AN EVALUATION OF INTEGRATED INTERVENTIONS TO IMPROVE ACCESS TO MALARIA TREATMENT IN TANZANIA (ACCESS PROGRAMME)

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Basel, den 2. März 2010

Prof. Dr. E. Parlow
Dekan

Dedicated to my dear parents

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List of abbreviations

ACT	Artemisinin-Based Combination Therapy
AMFm	Affordable Medicines Facility for malaria
ADDO	Accredited Drug Dispensing Outlet
ALu	Artemether-Lumefantrine (trade name: Coartem)
BMGF	Bill and Melinda Gates Foundation
CHF	Community Health Fund
CHMT	Council Health Management Team
CI	Confidence Interval
c/1000py	Cases per 1000 person years
c/1000pw	Cases per 1000 person weeks
DALDO	District Agriculture and Livestock Development Officer
DALY	Disability Adjusted Life Year
DDT	Dichlorodiphenyltrichloroethane
DHS	Demographic and Health Survey
DMO	District Medical Officer
DSS	Demographic Surveillance System
EIR	Entomological Inoculation Rate
EMIC	Explanatory Model Interview Catalogue
FGD	Focus-Group Discussion
GDP	Gross Domestic Product
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
GPS	Global Positioning System
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome
HMIS	Health Management Information Systems
HMM	Home Management of Malaria
IEC	Information, Education, Communication
IHI	Ifakara Health Institute
IMCI	Integrated Management of Childhood Illness
IMPACT-Tz	Interdisciplinary Monitoring Project for Antimalarial in Tanzania
IPTp	Intermittent Preventive Treatment for Pregnant Women
IQR	Interquartile Range
IRR	Incidence Rate Ratio
IRS	Indoor Residual Spraying
ITN	Insecticide Treated Net

KATRIN	Kilombero Agricultural Training and Research Institute
KINET	Kilombero Insecticide-Treated Net Project
LLIN	Long-Lasting Insecticidal Net
MARA	Mapping Malaria Risk in Africa
MIS	Malaria Indicator Survey
MICS	Multiple Indicator Cluster Survey
MCH	Mother and Child Health
MMV	Medicines for Malaria Venture
MOH(SW)	Ministry of Health (and Social Welfare)
MSD	Medical Stores Department
MSH	Management Sciences for Health
M&E	Monitoring and Evaluation
NBS	National Bureau of Statistics
NMCP	National Malaria Control Programme
OPD	Outpatients Department
OTC	Over-the-Counter
OR	Odds Ratio
PCA	Principal Components Analysis
PMI	United States President's Malaria Initiative
RBM	Roll Back Malaria
QIRI	Quality Improvement and Recognition Initiative
RDT	Rapid Diagnostic Tests
SES	Socio-Economic Status
SP	Sulphadoxine (or Sulphametoxipyrazine)-Pyrimethamine
STI	Swiss Tropical Institute
TEHIP	Tanzania Essential Health Interventions Project
TFDA	Tanzania Food and Drugs Authority
TSH	Tanzanian Shilling
UN	United Nations
USD	United States Dollar
WHO	World Health Organization

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Summary

Malaria causes an estimated one million deaths annually although it is a curable disease if treated promptly and correctly. Most cases occur in young children in sub-Saharan Africa, supporting a vicious circle of disease and poverty. Hence, ensuring access to malaria treatment is a major public health and development priority.

The purpose of this research was to evaluate the ACCESS programme, which aimed at understanding and improving access to malaria treatment in rural Tanzania. The programme was implemented in the Kilombero and Ulanga Districts in Southern Tanzania in two phases. This evaluation focuses on the first phase, which covered the years between 2004 and 2008. The ACCESS strategy is based on a set of integrated interventions at three levels: 1) community level; 2) public heath facilities; and 3) commercial drug sector. The interventions are accompanied by a comprehensive set of monitoring and evaluation activities.

Between 2004 and 2007 the ACCESS programme's main intervention at community level was a social marketing campaign for improved recognition of the disease and more effective care seeking. Various communication channels were used and material developed to disseminate information on malaria transmission, symptoms and prevention as well as to stress the importance of prompt and effective treatment. Road shows were the main activity and included role plays, public lectures and quizzes. In addition, promotional materials (e.g. stickers, leaflets, t-shirts) were distributed, and billboards and posters displayed in public places. The programme also organised special campaigns targeted at pregnant women and mothers of young children in Mother and Child Health (MCH) clinics.

In health facilities the ACCESS programme intervened to improve quality of care. The main activity was refresher training for health facility staff based on Integrated Management of Childhood Illness (IMCI) algorithms conducted in 2004 and 2005. In addition the study period saw the change of the first line treatment for malaria. In 2006 the Government of Tanzania switched from Sulphadoxine Pyrimethamine (SP) to the highly efficacious Artemether Lumefantrine (ALu), due to the high levels of resistance to SP. As ALu (trade name Coartem®) would be unaffordable at its market price the manufacturer Novartis sold it at-cost to Tanzania. Through support from the Global Fund to fight AIDS, TB and Malaria (GFATM) the drug was provided free to all government health care facilities.

In parallel the Accredited Drug Dispensing Outlets (ADDOs) programme was rolled out in the study area from 2006 onwards to improve access to treatment and quality of care in commercial drug shops. ACCESS undertook the local evaluation and monitoring of the programme. The private retail sector plays a very important role in the delivery of antimalarial treatment in most African countries as retailers tend to be more accessible and flexible, especially with regards to opening hours and charges. However, unqualified staff invariably sell drugs they are not allowed to stock, which often includes antimalarials. The aim of the ADDO programme is to improve access to quality care in drug shops with a mix of dispenser training, incentives, accreditation and regulation. ALu was made available to the programme at a highly subsidised price towards the end of 2007.

Findings from the monitoring and evaluation activities showed that access to malaria treatment improved in the study area following the interventions in health facilities and drugs shops. Drug shops became more available to the community (from 24 shops for every 100,000 people in 2004 to 39 in 2008) and more accessible (from 71% of households within 5km of a shop in 2004 to 87% in 2008) following the ADDO roll-out. In addition, the 2006 change of treatment policy from SP to ALu led to an increase in the availability of antimalarial drugs in health facilities (from 40% to 80% of months in stock of the drug). Treatment was generally more expensive in drug shops compared to health facilities and prices increased by 50-80% in shops between 2004 and 2008. Nevertheless, antimalarial sales in private retail grew (from 49% to 59% of market shares). This is likely to be a result of increased availability and accessibility of shops but better quality of care may also have played a role. Unfortunately the ADDO programme was not able to promote widespread availability of ALu in its outlets (only one third of outlets were found to stock the drug in 2008). This resulted in a low uptake of the new drug (19% of all malaria treatments sold or dispensed) despite the fact that it was available in almost all the health facilities in the area.

Results from treatment seeking surveys conducted in the community showed an improvement in malaria treatment between 2004 and 2008. This was ascribed to: 1) improved access to treatment; and 2) a better understanding of the importance of prompt treatment thanks to social marketing campaigns. The proportion of fever cases treated with an antimalarial increased (from 86% to 96% between 2004 and 2008) as well as the proportion of cases treated promptly (80% to 93-97% doses started within 24 hrs). However, there was no improvement in the reported adherence to the recommended dosage of drugs (43-76% of treatments dosed appropriately between 2004 and 2008). Moreover, the proportion of cases taking a recommended treatment was only 53% in 2008 since many

cases were treated in the private retail sector where the first line treatment ALu was not widely available.

Improved treatment appears to have had an impact on malaria morbidity and mortality, both at community and health facility level. At community level there was evidence of a 28% decrease in the incidence of fever (from 2.5 to 1.8 average cases per person per year between 2005 and 2008) while convulsions in children under the age of five (a sign of progression into severe malaria) decreased by 45% (from 4.3 to 2.3 cases for every 10 children per year). Under-five mortality decreased by 17% after the ACCESS interventions (from 28.4 cases per 1000 person years in the period 1997-2004 to 18.9 cases in 2008). However, due to the absence of a control it is difficult to know how much the ACCESS interventions contributed to this decrease compared to other malaria control strategies implemented in the area. The coverage with Insecticide Treated Nets (ITNs) is extremely high in the area (over 90% of household own at least one net). Although ITN ownership did not increase between 2004 and 2008 when the ACCESS interventions were implemented, they are likely to have continued to impact on transmission. Health facility fever rates decreased by 2-3% but the the absolute number of fever cases visiting health facilities remained unchanged due to population growth.

In conclusion this thesis has shown that an integrated approach tackling both users and providers can lead to tangible improvements in terms of access to malaria treatment and treatment seeking for the disease. This can in turn have a substantial impact on both morbidity and mortality. Interventions targeting providers in sub-Saharan Africa should recognise the important role of the private sector since. This thesis has shown that if drugs are not available in the private sector their uptake remains low. As far as user interventions are concerned, social marketing has proven to be a successful strategy to sensitise the population on the importance of prompt treatment but more efforts are needed to improve adherence to treatment regimens.

Zusammenfassung

Malaria verursacht schätzungsweise eine Million Todesfälle pro Jahr, obwohl es sich um eine heilbare Krankheit handelt, wenn sie schnell und richtig behandelt wird. Die meisten Fälle treten bei Kindern auf, die in Afrika südlich der Sahara leben, was den dort herrschenden Teufelskreis aus Krankheit und Armut verstärkt. Daher ist die Sicherung des Zugangs (access) zu Malaria-Behandlungen für das Gesundheitswesen und die Entwicklung von grosser Bedeutung.

Der Zweck dieser Arbeit war es, das ACCESS-Programm zu beurteilen, welches darauf abzielt das Verständnis und die Verbesserung des Zugangs zu Malaria-Behandlungen im ländlichen Tansania zu verbessern. Das Programm wurde im Kilombero und Ulanga Distrikt in Süd-Tansania in zwei Phasen durchgeführt. Die hier vorliegende Bewertung konzentriert sich lediglich auf die erste Phase, die in die Jahre zwischen 2004 und 2008 fällt. Die ACCESS-Strategie basiert auf einer Reihe von integrierten Interventionen auf dreierlei Ebenen: 1) der kommunalen Ebene, 2) den Einrichtungen des öffentlichen Gesundheitssystems, und 3) dem gewerblichen Medikamentenbereich. Die Interventionen werden durch ein umfassendes Paket zur Überwachung und Bewertung der Aktivitäten begleitet.

Zwischen 2004 und 2007 war die wichtigste Maßnahme des Access-Programms auf kommunaler Ebene eine soziale Marketing-Kampagne für eine bessere Erkennung der Krankheit und ein erfolgreiches Bemühen um Behandlung durchzuführen. Verschiedene Kommunikationskanäle wurden genutzt und Material entwickelt, um Informationen über Malaria-Übertragung, Symptome und Vorbeugung zu verbreiten, sowie die Bedeutung einer schnellen und wirksamen Behandlung hervorzuheben. Strassenvorführungen waren dafür die wichtigsten Aktivitäten. Sie beinhalteten Rollespiele, öffentliche Vorträge und Ratespiele. Darüber hinaus wurden Werbematerialien (z.B. Aufkleber, Flugblätter, T-Shirts) verteilt und Informationen auf Reklametafeln und Plakaten veröffentlicht. Das Programm organisierte auch spezielle Kampagnen welche speziell auf schwangere Frauen und Mütter mit kleinen Kindern in Mutter-Kind-Kliniken (MCH) abzielten.

In Gesundheitseinrichtungen hatte das ACCESS-Programm zum Ziel die Qualität der Versorgung zu verbessern. Die Haupttätigkeit bestand dabei in Auffrischungskursen für das Personal basierend auf den „Integrated Management of Childhood Illness“ (IMCI) Algorithmen aus den Jahren 2004 und 2005. Während der Studiendauer kam es zudem zu

einer Anpassung der Hauptbehandlung von Malaria. Aufgrund der vielen Resistenzen gegen Sulphadoxine Pyrimethamin (SP) wechselte die Regierung von Tansania im Jahr 2006 von SP zu dem hochwirksamen Artemether Lumefantrin (ALu) . Da ALu (Handelsname Coartem ®) zu den Marktpreisen des Herstellers Novartis unerschwinglich wäre verkaufte es das Unternehmen zum Herstellungskostenpreis nach Tansania. Durch die Unterstützung des Global Funds zur Bekämpfung von Aids, Tuberkulose und Malaria (GFATM) wurde das Medikament kostenlos an alle öffentlichen Einrichtungen des Gesundheitswesens bereitgestellt.

Parallel dazu wurde seit 2006 das Accredited Drug Dispensing Outlets (ADDOs) Programm im Untersuchungsgebiet durchgeführt, das den Zugang zu Behandlungen und die Qualität der Pflege bei gewerblichen Medikamenten-Geschäften zu verbessern sucht. ACCESS verpflichtete sich zur lokalen Auswertung und Überwachung des Programms. Der private Einzelhandel spielt eine sehr wichtige Rolle bei der Bereitstellung von Anti-Malaria Behandlungen in den meisten afrikanischen Ländern, da Einzelhändler tendenziell stärker verfügbar und flexibel einsetzbar sind, insbesondere in Hinblick auf Öffnungszeiten und Gebühren. Leider verkauft nicht qualifiziertes Personal beständig Medikamente, die es nicht bevorraten darf, wobei es sich häufig um Malariamittel handelt. Das Ziel des ADDO Programms ist es den Zugang zu einer hochwertigen Gesundheitsversorgung im Medikamentenverkauf mittels einer Mischung aus Arzneibesteller-Ausbildung, -Förderung, -Zulassung und -Regulierung zu verbessern. Gegen Ende des Jahres 2007 wurde ALu dem Programm zu einem stark subventionierten Preis zur Verfügung gestellt.

Ergebnisse der Beobachtung und Bewertung der Aktivitäten zeigten, dass der Zugang zur Malaria-Behandlung im Studiengebiet infolge der Eingriffe in Gesundheitsfürsorgeeinrichtungen und Medikamentengeschäfte verbessert werden konnte. Nach der Einführung von ADDO wurden Arzneimittelgeschäfte verfügbarer (24 Geschäften pro 100.000 Menschen im Jahr 2004 und 39 Geschäfte in 2008) und zugänglicher (von 71% der Haushalte im Umkreis von 5km von einem Geschäft im Jahr 2004 auf 87% in 2008) für die Gemeinschaft. Darüber hinaus führte die Änderung der Hauptbehandlungspolitik von SP zu ALu in 2006 zu einem Anstieg in der Verfügbarkeit von Medikamenten gegen Malaria in Gesundheitseinrichtungen (Monaten mit vorrätigen Medikamenten von 40% auf 80%). In der Regel war die Behandlung in Arzneimittelgeschäften im Vergleich zu Einrichtungen des Gesundheitswesens teurer. Zudem stiegen die Preise in den Geschäften um 50-80% zwischen 2004 und 2008. Dennoch stieg der Umsatz an Anti-Malaria Mitteln im privaten Einzelhandel von 49% auf 59% der Marktanteile. Dies dürfte eine Folge der erhöhten Verfügbarkeit und Zugänglichkeit von Geschäften sein, allerdings kann auch die verbesserte

Qualität der Betreuung eine Rolle gespielt haben. Leider war das ADDO Programm nicht in der Lage eine weit verbreitete Verfügbarkeit von ALu in seinen Verkaufsstellen zu fördern (nur ein Drittel der Filialen hatte das Medikament im Jahr 2008 auf Lager). Dies führte zu einer geringen Nutzung der neuen Arznei (bei 19% aller Malaria-Behandlungen verkauft oder ausgegeben) trotz der Tatsache, dass es in fast allen medizinischen Einrichtungen in der Region verfügbar war.

Ergebnisse von Studien über das Streben nach Behandlung in der Gemeinschaft durchgeführt wurden, zeigten eine Verbesserung der Malaria-Behandlung zwischen 2004 und 2008. Dies war zurückzuführen auf 1) eine Verbesserung des Zugangs zur Behandlung und 2) ein grösseres Verständnis für eine schnelle Behandlung dank der Kampagnen auf dem sozialen Sektor. Sowohl der Anteil der Fieber-Fälle, die mit Malariamedikamenten behandelt wurden (von 86% auf 96% zwischen 2004 und 2008), als auch der Anteil der Fälle, die umgehend behandelt wurden (von 80% auf 93-97% an Einnahmen innerhalb von 24 Stunden), erhöhte sich. Allerdings gab es keine Verbesserung zur gemeldeten Einhaltung der empfohlenen Dosierung von Medikamenten (43-76% der Behandlungen wurden zwischen 2004 und 2008 richtig dosiert). Darüber hinaus lag der Anteil an Fällen mit empfohlener Behandlung bei nur 53% im Jahr 2008, da viele Fälle im privaten Einzelhandel behandelt werden, in dem das Hauptmedikament ALu nicht überall verfügbar war.

Eine verbesserte Behandlung scheint einen Einfluss auf die Morbidität und Mortalität von Malaria zu haben, sowohl auf der kommunalen als auch auf der Gesundheitswesen-Ebene. Auf kommunaler Ebene gab es Anzeichen für eine 28%-ige Abnahme der Inzidenz von Fieber-Fällen (von 2,5 auf durchschnittlich 1,8 Fälle pro Person und Jahr zwischen 2005 und 2008), während Krämpfe bei Kindern unter fünf Jahren (ein Zeichen des Übergangs in die schwere Form der Malaria) um 45% abnahmen (von 4,3 auf 2,3 Fälle je 10 Kinder pro Jahr). Die Mortalität bei Kindern unter fünf Jahren sank um 17% nach den Interventionen des ACCESS Programms (von 28,4 Fällen pro 1.000 Personenjahre im Zeitraum 1997-2004 auf 18,9 Fälle im Jahr 2008). Aufgrund von fehlender Kontrolle ist schwierig zu wissen, inwieweit die ACCESS Interventionen im Vergleich mit anderen Strategien zur Bekämpfung der Malaria, die ebenfalls in der Region umgesetzt wurden, zu diesem Rückgang beitrugen. Die Abdeckung mit Insektizid-behandelten Moskitonetzen (ITN) in der Umgebung ist extrem hoch (über 90% der Haushalte besitzen mindestens ein eigenes Netz). Obwohl die Abdeckung zwischen 2004 und 2008 nicht zugenommen hat, als die ACCESS Interventionen umgesetzt wurden, ist es wahrscheinlich, dass die Auswirkungen auf die Übertragung sich fortgesetzt haben. Auf Ebene der Gesundheitseinrichtungen blieb die Zahl der Fälle, die mit Fieber in den Einrichtungen erschienen, aufgrund des Bevölkerungswachstums unverändert.

Zusammenfassend hat diese Arbeit gezeigt, dass ein integrierter Ansatz, der sowohl Nutzer als auch Anbieter einbezieht, zu konkreten Verbesserungen in Bezug auf den Zugang zu Malaria-Behandlung und zum Streben nach Behandlung führen kann. Dies kann wiederum einen wesentlichen Einfluss auf Morbidität und Mortalität haben. Es ist daher wichtig, dass Interventionen im Anbieterbereich die zentrale Rolle des privaten Sektors anerkennen. Die vorliegende Arbeit hat aufgezeigt, dass bei fehlender Verfügbarkeit von Medikamenten im privaten Sektor die Medikamentenverwendung in der Bevölkerung niedrig ist. Im Nutzerbereich haben sich soziale Marketing-Kampagnen auf kommunaler Ebene zwar als nützliche Strategien zur Sensibilisierung der Bevölkerung bezüglich der Wichtigkeit von frühzeitiger Behandlung erwiesen, doch muss die Befolgung der Behandlungsrichtlinien weiter verbessert werden.

Muhtasari

Malaria inasababisha takribani vifo milioni moja kila mwaka ingawa ni ugonjwa unaotibika iwapo tiba itachukuliwa mapema na kwa usahihi. Mashambulizi mengi yanatokea miongoni mwa watoto wadogo katika bara la Afrika, chini ya jangwa la Sahara, hali inayoendeleza mfumo mzima wa magonjwa na umasikini. Kwa mantiki hii, upatikanaji wa tiba ya malaria ni kipaumbele kikubwa katika swala zima la afya ya jamii na maendeleo.

Lengo la taarifa hii ya utafiti ilikuwa ni kutathmini mradi wa ACCESS uliokuwa na lengo la kuongeza uelewa na kuimarisha upatikanaji wa tiba ya malaria maeneo ya vijijini katika nchi ya Tanzania. Mradi huu ulitekelezwa kwa awamu mbili katika wilaya za Kilombero na Ulanga, kusini masharariki mwa Tanzania. Tathmini hii imelenga awamu ya kwanza ya mradi, iliyofanyika kati ya mwaka 2004 na 2008. Mkakati wa mradi wa ACCESS umelenga katika utekelezaji kwenye sehemu kuu tatu: 1) Ngazi ya jamii 2) Vituo vya afya, na 3) Ngazi ya maduka ya dawa.Utekelezaji huu unaambatana na zoezi la kina la ufatiliaji na tathmini.

Kati ya mwaka 2004 na 2007, utekelezaji mkubwa katika mradi wa ACCESS kwenye ngazi ya jamii ulikuwa uhamasishaji wa jamii masoko kwa ajili ya kuongeza utambuzi wa ugonjwa wa malaria na kupata tiba sahihi. Njia mbalimbali za mawasiliano zilitumika na vifaa kuandaliwa kwa ajili ya kutoa ujumbe juu ya maambukizo ya malaria, dalili zake na kinga, pia msisitizo juu ya umuhimu wa tiba sahihi na mapema. Maonyesho kwa njia ya barabara ilikuwa ni kazi kubwa iliyojumuisha michezo ya kuigiza, mhadhara na maswali na majibu. Pia vifaa vya uhamasishaji kama vipeperushi na fulana viligawiwa na mabango yalibandikwa kwenye sehemu za wazi. Mradi pia uliandaa uhamasishaji maalum uliowalenga akina mama wajawazito, wanawake wenye watoto wadogo na kliniki za watoto.

Katika vituo vya afya, mradi wa ACCESS ulijikita katika kuimarisha ubora wa huduma. Shughuli kubwa iliyofanyika ilikuwa ni kutoa mafunzo rejea kwa wafanyakazi wa vituo vya afya kulingana na mfumo ulikuwepo wa kutibu magonjwa yanayoshambulia watoto chini ya miaka mitano ikiwemo malaria, mfumo wa matibabu ya magonjwa ya watoto kwa uwiano unaojulikama kama IMCI (kwa lugha ya kiingereza ukimaanisha Integrated Management of Childhood Illness) uliofanyika mwaka 2004 na 2005. Pia katika kipindi cha utekelezaji wa mradi, kulitokea mabadiliko ya dawa ya kwanza ya kutibu malaria isiyo kali. Mwaka 2006, serikali ya Tanzania iibadili dawa ya malaria kutoka Sulphadoxine Pyrimethamine (SP) kwenda dawa iliyo bora zaidi iitwayo Artemether Lumefantrine (ALu) kutokana na SP kushindwa kupambana na vimelea vya malaria. ALu (jina la kibiashara Coartem) isingeweza

kupatikana kwa waanchi kwa sababu gharama zake zilikuwa juu kutokana na bei kubwa ya soko lake kutoka kwa watengenezaji (Norvatis) iliyouzwa Tanzania, lakini kutokana na msaada kutoka katika nfuko wa dunia wa kupambana na Ukimwi, Kifua Kikuu na Malaria, dawa ziliweza kutolewa bure kwa vituo vyote vya afya vya serikali.

Pamoja na hayo, mpango wa Maduka ya Dawa Muhimu (DLDM) ulizinduliwa katika eneo la mradi mwaka 2006 kwa ajili ya kuongeza upatikanaji wa tiba na huduma bora katika maduka ya dawa. Mpango wa ACCESS uliamua kufanya ufuatialji na tathmini ya mpango huu. Sekta binafsi inachangia kwa kiasi kikubwa katika utoaji wa tiba ya malaria katika nchi nyingi za Afrika kwa sababu maduka yanaweza kufikika kwa urahisi zaidi hususani kwenye kipengele cha muda wa kuwa wazi na suala la bei. Lakini wauzaji wasiokuwa na vigezo wamekuwa wakiuza dawa ikiwemo dawa za malaria. Lengo la mpango wa maduka ya dawa muhimu ni kuimarisha upatikanaji wa huduma bora katika maduka ya dawa na kuwapa mafunzo watoa huduma, motisha na kuongeza kiwango cha utendaji. Mwishoni mwa mwaka 2007 ALu zilipunguzwa bei katika eneo la mradi ili kusaidia jamii kuzipata kwa urahisi.

Matokeo ya shughuli za ufuatiliaji na tathmini ulionyesha kuwa upatiknaji wa tiba ya malaria umeongezeka katika eneo la mradi kutokana na utekelezaji katika ngazi za vituo vya tiba na maduka ya dawa. Maduka ya dawa yaliongezeka zaidi kwa jamii (kutoka maduka 24 kwa kila watu 100,000 mwaka 2004 mpaka maduka 38 mwaka 2008) na zaidi upatikanaji (kutoka asilimia 71 ya kaya zinazoishi ndani ya kilometa 5 kutoka duka la dawa mwaka 2004 mpaka asilimia 87 mwaka 2008) kutokana na uanzishwaji wa mpango wa Maduka ya dawa muhimu. Pia ubadilishwaji wa sera ya tiba kutoka SP kwenda ALu ilisababisha muongezeko wa dawa za malaria katika vituo vya tiba (kutoka asilimia 40 mpaka asilimia 80 ya miezi ya akiba ya dawa). Kwa ujumla matibabu yalikuwa ghali zaidi kwenye maduka ya dawa kuliko katika vituo vya tiba na bei iliongezeka kwa asilimia 50-80 kwenye maduka kati ya mwaka 2004 na 2008. Pamoja na hayo mauzo ya dawa za malaria kwenye maduka ya dawa ilikua (kutoka asilimia 49 mpaka 59 ya mgao wa masoko). Hii inaweza kuwa matokeo ya uongezekaji wa upatikanaji wa maduka lakini pia ubora wa huduma unaweza kuwa umechangia. Kwa bahati mbaya mpango wa maduka ya dawa muhimu haukuongeza uongezekaji wa ALu katika maduka haya (ni moja ya tatu tu ya maduka haya yalionekana kuwa na dawa za ALu mwaka 2008). Hii ilisababisha mapokeo machache ya dawa hii mpya (asilimia 19 ya dawa za malaria iliuzwa) pamoja na kwamba dawa hizi zilikuwepo pia kwenye vituo vya tiba katika eneo la mradi.

Matokeo ya tafiti za utafutaji matibabu zilizofanyika katika ngazi ya jamii zilionyesha kuongezeka kwa tiba ya malaria kati ya mwaka 2004 na 2008. Hii ilisababishwa na: 1)

kuimarika kwa upatikanaji wa tiba; 2) uelewa mzuri zaidi wa umuhimu wa tiba ya haraka ambao ulisisitizwa katika uhamasishaji wa masoko jamii. Kiwango cha matukio ya homa yaliyotibiwa kwa dawa za malaria kiliongezeka (kutoka aslimia 86 mpaka asilimia 96 kati ya mwaka 2004 na 2008) pamoja na kiwango cha matukio yaliyotibiwa mapema (asilimia 80 mpaka 93-97, dozi ilimezwa ndani ya masaa 24). Lakini kulikuwa hakuna mabadiliko kwa wale walioripoti kumaliza dozi iliyo sahihi (asilimia 43-76 ya tiba kamilifu kati ya mwaka 2004 na 2008). Zaidi kiwango cha matukio ya homa yaliyotumia tiba iliyopendekezwa ilikuwa asilimia 53 mwaka 2008 kwani matukio mengi yanatibika katika sekta binafsi ambapo dawa ya kwanza ya malaria (ALu) haikuwa inapatikana kwa kiasi kikubwa

Kuboreka kwa tiba kumeonekana kuwa na matokeo katika magonjwa na vifo, pote katika ngazi ya jamii na vituo vya tiba. Katika ngazi ya jamii imedhibitika kuwa asilimia 28 ya matukio ya homa yalipungua (kutoka wastani wa matukio 2.5 mpaka 1.8 kwa mtu.

kwa mwaka kati ya mwaka 2005 na 2008) wakati matukio ya degedege (dalili ya kuelekea kwenye malaria kali) kwa watoto chini ya miaka mitano yalipungua kwa asilimia 45 (kutoka matukio 4.3 mpaka 2.3 kwa kila watoto kumi kwa mwaka). Vifo vya watoto chini ya miaka mitano vilipungua kwa asilimia 17 baada ya utekelezaji wa mpango wa ACCESS (kutoka matukio 28.4 kwa watu 1000 kwa kipindi cha miaka 1997-2004 mpaka 18.9 mwaka 2008). Pamoja nah ii, kutokuwepo na kundi ambalo halikupewa utekelezaji, ni vigumu kujua ni kwa kiasi gani mpango wa ACCESS umechangia katika mabadiliko haya ukilinganisha na mikakati mingine ya kupambana na malaria katika eneo la mradi. Utumiaji wa vyandarua vilivyotiwa dawa ni mkubwa katika eneo la mradi (zaidi ya asilimia 90 ya kaya zinamiliki angalau chandarua kimoja). Ingawa hii haikuongezeka katika kipindi kati ya mwaka 2004 na 2008 wakati mradi wa ACCESS ulipotekelezwa, kuna uwezekano kukawa na muendelezo wa matokeo ya maambukizo. Katika ngazi ya kituo cha tiba idadi ya matukio ya homa yaliyofika vituo vya tiba hayakubadilika kutokana na muongezeko ya watu.

Kwa kuhitimisha taarifa hii ya utafiti imeonyesha kuwa njia ya muingiliano unaogusa watumiaji na watoaji inaweza kuongeza uimarikaji wa upatikanaji wa tiba ya malaria na utafutaji matibabu. Kwa njia nyingine, hii inaweza kuwa na matokeo katika magonjwa na vifo. Utekelezaji unaolenga watoa huduma kusini mwa jangwa la Sahara unatakiwa kuzingatia umuhimu wa sekta binafsi kutokana na kwamba utafiti huu umeonyesha kuwa kama dawa hazipatikani katika sekta binafsi matumizi yake yanakuwa madogo. Kwa namna ambavyo utekelezaji unaolenga watumia huduma unavyohusika, mkakati wa masoko jamii umeonyesha kufanikiwa kuhamasisha wananchi juu ya umuhimu wa tiba ya mapema lakini jitihada kubwa inatakiwa kuongezwa ili kuboresha uzingatiaji wa taratibu za matibabu.

1. Introduction

Malaria is the most important parasitic infection in humans and a major public health and development problem in sub-Saharan Africa. A brief overview of the transmission, clinical manifestations and geographical distribution of the disease is given in Section 1.1, with a focus on Africa. The current global strategy for malaria control is outlined in Section1.2. and Section 1.3 provides an overview of the mutually re-enforcing cycles of malaria and poverty, which challenge malaria control efforts in developing countries. The specifics of the malaria situation and control efforts to date in mainland Tanzania are described in Section 1.4. Section 1.5 focuses on existing strategies to improve access to malaria treatment. Finally Section 1.6 describes the Health Access Livelihood Framework and Section 1.7 provides a detailed description of the Tanzanian health system in terms of this framework.

1.1. Epidemiology of malaria

Malaria is a vector-borne infection caused by protozoan parasites belonging to the genus *Plasmodium*. It is transmitted by 40 main species of female *Anopheles* mosquitoes. These differ in behaviour which explains the many epidemiological patterns of the disease seen worldwide. Almost all human infections are caused by *P. falciparum*, *P. Vivax*, *P. malaria* and *P. ovale* although occasional infections with monkey malaria parasites*, such as P. knowlesi,* also occur*. P. falciparum* causes the most severe and life-threatening form of the disease and is mainly found in Africa [1].

Infection with *P. falciparum* may result in a wide variety of symptoms, ranging from very mild symptoms to severe disease and even death. Malaria is often categorised as uncomplicated (initial stages) or severe/complicated (later stages). The first symptoms of uncomplicated malaria include headache, fatigue, muscle and joint aches, followed by fever, vomiting and worsening malaise. In general, uncomplicated malaria is a curable disease if diagnosed and treated promptly and correctly. However, treatment delay can lead to severe malaria, which usually manifests itself with coma (cerebral malaria), metabolic acidosis, severe anaemia, hypoglycaemia and, in adults, acute renal failure or acute pulmonary oedema. If untreated, severe malaria is almost always fatal. Estimates suggest that approximately 2% of clinical malaria episodes in African children are severe and of these, 50% are fatal [1].

Malaria was widespread in many parts of Europe and North America but was progressively restricted to tropical areas in the 20th century as a result of general economic developement.

Cold winters facilitated the success of the control measures as they shorten mosquito life and prolong the time period required for the parasite to complete its life-cycle. Conversely, in tropical Africa and many parts of Asia, the measures to fight malaria are particularly challenging as the climatic conditions in these regions are more favourable for both the *Plasmodium* parasite and the *Anopheles* vector [2]. According to the World Health Organisation (WHO) malaria occurs in 108 countries and half of the world's population or 3.3 billion people are at risk of malaria [3]. However, it is in sub-Saharan Africa where 85-90% of malaria fatalities occur as most cases result from by *P. falciparum* infections [4].

Determination of the mortality and morbidity caused by malaria is difficult to achieve due to the lack of reliable data and the indirect effects of malaria. Estimates of the burden of malaria are based on different sources and assumptions as national health statistics of the countries concerned are often inadequate, incomplete and non representative [5]. Most estimates suggest that malaria directly causes about 1 million deaths per year, nearly 90% of which occur in children under five years of age in Africa (Figure 1) [3]. In 2004 malaria was given a Disability-Adjusted Life Year (DALY) score of 34 million worldwide (2.2% of the total) and 31 million in the African Region (8.2% of the total) [6]. However, these mortality and morbidity estimates do not allow sufficiently for malaria as an indirect cause of anaemia, low birth weight, growth retardation/undernutrition, and consequences of illness such as adverse reactions to treatment and neurological disabilities (Figure 2) [7, 8]. It has been estimated that the attributable mortality of malaria, taking into consideration its indirect effects, may be approaching three million, almost 3 times the WHO estimate [7].

Figure 1. Estimated deaths from malaria per 1000 population (source: RBM [4])

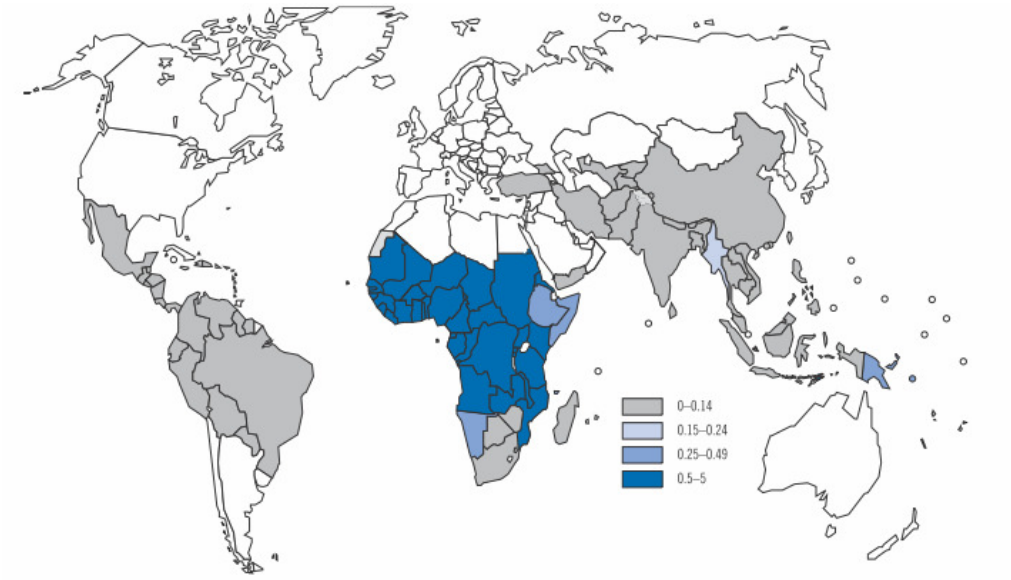
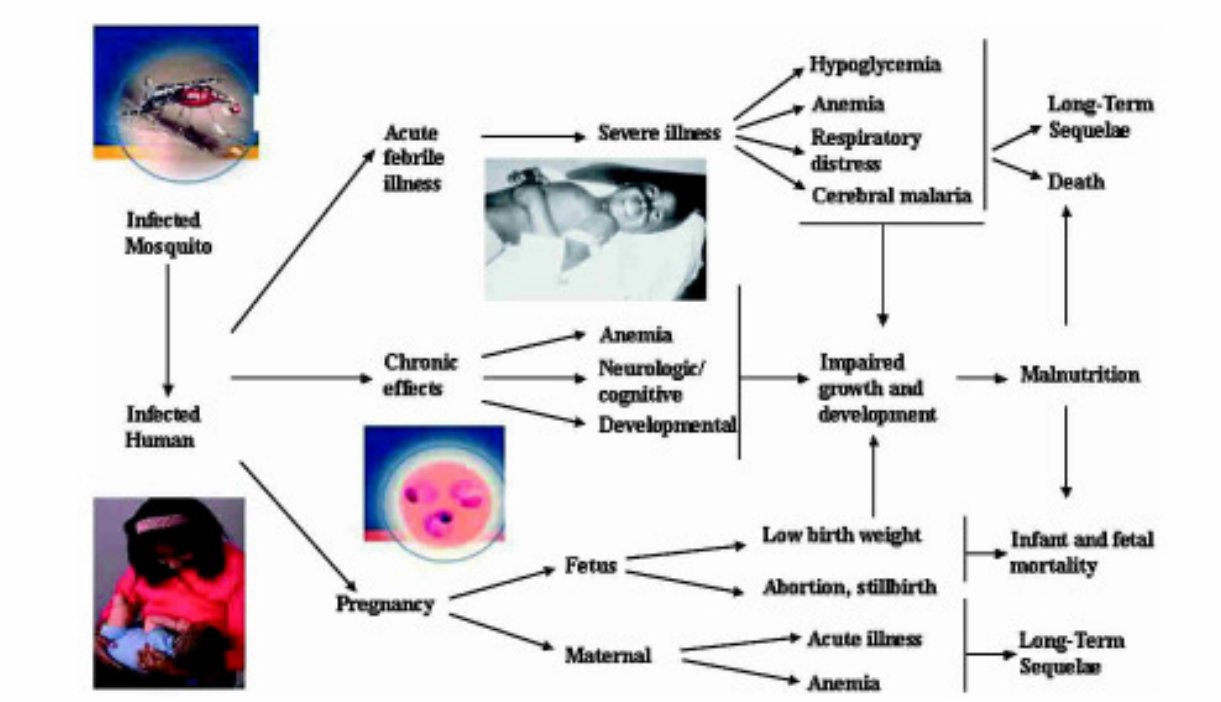


Figure 2. Acute, chronic and pregnancy related manifestations of malaria (source: Breman *et al* [7])



1.2. Malaria control

Following the elimination of malaria in temperate countries after the World War II, various malaria eradication campaigns were carried in the rest of the world with mixed outcomes. Countries such as the United States, Italy, Greece and Spain were the first to become free of autochthonous malaria in the 1930s to 1950s as a result of improved housing and intensive antimalarial interventions (draining of swamplands, use of DDT for indoor house spraying and effective case management, first with quinine and then with chloroquine). Confidence in the effectiveness of the available malaria control tools grew and in 1955 the World Health Assembly launched a global malaria eradication campaign conducted throughout the 1960s and 1970s. Malaria was eliminated in nations with temperate climates and seasonal malaria transmission, but in most countries progress was negligible or not sustained after control efforts ceased.

Following the failure to achieve eradication, WHO abandoned the campaign and reoriented its policy from eradication and elimination to control. In 1985 WHO adopted a resolution recommending that malaria control activities be developed as an integral part of primary health care systems at the district level. The lack of financial support and the integration of malaria programmes in rapidly decentralising and deteriorating primary health services, combined with an increase in parasite and vector resistance to the current antimalarial drugs

and insecticides led to an unprecedented increase in malaria mortality and morbidity in the 1980s [4, 7, 9].

The resurgence of malaria in the 1980s led to the creation of the Roll Back Malaria (RBM) Partnership to coordinate renewed global efforts in combating malaria in 1998. The Partnership was launched by the World Health Organization (WHO), the United Nations Children's Fund (UNICEF), the United Nations Development Programme (UNDP) and the World Bank. The partnership attempts to build upon the successes and lessons learnt from previous malaria control, elimination and eradication efforts by promoting universal coverage of effective interventions but also by strengthening health systems. The goal set by the partnership is to have achieved a 75% global reduction in incidence of malaria compared to 2000 levels in 2015 [10].

The current strategy of the partnership is outlined in the Global Malaria Action Plan (GMAP) [4] and comprises of three components: control, elimination and research. Control is thought of as a two stage process, whereby initially universal coverage of locally appropriate prevention and therapeutic interventions is reached for all populations at risk. Universal coverage is then sustained over time by strengthened health systems, which eventually leads the country into the elimination stage. The expert consensus is that elimination of malaria in certain countries will require new control tools in traditionally high-transmission areas. Therefore, continuous research into new tools, but also to inform policy and to develop intervention and operational strategies is necessary at every stage (Figure 3). Eradication is the long-term goal of the strategy which can be achieved by eliminating malaria country by country as new approaches and tools expand the geographical range of where elimination is possible. WHO currently estimates that 82 out of 109 malarious countries are currently in the control stage (Figure 4).

Figure 3. Three components of the global strategy (source: RBM [4])

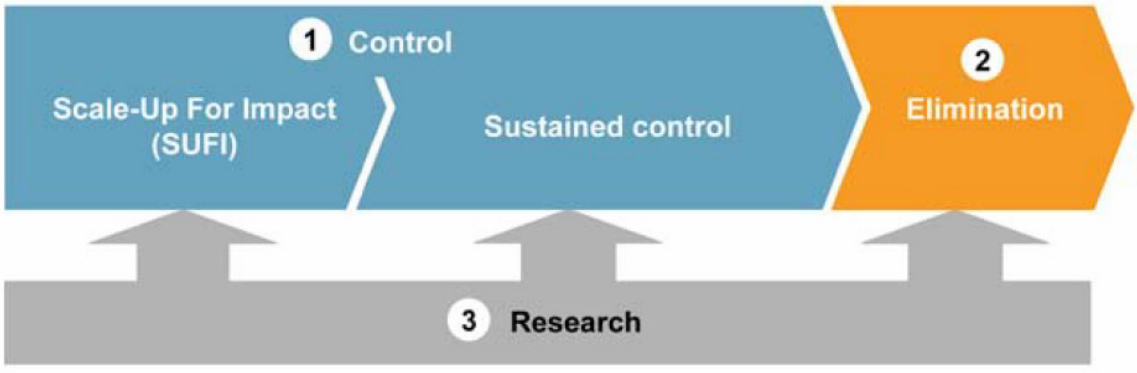
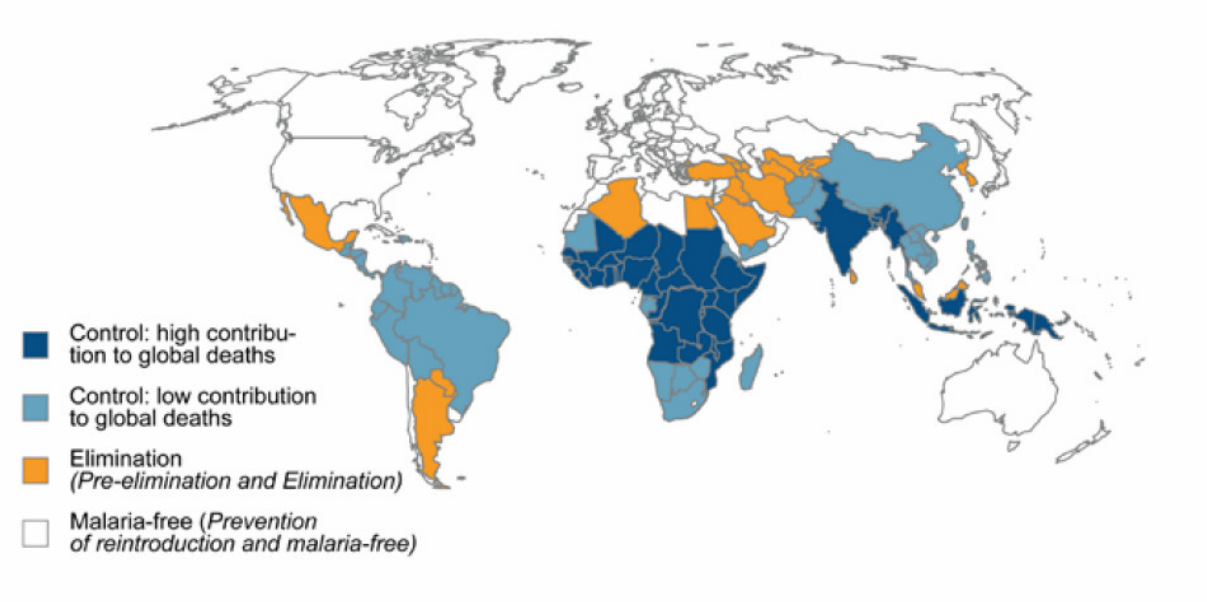


Figure 4. Country categorization by malaria status and burden (source: RBM [4])



The RBM Partnership advocates the universal coverage of preventive tools. The currently available preventive tools include Long-Lasting Insecticidal Nets (LLINs), Indoor Residual Spraying (IRS) and Intermittent Preventive Treatment for Pregnant women (IPTp). LLINs are recommended as a key vector control intervention which provides both personal protection with the net and the insecticide, and community protection by reducing the vector population when implemented at high coverage. Where LLINs are not available the use of Insecticide Treated Nets (ITNs) is recommended, with periodic insecticidal treatment. IRS is an effective method of vector control aimed at killing mosquitoes that enter houses and rest on sprayed surfaces (e.g. walls and ceilings). IRS is widely used in areas of seasonal transmission, but is only appropriate and advised in countries where the necessary logistics can be deployed. In high transmission settings, all pregnant women should receive at least 2 doses of Sulphadoxine-Pyrimethamine (SP) for IPT to reduce the risk of contracting malaria [4].

The appropriate case management recommended by the RBM Partnership is treatment with appropriate antimalarial drugs on malaria. Before treatment is started parasitological diagnosis is recommended to confirm malaria cases through quality-assured microscopy or Rapid Diagnostic Tests (RDTs). All confirmed uncomplicated *P. falciparum* infections should be treated with an artemisinin-based combination (ACT) therapy within 24hrs of onset. Conventional antimalarial monotherapies, such as chloroquine, SP and amodiaquine are no longer recommended due to widespread resistance. Four ACTs are currently recommended for use: artemether-lumefantrine, artesunate-amodiaquine, artesunate-mefloquine and artesunate-sulfadoxine-pyrimethamine. The choice of the ACT should be based on the efficacy of the partner medicine in the country or area of intended deployment. Severe

malaria should be treated parenterally with either an artemisinin derivative or quinine until the patient can swallow, when a complete course of ACT must be administered [4].

In its Global Strategic Plan 2005-2015 [4] the RBM Partnership set the following targets for 2010:

- 80% of people at risk from malaria are using locally appropriate vector control methods such as long-lasting insecticidal nets (LLINs), indoor residual spraying (IRS) and, in some settings, other environmental and biological measures;
- 80% of malaria patients are diagnosed and treated with effective anti-malarial treatments;
- in areas of high transmission, 100% of pregnant women receive intermittent preventive treatment (IPTp); and
- the global malaria burden is reduced by 50% from 2000 levels: to less than 175-250 million cases and 500,000 deaths annually from malaria.

1.3. Malaria and poverty

A strong correlation between malaria and poverty at country level and at individual/household level has long been recognised [11]. However, the strength and the causality of the relationship are still not clear. Most likely causality runs both ways and communities living in malaria endemic areas are trapped in reinforcing cycles of poverty and disease [11-13].

Studies investigating the association between poverty and malaria at individual or household level have reported mixed results. Results depend on how poverty is measured and are often confounded by clustering and education. Certainly, the poorest are more likely than their better-off peers to get sick (because they are more exposed to health risks and they have less resistance to disease due to under-nutrition and other hazards typical in poor communities) and less likely to access preventive and curative health care [14]. Furthermore expenditures for health care are more burdensome to the poorest. But the pathways between poverty, economic activity and healthcare seeking are complex and multidimensional: farming may increase the risk of malaria, but the wealth created by the activity may allow farmers to protect themselves from malaria; other remunerative activities may both increase risk and reduce access to health services [12, 15].

At a global level, malaria incidence is undoubtedly concentrated in the world's poorest countries. A study showed that countries with intensive malaria had income levels 33% that of countries without malaria in 1995, and grew 1.3% less per person per year between 1965

and 1990, controlling for confounding factors. The correlation could be explained in many different ways. As countries get richer, housing is improved, more public funding is available for control programmes (insecticide residual spraying, draining of swampland, etc) and strengthened health systems provide better quality of care. Conversely, it is also argued that malaria impedes long term economic growth and development by discouraging tourism and foreign investment and affecting schooling and worker productivity [11, 16].

The reduction of malaria, but more generally the improvement of public health, is therefore a key determinant of development. The inclusion of health related targets in Millennium Development Goals [17] reflects an acknowledgement by the international community that health and access to health are intrinsically linked to development. These goals have contributed to mobilise resources and improve the co-ordination of initiatives to fight malaria, but also HIV/AIDS and tuberculosis, in many countries. International initiatives and foundations which have made a significant contribution to malaria control include the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), The Bill and Melinda Gates Foundation (BMGF), the World Bank's Malaria Booster Programme, and the US President's Malaria Initiative (PMI).

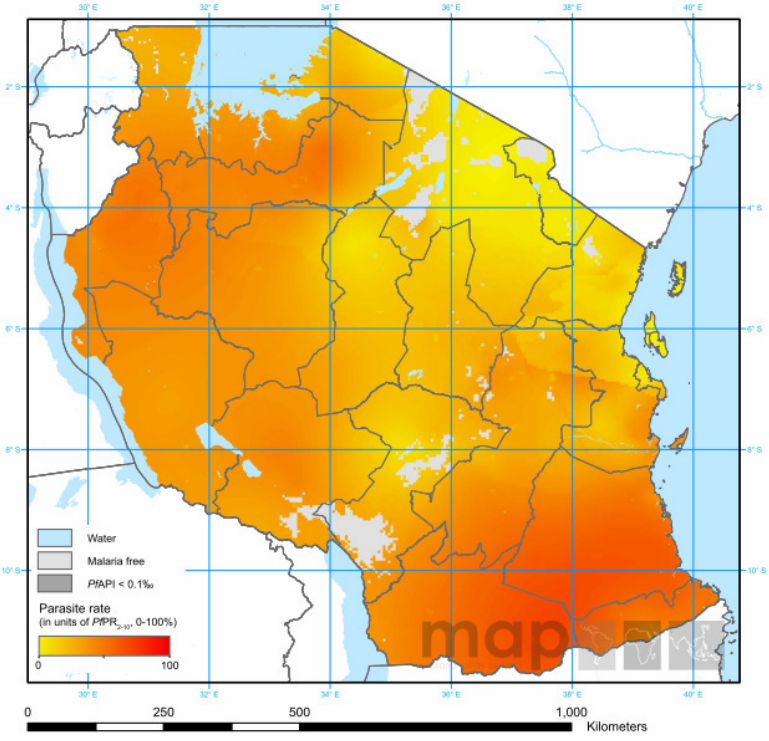
1.4. Malaria in Tanzania

In Tanzania malaria is a major public health problem. Malaria is endemic in almost all parts of the country (Figure 5). It accounts for over 30% of the disease burden and is a threat to every one of the estimated 32 million people (94% of the population) living in areas where transmission is possible The disease is estimated to cause between 100,000 and 125,000 deaths a year and is the leading cause of outpatient attendance for children under the age of five (38%) and for all other patients (32%) [18]. An estimated D 65 million is spent on the prevention and treatment of malaria in Tanzania each year, which amounts to 39% of all health expenditures and just under 1.1% of GDP [19].

Malarial control strategy

The current malarial control strategy is outlined in the National Malaria Control Programme's (NMCP) Medium Term Strategic Plan (MTSP) (2002-2007) and is based on strategies and targets from the 2000-2001 Roll Back Malaria Action Plan [18]. The strategy mainly promotes the use of ITNs coverage of prompt and effective treatment for malaria and the use of IPT of malaria among pregnant women. However it also includes other vector control measures such as IRS and epidemic prevention and control.

Figure 5. The spatial distribution of malaria endemicity in Tanzania (source: MAP [20])



Vector control with ITNs- Tanzania's current vector control strategy has mainly relied on intensive promotion of ITN use through a public private partnership approach. The National Insecticide Treated Nets programme (NATNETS) has four key components: 1) the ITN Cell in the NMCP coordinates and facilitates all ITN activities in the mainland of Tanzania; 2) the SMARTNET social marketing project creates demand, promotes behaviour change, supplies free-of-charge insecticide kits to the Tanzanian net manufacturers for bundling with all nets distributed on the Mainland and distributes subsidized insecticide re-treatment kits to the commercial sector; 3) the Tanzania National Voucher Scheme (TNVS) distributes discount vouchers to pregnant women and infants through clinics and dispensaries, allowing them to purchase ITNs from private retailers at approximately 75% discount [21-22] and 4) a mass "catch-up" distribution campaign to provide free LLINs to all children under five years since coverage of risk groups increased too slowly under the voucher scheme [23]. A national net re-treatment campaign is being carried out at the same time as the catch-up campaign.

Malaria case management - Until 2001 chloroquine was the main antimalarial used, but due to high levels of chloroquine resistance it was officially withdrawn and replaced by sulphadoxine-pyrimethamine (SP). Amodiaquine was the second line treatment and quinine third line and first choice in severe malaria. In 2006, SP was in turn abandoned in favour of Artemether-Lumefantrine (ALu, trade name Coartem®, Novartis AG). Quinine remained the

drug of choice for severe malaria. Through funding from the GFTAM the drug is provided free to all government health care facilities in Tanzania where it should be made available free to children under the age of five in accordance with the exemption policy and at asubsidised price of TSH 300 (USD 0.25) to all other patients. Subsidised ALu is also available in the private retail sector in Accredited Drug Dispensing Outlets (ADDOs). In all other private drug retail outlets it is currently unaffordable for most of the population at its current maker price of USD 8-10 for an adult dose.

Intermittent Preventive Treatment (IPT) - IPT with SP is recommended for pregnant women during antenatal visits as a prophylactic measure during pregnancy. The two doses should be given as directly observed therapy at 20-24 weeks and 28-32 weeks gestational age.

IRS - Although Tanzania was one of the pioneers in launching indoor residual spraying in the 1960s and 1970s, it has never been used systematically enough to have a significant impact. At present, the country plans to re-introduce IRS as a complement to the ITN programme to prevent and control malaria epidemics in 25 epidemic prone districts [24].

Epidemic prevention and control - The Malaria Epidemic Early Detection System (MEEDS) is based on plotting weekly and monthly malaria cases into a monitoring chart designed with a threshold representing alert and action lines derived from retrospective data for each health facility. Through this system, epidemic prone districts are required to note and report any substantial increase in the number of malaria cases and deaths.

Coverage achieved to date

A nationally representative survey has been conducted to provide information on the status and progress of the MSTP in 2007-08 [25] and results can be compared with a similar survey conducted in 2004-05 [26]. Results show improvements, but targets set for 2007 have not been reached. More than half of the children reported to have fever were given an antimalarial drug to treat the fever but only 34% were treated on the same day or the next, which is far below the 60% target for 2007. Household ownership of nets (both treated and untreated) increased in the country after the implementation of the ITN programme from 46% in 2004-05 to 56% in 2007-08 but ownership of ITNs is much lower (23% in 2004-05 and 39% in 2007-08). This resulted in 34-36% of children and pregnant women sleeping under a mosquito net and 26-27% under an ITN the night prior to the survey. This means that the 60% target set for 2007 was not reached. In 2007-08 57% of women with a live birth in the two years prior to the survey reported taking IPTp but only 30% took the two recommended doses. The 60% target set for 2007 was therefore not reached for IPTp either.

Coverage with IRS and MEEDS has not been implemented on a national scale. Since 2007, IRS operations in Mainland Tanzania have been limited to two districts (Muleba and Karagwe) in Kagera Region, where repeated spraying has been carried out in more than 10% of households. Plans are underway to scale up IRS coverage to about half the districts in Mainland Tanzania by the end of 2013. MEEDS mechanisms have been established in 19 districts of the county (less than 15%) [27].

1.5. Strategies to improve access to malaria treatment

Access to health services and interventions in developing countries is a much debated topic and has received an unprecedented level of funding in recent years. The impact of the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement on access to essential drugs in developing countries has been debated from a legal and trade related point of view [28-29]. A number of Public-Private Partnerships (PPPs) have been set up to develop much needed new efficacious treatments and prevention tools. As far as malaria is concerned the Medicines for Malaria Venture (MMV) [30], created in 1999, currently manages the world's largest malaria research and development portfolio and has a number of ACTs in its pipeline. However, resource-limited governments often need support from donor organisations to be able to purchase the newly developed medicines. This is especially the case for the ACTs as this new generation of drugs can be up to 10-20 times as expensive as conventional antimalarial monotherapies such as SP and chloroquine. The GFATM is the leading donor mechanism which supports governments to purchase newly developed malaria medicines. Thanks to support from the GFATM by 2009 108 million malaria drug treatments were delivered in 140 countries [31].

However, the availability and affordability of effective drugs at country level does not necessarily imply that people get the care they need. This is evidenced by recent surveys conducted between 2007 and 2008 in 11 African countries which found that despite large increases in the number of antimalarial treatments supplied through the public health sector, only 15% of children with fever were treated with ACTs [32]. Clearly there are many other issues that affect access to treatment. Care not only involves drugs but also appropriate infrastructure, health care personnel, diagnostic capacity, effective drug procurement systems and functioning financing or exemption mechanisms (provider level factors). Willingness and ability to pay, access to alternative health care providers, proximity to points of health care, trust in the health care system and providers also play an important role in determining health care seeking (user level factors).

Several interventions have been proposed and tested to improve access to malaria treatment by targeting providers or users. Smith *et al.*[33] recently conducted a systematic review on this topic. Interventions aimed at providers included optimising case-management and services in health facilities or improving dispensing practices of drug shop attendants as well as training community health dispensers. Two general approaches to improving user malaria treatment practices have been pursued: health education campaigns and interventions that specifically provide information on how to take anti-malarials, including pre-packaging and pictorial and verbal instructions.

The Integrated Management of Childhood Illnesses (IMCI) is a strategy designed to address major causes of child mortality in health facilities by targeting the behaviour of health facility providers. IMCI includes both preventive and curative interventions and it is designed to improve the case-management skills of health workers as well as to strengthen health system support for child health-service delivery. Studies that have tested the effectiveness of this strategy found higher levels of appropriate treatment of malaria in the facilities that had received the intervention compared with non-intervention facilities although the improvements were greater in Tanzania (88% versus 25%) [34] than in Uganda (49% versus 24%) [35].

WHO's strategy to improve access to malaria treatment has focused on the provision of antimalarial treatment through community health workers. This strategy, known as the Home Management of Malaria (HMM), [36] targets both users and providers. It comprises three fundamental pillars: 1) the selection and training of community members as community medicine distributors (CMDs) to correctly dispense anti-malarial medicines; 2) an information, education and communication campaign to sensitise caregivers to the importance of adhering to the correct treatment schedule; and 3) making effective antimalarial medicines available in every village, close to home, in unit-dosed and user-friendly blister packages. Although HMM clearly improves access to antimalarials, a review of the major studies carried out in Africa so far did not find substantial evidence that it has an impact on health outcomes [37]. However, proponents of HMM argue that the studies reviewed did not use pre-packaged antimalarial drugs, which are a key element of the strategy. Studies to confirm the validity of HMM in the era of ACT are currently underway [38].

A number of interventions have aimed at improving access to malaria treatment by improving the quality of care available in the private retail sector for drugs. The motivation for these initiatives comes from extensive research conducted in sub-Saharan Africa, which has shown that the private retail sector for drugs plays a very important role as a source of

antimalarial treatment [39-40]. Goodman *et al*. recently conducted a review of the interventions implemented to date [41]. A total of 16 interventions to improve malaria-related activities of medicine sellers in sub-Saharan Africa were identified (five in Nigeria, four in Kenya, two each in Uganda and Ghana and one each in Tanzania, Madagascar and Zambia). All involved a combination of training and job aids for providers as well as demand generation and consumer information components for users. Some also included pre-packaged drugs. The two key findings from the review were 1) medicine sellers are interested and willing to participate and 2) targeting this sector can have a substantial impact on the quality of care delivered and overall treatment outcomes.

On the basis of these positive experiences, a number of initiatives have been launched to distribute subsidised ACTs through the private sector. In 2005, MMV recognised the need for a concerted strategy to ensure the uptake of the products from its pipeline [42]. In collaboration with the Ugandan Ministry of Health, MMV Access piloted a study to assess if the provision of subsidised antimalarials through the private sector improves access, displaces ineffective products, and leads to health impact. In 2007 the Tanzanian Ministry of Health and Social Welfare and the Clinton Foundation [43] launched a pilot ACT subsidy project to assess the impact of a subsidy on the price and uptake of ACTs as well as the effect of a suggested retail price on those outcomes. Positive results from the Tanzanian and Ugandan experiences [44-45] have informed the creation of a global subsidy for the distribution of ACTs [46]. This subsidy, now known as the Affordable Medicines Facility for malaria (AMFm) is managed by the GFATM and aims to make ACTs available at the cost of the previous generation of antimalarials by negotiating with the manufacturers to supply very low-cost ACTs to first line buyers. It is expected that drugs will be available at about USD 0.20-0.50 to patients [47]. Tanzania is among the 11 AMFm pilot countries and implementation is expected to start in 2010.

Rapid Diagnostic Tests (RDT) for malaria have the potential to greatly improve the quality of management of malaria infections in areas when the main alternative form of diagnosis, high quality microscopy, is not readily available. It can therefore improve access by targeting drugs to only confirmed cases. The symptoms of malaria are very unspecific and current guidelines in many African countries recommend the presumptive treatment of fever with antimalarial drugs. However this strategy implies that the possibility that the fever is caused by another cause is overlooked and this leads to higher morbidity and mortality due to delay in giving appropriate treatment. Furthermore it leads to wastages of drugs and may foster parasite resistance [48]. Conversely, RDTs are easy-to-use and inexpensive and two meta-analyses have shown high levels of sensitivity and specificity [49-50]. It has been argued that

the introduction of the AMFm should be accompanied with the rollout of RDTs in drug shops to minimise unnecessary sales [51].

1.6. The Access to Health Livelihood Framework

An access to health care framework has been developed in the frame of the ACCESS programme as a conceptualisation of the various issues that affect access to malaria treatment. This framework places access to health in the broader context of livelihood insecurity and as such focuses on the community and health system barriers to accessing health care. Access is viewed as the interplay between the health care system on one side and individual/household's needs and resources on the other. The degree of fit between the two can be examined along the five dimensions of **availability**, **accessibility**, **affordability**, **adequacy**, and **acceptability** (Table 1). However, high levels of access only result in better health if the services are utilised and if the **technical quality of care** is adequate (Figure 6). Each of the five dimensions of access and quality of care is discussed in the next section with practical examples and references to malaria case management in Tanzania and the study area.

Figure 6. The ACCESS framework (source: Obrist *et al.* [52])

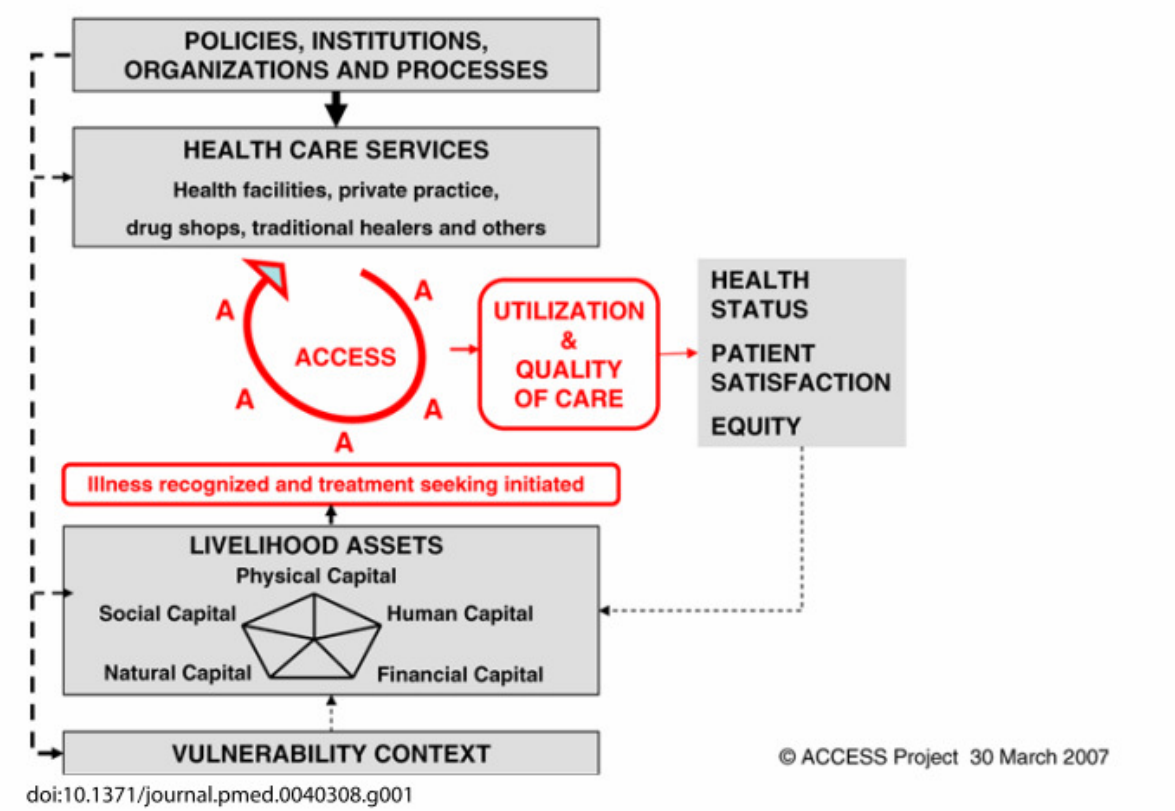


Table 1. Five dimensions of access to health care services (adapted from Obrist *et al.* [52])

Dimension	*Definition*	*Question*
Availability	The existing health services and goods meet client's needs	What types of services exist? Which organizations offer these services? Is there enough skilled personnel? Do the offered products and services correspond with the needs of poor people? Do the supplies suffice to cover the demand?
Accessibility	The location of supply is in line with the location of clients	What is the geographical distance between the services and the homes of the intended users? By what means of transport can they be reached? How much time does it take?
Affordability	The prices of services fit the clients' income and ability to pay	What are the direct costs of the services and the products delivered through the services? What are the indirect costs in terms of transportation, lost time and income, bribes, and other "unofficial" charges?
Adequacy	The organization of the health care meets the clients' expectations	How are the services organized? Does the organizational set up meet the patients' expectations? Do the opening hours match with schedules of the clients, for instance the daily work schedule of small-scale farmers? Are the facilities clean and well kept?
Acceptability	The characteristics of providers match with those of the clients	Does the information, explanation, and treatment provided take local illness concepts and social values into account? Do the patients feel welcome and cared for? Do the patients trust in the competence and personality of the health care providers?

1.7. Access to malaria treatment in Tanzania

Availability

The health care system in Tanzania is relatively well developed compared with other sub-Saharan African countries but treatment is not always available to people. The number of people per health facility/drug outlet is often used as a measure of availability of sources of care. In Tanzania, there is roughly one health centre for a population of 50,000 and a dispensary for a population of 10,000. However, the public sector is highly understaffed. The estimated ratios of currently active professionals per 100,000 population are 39 for nurses, 2.5 for physicians and 25 for medical cadres (i.e. medical officers, assistant medical officers and clinical officers) [53].

In addition, drug stock-outs are a recurrent problem in dispensaries and health centres. A study carried out in two districts in 2007 found that drug availability, defined as the presence of tracer items on the day of the survey, was on average 75% in hospitals and only 53% in public health facilities [54]. The Medical Stores Department (MSD) is responsible for the procurement, storage and supply of drugs to hospitals and health care facilities. MSD currently administers three different supply chains: 1) bulk distribution of essential drugs; 2)

distribution of kits and Indent packs and 3) and vertical programmes. The kit is a “push” system whereby each level of health facility receives a pre-determined quantity of medicines. In the indent “pull” system facilities decide on the quantity of products required and order them accordingly. Tanzania is in the process of converting the entire country to an Integrated Logistics Systems (ILS) which is an extension of the Indent system. Public health facilities experience regular stockouts in both kit and Indent systems but availability is much better with vertical programmes. Reasons for frequent stockouts include errors in quantification and forecasting by MSD (kit system) or by health facility staff (indent system) [55]. Stockouts also frequently cascade down from regional and central stores as MSD has to comply with long and complicated tendering procedures and does not always receive timely funds from the Ministry of Health and Social Welfare.(MOHSW). Generally stock-outs are more severe in dispensaries and health centres than in hospitals as the latter can more easily procure from the private drug market [54].

Given the shortcomings of the health care system commercial retail outlets also play an important role in the provision of malaria treatment close to people. The private retail sector for drugs in Tanzania includes three types of licensed drug shops and general shops. Although pharmaceutical regulation does not reach its targets, the retail market for drugs in Tanzania is fairly well ordered, even in rural areas [56]. Pharmacies have to be run by a pharmacist and are allowed to sell all registered prescription only drugs which are referred to as Part I drugs. Drug shops (also know as *duka la dawa baridi*) may sell Part II drugs such as analgesics and need to be staffed with a medically trained vendor. In addition since 2008 a new class of registered outlets known as Accredited Drug Dispensing Outlets (ADDOs) (also known as *duka la dawa muhimu*) is being rolled out country-wide. ADDOs are allowed to sell all Over the Counter (OTC) drugs, antimalarials and a selection of antibiotics and are staffed by formally trained retailers [57]. According to Goodman *et al.* [58], general shops are legally not authorized to stock any drugs but are in practice tolerated to sell common OTC drugs such as painkillers. Mobile drug sellers are not common in most of Tanzania. There are around 350 Part I pharmacies in Tanzania, mostly in the urban areas, and over 8000 Part II drug shops [59].

Affordability

In 1993 the Government of Tanzania introduced a policy of cost-recovery for health care as part of a Health Sector Reform (HSR). The rationale for the reform was to generate additional revenues to improve the availability and quality of health care services. One of the key components of the cost recovery scheme was the introduction of user fees for health care in public facilities. The reform also included schemes to protect the vulnerable and very

poor, such as exemptions (free public health care for children under five years, pregnant mothers and the elderly) and waivers (temporary entitlement to free care to those considered in need but unable to pay). Financing mechanisms such as the Community Health Fund (CHF), a district-level pre-payment scheme for primary care services, were also introduced to support the rural population and those working in the informal sector [60].

Findings from the study area show that the introduction of user fees has made health care less affordable because exemption, waiver and pre-payment mechanisms are not implemented properly. This is in line with various reviews which suggest that the introduction of user fees is more likely to reduce utilisation in the long term [61-63]. A study found that families visiting government facilities in a district (Kilombero) which had implemented a user-fee system were found to pay up to 15 times more than families in a district without (Ulanga) [64]. The least poor paid 2.5 times more than the poorest in seeking care for their child. Given that there is no evidence of differences in morbidity, this suggests that poorer people are not getting the care that they need because they cannot afford it. Experience to date also shows that the CHF fails to support the most vulnerable in meeting the costs of health care because of its low level of enrolment (10% of the target population after more than 10 years of operation) and due to various management issues [65].

In addition to all the official charges directly related to care and treatment, patients need to meet many other costs. A study was carried out in Tanzania in 2001 in two districts where cost sharing had been introduced (Kilombero and Ulanga) and one where there were no official fees in dispensaries (Rufiji) [66]. Results showed that on average about three quarters of the costs of treatment for fever is for drugs, the remainder spent on transport, food and lodging and non-drug fees such as registration, consultation, laboratory tests and syringes. Payments were reported in some government facilities where cost sharing had not been introduced, indicating that patients may have been unaware that payments were unofficial.

Accessibility

Tanzania has a fairly extensive network of health facilities throughout the country, but they are not evenly spread. The proportion of people living within a 5 km range from a source of care or treatment is usually used as a measure of accessibility. In Tanzania, it has been estimated that 75% of the people live less than 5 km from a health unit providing both curative and preventive services (68% in rural areas, 98% in urban areas) [53]. However most health facilities are found in the larger population and market centres. Usually the least poor are clustered near large centres while the poorest are widely dispersed and face the longest journeys to sources of care. A study carried out in southern Tanzania found that

children living over 5 km from a health facility had lower vaccine coverage, fewer nets, more anaemia, poorer care-seeking and higher infant mortality than those living closer [67].

The role of the private retail sector is crucial in terms of accessibility since shops can extend the coverage of treatment to very rural areas. A study carried out in the study area before the introduction of ACTs reported that over 85% of households live within a 5 km range of a commercial outlet selling antimalarials, although they often do not reach out into small villages or very remote areas [68]. The introduction of highly subsidised ACTs as a first line treatment for malaria in Tanzania in 2006 has sparked many debates on the best way to deploy these new and efficacious antimalarials in the retail sector. Confining ACTs to registered pharmacies, 76% of which are all concentrated in the major cities, would have substantially reduced accessibility.

Ensuring accessibility to sources of health care to mobile or dispersed communities is especially challenging. There are thought to be approximately 1.2 million pastoralists in Tanzania who move to very distant pastures to find suitable land and therefore live a nomadic or semi-nomadic existence [69]. Moreover, in many parts of the country such as in the study area, people move to sometimes very distant temporary shelters in their fields during the cultivation period. Geographical distance translates therefore not only in transport cost but also loss of income. The extent to which these factors influence access to malaria care has not been fully explored.

Acceptability

According to an early study carried out in the study area [70] the community gives great weight to inter-personal skills and perceptions of technical skills are conditioned by the judgement of inter-personal skills. The most severe community criticisms concerned the rudeness and insensitivity of staff. The poor attitudes of health staff was directly linked to the poor state of the infrastructure, lack of emergency curative services and to the late opening hours and long waiting times. Patients were also concerned about the lack of diagnostic facilities. The process of curative care is expected to begin with diagnosis, although obtaining drugs is amongst the most important factors determining health care use.

Adequacy

A study carried out on people's ability and willingness to pay for health care good provides a good example of how the organisation of the health care system is not adapted to client's socio-economic situation. The study showed that meeting the costs of a traditional treatment

is usually less burdensome to the individual or the household for two reasons: family and kin-members are under social pressure to contribute towards the payment of the type of diseases for which traditional treatment is sought; and many healers offer alternatives to cash payments, such as compensation in kind or in work, or payment on a credit basis. Malaria is a disease for which bio-medical treatment is considered the most effective and is usually treated in health facilities. Consequently people seeking malaria care usually do not benefit from wide community support and are faced with rigid payment modalities which are difficult to manage [71].

Technical quality of care

A number of problems with regards to the quality of care provided in the formal health sector have been reported in Tanzania. A report published in 2002 stated that between 56% and 80% of patients dying of suspected malaria had attended formal health services during their final illness and only 50% of children under-five years of age with uncomplicated malaria and 54% with severe malaria were correctly treated in the health facilities [18]. This was attributed partly to lack of diagnostic capacity, since laboratory services were inadequate and malaria parasitological confirmation was carried out in only 5-7% of total malaria reported cases. In addition, staff was often poorly trained and not adequately supervised. Only 11% of health workers had been trained in improved malaria case management in the previous two years. Council Health Management Teams had skills on supervisory activities but were lacking specific tools for malaria control issues and few of them had been trained on malaria case management. IMCI has now been integrated into all district health plans in Tanzania [64] but no nationwide assessment of its impact has been conducted to date. In addition since 2009 Tanzania is rolling out RDTs in the country's health facilities.

2. Study description

The ACCESS programme is a collaborative undertaking between the Ifakara Health Institute (IHI) in Tanzania and the Swiss Tropical and Public Health Institute (Swiss TPH), supported by the Novartis Foundation for Sustainable Development (NFSD). The aim of the programme is to improve access to prompt and effective malaria treatment with a set of integrated interventions targeting both users and providers. The programme was implemented in two phases and this thesis is concerned with the evaluation of its first phase (2004-2008). Section 2.1 outlines the aims and specific objectives of this thesis. The study area is described in section 2.2 with a focus on its physical and human geography since details on the health system have already been outlined in Section 1.7. Section 2.3 provides a detailed description of the interventions that are evaluated. This includes ACCESS interventions and the nation-wide change of treatment policy for malaria and the roll-out of the Accredited Drug Dispensing Outlets (ADDOs). Section 2.4. describes the data collection activities on which this evaluation is based.

2.1. Aims and objectives

The overall **aim** of this thesis is to provide an evidence base to assess effectiveness of the ACCESS interventions implemented between 2004 and 2008. This assessment is based on the input-output-outcome-impact framework [72]. For a programme to achieve its goals, *inputs* such as money or staff time must result in *outputs* showing that the programme is being implemented as planned. If these outputs reach the populations for which they were intended, the programme is likely to have positive short term effects or *outcomes.* These positive short-term outcomes should lead to a longer term *impact* on the health and wellbeing of the targeted populations.

Based on this framework the **specific objectives** of the studies presented here is to

1. Assess the output of the programme in terms of
    - accessibility
    - availability
    - affordability
    - use

    of malaria treatment from both the private retail sector and public health facilities (Chapter 3);

2. Assess the health outcome of the programme by estimating the proportion of fever cases in children under the age of five and in the whole population which were treated with an antimalarial/recommended antimalarial within 24 hours of onset of fever (Chapter 4);

3. Asses the impact of the programme on the community and health facility burden of malaria by measuring changes in the
    - incidence of community reported fever and convulsions in children less than five years (two week recall)
    - under five mortality rates
    - health facility utilisation for fever

    (Chapters 5 and 6).

2.2. Study area

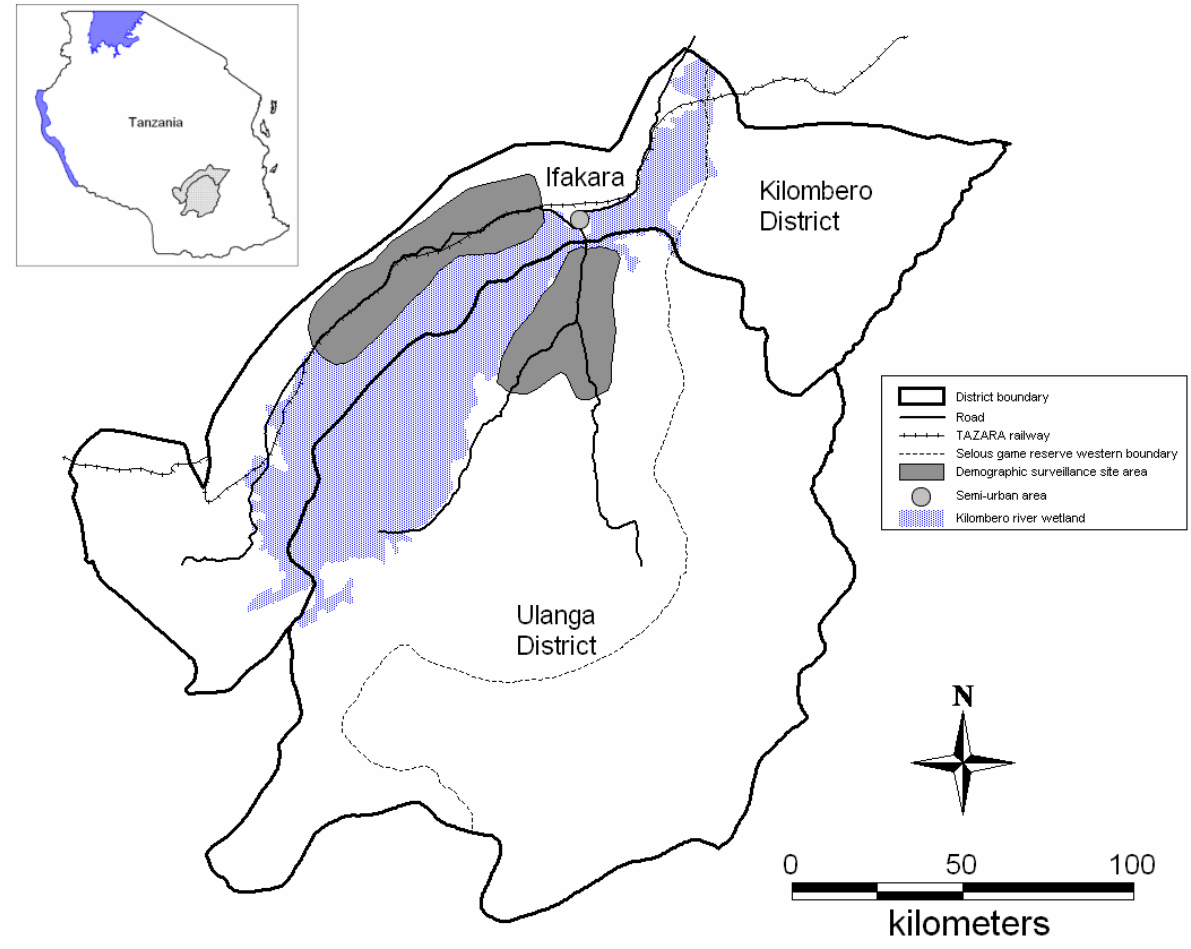
The programme's intervention area comprises the two districts of Kilombero and Ulanga in the south-east of Tanzania (Figure 7). The Kilombero River separates the two districts and forms the vast Kilombero Valley floodplain. Large parts of this valley are flooded during the rainy season which usually lasts from November to May. The valley is delimited by the Udzungwa Mountains in the north and the Mahenge Mountains in the south. In 2002, there were 517,000 people living in the 109 villages of the two districts. Ifakara, the administrative capital of Kilombero, is the major settlement in the valley with a population of approximately 46,000. Ulanga's capital Mahenge is smaller with 7,300 inhabitants.

Most people rely on subsistence farming for their livelihoods. Over 95% of the population reported farming as their main activity [73]. Rice is the main staple food and the most important cash crop in the area. Maize and cassava are also grown, but mainly for household consumption. Over 80% of total farmed land is used for growing paddy and farmers sell about 50% of what they grow [74]. Most of the rice paddies are lowland rainfed and production per hectare is fairly low compared to its potential [75]. This is explained partly by the low uptake of new high yield varieties, the reduced use of fertilisers and the reliance on manual labour for land preparation and weeding [74, 76]. As a consequence rice production and people’s livelihood in the area is extremely dependant on adequate rainfall.

The climatic and ecological conditions in the floodplain are favourable for mosquito breeding. Malaria transmission in the area is intense and perennial with differences between the rural and semi-urban settings. Overall transmission has been declining over the past 10 years. A

study conducted in the area between 2001 and 2003 reported an Entomological Inoculation Rate (EIR) of 349 infective bites per person per year (ib/p/y) [77], but according to recent data it has declined to 81 ib/p/y [78]. EIR data for Ifakara town suggest that the transmission rate is about a log order smaller than in the surrounding rural areas [79].

Figure 7. The Kilombero and Ulanga DSS area



2.3. Interventions

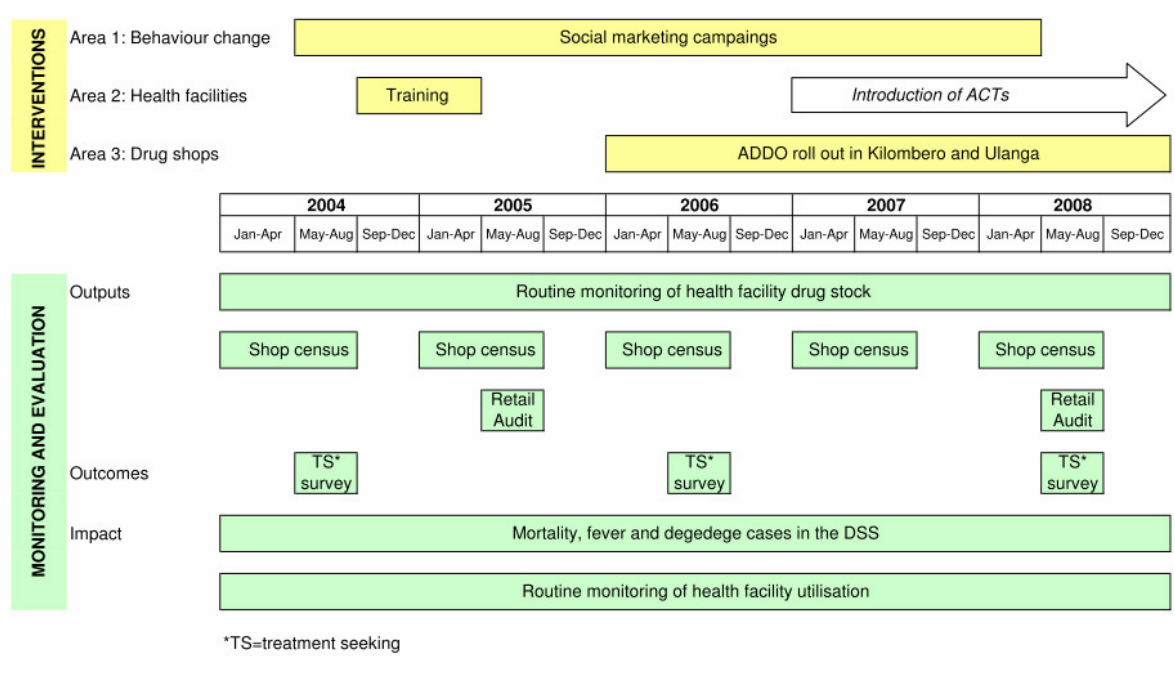
The ACCESS programme's interventions are conducted and studied at **user** and **provider** level:

- at *user level* a social marketing approach aims at creating demand for appropriate malaria diagnosis and treatment in the community;
- at *provider level* health facility and drug shop training, quality management, improved supportive supervision and new diagnostics aim to strengthen the supply of quality malaria case-management.

In addition to the activities implemented directly by the programme ACCESS also takes into consideration national interventions such as the 2006 changes of first line treatment from SP to ALu.

The main areas of intervention that are evaluated in this thesis are described below and summarized in Figure 8.

Figure 8. Timeline with ACCESS I interventions and monitoring and evaluation activities



Intervention area 1: Behaviour change campaigns for prompt and appropriate health care seeking

A social marketing approach was implemented to improve knowledge and awareness of malaria and to promote prompt and appropriate treatment seeking from reliable sources. The main target audience of the campaign were mothers and caretakers of children under five years of age and pregnant women. Messages stressed the importance of prompt recognition of malaria symptoms and immediate correct treatment with the recommended first-line drug, i.e SP until end 2006 and ALu from 2007 onwards. Health facilities and licensed drug stores (pharmacies, part II drug stores and Accredited Drug Dispensing Outlets i.e. ADDOs) were promoted as sources of proper treatment and advice. Prevention methods, such as the use of ITNs and IPTp were also advocated. Finally, one set of messages highlights high fever with convulsions (locally known as "degedege") as a sign of severe malaria that can and should be treated at health facilities (rather than by traditional healers) [80-81]. ACCESS

messages were in line with malaria-related messages on key family practices promoted by the community-based IMCI [82].

Communication channels and materials to disseminate behaviour change messages were developed to reach a poor rural audience. Road shows were the main vehicle for the campaign and included:

1. Dancing competitions to attract a large audience;
2. Comedies and role plays portraying appropriate treatment seeking and consequences of delaying treatment;
3. Public lectures on malaria transmission, signs and symptoms, dangers of malaria for young children and pregnant women, prevention and correct treatment. A question-and-answer sessions at the end of each part allowed interaction with the audience and distribution of promotion-materials (e.g. stickers, leaflets, T-shirts);
4. Cinema shows featuring stories on prompt and effective malaria treatment.

Other social marketing activities were developed to complement the road shows. Remote villages that were inaccessible with the truck were reached by a small 4WD vehicle branded with behaviour change slogans and airing radio spots. In addition permanent billboards were erected in major villages along the main road and posters affixed in public places. Special campaigns were implemented in Mother and Child Health clinics. They were targeted especially at pregnant women and mothers of young children who may not attend road shows if they overlap with household duties. During special sessions, ACCESS health promoters and MCH clinic staff informed mothers about malaria, its prevention and its proper treatment. The benefits of malaria prevention using ITNs and IPTp were particularly emphasised.

Intervention area 2: Improved quality of malaria treatment in health facilities

Health care services of good quality are a core element for the delivery of effective diagnosis and treatment for malaria. As a result of the social marketing activities, the demand for quality services is expected to increase. In order to meet this demand, health facility staff must be in the position and willing to deliver good quality of care. The ACCESS programme aimed to improve quality of care with a focus on the following areas:

1. Correct diagnosis through the proper use of the IMCI algorithm and/or with improved laboratory diagnosis;
2. Rational prescription of antimalarials, antipyretics and other drugs;
3. Appropriate advice on prescribed treatment and malaria prevention.

Key activities of this component include initial refresher training for health facility staff on malaria treatment, followed by the strengthening of routine supportive supervision and the implementation of a quality management scheme in all health facilities. Training was based on IMCI algorithms for diagnosis and treatment, which have been shown to be cost-effective in improving quality and efficiency of child health care in rural Tanzania [34]. A protocol for the refresher training was developed in close collaboration with the Council Health Management Teams (CHMT) of Kilombero and Ulanga. The training was targeted at clinical staff, lab technicians, and medical aids of public as well as private health facilities. It was carried out by the CHMT, appointed trainers and ACCESS staff with financial resources from the district and ACCESS.

Intervention area 3: Improved malaria case management in drug selling shops

Drug shops are often preferred to health facilities as a first treatment action [39-40]. However, despite the important service they offer drug shops are often poorly regulated. Common opportunistic practices include illegal stocking of prescription-only medicines, the use of unqualified staff and referral by health facility staff to private outlets in which they have a financial stake [56, 83-84]. This not only leads to bad treatment outcomes but can also foster the development of resistance to drugs. Experiences in Kenya [85] and Mali [86]) showed that training private drug retailers can considerably improve the services they offer. The programme's original plan to train general shop keepers had to be withdrawn because Tanzanian drug regulations do not allow general shops to sell the first-line antimalarial drugs (SP; or ACT since end 2006). Instead the ACCESS programme supported the Accredited Drug Dispensing Outlets (ADDOs).

The aim of the ADDO programme is to improve access to basic medicines by upgrading all Part II drug stores to well regulated and properly operated private medicine outlets manned by trained personnel [57]. ADDOs are the result of an innovative public-private partnership headed by the Ministry of Health and Social Welfare (MOHSW) through the Tanzanian Food and Drug Administration (TFDA) and with technical assistance from Management Sciences for Health (MSH). The ADDO programme involves a combination of dispenser training, incentives, accreditation and regulation with efforts to increase customer demand for quality products and services. ADDO operating standards include premise upgrades, minimum entry-level education and completion of a five week training curriculum. Incentives for owners to upgrade their existing premises and to open new outlets in underserved areas include business management training and link with a microfinancing bank [87]. The BMGF provided initial funding for the pilot projects in the Ruvuma region in 2002-2005 [88]. Motivated by the positive results from the pilot region, TFDA and the MOHSW rolled out the programme to

Rukwa and Mtwara Regions with funding from the government of Tanzania and to Morogoro region with financial support from USAID. Currently the MOHSW/TFDA plans are to convert most Part II drug stores into ADDOs by 2010 [89].

ADDOs are allowed to dispense a limited range of prescription-only drugs. Ideally at least one ACT should be available through this channel, most logically the one recommended as first-line treatment in the country (ALu, brand name Coartem®). For the districts of Kilombero and Ulanga, ACCESS could successfully negotiate the introduction of highly subsidized ALu in ADDOs. Subsidised ALu was made available in ADDOs in mid 2007 at the recommended retail price of ALu of TSH 500 (approximately USD 0.40) for children doses and TSH 1500 (approximately USD 1.30) for other patients. The ACCESS social marketing campaign promotes ADDOs as source of quality malaria treatment.

The programme's inputs – coverage achieved by 2008

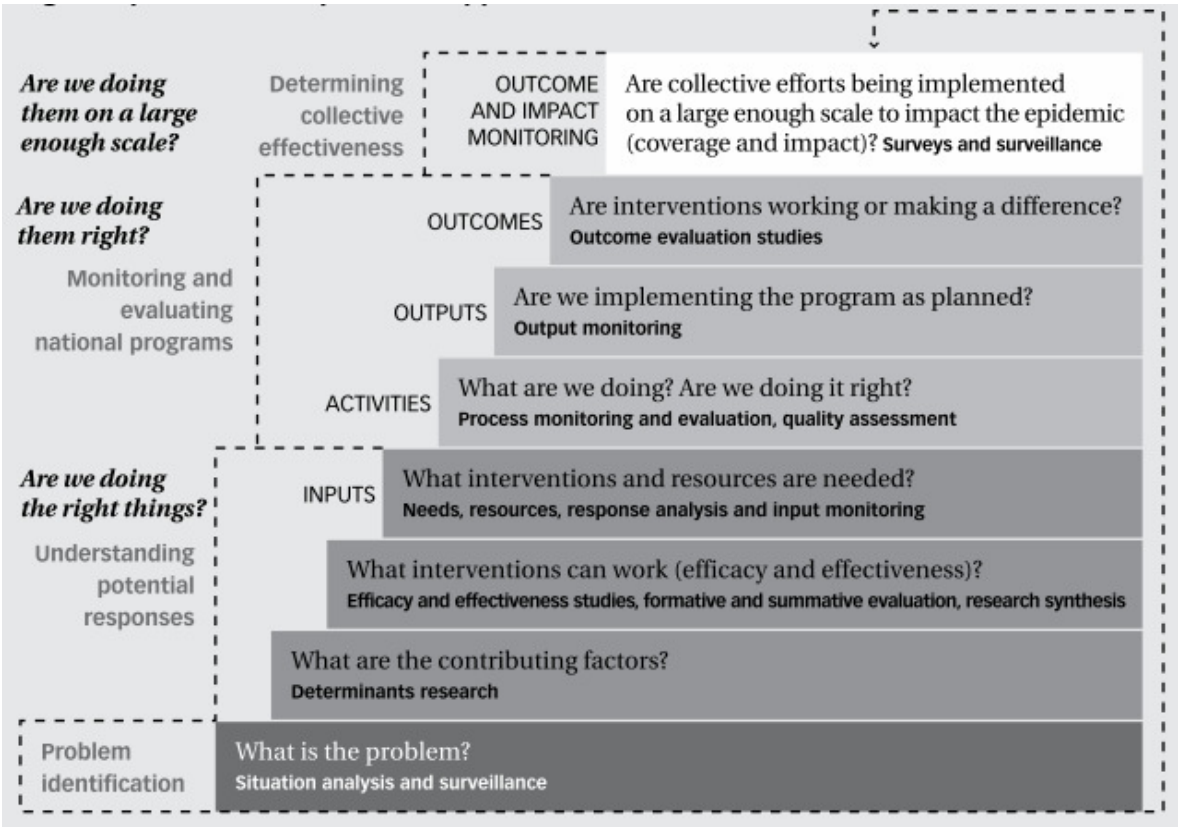
Between 2004 and 2008 the ACCESS and ADDO programmes achieved very high coverage. The ACCESS Social marketing road shows for improved treatment were conduced in 96% (78/81) of the villages in the Kilombero District and 95% (62/65) in the Ulanga District. In 2004 and 2005 93% (39/42) of clinical officers in the Kilombero District and 91% (94/97) of all health workers in the Ulanga District attended a refresher training on malaria case-management organised jointly organised by ACCESS and the CHMT. Between 2006 and 2008 135 ADDOs were opened the Kilombero district and 55 in the Ulanga district (equivalent to approximately three shops per 10 000 people in both districts). The switch from SP to ALu was successfully implemented in health facilities although actual introduction of ALu in health facilities was delayed until January 2007. Subsidised ALu was made available in ADDOs in the study area around July 2007.

2.4. Monitoring and evaluation

Monitoring and evaluation (M&E) activities provide the evidence base to ensure that programmes are fulfilling their objectives and to assess their effectiveness. *Monitoring* refers to the routine tracking of key elements of programme performance and epidemiological trends through record keeping, regular reporting and surveillance systems. *Evaluation* is the episodic assessment of the change in targeted results related to the programme's intervention. In other words, evaluation attempts to link outputs, outcomes and impact directly to an intervention (Figure 7) [72].

As experimental designs are often impossible or inadequate to evaluate large-scale programmes, this study relied on plausibility assessments [90]. With this type of design improvements are attributed to the programme and all other explanations can be formally discarded if improvements are found in every step of the causal pathway between intervention and impact. In an attempt to control for possible confounders, all other malaria control activities in both districts as well as other relevant parameters such as temperature and rainfall were closely monitored. A basic assumption was that the malaria transmission and other relevant epidemiological parameters remain largely unchanged during the period of observation with the exception of the factors that were monitored in the frame of the programme.

Figure 9. The Monitoring and Evaluation framework (source: GFTAM [72])



The M&E of the ACCESS programme was conducted in the area of the local Demographic Surveillance System (DSS) [73, 91]. The DSS served as a comprehensive epidemiological framework for the M&E activities. In the absence of a vital registration system, DSS field workers routinely record births, deaths and migrations for every household in a defined geographical area of 2400 km2 (Figure 7). Each household is visited every four months. The DSS area comprises 12 villages in Ulanga District and 13 in Kilombero District. The population in mid-2004 was around 74 000 people and increased at an average rate of 5%

per year, resulting in a population of just over 92 200 in mid-2008. There are six health facilities (three public dispensaries, one public health centre and two faith-based dispensaries) in the Kilombero DSS area and eight health facilities (five public dispensaries, one health centre and two faith-based dispensaries) in the Ulanga DSS area. The Designated District Hospital in Ifakara serves as a referral point for all the facilities in the study area. The DSS did not include Ifakara town at the time of the study but ACCESS monitoring and evaluation activities were also implemented there.

The M&E activities of ACCESS comprised qualitative and quantitative surveys, but this evaluation is based on a set of qualitative surveys which assessed the outputs, outcomes and impact of the programme. All the data from this evaluation was collected between 2004 and 2008. An overview of the timeline of the different M&E activities in relation to the programme's interventions is given in Figure 8. They are described in detail below and summarised in Table 2.

Table 2. Summary of ACCESS Monitoring and Evaluation (M&E) plan.

	Aim	*Primary Indicators*	*Surveys*
Output	Assess a difference in level of access to malaria treatment from private retail sector and health facilities	• Availability • Accessibility • Affordability • Use	1. Monitoring of drug stock in health facilities 2. Shop censuses 3. Retail audits
Outcome	Assess changes in treatment seeking	• Proportion fever cases in children under five and in all ages treated with an antimalarial within 24 hours of onset of fever	1. Treatment seeking surveys
Impact	Assess changes in the community and health facility burden of malaria	• Community fever and convulsions rate • Under-five mortality rate • Health facility and fever and malaria rate	1. DSS based surveys 2. Routine monitoring of health facility utilisation

Outputs

Output data was collected to assess a difference in the level of access to malaria treatment from the private retail sector and health facilities before and after the implementation of the interventions studied by ACCESS. This includes the 2006 change of treatment policy and the roll-out of ADDOs in the Kilombero and Ulanga districts. Results are presented in Chapter 3.

Indicators - Output indicators were based on the access to health framework developed within the ACCESS programme by Obrist et al. [52] (cf. Section 1.5 for details). The routine monitoring in health facilities and the shop censuses, combined with DSS data, provided information on *availability* and *accessibility* of sources of antimalarial drugs. The retail audits provided data on prices (and therefore, indirectly, on *affordability*) and *use* of antimalarial drugs. Separate studies which are not part of this evaluation assessed the quality of care in the private retail sector by using mystery shoppers [92].

Survey 1 : Routine monitoring of drug stock in health facilities - Every other month a team of trained field workers visited the ten public health facilities in the DSS area to collect end-of-month drug stock data from the Health Management and Information System (HMIS) ledger books, using validated data collection tools. Data could not be collected from the faith based facilities as they are not legally required to record drug stock in ledger books, rendering systematic collection of the data difficult. In 2004 the GPS locations of all the health facilities in the area were recorded with a hand-held GPS unit.

Survey 2: Shop censuses - Repeated cross sectional shop censuses were carried out every year in the Rural DSS area and in Ifakara town. All shops potentially selling drugs (general stores, kiosks, Part II drug stores and ADDOs) were visited by a team of nine trained field workers who recorded the outlet's stock and location.

Survey 3: Retail audits - Two retail audits of antimalarial drugs were conducted in the rural DSS areas during the shop censuses of 2005 and 2008. The retail audit included all outlets selling or dispensing drugs, i.e. all health facilities (public and faith-based) and drug shops (Part II drug shops and ADDOs), as well as the few general shops found to stock antimalarial drugs during the shop census. The retail audits enabled to estimate the prices and total antimalarial sales volume in the study area.

Outcomes

Outcome data was collected at community level to assess changes in treatment seeking following increased access to treatment and the implementation of a social marketing campaign which sensitised the community on the importance of prompt and effective treatment for malaria. Results are presented in Chapter 4.

Indicators - The primary outcome of interest was *the proportion of fever cases in children under the age of five and in all ages treated with an antimalarial within 24 hours of onset of fever* which is the indicator recommended by the Roll Back Malaria (RBM) partnership [93].

Other indicators related to the links of the community effectiveness chain developed by Hetzel *et al.* [88] as well as sources and actions for the treatment of fever.

Treatment seeking surveys - Three consecutive cross sectional surveys were conducted in the DSS areas and Ifakara Town in 2004, 2006 and 2008 to investigate treatment seeking for malaria and understanding of the disease. The interviewees included children and adults who had recently suffered a fever episode (caretakers responded to questions for children under the age of 12). The tool for data collection was a locally adapted Explanatory Model Interview Catalogue (EMIC) [94] which provided qualitative and quantitative data on patients' signs and symptoms associated with the fever episode (patterns of distress), as well as perceived causes and treatment seeking.

Impact

Health facility and community data was collected to assess changes in the community and health facility burden of malaria as a result of improved access to treatment and better treatment seeking for malaria. Results are presented in Chapters 5 and 6.

Indicators – The community burden of malaria is based on the monitoring of *under five mortality* rates and morbidity rates, which includes *community reported fever and convulsion* rates. Under-five mortality is a good indicator of the burden of malaria since malaria mortality is overwhelmingly concentrated in young children in malaria endemic countries. Therefore under five mortality is sensitive to changes in malaria-associated risk and captures both the direct and indirect effects of malaria [95]. Whereas fever refers to the incidence of un-complicated malaria, convulsions are a sign of progression towards cerebral malaria in children [96]. Both signs are not highly specific for malaria, but with other causes remaining stable, they provide useful markers of malaria morbidity. The health facility burden of malaria is based on *health facility fever and malaria* rates in children under the age of five.

Survey 1: DSS morbidity and mortality monitoring – Under five mortality rates were obtained from the DSS database. In addition ACCESS integrated the collection of community reported fever and convulsions cases (based on a two week recall) within the routine DSS data collection activities.

Survey 2: Routine monitoring of health facility utlisation data – Health facility utilisation data were collected continuously by the ACCESS project field workers from the Health Management and Information System (HMIS) records of all the private and public health facilities in the DSS area. Standard forms allowed rapid transcription of data from the health

facility records. The data collected included all in-patient and out-patient diagnoses disaggregated by age group (children under the age of five and all other patients) on a monthly basis. The combination of this data with population data from the DSS enables the calculation of fever and malaria health facility rates (where a fever is defined as any case diagnosed as either malaria pneumonia, respiratory infections, measles, typhoid fever or urinary tract infection).

3. Improvements in access to malaria treatment in Tanzania after switch to Artemisinin Combination Therapies and the introduction of Accredited Drug Dispensing Outlets – a provider perspective

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3.1. Abstract

Background

To improve access to treatment in the private retail sector a new class of outlets known as Accredited Drug Dispensing Outlets (ADDO) was created in Tanzania. Tanzania changed its first line treatment for malaria from Sulphadoxine-Pyrimethamine (SP) to Artemether-Lumefantrine (ALu) in 2007. Subsidized ALu was made available in both health facilities and ADDOs. The effect of these interventions on access to malaria treatment was studied in rural Tanzania.

Methods

The study was carried out in the villages of Kilombero and Ulanga Demographic Surveillance System (DSS) and in Ifakara town. Data collection consisted of 1) yearly censuses of shops selling drugs; 2) collection of monthly data on availability of antimalarials in health facilities; and 3) retail audits to measure antimalarial sales volumes in all public, mission and private outlets. The data were complemented with DSS population data.

Results

Between 2004 and 2008 access to malaria treatment greatly improved and the number of antimalarial treatment doses dispensed increased by 78%. Particular improvements were observed in the availability (from 0.24 shops per 1000 people in 2004 to 0.39 in 2008) and accessibility (from 71% of households within 5km of a shop in 2004 to 87% in 2008) of drug shops. Despite no improvements in affordability this resulted in an increase of the market share from 49% of antimalarial sales 2005 to 59% in 2008. The change of treatment policy from SP to ALu led to severe stock-outs of SP in health facilities in the months leading up to the introduction of ALu (only 40% months in stock), but these were compensated by the wide availability of SP in shops. After the introduction of ALu stock levels of the drug were relatively high in public health facilities (over 80% months in stock), but the drug could only be found in 30% of drug shops and in no general shops. This resulted in a low overall utilisation of the drug (19% of all antimalarial sales).

Conclusions

The public health and private retail sector are important complementary sources of treatment in rural Tanzania. Ensuring the availability of ALu in the private retail sector is important for its successful uptake.

3.2. Background

It is increasingly recognised that the Roll Back Malaria (RBM) Partnership target of "80% of malaria patients receiving effective treatment within 24 hours" cannot be achieved in sub-Saharan Africa unless antimalarial drugs are made available outside the formal health sector [85, 97-98]. The public health sector plays a central role in the delivery of key curative and preventative interventions for malaria in most African countries. However, health facilities alone do not guarantee satisfactory levels of access in countries where malaria is endemic. Surveys conducted between 2007 and 2008 in 11 African countries found that despite large increases in the number of antimalarial treatments supplied through the public health sector, only 15% of children with fever were treated with Artemisinin Combination Therapies (ACTs) [32].

As a result, it has been argued that the delivery of antimalarials needs to be supplemented by additional distribution mechanisms. This can be achieved through (1) community case management and (2) strengthening the role of the private retail sector. The World Health Organisation (WHO) is increasingly promoting the provision of antimalarial drugs through community health workers with its Home Management of Malaria (HMM) strategy [38]. However, the WHO also recognises the importance of private retailers [99] and various interventions aiming at improving their services have been developed and piloted in different country settings [41].

Reviews of the available literature reveal that shops are often preferred to health facilities as a first treatment action [39-40]. Retailers tend to be more accessible, have longer and more flexible opening hours, are willing to negotiate charges and offer credit, are more polite and friendlier and are generally perceived as being cheaper. Patients also seek treatment in the private sector out of necessity since public health facilities experience frequent stock-outs. However, the private retail sector is often poorly regulated in low and middle income countries. Common opportunistic practices include illegal stocking of prescription-only medicines, the use of unqualified staff and referral by health facility staff to private outlets in which they have a financial stake [56, 83-84]. The advent of ACTs compounds the problem further. In absence of regulation people are likely to buy cheaper and less effective drugs from the private retail sector. Furthermore the misuse of ACTs and the use of artemisinin monotherapies could contribute to the emergence and spread of artemisinin resistance.

In the past five years two major interventions which directly affect access to malaria treatment have been implemented in Tanzania. Firstly, in 2002 the Tanzanian Food and

Drug Administration (TFDA) registered a new class of drug shops known as Accredited Drug Dispensing Outlets (ADDOs). With over 8000 outlets nation wide, drug shops are an important source of antimalarial treatment in Tanzania but unqualified staff invariably sells drugs they are not legally authorised to stock [57, 59, 100]. The aim of ADDOs is to address this poor state of regulation by upgrading existing drug shops (known as Part II) to properly operated outlets through a combination of dispenser training, financial incentives, accreditation and regulation [87]. Motivated by the experience of pilots conducted in the Ruvuma Region with support from the Bill and Melinda Gates Foundation (BMGF), the Ministry of Health and TFDA have planned the conversion of all Part II drug shops in the country by 2010 [89].

Secondly, in 2006 SP was abandoned in favour of Artemether-Lumefantrine (ALu, trade name Coartem®, Novartis AG) as first line treatment for malaria due to high levels of resistance to SP. The actual introduction of ALu in health facilities was delayed until January 2007. ALu is currently unaffordable for most of the population because of the high market price of USD 8-10 for an adult dose. Thanks to support from the Global Fund to Fight AIDS TB and Malaria (GFATM) the drug is provided free to all government health care facilities, where it should be made available free to children under the age of five and pregnant women; and at subsidised price of TSH 300 (USD 0.25) to other patients. Subsidised ALu was also made available in ADDOs in mid 2007. Initial plans to upscale this scheme are likely to be superseded in 2010 by the Affordable Medicines Facility for malaria (AMFm). The AMFm aims to make ACTs available at the cost of the previous generation of antimalarials by negotiating with the manufacturers to reduce the price of their ACTs and subsidising them heavily for purchase by specified national importers. It is expected that drugs will be available at about USD 0.20-0.50 to patients. Tanzania and Zanzibar are among the 10 countries invited to pilot a first phase of this subsidy as from mid 2010 [47].

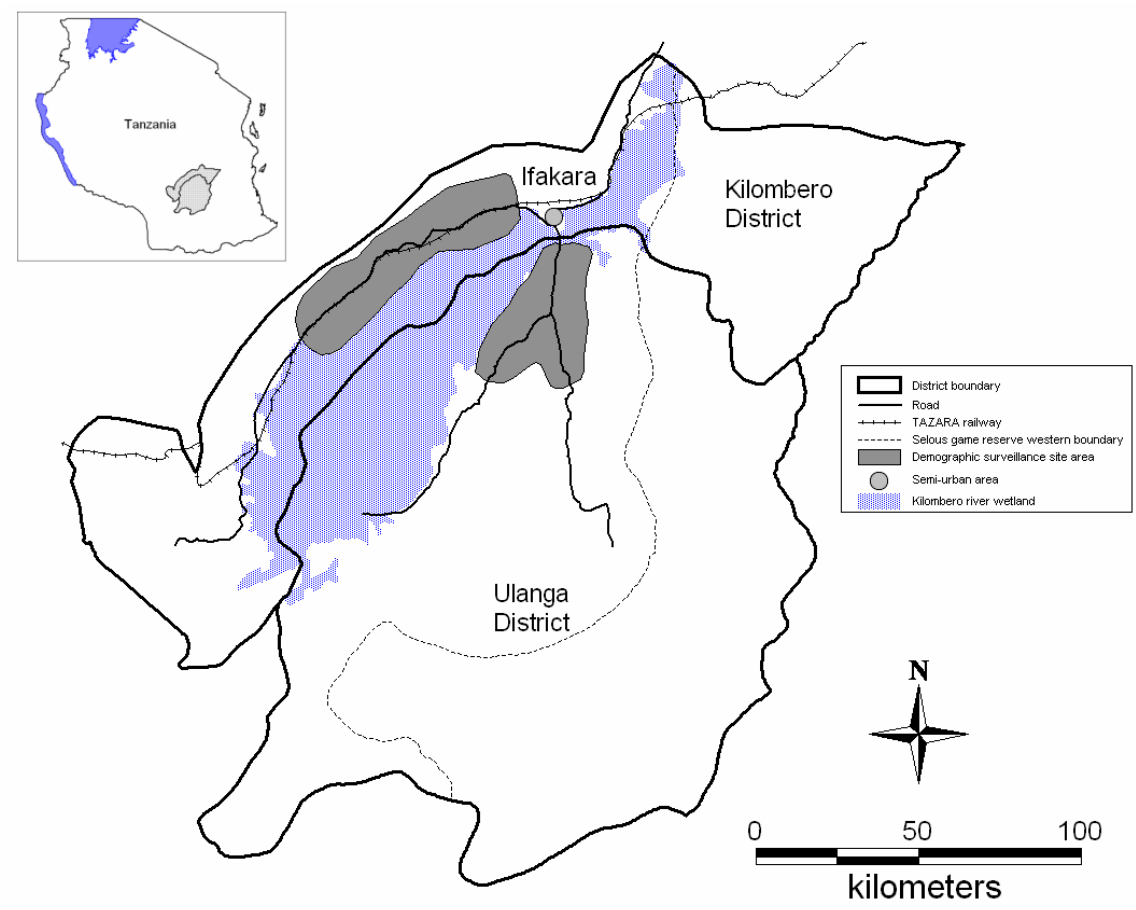
This study presents a unique set of longitudinal data on availability, accessibility, costs and uptake of antimalarial treatment in both the private retail and public health sectors. The data were collected between 2004 and 2008 in two districts of the Morogoro Region in the frame of the ACCESS programme, which aims at improving and understanding access to malaria treatment [101]. The results presented here are complemented by treatment seeking surveys which evaluated changes in treatment outcomes (i.e. the user perspective) [102] (cf. Chapter 4).This experience is of great relevance to other settings, as ACTs are being adopted throughout most of Africa as first line treatment for malaria and ACT subsidies will be introduced widely in the private sector through the AMFm.

3.3. Methods

Study setting

The study was carried out between 2004 and 2008 in the rural villages of the Kilombero and Ulanga Demographic and Surveillance System (Ifakara Rural DSS) and in the semi-urban setting of Ifakara town in south-central Tanzania (Figure 10). The Ifakara Rural DSS area covers 25 villages (13 in the Kilombero District and 12 in Ulanga District). The population in mid-2004 was 73,977 and increased at an average rate of 5% per year, resulting in a population of just over 92 203 in mid-2008. The population of Ifakara Town was 45,518 in 2002 according to the last national census [103].

Figure 10. Map of Kilombero and Ulanga Districts showing Ifakara Town and the Demographic Surveillance System (DSS).



Malaria transmission in the area is intense and perennial with differences between the rural and semi-urban settings. Overall transmission has been declining over the past 10 years. A

study conducted in the area between 2001 and 2003 reported an Entomological Inoculation Rate (EIR) of 349 infective bites per person per year (ib/p/y) [77], but according to recent data it has declined to 81 ib/p/y [78]. EIR data for Ifakara town suggest that the transmission rate is about a log order smaller than in the surrounding rural areas [79]. Treatment seeking surveys carried out in 2004, 2006 and 2008 within the frame of the ACCESS programme found on average twice as many fever cases in the rural areas compared to Ifakara Town (Alba *et al.,* unpublished data).

There are six health facilities (three public dispensaries, one public health centre and two faith-based dispensaries) in the Kilombero DSS area and eight health facilities (five public dispensaries, one health centre and two faith-based dispensaries) in the Ulanga DSS area. The Designated District Hospital in Ifakara serves as a referral point for all the facilities in the study area. There is only one Part I pharmacy in the study area, which is located in Ifakara town. The area has been described in more detail elsewhere [73, 101].

Data collection activities are summarised in Table 3 and described in detail below. The routine monitoring in health facilities and the shop censuses, combined with DSS data, provided information on availability and accessibility of sources of antimalarial drugs. The retail audits provided data on prices and uptake of antimalarial drugs.

Table 3. Summary of data collection activities

Activity	*Collection period (month.year or year)*	*Sample*	*Location*
Routine monitoring in health facilities			
• Collection of monthly data on availability of antimalarial drugs in all public health facilities from ledger books • GPS location of each health facility	1.2005 – 12.2008	10	Rural villages (DSS)
Shop census			
Census of all shops potentially selling drugs providing quantitative data on • Availability of shops selling antimalarial drugs • Availability of antimalarial drugs • GPS location of each shop	5.2004 – 7.2004 3.2005 – 7.2005 4.2006 – 7.2006 4.2007 – 8.2007 4.2008 – 9.2008	758 790 878 1074 1082	Rural villages (DSS) and Ifakara Town
Retail audits			
• Measurement of antimalarial sales during a two-week period in all outlets (shops and health facilities) • Retail prices of each antimalarial drug	4.2005 – 7.2005 4.2008 – 7.2008	78 66	Rural villages (DSS)

Routine monitoring in health facilities

Every other month a team of trained field workers visited the ten public health facilities in the DSS area (four in Kilombero and six in Ulanga) to collect end-of-month antimalarial drug stock data from the Health Management and Information System (HMIS) ledger books, using validated data collection tools. Data could not be collected from the faith based facilities as they are not legally required to record drug stock in ledger books, rendering systematic collection of the data difficult. In 2004 the GPS locations of all the health facilities in the area were recorded with a hand-held GPS unit (Garmin® e-Trex, Garmin® Ltd).

The percentage of facility-months in stock of a given antimalarial over the year was calculated as an indicator of drug availability. First an average estimate of yearly drug availability was calculated for each drug and each health facility. Unfortunately, the data on drug availability were missing in the ledger books for many months. Anecdotal evidence suggests that facility staff tended not to fill in the entry on end-of-month stocks when the drug was not available. As a result, and in the absence of any other information, months with missing data were considered as "out of stock". If a health facility had more than 25% missing values it was excluded from the average to avoid skewing estimates of yearly drug availability towards unrealistically low values. Then an average estimate of antimalarial availability for the area was calculated by averaging the yearly estimates from all the health facilities. The estimate was deemed inconclusive if more than 25% facilities had to be excluded from the average estimate.

The health facility data were complemented with population numbers and household locations to provide standardised indicators of availability and accessibility of health facilities. Population counts down to village level were available for every year between 2004 and 2008 from the DSS database. GPS positions were available from the DSS database for 85% (16141/18840) of households in 2004 and 90% (18580/20579) of households in 2008. An indicator of availability of health facilities was constructed as the number of shops per 1000 population, and an indicator of accessibility as the average distance between households and the nearest health facility.

Shop census

Repeated cross sectional shop censuses were carried out every year in the Rural DSS area and in Ifakara town. All shops potentially selling drugs (general stores, kiosks, Part II drug stores and ADDOs) were visited by a team of nine trained field workers who recorded the outlet's stock and location using tools and methodology developed and previously applied in the area [98][68]. The only Part I pharmacy was not visited. The primary aim of the census was to assess the type and brand of drugs available in each type of outlet. The analysis of the baseline study in 2004 was published by Hetzel et al [68] and the results presented here

provide a longitudinal assessment of the changes between 2004 and 2008. The secondary aim of the census was to assess shopkeepers' knowledge about signs, symptoms and treatment of malaria. Results will be presented elsewhere (Dillip *et al.*, in preparation).

Data were collected using a structured questionnaire and the location of each shop was recorded with a hand-held GPS unit. The field work was overseen by the same supervisor in all years. The supervisor visited all the village and hamlet leaders prior to the censuses to inform them and to answer any queries. Every year, field interviewers were provided with an inventory of all the outlets identified in the previous year's census and were instructed to visit every outlet on the list, as well as any new outlet they encountered. Random quality checks were performed by a research scientist who visited the field sites shortly after the field workers.

Estimates of availability and accessibility of shops stocking drugs were constructed using the methodology outlined for health facilities. Population counts were estimated for Ifakara Town by adjusting the 2002 census count with the annual growth rate in the DSS area.

Retail audits

Two retail audits of antimalarial drugs were conducted in the rural DSS areas during the shop censuses of 2005 and 2008. The methodology developed by Goodman *et al.* [104, 105] was applied. The retail audit included all outlets selling or dispensing drugs, i.e. all health facilities (public and faith-based) and drug shops (Part II drug shops and ADDOs), as well as the few general shops found to stock antimalarial drugs during the shop census. The aim of the study was to estimate total antimalarial sales volume in the study area and to compare the share of sales of each antimalarial drug across each type of outlet.

The retail audit data were collected over two consecutive visits two weeks apart. On the first visit, which coincided with the shop census visit, field interviewers recorded stock levels for each antimalarial drug. On the second visit they recorded stock levels and any deliveries since their last visit, as well as any drugs that had been given out for any other reason e.g. thrown away or returned to wholesalers. Two weeks was considered a reasonable recall period for wholesale deliveries. The exact number of tablets, bottles or vials was counted where possible. When tablets were kept in tins the following information was collected in order to estimate the number of tablets present: the height of the tablets in the tin when full, the height of tablets on the day of visit and the number of tablets in a full tin. In addition the reported retail price per single unit (be it a tablet, bottle or vial) was recorded. The retail audit was carried out once a year (in approximately the same months) as no significant seasonal

differences were found in the previous study in which two surveys per year were conducted [105].

Daily sales were calculated or estimated for each antimalarial. Sales between the two visits were calculated as: Sales = (total at first visit) + (deliveries between first and second visit) - (stocks thrown away or transferred to other shops/facilities) - (total at second visit). The number of tablets, bottles of syrup and vials was converted into the equivalent number of adult doses in order to calculate the total antimalarial sales of different types of antimalarials. Daily sales were calculated by scaling down up or down pro rata according to the number of days between the two audit visits. If total sales volumes could not be calculated (because drug levels were not recorded on the first or the second visit), they were estimated by a multiple imputation. With this statistical technique missing values are imputed several times based on random draws from the conditional distribution of the missing observations given the observed data and covariates (drug levels on the first or second visit, type of outlet, type of drug and drug formulation). In this case three draws were considered enough and the average between the three imputations kept for analysis. Multiple imputation was deemed appropriate as there were no indications that the data were not missing at random.

Reported drug prices were adjusted for inflation to reflect actual changes in purchasing power. The 2005 drug prices were inflated to real 2008 values on the basis of consumer price indices [106]. An inflation factor of 1.25 was derived from the mean yearly inflation values published by the Tanzania National Bureau of Statistics (NBS) [107].

Data entry and analysis

Data were double entered using Microsoft FoxPro and Microsoft Access (Microsoft Corp. Seattle, USA) and checked for coding errors and consistency. Intercooled Stata 10 (Stata Corp., College Station, TX, USA) was used for data management and analysis. Logistic and Poisson regressions provided Odds Ratios (OR) and Incidence Rate Ratios (IRR) to estimate changes over time or differences between areas. ORs and IRRs indicate an average increase per year between the years of observation (“year” is entered in the regression as a linear variable) unless it is explicitly stated that the increase is not linear and is from a given year to another (“year” is entered as a categorical variable). Differences in medians between years were tested using a two-sample Wilcoxon rank-sum (Mann-Whitney) test. Distances were calculated with ArcMap Version 9.1 (ESRI Inc.).

Ethics

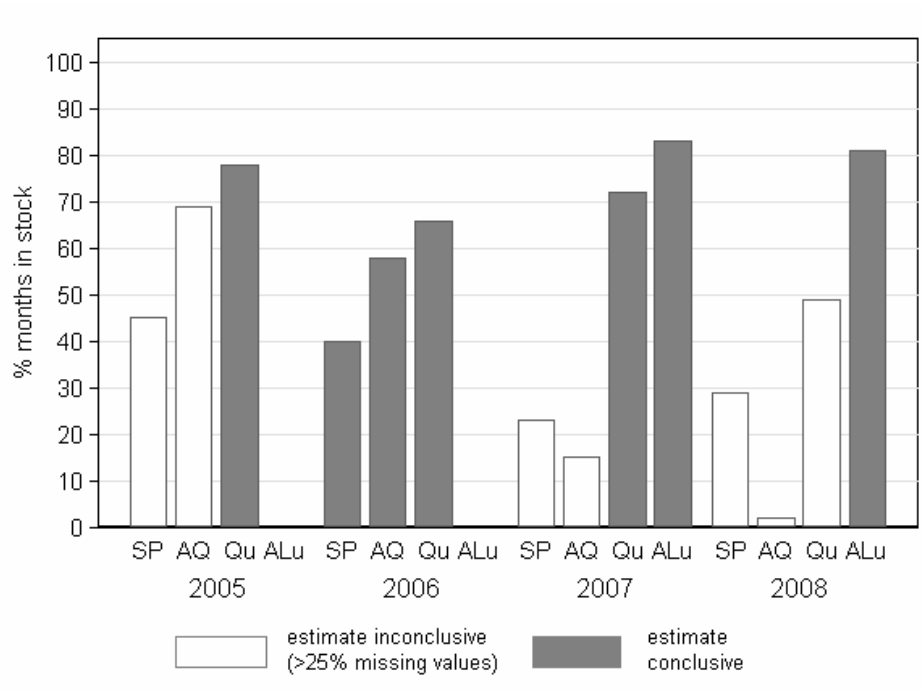
The National Institute for Medical Research of the United Republic of Tanzania (NIMR/HQ/R.8a/Vol.IX/236, 16th September 2003) granted ethical clearance for the study Shop keepers and health facility staff gave informed consent to participating in the study and were given feedback of the study results.

3.4. Results

Availability and accessibility of antimalarials in public health facilities

Drug availability data were collected for ten facilities over four years for four drugs (two years for ALu) i.e. 1680 facility-months but only 1380 facility-months of observation could be included in the analysis. As a result out of the 14 yearly overall availability estimates were deemed inconclusive (Figure 11).

Figure 11. Availability of antimalarial drugs in public health facilities in the rural DSS area (Note: ALu was introduced in January 2007).



Towards the end of 2006, just before the introduction of to ALu, health facilities experienced severe stock-outs of SP. On average throughout the year the drug was only available 40% (38/96) of the months with three facilities reporting stockouts for more than 10 months. This was mainly due a delay in the introduction of ALu without additional SP orders to compensate. The availability of quinine and amodiaquine was much higher as the drugs were reported to be available 66% (78/120) and 58% (70/120) of the time, respectively.

However, four facilities were out of stock of all three antimalarials for 2.8 (sd=1) months of the year. Since the introduction of ALu availability of antimalarial drugs has greatly improved. In 2007 and 2008 ALu was available for more than 80% of the months of the year (90/108 in 2007 and 88/108 in 2008).

The availability and accessibility of health facilities was only slightly affected by population growth. The availability of public health facilities decreased slightly but not significantly. In 2004 there were 0.13 facilities per 1000 people (10/73977) and in 2008 this figure declined to 0.11 (10/92203) (IRR=0.81 p=0.712 from 2004 to 2008). The median distance from a household to a facility marginally increased from 2.25 km (IQR=4.31) to 2.37 km (IQR=4.75) (z=-5.388 p<0.001) and the proportion of households located within 5km of a health facility decreased from 73% (11858/16141) to 70% (12990/18580) in 2008 (OR=0.90 p<0.001 from 2004 to 2008).

Availability and accessibility of malaria treatment in drug shops

The number of shops included in the census increased on a yearly basis (Table 4). Every year general shops (permanent structures and kiosks) consistently accounted for 95% of all shops potentially selling drugs, while the rest were Part II drug shops and ADDOs. The number of Part II drug shops decreased considerably after 2006 as they were progressively upgraded to ADDOs. Overall the number of drug shops (Part II drugs stores and ADDOs) increased from 34 to 59 between 2004 and 2008.

Table 4. Number of shops censused, by type

		2004	*2005*	*2006*	*2007*	*2008*
General shops (including kiosks)	Kilombero DSS	343	293	313	385	442
	Ulanga DSS	201	199	180	213	201
	Ifakara Town	185	256	341	421	380
	Total	**729**	**748**	**834**	**1019**	**1023**
Part II drug stores	Kilombero DSS	16	22	17	8	6
	Ulanga DSS	3	9	4	2	3
	Ifakara Town	10	11	17	1	1
	Total	**29**	**42**	**40**	**11**	**10**
ADDOs	Kilombero DSS	0	0	0	18	22
	Ulanga DSS	0	0	4	8	7
	Ifakara Town	0	0	0	17	20
	Total	**0**	**0**	**4**	**43**	**49**
Total	Kilombero DSS	359	315	330	412	470
	Ulanga DSS	204	208	190	223	211
	Ifakara Town	195	267	358	439	400
	Total	**758**	**790**	**878**	**1074**	**1083**

Across all years a high proportion of general shops stocked some type of drug and a high proportion of drug shops stocked antimalarials, but a varying and much smaller proportion of

general shops stocked antimalarials (Figure 12). Between 2004 and 2008 an average of 68% of general shops stocked drugs (mainly antipyretics), with no significant differences between districts or between the rural areas and Ifakara Town. However, few of these were found to sell antimalarial drugs. The proportion of general shops selling antimalarials never exceeded a peak of 9% (18/199 in Ulanga and 23/293 in Kilombero) in 2005 in the DSS villages and 3% in Ifakara in 2004 (5/185) and decreased considerably thereafter to 3% (5/501 in Ulanga and 10/442 in Kilombero) in the DSS and to 0% (0/380) in Ifakara in 2008 (DSS IRR=0.87 p=0.018, Ifakara IRR=0.64 p=0.013 between 2004 and 2008). The proportion of drug shops (Part II and ADDOs) storing antimalarial drugs was 86% (31/36) in 2004, 100% (42/42) in 2005, 84% (37/44) in 2006 and over 98% in 2007 (54/55) and 2008 (58/59) (Figure 14).

Table 5. Number of drugs shops per population[1]

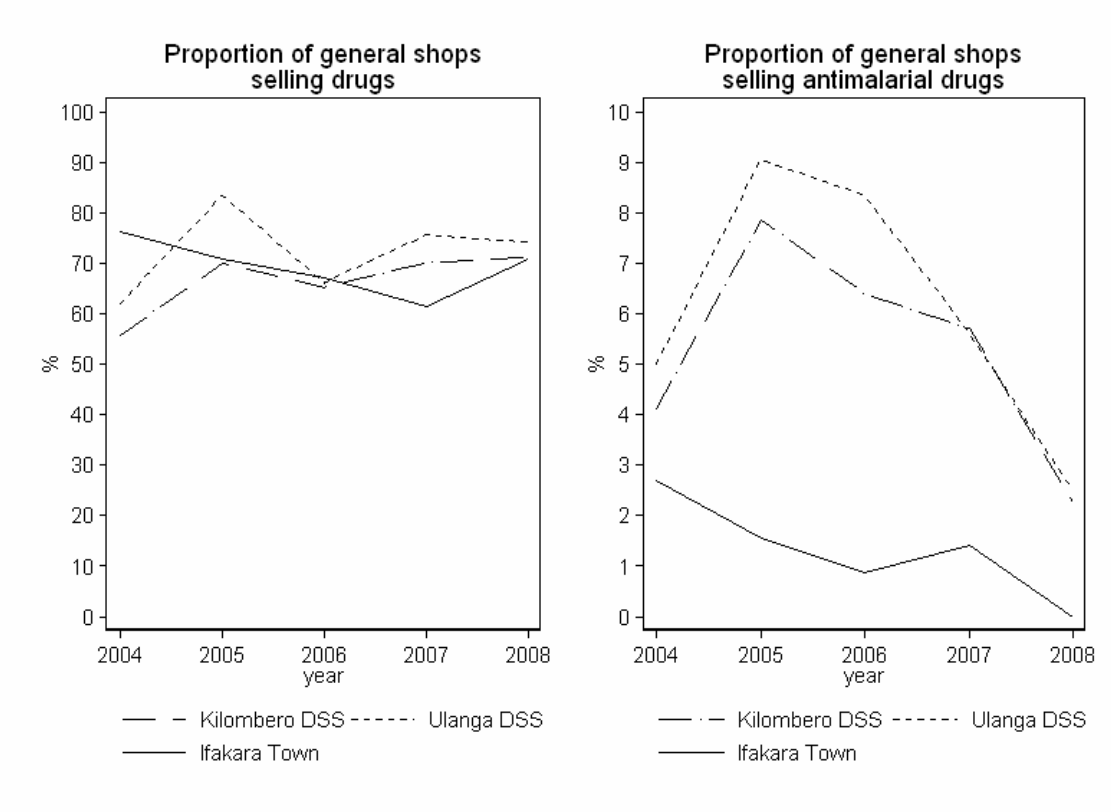
Village	*Drug shops*		*Population*		*Shops per 1000 people*		
	2004	*2008*	*2004*	*2008*	*2004*	*2008*	*Change*
Ulanga DSS							
Idunda	0	0	1837	1896	0	0	
Igota	0	0	1533	1506	0	0	
Igumbiro	0	0	2311	2220	0	0	
Iragua	1	0	3704	4676	0.26	0	-
Kichangani	0	2	3103	3236	0	0.62	+
Kidugalo	0	2	2539	4389	0	0.46	+
Kivukoni	0	1	5612	5581	0	0.18	+
Lupiro	1	2	4009	4085	0.25	0.48	+
Mavimba	0	1	2417	2896	0	0.34	+
Milola	1	1	1282	1783	0.77	0.56	-
Minepa	0	1	1964	2908	0	0.34	+
Nakafulu	0	0	919	891	0	0	
Subtotal	3	10	31230	36067	0.10	0.27	+
Kilombero DSS							
Idete	1	3	4661	4884	0.21	0.64	+
Igima	4	2	3793	5278	1.05	0.37	-
Ikule	3	3	2244	3587	1.34	0.86	-
Kisegese	0	1	1370	1928	0	0.52	+
Lukolongo	0	2	3821	4329	0	0.46	+
Mbingu	1	3	5380	7141	0.18	0.42	+
Mchombe	3	3	4452	4758	0.67	0.63	-
Miwangani	0	1	1702	2173	0	0.46	+
Mkangawalo	1	2	4675	6215	0.21	0.32	+
Mngeta	2	2	3399	3767	0.58	0.53	-
Mpofu	0	0	1897	2331	0	0	
Namawala	1	5	3675	7750	0.27	0.65	+
Njagi	0	1	1678	1995	0	0.50	+
Subtotal	16	28	42747	56136	0.37	0.50	+
Ifakara	10	21	48343	59057	0.21	0.36	

There is evidence of greater availability of drug shops, even accounting for population growth. While the absolute number of antimalarial retail points (drug shops and general

[1] This table was not included in the published version of this manuscript

shops) increased over the study period from 58 in 2004 to 74 in 2008, the number of shops per 1000 people did not change significantly over the years and fluctuated around 0.73 shops per 1000 people in rural DSS areas and 0.34 in Ifakara Town (Figure 13). In contrast, the availability of drug shops alone did increase over the years, although not linearly, from 0.23 (29/123260) shops per 1000 people in 2004 to 0.39 (59/151260) in 2008 (IRR=1.72 from 2004 to 2008 p=0.019). Average rates mask differences at district and village level. The Kilombero District generally had higher availability of both general shops selling drugs (IRR=0.71 p=0.005) and drug shops (IRR=0.53, p=0.001) compared to the Ulanga District. Moreover, half of the 14 villages which did not have drug shops in 2004 still did not have any in 2008 (Table 5). Three of these did not have any health facilities either, and this accounts for 6% (5442/92203) of the total rural DSS population.

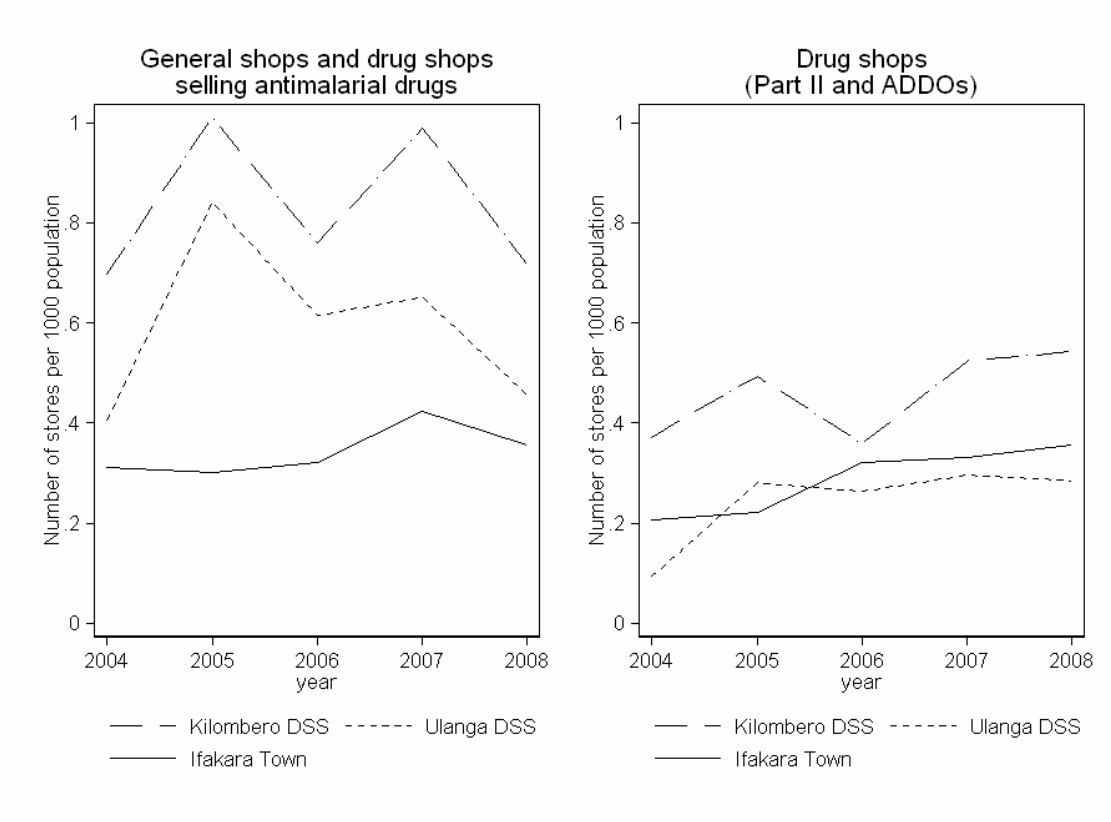
Figure 12. Proportion of general stores selling any drugs and antimalarials (Note: vertical axis differs between two graphs)



Amodiaquine and SP were the most commonly available antimalarials in both general shops and drug shops (Figure 14). In drug shops the antimalarial most commonly available was SP (90% of shops i.e. 210/234 over the study period), closely followed by amodiaquine (86% i.e. 200/234) and quinine (80% i.e. 187/234). ALu was available in 2% (1/43) of the drugs stores in 2006 (unsubsidised), 7% (4/54) in 2007 and 29% (17/58) in 2008. Interestingly,

chloroquine could still be found in 2004 and in 2005 in one drug shop in a remote village of the Kilombero DSS area. Figure 14 gives a break down by year of these figures.
While artemisinin monotherapies were mainly found in the drug shops of Ifakara, ALu was also available in the more rural areas. The proportion of shops storing artemisinin monotherapies grew until 2007, when up to 11 out of 55 (20%) shops stored drugs containing either artesunate, artemether or dihydroartemisinin (Figure 14). In 2008 this proportion decreased to 12% (7/59), probably as a result of tighter national and international regulations on the distribution of artemisinin monotherapies. However, it is worth noting that these artemisinin derivatives could be found in Ifakara but hardly reached the more rural villages, most likely because of their very high prices. ALu tended to be more available in Ifakara than in rural areas (Ifakara 8/13 i.e. 38.1% of drug shops stored ALu, Kilombero DSS 7/27 i.e. 25.9%, Ulanga DSS 2/10 i.e. 20%).

Figure 13. Availability of retail outlets selling drugs, per 1000 population



Drug shops became more accessible after the introduction of ADDOs. Across all years drugs shops were more likely to be found in the most populous areas, but different patterns were noted for ADDOs and drug shops. Both in 2004 and in 2008 a significant association was found between the presence of any drug shop in a village and the size of the village (2004 OR=2.6 for every 1000 increase in population p=0.016, 2008 OR=2.6 p=0.048). However, in 2008 the association between the presence of an ADDO in a village and the size of the

village was much smaller (OR=1.7 p=0.077) suggesting that ADDOs were also opened purposefully in less populous areas. This resulted in an increase in the number of households located within 5 km from a drug shop from 71 % (3848/16141) to 87% (11662/18580) (OR= 5.38 p<0.0001 from 2004 to 2008) (Figure 15). The median distance from a drug shop to a household nearly halved during the study period, decreasing from 2.2km (IQR=4.8) to 1.2km (2.6) (z=32.234 p<0.0001).

Figure 14. Availability of different antimalarial drugs in private retail outlets (Note: vertical axis differs between two graphs)

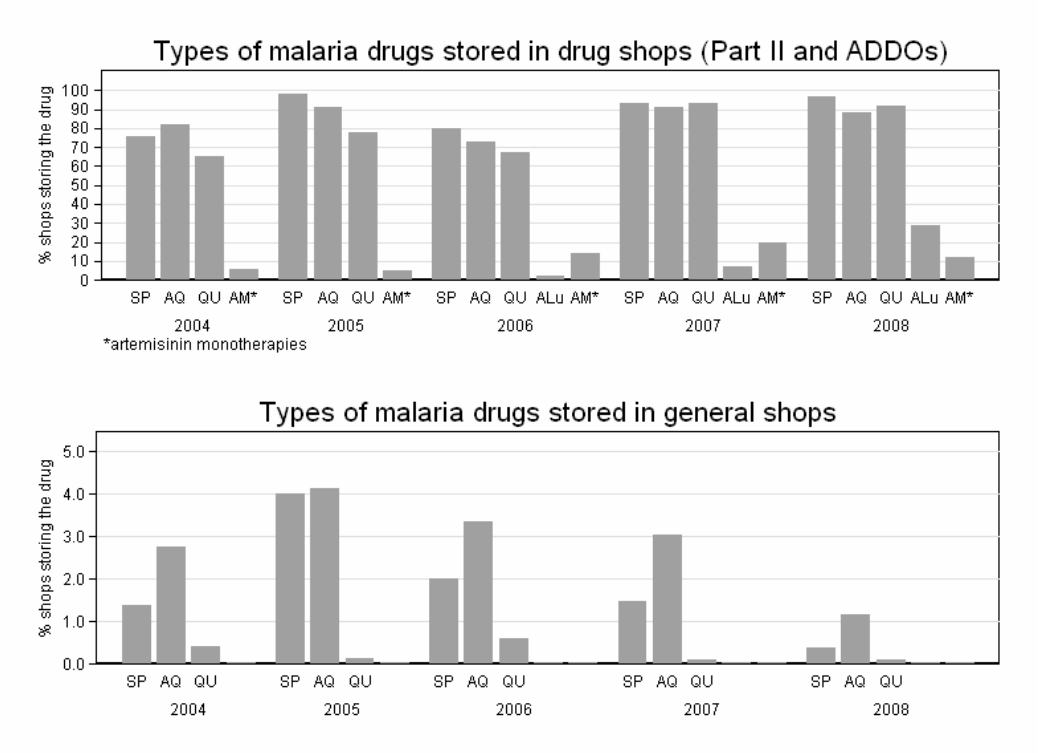
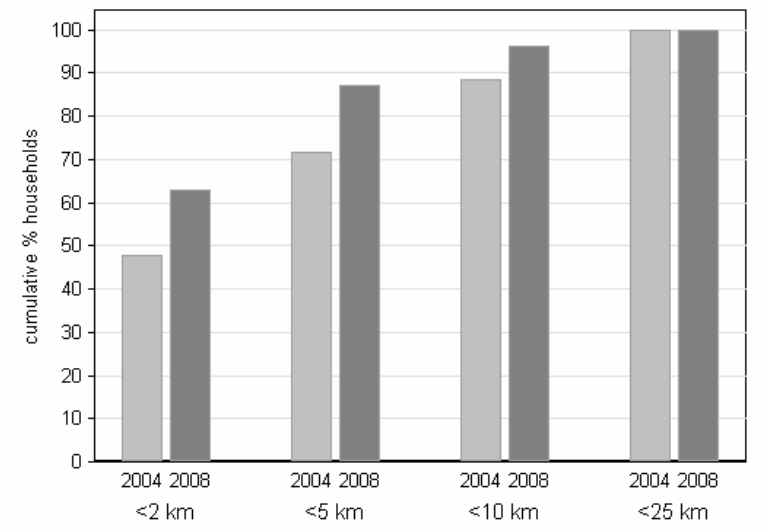


Figure 15. Cumulative percentage of households within a given distance to the nearest drug shop.



Sales of antimalarial drugs in shops and health facilities

In 2005 a total of 366 antimalarial products were followed from 77 retail outlets (31 drug stores, 37 general stores, five kiosks and 14 health facilities). In 2008 a total of 409 products were followed from 66 outlets (10 drug stores, 12 general stores, three kiosks, 27 ADDOs and 14 health facilities). Sales levels could not be calculated and were estimated for 6% (44/775) items because drug levels were not recorded either in the first or in the second visit (see methods).

The analysis of daily sales revealed a near doubling in the number of antimalarials doses dispensed between 2005 and 2008 and the increasing importance of drug shops as a source of antimalarials. An estimated 315 equivalent adult antimalarial doses were dispensed per day from all facilities and shops in the DSS areas in 2005 while 560 doses were dispensed in 2008 (78% increase). The proportion of antimalarial drugs sold in drug shops increased from 49% (153.5/315.3) in 2005 to 59% (330.2/560.3) in 2008 (OR=1.51 p=0.036) (Table 6 and Figure 16). The increase in the use of drug shops was not at the expense of public health facilities, but at the expense of general shops and faith based facilities. Indeed, the proportion of doses sold in general shops and faith based health facilities decreased but there was no significant difference in terms of antimalarials dispensed in health facilities (79.4/315.3 i.e. 25% in 2005 vs. 169.9/560.3 i.e. 30% in 2008 OR=1.29 p=0.115).

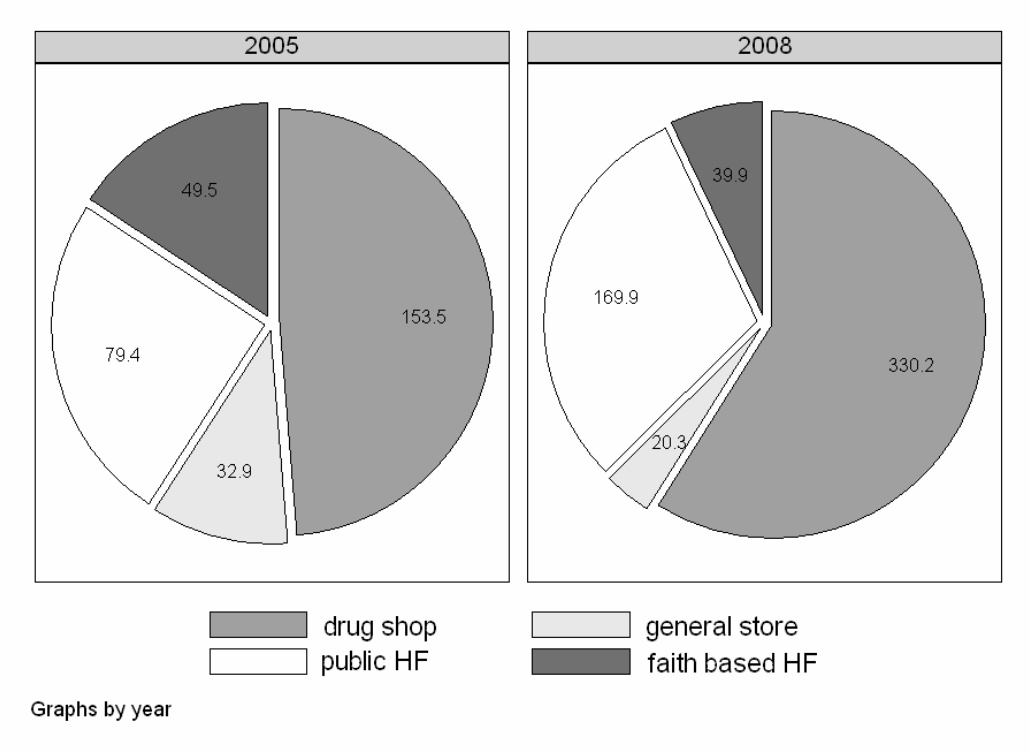
Table 6. Number of equivalent adult doses sold per day in all shops and health facilities (HF) in the DSS rural areas and share out of total in the type of outlet

	2005					*2008*				
	Public HF	*Faith Based HF*	*Drugs shops*	*General shops*	*Total*	*Public HF*	*Faith Based HF*	*Drugs shops*	*General shops*	*Total*
Amodiaquine	22.4 (28.2%)	21.0 (42.4%)	43.4 (28.3%)	10.8 (32.8%)	97.6 (30.9%)	64.7 (38.1%)	9.6 (29.2%)	62.1 (18.8%)	4.3 (21.2%)	140.7 (25.1%)
Chloroquine			0.9 (0.6%)		0.9 (0.3%)					-
SP	54.9 (69.2%)	26.8 (54.2%)	97.9 (63.8%)	21.9 (66.6%)	201.5 (63.9%)	26.6 (15.7%)	7.9 (24.0%)	233.6 (70.7%)	15 (78.8%)	284.1 (50.7%)
Quinine	2.1 (2.6%)	1.7 (3.4%)	11.3 (7.3%)	0.2 (0.6%)	15.3 (4.9%)	7.5 (4.4%)	7.5 (22.8%)	16.1 (4.9%)	<0.1 (<0.1%)	31.1 (5.1%)
Alu	-	-	-	-	-	71.1 (41.8%)	14.8 (50%)	18.1 (5.5%)		104.0 (18.6%)
Artemisinin monotherapy	-	-	-	-	-	0.1 (<0.1%)		0.3 (<0.1%)		0.3 (<0.1%)
Total	**79.4**	**49.5**	**153.5**	**32.9**	**315.3**	**169.9**	**32.9**	**330.2**	**20.3**	**560.3**

The sales of SP remained very high in 2008 despite the change of treatment policy to ALu. In 2005 64% of all antimalarial sales consisted of SP and in 2008 it still accounted for 51% of all

antimalarial sales. ALu only accounted for 19% of total sales in 2008, 68% (71.1/104.0) of which were in public health facilities, 14% (14.8/104.0) from faith based health facilities and 17% (18.1/104.0) from drug shops.

Figure 16. Share of total antimalarial sales through each outlet type



Prices were generally higher in drug shops where they also increased considerably over time. Prices of antimalarials were compared between 2005 and 2008 in drug shops and public health facilities only (Table 7) although six out of 10 health facilities did not provide any pricing information. In 2005 health facilities reported selling SP adult doses at an average of USD 0.25 (USD 0.32 in 2008 prices) whereas it was sold for USD 0.37 (USD 0.45 in 2008 prices) on average in drug shops. In 2008 two of the facilities which provided prices reported dispensing ALu packs for children under the age of eight free, whereas two reported selling them for USD 0.25. Adult ALu and SP doses were reported to be sold for USD 0.25 in health facilities. Both SP and ALu were much more expensive in shops where sellers reported selling an ALu dose for USD 1.27 and SP doses for USD 0.67. Adjusting for inflation these price differences translate into a 20% decrease in the price of the first line treatment in public health facilities. In drug shops prices increased by 51% when comparing the price of SP in 2005 and in 2008 and by 84% when comparing the price of SP in 2005 and the price of ALu in 2008.

Table 7. Reported retail price in US Dollars (TSH) in drug shops and public Health Facilities (HF) of a single adult antimalarial dose - unless otherwise specified (USD 1= TSH 1180 in 2008 and USD 1= TSH 1130 in 2005)

	2005				*2008*			
	Drugs shops		*Public HF*		*Drug Shops*		*Public HF*	
	N	*Median (IQR)*	*N*	*Median (IQR)*	*N*	*Median (IQR)*	*N*	*Median (IQR)*
Amodiaquine								
Tablets	35	0.35 (0.35 to 0.94)	4	0.35 (0.32 to 0.44)	31	0.42 (0.42 to 0.67)		-
syrup [1]	36	0.72 (0.62 to 0.83)	1	0.25 (0.25 to 0.25)	38	0.99 (0.78 to 0.99)		-
Chloroquine tablets	1	0.26 (0.26 to 0.26)		-		-		-
SP	100	0.37 (0.26 to 0.79)	5	0.26 (0.26 to 0.26)	103	0.67 (0.25 to 1.27)	4	0.25 (0.13 to 0.25)
Quinine								
Tablets	26	1.85 (1.85 to 1.85)	3	1.85 (1.85 to 1.85)	28	3.56 (3.56 to 3.56)	3	2.85 (1.78 to 3.56)
syrup [1]	15	3.35 (2.79 to 4.18)		-	38	5.34 (5.34 to 5.34)		
Injection [2]	18	9.29 (7.43 to 9.29)	5	7.43 (5.58 to 9.28)	30	8.90 (8.90 to 0.68)	2	8.89 (8.89 to 8.89)
Artemether-Lumefantrine								
3 m – 3 y		-		-	8	0.42 (0.42 to 1.06)	4	0.05 (0 to 0.18)
3 – 8 y		-		-	9	0.42 (0.42 to 0.84)	3	0.25 (0 to 0.25)
8 – 12 y		-		-	8	1.27 (1.14 to 6.99)	4	0.13 (0 to 0.13)
12 y +		-		-	7	1.27 (1.27 to 1.69)	4	0.25 (0.13 to 0.25)
Artemisinin monotherapies		-		-	2	4.68 (4.29 to 5.08)		

[1] dose for a child between 1 and 3 years of age
[2] calculated assuming a full course of quinine is taken intra-muscularly for 7days

3.5. Discussion

The findings presented here provide an independent assessment of the changes in access to antimalarial treatment in the private and the public sector after the roll-out of ADDOs and the introduction of ACTs in the Kilombero and Ulanga Districts of Tanzania. A framework recently published by Obrist *et al*. views access as the degree of fit between providers' services and users' means along the five dimensions of availability, accessibility, affordability, adequacy and acceptability [52]. Appropriate levels of access lead to utilisation of treatment and eventually to improved health, provided the treatment is of high quality. This study has concentrated on the provider side of access. Changes in levels of availability, accessibility and affordability of treatment in both the private health sector and the commercial retail sector are summarised in Table 8 and Table 9. These access indicators can be viewed as outputs in the standard evaluation terminology [72] whereas the treatment

seeking surveys conducted alongside this study focused on treatment outcomes [102] (cf. Chapter 4).

Table 8. Summary of changes in access to malaria treatment from the public health sector

Dimension	*Indicator*	*Difference*	*Change*
Availability	Facilities per 1000 population	**0.13** in 2004 vs. **0.11** in 2008 (p=0.712)	
	Proportion of months in stock of antimalarial drugs	Data not conclusive	
	Proportion of months in stock of the first line antimalarial	**40%** SP stock in 2006 vs. **81%** ALu stock in 2008 (p<0.001)	+
Affordability	Median price of an adult antimalarial dose	SP TSH **375** (in 2008 prices) in 2005 vs. SP TSH **300** in 2008 and ALu TSH **300** in 2008	-
Accessibility	Population within 5 km from a facility	**73%** in 2004 to **70%** in 2008 (p<0.001)	-
	Median distance from a household to a facility	**2.2 km** in 2004 vs. **2.3 km** in 2008 (p=0.457)	
Utilisation	Number of equivalent adult doses dispensed per day	**79** in 2005 vs. **170** in 2008	+
	Share of total sales through public health facilities	**25%** in 2005 vs. **30%** in 2008 (p=0.115)	

Table 9. Summary of changes in access to malaria treatment from the private retail sector

Dimension	*Indicator*	*Difference*	*Change*
Availability	Shops per 1000 population	**0.24** in 2004 vs. **0.39** in 2008 (p=0.05)	+
	Proportion of licensed drug shops storing antimalarials	**86%** in 2004 vs. **98%** in 2008 (p=0.019) but not a constant trend over the years	
	Proportion of licensed drug shops storing the first line antimalarial	**86%** selling SP in 2004 vs. **29%** selling ALu in 2008 (p<0.001)	-
Affordability	Median price of adult antimalarial dose	SP TSH **493** (in 2008 prices) in 2005 vs. SP TSH **800** in 2008 and ALu TSH **1500** in 2008	-
Accessibility	Population within 5 km from a shop	**72%** in 2004 vs. **87%** in 2008 (p<0.001)	+
	Median distance from a household to a shop	**2.2 km** in 2004 vs. **1.2 km** in 2008 (p<0.001)	+
Utilisation	Number of equivalent adult doses dispensed per day	**154** in 2005 vs. **330** in 2008	+
	Share of total sales through drug shops	**49%** in 2005 vs. **59%** in 2008 (p=0.036)	+

Overall there has been a great improvement in access to malaria treatment. The number of antimalarial doses dispensed nearly doubled over the three years of observation. Major gains were made in the private retail sector in terms of availability and accessibility of treatment, but availability of drugs also improved in health facilities following the introduction of ALu. The treatment seeking surveys [102] (cf. Chapter 4) conducted in the study area found that this was accompanied by an increase in the promptness of treatment. The data show that the proportion of antimalarial doses taken within 24 hours of symptom onset increased from form 80% in 2004 to 93-97%.

A great improvement was noted in the public health sector as far as the availability of the first line treatment is concerned. In 2008 health facilities were in stock of ALu in over 80% of the months of the year compared to 40% in stock of SP in 2006. It is worth noting that the value of 80% ALu stock was determined using a very conservative method of estimation whereby missing values were considered out of stock (see methods). A more liberal calculation of estimation which excludes missing values from any calculation yields values of 94% stock in 2007 and 91% in 2008 compared to 60% SP stock in 2005. This presents a noteworthy improvement compared to previous years. There is still room for improvement though, and ACCESS is continuously working with the District Health Management Teams to close the gap. The severe stock-outs of SP in 2006 during the months leading up to the introduction of ALu showed the importance of having an alternative source of antimalarials in the community.

The high levels of stock of ALu in 2007 and 2008 are the result of the “push” system of delivery which was implemented as a temporary measure for the distribution of ALu to ensure its wide availability. Although this system has led to high levels of stock, it is argued not to be desirable in the long as it leads to wastages when number of malaria patients is lower than expected (e.g. as a result of malaria control or the introduction of diagnostics). The National Malaria Control Programme (NMCP) has been progressively integrating the delivery of ALu into the national drug delivery system and by the beginning of 2010 all facilities should be placing orders for ALu along with other items (Dr Mkude, NMCP, personal communication). The impact of this change on stock levels need to be closely monitored and evaluated.

Two other issues concerning the public health sector emerged from the retail audits: 1) the low rate of prescription of ALu and 2) the non-adherence to user fee exemptions. Although ALu was widely available in public health facilities, it only accounted for 42% of antimalarials dispensed in health facilities. Similar findings have been documented in Kenya [108-109]. In

this study amodiaquine was still largely dispensed (32%), although the drug was no longer in stock (which does not exclude it from being in the dispensing room). These findings differ from information extracted from user surveys carried out a few months later (June to August) according to which 63% of patients who were treated in health facilities received ALu, 17% SP and 6% amodiaquine. A deliberate attempt by health facility staff to clear out any remaining stocks of amodiaquine in the first half of the year could be an explanation for this. This would be consistent with reasons documented in Kenya for low ALu prescription. Indeed, factors determining low prescription of ALu by health workers were not so much related to distrust in the drug, but more with concerns over the cost of ALu, fears of future stockouts and excess stocks of non-recommended antimalarial drugs [108]. The data presented here clearly suggested a non-adherence to the user fee exemption given that half of the health facilities reported selling ALu packs for children under the age of eight. However, the findings are not conclusive as only four out of 10 health facilities provided pricing.

As far as the private sector is concerned both availability and accessibility of drug shops greatly increased after the introduction of ADDOs. Interestingly, there is evidence that ADDOs were opened in less populated areas where there were previously no Part II drug shops, suggesting that the programme may have succeeded in encouraging shop owners to open ADDOs in more remote areas.

General shops no longer play an important role in the provision of antimalarial treatment in the study area. A study carried out in 2001 found that 27% of the general shops selling drugs had antimalarials in stock [98] . This study found that the proportion of general shops selling antimalarial drugs decreased constantly between 2004 and 2008. There are a few possible explanations for this. On one hand this may be due to tighter supervision by district authorities as a result of the ADDO pilot in the area. However market mechanisms could also be operating. General shops may have been competed out of the market by the increase in the number of licensed drug shops or the increase in prices of antimalarials.

The use of the private retail sector for malaria treatment increased despite increases in prices and much higher prices than in health facilities. Although prices of antimalarials alone do not serve as an indication of affordability, price changes over a relatively short period of time provide a good indication of relative changes in affordability. The price of the first line treatment for malaria increased by 84% and the price of SP by 51% in drug shops whereas both decreased by 20% in health facilities. Nevertheless, the share of doses sold in the private retail sector increased from 49% to 59%. There are many possible reasons behind

this. Certainly improvements in availability and accessibility of shops must have contributed to their increased use. It might also be the result of greater demand for ADDO products compared to the previous Part II drug shops. Indeed, results from mystery shopper surveys conducted in parallel to the shop censuses suggest a major improvement in the quality of care in drug shops after the introduction of ADDOs. The percentage of mystery shoppers reporting with malaria symptoms increased from just above 30% to nearly 80% between 2004 and 2008 (Dillip et al., unpublished data). Another possible explanation could be the referral by health facility staff to shops in which they have a financial stake in, given that many ADDOs and Part II drug shops are owned directly or indirectly by health facility workers, but data from treatment seeking surveys suggest that this was not a major problem in the study area.

Despite the many improvements seen, the low availability of ALu in ADDOs is a major concern. Most ADDO shop keepers reported selling ALu at its recommended retail price of TSH 500 (approximately USD 0.40) for children doses and TSH 1500 (approximately USD 1.30) for other doses. The results presented here indicate that this level of subsidy did not result in widespread availability of the drug. Discussions with ADDO dispensers highlighted two main reasons for this: firstly the drug can only be procured from one wholesaler in Morogoro, a city approximately 200km from Ifakara; secondly the drug is too expensive and leads to low profit margins. A typical pre-packaged adult dose of SP was bought for TSH 900 (USD 0.80) and sold for TSH1500 (USD 1.30). Un-packaged SP was bought at the lower price of TSH 180 (USD 0.15) and sold for TSH 300 (USD 0.25). Conversely, a dose of ALu was bought for TSH 1150 (USD 1) which leaves a much lower profit margin than for other drugs. The experience from two studies which piloted the AMFm in Tanzania and Uganda where retail mark-ups were higher found higher stocking rates [44-45].

The findings presented here are highly relevant to the imminent roll-out of the AMFm and confirm that ensuring wide availability of ALu in the private retail sector is paramount to its uptake. ADDOs are a suitable distribution channel for ALu, since in the districts where they exist, they are available, accessible and highly utilised in both the district town and rural areas. The data presented here suggest that the low affordability of ALu in ADDOs ultimately restricted its availability. Cheaper drugs such as amodiaquine and SP were still the most dispensed drugs. AMFm plans to subsidise ACTs high in the distribution chain and to facilitate their distribution at competitive prices along the same channels as other antimalarials could present a viable solution to the problems encountered in the study area.

3.6. Conclusions

The public and private retail sector are important complementary sources of malaria treatment in rural Tanzania and efforts to improve access to prompt and effective malaria treatment should take both sectors into account. This duality of sources also offers a backup solution when drugs are out of stock in the public heath system. A high proportion of patients seek treatment for malaria from shops rather than health facilities despite higher prices possibly since shops are more available and more accessible. The introduction of subsidised ACTs in the private retail sector was piloted in the study area through the ADDO programme but did not lead to high availability of the drug, probably because the final price was not affordable. This resulted in a low uptake of ACTs despite its wide availability in public health facilities. If a high quality of services is ensured in the private sector the public health impact of ACTs can be maximised by making this class of drugs available in at affordable prices in the private sector.

3.7. Competing interests

AS is employed by the Novartis Foundation for Sustainable Development (NFSD) which funded the ACCESS programme. The Foundation works independently from the company's business and supports not-for-profit health programmes in developing countries.

3.8. Authors' contributions

SA coordinated the surveys between 2007 and 2008, analysed the data, drafted and finalised the manuscript. MWH coordinated the surveys between 2004 and 2006 and contributed to the manuscript. CG contributed to the coordination of the 2005 retail audit survey and contributed to the manuscript. AD contributed to the data collection and to the manuscript. JL coordinated the implementation of the ADDO programme and contributed to the manuscript. HM provided overall coordination and contributed to the discussion on the manuscript. CL contributed to the study design, the data analysis and the manuscript. The final manuscript was approved by all authors.

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4. Improvements in access to malaria treatment in Tanzania following community, retail sector and health facility interventions – a user perspective

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4.1. Abstract

Background

The ACCESS programme aims at understanding and improving access to prompt and effective malaria treatment. Between 2004 and 2008 the programme implemented a social marketing campaign for improved treatment seeking. To improve access to treatment in the private retail sector a new class of outlets known as Accredited Drug Dispensing Outlets (ADDO) was created in Tanzania in 2006. Tanzania changed its first line treatment for malaria from Sulphadoxine-Pyrimethamine (SP) to Artemether Lumefantrine (ALu) in 2007 and subsidized ALu was made available in both health facilities and ADDOs. The effect of these interventions on understanding and treatment of treatment was studied in rural Tanzania. The data also enabled an investigation of the determinants of access to treatment.

Methods

Three consecutive treatment seeking surveys were conducted in 2004 2006 and 2008 in the rural areas of the Ifakara Demographic Surveillance System (DSS) and in Ifakara Town. Each survey included approximately 150 people who had suffered a fever case in the previous 14 days were interviewed.

Results

Treatment seeking and awareness of malaria was already high at baseline, but various improvements were seen between 2004 and 2008, namely: better understanding causes of malaria (from 62% to 84%); an increase in health facility attendance as first treatment option for patients older than five years (27% to 52%); higher treatment coverage with antimalarials (86% to 96%) and more timely use of antimalarials (80% to 93-97% treatments taken within 24 hrs). Unfortunately, the change of treatment policy led to a low availability of ALu in the private sector and therefore to a drop in the proportion of patients taking a recommended malaria treatment (85% to 53%). The availability of outlets (health facilities or drug shops) is the most important determinant of whether patients receive prompt and effective treatment, whereas affordability and accessibility contribute to a lesser extent.

Conclusions

An integrated approach aimed at improving understanding and treatment of malaria has led to tangible improvements in terms of people's actions for the treatment of malaria. However, progress was hindered by the low availability of the first line treatment after the switch to ACTs.

4.2. Background

The cornerstone of the World Health Organisation's malaria control strategy is prompt and effective treatment for all episodes of malaria [3] [4]. Largely thanks to international support through the Global Fund to Fight AIDS Tuberculosis and Malaria (GFATM) and the World Bank's Malaria Booster programme, most sub-Saharan African countries have now switched to the highly efficacious artemisinin-combination therapies (ACT). International initiatives such as Medicines for Malaria Venture (MMV) are increasingly speeding up the development of new antimalarials. However, the public health impact of such drugs relies to a large extent on patient's ability to access them and little progress will be made unless broader access issues are tackled. Despite large increases in the number of antimalarial drugs supplied internationally, surveys conducted between 2007 and 2008 in 11 African countries found that only 15% of fever cases were treated with ACTs [3].

Several strategies have been proposed and tested to improve access to malaria treatment by targeting providers or users. Smith et al.[33] recently conducted a systematic review of the effectiveness of various such interventions in improving prompt and effective treatment of malaria. Interventions reviewed included optimising case-management and services in health facilities [34-35, 110-112] or improving dispensing practices of drug shop attendants and private practitioners [85, 113-117] as well as community based approaches [86, 118-119]. Two general approaches to improving user malaria treatment practices have been pursued 1) health education campaigns [120-121] and 2) interventions that specifically provide information on how to take anti-malarials [122], including pre-packaging and pictorial and verbal instructions [123-125]. The main finding from the review is that most interventions so far have been conducted on a rather small scale and that few have been appropriately evaluated. As a consequence, despite the wealth of research conducted on the topic, little is known about interventions that can promote sustained change.

The ACCESS programme in the Kilombero and Ulanga Districts in southern Tanzania aims to improve understanding of and access to prompt and effective malaria treatment through an integrated approach targeting both users and providers [101]. The programme's activities are based on a conceptual framework which defines access as the degree of fit between the needs and means of patients (users) and the existing services (providers) along the five dimensions of availability, accessibility, affordability, adequacy and acceptability [52]. Interventions are carried out at three levels: 1) the community, 2) the formal health sector and 3) the private retail sector for drugs. A comprehensive monitoring and evaluation plan accompanied each of these interventions. The implementation of the programme started in 2004 and the second phase will be completed in 2011.

Between 2004 and 2007 the ACCESS programme's main intervention at community level was a social marketing campaign for improved recognition of the disease and more effective care seeking. It followed on the work by the KINET project which used a social marketing approach to promote the use of insecticide treated nets in the same area [126]. Various communication channels were used and material developed to disseminate information on malaria transmission, symptoms and prevention as well as to stress the importance of prompt and effective treatment. Road shows were the main activity and included role plays, public lectures and quizzes. In addition, promotional materials (e.g. stickers, leaflets, t-shirts) were distributed, and billboards and posters displayed in public places. The programme also organised special campaigns targeted at pregnant women and mothers of young children in Mother and Child Health (MCH) clinics. Social marketing campaigns were conducted in 96% (78/81) of the villages in the Kilombero District and 95% (62/65) of the villages in the Ulanga District. More detailed information on the ACCESS social marketing campaigns can be found elsewhere [101].

The ACCESS programme also intervened in the public health sector to improve quality of care. Key activities included strengthening of routine supervision and refresher training for health facility staff based on Integrated Management of Childhood Illness (IMCI) algortithms [101]. In 2004 and 2005 91% (94/103) of all health workers in the Ulanga District and 93% (39/42) of clinical officers in the Kilombero District attended a refresher training. In addition the study period saw a change of first line treatment for malaria. In 2006 the Government of Tanzania switched from Sulphadoxine Pyrimethamine (SP) to Artemether Lumefantrine (ALu). Actual introduction of ALu in health facilities was delayed until 2007, with resulting stock-outs in the transition period [127] (Cf. Chapter 3).

In parallel the Accredited Drug Dispensing Outlets (ADDOs) programme was rolled out in the study area from 2006 onwards to improve access to treatment and quality of care in the private drug retail sector [87]. ACCESS undertook the local evaluation and monitoring of the programme. The private retail sector plays a very important role in the delivery of antimalarial treatment in most African countries as retailers tend to be more accessible and flexible, especially with regards to opening hours and charges [39-40]. The aim of the ADDO programme is to improve access to basic medicines by upgrading all existing drug shops to well regulated and properly operated outlets manned by specifically trained personnel [57]. The intervention involved a combination of private drug shop dispenser training, incentives, accreditation and regulation. The ADDO programme greatly improved the availability and accessibility of drug shops and, most importantly the quality of advice and dispensing (Dillip

et al. unpublished data). ALu was made available to the programme at a very highly subsidised price towards the end of 2007, but this did not result in widespread availability of the drug , allegedly because of low profit margins and long distances to the wholesalers.[127] (cf. Chapter 3) between 2006 and 2008 55 ADDOs were opened the Ulanga District and 135 in the Kilombero District (equivalent to approximately three shops per 10,000 people in both districts).

The primary aim of this study was to evaluate changes in understanding and treatment seeking for malaria in the Kilombero and Ulanga Districts during the period 2004-2008 and to assess how such changes could be attributed to the three interventions evaluated by the ACCESS programme. The results presented here are complemented by a study which focused on changes in availability, accessibility and affordability of treatment over the same period (i.e. the provider perspective) [127] (cf. Chapter 3). The data also provided a unique opportunity to apply a recent analytical framework on access to treatment [52] in a real-life situation and to assess the determinants of access to prompt and effective treatment.

4.3. Methods

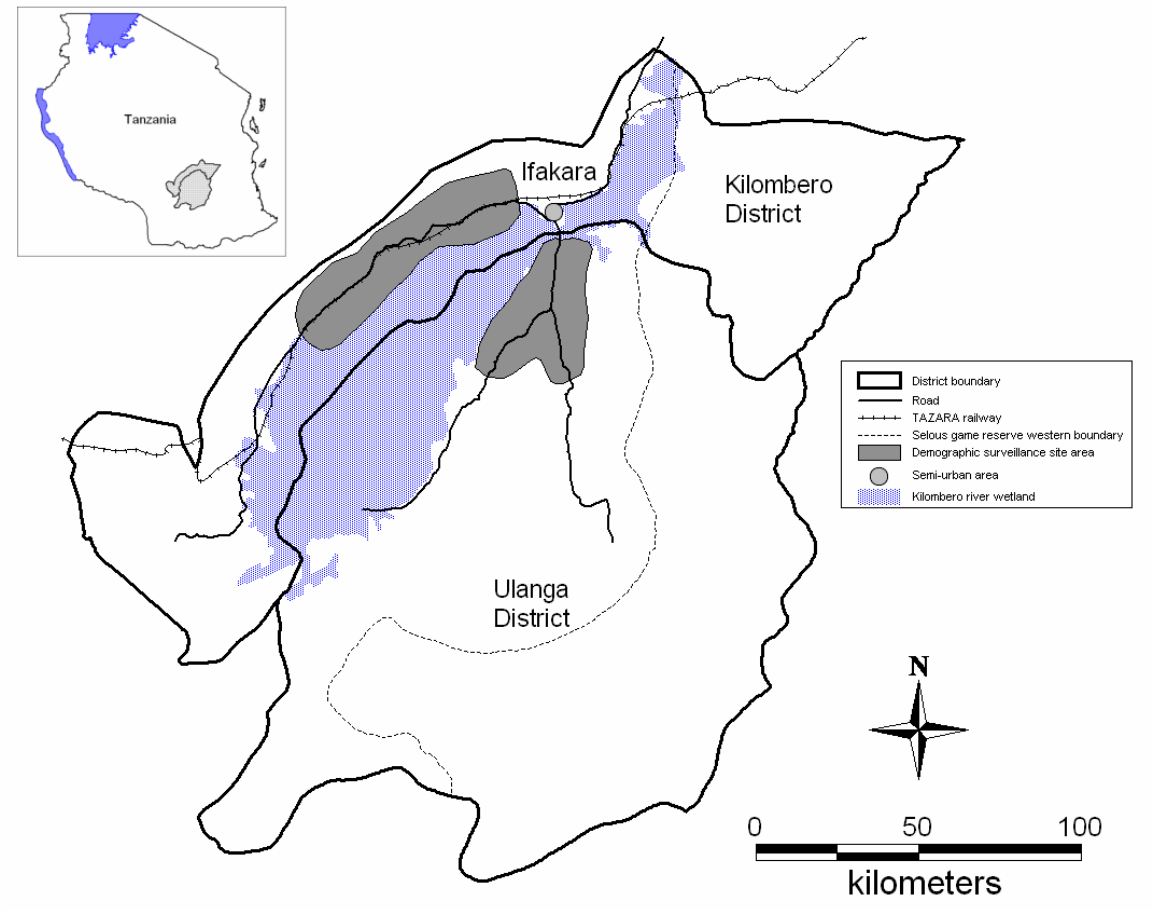
Study setting

The study was carried out in the Kilombero and Ulanga Demographic Surveillance System (Ifakara Rural DSS) and in the semi-urban setting of Ifakara town between 2004 and 2008 (Figure 17). In the DSS area every household is visited every four months to collect a set of basic demographic data. As a result, a comprehensive and continuously updated database of the resident population is maintained for the study area. The Ifakara Rural DSS covers 25 villages (13 in Kilombero and 12 in Ulanga). The population in 2004 was almost 74,000 and just over 92,000 in 2008. The population of Ifakara Town was 45,700 according to the national census of 2002 [103]. A study conducted in the area between 2001 and 2003 reported an Entomological Inoculation Rate (EIR) of 349 infective bites per person per year (ib/p/y) [77], but according to recent data it has declined to 81 ib/p/y [78]. EIR data for Ifakara town suggest that the transmission rate is about a log order smaller than in the surrounding rural areas [79]. The area has been described in more detail elsewhere [73, 101].

The formal health sector **-** There are six health facilities in the Kilombero DSS area and eight health facilities in the Ulanga DSS area. The Designated District Hospital in Ifakara serves as a referral centre for the entire area and there are also two other health facilities in town. Government and faith-based facilities in Kilombero and Ulanga charge user fees. In the

Ulanga District the Community Health Fund (CHF) offers a form of risk protection to its members but very few people were enrolled during the study period (around 3% of the population in 2005 - personal communication from the District Medical Officer). Children under five years of age, pregnant women and elderly people should receive services and drugs free of charge but there is ample evidence that the exemption mechanism is not properly implemented [64, 88].

Figure 17. Map of Kilombero and Ulanga Districts showing Ifakara Town and the Demographic Surveillance System (DSS).



Retail sector for drugs - By 2008 90% (49/54) of drug shops in the study area were ADDOs. Between 2004 and 2008 the number of shops per 1000 people increased from 0.24 to 0.39 and as a result the proportion of people living within 5km from a shop increased from 71% in 2004 to 87% in 2008. The roll out of ADDOs coincided with a stark decrease in the availability of antimalarial drugs in non-licensed general shops. Mystery shopper surveys showed that the proportion of customers with malaria symptoms who got correct advice and treatment in drug shops increased from just above 30% to nearly 80% between 2004 and 2008 (Dillip *et al*., unpublished data) after the introduction of ADDOs. Although ALu was

made available in ADDOs in mid 2007 with a high level of subsidy by 2008 it was only stocked by a third of shops. SP and other older antimalarials remained much more widely available and sold [127] (cf. Chapter 3).

Treatment seeking surveys

Three cross sectional surveys were conducted in the DSS areas and Ifakara Town in 2004, 2006 and 2008 to investigate treatment seeking for malaria and understanding of the disease. The interviewees included children and adults who had recently suffered a fever episode (caretakers responded to questions for children under the age of 12). Data collection was carried out every other year between May and August, a time of the year which coincides with the dry season and is characterised by a lower intensity of transmission. An analysis of the baseline study in 2004 was published by Hetzel *et al.* [88] and the results presented here provide a longitudinal assessment of the changes between 2004 and 2008.

Sampling procedure - Different sampling procedures were applied in the DSS area and in Ifakara Town. In the DSS area, a village-stratified random sample of households was drawn from the existing comprehensive DSS register. Only households with at least one child under the age of five years were eligible. In Ifakara such a sampling frame was not available. Therefore, the local administrative structure was used to draw a two-stage random sample of households, using ten-cell leaders (*balozi*) as first level of sampling. Given a background of decreasing fever incidence rates (cf. Chapter 5), every year a greater number of households were sampled to ensure that approximately 150 fever cases could be followed up (Table 10). All individuals from the sampled households who reported an episode of fever within the previous 14 days were included in the study. Patients who had not recovered clinically were not included and they were instead advised to seek care from a health facility. More details on the sampling and interviewing procedure can be found in the baseline paper [88].

Table 10. Sample size and number of fever cases followed up in each survey round

	DSS areas		*Ifakara Town*	
	Households sampled [1]	*People interviewed*	*Households sampled (ten-cells x households per ten-cell)* [2]	*People interviewed*
2004	318	110	223 (40 x 6)	44
2006	561	103	410 (50 x 9)	50
2008	750	86	739 (75 x 10)	41

[1] Village-stratified sampling proportional to number of households per village
[2] Two-stage sampling of households within ten-cells. The final number of households is lower than the product of the parts as some ten-cells have less than the chosen number of households

Data collection tool - The tool for data collection was a locally adapted Explanatory Model Interview Catalogue (EMIC) [94] based on focus group discussions and prior research carried out in the study area [81, 128]. This semi-structured questionnaire provides qualitative and quantitative data on patients' signs and symptoms associated with the fever episode (patterns of distress), as well as perceived causes and treatment seeking. Patients were also asked to label the disease according to their own understanding. In the study area most cases were labelled as malaria, *homa* (fever) and *degedege* (fever-related disease with neurological involvement [81]).

Distance from households to nearest point of care - Distances from households to the nearest health facility or drug shop were calculated by combining the Global Positioning System (GPS) locations of households from the DSS database and the GPS positions of outlets obtained from providers surveys [127] (cf. Chapter 3). The households GPS values were available for 91% (100/110) households in 2004 97% (100/103) in 2006 and 87% (73/87) in 2008.

Measuring socio-economic status - A relative index of socioeconomic status (SES) was calculated for the households in the DSS villages using asset ownership and household characteristics data stored in the DSS database. A principal components analysis (PCA) defined the weights of an SES index [129] [130] for the households in the survey, relative to all other households in the area. Households were divided into five wealth quintiles based on their SES score. The score was available for 97% (107/110) households in 2004, 93% (96/103) in 2006 and 93% (81/87) in 2008. The variables included in the analysis and the weight given to each is shown in Table 11.

The variables collected for SES assessment in 2004 differed from the ones collected in subsequent years but this was not considered to bias analyses. Comparing SES quintile groupings in the DSS households showed similar year on year comparability across all years in the poorest and richest category. Indeed 40% (871/2157) of households categorised as poorest in 2004 were categorised as poorest in 2006 and 47% (1256/2686) households categorised as richest in 2004 were categorised as richest in 2006. Similar, albeit higher values were found comparing categories in 2006 and 2008, that is 53% (1341/2540) and 61% (1752/2882) respectively. As year on year comparability in the three middle quintiles was poor, the middle quintiles were grouped into one category which resulted in 66% (4470/6813) of household categorised as middle in 2004 also categorised as middle in 2006 and similarly 73% (5930/8104) comparing the 2006 and 2008 groupings. With these

regroupings it was assumed that the difference in the type of assets collected would not introduce substantial bias.

Table 11. Results of principal components analysis of socio-economic status (SES) variables

Item	*2004*		*2006*		*2008*	
	Mean	*weight*	*Mean*	*weight*	*Mean*	*weight*
Meals consumed per day in past 2 days	2.31	0.42				
Days per week that the following is consumed:						
Meat	0.71	0.29				
Rice	3.92	0.23				
Tea	2.37	0.42				
Main source of food:						
Market	0.52	-0.34				
Own farm	0.44	0.37				
Source of water : 1=tap 2=well with pump 3=well 4=river	2.49	-0.06				
Household owns at least 1:						
Bicycle	0.45	0.32	0.57	0.42	0.65	0.44
Radio	0.49	0.34	0.65	0.38	0.66	0.42
Animal			0.09	0.17	0.10	0.23
Mobile phone			0.07	0.28	0.28	0.42
Corrugated iron roof			0.32	0.35	0.34	0.34
Small business as source of income			0.09	0.09	0.11	0.13
Rented accommodation			0.10	-0.02	0.10	0.02
Number of mosquito nets			1.97	0.46	2.03	0.35
Number of rooms	2.09	0.17	2.18	0.45	2.23	0.38
Toilet or latrine			0.92	0.15	0.93	0.06
Number of households included	14515 / 14997		16762 / 16888		17764 / 18813	
Variation explained by first principal component	24%		23%		24%	

Ethical clearance - All study participants provided oral informed consent prior to the interview. The National Institute for Medical Research of the United Republic of Tanzania granted ethical clearance for the study (NIMR/HQ/R.8a/Vol.IX/236, 16th September 2003).

Analyses

Various indicators were constructed and compared between 2004 and 2008. Indicators of understanding of malaria focused on perceived causes and patterns of distress.. Indicators of treatment included: actions, sources and type of drugs used for the treatment of fever and links of the community effectiveness chain based on the approach developed by Hetzel et al [88]. The community effectiveness chain breaks down the full Roll Back Malaria (RBM) [4]

indicator into its primary components [131] and includes: the proportion of fever cases 1) treated; 2) treated with a drug; 3) treated with an anti-malarial; 4) treated with a recommended anti-malarial; 5) treated with a recommended anti-malarial on the same or next day; 6) treated with a recommended anti-malarial the on same or next day and following the correct regimen (correct number of tablets, timely intake and duration), i.e. the full RBM indicator; 7) treated with a recommended anti-malarial on the same or next day, following the correct regimen and appropriately considering reported symptoms (with quinine if symptoms of severe malaria are reported). Since the change of treatment policy only effectively took place one year before the last 2008 survey, two scenarios were presented for 2008. The first scenario is strictly according to guidelines, following which only ALu qualifies as a recommended treatment, whereas the second scenario also allows for SP as a recommended treatment. Logistic regressions estimated the effect of changes over time from 2004 to 2008 with time entered in the model as a categorical variable. Estimates of change over time were reported crude as well as adjusted by SES groupings since SES score was higher in the last two surveys compared to the first survey.

The recently developed access to treatment framework [52] was applied to the data to estimate the determinants of access in the study area. The framework defines five dimensions of access, namely availability, accessibility, affordability, adequacy and acceptability. Availability refers to the existence of appropriate service. Thus, an indicator of availability was defined as the presence of an outlet (health facility or drug shop) stocking anti-malarial drugs in the village of residence of the patient. Accessibility refers to the geographical distance between the services and the homes of intended users. The main indicator of accessibility was thus defined as the distance from the patient's main residence to the nearest outlet stocking anti-malarials (health facility or drug shop). But since patients in the study area often spend a significant amount of time in farming fields far away from households and outlets [132], a secondary indicator of accessibility was defined as whether the patients were in their main residence or away in farming fields at onset of fever. Affordability refers to whether the prices of services fit the patients' income and ability to pay. The patient's SES quintile was taken as a surrogate indicator for income and how much they spent on their treatment (drug and consultation) as an indicator of their ability to pay. The data necessary to construct indicators of acceptability and adequacy were not available The analysis only included patients from the rural DSS villages as data on SES and distances to nearest shop or health facility were not available for households in Ifakara town.. Univariate logistic regressions assessed contribution of each of the access indicators on the odds of the patient receiving of prompt and effective treatment within 24 hours. A multivariate model was

built (by backward elimination of variables with a log-likelihood ratio test greater than 0.2) to assess the relative contribution of each of the access indicators.

Epi Info 6 and Intercooled Stata 9 (College Station, Texas, USA) were used for random sampling procedures. Data were double entered in Microsoft FoxPro and Microsoft Access (Microsoft Corp.) and checked for coding errors and consistency. Statistical analysis was done with Intercooled Stata 9. Distance calculations were carried out with ArcMap Version 9.1 (ESRI Inc.).

4.4. Results

The cross-sectional samples were similar over the three years of observation in terms of age, sex, residence, religion and years of formal education. Despite being marginally wealthier, households in 2008 were located further away from drug shops and health facilities (Table 12).

Table 12. Sample characteristics

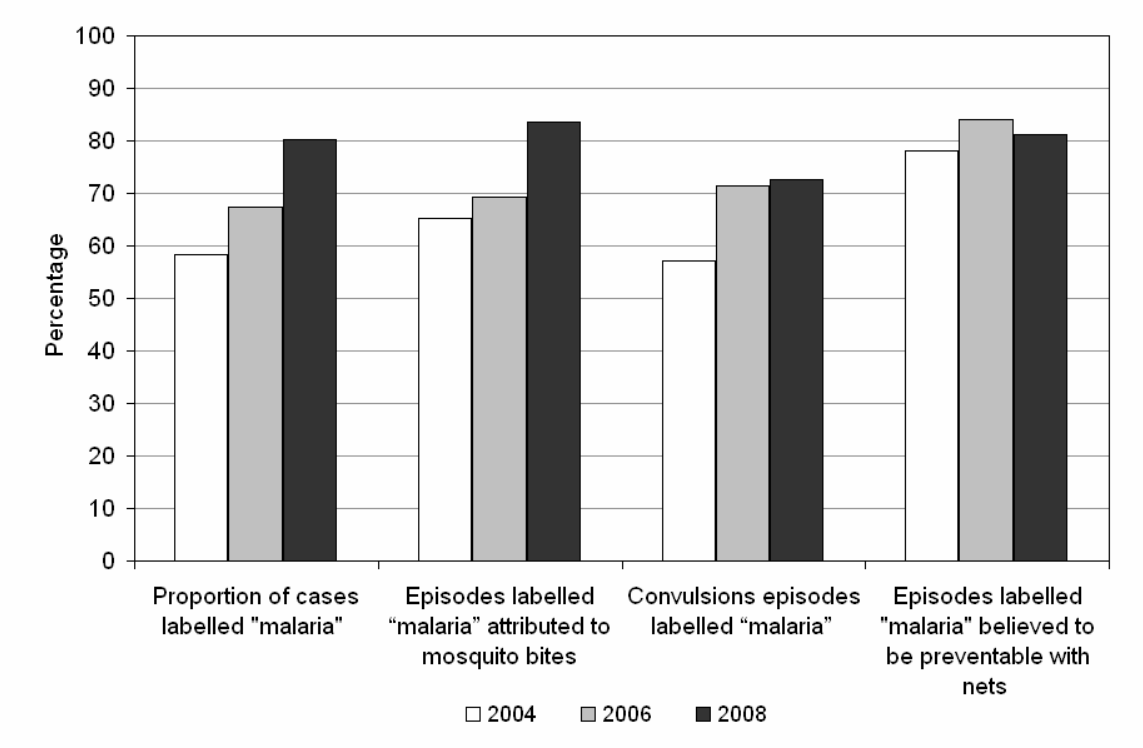
	2004		*2006*		*2008*	
	N	*n (%)**	*N*	*n (%)**	*N*	*n (%)**
Age group	154		153		127	
Under 5 years		81 (52.6%)		76 (49.7%)		50 (39.4%)
Over 5 years		73 (47.4%)		77 (50.3%)		77 (60.6%)
Sex	154		153		127	
Male		71 (46.1%)		63 (41.2%)		54 (42.5%)
Female		83 (53.9%)		90 (58.8%)		73 (57.4%)
Residence	154		153		153	
Ulanga DSS		61 (39.6%)		41 (26.8%)		40 (31.5%)
Kilombero DSS		49 (31.8%)		62 (40.5%)		46 (36.2%)
Ifakara		44 (28.6%)		50 (32.7%)		41 (32.3%)
Religion*	154		152		125	
Muslim		63 (40.9%)		51 (33.5%)		50 (40.0%)
Christian		91 (59.1%)		101 (66.4%)		75 (60.0%)
Years of formal education**	137		150		125	
< 7 years		56 (40.9%)		45 (30.0%)		38 (30.4%)
= 7 years		70 (51.1%)		99 (66.0%)		80 (64.0%)
> 7 year		11 (8.0%)		6 (4.0%)		7 (5.6%)
SES score ***	107		96		81	
Poorest		20 (18.7%)		6 (6.3%)		10 (12.4%)
Middle		63 (58.9%)		62 (64.6%)		52 (64.2%)
Richest		24 (22.4%)		28 (29.2%)		19 (23.5%)
SES score *** *[mean (SD)]*	107	0.09 (1.53)	96	0.41 (1.28)	81	0.44 (1.45)
Distance to nearest health facility (km) *** *[median (IQR)]*	105	1.69 (2.74)	100	1.67 (3.43)	73	2.25 (3.83)
Distance to nearest Part II or ADDO drug shop (km) *** *[median (IQR)]*	105	1.70 (4.13)	100	1.79 (3.30)	73	2.49 (1.94)

* unless otherwise stated
** of caretaker if patient <12 years
*** DSS only (110 observations in 2004, 103 in 2006 and 86 in 2008)

Understanding of malaria

The population appears to be more aware of malaria, its causes and its prevention in 2008 compared to 2004 (Figure 18). While in 2004 57% (80/137) of people labelled their fever case as malaria, the proportion rose to 80% (102/127) in 2008 (crude OR=3.14 p<0.001, adjusted for SES OR=2.31 p=0.008. The proportion of cases labelled malaria attributed to mosquito bites significantly increased from 62% (79/127) to 84% (97/116) (crude OR=3.10 p<0.001, adjusted for SES OR=2.02 p=0.056). The proportion of fever episodes with symptoms of convulsions (twitching, stiff body, delirium, white eyes, kicking limbs) labelled as malaria also consistently increased from 57% (16/28) to 73% (8/11), although not significantly so due to the small number of cases with such symptoms (OR=2.00 p=0.373). The proportion of fever cases believed to be preventable with the use of mosquito nets did not increase, most likely because of the already very high value of 81% at baseline.

Figure 18. Changes in understanding of malaria

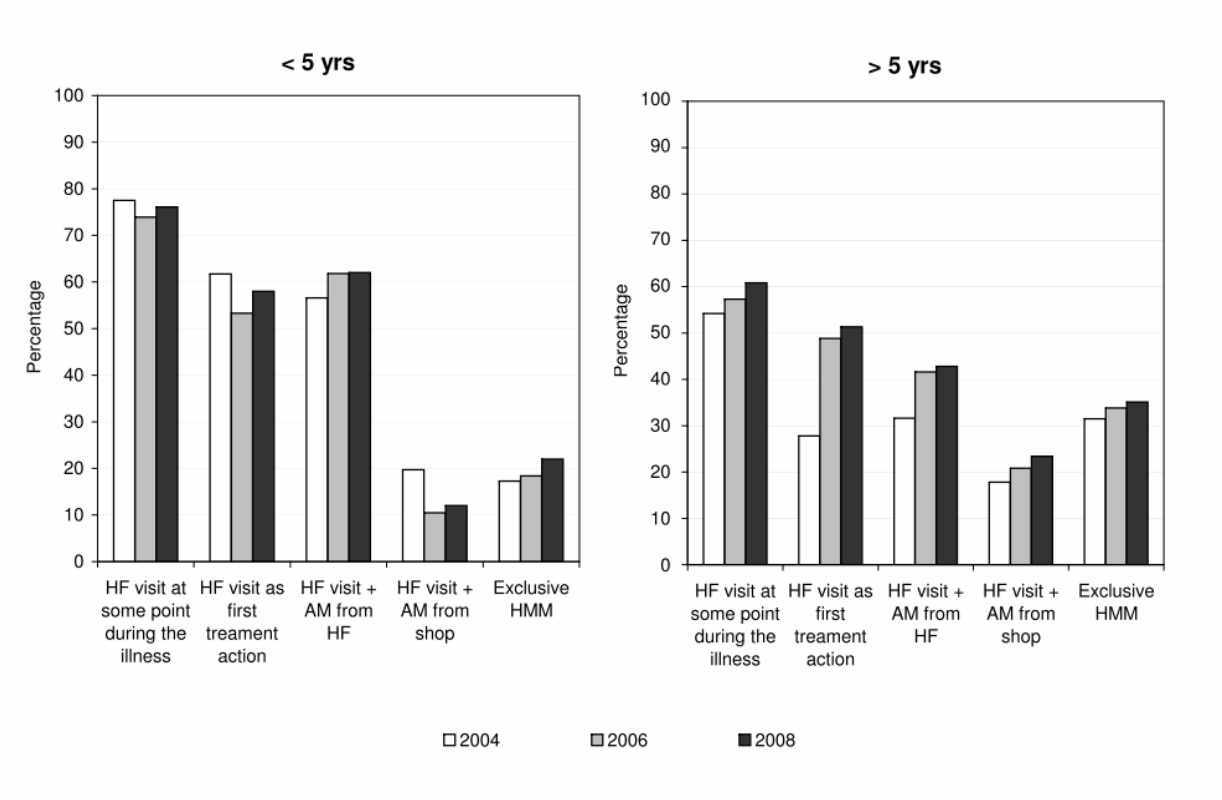


Treatment of fever

There was no difference in health facility attendance and treatment in children, but the proportion of older patients who sought treatment in health facilities increased significantly . Health facility attendance and treatment was already very high at baseline in children and did not change over the study period (health facility attendance at some point during the illness

148/195 i.e. 76%; health facility attendance as first treatment action 119/201 i.e. 58%; treatment with antimalarial from a health facility 123/207 i.e. 59%). Conversely the odds of older patients attending a health facility as a first treatment option increased three-fold between 2004 and 2008 (from 20/73 i.e. 27% to 40/77 i.e. 52% OR=2.9 p=0.002) crude and nearly 5-fold adjusting for SES (OR=4.6 p=0.001). The odds of older patients being treated in a health facility also increased although not significantly (from 23/73 i.e. 32% to 33/77 i.e. 43% OR=1.63 p=0.152) crude and nearly three-fold adjusting for SES (OR=2.9 p=0.012).

Figure 19. Sources of treatment for fever and actions undertaken (Note: HF=Health facility; AM=antimalarial; HMM=home management of malaria



The receipt of treatment from the private retail sector increased over the study period. Overall the proportion of cases treated with an antimalarial from a drug shop significantly increased from 31% (47/154) in 2004 to 31% (47/153) in 2006 and 43% (54/127) in 2008 (OR=1.68, p=0.038). Three points should be highlighted with regards to this. Firstly, this effect is confounded by SES (adjusted OR=1.18 p=0.632). The proportion mainly increased in the three middle wealth quintiles from 19% (12/63) to 26% (12/46) and actually decreased in the poorest quintile from 25% (5/20) to 20% (2/10) whereas it stayed stable in the richest quintile (20/74 i.e. 27%). Secondly the increase was mainly in patients over the age of five (38% in 2004 to 52% in 2008) and not in children (25% in 2005 to 28% in 2008). Thirdly the increase in the use of the private sector in patients older than five was due more to an

increase in people who attended health facilities and obtained treatment from a shop (23/73 i.e 31% in 2004 to 33/77 i.e. 43% in 2008) than in people who treated themselves directly from shops without ever visiting a health facility (23/73 i.e. 32% in 2005 to 27/77 i.e 35% in 2008). Few patients were treated from a general shop (30/434 i.e. 7%) (Table 13).

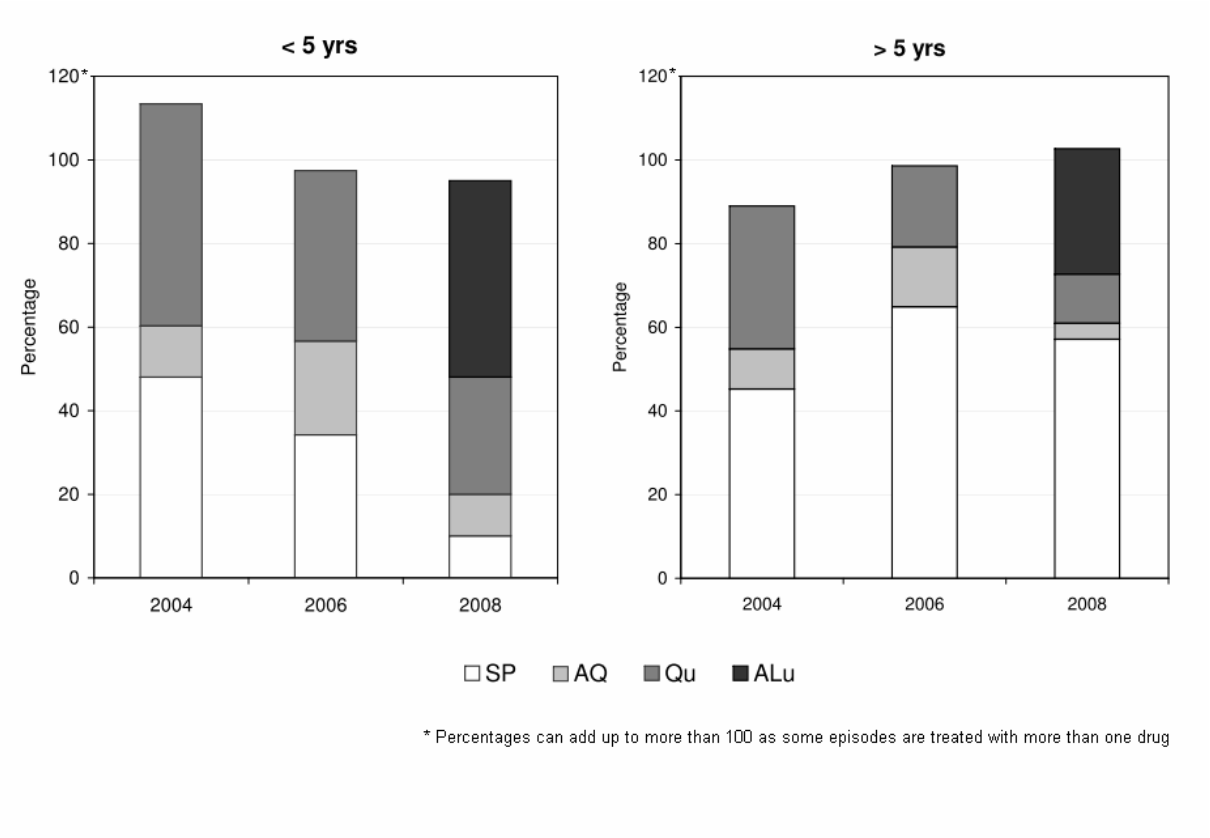
Table 13. Breakdown of types of antimalarials received from each of the sources of treatment (number of cases and percentages)

	2004			*2006*			*2008*		
	Health facilities	*Drug shops*	*General shops*	*Health facilities*	*Drug shops*	*General shops*	*Health facilities*	*Drug shops*	*General shops*
Chloroquine*		1 (2.1%)							
Artemether-Lumefantrine							40 (62.5%)	7 (13.0%)	1 (16.7%)
Sulphadoxine-Pyrimethamine	40 (58.5%)	20 (42.6%)	10 (90.9%)	41 (51.2%)	33 (70.2%)	10 (83.3%)	11 (17.2%)	35 (64.8%)	3 (42.9%)
Amodiaquine	10 (14.7%)	9 (19.2%)		16 (20.0%)	9 (19.2%)	1 (8.3%)	4 (6.3%)	4 (7.4%)	
Quinine	38 (55.9%)	26 (55.3%)	3 (27.3%)	24 (42.5%)	13 (27.7%)	3 (25%)	12 (18.8%)	11 (20.4%)	2 (28.5%)
Total	68	48	11	80	47	12	64	54	6

* 2 patients took chloroquine in 2004 but information on source of treatment was available for 1 patient

A breakdown of the types of antimalarials taken also shows some improvements over time although the low uptake of ALu is disappointing (Figure 20). Treatment coverage with antimalarials is extremely high in the study area. In 2004 the use of multiple antimalarials to treat a single fever case in children under the age of five was common but it decreased in 2006 and 2008. The most commonly used drug over the study period was SP. In 2008, more than a year after the change of treatment policy, only 39% (48/124) of cases were treated with ALu. The low uptake of ALu is partly explained by the fact that even in health facilities not all cases received ALu (only 63%) and partly because most of the people who were treated in shops either received SP (65%), quinine (20%) or amodiaquine (7%) and only 13% received ALu (Table 13). Children were more likely to be treated with the new drug than older patients but not significantly so (23/50 i.e. 46% of children and vs. 23/77 i.e. 30% older patients OR=1.28 p=0.439). Interestingly, patients in the middle quintiles were the least likely to be treated with ALu (poorest to middle quintiles OR=3.56 p=0.029, richest to middle quintiles OR=3.15 p=0.004).

Figure 20. Types of antimalarials taken for treatment of fever (Note: SP=Sulphadoxine-Pyrimethamine, AQ=amodiaquine, Qu=Quinine, ALu=Artemether-Lumefantrine)



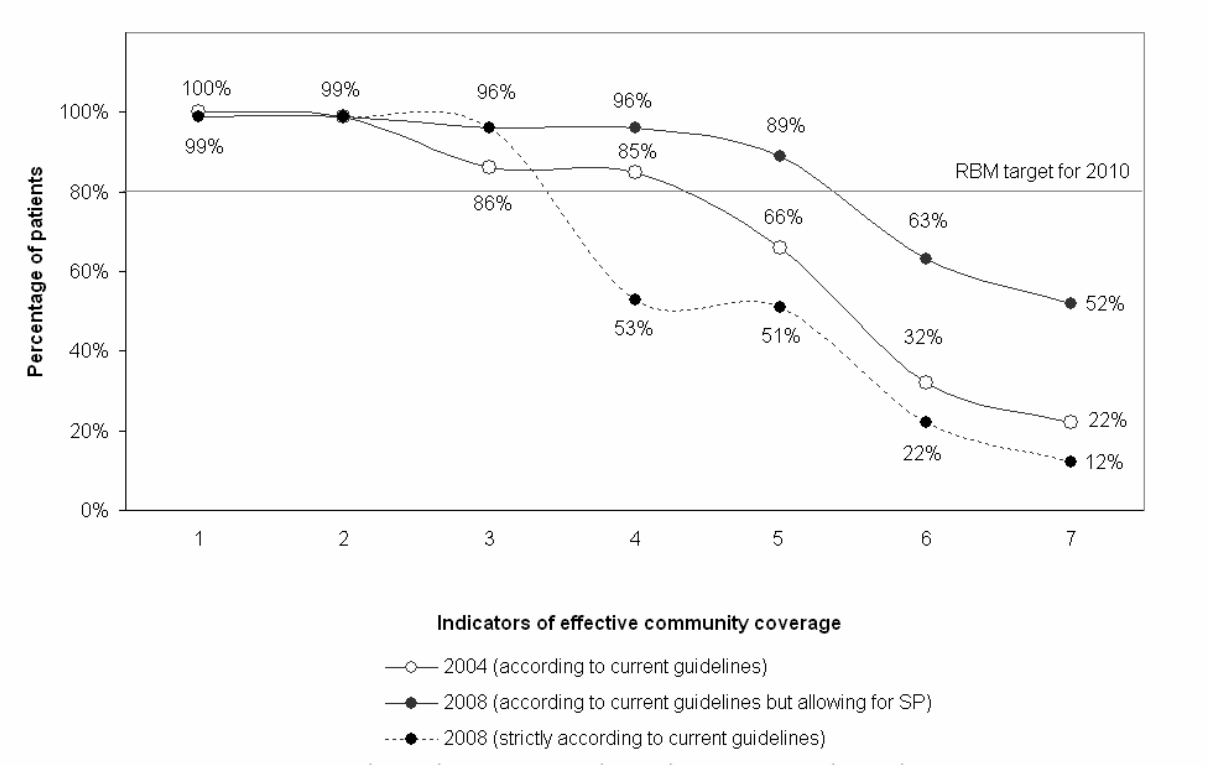
Community effectiveness of malaria treatment

The comparison of the community effectiveness of malaria treatment in 2004 and 2008 shows a clear improvement over time (Figure 21). Despite a sharp fall in the proportion of people taking a recommended treatment for malaria after the switch to ALu, there were appreciable improvements in terms of timeliness of treatment. Comparing the number of people who took an appropriate anti-malarial (indicator 4) and the number who took it within 24 hours (indicator 5) shows that whereas in 2004 80% (101/127) of were treated promptly, in 2008 this figure rose to 97% (65/67) of patients who took ALu or quinine (crude OR=8.36 p=0.005, adjusted for SES OR=6.39 p=0.018), and 93 % (113/122) of patients who took a ALu, quinine or SP (crude OR=3.23 p=0.004, adjusted for SES OR=4.23 p=0.015).

The self-reported adherence to the recommended drug regimen. only marginally improved. Adherence to SP treatment regimens improved over time (55/72 i.e. 76% in 2004 vs. 41/49 i.e. 84% in 2008). However, just over two thirds of patients completed their courses of ALu (22/32 i.e. 69%). Quinine treatments were always under-dosed because the course was not taken for the full seven days. Overall, comparing the number of people who took an appropriate anti-malarial within 24 hours (indicator 5) and those who took it adhering full to its regimen (indicator 6) shows that in 2004 32% (32/101) of timely treatments were taken

following regimen and in 2008, although this figure rose to 51% (58/113) of patients who took ALu, quinine or SP, only 31% (20/65) of patients who took quinine or SP fully adhered to their regimen (strictly according to guidelines: crude OR=1.12 p=0.809, adjusted for SES OR=0.94 p=0.910; allowing for SP as appropriate treatment in 2008: crude OR=1.63 p=0.212, adjusted for SES OR=1.40 p=0.475).

Figure 21. Estimated effective coverage of fever treatment based on patients' or caretakers' accounts. Percentages are the proportion of fever cases 1) treated; 2) treated with a drug; 3) treated with an anti-malarial; 4) treated with a recommended anti-malarial; 5) treated with a recommended anti-malarial on the same or next day; 6) treated with a recommended anti-malarial on the same or next day and following the correct regimen (correct number of tablets, timely intake and duration), i.e. the full RBM indicator; 7) treated with a recommended anti-malarial on the same or next day, following the correct regimen and appropriately considering reported symptoms (quinine if symptoms of severe malaria are reported).



There were some difference between adults and children. Generally coverage was higher in children under the age of five compared to the rest of the population. The proportion of cases treated with a recommended anti-malarial (including SP) within 24hrs increased from 73% (59/81) in 2004 to 88% (44/50) in 2008 in children under the age of five (OR=1.30, p=0.030) and from 57% (42/73) in 2004 to 90% (69/77) in patients over the age of five (OR=1.56 p<0.001). The proportion of cases treated with either ALu or quinine within 24hrs in 2008 was 72% (36/50) in children under the age of five and 38% (29/77) in all other patients. However the proportion of cases treated promptly and effectively and following the recommended regimen tended to be slightly lower in children under five than in adults. Allowing for SP the

proportion in children under five increased from 37% (16/43) to 56% (19/34) and in adults from 28% (16/58) to 67% (39/58) between 2004 and 2008. Strictly according to guidelines, i.e. excluding SP and conforming to the full RBM indicator for prompt and effective treatment of malaria, the figure in 2008 is 39% (13/33) for children and 12% (7/58) in adults.

Determinants of access

An analysis of the contribution of each of the access dimensions suggests that the **availability** of antimalarials thanks to the presence of a drug outlet (health facility or drug shop) is the main determinant of whether people get prompt and effective treatment for malaria (Table 14). There was no significant difference in promptness of treatment between patients who had been treated in health facilities and those treated in drug shop (OR=1.28 p=0.613), but patients treated in drug shops were less likely to be treated with the appropriate drugs (OR=0.14 p=0.001). Patients living in villages with either a drug shop or a health facility were four times as likely to get prompt and effective malaria treatment than people from villages without outlets (OR=4.10 p<0.001 adjusting for differences in affordability and accessibility). The presence of outlets influenced promptness (OR=5.83 p<0.001) and appropriateness (OR=4.75 p<0.001) of treatment to a similar extent.

Affordability contributed to a lesser extent to receipt of treatment. Both the univariate and multivariate model showed no difference in receipt of prompt and effective treatment across socio-economic groups. However, people who paid more for their treatment were more likely receive it promptly and effectively (OR=1.74 p=0.008). This implies that even poorer people manage to find the resources to afford treatment. The cost of treatment influenced the appropriateness of treatment (OR=3.34 p<0.001) more than the timeliness (OR=1.67 p=0.017). It is worth recalling here that a somewhat un-expected pattern of ALu uptake was observed in 2008 whereby the three middle quintiles were less likely to be treated with ALu (cf. results in “Treatment of fever”).

Accessibility is a determinant of access to treatment, but only if people are in far away farms at onset of their disease. People were twice as likely to be treated promptly and effectively if they were residing in their main homestead rather than in the farming fields at the onset of their fever (OR=2.08 p=0.032 in the multivariate model). The location at onset of disease mainly influenced the receipt of a recommended anti-malarial (OR=2.48 p=0.004) rather than the timeliness of treatment (OR=1.63 p=0.133). However, if people were in their main homestead at onset of disease, the distance to the nearest outlet did not have a major impact on treatment provided the outlet was present in their village (OR=0.88 p=0.082).

Table 14. Determinants of receiving prompt and effective antimalarial treatment according to current guidelines from either a health facility or a drug shop in the rural DSS villages between 2004 and 2008

			Univariate model		*Multivariate model (n=264)*	
		N	*OR (95% CI) **	*p*	*OR (95% CI) **	*p*
Availability	Presence of outlet in the village of residence **	297	**3.32 (1.96 to 5.63)**	**<0.001**	**4.10 (2.17 to 7.73)**	**<0.001**
Affordability	SES (baseline: middle quintiles)	282		0.951		
	Poorest		0.94 (0.44 to 2.03)	0.893		
	Richest		1.07 (0.59 to 1.95)	0.803		
	Cost of treatment *** (TSh1000)	297	**1.73 (1.26 to 2.43)**	**0.002**	**1.74 (1.16 to 2.60)**	**0.008**
Accessibility	Distance household to nearest outlet ** (1km)	276	**0.84 (0.73 to 0.95)**	**0.006**	0.88 (0.75 to 1.01)	0.082
	Location at onset of fever (home vs. farming site)	295	**1.83 (1.03 to 3.27)**	**0.039**	**2.08 (1.07 to 4.09)**	**0.032**

* Adjusted for the effect of year of study
** Presence/distance to health facility for those treated in a health facility and presence/distance to drug shop for those treated in a drug shop
*** Drug + consultation

4.5. Discussion

The results presented here show improvements in understanding and treatment seeking for malaria in two rural districts in Tanzania after the implementation of the ACCESS programme. Specific improvements include a better understanding of the causes of malaria, an increase in health facility attendance and treatment in patients older than five years, and more timely use of antimalarials. Unfortunately, the change of malaria treatment policy from SP to ALu during the same period led to a lower availability of the first line drug in the private retail sector. As a consequence the proportion of patients taking a recommended malaria treatment dropped significantly in 2008.

Given the before-after nature of this study and the absence of a control group it is difficult to attribute specific improvements to ACCESS interventions. However, plausible explanations can be given on the basis of accepted frameworks [72, 90].With this type of design improvements are attributed to the programme if improvements are found in every step of the causal pathway between intervention and outcomes and all other explanations can be formally discarded. In this study the main outcome of interest is prompt and effective treatment and steps in the causal pathway include :1) changes in understanding of malaria; 2) changes in actions for the treatment of malaria and; 3) changes in access outputs, i.e the accessibility, availability and affordability of treatment, which were reported in a separate study [127] (Cf. Chapter 3).

It seems reasonable to credit the ACCESS social marketing campaigns for the observed changes in the understanding of malaria and the increased use of health facilities as a first treatment action. Indeed, no other efforts of this magnitude took place concurrently in the area. With regard to the lack of increase in health facility attendance in children, it is important to bear in mind that health facility attendance in this age group was already very high for a rural African setting with over 75% of children visiting a facility at some point during their illness. The high level of action already undertaken by mothers of small children at the start of ACCESS is undoubtedly the result of a long-standing effort in the area to improve comprehensively malaria control parameters [91, 126]. It is especially worthy of note that increases in health facility attendance were higher once adjusted for SES status. This would suggest the ACCESS social marketing campaigns were able to target even the less well off, which is far from always being the case [133]. This result is consistent with data from the evaluation of the Tanzania National Voucher Scheme, which found that road shows are able to disseminate messages more equitably than any other means of communication such as radios and billboards (Hadji Mponda, unpublished data).

The more timely use of anti-malarials can be attributed to the combination of the ACCESS social marketing campaigns and the ADDO intervention. On one hand the ACCESS social marketing campaigns stressed the importance of prompt and effective treatment for malaria. On the other hand following the ADDO intervention treatment became more available and accessible [127] (Cf. Chapter 3). The good avaialabiltiy of ALu in health facilities in 2008, combined with the increase in health facility visits as a first treatment action is likely to also have contributed to the improved timeliness of treatment. It is worth highlighting here two positive outcomes with regards to the role of ADDOs and health facilities which emerged from this evaluation. Firstly self treatment at home did not increase significantly in neither children nor older patients suggesting that ADDOs did not undermine the role of the formal health sector, but rather complemented it. Secondly, after the introduction of ADDOs, the proportion of children who were taken to a health facility and received an anti-malarial from a shop did not change (10-12%), which refutes claims that health facility staff refer patients to outlets in which they have a financial stake. It is important the ADDOs continue to be adequately supervised for these gains to be sustained.

The results presented here largely compatible with findings from the Smith *et al.* review [33], which concluded that interventions targeted at private sector providers generally show a good impact on provider practices. Similarly to the Kilifi Shopkeeper programme in Kenya [85, 113] and other studies targeting the private retail sector [114, 116-117] (but contrary to results by Winch *et al*. in Mali [86]), the ADDO programme has achieved notable gains in

terms of the quality of advice given by shopkeepers. Ignoring the treatment policy change, the increase in the proportion of patients treated promptly and effectively according to the recommended regimen in the present study (from 32% to 63%) is comparable to the outcomes in Kilifi (from 2% to 29% treated promptly and effectively with the right dosage and duration) or in Mali (from 2% to 42% treated effectively with the right dosage and duration). However, this study has shown for the first time that improvements can be sustained even at much higher levels. Therefore key parameters can continue to be improved with targeted interventions, up to the 80% levels targeted by the Roll Back Malaria (RBM) Partnership [4].

The results presented here also confirm the reviewers' conclusion that improving user practice is more challenging. Noticeable gains were made in terms of people's actions for the treatment of fever (health facility attendance for patients older than five years, timeliness of treatment) but there was no clear improvement in the proportion of cases following the recommended regimen of anti-malarials. This appears to be the result of poor patient adherence, since mystery shopper surveys showed a substantial improvement in provider practice (Dillip et al, unpublished data). It is likely to be due to: 1) the introduction of a new treatment (ALu) with a more complicated regime than the previously recommended SP combined with; 2) the absence of messages targeted at users specifically focusing on the importance of adhering to treatment regimens (although ALu was pre-packaged with clear instructions and pictograms).Future social marketing campaigns in the area should put more emphasis on this component.

The community effectiveness chains show that treatment coverage with antimalarials is very high in the study area, but the change of treatment policy led to a significant drop in the proportion of patients taking a recommended malaria treatment. . Despite high levels of ALu stock in health facilities, the proportion of patients treated with ALu remained low partly because the drug was not widely available in drug shops. The decrease in the proportion of patients treated strictly according to guidelines should be seen in the light of the fact that already in 2003 SP had a treatment efficacy of 50% [133], while ALu had a treatment efficacy of more than 95% [134]. The low availability of the first line drug in the private retail sector following the change of treatment policy from SP to ALu, coupled with the multiple stockouts of SP in public health facilities during the treatment transition clearly indicate that malaria treatment policy changes need to be considered in a more comprehensive way. Fortunately, ACTs will be made available in ADDOs in Tanzania in 2010 in the frame of the Affordable Medicine Facility for malaria [47].

Strategies to improve access to treatment should focus especially on the availability of points of care. The presence of a health facility or drug shop in the village of residence was the strongest predictor of prompt and correct treatment, whereas affordability (within the observed range of prices) and accessibility indicators contributed to a lesser extent. These results differ from those presented in a paper, which focused specifically on the farming season, and according to which fever cases which occurred in the farming sites were as less likely to be treated promptly and effectively as those which occurred in the main homestead [132]. This discrepancy is probably because of design issues, but the considerations from this analysis are largely consistent with a qualitative study on livelihood and health care which revealed that patients make considerable efforts to access treatment, including walking long distances and selling important livelihood assets [135]. Hence future interventions aimed specifically at improving access to treatment should focus on extending the network of health facilities and ADDOs to underserved villages and ensuring that drugs are available.

The main limitation of this study is the selection of cases on the basis of reported fever only, since not every fever case is due to malaria. However considering every fever as a potential malaria case is consistent with the Integrated Management of Childhood Illness (IMCI) guidelines for treatment in areas of stable malaria [136]. This approach was warranted when the survey was designed in 2003 and the area experienced very high levels of transmission. This is no longer justified in the study area since 1) recent data suggest a drastic change in the epidemiology of malaria in the study area, and 2) a recent study piloting the use of Rapid Diagnostic Tests (RDT) for malaria in local health facilities found that only 40% of fever cases were actually due to malaria (D'Acrémont *et al*. unpublished data). It is difficult to assess how much the presence RDTs at the time of our surveys would have changed our observations.

Another limitation concerns the variability observed in the samples and the inconsistency of a finding with another study conducted in the area. Despite a random sampling from the comprehensive DSS database households in 2008 were located further away from health facilities and drug shops despite an increase in the accessibility of these outlets [127] (cf. Chapter 3). Furthermore the distribution of patients across SES appeared to be unequal over the years, with wealthier households over-represented in the 2006 and 2008 samples. To account for differences in SES across years all ORs of significant effects were reported crude and adjusted for SES.

Finally, it is worth pointing out that additional positive patterns of treatment emerged from this analysis which are not consistent with conclusions one might draw from provider survey carried out in the study area [127] (cf. Chapter 3). Firstly, no patient in Ifakara was reported treated with artemisinin monotherapy although they were available in 10-20% of shops. And secondly, the severe stockouts of SP in the study area in 2006 did not appear to have an impact on treatment since the proportion of patients who obtained the drug did not decrease as a result. The reason for this apparent paradox is that availability data from health facilities is based on end-of-month balance in the store rooms. Hence, stocks may be delivered at the beginning of the month and dispensed in their entirety by the end of the month or drugs may not be in the store-room but still present in the dispensing room.

4.6. Conclusions

An integrated approach aimed at improving understanding and treatment of malaria has led to tangible improvements in terms of people's perception and actions for the treatment of malaria. The positive results testify that even in a poor and remote African setting, the Abuja targets for access to treatment can be achieved. A higher impact on prompt and effective treatment according to treatment guidelines was hindered by a change of treatment policy, which led to low availability of the first-line drug (ALu) in the private retail sector. This shows clearly that ensuring consistent stocks of ALu in the private retail sector is crucial to improve prompt and effective treatment for malaria. Future interventions aimed at improving access to treatment by targeting users should have a focus on adherences to treatment regimens. Interventions targeting providers should aim at extending the network of health facilities and ADDOs to underserved villages.

4.7. Competing interests

AS is employed by the Novartis Foundation for Sustainable Development (NFSD) which funded the ACCESS programme. The Foundation works independently from the company's business and supports not-for-profit health programmes in developing countries.

4.8. Authors' contributions

SA participated in the supervision of the data collection in 2008, analysed the data, drafted and finalised the manuscript. AD participated in the supervision and training for the data collection in 2006 and 2008 as well as contributing to the manuscript. MWH participated in the design of the survey, coordinated the data collection in 2004 and 2006 and contributed to

the manuscript. CM and AM designed and conducted the social marketing campaigns. MA was responsible for the DSS, performed the sampling for the DSS surveys and supervised the data collection. IM participated in the data collection and contributed to the discussion on the manuscript. CM and AM implemented the social marketing campaigns and contributed to the manuscript. MA did the sampling of households, supervised the field work and contributed to the manuscript. BO and AS participated in the design of the surveys and contributed to the discussion on the manuscript. HM and FK provided overall coordination and contributed to the discussion on the manuscript. CL contributed to the study design, the data analysis and the manuscript. The final manuscript was approved by all authors.

4.9. Acknowledgements

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5. Assessing the impact of malaria interventions on morbidity through a community-based surveillance system

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5.1. Abstract

Background

The ACCESS programme aims at understanding and improving access to prompt and effective malaria treatment in rural Tanzania with a set of integrated interventions targeting both users and providers. The aim of this paper is to evaluate the programme's impact on the community and health facility burden of malaria and to investigate the value of community-based reporting for routine malaria control programme monitoring.

Methods

This work was implemented within the Ifakara Demographic Surveillance System (DSS) between 2004 and 2008. At community level the DSS staff routinely collected data on reported history of fever and severe malaria (convulsions) based on a two-week recall. In parallel we collected in-patient and out-patient fever and malaria diagnoses data from the 15 health facilities in the area. Treatment seeking surveys conducted in the study area and nationally representative data were used to validate our measure of community fever.

Results

Between 2005 and 2008 community reported fever incidence rates in children under the age of five declined by 34%, from 4.9 to 3.2 average cases per child per year, while convulsions, a marker of severe malaria morbidity in children, decreased by 46%, from 4263 to 2320 cases for every 100 000 children per year. The decrease in the community rates was paralleled by a decrease in the health facility fever rates in children, although the number of fever cases seen in health facilities did not change because of population growth. Our data showed very good internal and external consistency with independent local and national surveys.

Conclusions

There is evidence of a substantial decline in the community burden of malaria morbidity between 2005 and 2008 in the Kilombero and Ulanga DSS areas in Tanzania, most likely as a result of malaria control efforts. Meanwhile the health facility burden remained unchanged due to population growth. The good internal and external consistency of the data shows that history of fever in the previous two weeks in children under the age of five can be used as a morbidity monitoring tool.

5.2. Background

“Without high quality surveillance, the billion dollar malaria effort is flying blind” [137].

The massive increase in resources mobilised for malaria control calls for careful monitoring to ensure that money is spent effectively. Surveillance data are crucial at country level to know when targets are met and even more importantly to initiate mid-course corrections if progress is inadequate. Reliable evaluation data are also important as an evidence base to up-scale effective new interventions. The need for a comprehensive monitoring and evaluation plan has been recognised by donors and international technical agencies. This has led to the development of a comprehensive Monitoring and Evaluation (M&E) toolkit by the Global Fund to fight AIDS TB and Malaria (GFATM) to assist countries in developing robust M&E systems [72].

The GFATM’s M&E toolkit is based on the widely applied input-output-outcome-impact framework and includes mortality and morbidity impact indicators. Mortality indicators are based on robust and validated methodologies [138-139]. They are widely used for the evaluation of malaria control efforts since the data can be obtained from nationally representative, cross sectional retrospective surveys such as the Demographic Health Surveys (DHS) [140], and the Multiple Indicator Cluster Surveys (MICS) [141]. However, mortality is multi-factorial and it is always difficult to tease apart the effect of malaria control from secular changes. The recommended morbidity indicators are parasite prevalence and anaemia prevalence. The Malaria Indicator Survey (MIS) [142] was especially designed to capture these two measures. Although the DHS, MICS and MIS also collect history of fever during the past two weeks, this measure is not widely used as a morbidity indicator and is not recommended in the M&E toolkit. Instead it is used as a basis for operational indicators such as “the percentage of children with fever in the previous two weeks who were treated with an antimalarial drug”. However, although parasite prevalence gives important information on the impact of control efforts on malaria transmission [143], it is not directly a morbidity indicator. In high endemicity areas control efforts may first have an impact on fever and then only later on prevalence due to the reduction of multiplicity of infections which reduces clinical episodes [144]. Anaemia prevalence has been shown to be a reliable indicator or malaria morbidity but is also an indirect measure with multi-factorial causality [145].

The ACCESS Programme was implemented in two Tanzanian districts with the aim of improving access to malaria treatment. The programme’s interventions are based on an integrated approach which targets both users and providers and were accompanied by

monitoring and evaluation activities to assess its outcomes and impact [101]. Between 2004 and 2008, the ACCESS Programme's main intervention at user level was the implementation of social marketing campaigns for improved care seeking. At provider level key activities in health facilities included strengthening routine supportive supervision and the implementation of a quality management scheme. In parallel, the Accredited Drug Dispensing Outlets (ADDO) programme was piloted in the study area from 2006 onwards to improve the availability of drugs and quality of care people obtain from the private retail sector [87].

The ACCESS M&E plan included the measurement of both outcome and impact indicators. Provider and user surveys conducted within the frame of programme showed an improvement in access outputs and treatment outcomes [102-127] (cf. Chapters 3 and 4) although treatment with antimalarials was already very high at baseline [88]. The proportion of recent fever cases treated with an antimalarial increased from 86% to 96% between 2004 and 2008. This paper is concerned with the programme's impact on morbidity and aims at assessing changes in the community and health facility burden of malaria between 2004 and 2008 [146], In this frame we investigated the value of collecting history of fever in the previous two weeks at community level as a morbidity monitoring tool.

5.3. Methods

Study setting

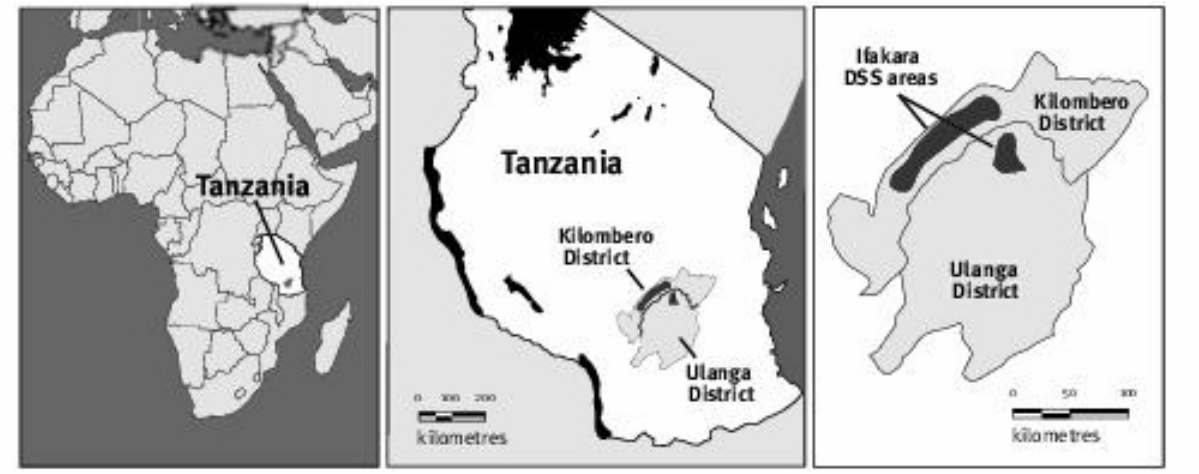
The ACCESS Programme's monitoring and evaluation activities were imbedded within the Kilombero and Ulanga Demographic Surveillance System (DSS) in south-central Tanzania (Figure 22). It was established in 1996 and covers 25 villages (13 in Kilombero District and 12 in Ulanga District). The population in 2004 was almost 74,000 and it increased to just over 92,000 in 2008. There are six health facilities (one health centre and five dispensaries) in the Kilombero area and eight health facilities (one health centre and seven dispensaries) in Ulanga. Malaria transmission was intense and perennial with an entomological inoculation rate (EIR) of 350 [77], but has been declining over the past 10 years [78]. The area is characterised by a rainy season from November to May, with rain levels consistently increasing month by month until April [147]. More details on the study area can be found elsewhere [73, 101].

Data collection and processing

We collected data at community and health facility level between 2004 and 2008 with three independent instruments. The community based data included: 1) the collection of history of

fever and convulsions during the past two weeks with DSS based surveys and 2) three cross sectional treatment seeking surveys in 2004, 2006 and 2008 to elicit information about people's actions in the event of fever. At health facility level we collected Health Management and Information Systems (HMIS) data from all the facilities in the area.

Figure 22. Location of the Ifakara DSS site (source: Schellenberg et al. [73])



History of fever and convulsions - We integrated the collection of community reported fever and convulsions cases within the routine DSS data collection activities between May 2004 and December 2008. Whereas fever (locally termed *homa*) is a proxy indicator for un-complicated malaria, convulsions (*degedege*) are a sign of severe febrile illness, which includes cerebral malaria in children [96, 148]. Both signs are not highly specific for malaria, but under the assumption that other causes remain stable, they provide useful markers of malaria morbidity. DSS field workers visit every household in the area at four month intervals (three rounds per year) to collect data on birth, death, in-migration and out-migration. Field workers collect information at village level by following a fixed schedule of household visits. Therefore, although each household is visited only every four months, data is effectively collected on a daily basis in each village. Given that each recorded case refers to fever in the past two weeks, each interviewed individual contributes two person weeks of observation. We therefore constructed the following approximated monthly fever and convulsions incidence rates for each of the 25 DSS villages [expressed in cases per 1000 person weeks (c/1000pw)]:

$$community\ fever\ rate = \frac{number\ of\ community\ reported\ fever\ cases\ per\ month}{total\ number\ of\ people\ interviewed\ per\ month \times 2}$$

$$community\ convulsions\ rate = \frac{number\ of\ community\ reported\ fever\ convulsions\ per\ month}{total\ number\ of\ people\ interviewed\ per\ month \times 2}$$

Unfortunately, due to logistical constraints the data could only be collected on two thirds of the DSS population. However there was no indication that certain villages were consistently less visited than others and the distribution across ages was similar in every round and reflective of the DSS age distribution. Hence there is no reason to for this incomplete coverage to be biasing our estimates.

Treatment seeking surveys - In 2004, 2006 and 2008 a village stratified random sample of approximately 100 community reported fever cases were followed up with treatment seeking surveys. These surveys were conducted by the DSS field workers between May and August each year (second round of data collection). Patients who had not recovered were not included and they were instead advised to seek care from a health facility. For the purpose of this analysis we only extracted data on the proportion of fever cases brought to a health facility at some point during the illness. A detailed analysis of the treatment seeking surveys is presented elsewhere [102] (cf. Chapter 4).

HMIS data from dispensaries and health centres - Health facility data was collected by specifically trained field workers who visited all the 14 facilities in the area (two health centres and 12 dispensaries) on a two-monthly basis between January 2004 and December 2008. The data collected included all in-patient and out-patient diagnoses disaggregated by age group (children under the age of five and all other patients) on a monthly basis. We created catchment areas for each facility based on the village in which they are located. Some catchment areas included more than one health facility due to their proximity. Villages without a health facility were distributed equally between two health facilities were arbitrarily allocated to a given catchment area. By combining the data from the health facilities with the person time exposure data from the DSS database, we calculated the following monthly health facility fever and malaria incidence (c/1000pw) for each health facility catchment area:

$$Health\ facility\ fever\ rate = \frac{(malaria + pneumonia + respiratory\ in fections + measles + \\ + typhoid + urinary\ tract\ in fections)\ diagnoses\ per\ month}{person\ weeks\ exposed\ per\ month\ (DSS)}$$

$$Health\ facility\ malaria\ rate = \frac{malaria\ diagnoses\ per\ month}{person\ weeks\ exposed\ per\ month\ (DSS)}$$

Mean imputation was carried out for the months were the data could not be obtained from health facilities: missing entries for a given month in a given health facility were replaced by the mean number of patients seen in the health facility over the years of observation. This method was considered appropriate since only 7.7% (153/1984) records were missing.

Statistical analysis

We first estimated trends over time of the community fever and convulsions as well as the health facility fever and malaria rates. We then explored the validity of monitoring history of fever at community level by assessing the internal and external consistency of our data with surveys conducted in the study area and nationally representative surveys.

Trends over time - Poisson regression models were fitted to estimate changes in the community and health facility burden of malaria. The fever, convulsions and malaria cases *N* in village or catchment area *i* were assumed to have arisen from a Poisson distribution, as is most appropriate for count data. We thus assumed that the rate of incidence is constant for every individual and that the variance is equal to the mean. Hence the following model was fitted:

$$\log \mu_i = \log(Y_i) + \alpha + \beta_1 year_i + \beta_2 month2_i + ... + \beta_{12}\, month12_i + u_i \qquad \text{(Model 1)}$$

where μ_i is the expected value of the rate N_i/Y_i in village or catchment area *i*, Y_i are the person weeks exposed per month and $\log(Y_i)$ is an offset term that ensures that the rate is being modelled on the log scale. The coefficient α is the intercept term. Year is a continuous variable (from 2004 to 2008) and the exp(β_1) is the estimated incidence rate ratio (IRR) of changes over the years and months. Month is a categorical variable denoting month of the year (from 1 to 12) which ensures that the estimate of exp(β_1) is not confounded by monthly variations (seasonality). The random effect u_i explicitly allows for the clustering of rates in villages or catchment areas i and is assumed to follow a gamma distribution $u_i \sim Gamma(1/\alpha, \alpha)$ with implies a mean 1 and variance α.

Internal consistency - To address the internal consistency, we first correlated the health facility fever and community fever monthly rates to assess the temporal correlation between the two sources of data. We then fitted a Poisson regression model on the community and health facility rates combined to estimate health the proportion of fever cases in the community that are brought to a health facility as well as changes in this proportion over time. These estimates were compared with independent information from the treatment seeking surveys. For this purpose cases and exposures were aggregated over villages and health facilities and the following models were fitted:

$$\log \mu = \log(Y) + \alpha + \beta_1 year + \beta_2 month2 + ... + \beta_{12}\, month12 + \gamma_1 HF \qquad \text{(Model 2)}$$

$$\log \mu = \log(Y) + \alpha + \beta_1 year + \beta_2 month\,2 + ... + \beta_{12}\ month\,12 + \gamma_1\ HF + \gamma_2 HF * year \qquad \text{(Model 3)}$$

where HF indicates the type of case that is being modelled and takes the value of 1 if the cases are health facility recorded cases and 0 if the cases are community reported. The coefficient exp(γ_1) in Model 2 is an estimate of the ratio of health facility rates to community rates and therefore provides an estimate proportion of fever cases in the community that are brought to a health facility. The coefficient exp(γ_2) of the interaction between type of case and year in Model 3 estimates the change over time of the proportion of fever cases brought to a health facility.

External consistency - To assess the external consistency of our data, we compared our estimates with data from the 2004/5 DHS [26] and 2007/8 MIS [25]. Both surveys were carried out on a nationally representative sample of the population between October and January. First we compared the decrease in community fever from our surveys between 2004 and 2007 with the decrease in fever reported in the DHS and MIS. We then compared the decreases in fever rates with decreases in under five mortality in both settings. Under five mortality rates for our study area were obtained from the DSS for 2004 and 2007 and were expressed as the number of cases per 1000 person years (c/1000py). Nation-wide estimates of under-five mortality for 2004 and 2007 were derived by disaggregating the 2007/8 MIS estimate using the methodology described by Masanja *et al.* [149] and are expressed as a probability of dying between birth and the fifth birthday for every 1000 live births (5q0).

All data were double entered using Microsoft FoxPro and Microsoft Access (Microsoft Corp. Seattle, USA) and checked for coding errors and consistency. Intercooled Stata 10 (Stata Corp., College Station, TX, USA) was used for data management and analysis.

Ethics

The National Institute for Medical Research of the United Republic of Tanzania (NIMR/HQ/R.8a/Vol.IX/236, 16th September 2003) granted ethical clearance for the study.

5.4. Results

The number of fever cases reported in 2004 appeared to be unrealistically high at community level and unrealistically low at health facility level (Table 15 and Figure 23) compared to values in subsequent years. A visual inspection of the rates suggests that more accurate reporting was achieved both at community level (Figure 23a and Figure 23b) and in health

facilities (Figure 23c and Figure 23d) after a year of data collection. All the 2004 data was therefore excluded from any analysis.

Table 15. Number of cases and person weeks of observation of community reported and health facility recorded cases between 2004 and 2008

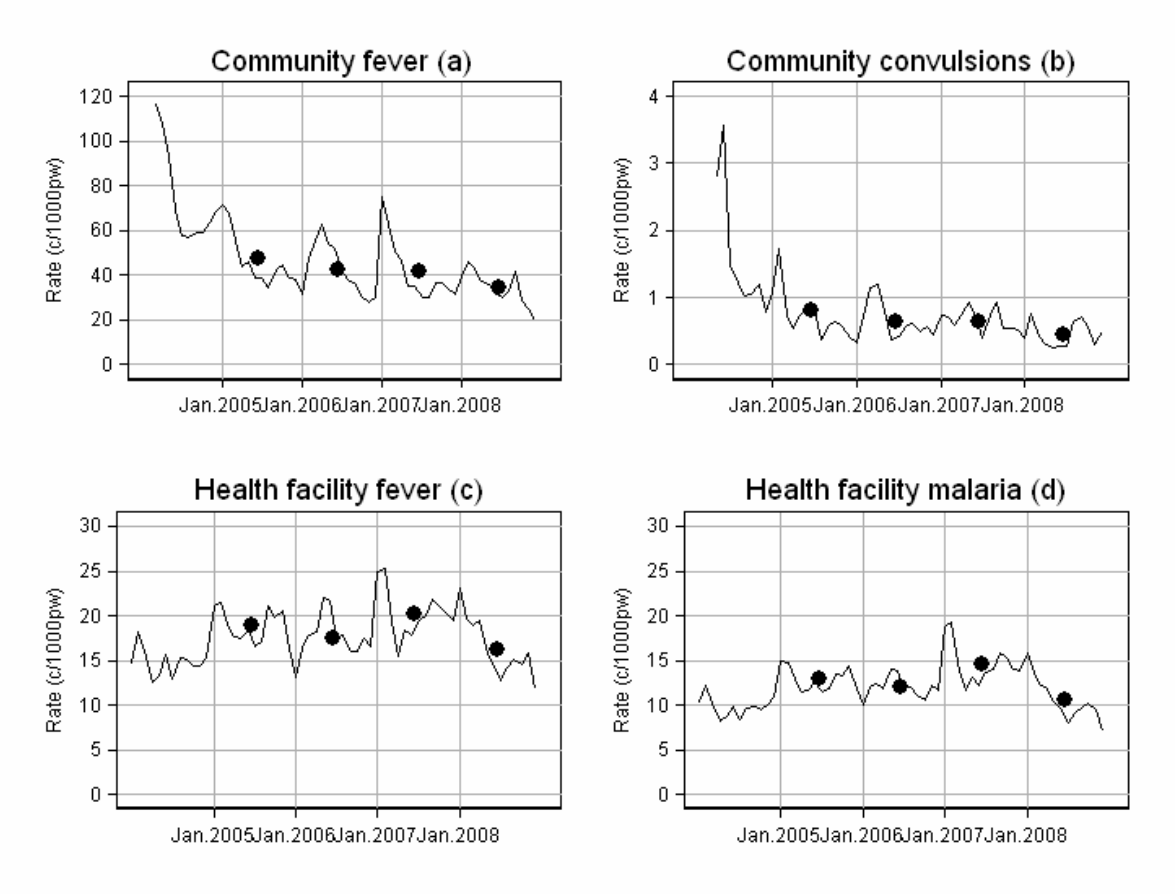
Level	*Type of cases*	*Year*	*Cases*	*Person weeks of observation (x 1000)*
Community	Fever	2004	18844	289,764
		2005	16350	346,311
		2006	14032	329,306
		2007	18691	451,228
		2008	11567	336,474
	Convulsions	2004	590	291,321
		2005	284	346,427
		2006	213	330,576
		2007	292	451,292
		2008	152	340,666
Health facility	Fever	2004	52875	3579,456
		2005	67335	3573,468
		2006	65342	3729,097
		2007	77398	3818,092
		2008	65223	4008,284
	Malaria	2004	35011	3579,456
		2005	45931	3573,468
		2006	44562	3729,097
		2007	55788	3818,092
		2008	42358	4008,284

The community fever and convulsions rates follow a clear seasonal pattern and have been decreasing over time. Seasonal peaks correspond with the middle of the rainy season (January to March) (Figure 23a and Figure 23b). The rates averaged over the year show a constant decrease in community fever rates between 2005 and 2008 from 47.2 c/1000pw (16350/346311) to 34.4 c/1000pw (11567/336475) in all ages. This corresponds to a decrease from 2.5 to 1.8 average cases per person per year i.e. an overall reduction of 28%. In children under the age of five fever rates decreased by 34% from 93.9 c/1000pw (5298/56403) to 61.6 c/1000pw (3419/55490), which means a decrease from 4.9 cases to 3.2 cases per child per year. Convulsions are a much rarer event than fever and also decreased. Convulsion rates were 0.82 c/1000pw (284/346427) in 2005 (4263 cases for every 100 000 children per year) and 0.45 c/1000pw (152/340.667) in 2008 (2320 cases for every 100 000 children per year) which is equivalent to an overall reduction of 46% (Table 15).

The health facility rates exhibited much less seasonal variation and there was a less discernable pattern of change over time. Between 2005 and 2007 there appeared to be a trend of increasing rates but this was followed by a low value in 2008 driven by a particularly

low attendance in one of the health centres. In 2005 the median number of patients recorded per month was 523 (IQR=339 to 658) in dispensaries and 856 (IQR=693 to 1079) in health centres. These figures hardly changed in 2008 when the median number of patients recorded per month was still 523 (IQR=347 to 410) in dispensaries and 840 (IQR=745 to 1220) in health centres. Between 2005 and 2008 malaria diagnoses consistently accounted for 67.4% of all fever cases in all the months of data collection (Table 15 and Figure 23c and Figure 23d).

Figure 23. Community and health facility rates (note: y-axes differ across graphs)



Trends over time

Fitting Model 1 on the community reported rates shows a decrease in the incidence of both fever and convulsions. Overall community fever decreased by 10% per year (IRR=0.90 95%CI=0.87 to 0.89) between 2005 and 2008. Rates decreased more steeply in children under the age of five at a rate of 13% per year (IRR=0.87 95%CI=0.85 to 0.87) (Table 16 and Figure 23). The incidence of convulsions in children also decreased considerably over the study period at an estimated rate of 21% per year (IRR= 0.79 95%CI=0.74 to 0.92).

Table 16. Estimated Incidence Rate Ratios (95% CI) and between village variance alpha (95% CI) of Poisson regressions fitted on monthly community reported fever and convulsion rates (2005 to 2008) with gamma distributed random effects to account for between village variance

	Fever		*Convulsions*
	All ages (n=1064)	*<5 years (n=1047)*	*<5 years (n=1046)*
Year	0.90 (0.87 to 0.89)	0.87 (0.85 to 0.87)	0.79 (0.74 to 0.92)
Month*			
Jan	1	1	1
Feb	1.01 (0.97 to 1.05)	0.99 (0.91 to 1.07)	1.32 (0.90 to 1.94)
Mar	0.91 (0.88 to 0.95)	0.89 (0.82 to 0.97)	1.02 (0.70 to 1.50)
Apr	0.86 (0.82 to 0.90)	0.83 (0.75 to 0.91)	1.03 (0.66 to 1.61)
May	0.74 (0.70 to 0.78)	0.70 (0.63 to 0.77)	0.83 (0.52 to 1.34)
Jun	0.70 (0.66 to 0.72)	0.66 (0.61 to 0.72)	0.65 (0.43 to 0.97)
Jul	0.62 (0.59 to 0.65)	0.61 (0.58 to 0.68)	0.62 (0.41 to 0.94)
Aug	0.61 (0.57 to 0.65)	0.60 (0.54 to 0.68)	0.68 (0.39 to 1.20)
Sep	0.71 (0.67 to 0.74)	0.79 (0.72 to 0.87)	1.04 (0.67 to 1.62)
Oct	0.63 (0.60 to 0.65)	0.71 (0.66 to 0.77)	0.74 (0.49 to 1.11)
Nov	0.57 (0.54 to 0.60)	0.66 (0.61 to 0.72)	0.63 (0.41 to 0.97)
Dec	0.54 (0.50 to 0.57)	0.60 (0.53 to 0.68)	0.47 (0.24 to 0.89)
Alpha	0.07 (0.04 to 0.12)	0.04 (0.02 to 0.08)	0.20 (0.11 to 0.38)

*LLR test of inclusion: fever all ages chi=2514.23 p<0.001, <5yrs chi=562.93 p<0.001, convulsions chi=63.27 p<0.001

Model 1 was also used to estimate the extent to which the community fever cases were overreported in the first year of data collection (first round January to April 2004 but data was only collected from March onwards, second round May to August 2004 and third round September to December 2004). The extrapolation suggests an overall overestimation of 79.6% in the first round of collection (actual number of cases reported 9456 vs. estimated 5265 for 83 434 person weeks of observation); 43.7% in the second round of data collection (6432 vs. 4469 cases for 95 718 person weeks); and 39.7% in the third round (6048 vs. 4329 cases for 99087 person weeks).

Health facility rates were also estimated to have decreased over the study period, but to a much lesser extent. The IRR of fever and malaria rates in adults over time were estimated at values very close to one (fever IRR=0.98 95%CI=0.98 to 0.98, malaria IRR=0.97 95%CI=0.97 to 0.98) suggesting an only very slight decrease over time. A more appreciable decrease was estimated for rates in children; health facility fever rates were estimated to have decreased by 6% per year (IRR=0.94 95%CI=0.94 to 0.95) and malaria rates by 7% per year (IRR=0.93 95%CI=0.92 to 0.93) (Table 17).

Accounting for the seasonality of the data by including a categorical factor for the month of the year did not affect the estimated change over time. The log likelihood ratio test for the inclusion of months of the year was highly significant in all the models estimating trends over time (Table 16 and Table 17). However the inclusion of this variable only slightly affected the size of the IRR estimating the changes over the years in the community rates. More

specifically the models fitted excluding months of the year overestimated the decrease over time, but only by 1% point (fever all ages IRR=0.90 95%CI=0.89 to 0.91, fever children <5 IRR=0.86 95%CI= 0.85 0.88, convulsions IRR=0.78 95%CI= 0.74 to 0.84). The exclusion of the variable did not affect the size of the IRRs for the health facility rates.

Table 17. Estimated Incidence Rate Ratios (95% CI) and between health facility catchment variance alpha (95% CI) of Poisson regressions fitted on monthly health facility fever cases and malaria diagnoses rates (2005 to 2008) with gamma distributed random effects to account for between area variance (n=432)

	Fever cases		*Malaria diagnoses*	
	All ages	*<5 years*	*All ages*	*<5 years*
Year	0.98 (0.98 to 0.98)	0.94 (0.94 to 0.95)	0.97 (0.97 to 0.98)	0.93 (0.92 to 0.93)
Month*				
Jan	1	1	1	1
Feb	1.00 (0.98 to 1.02)	0.99 (0.97 to 1.01)	0.99 (0.97 to 1.01)	0.97 (0.95 to 1.00)
Mar	0.91 (0.89 to 0.92)	0.92 (0.89 to 0.93)	0.86 (0.85 to 0.88)	0.87 (0.84 to 0.89)
Apr	0.86 (0.84 to 0.87)	0.94 (0.92 to 0.96)	0.77 (0.76 to 0.79)	0.85 (0.83 to 0.87)
May	0.89 (0.87 to 0.91)	0.87 (0.85 to 0.89)	0.81 (0.79 to 0.83)	0.79 (0.76 to 0.81)
Jun	0.87 (0.85 to 0.88)	0.85 (0.83 to 0.87)	0.79 (0.77 to 0.81)	0.78 (0.75 to 0.80)
Jul	0.80 (0.78 to 0.81)	0.77 (0.76 to 0.79)	0.74 (0.72 to 0.75)	0.72 (0.70 to 0.74)
Aug	0.84 (0.82 to 0.85)	0.81 (0.79 to 0.83)	0.78 (0.76 to 0.79)	0.76 (0.74 to 0.79)
Sep	0.90 (0.88 to 0.91)	0.89 (0.87 to 0.92)	0.83 (0.81 to 0.85)	0.84 (0.82 to 0.86)
Oct	0.87 (0.85 to 0.88)	0.90 (0.88 to 0.92)	0.82 (0.80 to 0.83)	0.85 (0.83 to 0.86)
Nov	0.90 (0.88 to 0.91)	0.88 (0.86 to 0.91)	0.83 (0.81 to 0.84)	0.83 (0.81 to 0.86)
Dec	0.78 (0.77 to 0.79)	0.76 (0.74 to 0.77)	0.74 (0.72 to 0.75)	0.73 (0.71 to 0.76)
Alpha	0.30 (0.12 to 0.72)	0.36 (0.15 to 0.86)	0.23 (0.10 to 0.57)	0.27 (0.11 to 0.65)

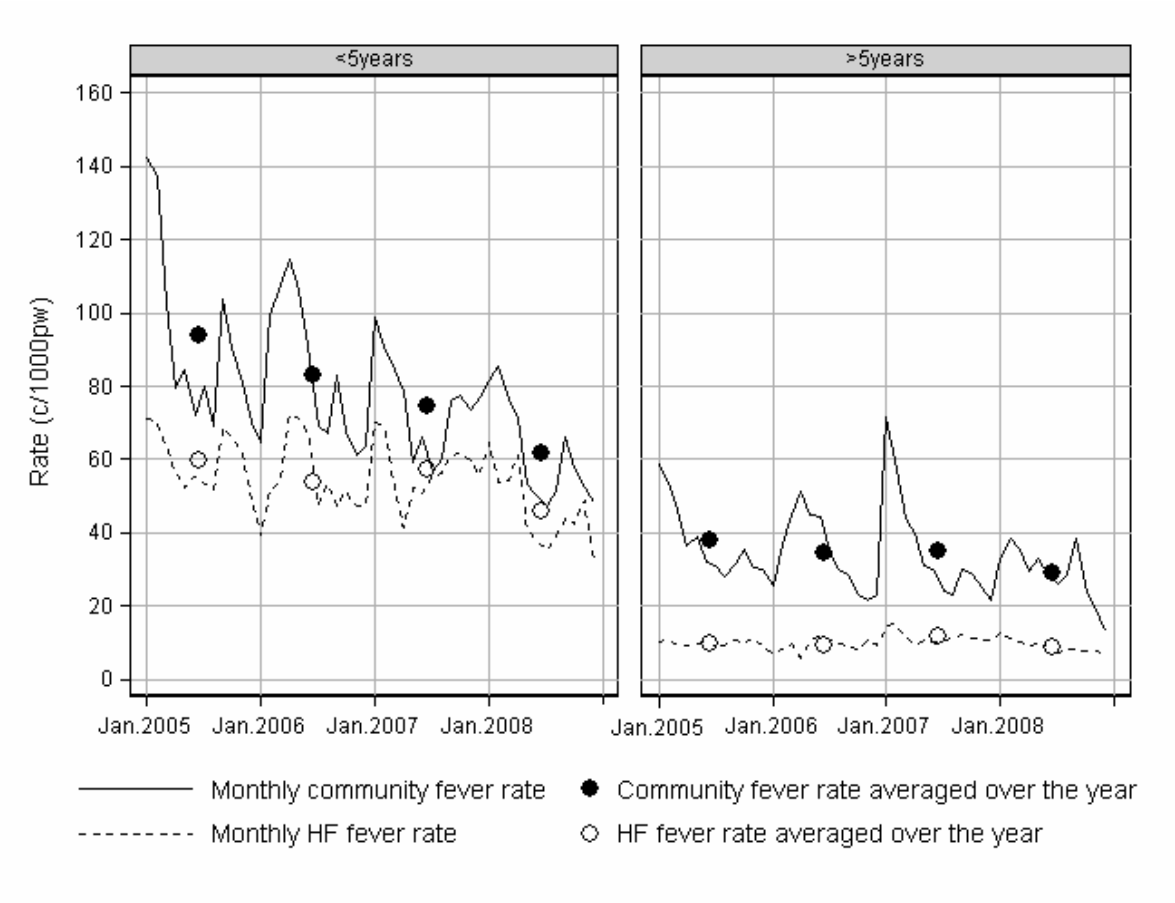
*LLR test of inclusion fever all ages chi=1440.82 p<0.001, <5yrs chi=1063.87 p<0.001; malaria diagnoses all ages chi=1730 p<0.001, <5yrs chi=1005.58 p<0.001

The inclusion of a random effect to account for the fact that different villages or catchment areas might have different rates did not affect the estimated change over the years either. However, the variance alpha of the random effects was significantly different from zero in all the models fitted (Table 16 and Table 17), suggesting that there is clustering between villages or catchment areas and that random effects should be included in the models to account for this.

Internal and external consistency of the data

The community fever rates correlate very well with fever rates from health facilities in children under the age of five (r=0.81 p<0.001) but less so in all patients (r=0.67 p<0.001) (Figure 24).

Figure 24. Community fever rates and health facility fever rates by age group between 2005 and 2008



Combining the fever rates at health facility and community level and comparing the results with the treatment seeking surveys shows reasonable but not all round internal consistency. According to the independent cross-sectional treatment seeking surveys, the proportion of fever cases brought to a health facility did not change significantly between 2006 and 2008 and was estimated around 68% in children and 65% in all ages [children from 67.3% (37/55) in 2006 to 69.2% (27/39) in 2008 OR=1.05 95%CI = 0.67 to 1.63, all patients 61.2% (63/103) in 2006 to 69.7% (60/86) in 2008 OR=1.21 95% CI=0.89 to 1.64]. Model 2 estimated the proportion of fever cases brought to a health facility to be 72% (IRR=0.72 95%CI=0.70 to 0.73) in children under the age of five and 45% (IRR=0.45 95%CI=0.45 to 0.46) in all patients between 2006 and 2008. According to Model 3 the proportion of fever cases brought to a health facility increased by 8% per year (IRR=1.08 95%CI=1.07 to 1.10) in children and by 9% per year in all patients (IRR=1.09 95%CI=1.08 to 1.10) between 2006 and 2008. Hence the estimated proportion of fever cases brought to a health facility was the same according to the treatment seeking surveys and Model 2 in children (but not in adults); and Model 3 suggests a higher increase over time in proportion of fever cases brought to a health compared to the treatment seeking surveys.

There is very good external consistency between our data and data from the national DHS and MIS. These surveys report a decrease in the percentage of fever in the past two weeks from 25% for the period October 2004 to January 2005 to 18% for the period October 2007 to January 2008. This is equivalent to a 26% decrease in fever prevalence over the three years of observation. This was associated with a 8% decrease in mortality from 97.2 5q0 in 2004 to 89.5 5q0 in 2007 (ratio of fever to mortality decrease = 3.3). An extrapolation of our fever data (Model 1) estimated a fever incidence of 107.3 c/1000pw for the period October 2004 to January 2005 and 73.2 c/1000pw for the period October 2007 to January 2008. This is equivalent to a 32% decrease in fever, very close to the 26 % decrease at national level. In the Kilombero and Ulanga DSS this was associated with a 12% decrease in mortality from 25.3 c/1000py to 22.2 c/1000py (ratio of fever to mortality decrease = 2.6).

5.5. Discussion

The data presented here document a decline in malaria morbidity between 2005 and 2008 in the highly malaria-endemic Kilombero and Ulanga DSS areas. Community reported fever incidence rates declined by 10% per year in the overall population and by 13% per year in children under the age of five. There is also an indication of a decrease in severe malaria morbidity as indicated by a 21% decrease in the incidence of reported convulsions in children. The decrease in the community burden of malaria in children is accompanied by decrease in the health facility fever rate in children (6% and 7% per year respectively) but not as much in the overall population (2% and 3% per year). However, due to population growth the average number of cases per month in health facilities remained constant, implying that there was no change in the health facility burden of fever and malaria.

Data available from separate studies conducted in the study area provide evidence that the decline in community fever and convulsions is paralleled by a decline in malaria transmission. Data from two other projects documented a decrease in parasitaemia in children under five from 25% in 2004 [150] to 10% in 2008 (Mulokozi *et al.,* unpublished data). While an older study reported an Entomological Inocluation Rate (EIR) of 349 infective bites per person per year (ib/p/y) between 2001 and 2003 [81], by 2008 the EIR had declined to 81 ib/p/y [78]. Under-five mortality decreased from 24.5 c/1000py to 18.9 c/1000py (cf. Chapter 6). These data for other malariometric indicators gives us confident that the decrease we observed in fever rates is to a large extent malaria-related. This is obviously important because we could not assess independently the proportion of true malaria cases among all the fever episodes.

The increased treatment coverage may have contributed to the decrease in morbidity. The first line treatment for malaria in Tanzania was Sulphadoxine Pyrimethamine (SP) until 2006 when it was replaced by the Artemisinin Combination Therapy (ACT) Artemether-Lumefantrine (ALu) due to high levels of resistance to SP. The long half life of SP [151] and its prophylactic effect have been clearly documented [152]. The treatment of any potential malaria case with SP not only clears parasites in true cases of malaria but also provides chemoprophylaxis for four weeks in both those who were and those who were not infected, which in turn reduces the parasite burden in individuals and the infectious reservoir in the community. This has led to the hypothesis that widespread presumptive treatment with the drug contributes to a decrease in transmission based on the observation the malaria started decreasing in Kenya before the widespread use of ITNs [153]. Conversely ACTs have gametocidal properties [154-156] and it has been suggested that this can have an impact on transmission [157]. In our study area malaria treatment has reached very high levels, with an increase in the proportion of fever cases treated with an antimalarial from 86% in 2004 to 96% in 2008. SP was used to treat 30-40% of all identified cases between 2004 and 2008, while ALu was used in a third of cases in 2008 (with most of the remaining cases still treated with SP). Hence, it is reasonable to ascribe part of the observed decrease in malaria-related fevers to improved treatment.

The increased vector control in the area over the same period most likely also explains a large part of the decrease in transmission and morbidity. A very high mosquito net coverage has been achieved in the study area following the nation-wide up-scaling [77, 158] of the KINET scheme for the promotion and subsidisation of nets [91]. Mosquito net coverage remained largely unchanged between 2005 and 2008 with over 90% of household ownership. However, this does not rule out continued effect over time since recent modelling work suggests that sustaining coverage with ITN at such levels may lead to constant decreases in transmission even if coverage does not increase (personal communication, Prof. Tom Smith, Swiss Tropical and Public Health Institute, Basel). Furthermore most nets were untreated in 2005 [77] but by 2008 nearly half of the nets were treated [78]. A recent study concluded that the addition of long-lasting insecticide treatment of bednets in the area was able to reduce the intensity malaria transmission 4.6-fold [78]. Increased IPTp may also have played a role in decreasing morbidity, especially in children. According to regional data the proportion of women who received two doses of SP during their pregnancy increased from 23% in 2004 to 44% in 2007 [25-26]. Unfortunately there is no way to conclusively estimate the relative contribution of each intervention to the observed decrease in transmission and morbidity on the basis of only empirical data. Future mathematical modelling may provide answers to these questions.

The good internal and external consistency of our data shows that reported history of fever in the previous two weeks can be used to monitor the community burden of malaria in children under the age of five reliably in highly malaria endemic areas. As far as internal consistency is concerned, we were able to show that: 1) community fever rates were very highly correlated health facility fever rates in children under the age of five and; 2) estimates of health facility attendance for fever (i.e. the proportion of fever cases in the community brought to a health facility) resulting from the ratio of health facility to community rates are similar to those obtained from and independent treatment seeking survey. In addition our data showed good external consistency with national data. Although a slightly lower decrease in incidence of fever was observed at national level compared to our study site between 2004 and 2007 (25% vs. 32%), the ratio of fever incidence decrease to under-five mortality decrease was comparable in both settings (3.3 vs. 2.5). This finding is of high interest to malaria control programmes because it offers for the first time a validated community-based measure of malaria morbidity that can be used for monitoring. It follows that fever recall data collected by representative household surveys such as the DHS, MICS and MIS can be analysed to monitor morbidity trends and impact.

However, there is an important caveat associated with the use of fever recall as a morbidity monitoring tool. Our experience shows that cases are substantially over-reported when the question “Have you had fever in the past two weeks” is asked for the first time, and this is consistent with finding from other studies [159-160]. A possible explanation is that respondents do not only report episodes which occurred in the past two weeks but also previous ones. According to our data, respondents are better able to limit reporting to episodes that occurred strictly within the requested time interval after three rounds. Therefore fever rates based on a two week recall in cross-sectional household surveys such as the DHS, MICS and MIS are likely to be overestimated. Fortunately, consistency checks between our data and the 2007/8 Tanzania MIS and the 2004/5 DHS suggested that over reporting is consistent between surveys and therefore does not jeopardise the comparability of data collected in the frame of different surveys and these estimates can still be used to assess changes over time. However, it implies that such data should not be used for example to derive the number of fever-related commodities required in a given population (typically antimalarial drugs and diagnostic tests) as estimates are likely to be too high.
We were not able to validate the use of history of convulsions in the past two years in the frame of this study. It can be argued that the incidence of convulsions it the only marker of severe malarial disease that can be monitored at community level. There is evidence from a hospital study conducted in the Kilifi District Hospital in Kenya [161] that approximately 50% of convulsions in malaria endemic settings can be attributed to malaria. However we cannot

exclude the possibility that estimates of incidence of convulsions based on reported data are biased. Our estimates were about 10 times higher than those reported in Kilifi (from 4300 to 2300 cases for every 100 000 children per year between 2005 and 2008 compared to 235 cases per 100 000 per year in 2006). On one hand it is recognised that hospital estimates of incidence are lower than what would be expected at community level in most of sub-Saharan Africa where many cases are managed at home [5]. The authors themselves caution that many children with convulsions may have died without reaching the hospital and that a few may have been treated successfully in peripheral health facilities. On the other hand, it is likely that our estimates are too high because the same recall bias that was seen for simple fever estimates may have led to reporting bias. It is well possible that a rare and dramatic event such as a convulsion in a small child might have led to recall beyond the two weeks that we were asking for.

Our data confirm that “caution is required when using health facility-based data to evaluate the health impact of malaria control efforts in Africa” [146]. The main concern with health facility records is obviously their quality. Our experience shows that in absence of constant supervision records were often not filled in. Acceptable reporting was only achieved after one year of repeated visits and we had to discard the data from the first year of data collection. Furthermore, health facility staff mostly relies on presumptive diagnosis of malaria in malaria endemic countries [82]. The data we presented here shows that the proportion of fever cases diagnosed did not change throughout the year. Both during the months of high transmission and during the months of low transmission approximately two thirds of fever cases were systematically diagnosed as malaria. Rapid diagnostic tests (RDT) for malaria were introduced in three out of the 14 health facilities in the area in late 2007. Although a decrease in malaria diagnoses was observed in those facilities (Robert Tillya, in preparation), this effect was diluted in our study when the data was aggregated over all the facilities

Beyond data quality issues, relying exclusively on health facility data can lead to biases. Firstly, they do not take population growth into account. Our results clearly show that population growth can affect results, since despite decreases in health facility fever and malaria rates there was no impact on the absolute number of cases seen in health facilities which ultimately represents the burden of malaria at health facility level. Secondly, health facility users are not necessarily representative of the population at large when the proportion of cases brought to a health facility is low, which is often the case in resource-limited countries [5]. In our study, the decline in community fevers was matched by a decline in health facility fevers in children under the age of five, the majority of which attended a health

facility (72%) but not in the overall population for which health facility attendance was much lower (estimated between 45% and 57%).

5.6. Conclusions

The community burden of malaria morbidity declined between 2005 and 2008 in the Kilombero and Ulanga DSS most likely as a result of malaria control efforts. Meanwhile the health facility burden of the disease remained unchanged due to population growth. The good internal and external consistency of our data strengthens our conclusions and shows that history of fever in the previous two weeks can be used as a community-based morbidity monitoring tool.

5.7. Authors' contributions

SA oversaw the collection of the health facility data from 2007 to 2008, coordinated the treatment seeking survey in 2008, analysed the data, drafted and finalised the manuscript. RN and MA head the Ifakara DSS and oversaw the collection and entry of the history of fever and convulsions data. MWH participated in the design of the treatment seeking surveys, coordinated the treatment seeking surveys in 2004 and 2006, developed the forms for the collection health facility data and oversaw the collection of the health facility data from 2004 to 2006. CL did the original study design and contributed to the data analysis as well as the manuscript. The final manuscript was approved by all authors.

5.8. Acknowledgements

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6. Under-five mortality patterns before and after the implementation of the ACCESS programme in Tanzania.

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6.1. Abstract

Background

The ACCESS Programme was implemented between 2004 and 2008 in the Kilombero and Ulanga Districts of south-central Tanzania to improve access to malaria treatment with a set of interventions targeting users and providers. This paper aims at assessing the ACCESS programme's impact on mortality.

Methods

The local Demographic Surveillance System (DSS) provided monthly and yearly estimates of under-five, infant and child mortality rates expressed as cases per 1000 person years (c/1000py) between 1997 to 2008. We used Poisson regressions to assess the impact of the ACCESS interventions accounting for the effect of other malaria interventions and contextual factors. We also attempted to understand the relative contribution of malaria risk and food availability to monthly variations in mortality.

Results

Under five mortality decreased from an average of 28.4 c/1000py in the years before 2004 to 18.9 c/1000py in 2008 but this was part of a longer secular trend dating back to 1997. The ACCESS interventions and Insecticide Treated Nets (ITN) coverage were independently associated with decreases in mortality, accounting for the effect of other malaria interventions and contextual factors (ACCESS: IRR comparing before 2004 vs. 2008=0.83, 95%CI=0.68 to 0.99; ITNs: IRR for every 10% increase in net ownership=0.97, 95%CI=0.95 to 0.98). Decreases in under five mortality were largely driven by decreases in infant mortality while child mortality (ages 1-4 years) remained constant. Infant deaths were more likely to occur in months of high transmission whereas child deaths were more frequent in months of low household food availability.

Conclusions

Improving access to malaria treatment appears to be a successful strategy along with increasing ITN coverage. Most of the decrease in under-five mortality has been driven by decreases in infant mortality. Little gains have been made in child mortality, which appears to be mainly driven by household food insecurity. Child survival programmes should recognise the important contribution of malnutrition to morbidity and mortality.

6.2. Background

Prompt treatment of malaria episodes is a core component of malaria control and elimination strategies [4]. Impressive progress has been achieved in product development and in securing a substantial international support, so that most African countries have now switched to the highly efficacious Artemisinin-Combination Therapies (ACT). Despite this, surveys conducted between 2007 and 2008 in 11 African countries found that despite large increases in the supply of antimalarial treatments, only 32% of children with fever were treated with antimalarial drugs and only 15% with ACTs [32].

The low coverage of antimalarial treatment is largely explained by people's inability to access this class of drugs, and little progress will be made unless broader access issues are tackled. The ACCESS programme implemented between 2004 and 2008 in the Kilombero and Ulanga Districts of south central Tanzania was one of the first initiatives to address access issues in a comprehensive way, with a set of interventions and monitoring and evaluation (M&E) activities targeting users and providers [101]. Since, a number of initiatives have also put access on their agenda, including the Medicines for Malaria Venture (MMV) [162], the ACT consortium [163] and the Clinton Foundation [164]. Recently, the Global Fund to Fight AIDS Tuberculosis and Malaria (GFATM) has started planning the implementation of an innovative funding mechanism which aims at improving the availability and accessibility of effective antimalarial drugs in the private retail sector - the Affordable Medicines Facility for malaria (AFMm) [47].

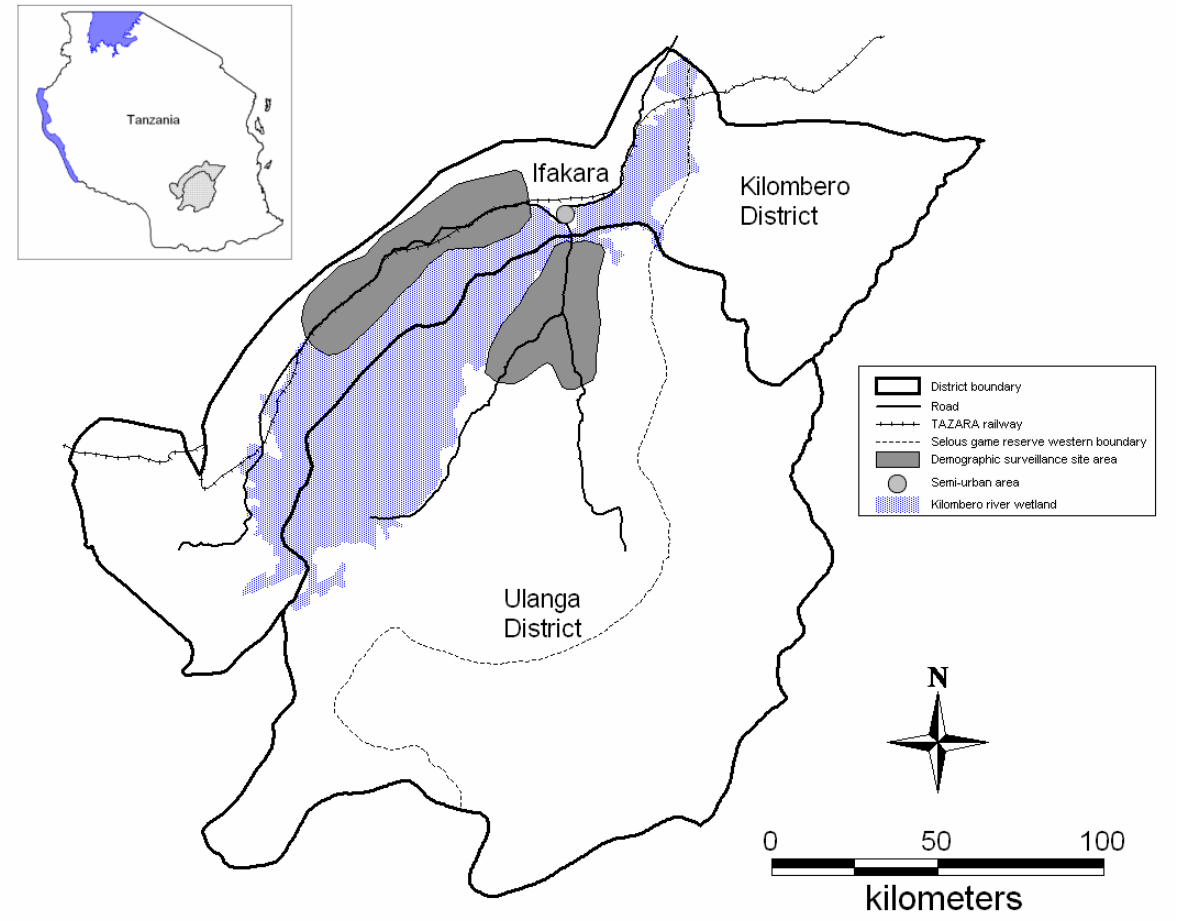
As a result of ACCESS interventions there is evidence of an increase in access to malaria treatment [127] (cf. Chapter 3) and better quality treatment for malaria [102] (cf. Chapter 4). Recently, an impact on morbidity has been documented in the study area (cf. Chapter 5). The present paper is concerned with the impact on infant and child mortality of improved treatment seeking and treatment quality. While technically feasible because of the presence of a full demographic surveillance site in the area, the major problem with such an assessment is the multiplicity of causes of death, and the difficulty to distinguish them. Not only do most children die at home [5] but causes are multifactorial in the sense that more than one cause is required to overwhelm a child's body and lead to death. Here we investigated the relative contribution of malaria risk, climate and food availability to monthly variations in infant and child mortality.

6.3. Methods

Study setting

The ACCESS Programme was implemented in the Kilombero and Ulanga Districts in south-central Tanzania (Figure 25). The area has been extensively described elsewhere [73, 101]. The total population of the two districts was 517,000 in 2002 according to the national census [165]. Malaria transmission in the area is intense and perennial [77, 78]. The area is characterised by a rainy season from November to May.

Figure 25. Location of the Ifakara DSS site



The area is predominantly rural with over 95% of its population reporting farming as their main activity [73]. Rice is the main staple food and the most important cash crop in the area. Maize and cassava are also grown, but mainly for household consumption. Over 80% of total farmed land is used for growing paddy and farmers sell about 50% of they grow [74]. Most of the rice paddies lie in lowlands and are rainfed. Production per hectare is fairly low compared

to its potential [75], partly due to the low uptake of new high yield varieties and the reduced use of fertiliser, but also because of the reliance on manual labour for land preparation and weeding [74] [76]. As a consequence, rice production and people's livelihood in the area is extremely reliant on adequate rainfall.

Malaria control interventions

Coverage and outcomes of ACCESS Interventions - The ACCESS programme was implemented in the whole of the Kilombero and Ulanga Districts between 2004 and 2008 to improve access to prompt and effective malaria treatment by targeting both users and providers [101]. Interventions were carried out at three levels: 1) the community, 2) the formal health sector and 3) the private retail sector for drugs. The community intervention consisted of a social marketing campaign for more effective care seeking. Key activities in the public health sector included refresher training for health facility staff based on Integrated Management of Childhood Illness (IMCI) algorithms and strengthening the role of the Council Health Management Teams (CHMT). The intervention in the private retail sector were implemented by the Tanzanian Food and Drug Administration (TFDA) and Management Science for Health (MSH) and consisted of the roll out of Accredited Drug Dispensing Outlets (ADDOs) in the study area from 2006 onwards to improve access to quality treatment in the private retail sector for drugs [57, 87]. In addition in 2006 Tanzania changed its first line treatment for malaria from Sulphadoxine-Pyrimethamine (SP) to Artemether-Lumefantrine (ALu).

Between 2004 and 2008 the ACCESS and ADDO programmes achieved a very high coverage. The ACCESS Social marketing campaigns were conduced in 96% (78/81) of the villages in the Kilombero District and 95% (62/65) of the villages in the Ulanga District. Between 2006 and 2008, 135 ADDOs were opened in the Kilombero District and 55 the Ulanga District (equivalent to approximately three shops per 10 000 people in both districts). In 2004 and 2005 91% (94/103) of all health workers in the Ulanga District and 93% (39/42) of clinical officers in the Kilombero District attended a refresher training on malaria case management within the framework of IMCI organised jointly organised by ACCESS and the CHMT. Between 2006 and 2008 55 ADDOs were opened the Ulanga district and 135 in the Kilombero district (equivalent to approximately three shops per 10 000 people in both districts). The programme's monitoring and evaluation activities showed and an improvement in access outputs in terms of availability and accessibility of retail outlets [127] (cf. Chapter 3) and hence better treatment outcomes: the percentage of fever cases treated within 24hrs increased from 67% to 89% between 2004 and 2008 [102] (cf. Chapter 4).

Other malaria control interventions - Three other major interventions took place in the study area and needed to be controlled for in the analysis. The KINET project for the promotion and subsidisation of Insecticide Treated Nets (ITNs) [126] was implemented between 1997 and 1999 and resulted in a 73% ownership of nets by 2000 [77, 91] from an initial coverage of 37%. Since 2000, the KINET model has been upscaled nation-wide within the frame of the Tanzania National Voucher Scheme (TNVS) programme [158]. The area has also seen two changes in the national treatment policy for malaria. Chloroquine was abandoned in favour of Sulphadoxine-Pyrimethamine (SP) in 2001 due to widespread resistance. However, high levels of resistance to SP developed within two years of its introduction [133] and in 2007 the ACT Artemether-Lumefantrine (ALu, trade name Coartem®) replaced SP as the first line treatment for malaria. This change of treatment policy resulted in improved availability of antimalarials in health facilities in 2007 and 2008 due to the implementation of a push system of delivery [127] (cf. Chapter 3). In addition, in 2000 the Kilombero and Ulanga Districts decided to implement the "facility based" IMCI interventions which aim at improving case-management in health facilities while at the same time strengthening the health system [34] [166].

Data collection and processing

Mortality rates - The Ifakara Demographic and Surveillance System (DSS) area provided data on mortality. The DSS was established in 1996 and covers 25 villages (13 in Kilombero and 12 in Ulanga) [73]. The population in 2004 was almost 74,000 and just over 92,000 in 2008. We calculated estimates of under-five annual mortality rates (ages 0 to 5 years), infant mortality rates (ages 0 to 1) and child mortality rates (ages 1 to 5) as the number of deaths per 1000 person years of exposure (c/1000py).

Malaria control interventions – In the absence of a control group we could only evaluate the effect of the ACCESS interventions and the changes of national treatment policy by comparing mortality rates before and after their introduction. One issue is the quantification of the year-to-year development in coverage of the interventions. We could at least obtain yearly ITN coverage data (percentage of households owning at least one mosquito net) from the DSS routine data collection for the 12 years of observation, and the time point for the two changes in first-line antimalarial is also well defined. To the best of our knowledge, no major other malaria or health intervention took place in the area during the period of observation. The number of health facilities did increase less rapidly than population growth.

Contextual factors - We collected data on rainfall and agricultural production as the two main potential confounding factors. The Kilombero Agricultural Training and Research Institute

(KATRIN) provided monthly rainfall data (mm) which it collects from gauges located just outside Ifakara. We obtained yearly agricultural yield (tons/ha) of rice and maize from the Kilombero District Agricultural and Livestock Development Office (DALDO). Because of the similarity of the environment in both districts we extrapolated the values for Ulanga from those of the Kilombero District.

We constructed a proxy for monthly food availability (kg per household) on the basis the agricultural yield data and information describing the agricultural practices of the local farmers. We estimated food availability in a given month as the sum of the availability of rice and maize, with rice availability peaking in June and maize availability in March, when they are harvested [74, 167]. The initial amount of rice and maize in a given year was calculated by multiplying the rice yield of that year by 1.5 hectare (ha) for rice and 0.24 ha for maize, the average areas that a household dedicated to each of the two crops [74]. We assumed that 1/10 of the rice harvest was already available in May when harvesting starts. Given that on average farmers sell half of their rice crops [74, 76], we applied a composite decay function for rice. The half that is kept for personal consumption was assumed to decrease linearly every month (1/12 of half of the initial amount per month). The half that is sold was assumed to decrease at an exponential rate (1/2 of the amount in the previous month every month), which ensured that bigger quantities are sold in the months following the harvest and most of the rice is sold by the beginning of the rainy season [167]. We applied a linear decay to maize (1/12 of half of the initial amount per month), given that it is usually only used for household consumption [167].

Statistical analysis

We estimated the change in yearly under-five mortality rates before and after the ACCESS intervention, (excluding the years of intervention between 2004 and 2008) by means of a Poisson regression. The effect of ACCESS was assessed with a binary variable taking the value zero in the years from 1997 to 2004 and one in 2008. The following variables accounted for the effect of the other malaria interventions: 1) a binary variable denoting years before and after the IMCI training with value zero before 2003 and one thereafter; 2) a categorical variable denoting the first line treatment for malaria; 3) a binary variable denoting years of change in treatment policy with value one in years coinciding with a the first year of introduction of a new drug and zero otherwise; 4) a continuous variable denoting household mosquito net ownership. In addition the two following continuous variables accounted for the effect of contextual factors: 1) total annual rainfall; and 2) agricultural yield.

First. we explored the univariate relationship between mortality and all the explanatory variables. We then fitted two multivariate Poisson models, one including the effect of

ACCESS and one excluding them. This was necessary because the change of treatment policy took place during the ACCESS years and their effects cannot be estimated in the same model due to co-linearity.

To better understand the determinants of the inter-annual variations in under five mortality we regressed monthly infant and child mortality rates against monthly rainfall and food availability data. We used monthly rainfall as a proxy for malaria transmission on the basis of the very high correlation between monthly rainfall and the entomological inoculation rate (EIR) in the study area [78]. We also lagged rainfall by one and two months [168] since health facility studies conducted in the area show that the proportion of children with malaria infections is highest in January and February (Valérie D'Acrémont, personal communication), whereas rainfall peaks in March and April (probably because larval habitats get washed away with very heavy rain [169]). We used food availability as a combined proxy for nutrition and this was also lagged by one and two months to allow for delayed and cumulative effects of food availability on children's health. We explored the relationships between mortality and these explanatory variables with univariate and multivariate models.

Intercooled Stata 10 (Stata Corp., College Station, TX, USA) was used for all data management and analysis. Multivariate models were built by stepwise elimination of variables with a Wald test probability values less than 0.2.

6.4. Results

Impact of ACCESS interventions

Annual under five mortality decreased from an average of 28.4 c/1000py (2405/84,576) in the years before 2004 to 18.9 c/1000py (299/15,793) in 2008. However, this decrease is part of a longer secular trend which started at least in 1997, when mortality was as high as 31.7 c/1000py (284/8.951) (Table 18 and Figure 26). ITN household ownership increased steadily from 37% in 1997 to above 90% in 2005, remaining constant at this level throughout the study period (Figure 27). Over the study period the average rice yield was 1.8 ton/ha (SD=0.36) and the total annual rainfall was 1510mm (SD=392). There was no secular trend in rice yield or annual rainfall. Rice yield is very highly correlated with rainfall ($r=0.835$ $p<0.0001$). In 2003 mortality peaked to 1997 levels and this coincided with a severe drought which affected rice crops very negatively. Two lesser peaks in mortality (in 2000 and 2005) also coincided with lower than average rainfall and hence agricultural yield (Figure 26 and Figure 28).

Table 18. Under five annual mortality rates between 1997 and 2008

Year	*Cases*	*Person years exposed*	*Rate (c/1000py)*
1997	284	8952	31.7
1998	249	8879	28.0
1999	246	8673	28.4
2000	298	10078	29.6
2001	284	11266	25.2
2002	345	11968	28.8
2003	392	12167	32.2
2004	307	12593	24.4
2005	346	12824	27.0
2006	318	13732	23.2
2007	325	14657	22.2
2008	299	15793	18.9

There is evidence of a significant decrease in under five mortality from 1997 to 2008. Between 1997 and 2008 under five mortality decreased by 3% per year (IRR=0.97 95%CI=0.96 to 0.98). This decrease was mainly driven by a decrease in infant mortality whereas child mortality did not change significantly. Infant mortality decreased from 99.68 c/1000py (181/1,815) in 1997 to 62.48 c/1000py (186/2,977) in 2008 which is equivalent to a 3% decrease per year (IRR=0.97 95%CI=0.96 to 0.98). The average child mortality over the study period was 10.68 c/1000py (417/39,041) (IRR=1.00 p=0.849).

Figure 26. Yearly Under five mortality rates in the Kilombero and Ulanga DSS 1997 and 2008

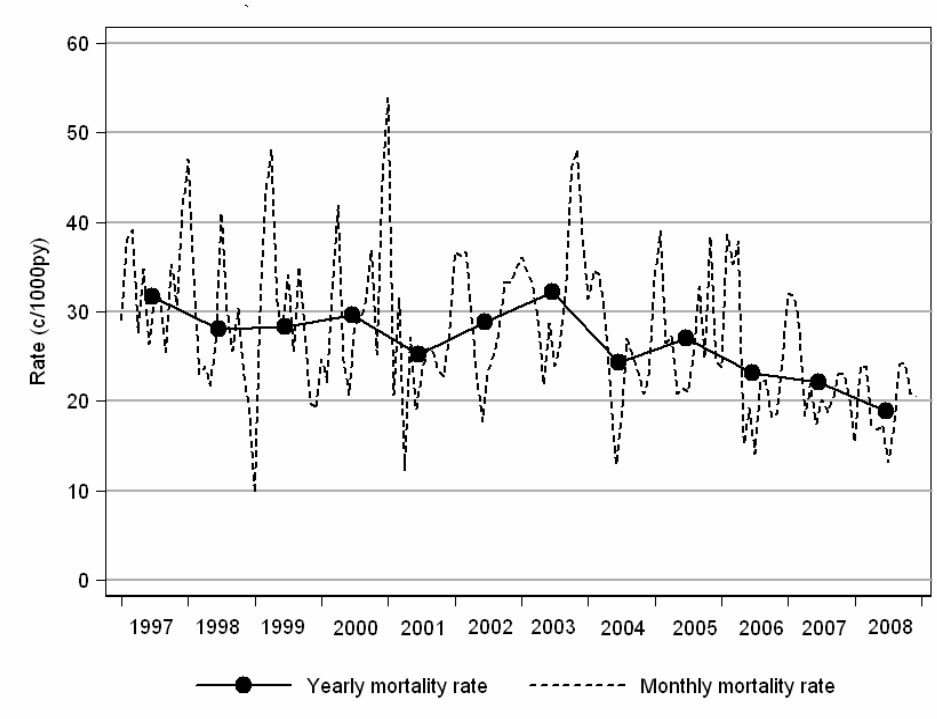


Figure 27. ACCESS interventions and other major malaria control interventions

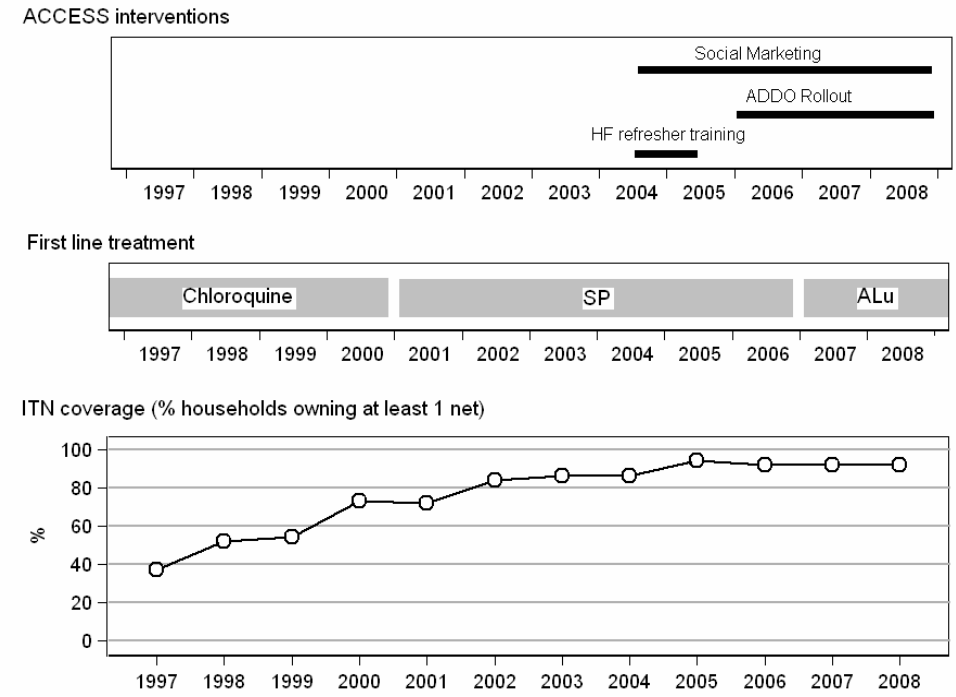
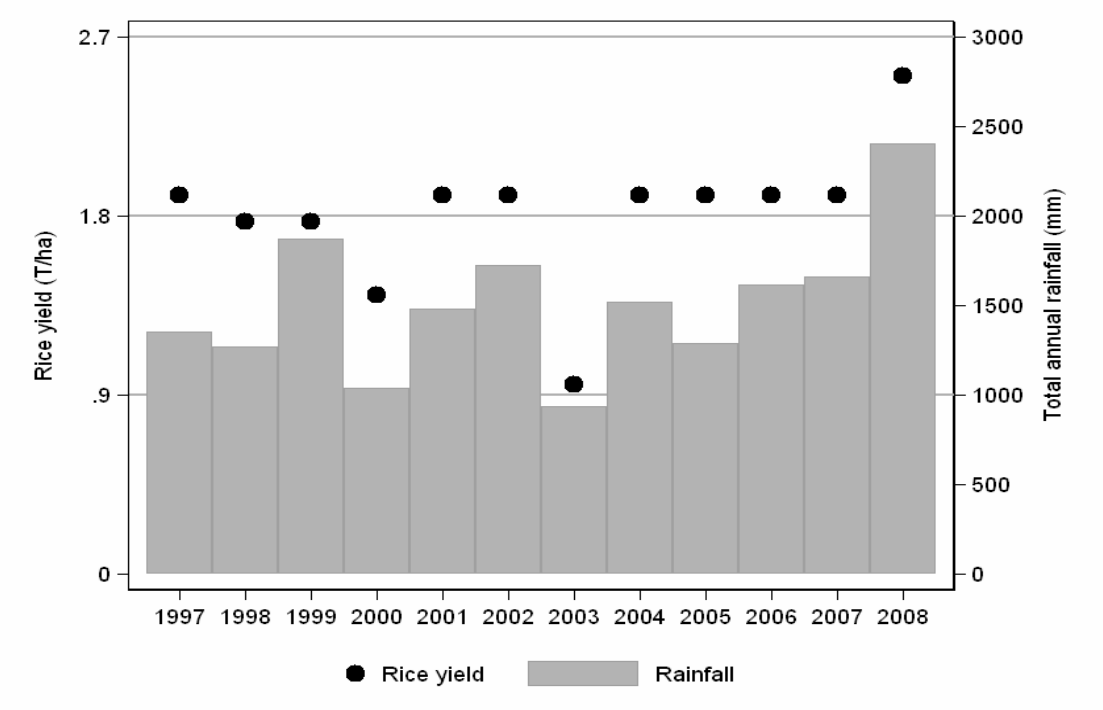


Figure 28. Rainfall and rice production in the Kilombero Valley, between 1997 and 2008



The only malaria control interventions which were found to be independently associated with a decrease in mortality were (1) the package of ACCESS interventions, and (2) the ownership of ITNs (Table 19). Mortality rates were 17% lower in 2008 compared to 2004 (before the ACCESS interventions – IRR 0.83 95% CI 0.68-0.99) and every 10% increase in mosquito net ownership was associated with a 5% decrease in mortality (IRR 0.95 95%CI

0.93-0.98). The IMCI training of health facility staff and the changes of treatment policy did not affect mortality significantly. There was no effect following the first year of introduction of a new antimalarial drug, but a 19% increase in mortality was estimated in the second year of introduction of a new drug. An analysis performed separately during the SP years and the ALu years suggests that this effect is entirely driven by increases in mortality during the second year of SP introduction (IRR=1.18, 95%CI=1.04 to 1.35 excluding the effect of ACCESS) whereas there was no significant effect associated with the second year of introduction of ALu. The effect of interventions did not vary significantly whether the variable denoting the ACCESS interventions was included in the model or not, i.e whether the model was fitted on 9 or 12 years of data (effect of the second year of a drug IRR=1.16 95%CI 1.04 to 1.31, effect of ITN ownership IRR=0.97 95%CI=0.95 to 0.98, all others non significantly different from zero, Pseudo R-sq=0.430 LR Chi-sq=77.53 p<0.001).

Table 19. Estimated effect of malaria control interventions and contextual factors from Poisson regression fitted on yearly under-five mortality rates between 1997 to 2008

	Univariate model (n=12)		*Multivariate model (n=9) **	
	IRR (95% CI)	*Sig.*	*IRR (95% CI)*	*Sig.*
Malaria control interventions				
ACCESS (before 2004 vs. 2008)	0.66 (0.59 to 0.79)	<0.001	0.83 (0.68 to 0.99)	0.035
IMCI (before vs. after 2003)	0.85 (0.79 to 0.91)	<0.001		
1st line treatment (baseline=CQ)	1			
SP	0.91(0.84 to 0.98)	0.010		
Alu	0.70 (0.63 to 0.77)	<0.001		
1st year of a drug	0.88 (0.81 to 0.96)	0.004		
2nd year of a drug	0.87 (0.80 to 0.94)	0.001	1.19 (1.04 to 1.37)	0.011
ITN ownership (10% increase)	0.95 (0.94 to 0.97)	<0.001	0.95 (0.93 to 0.98)	0.001
Contextual factors				
Total annual rainfall (500 mm)	0.86 (0.82 to 0.89)	<0.001		
Rice yield (500 kg/ha)	0.85 (0.82 to 0.89)	<0.001	0.86 (0.79 to 0.92)	<0.001

* Pseudo R-sq=0.454 LR Chi-sq=80.82 p<0.001

There is evidence that non-malaria control factors also explain variations in mortality. Rice yield and rainfall were both strong independent predictors of mortality (Table 19), with increased rainfall and increased yield significantly associated with decreases in mortality. However, overall the multivariate models explained only approximately 20% of the variation in mortality (Model including the effect of ACCESS R-sq= R-sq=0.454, model excluding the effect of ACCESS Pseudo R-sq=0.430). This suggests that many other variables not accounted for also explain the observed decrease in mortality.

Determinants of intra-annual variations in infant and child mortality rates

Infant and child mortality both exhibited strong intra-annual variation (Table 20). Mortality rates in children were between 6 and 10 times higher than in infants. There was no evident

seasonal pattern, although monthly infant mortality rates tended to be lower between May and July, while child mortality rates were lower between June and September (the months with lower rainfall and higher food availability). The accepted pattern of the rainy season is from November to May with peaks in March and April, but our data suggest a strong year on year variability in monthly rainfall The average rice harvest produced a mean of 2675kg (SD=443kg) per household and the average maize harvest was 540kg (SD=100kg) per household. Food availability was at its maximum in June after the harvest and decreased constantly thereafter, reaching its minimum in January and February (Figure 29 and Figure 30).

Table 20. Descriptive statistics of inter-annual variation in infant and child mortality, rainfall and estimated food availability between 1997 and 2008

	Infant mortality	*Child mortality*	*Total rainfall (mm)*	*Estimated household food availability (kg)*
	Rate (c/1000py)	*Rate (c/1000py)*	*Median (IQR)*	*Median (IQR)*
Jan	88.9(215/2.419)	11.0 (38/3.463)	215.1 (110.0)	525 (40)
Feb	89.5 (196/2.191)	12.0 (40/ 3.089)	203.0 (136.1)	360 (30)
Mar	86.7 (210/2.422)	13.9 (47/3.379)	307.2 (228.5)	730 (75)
Apr	81.6 (192/2.353)	12.3 (40/3.255)	380.4 (289.0)	570 (65)
May	66.4 (162/2.441)	10.7 (36/3.375)	83.9 (88.5)	980 (70)
Jun	60.7 (144/2.372)	8.9 (29/3.245)	14.1 (22.3)	1810 (130)
Jul	69.5 (171/2.459)	9.5 (31/3.263)	1.1 (6.0)	1860 (130)
Aug	77.6 (193/2.489)	9.4 (31/3.282)	1.1 (24.8)	1520 (110)
Sep	86.8 (209/2.408)	7.9 (25/3.148)	0.2 (5.5)	1260 (90)
Oct	83.3 (208/2.496)	12.4 (40/3.216)	1.2 (14)	1060 (80)
Nov	79.1 (193/2.439)	7.7 (24/3.098)	27.6 (80)	870 (60)
Dec	79.2 (202/2.549)	11.1(36/3.229)	159.1 (206.8)	690 (40)

Rainfall and food availability in the same month were strong predictors of infant and child mortality in univariate analyses, with every mm of rain increasing the death rate by 20-35%, and every 500kg increase in household food availability decreasing it by 8-12%. Child mortality was also negatively associated with food availability in the previous month and the previous two months. Strangely, rainfall in the previous two months appeared to have a protective effect on infant mortality (Table 21).

Figure 29. Monthly rainfall, food availability and infant mortality between 1997 and 2008.

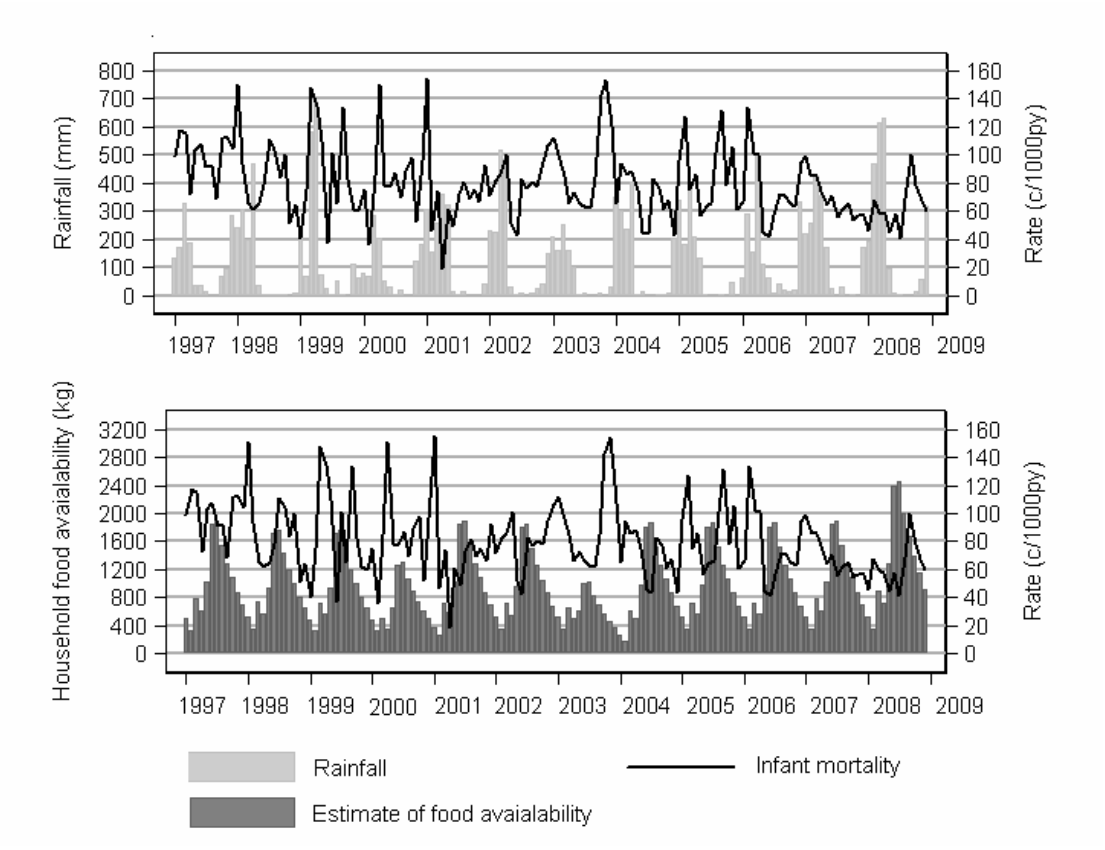


Figure 30. Monthly rainfall, food availability and child mortality between 1997 and 2008

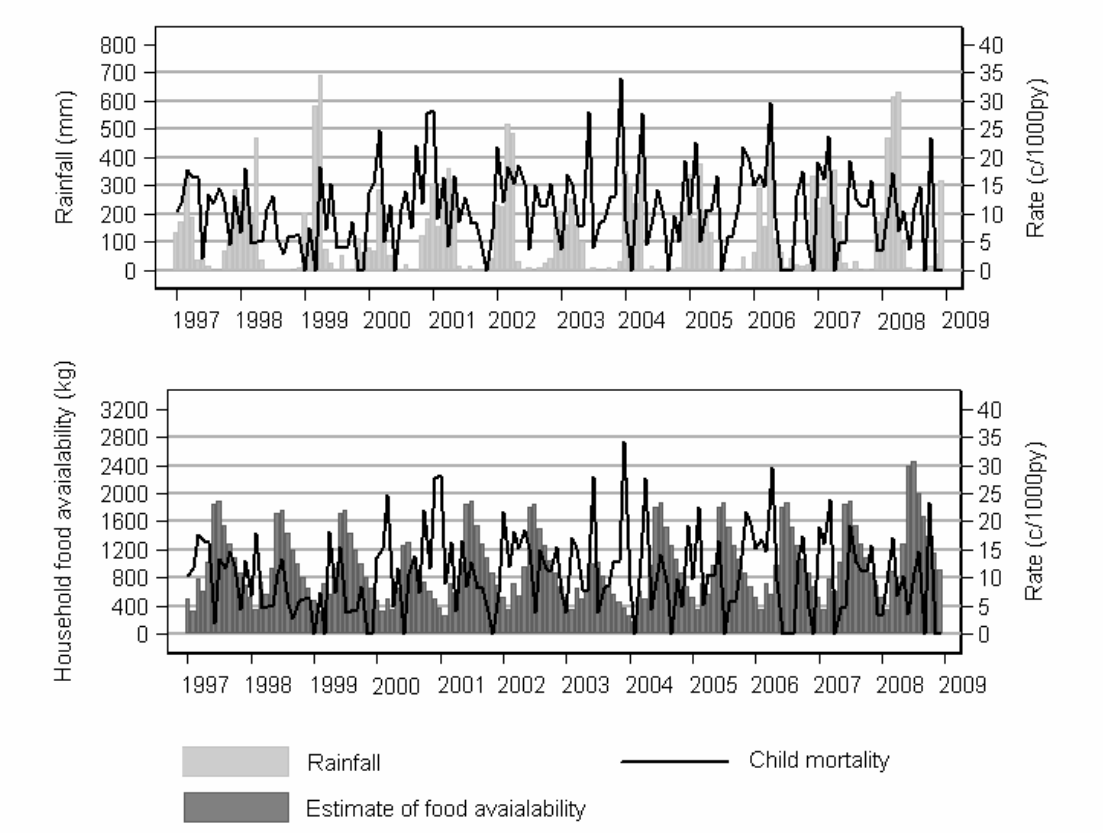


Table 21. Estimated effect of rainfall and food availability from Poisson regressions fitted on monthly infant and child mortality rates between 1997 and 2008 (all effects adjusted for the effect of year)

		Univariate model		*Multivariate model (n=142) **	
	n	*IRR (95% CI)*	*Sig.*	*IRR (95% CI)*	*Sig.*
Infant Mortality					
Rainfall (500 mm)	144	1.20 (1.06 to 1.36)	0.005	1.19 (1.01 to 1.40)	0.038
Rainfall (500 mm) lag 1	143	1.02 (0.90 to 1.16)	0.814		
Rainfall (500 mm) lag 2	142	0.79 (0.69 to 0.90)	0.001	0.76 (0.65 to 0.89)	0.001
Food availability (500 kg)	144	0.92 (0.89 to 0.96)	<0.001	0.96 (0.91 to 1.01)	0.103
Food availability (500 kg) lag 1	143	0.97 (0.94 to 1.01)	0.133		
Food availability (500 kg) lag 2	142	1.01 (0.97 to 1.05)	0.607		
Child mortality					
Rainfall (500 mm)	144	1.35 (1.02 to 1.80)	0.036		
Rainfall (500 mm) lag 1	143	1.21 (0.90 to 1.62)	0.199		
Rainfall (500 mm) lag 2	142	1.14 (0.84 to 1.53)	0.394		
Food availability (500 kg)	144	0.88 (0.80 to 0.97)	0.009	0.90 (0.82 to 0.99)	0.044
Food availability (500 kg) lag 1	143	0.90 (0.82 to 0.98)	0.021		
Food availability (500 kg) lag 2	142	0.90 (0.82 to 0.99)	0.029	0.93 (0.84 to 1.03)	0.158

* Infant mortality Pseudo R-sq=0.0523 LR chi-sq(4)=46.16 p<0.0001 Child mortality pseudo R-sq=0.0160 LR chi-sq(2)=9.13 p=0.0140

6.5. Discussion

Under five mortality significantly decreased by 17% following the ACCESS package of interventions, from an average of 28.4 c/1000py in the years before the interventions to 18.9 c/1000py in 2008, accounting for other malaria interventions (ITN coverage, changes in treatment policy and IMCI training of health facility staff) and contextual factors (rice yield and rainfall). The only other malaria control intervention which was found to be independently associated with under-five mortality is ITN coverage, with every 10% increase in household ownership decreasing the incidence of death by 3-5%. The decrease in under-five mortality was mainly driven by a decrease in infant mortality whereas child mortality remained constant between 1997 and 2008. An analysis of the inter-annual determinants of infant and child mortality suggests that this may be because the main determinant of child mortality is household food availability, which has not changed significantly over the study period.

Our conclusion that the improvement in access to treatment has resulted in a decrease in mortality is based on a before-after assessment [90]. This type of design assumes a plausibility argument, i.e. that mortality reductions can be attributed to programmatic efforts. Plausibility is often defined by demonstrating improvements in population-level measurements of steps in the causal pathway. In our study area we have evidence that a social marketing campaign for improved malaria treatment seeking for malaria combined with a strategy to strengthen the role of the private retail sector and changes in the delivery system of drugs in health facilities resulted in improved access to treatment at both the

provider and the user levels from 2004 to 2008 (cf. Chapters 3 and 4). The percentage of fever cases treated with an antimalarial increased from 85% to 96% (infants from 89% to 90%, children under five from 90% to 94%) and the percentage treated within 24hrs increased from 67% to 89% (infants from 67% to 90%, children under five from 73% to 88%). These are very high treatment coverage indicators, well in excess of the 30% average in Sub-Saharan Africa [32].

The very high levels of treatment obtained in the study area imply that virtually any potential malaria case is treated with an antimalarial. This is in some ways this is confirmed by an independent survey demonstrating a very high average drug level for antimalarials in the population [170]. It is important to point out that a significant proportion of fever patients was treated with SP even after the change of treatment policy. Although a high resistance to the drug had been documented in the area [133] it has been argued that using SP for presumptive treatment may have a significant impact on transmission thanks to its prophylactic effect [153]. The uptake of ALu was not as high as expected (only used in third of cases in 2008), it had a very high treatment efficacy upon its introduction [134] in 2007. Therefore it is reasonable to assume that the treatment access improvements we have observed have contributed to a decrease in mortality.

A concurrent decrease in malaria morbidity and transmission indicators gives an independent argument that the decrease in under five mortality is driven by a decrease in the malaria burden. The incidence of fevers in the area decreased from 47 cases per 1000 weeks (c/1000pw) in 2005 to 34 c/1000pw in 2008 and the incidence of convulsions in young children decreased from 4263 to 2320 cases for every 100 000 children per year (cf. Chapter 5). An older study reported an EIR of 349 infective bites per person per year (ib/p/y) between 2001 and 2003 [77], but by 2008 the EIR had declined to 81 ib/p/y [78]. Similarly, data from two other projects documented a decrease in parasitaemia in children under the age of five years from 25% in 2004 [150] to 10% in 2008 (Mulokozi *et al.,* unpublished data). However it is important to recognise that this decrease started already in the mid-nineties when an EIR of up to 1400 ib/p/y was recorded [171] and parasitaemia in infants and children under the age of two years was over 50% [172-173].

Given the imperfect study design and the complex nature of malaria transmission dynamics any attribution of the observed mortality decreases to specific interventions should be interpreted with caution. Before-after designs are often the only feasible way to assess the impact of health interventions at population level (when it is not possible to have a concurrent and comparable control group) but they provide a weak argument for causality. The main concern is that there may be other factors explaining the observed decrease in mortality and

which can not be taken into account. With regards to malaria transmission, there is evidence of a non linear relationship between ITN coverage and EIR. It has been estimated that 35%-65% use of nets in all adults and children can achieve community-wide benefits equivalent to or greater than personal protection [174]. Further, recent modelling work suggests that sustaining coverage with ITN at such levels may lead to constant decreases in transmission even if coverage does not increase (personal communication, Prof. Tom Smith, Swiss Tropical and Public Health Institute, Basel) It is therefore likely that the effect of improved treatment following ACCESS interventions is lower than what our analyses suggest and may perhaps only explain half of the 17% decrease that we have observed.

Despite these study design limitations, our conclusions are strengthened by the broad consistency with other studies conducted in the study area. The 3-5% decrease in mortality for every 10% increase in bednet ownership is very similar to the results of a Cochrane review which synthesised the evidence from five cluster randomised trials conducted in sub-Saharan Africa. Results showed a 17% protective efficacy of ITNs for an average of 60% coverage compared to control areas with no nets [175]. The absence of an impact in the first and second years of introduction of a new antimalarial drug in the public sector is disappointing, but is not entirely surprising considering that both in 2001 and in 2007 the change of treatment policies resulted in a decreased availability of the first line treatment [68] (cf. Chapters 3 and 4). The increase in mortality in the second year of introduction of SP is most likely due to the rapid onset of resistance to the drug [133]. We were not able to find an impact of the introduction of IMCI in the study area. This is surprising since a study conducted in Tanzania which used our study as a control, found that under five mortality was 13% lower in IMCI than in comparison districts [34]. This may reflect differences in the implementation of this strategy in programmatic versus non-programmatic settings.

We found that the decrease in under-five mortality was mainly driven by decreases in infant mortality, whereas child mortality remained constant over the study period. This is consistent with various studies which showed that in highly endemic settings most malaria deaths occured in the first year of life [176-178], and that decreasing transmission mainly reduces infant mortality [179]. On the other hand, it is likely that the reason why child deaths (ages 1-4 years) have not been decreasing between 1997 and 2008 is because they are only indirectly caused by malaria, whereas the primary driver is food availability and therefore malnutrition. It is important to stress that the fact that household food availability emerged as the only independent correlate of child deaths does not exclude that malaria is an important cause of death in this age group. Firstly, because months with higher rainfall largely coincide with the months of lower food availability, and the exact relationship between the amount and timing of rainfall, EIR and malaria infection in humans is not fully understood. Secondly,

because there is considerable body of evidence showing that children who are malnourished are more susceptible to malaria morbidity and mortality [180]. Animal and human epidemiological studies suggest that this is a consequence of a reduction in the function of the immune system [181]. Moreover in a cash crop society household food availability is also strongly related to the ability to mobilise resources to afford treatment [135]. It has also been argued that household food insecurity and its related stress [182] could impair mother's ability to successfully prevent and treat malaria in their children [183].

There are a number of factors which could affect our analyses, including changes in HIV/AIDS prevalence and treatment and other non malaria health interventions. However, regional data suggests that there the proportion of women living with HIV/AIDS has remained constant at around 7% between 2004 and 2008 [25,184] and knowledge of the HIV/AIDS epidemic suggests that it can only have risen between the mid nineties and 2004 [185]. Anti Retroviral Treatment (ART) was introduced in 2004 but only around 11-13% of HIV infected people in the DSS area received treatment by 2008 (Dr Erik Mossdorf, Chronic Diseases Clinic Ifakara, Tanzania and University Hospital Basel, Switzerland personal communication). The coverage of other child-survival interventions such as vitatmin A supplementation increased after its introduction in the routine Essential Drugs Programme (EDP) in 1997 [186]. Other interventions such as oral rehydration therapy and iron supplementation for children also increased but antenatal care and immunisation coverage were already high and did not change [149].

Finally, Economic growth and development could also explain part of the decrease in mortality and confound our results. The Gross Domestic Product (GDP) of Tanzania increased from 7.68 billion USD to 20.5 billion USD between 1997 and 2008 [187]. However most of the inhabitants of the study area are subsistence rice farmers. GDP figures do not reflect changes in their wealth and it is difficult to estimate how much better off they are as a result of the nation's economic growth.

6.6. Conclusions

Malaria control interventions in the Kilombero and Ulanga districts are likely to be associated with decreases in under five mortality. It is difficult to quantify the individual contribution of each malaria control intervention given the before-after nature of the study and the lack of information on the many other factors which may provide alternative explanations for this decrease. However, plausibility arguments suggest that improving access to malaria treatment with social marketing campaigns and by strengthening the role of the private retail sector for drugs is a successful strategy. Most of the decrease in under-five mortality has

been driven by decreases in infant mortality, while child mortality appears to be mainly driven by household food insecurity. Future malaria control interventions should recognise and act upon the important contribution of malnutrition to malaria morbidity and mortality.

6.7. Authors' contributions

SA analysed the data, drafted and finalised the manuscript. RN and MA head the Ifakara DSS and oversaw the collection and entry of all DSS related data between 1996 and 2008. MWH, AD, AS, FK and HM contributed to the collection of contextual data, and contributed to the design of the study and the manuscript. CL generated the study design and contributed to the data analysis as well as the manuscript. The final manuscript was approved by all authors.

6.8. Acknowledgements

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7. Overall discussion and conclusions

This aim of this thesis was to evaluate the ACCESS Programme. Findings should feed into a better understanding of access to malaria treatment and inform future interventions. The methodological issues of the analysis are presented in 7.1 with a focus on the design and the choice of study area. Sections 7.2 outlines the study's implication for the interventions and monitoring and evaluation activities of the second phase of ACCESS (2008-2011) while section 7.3 examines the study's implications for practice.

7.1. Methodological issues

Study design

The main limitation with the evaluation presented in this thesis is the weakness of the arguments attributing causality. Randomised controlled trials are considered the gold standard to establish a causal relationship but it is not always possible to randomise people and results are typically not very generalisable since they offer an indication of controlled efficacy rather than real life effectiveness [188]. In the case of the ACCESS programme it would not have been practical or politically acceptable to randomise communities. It would have also excluded the possibility of monitoring the community impact of the programme since too few communities would have been in the DSS area. Hence a plausibility assessment [90] was the only feasible way to assess the impact of ACCESS interventions. With this type of design improvements are attributed to the programmes if improvements are found in every step of the causal pathway between intervention and impact and all other explanations can be formally discarded. The comprehensive M&E plan of the ACCESS programme enabled to reach a high level of plausibility but it was not possible to rule out that improvements could have happened independently from the project, especially as a result of a secular trend.

There would have been two ways to reach a higher level of plausibility: 1) by documenting changes in the understanding of malaria and its treatment and 2) by choosing a comparison group to control for the influence of confounding factors. The main health outcome of the programme was the increase in the proportion of fever cases treated with an antimalarial within 24 hours. This improvement was ascribed to the ADDO intervention and the social marketing campaigns, on the basis of improved access outputs, (i.e. better availability and accessibility of treatment) and better knowledge. The access outputs were measured, and indeed improvements were noted [102] (cf. Chapter 4) but better knowledge was only

assumed as a necessary consequence of exposure to social marketing campaigns. Although it might be a perfectly reasonable assumption, measuring improvements in understanding within the frame of the EMIC treatment seeking surveys or with a household survey before and after the implementation of the interventions would have added strength to the argument that the social marketing campaigns were able to promote behaviour change.

As far as the choice of a control is concerned, the Rufiji Demographic Surveillance Site (DSS) could have been an ideal comparison group. Two other large scale studies have evaluated interventions by comparing the Ifakara and the Rufiji DSS. The Interdisciplinary Monitoring Project for Antimalarial Combination Therapy in Tanzania (IMPACT-Tz) [105] [150] and the Integrated Management of Childhood Illness Multi-Country Evaluation (IMCI-MCE) [34, 166] have made use of this design. The choice of an external control would have enabled, for example, to rule out the possibility that improved access outputs were just the result of a natural growth in the retail sector for drugs, and that better treatment outcomes are just a consequence of that. It would have also enabled to quantify better the impact of the programme on morbidity and mortality.

Choice of location

There were numerous advantages to conducting this study in the Ifakara DSS. The DSS provided an excellent epidemiological framework for this study. The constant demographic surveillance enabled the assessment of the mortality and morbidity impact and facilitated the selection of random sample of households for the treatment seeking surveys [102] (Chapter 4). The findings from qualitative investigations of people's perception and understanding of disease could guide the adaptation of the questionnaire used for the treatment seeking surveys [81, 128]. Furthermore, there was a wealth quantitative data to support the interpretation of the findings of this thesis. This includes entomological and parasitological data [77, 173, 189-190] (Chapters 5 and 6) collected since the 1990s. This data was further complemented by in depth descriptions of the agricultural practices of the farmers of the Kilombero Valley [74, 76, 167] and comprehensive agricultural production data from the Kilombero District Agricultural and Livestock Development Office (DALDO), most likely due to the proximity to the Kilombero Agricultural Research and Training Institute (KATRIN). In addition KATRIN itself had been collecting rainfall data since the nineties which it kindly agreed to share.

However, studies conducted in DSS areas are not necessarily very generalisable to the rest of the country. The Kilombero and Ulanga Districts in general, and their DSS areas in particular, have been the object of continued donor and research attention for decades. The

use of antimalarials to treat fever was already much higher in the study area (73% feverish children treated within 24 hours) compared to the rest of the country (51%) [26]. The continued visits by DSS staff could be causing respondent fatigue and biasing our results. The possibility of a Hawthorne effect also needs to be considered [191-192], whereby people may be adapting their responses (and behaviour) simply because they are being studied, not necessarily in response to a particular intervention.

Interventions

Unfortunately this evaluation was not able to fully assess the effect of interventions at health facility level. A refresher course training was conducted between 2004 and 2005 in the health facilities of the Kilombero and Ulanga District to improve quality of care. A follow-up was planned with a Quality Improvement and Recognition Initiative (QIRI). QIRI offers an integrated approach for the evaluation of quality of care combined with a strategy to establish the root causes of performance gaps and to develop implementable strategies to address them. A central element of this component is capacity building for joint supportive supervision and quality management, conducted by the regional and district health management teams together with community representatives. Due to logistic constraints the implementation of QIRI excercises had to be postponed to 2007 and hence their effect could not be evaluated in this thesis.

7.2. Implications for the second phase of ACCESS

Building on the experiences and results from the first phase, the aim of ACCESS II (2008-2011) is to strengthen resources at community, health facility level, with a particular emphasis on sustainability. The activities of the second phase will focus on:

1) Improving households' economic (income) base needed for improved health seeking and outcomes through strengthened Community Health Fund (CHF) and micro-finance for income generation activities;
2) Intensifying community sensitization on correct and prompt malaria treatment with ALu, as well as the empowerment of patients to demand their rights and quality services through a social marketing approach;
3) Strengthening routine supportive supervision and implementation of quality (malaria) case management in all health facilities through the Quality Improvement and Recognition Initiative (QIRI), as well as the introduction of RDTs for malaria;
4) Enhancing the flow of the project's main findings and outcomes to the different stakeholders such as communities, district health authorities, and national and international policy makers in order to influence access policies and practices.

Recommendations for ACCESS II interventions

Results from the treatment seeking surveys [102] (cf. Chapter 4) showed that the use of ALu was not widespread. This was largely due to the low availability of the drug in drug shops, but also because the drug was only prescribed to 2/3 of patients who visited health facilities, although it was present in virtually all the health facilities during the survey period. Possible reasons have already been elaborated on (Section 3.5) and include health facility staff rationing and patient preference for other drugs with simpler regimens. Future interventions in health facilities and social marketing campaigns should aim to address these issues. The introduction of Rapid Diagnostic Tests (RDT) for malaria should facilitate the process since studies suggest that providers and patients alike are more keen to use ALu in a cases of confirmed malaria (D'Acremont, in preparation).

It is important that the availability of ALu in ADDOs continues to be monitored. This will be undertaken by the nation-wide evaluation of the Affordable Medicines Facility for malaria (AMFm) (Mwita, National Malaria Control Programme, personal communication). But within the frame of enhancing the flow of the programme's main findings to district health authorities and strengthening routine supervision, ACCESS II should ensure that the Council Health Management Teams (CHMT) are fully aware of the importance of the availability of the first line treatment for malaria in the private health sector.

Results from the treatment seeking surveys [102] (Chapter 4) suggest that more research is needed on methods to improve patient adherence to treatment. Noticeable gains were made between 2004 and 2008 in terms of timeliness of treatment (from 80% to 92-97% of doses taken within 24 hours), but no significant changes with regards to dosage (between 43% and 76% of doses taken in the right dose). Data from mystery shoppers surveys conducted in between 2004 and 2008 in drug shops showed that the proportion of shopkeepers who gave correct advice for the treatment of malaria along with the antimalarial they sold improved significantly after the introduction of ADDOs (from 30% to 80%, Dillip *et al.*, unpublished data). This suggests that inappropriate dosage of treatment is more likely to be the result of patient adherence rather than provider compliance, and that future social marketing campaigns should aim to address this component.

Recommendations for ACCESS II monitoring and evaluation

This thesis has shown the strength of combining an analytical framework with epidemiological methods to investigate the determinants of access to treatment. On the basis of the Access framework [52] (cf. Section 1.6 for details), data from provider surveys were combined with data from treatment seeking surveys to determine the relative

contribution of the availability, accessibility and affordability of malaria drugs to prompt and effective treatment. Unfortunately the data generated in this evaluation did not able a systematic and quantified assessment of the effect of each access dimensions. Table 22 and Table 23 give an overview of all the dimensions which should be extracted in future provider and user surveys to quantify the contribution of all the access.

Table 22. Determinants of malaria treatment at user level

Dimension	*Indicators*		*Available in this evaluation*
Availability	(does not need to be assessed at user level for the purpose of this evaluation)		
Affordability	1.	SES of household	YES
	2.	Ability and willingness to pay for treatment	NO
	3.	Amount paid for drug and treatment	YES
	4.	Indirect costs (transport, bribes)	NO
Accessibility	5.	GPS location of household	YES
	6.	Location at onset of fever	YES
	7.	Loss of time/time taken to travel to the outlet	NO
Adequacy	8.	Waiting hours	NO
	9.	HF workers/shop attendants perceived as polite and professional	NO
	10.	Patient expectation to be diagnosed with a diagnostic tool (microscopy or RDT)	NO
Acceptability	11.	Personal opinion about each drug	NO
	12.	Personal opinion about importance of prompt treatment for fever	NO
	13.	Advice to take the drug by a community member	NO
	14.	Advice from community member about importance of promptness of treatment	NO

Table 23. Determinants of malaria treatment at provider level

Dimension	*Indicators*		*Available in this evaluation*
Availability	1.	Availability of outlets (HF and drug shops)	YES
	2.	Availability of drugs in outlets	YES
Affordability	3.	Prices of drugs	YES
Accessibility	4.	GPS location of outlets	YES
Adequacy	5.	Waiting hours	NO
	6.	Opening hours	NO
	7.	HF staff qualification	NO
	8.	HF staff operate on a first come first served basis	NO
	9.	presence of diagnostic tools in the HF	NO
Acceptability	10.	Providers' opinion (HF staff or shop attendants) about each drug and the importance of prompt treatment of fever	NO
	11.	Providers' opinion about diagnostic tools in the HF	NO

7.3. Implications for practice

This evaluation has shown that with a set of integrated interventions the Abuja target of "80% of children treated with an antimalarial drug within 24hours of fever onset" is reachable even in a rural Africa setting. A recent review conducted by Smith *et al.* concluded that very little is known about what interventions work in improving prompt and effective treatment for malaria [33]. The overwhelming finding from the review was that despite the wealth of research conducted on the topic, few interventions have been thoroughly evaluated - out of 58 studies conducted on the topic only 23 met the inclusion criteria. This thesis has presented data from a thorough evaluation and has shown that: 1) social marketing campaigns stressing the importance of prompt treatment for malaria combined with 2) a private sector intervention which has improved the availability of quality malaria care in drug shops and 3) good availability of antimalarial drugs in the public sector following the implementation of a push system of delivery can result in over 80% of fever cases in children treated promptly for malaria. Only 56% of cases reported adhering to the recommend drug dosage, but these are still very high values for a rural sub-Saharan African setting. A recent report found that on average only 30% of fever cases in children are treated promptly and adequately for malaria in sub-Saharan Africa [32]. Most importantly, it means that the 2007 targets set by the MTSP were nearly reached in the study area (cf. Section 1.4).

However, this evaluation has also shown the importance of integrated strategies. Improvements in treatment for malaria were associated with a decrease in malaria morbidity and morbidity, but the high level of ITN ownership in the study area also contributed to these decreases. Nevertheless, despite the improvements seen in terms of reduced malaria, little gains have been made in terms of child mortality (ages 1 to 5) as the main driver of mortality in this age group appears to be food availability and malnutrition. It is crucial that policy makers and donors recognise the need for integrated approaches rather than focusing only on one element of child survival. Furthermore, malaria control strategies should be implemented within a wider frame of child survival interventions which recognises and acts upon the synergy between malnutrition and infectious diseases. As it is beyond the scope of this evaluation to advise on these issues, the following sections will concentrate on the implications for the scale up the strategies evaluated in this thesis.

Behaviour change campaigns

Experiences from the Kilombero Valley offer a compelling case to justify the use of heath education campaigns to improve people's understanding of malaria and their actions for its treatment. This evaluation documented impressive improvements in terms of prompt and

effective treatment for malaria, but treatment coverage was already much higher at baseline than in the rest of the country. This is most likely due to the long standing efforts in the area to improve malaria control parameters comprehensively since the mid 1990s with the KINET social marketing campaigns [126]. The Smith *et al*. review pointed out that most interventions targeting users alone with education campaigns have only been assessed in terms of changes in knowledge [121-122, 193] and the reviewers have argued that this is not enough to show that they can change behaviour. This evaluation has shown that changes in knowledge can translate into changes in practice if efforts are made on the provider side to improve the availability and accessibility of sources of treatment. This is confirmed by results from two other interventions which involved both users and providers contemporarily such as the HMM strategy by Pagnoni *et al.* in Burkina Faso [118] and the shopkeeper programme reported by Marsh *et al.* in Kenya [113] .

However, there are two main caveats with regards to social marketing campaigns. Firstly they do not seem to be able to change user behaviour in terms of adherence to recommended treatment regimens. The results from this evaluation are confirmed by a study conducted in Kenya [194] that targeted users with a health education campaign and showed a significant effect with regards to the use of a correct antimalarial, but not on dosage. Generally interventions that specifically provide information on how to take antimalarial, including pre-packaging and pictorial instructions have shown greater improvements on patient adherence [124, 195] . This evaluation was unable to find a significant difference between adherence to ALu, which had been pre-packaged with pictograms, and to other drugs such as SP and amodiaquine. However, it is worth pointing out that ALu had just been introduced and its dosage is not as straight forward as the other drugs (quinine, SP and amodiaquine). Had it not been pre-packaged adherence to it might have been even lower than observed. Furthermore adherence was only based on patient report, while another study conducted in the area, which followed up patients from the clinic to their homes and counted the pills left in their blister packs, found over 90% adherence (Mulokozi *et al*., unpublished data).

Secondly more sustainable approaches need to be developed. The ACCESS social marketing campaigns evaluated in this thesis are too costly to be uspscaled. This issue is currently being addressed in the frame of the ACCESS II where community based strategies which make use of existing structures are being explored. This includes using women's groups as a platform to disseminate public health messages and introducing malaria "modules" in the school curriculum.

Strengthening the role of the private sector

ADDOs have proven to be a successful model and upscaling them nation-wide, as is planned, can potentially extend the improvements observed in the study area to the rest of the country. The results from this evaluation confirm considerations from Smith *et al*. that interventions targeting the private retail sector generally have a positive impact on provider practice and can improve community drug use. The implementation of the ADDO programme in the study setting had all features outlined by Goodman *et al* as key for a successful private sector implementation [41]: 1) the planning process began with a comprehensive situation analysis including the legal and market environment [57]; 2) the intervention had a wide "buy-in" since it was developed closely with the national drug regulatory authorities, with support from central and local officials and 3) it was accompanied with a community intervention promoting its use (i.e. the ACCESS social marketing campaigns).

However, for the successes documented in this thesis to be sustained, it is crucial that the programme continues to be monitored closely. There is limited evidence that private sector interventions such as the ADDO programme can operate at a nationwide scale [41]. Furthermore many concerns have been raised with regards to private sector health care delivery in developing countries [196]. The two main sources of objection are that 1) private provision increases inequity because it naturally favours those who can afford treatment and 2) the quality of care is not up to the standard offered in health facilities and can put lives at risk. In the specific case of malaria a further concern is that the misuse of ACTs and the use of artemisin monotherapies could compromise the effectiveness of artemisin derivatives.

In view of its upscaling it is important that ADDOs remain a system that is complementary to health facilities and stick to their mandate to "improve the quality of medicines and pharmaceutical services in previously under served areas" [87]. With regards to equity concerns, this evaluation has found that the main determinant of prompt and effective treatment is the availability of outlets whereas there were no differences across SES groups. Despite increases in prices in drug shops the market shares of the private sector continued to grow since shops were more available and accessible. Based on these considerations the ADDO programme could even contribute to more equitable access, if it manages to promote the opening of its outlets even in remote areas where there are currently no facilities. This evaluation has provided some evidence that ADDOs were opened in previously underserved areas but three out of 25 villages in the DSS area still have neither a health facility nor an ADDO. Some schemes which include reduced accreditation fees have been suggested to encourage the opening of ADDOs in more remote areas (Liana, MSH Tanzania, personal communication), but MSH and TFDA will have to ensure that these schemes are fulfilling their aims, or come up with other ones. As far as quality of care is concerned, experience to

date suggests that the quality of the advice given by ADDO dispensers is good and that they usually refer cases they cannot manage to health facilities (Dillip *et al.*, in preparation). However constant supervision and refresher courses will be needed to ensure that they continue to do so. Finally, TFDA, in collaboration with district health authorities should enforce a ban on the sale of cheap artemisinin monotherapies so that they are not available in ADDOs. This thesis found that no patients were treated with such drugs in the study area because of their high price, but their availability at low prices is bound to change this picture.

However, for the full potential of the ADDO programme to be realised, ACTs need to be made available in all outlets at an affordable price. This evaluation has shown that the main failure of the programme was its inability to promote the widespread availability of ALu in its outlets [127] (cf. Chapter 3). ALu was made available at a highly subsidised price to ADDO retailers but the end user price was still 2-5 times as expensive as other monotherapies such as SP. This appears to have led to low demand for the drug and therefore low stocking rates, which in turn resulted in a very low use of ALu in the community despite it being widely available in all health facilities: although 63% of all fever cases were treated promptly and effectively only 22% were treated with a recommend antimalarial (ALu or quinine). The introduction of the AMFm in Tanzania could provide a viable solution to these types of problems, by subsidising ACTs at source and making them available at a similar price to previous generations of drugs. If ADDOs can be upscaled by maintaining the good quality of care shown in this evaluation, they will provide an ideal platform for the implementation of the AMFm and access to malaria treatment could be substantially improved.

Drug distribution systems in the public health sector

A “push” system of drug distribution in public health facilities has led to impressive drug stock levels, which would suggest it is a successful approach. Tanzania has nearly completed its conversion from the kit system of drug delivery (a “push” mechanism), to the Indent/ILS (a “pull” mechanism) (cf. Section 1.7). This transition was motivated by recurrent drug stock-outs due to the inelasticity of the kit system, but this evaluation suggests better stocks can be achieved with this type of system. Antimalarials were only available 40% of the time when the Indent system was operating but over 80% when a temporary push system was implemented as a short term strategy. Nevertheless, it is important to recognise that this evaluation did not focus on drug delivery mechanisms. Based on the studies that have been conducted in Tanzania on drug procurement it is likely that the wide availability of ALu in health facilities was as much a result of its availability at central level as a consequence of the delivery system (cf. Section 1.7). There are many reasons why push systems are not desirable: they typically do not respond rapidly to differing seasonal and geographical needs

and this often leads to either stockouts or wastages. Such issues were not studied here and therefore recommendations should not be made in terms of drug delivery mechanisms based on this evaluation.

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Hetzel MW, **Alba S**, Fankhauser M, Mayumana I, Lengeler C, Obrist B, Nathan R, Makemba AM, Mshana C, Schulze A, Mshinda H; *Malaria risk and access to prevention and treatment in the paddies of the Kilombero Valley, Tanzania*. Malar J. 2008 Jan 9;7:7.

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