drug name, dosage, duration of treatment, and whether instructions were given on how to use the purchased medicines.

The data were entered separately for the household and exit interviews in Epi data software, and they were analyzed using SPSS. Ethical approval was obtained from the Makerere University School of Public Health Higher Degrees Research and Ethics Committee as well as the Uganda National Council of Science and Technology. Informed consent was obtained from all the study participants.

RESULTS

The median (interquartile range [IQR]) age of the primary caregiver, number of children less than 5 years old, and household size were 28 (23, 35) years, 2 (1, 2) children, and 6 (4, 8), respectively (Table 1). The decision to seek treatment of the ill child was usually made by the mother in 854 (53.2%) households, whereas the father/husband mainly authorized expenditure for treatment of sick children in 1,173 (73.1%) households.

Up to 934 (58%) children had been sick within the previous 2 weeks of the study (Table 2). The number of children with an illness within the last 2 weeks who first sought treatment in the private sector (private clinics and drug shops) was 496 (53.1%) versus 154 (16.5%) in a government health facility. Caregivers who first managed the sick child at home were 228 (24.4%), whereas 31 (3.3%) caregivers first visited a community health worker, 13 (1.4%) caregivers first visited a traditional healer, and 12 (1.3%) caregivers first visited a spiritual healer or the church.

The median (IQR) age of children for whom treatment was sought at the drug shop was 15 (9, 36) months; 65% of the caretakers who bought drugs for sick children at the drug shops were female, and their education level was primary in 75 (52.8%) and ordinary level in 53 (37.3%) women. The main presenting complaint/symptoms for which treatment was sought at the drug shop was fever in 145 (89%), cough in 100 (61.3%), and diarrhea in 56 (34.4%) children. Both cough

TABLE 1
Baseline characteristics of the study population ($N = 1,604$)

Median age (years) of primary caregiver/respondent (IQR)	28 (23, 35)
Median age (months) of child (IQR)	14 (7, 24)
Median household size (IQR)	6 (4, 8)
Median number of children less than 5 years old in the household (IQR)	2 (1, 2)
Educational background of caretaker/respondent	
No education	308 (19.2%)
Primary level	908 (56.6%)
Secondary level	362 (22.6%)
Higher education	26 (1.6%)
Household head	
Self (caretaker/respondent)	212 (13.2%)
Partner/husband	1,323 (82.5%)
Other male adult	52 (3.2%)
Other female adult	17 (1.1%)
Educational background of partner/husband ($N = 1,568$; some have no partner)	
No education	138 (8.8%)
Primary level	809 (51.6%)
Secondary level	422 (26.9)
Higher education	72 (4.6%)
Do not know	127 (8.1%)
Occupation of partner/husband ($N = 1,568$)	
Farmer	896 (57.1%)
Trader	91 (5.8%)
Civil servant	94 (6.0%)
Other office work	54 (3.4%)
Business man/self-used	346 (22.1%)
Unemployed	26 (1.7%)
Do not know	61 (3.9%)
Who makes the decision to seek medical treatment when a child is sick?	
Mother	854 (53.2%)
Husband	312 (19.5%)
Mother and husband together	402 (25.1%)
Relatives/others	36 (2.2%)
Who authorizes expenditure for treatment of sick children in household?	
Mother	163 (10.2%)
Husband	1,173 (73.1%)
Mother and husband together	220 (13.7%)
Relatives/others	48 (3%)
Ownership of house	
Self-owned	1,394 (86.9%)
Rented	123 (7.7%)
Relative (pays no rent)	85 (5.3%)
Other	2 (0.1%)

TABLE 2
First point where care was sought for illness within the last 2 weeks in a child less than 5 years of age ($N = 934$)

Healthcare service provider	Number (%)
Private health provider	496 (53.1)
Drug shop	279 (29.9)
Private clinic	217 (23.2)
Managed at home	228 (24.4)
Government health facility	154 (16.5)
Rural health center	120 (12.8)
Hospital	34 (3.6)
Community health worker	31 (3.3)
Traditional healer	13 (1.4)
Spiritual healer/church	12 (1.3)

Symptoms of the child for whom treatment was sought at the
drug shop

Symptom/complaint (N = 163)	Number (%)*
Fever	145 (89)
Cough	100 (61.3)
Rapid/difficult breathing	40 (24.5)
Cough and rapid/difficult breathing	32 (19.6)
Diarrhea	56 (34.4)
Vomiting	20 (12.3)
Others	37 (22.7)

*The total is more than 100%, because more than one complaint is possible.

and rapid/difficult breathing were the presenting complaint in
32 (19.6%) children (Table 3).

Of all children with fever for whom treatment was sought at
a drug shop, only 15 (10.3%) children received appropriate
treatment according to current national guidelines with an
ACT for 3 days and within 24 hours of onset of illness (Table 4).
For children who presented with cough and fast breathing—
defined as pneumonia according to the iCCM guidelines—
23 (71.9%) children received an antibiotic, although it was
mainly cotrimoxazole (56.3%). Only 5 (15.6%) children were
treated with the recommended first-line drug of amoxicillin.
However, zero children with cough and fast breathing received
amoxicillin for the recommended duration of 5–7 days. Similarly,
only 8 (14.3%) children with diarrhea were treated with ORS,
and none of the children with diarrhea received zinc tablets.

Appropriateness of treatment obtained from drug shops

Appropriateness of treatment of fever, cough with rapid/fast breathing and diarrhoea	Number (%)
Treatment of fever (N = 145)	
Proportion of children with fever receiving any ACT drug	37 (25.5)
Proportion of children with fever receiving any ACT for 3 days	27 (18.6)
Proportion of children with fever receiving any ACT within 24 hours	22 (15.2)
Proportion of children with fever receiving any ACT within 24 hours of onset of fever and for 3 days	15 (10.3)
Proportion of children with fever receiving any ACT within 24 hours of onset of fever and for less than 3 days	1 (0.7)
Proportion of children with fever receiving any ACT within 24 hours of onset of fever and for more than 3 days	6 (4.1)
Treatment of cough with rapid/fast breathing (N = 32)	
Proportion of children with both cough and fast breathing treated with any antibiotic (amoxicillin, cotrimoxazole, or any other antibiotic)	23 (71.9)
Proportion of children with both cough and fast breathing treated with cotrimoxazole only	18 (56.3)
Proportion of children with both cough and fast breathing treated with amoxicillin	5 (15.6)
Proportion of children with both cough and fast breathing treated with amoxicillin for 5–7 days	0
Treatment of diarrhea (N = 56)	
Proportion of children with diarrhea treated with ORS	8 (14.3)
Proportion of children with diarrhea treated with ORS and zinc	0

Accessibility and affordability of drugs from the drug shop (N = 163)

Bought drugs without a prescription	108 (66.3%)
Reason for choosing the drug shop	
Good service/customer care	101 (62%)
Distance (proximity)	34 (20.9%)
Good/trained staff	32 (19.6%)
Regular supply of drugs	23 (14.1%)
Drug seller is my friend	22 (13.5%)
How long does it take to walk from home to this drug shop?	
Less than 15 minutes	51 (31.3%)
15–30 minutes	42 (25.8%)
30–60 minutes	39 (23.9%)
1–2 hours	19 (11.7%)
Spent money to get to drug shop?	60 (36.8%)
Median amount spent (range)	1,000 Ugshs (200–7,500)
Walking distance to the nearest public health facility	
Less than 15 minutes	34 (20.9%)
15–30 minutes	39 (23.9%)
30–60 minutes	35 (21.5%)
1–2 hours	28 (17.2%)
Was not able to afford all drugs prescribed/advised	47 (28.8%)
Why not able to buy all drugs? (N = 47)	
I did not have enough money	42 (89.4%)
When buying drugs, what determines the amount that you buy?	
The dosage prescribed	65 (39.9%)
The amount of money that I have	78 (47.8%)
Other	20 (12.3%)
How do you rate prices in the drug shop with respect to your ability to buy them?	
Too expensive	50 (30.7%)
Prices within my reach	113 (69.3%)

Up to 108 (66.3%) caretakers bought drugs from the drug
shops without a prescription (Table 5). Although the amount
of money available to a care-seeker determined the amount of
drugs bought in 78 (47.8%) cases, the prices of drugs were
reported to be within reach of the majority (113; 69.3%). The
main reasons for seeking care at the drug shop included per-
ceived good service/customer care in 101 (62%) cases, dis-
tance/proximity in 34 (20.9%) cases, good/trained staff in
32 (19.6%) cases, regular supply of drugs in 23 (14.1%) cases,
and the drug seller being a friend in 22 (13.5%) cases (Table 5).

DISCUSSION

In this study, we have documented that the majority of
parents/caretakers in two districts in rural Uganda take their
febrile children to the private sector and that the care that
they receive at drug shops for treatment of the main diseases
causing pediatric death is inadequate. The significant role of
the private sector in healthcare delivery has been previously
described. The work by Rutebemberwa and others[3] showed
that 62.7% of care for febrile children sought outside the
home was first obtained from drug shops/private clinics. Our
study confirms this finding, with more than one-half of all care
for children less than 5 years of age being first sought in
private drug shops and clinics. This finding is also in agree-
ment with the finding in the work by Konde-Lule and others[4]
that private providers play a major role in healthcare delivery
in rural Uganda.

However, we document that the care received at private drug shops is poor. According to the current Ugandan iCCM guidelines for management of fever, cough, and diarrhea, only 10% of febrile children were correctly managed in our study (that is, correct treatment with ACT for the correct duration and within 24 hours of onset of illness). Management of cough with fast breathing at the drug shops was even worse, with no children receiving the recommended drug—amoxicillin—for the correct duration of time. Also, no child with diarrhea received ORS with zinc tablets according to current treatment guidelines. This more comprehensive assessment of correct management for a range of symptoms shows similar results to previous studies of the appropriateness of care provided by the private sector to sick children less than 5 years of age.[5,12,13]

Although drug shops in Uganda are commonly owned and registered by middle-level health workers, they are usually manned by either lower-level nurses (nursing assistants who have some level of medical training that allows them to manage simple health problems like treatment of fever) or people with no previous medical training.[14] Generally, most drug shop attendants have some secondary school education. Given the poor management of childhood malaria, pneumonia, and diarrhea by drug shop attendants and their limited medical training, there is urgent need for more effective training and supervision in this part of the private sector.[5,14]

Although both drug shops and government facilities were a similar distance from their homes, 62% of the caretakers interviewed reported that the reason that they chose to seek care at a drug shop was because of good service/customer care. Poor interpersonal handling of patients and longer waiting time at government facilities as well as lack of trust in staff at public health facilities have been reported as reasons for preferred use of private drug shops for acute febrile illness.[15] Improving customer experience at public health facilities could, thus, contribute to increased use of these facilities.

The Global Fund now supports the AMFm with subsidized ACT through the private sector in eight countries. It has ambitions to increase prompt access to effective antimalarials, particularly to increase ACT affordability, availability, and use and crowd out artemisinin monotherapies, chloroquine, and sulfadoxine-pyrimethamine by gaining market share. Challenges for the AMFm include ensuring that the subsidy is passed on to consumers, increasing access to diagnostic confirmation, reaching the poor and remote, and identifying appropriate benchmarks to evaluate the AMFm pilots.[16] Although increasing prompt access to ACT through the private sector through subsidies has been shown to be feasible,[7] this access may well come at the expense of rational use when ACT is used to treat fever presumptively. The experience of introducing ACT and malaria RDT in the private sector in Cambodia over the last 10 years has shown challenges in maintaining constant supply and determining effective incentives for private providers and consumers to use the RDT and adhere to their results.[17] There may also be inadvertent effects on the use of antibiotics. Studies from Zanzibar[18] and mainland Tanzania[9] have shown dramatically increased prescription rates for antibiotics when RDTs were introduced, particularly in RDT-negative cases.

We hypothesize that adherence to test results, adequate management of the febrile child, and rational use of ACT as well as antibiotics may be dependent on diagnostics for malaria as well as pneumonia (respiratory timers) and alter-native appropriate treatment being provided, including paracetamol, to the likely majority of patients who do not fulfill the criteria for antimalarial or antibiotic treatment. With changing epidemiology of malaria and pneumonia, this group will be a higher and higher proportion of children.[19]

To realize the full potential of ACT and RDT to treat malaria and adequately cater to the febrile child, it may, therefore, be important to extend the logic and policy recommendation of integrated community case management of febrile illness to the private sector. This extension will be in support of the World Health Organization (WHO)/United Nations Children's Fund (UNICEF) recommendations for managing childhood febrile illnesses[20] and further explore opportunities to enhance public–private partnerships. We are now undertaking a proof-of-concept study of iCCM in registered drug shops in Uganda and encourage others to do the same in other settings.

Methodological considerations. Part of the data presented was based on caretaker's report of child's illness. This method is prone to both recall and reporting bias, where a respondent may not remember relevant details of the illness and may report what they think is expected of them, respectively. The use of exit interviews minimized recall bias, because we asked about a child's current illness and which drugs were bought at a drug shop. We also minimized recall bias by considering only illness that occurred within 2 weeks of the household interviews, which is a standard and acceptable method applied in similar cross-sectional surveys. The results obtained are comparable with other studies. However, selection bias remains relevant when exit interviews are used, because people who seek care from private drug shops may be different from the general population.

Conclusion. The majority of parents in Uganda first seek care for febrile children in the private sector, notably drug shops and private clinics. However, febrile children mostly receive inappropriate treatment at the private sector drug shops. This finding means that there is a missed opportunity for them to access appropriate and timely treatment of fever, cough, and diarrhea at this level. There is urgent need to improve the standard of care provided at drug shops through a mix of appropriate technical solutions (drugs and diagnostics), training, incentives, regulation, supervision and information, education, and communication. Public–private partnerships would provide an adequate avenue for such improvements.

Authors' addresses: Phyllis Awor, Mulago Hospital, Kampala, Uganda, E-mail: pawor@musph.ac.ug. Henry Wamani, Makerere University, College of Health Sciences, School of Public Health—Community Health and Behavioral Sciences, Kampala, Uganda, E-mail: hwamani@musph.ac.ug. Godfrey Bwire and George Jagoe, Global Access Division, Medicines for Malaria Venture, Kampala, Uganda, E-mails: sgbwire@yahoo.com and jagoeg@mmv.org. Stefan Peterson, Division of Global Health, Karolinska Institute, Stockholm, Sweden and International Maternal and Child Health Unit, Uppsala University, Uppsala, Sweden, E-mail: s.peterson@ki.se.

REFERENCES

1. Black RE, Morris SS, Bryce J, 2003. Where and why are 10 million children dying every year? *Lancet 361:* 2226–2234.

2. Ministry of Health, 2010. *Intergrated Community Case Management of Childhood Malaria, Pneumonia and Diarrhoea: Implementation Guide*. Kampala, Uganda: Ministry of Health.

3. Rutebemberwa E, Pariyo G, Peterson S, Tomson G, Kallander K, 2009. Utilization of public or private health care providers by febrile children after user fee removal in Uganda. *Malar J 8:* 45.

4. Konde-Lule J, Gitta SN, Lindfors A, Okuonzi S, Onama VO, Forsberg BC, 2010. Private and public health care in rural areas of Uganda. *BMC Int Health Hum Rights 10:* 29.

5. Tawfik Y, Nsungwa-Sabitii J, Greer G, Owor J, Kesande R, Prysor-Jones S, 2006. Negotiating improved case management of childhood illness with formal and informal private practitioners in Uganda. *Trop Med Int Health 11:* 967–973.

6. Global Fund, 2011. *Affordable Medicines Facility—Malaria*. Available at: http://www.theglobalfund.org/en/amfm/. Accessed October 28, 2011.

7. Kangwana BP, Kedenge SV, Noor AM, Alegana VA, Nyandigisi AJ, Pandit J, Fegan GW, Todd JE, Brooker S, Snow RW, Goodman CA, 2011. The impact of retail-sector delivery of artemether-lumefantrine on malaria treatment of children under five in Kenya: a cluster randomized controlled trial. *PLoS Med 8:* e1000437.

8. Sabot OJ, Mwita A, Cohen JM, Ipuge Y, Gordon M, Bishop D, Odhiambo M, Ward L, Goodman C, 2009. Piloting the global subsidy: the impact of subsidized artemisinin-based combination therapies distributed through private drug shops in rural Tanzania. *PLoS One 4:* e6857.

9. D'Acremont V, Kahama-Maro J, Swai N, Mtasiwa D, Genton B, Lengeler C, 2011. Reduction of anti-malarial consumption after rapid diagnostic tests implementation in Dar es Salaam: a before-after and cluster randomized controlled study. *Malar J 10:* 107.

10. D'Acremont V, Lengeler C, Mshinda H, Mtasiwa D, Tanner M, Genton B, 2009. Time to move from presumptive malaria treatment to laboratory-confirmed diagnosis and treatment in African children with fever. *PLoS Med 6:* e252.

11. Kallander K, Hildenwall H, Waiswa P, Galiwango E, Peterson S, Pariyo G, 2008. Delayed care seeking for fatal pneumonia in children aged under five years in Uganda: a case-series study. *Bull World Health Organ 86:* 332–338.

12. Nshakira N, Kristensen M, Ssali F, Whyte SR, 2002. Appropriate treatment of malaria? Use of antimalarial drugs for children's fevers in district medical units, drug shops and homes in eastern Uganda. *Trop Med Int Health 7:* 309–316.

13. Ringsted FM, Massawe IS, Lemnge MM, Bygbjerg IC, 2011. Saleability of anti-malarials in private drug shops in Muheza, Tanzania: a baseline study in an era of assumed artemisinin combination therapy (ACT). *Malar J 10:* 238.

14. Konde-Lule J, Okuonzi S, Matsiko C, Mukanga D, Onama V, Nakacubo SG, 2006. *The Potential of the Private Sector to Improve Health Outcomes in Uganda*. Kampala, Uganda: Makerere University School of Public Health.

15. Chuma J, Gilson L, Molyneux C, 2007. Treatment-seeking behaviour, cost burdens and coping strategies among rural and urban households in coastal Kenya: an equity analysis. *Trop Med Int Health 12:* 673–686.

16. Adeyi O, Atun R, 2010. Universal access to malaria medicines: innovation in financing and delivery. *Lancet 376:* 1869–1871.

17. Yeung S, Patouillard E, Allen H, Socheat D, 2011. Socially-marketed rapid diagnostic tests and ACT in the private sector: ten years of experience in Cambodia. *Malar J 10:* 243.

18. Msellem MI, Martensson A, Rotllant G, Bhattarai A, Strömberg J, Kahigwa E, Garcia M, Petzold M, Olumese P, Ali A, Björkman A, 2009. Influence of rapid malaria diagnostic tests on treatment and health outcome in fever patients, Zanzibar: a crossover validation study. *PLoS Med 6:* e1000070.

19. English M, Scott JA, 2008. What is the future for global case management guidelines for common childhood diseases? *PLoS Med 5:* e241.

20. WHO/UNICEF, 2004. *Management of Pneumonia in Community Settings*. Geneva: World Health Organization/United Nations Children's Fund.

Paper II

Increased Access to Care and Appropriateness of Treatment at Private Sector Drug Shops with Integrated Management of Malaria, Pneumonia and Diarrhoea: A Quasi-Experimental Study in Uganda

Phyllis Awor[1,2]*, **Henry Wamani**[2], **Thorkild Tylleskar**[1], **George Jagoe**[3], **Stefan Peterson**[2,4,5]

1. Centre for International Health, Department of Global Public Health and Primary Health Care, University of Bergen, Bergen, Norway, **2.** School of Public Health, College of Health Sciences, Makerere University, Kampala, Uganda, **3.** Medicines for Malaria Venture, Geneva, Switzerland, **4.** Global Health, Karolinska Institutet, Stockholm, Sweden, **5.** International Maternal and Child Health Unit, Uppsala University, Uppsala, Sweden

*aworphyllis@yahoo.co.uk

Abstract

Introduction: Drug shops are a major source of care for children in low income countries but they provide sub-standard care. We assessed the feasibility and effect on quality of care of introducing diagnostics and pre-packaged paediatric-dosage drugs for malaria, pneumonia and diarrhoea at drug shops in Uganda.

Methods: We adopted and implemented the integrated community case management (iCCM) intervention within registered drug shops. Attendants were trained to perform malaria rapid diagnostic tests (RDTs) in each fever case and count respiratory rate in each case of cough with fast/difficult breathing, before dispensing recommended treatment. Using a quasi-experimental design in one intervention and one non-intervention district, we conducted before and after exit interviews for drug seller practices and household surveys for treatment-seeking practices in May–June 2011 and May–June 2012. Survey adjusted generalized linear models and difference-in-difference analysis was used.

Results: 3759 (1604 before/2155 after) household interviews and 943 (163 before/ 780 after) exit interviews were conducted with caretakers of children under-5. At baseline, no child at a drug shop received any diagnostic testing before treatment in both districts. After the intervention, while no child in the non-intervention district received a diagnostic test, 87.7% (95% CI 79.0–96.4) of children with fever at the

intervention district drug shops had a parasitological diagnosis of malaria, prior to treatment. The prevalence ratios of the effect of the intervention on treatment of cough and fast breathing with amoxicillin and diarrhoea with ORS/zinc at the drug shop were 2.8 (2.0–3.9), and 12.8 (4.2–38.6) respectively. From the household survey, the prevalence ratio of the intervention effect on use of RDTs was 3.2 (1.9–5.4); Artemisinin Combination Therapy for malaria was 0.74 (0.65–0.84), and ORS/zinc for diarrhoea was 2.3 (1.2–4.7).

Conclusion: iCCM can be utilized to improve access and appropriateness of care for children at drug shops.

Introduction

After the first month of life, about half of mortality in children under five years of age in sub-Saharan Africa is caused by malaria, pneumonia and diarrhoea. [1] These three illnesses usually manifest as an acute febrile illness, with overlapping symptoms. Following on from lessons learned in the public sector roll out of Integrated Management of Childhood Illness (IMCI) [2, 3], the integrated Community Case Management (iCCM) of malaria, pneumonia and diarrhoea targets the community level for integration of diagnostics with pre-packaged drugs for these illnesses. iCCM is now being scaled up through the efforts of UNICEF, WHO and several large donors. [4]

Under the iCCM strategy, lay community members are empowered to diagnose and treat malaria, pneumonia and diarrhoea using diagnostics (malaria rapid diagnostic tests - RDTs - and respiratory timers) and the dose specific pre-packaged drugs: artemisinin combination therapy (ACTs), dispersible amoxicillin tablets and oral rehydration salts/zinc sulphate (ORS/zinc) respectively. Consequently, Uganda [5] and other low income countries have now adopted a policy of iCCM implemented primarily through Community Health Workers (CHW).

However, about 60% of parents with febrile children in Uganda first seek care in the private sector, especially at drug shops. [6] Unfortunately, the standard of care in these drug shops is poor. [7, 8]

Recognizing the high utilization of the private sector and drugs shops for fever treatment in low income countries, the Global Fund through the Affordable Medicines Facility – Malaria (AMFm) in 2010 subsidized ACTs for both the public and private sector in a pilot study in 8 countries. [9] An independent evaluation of the AMFm pilot concluded that subsidies combined with supporting interventions were effective in rapidly improving availability, price and market share of quality assured ACTs in the private-for-profit sector. [10, 11] However, the lack of programmatic integration of RDTs in the AMFm presumably led to widespread presumptive treatment of fever with anti-malaria drugs only.

While the AMFm may have encouraged presumptive treatment of fever with antimalaria drugs, malaria RDTs are now available, allowing rapid detection of "RDT-negative fever", prompting the need for alternative appropriate treatment. Also, WHO now recommends parasitological diagnosis of malaria for all patients, including children less than 5 years, prior to treatment. [12]The challenge now is to integrate both diagnostics, and alternative appropriate treatment, [13] in order to simultaneously achieve rational use of drugs for both antimalarials and antibiotics, at the same time as good quality of care for the febrile child, irrespective of cause of fever.

As drug shops remain a major source of care for febrile children in low income countries, there is a need to study interventions aimed at improving their quality of care in the management of common febrile childhood illnesses. We set out to assess the feasibility and effect on access and appropriateness of treatment when we introduce diagnostics (RDT and respiratory timers) and promote pre-packaged paediatric-dosage drugs for acute febrile illnesses (malaria and pneumonia) and diarrhoea at private sector drug shops.

Methods

Study site
The study was conducted in two rural neighbouring districts of eastern Uganda located approximately 150 km north-east of the capital Kampala: Kaliro district (est. 216,000 inhabitants 2010) as the intervention district and Kamuli district (est. 270,000 inhabitants 2010) as the non-intervention or comparison district. This is a high malaria transmission area with estimated parasite prevalence of over 60% in school-age children. [14] These districts were also chosen because they had both participated in a previous study, the Consortium for ACT Private Sector Subsidy (CAPSS) pilot study where ACTs for malaria had been made available in registered drug shops. [15]

Study design
This was a quasi-experimental study in one intervention and one non-intervention or comparison district using a plausibility design with before and after measurement, in line with current WHO/Alliance for Health Policy and Systems research recommendations. [16] The chosen plausibility design comparing two entire districts was deemed the most suitable given that the registered drug shops are supervised from district level, and that both supervisors and patients would likely have contaminated the study if individual drug shops had been randomized in a probability design.

This was a two phased study. In the first phase, prior to the intervention, we set out to determine the community care seeking and treatment practices as well as drug-seller treatment practices. Given that appropriateness of treatment for

children with fever, cough with fast breathing or diarrhoea within the community and at drug shops was not known, we set out to determine these.

In phase two, (one year later after the intervention) we then determined the effect of the intervention on access to care and appropriateness of treatment in the community as well as at drug shops.

The intervention

There were three main components of the intervention: 1) provision of dose specific pre-packaged and subsidized drugs and diagnostics to registered drug shops drugs; 2) training of drug shop attendants and 3) a community awareness campaign.

Modelled on the public sector iCCM intervention for community health workers, all registered drug shops in the intervention district received the following: **subsidised drugs:** The drugs were pre-packaged as unit doses and included: dispersible ACTs from Uganda's AMFm pilot; amoxicillin tablets (dispersible); low osmolar oral rehydration solution (ORS) and zinc sulphate tablets (dispersible) which were sold at a mark-up of 50–80% (typically buying at USD 0.25 and selling at USD 0.38). **Free diagnostics:** malaria RDTs; respiratory timers and diagnostic algorithms/charts. **Training:** Two drug shop attendants per drug shop received a 5-day training on how to use the diagnostics and dispense pre-packaged drugs including daily clinical sessions in a public health facility. The training was conducted by the Ministry of Health using the national iCCM training manual for community health workers, adapted for drug shop attendants. Drug shop attendants were trained to perform RDTs in each fever case and count respiratory rate in each case of cough with fast/difficult breathing prior to dispensing the appropriate recommended treatment.

The non-intervention district continued the current practice of distributing subsidized ACTs only under AMFm support and guidelines, relying upon previous training. This previous training was conducted by Ministry of Health trainers and the (CAPSS) pilot study [15] which had ended just prior to the start of our intervention and focused on treatment of malaria. The non-intervention district had also received an awareness campaign on improved treatment seeking for febrile children which was conducted by the CAPSS pilot study. Additional awareness information on appropriate care-seeking was provided through the district/community radios in the non-intervention area during the intervention period.

The community awareness campaign in the intervention district was conducted by Population Services International (PSI)/Programme for Accessible Health Communication and Education (PACE) in Uganda. This included branding of the drug shops, communicating with caretakers of children and providing information at markets, public gatherings and on community radios, on appropriate care-seeking.
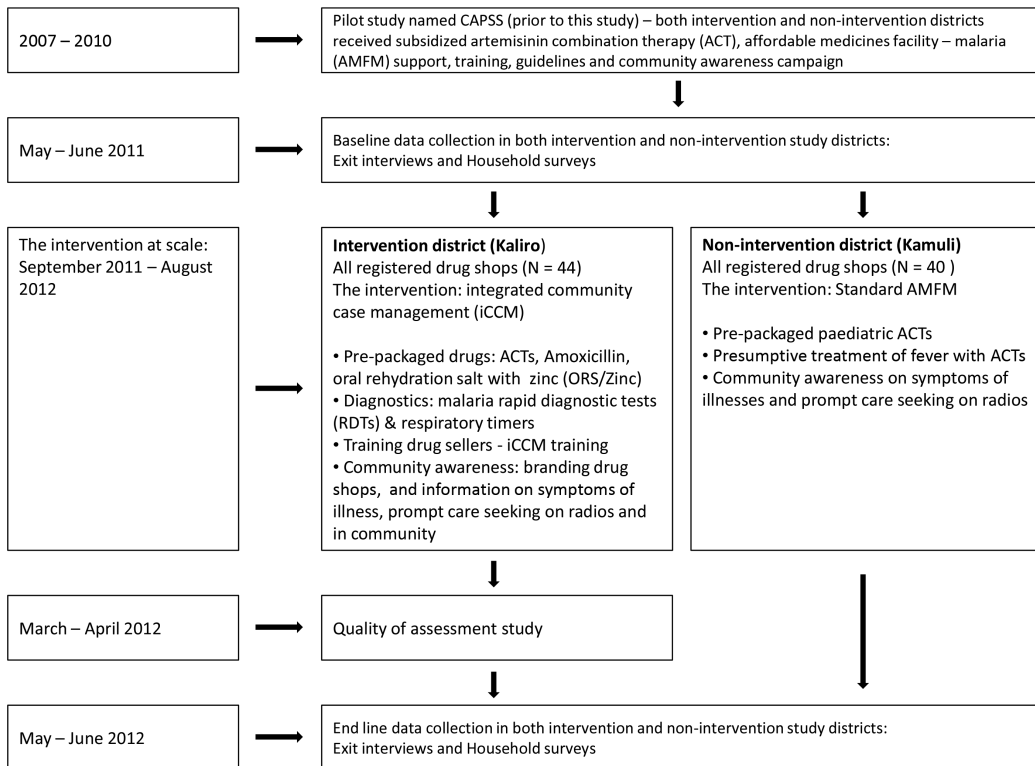
| 2007 – 2010 | → | Pilot study named CAPSS (prior to this study) – both intervention and non-intervention districts received subsidized artemisinin combination therapy (ACT), affordable medicines facility – malaria (AMFM) support, training, guidelines and community awareness campaign |

↓

| May – June 2011 | → | Baseline data collection in both intervention and non-intervention study districts: Exit interviews and Household surveys |

↓   ↓

| The intervention at scale: September 2011 – August 2012 | → | **Intervention district (Kaliro)** All registered drug shops (N = 44) The intervention: integrated community case management (iCCM)

• Pre-packaged drugs: ACTs, Amoxicillin, oral rehydration salt with zinc (ORS/Zinc)
• Diagnostics: malaria rapid diagnostic tests (RDTs) & respiratory timers
• Training drug sellers - iCCM training
• Community awareness: branding drug shops, and information on symptoms of illness, prompt care seeking on radios and in community | **Non-intervention district (Kamuli)** All registered drug shops (N = 40) The intervention: Standard AMFM

• Pre-packaged paediatric ACTs
• Presumptive treatment of fever with ACTs
• Community awareness on symptoms of illnesses and prompt care seeking on radios |

↓   ↓

| March – April 2012 | → | Quality of assessment study |

↓

| May – June 2012 | → | End line data collection in both intervention and non-intervention study districts: Exit interviews and Household surveys |

Fig. 1. Study design and timing of interventions and data collection.

doi:10.1371/journal.pone.0115440.g001

The intervention began in August 2011 and was implemented at full scale from September 2011 until August 2012. Fig. 1 shows the study design and timing of the intervention and data collection.

Eligibility criteria

All 84 drug shops registered by the Uganda National Drug Authority (NDA) in the intervention (44 shops) and non-intervention district (40 shops) were included in the study. Un-registered drug shops, small shops and mobile medicine vendors were excluded as required by the NDA.

All caretakers and children for whom care was sought in a drug shop or who were residing in the participating districts were eligible to participate in the study.

Data collection

Data collection was conducted both at baseline from May–June 2011 and at follow-up from May–June 2012 in both the intervention and non-intervention districts, using structured questionnaires. A 5-day training was conducted for data collectors including a pilot assessment outside the study clusters.

We conducted household interviews for community treatment practices (1604 before/2155 after) and exit interviews at drug shops for drug seller treatment practices (163 before/780 after).

Exit interviews at drug shops

All clients exiting the drug shops were approached and asked to participate in an interview using a semi-structured questionnaire, if they had come to the drug shop seeking treatment for a child less than 5 years of age. Data collectors were at the drug shop all day, from 8:30 am–7:00 pm for a total of four weeks. We also recorded information on the medicines purchased including the drug name, dosage and duration of treatment.

Household survey

A two stage cluster sampling using probability proportional to population size was used to select 1604 households in both the intervention and non-intervention districts at baseline and 2155 households at follow up, with children less than 5 years of age. At the first stage a probability sample of 30 villages/clusters were sampled, the same before and after. At the second stage, individual households were sampled from each cluster, not identical before and after. The study team randomly identified a starting point from a list of households obtained from the local leaders (village level household enumeration lists for local elections) and thereafter sampled every fifth household with children less than 5 years of age. The main caretaker (usually the mother) aged 15 years and above was interviewed face-to-face using a semi-structured questionnaire, designed to elicit treatment and care seeking practice for the most recent illness, less than 2 weeks prior to the interview. If there was no child under 5 years of age at the sampled house, the very next house was visited.

Direct observation

In order to directly assess quality of management of sick children by drug sellers, we randomly selected half of the participating drug shops in the intervention area and directly observed the drug sellers manage 2–3 sick children each. A field supervisor (a nurse) trained in iCCM, observed the drug sellers. This person recorded all the presenting complaints of the children observed, the assessment done by the drug seller and treatment given. At the same time, she made her own assessment of the child and recorded this.

Sample size calculation

This was a two phased study. During phase one, sample size for the household survey was calculated to determine prevalence of appropriate treatment of sick

children in the study area which was previously unknown and so was taken as 50%, using 95% confidence interval; a 5% margin of error and a design effect of 2. For exit interviews, data from all children with fever or cough with fast/difficult breathing or diarrhoea, for whom care was sought at all participating drug shops (both intervention and non-intervention combined) was collected, in order to estimate appropriateness of treatment provided at drug shops as previously published [7].

Phase 2: Informed by the baseline findings, the sample size (end line) for household survey was calculated based on baseline prevalence of appropriate treatment of fever and cough with rapid/difficult breathing, assuming 50% increase in correct treatment between baseline and end line, a 5% margin of error and a design effect of 2.

The outcome of interest was "appropriate treatment" of children in the community with each of the three symptoms: fever, cough and rapid/difficult breathing, or diarrhoea. Appropriate treatment was thus defined as: a child with fever in the community treated with ACTs; a child with cough and rapid/difficult breathing treated with amoxicillin and a child with diarrhoea treated with ORS/zinc.

For the exit interviews, end line sample size was calculated based on the prevalence of appropriate treatment of children at drug shops of 10%; 100% increase in appropriate treatment of children (i.e. 10% to 20%); 95% confidence level; and a 5% margin of error. For logistical reasons, in order to answer a different objective on community adherence to drugs, the sample size at end line in the intervention area is higher than that in the non-intervention area.

Data analysis

The data was entered in Epi Data (www.epidata.dk), and was analysed using stata version 12 (www.stata.com). Baseline and follow up data was analysed separately and the baseline findings of the 2 districts combined have now been published. [7]

For this paper, survey-adjusted generalized linear models (log transformation and binomial distribution) and difference-in-difference analysis was used for both exit interviews and household surveys data. Descriptive statistics were generated separately for the intervention and non-intervention districts at each of the data collection rounds (before and after) and the differences between/within intervention and non-intervention areas are presented in terms of p-values. Survey-adjusted differences in management of children before and after the intervention were also calculated with intervention status as the exposure. Finally, survey-adjusted prevalence ratios of the intervention effect on appropriate treatment of malaria, pneumonia and diarrhoea were derived, adjusting for confounding. In the step-wise multivariate regression analysis, covariates were included in the model in descending order of their strength of association with the outcome variable in univariate analysis (p value $<=0.1$). If inclusion of a covariate into the model produced a $>10\%$ difference in the prevalence ratios, it was considered a confounder and left in the model. In the final models, the

presence of interaction was also assessed. For the difference-in-difference analysis, an interaction term for intervention status and time of assessment (baseline or end-line) was included in the models and if significant, the coefficient of the interaction was presented.

Ethical approval

Ethical approval was obtained from Uganda National Council of Science and Technology (# HS 1184), the Uganda National Drug Authority (# 0456/ID/ NDA) and Makerere University School of Public Health (# 166). Written consent was obtained from the child caretaker who was interviewed during the household survey and exit interviews.

We report according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement. [17]

Role of the funding sources

The Einhorn Family Foundation had no role in study design, data collection, data analysis, interpretation or writing the report. Medicines for Malaria Venture participated in all the above stages. The corresponding author had full access to all the data in the study and had the final responsibility for the decision to submit for publication.

Results

We completed 3759 (1604 before/2155 after) households interviews and 943 (163 before/780 after) drug shop exit interviews with caretakers of children less than 5 years of age. From the baseline household survey, the comparison areas (districts) were generally similar before the intervention with some differences only in terms of the source of water used and the head of the household (Table 1).

From drug shop exit interviews, all febrile children were treated presumptively with malaria drugs in both intervention and non-intervention areas before the intervention and there were no diagnostic tests used prior to treatment. At follow-up, while no child with fever received any diagnostic test in the non-intervention district drug shops, nearly 90% in the intervention district had a parasitological diagnosis of malaria with an RDT and over half with symptoms of cough and fast breathing first had their respiratory rate counted. Treatment of diarrhoea with the recommended drug ORS/zinc, in the intervention district drug shops was 77% compared to only 5% in the non-intervention district, Table 2.

The effect of the intervention at the level of the drug shop was: almost total replacement of the obsolete antibiotic cotrimoxazole from the intervention area, three times better access to amoxicillin, the recommended drug for pneumonia and a reduction in overall antibiotic use by 18% in the intervention area as compared to the non-intervention area (Table 3). In addition, there was thirteen times better access to ORS/zinc for diarrhoea in the intervention district compare

Table 1. Characteristics of participating children and caretakers from household survey.

	BEFORE			AFTER	
	Non-Intervention	Intervention	p-value	Non-Intervention	Intervention
	N=811	N=794		N=1076	N=1079
	n (%)	n (%)		n (%)	n (%)
Child's gender – male	371 (48.2)	392 (49.9)	0.5	516 (48.9)	548 (51)
Caretaker's highest level of education - primary school	451 (55.7)	457 (57.6)	0.4	637 (59.2)	668 (61.9)
Marital status – married	744 (91.7)	725 (91.3)	0.8	952 (88.5)	992 (91.9)
Caretaker's employment – subsistence farmer/housewife	726 (89.5)	727 (91.6)	0.2	993 (92.3)	1029 (95.4)
Floor type – hard earth/mud	625 (77.1)	623 (79.6)	0.2	828 (77.1)	904 (83.8)
Main type of fuel for cooking – firewood	745 (91.9)	745 (93.8)	0.1	985 (91.5)	1,015 (94.1)
Main source of water – bore hole	691 (85.2)	737 (92.8)	<0.01	953 (88.6)	1,022 (94.7)
Head of household – partner/husband*	716 (88.4)	607 (76.5)	<0.01	927 (86.2)	869 (80.5)
Continuous variables	**Mean (SD)**	**Mean (SD)**		**Mean (SD)**	**Mean (SD)**
Child's age (months)	18.1 (13.6)	17.6 (13.1)	0.5	20.3 (14.2)	17.5 (12.2)
Caretaker's age (years)	29.5 (8.6)	30.1 (9.7)	0.2	28.5 (7.9)	27.9 (8.1)

*This reflects that the caregiver is often not the head of the household.

doi:10.1371/journal.pone.0115440.t001

to the non-intervention district. From the direct observation of drug sellers, 88% of sick children presenting at drug shops with fever, cough or diarrhoea were appropriately managed according to the iCCM guidelines (Fig. 2; Table 4).

Table 2. Symptoms and management of fever, cough with fast breathing and diarrhoea in children below 5 years of age at drug shop exit interviews (survey adjusted).

	Non-intervention		Intervention		Difference	
	Before	After	Before	After	% (95% CI)	
	N=83	N=283	N=80	N=497		
Management	n (%)	n (%)	n (%)	n (%)		p-value
Children who had fever	71/83 (85.5)	275/283 (97.2)	74/80 (92.5)	487/497 (98.0)		
- Malaria RDT used to make diagnosis	0/71 (0)	0/275 (0)	0/74 (0)	427/487 (87.7)	87.7 (79.0–96.4)	<0.000-1
– Malaria RDT used and ACT dispensed	0/71 (0)	0/275 (0)	0/74 (0)	343/487 (70.4)	70.4 (60.4–80.4)	<0.000-1
Children with cough & fast breathing (pneumonia)	8/83 (9.6)	45/283 (15.9)	24/80 (30)	73/497 (14.7)		
- Amoxicillin (5–7 days) dispensed	0/8 (0)	12/45 (26.7)	0/24 (0)	55/73 (75.3)	48.6 (44.3–53.1)	<0.000-1
- Respiratory timer used	0/8 (0)	0/45 (0)	0/24 (0)	40/73 (54.8)	54.8 (33.8–75.8)	<0.000-1
- Respiratory timer used and amoxicillin dispensed	0/8 (0)	0/45 (0)	0/24 (0)	36/73 (49.3)	49.3 (27.4–71.2)	<0.000-1
Children with diarrhoea	25/83 (30.1)	111/283 (39.2)	31/80 (38.8)	176/497 (35.4)		
- ORS and zinc dispensed	0/25 (0)	6/111 (5.4)	0/31 (0)	136/176 (77.3)	71.9 (67.7–74.1)	<0.000-1

doi:10.1371/journal.pone.0115440.t002

Table 3. The effect of the intervention on treatment using antibiotics, ACTs and ORS/zinc, by survey-adjusted prevalence ratios using difference in difference analysis and generalized linear models.

	Non-intervention		Intervention		Prevalence ratios
	Before	After	Before	After	PR (95% CI)
	N=83	N=283	N=80	N=497	
Management	n (%)	n (%)	n (%)	n (%)	
Children with pneumonia treated with amoxicillin (5–7 days)	0/8 (0)	12/45 (26.7)	0/24 (0)	55/73 (75.3)	[a]2.8 (2.0–3.9)
Children with pneumonia treated with cotrimoxazole	3/8 (37.5)	11/45 (24.4)	19/24 (79.2)	2/73 (2.7)	0.07 (0.01–0.39)
Overall antibiotic use	54/80 (65.1)	208/283 (73.5)	36/86 (45.0)	298/497 (60.0)	0.82(0.69–0.97)
Children with fever treated with ACT	27/71 (38.0)	[d]113/275 (41.1)	12/74 (16.2)	393/487 (80.7)	[c,]4.2 (1.9–9.4)
Children with diarrhoea treated with ORS/zinc	0/25 (0)	6/111 (5.4)	0/35 (0)	136/176 (77.3)	[a,b]12.8 (4.2–38.6)

Note: Adjustment for various possible confounders including age, caretaker's gender, caretaker's highest education, employment etc did not change most results. Adjusted results are reported below only where changes were statistically significant.
[a]Computed between intervention and control, at end-line only because of presence of zero cells at baseline.
[b]Adjusted for child-age (un-adjusted =14.3, 95% CI 4.8–42.4).
[c]Adjusted for employment status (unadjusted =4.1, 95%CI 1.8–9.2).
[d]Additional febrile children were treated with quinine (23%), chloroquine (5%) and sulfadoxine/pyrimethamine (4%).

doi:10.1371/journal.pone.0115440.t003

Results similar to those obtained from the direct observation exercise were obtained during repeated routine support supervision visits.

The effect of the intervention at household survey level was: three times better access to malaria rapid diagnostic tests for children reported to have fever in the

Observation of management of children at drug shops according to iCCM guidelines (N = 49)
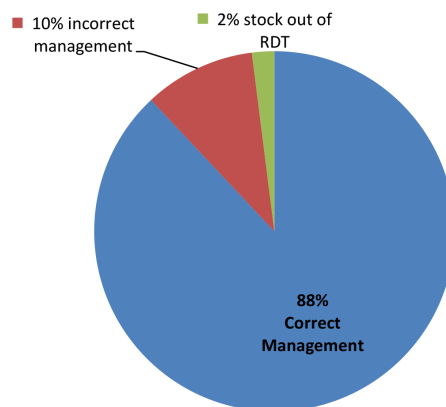
- 10% incorrect management
- 2% stock out of RDT
- 88% Correct Management

Fig. 2. Quality of assessment of children at drug shops, from direct observations in the intervention area.

doi:10.1371/journal.pone.0115440.g002

Table 4. Appropriateness of management of children at drug shops, from direct observation in the intervention area (N=49).

Management	n (%)
Fever management	
Complained of fever	47/49 (96)
Number who received malaria RDT test	44/47 (94)
Positive malaria RDT	33/44 (75)
Received recommended treatment with ACTs	33/33 (100)
Number with negative RDT who received anti-malaria drug	1/11 (9)
Pneumonia management	
Complained of cough	30/49 (61)
Respiratory rate counted	30/30 (100)
High respiratory rate (diagnosis pneumonia)	25/30 (83)
High respiratory rate and received amoxicillin	24/25 (96)
High respiratory rate and no amoxicillin	1/25 (4)
Low respiratory rate and no amoxicillin given	5/5 (100)
Challenge with counting respiratory rate	2/30 (7)
Respiratory rate counted when no cough	4/49 (8)
Diarrhoea Management	
Children with diarrhoea	14/49 (29)
Children with diarrhoea who received ORS/Zinc	13/14 (93)

doi:10.1371/journal.pone.0115440.t004

intervention district compared to the non-intervention district (Prevalence ratio 3.2, 95% CI 1.9–5.4) and about 30% less use of artemisinin combination therapy in the intervention district for fever in children as compared to the non-intervention district (Prevalence ratio 0.74, 95% CI 0.65–0.84), Table 5. There was also decreased use of the obsolete antibiotic cotrimoxazole for reported pneumonia symptoms in the intervention area compared to the non-intervention district (Prevalence ratio 0.45, 95% CI 0.27–0.47) while treatment of diarrhoea with ORS/zinc was two times better in the intervention district as compared to the non-intervention district (Table 5).

Treatment seeking at a government health facility for children with an illness less than 2 weeks prior to the interview remained the same between baseline and follow-up in the intervention and non-intervention districts (Table 6). In the intervention district, utilization of registered drug shops increased from 29.4% at baseline to 55.1% at follow-up and this increase came mainly from unregistered drug shops and other informal private sector.

Discussion

We demonstrate that it is possible to adopt and utilize iCCM for management of fever in children in private-sector registered drug shops to improve access and appropriateness of treatment.

Table 5. Survey adjusted appropriateness of management of illness within the last 2 weeks, from household survey.

Management	Non-intervention		Intervention		
	Before	After	Before	After	Prevalence Ratio (CI)
	N=457	N=711	N=483	N=748	
	n (%)	n (%)	n (%)	n (%)	
Children who had fever	426/457 (93.2)	695/711 (97.7)	452/483 (93.4)	718/748 (96)	
- Malaria RDT used to make diagnosis	-	30/695 (4.3)	-	99/718 (13.8)	3.2 (1.9–5.4)
- Parasitological test for malaria performed (RDT or microscopy)	-	133/695 (19.1)	-	170/718 (23.7)	1.2 (1.01–1.5)
- Received Artemisinin combination therapy	203/426(47.7)	468/695 (67.3)	152/452 (33.6)	362/718 (50.4)	0.74 (0.65–0.84)
Children with cough + fast breathing (pneumonia)	130/457 (28.4)	216/711 (30.4)	143/483 (29.6)	219/748 (29.3)	
- Respiratory rate timer used	0	0	0	9/219 (4.1)	
- Cotrimoxazole treatment	120/184 (65.2)	155/278 (55.8)	84/193 (43.5)	46/219 (21.0)	0.45 (0.27–0.74)
- Amoxicillin treatment	40/130(30.8)	62/216 (28.7)	45/143 (31.5)	56/219 (25.6)	0.82 (0.58–1.2)
Children with diarrhoea	246/457 (53.8)	387/711 (54.4)	270/483 (55.9)	432/748 (55.1)	
- ORS and Zinc treatment	0	10/387 (2.6)	0	26/432 (6)	2.3 (1.2–4.7)

doi:10.1371/journal.pone.0115440.t005

At follow up, nearly 90% of febrile children who sought care at registered drug shops in the intervention district received a malaria rapid diagnostic test and more than half of children with cough and fast breathing first had their respiratory rate counted prior to receiving treatment. About three quarters of children with diarrhoea received the recommended treatment with ORS/zinc.

Furthermore, from both household surveys and exit interviews, overall antibiotic use reduced in the intervention area and the use of the obsolete antibiotic, cotrimoxazole, for treatment of pneumonia was greatly reduced (97% at the level of drug shops and 55% at population level). Also, from the household survey, parasitological diagnosis of malaria was higher in the intervention area contributing partly to the lower use of ACTs there.

While we found increased utilization of drug shops in the intervention district, this increase came from people already utilizing the private sector with a shift

Table 6. First source of care for children with an illness less than 2 weeks prior to interview, in the household interviews.

	Non-intervention			Intervention		
	Before	After	p-value	Before	After	P value
	N=457	N=711		N=483	N=748	
	n (%)	n (%)		n (%)	n (%)	
Government health facility	84 (18.3)	127 (17.9)	0.8	101 (20.9)	154 (20.6)	0.9
Managed at home	149 (32.6)	305 (42.9)	<0.001	79 (16.4)	130 (17.4)	0.7
Drug shop	137 (30)	246 (34.6)	0.1	142 (29.4)	412 (55.1)	<0.001
Other private sector*	72 (15.8)	31(4.4)	<0.001	145 (30.0)	41 (5.5)	<0.001
Others	15 (3.3)	2 (0.3)	<0.001	16 (3.3)	11 (1.5)	0.04

*his was mainly the informal/unregistered private sector.

doi:10.1371/journal.pone.0115440.t006

mainly from unregistered drugs shops and vendors to the participating, registered drug shops. The overall utilization of government health facilities (rural health centre and hospital) as the first source of care remained the same in the intervention district both at baseline (20.9%) and at follow up (20.6%). We could therefore allay fears in this context that interventions at drug shops will distort the health system at the expense of the public sector. [18, 19] Similar results have been shown from Kenya after intervention with subsidized ACTs in retail shops. [20]

The proportion of children managed at home in the intervention district remained the same both at baseline (16.4%) and at follow up (17.4%) and increased in the non-intervention district. This indicates continued need for interventions targeting caretakers for better home care, e.g. by means of Community Health Workers and iCCM.

Recently, there has been considerable debate about the role of the AMFm in improving access to quality malaria treatment in low income countries through drug shops. [10, 15, 18, 21, 22, 23] The Global Fund board decided in November 2012 to integrate the AMFm into core grant management and financial processes. [22] From 2014, countries will now apply for funding to subsidize ACTs through their usual Global Fund applications. In many cases these efforts will be combined with malaria RDT introduction in private sector. As countries enter this next phase of private sector intervention, it will be imperative to ensure correct management of febrile children with appropriate differential diagnosis and treatment also of non-malaria fevers.

The iCCM strategy is effective in reducing both morbidity and mortality in febrile children. [24, 25, 26] However, there are numerous challenges with scaling-up iCCM, especially around the sustainability of the intervention in terms of salaries and motivation of community health workers and national ownership of the intervention [27]. In some countries like Uganda, only 30% of the districts have trained and active CHWs. Private sector drug shops will therefore remain an important source of care for the foreseeable future. Involving them in the campaign for better care for children is a potential game changer that could contribute to lowering child mortality. Private and public sector care must both be embraced and enhanced to ensure well-functioning pluralistic health systems. [28, 29, 30]

Care should be taken when interpreting and generalizing these results. First, we used one intervention and one non-intervention district in a high malaria transmission area in Uganda and collected data at two time points, at baseline and at follow up. However, the use of multiple methods of data collection - exit interviews, direct observation and household surveys - which produced similar results improves the strength of the results. Secondly, the malaria rapid diagnostic tests used in this study were provided free of charge so different subsidy levels for RDTs need to be explored for iCCM at drug shops. Finally, we did not cross check the diagnostic test results real time during the exit interviews in order not to interfere with drug seller practice. However, we conducted the quality of assessment exercise where a nurse trained in iCCM observed the drug sellers diagnosing and treating children and then re-assessed the children, for

comparison. This quality of assessment exercise showed about 90% correct management of children by drug sellers.

This study shows that in high malaria prevalence areas in rural Uganda, the iCCM strategy may be adapted for utilization at registered drug shops to diminish the presumptive treatment of malaria and to increase the integrated assessment and care of children with fever. AMFm and other private sector initiatives should follow the path of the public sector from presumptive, vertical management of malaria only to integrated management of the sick child. Further research is necessary in low malaria prevalence areas and on methods for cost recovery of RDTs.

Author Contributions

Conceived and designed the experiments: PA HW SP. Performed the experiments: PA HW SP GJ. Analyzed the data: PA HW SP. Contributed reagents/materials/analysis tools: PA HW GJ TT SP. Wrote the paper: PA HW GJ TT SP.

References

1. **Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, et al.** (2012) Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 380: 2095–2128.

2. **WHO** (2005) Integrated Management of Childhood Illness - Handbook. Geneva: World Health Organization.

3. **Armstrong Schellenberg JR, Adam T, Mshinda H, Masanja H, Kabadi G, et al.** (2004) Effectiveness and cost of facility-based Integrated Management of Childhood Illness (IMCI) in Tanzania. Lancet 364: 1583–1594.

4. **Young M, Wolfheim C, Marsh DR, Hammamy D** (2012) World Health Organization/United Nations Children's Fund Joint Statement on Integrated Community Case Management: An Equity-Focused Strategy to Improve Access to Essential Treatment Services for Children. Am J Trop Med Hyg 87: 6–10.

5. **MoH** (2010) Intergrated Community Case Management of Childhood Malaria, Pneumonia and Diarrhoea: Implementation Guide. In: Ministry of Health CHD, editor. Kampala.

6. **Rutebemberwa E, Pariyo G, Peterson S, Tomson G, Kallander K** (2009) Utilization of public or private health care providers by febrile children after user fee removal in Uganda. Malar J 8: 45.

7. **Awor P, Wamani H, Bwire G, Jagoe G, Peterson S** (2012) Private sector drug shops in integrated community case management of malaria, pneumonia, and diarrhea in children in Uganda. Am J Trop Med Hyg 87: 92–96.

8. **Smith F** (2009) The quality of private pharmacy services in low and middle-income countries: a systematic review. Pharm World Sci 31: 351–361.

9. **Global-Fund** (2011) Affordable Medicines Facility - malaria. Geneva.

10. **Tougher S, Ye Y, Amuasi JH, Kourgueni IA, Thomson R, et al.** (2012) Effect of the Affordable Medicines Facility–malaria (AMFm) on the availability, price, and market share of quality-assured artemisinin-based combination therapies in seven countries: a before-and-after analysis of outlet survey data. Lancet 380: 1916–1926.

11. **Fink G, Dickens WT, Jordan M, Cohen JL** (2013) Access to subsidized ACT and malaria treatment–evidence from the first year of the AMFm program in six districts in Uganda. Health Policy Plan.

12. **WHO** (2010) Guidelines for the Treatment Malaria. Second Edition. Geneva.

13. **WHO** (2013) WHO informal consultation on fever management in peripheral health care settings: A global review of evidence and practice. Geneva: World Health Organization.

14. **CAPSS** (2011) Closing the affordability gap: Ensuring affordable and effective malaria treatment for children in rural Uganda.

15. **Talisuna AO, Daumerie PG, Balyeku A, Egan T, Piot B, et al.** (2012) Closing the access barrier for effective anti-malarials in the private sector in rural Uganda: consortium for ACT private sector subsidy (CAPSS) pilot study. Malar J 11: 356.

16. **de Savigny D, Teghreed A (eds)** (2009) Systems Thinking for Health Systems Strengthening; Don de Savigny TA, editor: Alliance for Health Policy and Systems Research, WHO.

17. **von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, et al.** (2007) The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet 370: 1453–1457.

18. **Oxfam** (2012) Salt Sugar and Malaria Pills. How the Affordable Medicines Facility-malaria endangers public health. Oxford: Oxfam GB.

19. **Kamal-Yanni MM, Potet J, Saunders PM** (2012) Scaling-up malaria treatment: a review of the performance of different providers. Malar J 11: 414.

20. **Kangwana BP, Kedenge SV, Noor AM, Alegana VA, Nyandigisi AJ, et al.** (2011) The impact of retail-sector delivery of artemether-lumefantrine on malaria treatment of children under five in Kenya: a cluster randomized controlled trial. PLoS Med 8: e1000437.

21. **I.O.M IoMotNA** (2004) Saving Lives Buying Time. Economies of Malaria Drugs in an Age of Resistance. Washington DC: National Academies Press.

22. **Global-Fund** (2012) BOARD APPROVES INTEGRATION OF AMFM INTO CORE GLOBAL FUND GRANT PROCESSES. Geneva: Global Fund.

23. **Arrow KJ, Danzon PM, Gelband H, Jamison D, Laxminarayan R, et al.** (2012) The Affordable Medicines Facility–malaria: killing it slowly. Lancet 380: 1889–1890.

24. **Marsh DR, Hamer DH, Pagnoni F, Peterson S** (2012) Introduction to a special supplement: Evidence for the implementation, effects, and impact of the integrated community case management strategy to treat childhood infection. Am J Trop Med Hyg 87: 2–5.

25. **Chinbuah MA, Kager PA, Abbey M, Gyapong M, Awini E, et al.** (2012) Impact of community management of fever (using antimalarials with or without antibiotics) on childhood mortality: a cluster-randomized controlled trial in Ghana. Am J Trop Med Hyg 87: 11–20.

26. **Mukanga D, Tiono AB, Anyorigiya T, Kallander K, Konate AT, et al.** (2012) Integrated community case management of fever in children under five using rapid diagnostic tests and respiratory rate counting: a multi-country cluster randomized trial. Am J Trop Med Hyg 87: 21–29.

27. **Bennett S, George A, Rodriguez D, Shearer J, Diallo B, et al.** (2014) Policy challenges facing integrated community case management in Sub-Saharan Africa. Trop Med Int Health.

28. **Forsberg BC, Montagu D, Sundewall J** (2011) Moving towards in-depth knowledge on the private health sector in low- and middle-income countries. Health Policy Plan 26 Suppl 1: i1–3.

29. **Meessen B, Bigdeli M, Chheng K, Decoster K, Ir P, et al.** (2011) Composition of pluralistic health systems: how much can we learn from household surveys? An exploration in Cambodia. Health Policy Plan 26 Suppl 1:: i30–44.

30. **Bloom G, Standing H, Lucas H, Bhuiya A, Oladepo O, et al.** (2011) Making health markets work better for poor people: the case of informal providers. Health Policy Plan 26 Suppl 1: i45–52.

Paper III

MALARIA
JOURNAL

RESEARCH

CrossMark

Drug seller adherence to clinical protocols with integrated management of malaria, pneumonia and diarrhoea at drug shops in Uganda

Phyllis Awor[1,2*], Henry Wamani[2], Thorkild Tylleskar[1] and Stefan Peterson[2,3,4]

Abstract

Background: Drug shops are usually the first source of care for febrile children in Uganda although the quality of care they provide is known to be poor. Within a larger quasi-experimental study introducing the WHO/UNICEF recommended integrated community case management (iCCM) of malaria, pneumonia and diarrhoea intervention for community health workers in registered drug shops, the level of adherence to clinical protocols by drug sellers was determined.

Methods: All drug shops (N = 44) in the intervention area were included and all child visits (N = 7,667) from October 2011–June 2012 to the participating drug shops were analysed. Drug shops maintained a standard iCCM register where they recorded the children seen, their symptoms, diagnostic test performed, treatments given and actions taken. The proportion of children correctly assessed and treated was determined from the registers.

Results: Malaria management: 6,140 of 7,667 (80.1%) total visits to drug shops were of children with fever. 5986 (97.5%) children with fever received a malaria rapid diagnostic test (RDT) and the RDT positivity rate was 78% (95% CI 77–79). 4,961/5,307 (93.4%) children with a positive RDT received artemisinin combination therapy. Pneumonia management: after respiratory rate assessment of children with cough and fast/difficult breathing, 3,437 (44.8%) were categorized as "pneumonia", 3,126 (91.0%) of whom received the recommended drug—amoxicillin. Diarrhoea management: 2,335 (30.5%) child visits were for diarrhoea with 2,068 (88.6%) correctly treated with oral rehydration salts and zinc sulphate. Dual/Triple classification: 2,387 (31.1%) children had both malaria and pneumonia and 664 (8.7%) were classified as having three illnesses. Over 90% of the children with dual or triple classification were treated appropriately. Meanwhile, 381 children were categorized as severely sick (with a danger sign) with 309 (81.1%) of them referred for appropriate management.

Conclusion: With the introduction of the iCCM intervention at drug shops in Eastern Uganda, it was possible to achieve high adherence to the treatment protocols, which is likely compatible with increased quality of care.

Background

Every year, over 30 million cases of malaria, pneumonia and diarrhoea in children go untreated in Uganda [1]. Under-five mortality from these three illnesses is 13, 15 and 9%, respectively [2]. This large treatment gap and high under-five mortality can be reduced by ensuring high access to life saving preventive and curative services for these illnesses. However, access to health services in Uganda is variable, ranging from 7 to 100% in different parts of the country. Even where health facilities are available, low staffing, lack of necessary supplies and equipment and various health system challenges make access to basic care uncertain [1]. As a result of gaps within the

*Correspondence: pawor@musph.ac.ug
[1] Department of Global Public Health and Primary Health Care, Centre for International Health, University of Bergen, PO Box 7800, 5020 Bergen, Norway
Full list of author information is available at the end of the article

Awor *et al. Malar J* (2015) 14:277

Page 2 of 6

public health sector, the private sector—dominated by drug shops in rural areas—has proliferated and is a major source of care for sick children [3]. More than half of sick children in Uganda seek care at the level of a drug shop when ill [4, 5]. However, without any interventions at this level, the quality of care has been documented to be poor [6, 7].

Meanwhile, evidence shows that health workers, both public and private generally have low adherence to clinical protocols. For example, health workers in malaria endemic areas continue to prescribe artemisinin combination therapy to patients whose malaria diagnostic test result is negative, for various reasons including mistrust of test results [8–11]. Lower level health workers for example community health workers have been shown to follow clinical protocols more strictly [12, 13]. However, the adherence of drug shop attendants to treatment protocols for malaria, pneumonia and diarrhoea is largely unknown. Given the role of drug shops in the care for children in Uganda and other low-income countries, it is necessary to understand adherence to treatment protocols in this group of health providers.

The objective of this study was to determine the level of adherence by drug shop attendants in eastern Uganda, to the integrated community case management (iCCM) of malaria, pneumonia and diarrhoea treatment guidelines.

Methods

This analysis was done with data collected during a quasi-experimental study determining the feasibility and effect on access and appropriateness of treatment with the introduction of the integrated community case management of malaria, pneumonia and diarrhoea intervention at drug shops. The study site, intervention, methods and results of the main study are published elsewhere [4]. For this paper, all drug shops (N = 44) in the intervention area were included and all child visits (N = 7,667) from October 2011–June 2012 to the participating drug shops were analysed.

Data collection

Drug shops maintained a standard iCCM register (see Additional file 1) where they recorded the children seen, their symptoms (fever, cough, fast/difficult breathing etc.), diagnostic test performed, the test results, treatment given and actions taken. For every child with fever, drug shop attendants were trained to perform a malaria rapid diagnostic test (RDT) and record the test result as positive or negative. Similarly for every child with cough and fast/difficult breathing, the drug shop attendants were trained to count the respiratory rate using the UNICEF respiratory rate (RR) counter and record the findings. Based on the standard iCCM sick-child-job-aid

provided (see Additional files 2, 3), this child was then categorized as having pneumonia or not, taking into consideration the age and respiratory rate. Children with diarrhoea were also recorded in the register. After assessment, appropriate treatment was then given to the children.

Quality control of diagnostic testing and treatment

Quality control was done during the main study through support supervision. Both the local district drug inspector and a study nurse supervised the drug shops separately. After the iCCM training, a full time study nurse was employed to provide support supervision to the drug shop attendants. Initial support supervision was weekly at each drug shop and this was later reduced to monthly as less support became necessary. During the supervision visits, the study nurse observed the drug shop attendants manage children from the initial diagnosis of malaria, pneumonia or diarrhoea with utilization of the respective diagnostic test (RDT or RR counter), to the provision of appropriate treatment. The study nurse then discussed with the drug shop attendant the positive aspects and weaknesses observed during the management of the child. Continuous training was also provided to the drug shop attendant as necessary. More details of the support supervision process and results from some of the direct observation exercises have been previously published [4].

Sample size

To determine prevalence of adherence to clinical protocol from the registers, we used all records of children seen at the drug shops during the entire study period (8 months). The total sample size was 7,667 child visits to the drug shops.

Analysis

Data was double-entered in epi data [14] and was analysed using STATA, version 12 [15]. During the analysis, the symptoms and test results recorded in the iCCM registers were utilized, and every child was re-classified according to the iCCM algorithm. For children recorded as having fever, the analysis checked that an RDT result was recorded and whether appropriate treatment was given. For children recorded as having cough and fast/difficult breathing, the analysis checked that a respiratory rate was recorded, then this respiratory rate was reclassified as fast or not (thus presence or absence of 'pneumonia'), based on the age of the child, as required by the guidelines. The appropriateness of treatment provided for pneumonia was assessed. For all children recorded as having diarrhoea, the analysis checked whether the recorded treatment was appropriate. Finally, the quality of integrated management of several concurrent

Awor *et al. Malar J* (2015) 14:277

Page 3 of 6

symptoms was assessed. The proportion of children receiving a single, double, or triple illness classification was determined, and then the proportion of these children correctly assessed and treated was calculated. Confidence intervals around the estimates are provided.

Ethics, consent and approvals

Ethical approval was obtained from Uganda National Council of Science and Technology (# HS 1184), the Uganda National Drug Authority (# 0456/ID/NDA) and Makerere University School of Public Health (# 166). Written consent was obtained from the drug sellers who participated in this study.

Results

A total of 7,667 children were seen at the drug shops during the eight months study period, from October 2011–May 2012. Of all recruited drug shops (N = 44), two dropped out of the study in the initial months and another two were closed permanently, leaving 40 participating drug shops for the duration of the study. While half (22/40) of the drug shops saw almost 90% of the children, just five drug shops saw nearly half of all the children. Table 1 shows the total number of children seen every month. Over the first 3 months the percentage of children seen at the drug shops was constant at about 11% of the total number of children seen. Over the remaining months of the study, there was an increase in the number of children seen ($p \leq 0.001$).

The children seen at the drug shops had a mean age of 21 months (range 0–84) and 47% were 12 months and below, (Table 2). Eighty percent (6,140/7,667) of all the children were recorded as having fever. Of these, 5986 (98%) were tested for malaria with an RDT and the overall RDT positivity rate was 78% (95% CI 77–79). Further, 94% of all children with a positive RDT test received the recommended malaria treatment, ACT.

Table 1 Total number of children seen at drug shops by month of study

Month	Frequency	Percent	Test for trend
October 2011	858	11.2	P ≤ 0.001
November	900	11.7	
December	883	11.5	
January 2012	784	10.2	
February	950	12.4	
March	1,291	16.9	
April	850	11.1	
May	1,151	15.0	
Total	7,667	100	

In this study, 5,203 (67.9%) were assessed for fast breathing and 45% (3,437/7,667) were classified as having 'pneumonia' according to the MoH/WHO ICCM guidelines. The mean respiratory rate recorded was 48 breaths per minute (standard deviation 11.9). Of the children classified as having pneumonia, 91% received the recommended drug, amoxicillin. Thirty-one percent (2,335/7,667) of all the children seen at the shops had diarrhoea and 89% of these were recorded as having received the recommended treatment, ORS/zinc. Further, a total of 5% of children in the sample were classified as severely ill (having a danger sign) and the majority of these children were reported to have been referred to the health centre.

The proportion of children in the sample who were classified with both malaria and pneumonia was 31% and most of these (93%) were recorded as having received both ACT for malaria and amoxicillin for pneumonia—Table 3. Meanwhile, 9% of all the children seen at drug shops were found to have all three illnesses (malaria, pneumonia and diarrhoea) and the majority was treated appropriately.

Discussion

This analysis of treatment registers shows high adherence to the iCCM guidelines by drug shop attendants. Over 90% of all children with pneumonia-related symptoms, fever or diarrhoea were appropriately assessed, classified and treated according to guidelines. This is likely to represent an enormous step up in quality of care as illustrated by our previous paper where exit interviews and household surveys were used to assess appropriateness of treatment of children at the drug shops. That study found 3–13 times better management of children at drug shops with the introduction of iCCM [4]. Beside these two studies, there is limited additional evidence on the utilizing the iCCM strategy at the level of drug shops as studies at drug shops in low income countries have focused on single diseases especially malaria, at the expense of other febrile illness [16].

Similarly high levels of adherence to malaria RDT results by community health workers (97%) have been demonstrated in Uganda and other African countries [12, 13, 17]. However, in two of these studies, the classification and treatment of pneumonia by CHWs was demonstrated to be poor with for example, only 40% of children with pneumonia symptoms being prescribed an antibiotic [12]. One child in three (31%) received treatment for both malaria and pneumonia. While this confirms earlier findings by Källander et al. of a 30% symptom overlap [18], it also means that there was little further reduction in drug use from inclusion of RDTs compared to presumptive management. However, this was a high malaria

Awor et al. Malar J (2015) 14:277

Page 4 of 6

Table 2 Classification and treatment of children attending drug shops

Characteristic	Proportion	95% Confidence Intervals
Child age		
Up to 1 year	3,596 (46.9%)	
Greater than 1 year	4,071 (53.1%)	
Child sex—male	3,732 (48.8%)	
Diarrhoea		
Proportion with diarrhoea	2,335/7,667 (30.5%)	29.4–31.5
Received ORS packet	2,068/2,335 (88.6%)	87.3–89.9
Fever		
Proportion with fever	6,140/7,667 (80.1%)	79.2–81.0
Fever and received Rapid Diagnostic test (RDT)	5,986/6,140 (97.5%)	
Fever and RDT positive	5,096/6,140 (83.0%)	82.1–83.9
Received an RDT (ALL RDT tests done)	6,801/7,667 (88.7%)	
RDT positive (overall RDT positivity)	5,307/6,801 (78.0%)	77.0–79.0
RDT positive and got ACT	4,961/5,307 (93.5%)	92.8–94.1
Any ACT dispensed	5,218/7,667 (68.1%)	67.0–69.1
Pneumonia		
Respiratory rate counted (all RRs counted)	5,203/7,667 (67.9%)	
Proportion with pneumonia	3,437/7,667 (44.8%)	
Pneumonia and amoxicillin dispensed	3,126/3,437 (91.0%)	
Any amoxicillin dispensed	3364/7,667 (43.9%)	42.8–45.0
Danger signs		
Proportion with any danger sign	381/7,667 (5.0%)	
Danger sign and referred	309/381 (81.1%)	
Outcome		
Referred	477/7,667 (6.2%)	5.7–6.8
Adverse drug reaction	2/7,667	
Died	2/7,667	

Table 3 Management of double or triple illnesses in children, at drug shops

Both malaria and pneumonia		
Children with both malaria and pneumonia	2,387/7,667 (31.1%)	
Received ACT	2,237/2,387 (93.7%)	
Received Amoxicillin	2,211/2,387 (92.6%)	
Malaria, pneumonia and diarrhoea		
Children with all 3 illnesses	664/7,667 (8.7%)	
Received ACT	624/664 (94.0%)	
Received Amoxicillin	607/664 (91.4%)	
Received ORS/zinc	580/664 (87.3%)	

transmission area with estimated parasite prevalence of 60% in school-age children [19, 20] and the RDT positivity rate at the drug shops from this study was 77%. Limited penetration of malaria bed nets in this high malaria transmission area is likely to explain the high RDT positive rate, which will further have been augmented by the inherent problem of false positivity with malaria RDT—due to persistence of *Plasmodium falciparum* histidine-rich protein 2 (*Pf*HRP2) antigens four up to 1 month in the blood stream, following elimination of parasites [21, 22]. In comparison, Nankabirwa et al. reported 51% malaria parasite prevalence using the gold-standard, microscopy, in children 0–59 months at public health facilities in regions with moderate-high malaria transmission in Uganda [23].

The high malaria positivity rate and the 45% of children whose respiratory rate was found high after assessment, meant that the drug shops could have continued, and perhaps even increased, the number of drugs sold per child, which coupled with the 25% increased utilization of these drug shops [4] likely increased their total financial turnover. Exactly how this affected total profits is not clear since we do not know profit margins of drugs earlier sold, although it was noted anecdotally that shopkeepers were almost uniformly happy saying "this has increased

Awor *et al. Malar J* (2015) 14:277

Page 5 of 6

my business". However, how drug shop attendants would react in lower malaria endemic settings where a lower proportion of RDTs were positive and an increasing proportion of children are supposed to be treated with lower-profit-margin paracetamol is not clear, but needs to be subject to further study.

While we followed up 40 drug shops for the entire study period, care seeking tended to concentrate around particular drug shops. Five drug shops saw nearly half of all the children, during the entire study period. While this was unexpected, it is logical that parents may prefer certain characteristics of health workers/drug shop attendants and thus choose to take their children to these health workers. This concentration of care seeking has the potential to allow closer supervision, and also gaining more experience.

The discourse around governance of the private sector in pluralistic health systems emphasizes balancing both regulation and incentives [24, 25]. Regulation alone may be insufficient as state regulation is weak and the processes for self-regulation are lacking. Incentives available to drug sellers for example through this iCCM intervention can improve quality of care, but there are limits to positive incentives alone. Community awareness to enable demand for quality service is also very important. This will likely need to involve aspects of asking for, and respecting test results, and an acceptance of treatment of children not with anti-malarials or antibiotics, but with for example paracetamol only if they have no malaria and no pneumonia.

This study has two important limitations that should be considered. First, the analysis is based on data from drug shop registers, which was not validated. However, this data was collected during a prospective experimental study and these results are very similar to results from the main study which used different data collection techniques like exit interviews and household surveys [4]. Secondly, the case definition of "pneumonia" in this study is not for confirmed pneumonia diagnosis, but for the iCCM classifications of 'pneumonia'—cough with fast/difficult breathing. This classification tends to result in more children being classified as having "pneumonia" than in reality.

Conclusion

This paper shows that with the introduction of the iCCM intervention at drug shops in Eastern Uganda, it was possible to achieve high adherence to the treatment protocols, which is likely compatible with increased quality of care.

Additional files

Additional file 1: The ICCM register: This is a copy of the standard book, where drug shop attendants (and community health workers) record all children seen with symptoms of malaria, pneumonia or diarrhoea.

Additional file 2: The sick child job aid 1. This is a visual aid that contains the iCCM treatment algorithm. It is printed in A3 size and displayed in the drug shop for easy reference when managing children.

Additional file 3: The sick child job aid 2. This is a visual aid that contains the iCCM treatment algorithm. It is printed in A3 size and displayed in the drug shop for easy reference when managing children.

Authors' contributions

PA, HW and SP conceptualized and designed the study; PA analysed the data and drafted the manuscript which all authors edited and approved. All authors read and approved the final manuscript.

Author details

[1] Department of Global Public Health and Primary Health Care, Centre for International Health, University of Bergen, PO Box 7800, 5020 Bergen, Norway. [2] Department of Community Health and Behavioural Sciences, School of Public Health, College of Health Sciences, Makerere University, PO Box 7072, Kampala, Uganda. [3] Global Health, Karolinska Institutet, Stockholm, Sweden. [4] International Maternal and Child Health Unit, Uppsala University, Uppsala, Sweden.

References

1. MoH (2010) Integrated community case management of childhood malaria, pneumonia and diarrhoea: implementation guide. Ministry of Health CHD, Kampala
2. Uganda Health Profile (http://www.who.int/gho/countries/uga.pdf?ua=1). Accessed 1 Dec 2014
3. Tougher S, Ye Y, Amuasi JH, Kourgueni IA, Thomson R, Goodman C et al (2012) Effect of the Affordable Medicines Facility–malaria (AMFm) on the availability, price, and market share of quality-assured artemisinin-based combination therapies in seven countries: a before-and-after analysis of outlet survey data. Lancet 380:1916–1926
4. Awor P, Wamani H, Tylleskar T, Jagoe G, Peterson S (2014) Increased access to care and appropriateness of treatment at private sector drug shops with integrated management of malaria, pneumonia and diarrhoea: a quasi-experimental study in Uganda. PLoS One 9:e115440
5. Rutebemberwa E, Pariyo G, Peterson S, Tomson G, Källander K (2009) Utilization of public or private health care providers by febrile children after user fee removal in Uganda. Malar J 8:45
6. Wafula FN, Miriti EM, Goodman CA (2012) Examining characteristics, knowledge and regulatory practices of specialized drug shops in sub-Saharan Africa: a systematic review of the literature. BMC Health Serv Res 12:223

Awor *et al. Malar J* (2015) 14:277

Page 6 of 6

7. Awor P, Wamani H, Bwire G, Jagoe G, Peterson S (2012) Private sector drug shops in integrated community case management of malaria, pneumonia, and diarrhea in children in Uganda. Am J Trop Med Hyg 87:92–96

8. Chandler CI, Whitty CJ, Ansah EK (2010) How can malaria rapid diagnostic tests achieve their potential? A qualitative study of a trial at health facilities in Ghana. Malar J 9:95

9. Kyabayinze J (2010) Use of RDTs to improve malaria diagnosis and fever case management at primary health care facilities in Uganda. In: World Malaria Day 3rd Technical and Scientific Symposium. Protea Hotel, Kampala, Uganda: Ministry of Health, Uganda

10. Ansah EK, Narh-Bana S, Epokor M, Akanpigbiam S, Quartey AA, Gyapong J, et al. (2010) Rapid testing for malaria in settings where microscopy is available and peripheral clinics where only presumptive treatment is available: a randomised controlled trial in Ghana. Bmj 340:c930

11. Bastiaens GJ, Bousema T, Leslie T (2014) Scale-up of malaria rapid diagnostic tests and artemisinin-based combination therapy: challenges and perspectives in sub-Saharan Africa. PLoS Med 11:e1001590

12. Mukanga D, Babirye R, Peterson S, Pariyo GW, Ojiambo G, Tibenderana JK et al (2011) Can lay community health workers be trained to use diagnostics to distinguish and treat malaria and pneumonia in children? Lessons from rural Uganda. Trop Med Int Health 16:1234–1242

13. Kalyango JN, Rutebemberwa E, Alfven T, Ssali S, Peterson S, Karamagi C (2012) Performance of community health workers under integrated community case management of childhood illnesses in eastern Uganda. Malar J 11:282

14. EpiData software (http://www.epidata.dk). Accessed 1 Dec 2014

15. STATA data anlysis and statistical software (http://www.stata.com). Accessed 1 Dec 2014

16. Awor P, Miller J, Peterson S (2014) Systematic literature review of integrated community case management and the private sector in Africa: relevant experiences and potential next steps. J Glob Health 4:020414

17. Mukanga D, Tiono AB, Anyorigiya T, Källander K, Konate AT, Oduro AR et al (2012) Integrated community case management of fever in children under five using rapid diagnostic tests and respiratory rate counting: a multi-country cluster randomized trial. Am J Trop Med Hyg 87:21–29

18. Kallander K, Nsungwa-Sabiiti J, Peterson S (2004) Symptom overlap for malaria and pneumonia–policy implications for home management strategies. Acta Trop 90:211–214

19. CAPSS (2011) Closing the affordability gap: Ensuring affordable and effective malaria treatment for children in rural Uganda. Subsidized ACTs in the private sector, CAPSS MOH-MMV Pilot, 2011. http://www.mmv.org/sites/default/files/uploads/docs/access/Access_projects/Closing_the_Affordability_Gap.pdf

20. UBOS (2015) Uganda Malaria Incator Survey 2014–2015: key indicators. Uganda Bureau of statistics (UBOS)and ICF international, Kampala, Uganda and Rockville

21. Mouatcho JC, Goldring JP (2013) Malaria rapid diagnostic tests: challenges and prospects. J Med Microbiol 62:1491–1505

22. Moody A (2002) Rapid diagnostic tests for malaria parasites. Clin Microbiol Rev 15:66–78

23. Nankabirwa J, Zurovac D, Njogu JN, Rwakimari JB, Counihan H, Snow RW et al (2009) Malaria misdiagnosis in Uganda–implications for policy change. Malar J 8:66

24. Bennett S, Bloom G, Knezovich J, Peters DH (2014) The future of health markets. Global Health 10:51

25. Bloom G, Henson S, Peters DH (2014) Innovation in regulation of rapidly changing health markets. Global Health 10:53