Malaria surveillance and control in Central Africa: the challenges of instability and access

Inauguraldissertation

zur
Erlangung der Würde eines Doktors der Philosophie

vorgelegt der
Philosophisch-Naturwissenschaftlichen Fakultät
der Universität Basel

von
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Dorset, England, United Kingdom

Basel, 2019

Genehmigt von der Philosophisch-Naturwissenschaftlichen Fakultät auf Antrag von Prof. Dr. Christian Lengeler und Dr. Umberto D'Alessandro.

Basel, den 23. Mai 2017

Prof. Dr. Martin Spiess
The Dean of Faculty

Dedicated to my parents
and to my beloved husband, Tobias.

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Acknowledgements

This PhD has been a great adventure and a journey of collaborative effort. It has taken me to new places and provided many exciting albeit challenging twists and turns along the way. It has been made possible thanks to the continual support and contribution of a number of people who walked with me through this journey. I would therefore like to take this opportunity to acknowledge with heartfelt thanks and appreciation those who contributed to the completion of this thesis and supported me through the whole process ultimately making this work possible.

My sincere thanks first and foremost go to my supervisor, Christian Lengeler who has proven to be a great mentor from whom I have learnt so much. This work would not have been possible without his guidance and contributions. I deeply appreciated all the time invested into the process of shaping these projects and studies together and the assistance in scientific thinking and writing that has helped me grow as a scientist and will stick with me through the rest of my career. Thank you for always being available to talk through challenges from the field and motivating me and inspiring me through your own devotion to public health and epidemiology.

I am so grateful to Umberto D'Alessandro who accepted to act as co-referee for this thesis and to Antoinette Tshefu for the stimulating discussions and encouragement during my time in DRC.

For my fieldwork in DRC, I thank all my colleagues at the Swiss TPH office in Kinshasa who supported me throughout and had endless patience and grace with my French. Particular thanks to Didier Kalemwa Mitembo for always being available to help in any way he could and to Jean-Emmanuel Julo-Réminiac for being a great friend and colleague who was always available to bounce ideas off and lend an understanding ear during the chaos of Kinshasa life. For the team who helped collect the data in the field, thank you for all your efforts, and for Antoine Masendi and Winny Kialanda for the good friendships on the road. Finally, for Henry Ntuku for his constant support, help and for making me feel at home in Kinshasa, the experience wouldn't have been the same without you.

For my time in CAR, I would like to thank the MENTOR Initiative for allowing me to come back and work on a project so close to my heart. I am particularly indebted to Richard Allen, Helle Garro and Sarah Hoibak for their personal interest in my career from the beginning. You all believed in me when I was fresh faced from University and gave me the opportunities and experience that lead me to where I am today. Special thanks to Sarah for recruiting me for my very first job in malaria

and pushing me to fulfill my dreams ever since. Thank you to Helle, who first encouraged me to learn French all those years ago, this has opened all the doors I have walked through ever since and completely changed my life. I sincerely look forward to continuing our collaboration in the future.

Thanks to all who contributed to the field studies in both CAR and DRC, the supervisors, interviewers, lab technicians, medical doctors, nurses and community health workers for their excellent work and determination, you all inspire me. Thank you for the approval and collaboration from the health authorities, village chiefs and all the survey participants.

At the Swiss TPH in Basel, thank you to Christian Burri, Melissa Penny, Christine Mensch, Dagmar Batra and Laura Innocenti for the invaluable support and encouragement. To all the PhD students whose support, friendship, company and ability to completely understand the challenges we faced together so often lifted my spirits and got me through the tough times. I am so grateful for the support and all the memories I will take with me.

A big thank you to my wonderful in laws, Astrid and Christoph who have made Basel a very special place over the years and made sure I always felt at home.

And then there is my support network in England without which I could not have done this. To my amazing little sister Alexandra, who has an incredible ability to cheer me up and make me smile when I need it most. To Hannah and Sarah, for always being there to share in both the tears and the laughter, over Skype or in person. Thank you for helping me remember what's important in life and for standing with me in prayer throughout this and so much more. To my parents, I am forever indebted for the sacrifices made to ensure I had the best education and opportunities. For the endless patience as I figured it all out and unwavering support even when my adventures took me far from home. Thanks for being the first to make me believe that I can go anywhere and do anything. Also in memory of my Grandma who always said I should write a book one day – I think this counts Nana.

Last but not least, my heartfelt gratitude goes to my husband, Tobias, for his endless love and unwavering support. He tolerated my long absence in the field but never made me feel alone. He taught me to love what I do with all my heart. Thank you for embarking on life's adventures with me and for valuing this work. I could not have done this without you.

List of abbreviations

ACT	Artemisinin-based Combination Therapy
AL	Artemether plus Lumefantrine
AS-AQ	Artesunate plus Amodiaquine
ASF	Association de Santé Familiale
ANC	Ante Natal Care
CAR	Central African Republic
CI	Confidence Interval
DDT	Dichlorodiphenyltrichloroethane
DfID	Department for International Development
DHIS2	District Health Information System 2
DHS	Demographic and Health Survey
DRC	Democratic Republic of Congo
EIR	Entomological Inoculation Rates
EPI	Expanded Programme on Immunisation
EKBB	Ethikkommission Beider Basel
FOREAMI	Fondation Reine Elisabeth pour l'Assistance Médicale aux Indigènes
GFATM	Global Fund to fight AIDS Tuberculosis and Malaria
GIS	Geographic Information System
GMEP	Global Malaria Eradication Programme
GPS	Global Positioning System
GRH	General Reference Hospital
GTS	Global Technical Strategy
HA	Health Area
Hb	Haemoglobin
HDI	Human Development Index
HMIS	Health Management Information System
HRP2	Histadine-rich protein 2
HZ	Health Zone
iCCM	Integrated Community Case Management
ICRC	International Committee of the Red Cross
INFORM	Information For Malaria Project
IRS	Indoor Residual Spraying
IPTc	Intermittent preventive treatment in children

ITPp	Intermittent Preventive Treatment in pregnancy
ITN	Insecticide Treated Net
KSPH	Kinshasa School of Public Health
LLIN	Long Lasting Insecticidal Net
MAP	Malaria Atlas Project
MDG	Millennium Development Goal
MERG	Monitoring and Evaluation Reference Group
MICS	Multiple Indicator Cluster Survey
MIS	Malaria Indicator Survey
MoH	Ministry of Health
mRDT	Rapid Diagnostic Test
MSF	Médecins sans Frontieres (Doctors without borders)
NGO	Non-Governmental Organisation
NMCP	National Malaria Control Programme
OR	Odds Ratio
PCA	Principal Components Analysis
PSI	Population Services International
SDG	Sustainable Development Goal
SELCA	Service d'Etude et Coordination de la Lutte Antipaludique au Congo
SMC	Seasonal Malaria Chemoprevention
SP	Sulfadoxine-Pyrimethamine
Swiss TPH	Swiss Tropical and Public Health Institute
UI	Uncertainty Interval
UNDP	United Nations Development Programme
UNICEF	United Nations International Children's Emergency Fund
UMHK	Union Minière du Haut Katanga
USAID	United States Agency for International Development
WHO	World Health Organisation
WHOPES	World Health Organisation Pesticide Evaluation Scheme

Summary

Scientific discovery and endeavour has led to significant advances in the development of tools available to fight malaria. Long-Lasting Insecticidal Nets, Rapid Diagnostic Tests and Artemisinin-based Combination Therapy have all been well designed to combat the complex biology of the *Plasmodium* parasite and its vector. They have significantly contributed to the reduction of malaria associated morbidity and mortality in many different settings worldwide. Despite an estimated 6.8 million malaria deaths averted between 2000 and 2015, malaria remains one of the leading causes of death in sub-Saharan Africa where just 12 countries account for 69% of the global malaria associated mortality (almost 500,000 deaths a year).

When looking at country level estimations over time, it is clear that access to these anti-malarial tools is increasing. However, there are large inequalities in access at sub-national level. As a disease shaped by broad patterns of social and economic development, it is the poorest, most isolated and difficult-to-reach communities that remain disproportionately underserved by malaria control programmes and consequently have the highest burden of disease. These areas often have weak health systems as well as inadequate infrastructure and governance to effectively implement programmes and this can be further exacerbated by political instability and armed conflict. Yet, there is little evidence on how to effectively tailor traditional control programmes to such settings.

This PhD thesis focuses on Central Africa, more specifically the Democratic Republic of Congo (DRC) and the Central African Republic (CAR). Both countries have been classified as "fragile states", meaning they face particularly difficult political, social and economic conditions. They have extremely limited access to health care in many areas and experience a large amount of social unrest, political instability and conflicts. This thesis aims to contribute quality evidence on how to explore and overcome the challenges presented by isolated or conflict-affected settings and explores how malaria control programmes can be adapted to see malaria effectively controlled and associated morbidity and mortality reduced.

Evidence-based adaptations of control programmes at the sub-national level are essential to develop more flexible strategies, integrated into the national infrastructure. This in turn will be key to accelerate progress among the most vulnerable populations towards Roll Back Malaria's ambitious global malaria targets to reduce malaria associated mortality and case incidence by 90% by 2030 compared to 2015. Ultimately, malaria control programmes also contribute to achieving universal health coverage.

This thesis begins by examining the history of malaria control in DRC to complete and update the state of knowledge in this vast and diverse country. It is the second largest country in Africa carrying the second highest global malaria burden after Nigeria (estimated 14 million cases per year). It reviews the historic evidence from the colonial period through to early years of independence, until the creation of the national malaria control programme. It explores particularly how programmes could build on successes and learn from failures during a time that was rife with political turmoil. It then explores current malaria control programmes, assessing how to maximise the use of LLINs in remote communities in DRC through different distribution strategies. Additionally, it investigates how a network of community health workers can continue malaria case management services during the on-going conflict in CAR in spite of a highly volatile situation. Finally, this thesis assesses the role surveillance is currently playing, its limitations in accurately estimating malaria burden in the community, and ways this could be improved to better inform policy makers and hence lead to better programming.

Combined, these projects provide a unique perspective on how malaria control programmes can overcome the issue of access to healthcare in isolated or conflict-affected communities. The evidence presented here builds a case for placing a stronger emphasis on decentralising care and surveillance through community health workers and sentinel site systems. In areas where health facility surveillance is weak, these strategies can offer a sustainable solution to capture changes in the epidemiological profile of diseases and better understand the health burden at the local level. The thesis also identifies challenges that need to be overcome for such programmes to be sustainable, including the role of private pharmacies to increase access to treatment and representativeness of surveillance and national financing.

Résumé

Les découvertes scientifiques et les efforts menés dans le cadre de la lutte contre le paludisme ont conduit à des avancées significatives, notamment le développement d'outils tels que les Moustiquaires Imprégnées à Longue Durée d'Action (MILD), les Tests de Diagnostic Rapides (TDR) et la Thérapie Combinée à base d'Artémisinine (CTA). Ces outils ont été conçus pour lutter contre la biologie complexe du parasite *Plasmodium* et de son vecteur. Ils ont considérablement contribué à la réduction de la morbidité et de la mortalité liées au paludisme dans de nombreuses zones dans le monde entier. Malgré les 6,8 millions décès évités entre 2000 et 2015, le paludisme demeure l'une des principales causes de mortalité en Afrique subsaharienne. Douze pays de l'Afrique subsaharienne représentent à eux seuls 69% de la mortalité mondiale associée au paludisme (environ 500.000 décès par an).

En examinant les estimations de cas au niveau des pays endémiques, on voit clairement que l'accès à ces outils antipaludiques a considérablement augmenté. Cependant, il existe d'énormes inégalités d'accès au niveau infranational. Comme le niveau développement social et économique détermine largement la prévalence de cette maladie, ce sont les communautés les plus pauvres, les plus isolées et les plus difficiles à atteindre qui restent disproportionnément non desservies par les programmes de lutte contre le paludisme. Par conséquent, ces communautés portent le plus grand fardeau de cette maladie. Ces zones ont souvent des systèmes de santé faibles, et une infrastructure et une gouvernance inadéquate pour mettre en œuvre efficacement ces programmes. Cela peut encore être exacerbé par l'instabilité politique et les conflits armés. Jusqu'à présent, peu d'expérience a été générée sur la façon d'adapter efficacement des programmes de contrôle traditionnels à de telles zones.

Cette thèse se concentre sur l'Afrique centrale, plus précisément sur la République Démocratique du Congo (RDC) et la République Centrafricaine (RCA). Ces deux pays ont été classés comme des « États fragiles », car ils sont confrontés à des conditions politiques, sociales et économiques particulièrement difficiles. Ils sont caractérisés par un accès limité aux soins de santé dans de nombreuses zones et connaissent des troubles sociaux, de l'instabilité politique et des conflits. Cette thèse explore les défis spécifiques rencontrés dans ces pays et évalue comment les programmes de lutte peuvent être adaptés afin de mieux contrôler le paludisme et diminuer la morbidité et la mortalité qui lui sont associées.

Idéalement, les programmes de contrôle doivent être basés sur des recherches scientifiques au niveau infranational, afin d'élaborer des stratégies plus souples et bien intégrées dans l'infrastructure nationale. Ceci est essentiel pour accélérer le progrès parmi les populations les plus vulnérables, en vue des ambitieux objectifs mondiaux de « Roll Back Malaria », visant à réduire la mortalité associée au paludisme et l'incidence des cas de 90% par rapport à 2015. Ce faisant, le contrôle du paludisme contribue aussi à la couverture universelle de santé.

Cette thèse examine d'abord l'histoire de la lutte contre le paludisme en RDC dans le but de compléter et mettre à jour l'état des connaissances dans ce pays vaste et diversifié. La RDC est le deuxième plus grand pays d'Afrique et se trouve au deuxième rang mondial du paludisme (environ 14 millions de cas par an) après le Nigéria. Les données historiques, de la période coloniale jusqu'aux premières années après l'indépendance et après la création du programme national de lutte contre le paludisme, ont été examinées afin d'explorer la manière dont les programmes peuvent profiter des réussites passées et apprendre des échecs rencontrés au cours de ces temps de troubles politiques. La thèse explore ensuite les programmes actuels de lutte contre le paludisme, en évaluant comment maximiser l'utilisation des MILD dans des communautés éloignées en RDC par le biais de différentes stratégies de distribution. De plus, elle étudie comment un réseau de travailleurs de la santé communautaire peut poursuivre les services de gestion des cas de paludisme pendant le conflit armé en cours en RCA. Enfin, cette thèse étudie le rôle que la surveillance joue actuellement, ainsi que ses limites, pour estimer avec précision la charge de lutte contre le paludisme dans la communauté et les moyens d'améliorer cette situation pour mieux informer les décideurs politiques.

L'ensemble de ces projets offre une perspective unique sur la façon dont les programmes de lutte contre le paludisme peuvent surmonter la question de l'accès aux soins de santé dans les communautés isolées ou en conflit. Les éléments de preuve présentés ici permettent de mettre l'accent sur la décentralisation des soins et la surveillance par le biais des agents de santé communautaires et des systèmes de sites sentinelles. Dans les zones où la surveillance des établissements de santé est faible, ces stratégies peuvent offrir une solution durable pour appréhender les changements dans le profil épidémiologique des maladies, et pour mieux comprendre le fardeau de la santé au niveau local. La thèse identifie également les défis à surmonter pour que ces programmes soient durables, y compris les rôles que les pharmacies privées pourraient jouer pour accroître l'accès aux soins et la représentativité de la surveillance, ou l'importance des financements nationaux.

1. Introduction

1.1 Discovering malaria

Malaria is a poverty-related disease that places an enormous burden on populations and health systems around the world. It is an ancient disease and is thought to have killed more people throughout history than any other infectious disease (Carter and Mendis, 2002). For centuries it was believed to be caused by miasmas rising from swamps, but in 1880 our understanding of malaria was transformed when Alphonse Laveran discovered that malaria was caused by a protozoan parasite of the genus *Plasmodium* (Bruce-Chwatt, 1981). Today, there are five *Plasmodium* species known to infect humans: *P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale* and *P. Knowlesi* (Warrell and Gilles, 2002, Singh *et al.*, 2004). Of these, *P. falciparum* is responsible for the most severe and fatal cases of malaria, accounting for 99% of all malaria deaths worldwide (WHO, 2016).

Another milestone in our understanding of malaria came by the end of the 19th Century, when the mosquito was identified as the vector of the disease. This was first discovered for avian malaria by Ronald Ross in 1897 who observed *Plasmodium* parasites in the stomach of a mosquito. Then, in 1898 an Italian group lead by Giovanni Battista Grassi discovered that the human form of malaria was transmitted by the female *Anopheles* mosquito *(Cox, 2010)*. There are approximately 400 species of *Anopheles* mosquitoes known today, of which 70 can transmit malaria and 40 are considered of public health importance (Service and Townson, 2002). In Africa, the *An. gambiae* and *An. Funestus* complexes are the dominant vectors of human malaria due to their anthropophagic, endophagic and endophilic characteristics (preferring to feed on humans, indoors and rest indoors after a blood meal) (Sinka *et al.*, 2012).

While these early pioneers elucidated the general *Plasmodium* life cycle, it took decades of continued scientific inquiry to reveal the complex life cycle of the parasite. The parasite transforms itself several times (Figure 1.1) and is able to adapt to two very different hosts, overcoming the hostile environment of the cold-blooded mosquito vector and evading attack from the immune system in the warm-blooded human host. Exploring these complexities sheds some light as to why malaria remains such a problem today, despite having known how to both prevent it and cure it for decades.

Human infection is initiated when a female *Anopheles* mosquito, infected with the *Plasmodium* parasite, bites a susceptible human being. During that blood meal, the mosquito injects sporozoites

(the immature form of the *Plasmodium* parasite) with its saliva. These travel quickly in the blood stream to the liver, where they invade the hepatocytes. Here, the parasite undergoes asexual reproduction, developing into mature schizonts that contain thousands of uninucleate merozoites. This stage of the infection causes no symptoms and about 7 to 10 days after initial infection the schizont ruptures the hepatocyte, releasing thousands of merozoites into the blood stream, where they rapidly invade healthy red blood cells (erythrocytes). Inside the red blood cells the parasites can hide from the body's immune system and develop into trophozoites that undergo asexual reproduction once again, forming schizonts containing merozoites. Infected erythrocytes eventually burst, liberating more merozoites back into the blood stream that will penetrate new erythrocytes creating a cycle of infection and eruption. It is this destruction of the red blood cells that triggers the clinical symptoms of malaria of repeated bouts of fever, chills and sweating (Warrell and Gilles, 2002). Eventually, some of the merozoites differentiate into sexual forms of the *Plasmodium* parasites and form either male or female gametocytes (gametocytogenesis). While they do not harm the human host, they circulate in the peripheral blood where they can be taken up by a female *Anopheles* mosquito during another blood meal thus initiating the next stage of the cycle.

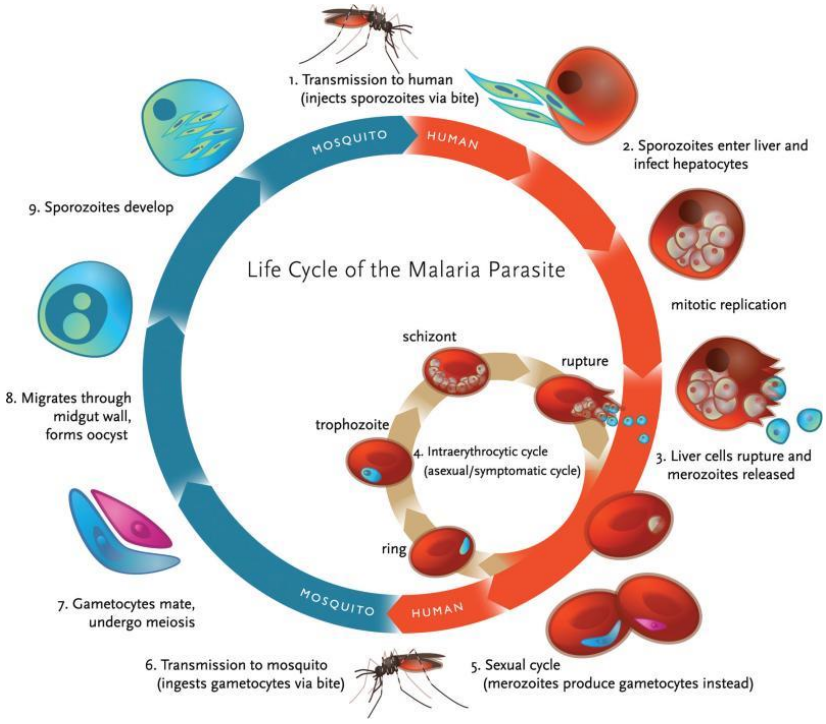


Figure 1.1 Life cycle of the malaria parasite in humans and mosquitoes. Source: Klein (2013)

In the gut of the mosquito, these gametocytes develop into mature male and female sex cells called gametes that fuse to produce a zygote (sporogony). The zygote matures into a motile cell called an ookinete that migrates and burrows into the mosquito's midgut wall and forms an oocyst. Inside the oocyst another phase of multiplication occurs, producing thousands of active sporozoites until it

eventually bursts, releasing sporozoites into the body cavity of the mosquito that travel to its salivary glands ready to be injected with the next blood meal (Greenwood *et al.*, 2008).

1.2 Early malaria control programmes

The discovery of malaria parasites, identification of its vector and the understanding of its complex life cycle shaped early control interventions (summarised in Figure 1.2). Initial attempts were non-specific, often costly to the local communities, and consequently had limited success in the areas where burden was highest. However, available tools evolved during World War II when in 1939 Paul Müller developed in Basel the synthetic pesticide dichlorodiphenyltrichloroethane (DDT) which proved to be an extremely effective and cheap means of killing mosquitoes. It catalysed investment in the development of insecticide spray equipment and subsequently became the major instrument for fighting malaria (Packard, 2011).

The success seen with DDT was a major contributor in the world health assembly's decision to vote for the Global Malaria Eradication Programme (GMEP) in 1955. This was the first globally coordinated push for malaria control. It had major successes in the more temperate areas of the world, and even permanently eliminated malaria from many regions. However, the contribution that well-developed primary health care systems made in these countries should not be underestimated. Consequently, in poorer, more remote tropical areas where the burden of disease was much higher and infrastructure much weaker, the programme failed and was subsequently abandoned in 1969 (WHO, 1969). Gains were rapidly lost across sub-Saharan Africa, international support declined and malaria resurged to worse levels than before. In fact, this lead the WHO's Director of the malaria control division (1971-1973), Tibor Lepes, to conclude that the campaign was 'one of the greatest mistakes ever made in public health'. The GMEP era had shown that a one-size-fits-all approach did not work when combatting malaria and that long-term malaria control strategies must be adapted to the local epidemiology and conditions, especially in sub-Saharan Africa (Najera *et al.*, 2011). Subsequently, this era was followed by a period of neglect in terms of global coordination to fight the disease. A full chapter of this thesis is dedicated to the history of malaria control interventions specifically in the Democratic Republic of Congo (DRC) (chapter 3).

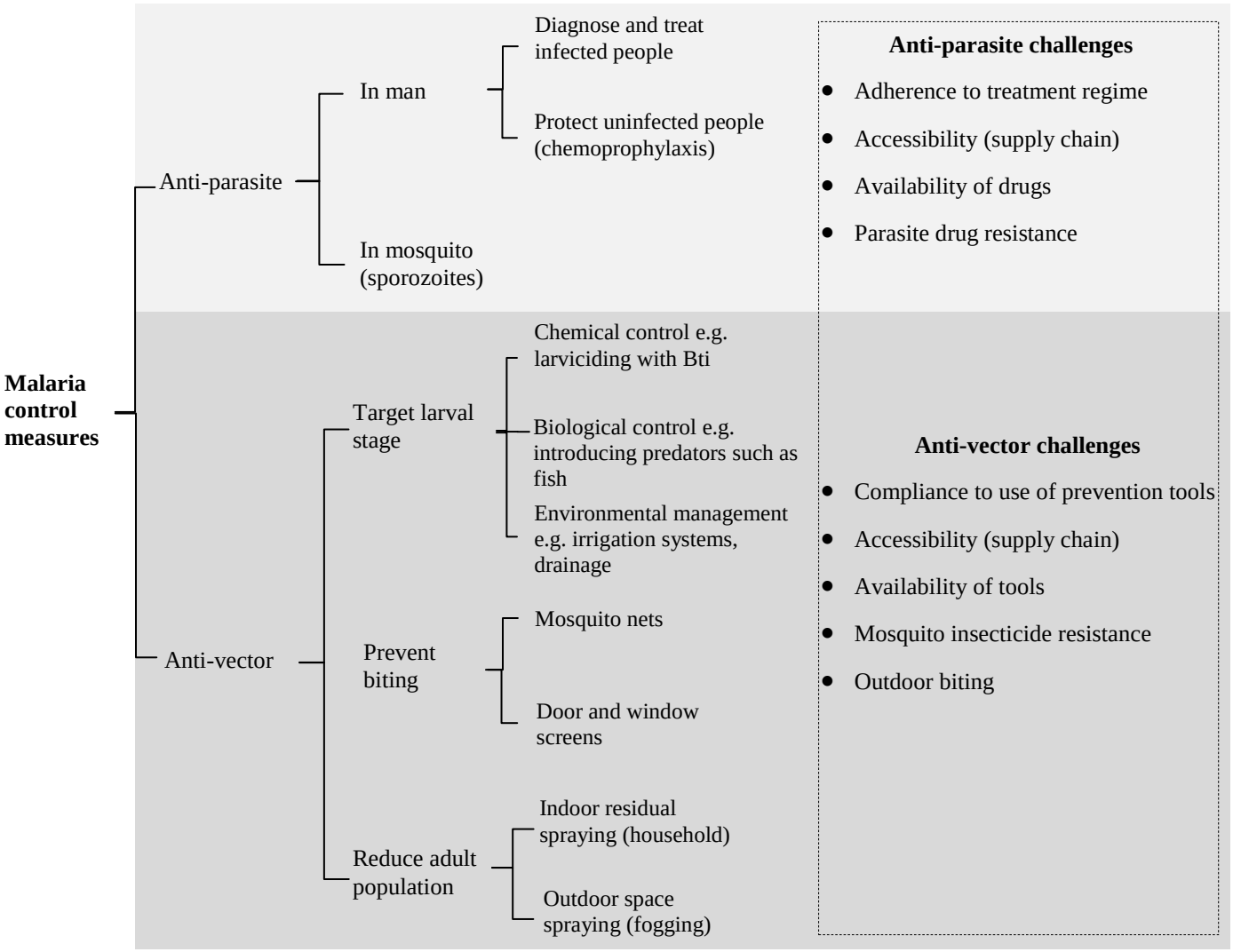


Figure 1.2 Malaria control measures against parasite and mosquito and the main challenges faced. Adapted from (Shuler, 1985).

1.3 Relevance of malaria in today's broader development agenda

The interest in malaria control was renewed in 1992 with the ministerial conference held in Amsterdam. In 1998, a new global malaria strategy was launched when WHO, World Bank, United Nations Development Fund (UNDP) and United Nations International Children's Emergency Fund (UNICEF) founded the Roll Back Malaria (RBM) partnership. It set ambitious goals to halve malaria-associated mortality by 2010 and halve it again by 2015 (Nabarro and Tayler, 1998). Subsequently, this partnership triggered renewed recognition of malaria as a priority global health issue and therefore saw it included in the universal Millennium Development Goals (MDGs). For malaria, the results at the end of the following 15 years period were spectacular. An estimated 6.8 million malaria deaths were averted (94% of which were in the WHO African region and 97% of

which were in children less than 5 years old). Furthermore, the number of global malaria cases is estimated to have decreased by 41% and malaria mortality rates declined by 62% in this time period. While approximately 70% of these cases averted are thought to be directly due to the control interventions (WHO, 2016), it is also important to recognise the role general economic and social development had in reducing malaria burden and improving the health in a sustainable way. It is after all how Europe and the United States eliminated malaria. They not only tackled the parasite and the vector, but also the poor living conditions and inadequate sanitation that further promoted the malarious way of life.

Despite these significant advances, gains remain fragile and are unevenly distributed. Malaria is still an enormous public health problem and one of the major diseases of poverty. Over 3 billion people are still at risk worldwide and there were an estimated 212 million cases in 2015 (UI: 148-304 million). Annual malaria mortality continues to oscillate around 500,000 people, 70% of whom are children less than 5 years old and 92% of these deaths occurring in sub-Saharan Africa. In the new 'post-2015' era of Sustainable Development Goals (SDG), optimising malaria control interventions continues to be an integral component to see these targets reached (RBM, 2015). Furthermore, as a disease shaped by broad patterns of social and economic development, it is widely acknowledged that programmes need to develop more flexible strategies, integrated into the national health infrastructure, to contribute to achieving universal health coverage. WHO defines this as all individuals and communities receiving the health services they need (preventive and curative) without suffering financial hardship (WHO, 2010b).

In line with the timeframe for the SDGs (2016 – 2030), RBM has produced new and updated malaria targets that take into account progress to date, the newest tools available and a deeper understanding of the challenges that have hindered achieving previous goals in some countries (Table 1.1).

Table 1.1 Goals, milestones and targets for the global technical strategy (GTS) for malaria 2016-2030.

Goals	Milestones		Targets
	2020	2025	2030
1. Reduce malaria mortality rates globally compared with 2015	At least 40%	At least 75%	At least 90%
2. Reduce malaria case incidence globally compared with 2015	At least 40%	At least 75%	At least 90%
3. Eliminate malaria from countries in which malaria was transmitted in 2015	At least 10 countries	At least 20 countries	At least 35 countries
4. Prevent re-establishment of malaria in all countries that are malaria-free	Re-establishment prevented	Re-establishment prevented	Re-establishment prevented

1.4 Malaria control tools and interventions

With these goals in mind, there are many effective malaria tools that have been developed through decades of scientific endeavour to reduce malaria associated morbidity and mortality. The key pillars recommended by WHO and used by national malaria control programmes (NMCP) across sub-Saharan Africa can be grouped into two categories discussed below:

1) Malaria case management tools including prompt diagnosis with microscopy or malaria rapid diagnostic tests (mRDTs), and timely treatment with artemisinin-based combination therapy (ACT).
2) Malaria prevention tools including Long Lasting Insecticidal Nets (LLINs), Indoor Residual Spraying (IRS) and Intermittent Preventative Treatment (IPTp) for pregnant women.

Each control method acts on at least one stage of the malaria life cycle outlined in section 1.1 and therefore has the potential to reduce transmission, morbidity or mortality in several ways (Figure 1.1).

1.4.1 Malaria case management tools

Malaria can progress to severe disease within 24 hours of the onset of symptoms, therefore, access to prompt diagnosis and timely treatment for all is essential for reducing malaria morbidity and mortality. Parasitological confirmation is recommended for all suspected malaria cases and this has been made easier in the most remote communities through the development of mRDTs. In Africa in

2005, only 36% of suspected malaria cases were tested, while in 2014, 65% were tested - of which 71% were tested with an mRDT. However, despite the increased number of cases tested, the proportion of children less than 5 years old with *P. falciparum* who received the recommended treatment with ACT remained significantly below universal access for malaria case management, increasing from 1% in 2005 to only 16% in 2014 (WHO 2015).

In addition to this challenge of needing to increase access to ACTs, parasite resistance to artemisinin, the key component in ACTs, has been detected in four countries in Southeast Asia. This resistance means the clearance of parasites from the human's blood is either delayed or incomplete. This threatens the efficacy of this drug if the resistance spreads, particularly to Africa. While this has not yet led to programme failure, historic drug resistance in all antimalarial medicines used so far except quinine, resulted in treatment failure and an associated increased malaria burden (WHO, 2010a). As there are currently no alternative antimalarial drugs available that have the same level of efficacy and tolerability as ACTs, there is an urgent need for the development of alternative treatments. In the meantime, considering the potential spread of drug resistance and the fragile health infrastructures that provide these drugs, the need for malaria prevention becomes ever more urgent (Endo and Eltahir, 2016).

1.4.2 Malaria prevention tools

The main malaria prevention tools are those that target the mosquito to reduce human exposure to the infectious malaria vector. According to Macdonald (1956), longevity of the mosquito is the weakest link in the malaria life cycle due to the length of time required for sporogony. Therefore, the interventions that reduce either 1) the probability of a mosquito living long enough to become infected 2) the probability of a mosquito living long enough to become infectious or 3) the number of infectious bites, have the greatest potential for reducing transmission (Macdonald, 1956, Smith *et al., 2012a).*

Vector control tools exploit the indoor biting and resting habits of the *Anopheles* mosquito and it is LLINs that have had the largest impact. There is considerable evidence showing the effectiveness of LLINs in substantially reducing malaria associated morbidity and mortality across several settings (D'Alessandro *et al.*, 1995, ter Kuile *et al.*, 2003). A Cochrane Review showed that they could reduce child mortality by about 20%, leading to the scale up of LLINs as primary vector control tool (Lengeler, 2004). The proportion of the population sleeping under an LLIN subsequently

increased in sub-Saharan Africa from less than 2% in 2000 to 55% in 2015 (although this varies between and within countries). As a result, it is estimated that LLINs accounted for 68% of all cases averted between 2000 and 2015 (Bhatt *et al.*, 2015). The efficacy of an LLIN is found in the fact that they not only offer a physical barrier between the vector and human, but are also impregnated with a safe, quick-acting insecticide that kills, irritates or repels mosquitoes. Furthermore, when over 80% of the population sleeps under an LLIN, they provide a 'community' effect by reducing mosquito densities and longevity thus reducing malaria transmission (Killeen *et al.*, 2007, Azondekon *et al.*, 2014). Unfortunately, there is currently only one class of insecticide (pyrethroids) approved by the WHO Pesticide Evaluation Scheme (WHOPES) that can be used for LLINs, and therefore vector resistance to this insecticide is a great concern (Ranson *et al.*, 2011). While some evidence suggests LLINs can continue to have a powerful effect despite high levels of resistance, the need for developing novel insecticides or finding new ways to use other classes of available insecticides on nets is urgent. Furthermore, behavioural adaptive changes of mosquitoes threaten the future effectiveness of LLINs as mosquitoes have been seen to change biting habits to earlier in the day or outdoors (before people go to sleep indoors) (Pates and Curtis, 2005, Ferguson *et al.*, 2010, Ranson *et al.*, 2011, Gatton *et al.*, 2013).

While LLIN coverage has increased, the WHO recommendation of universal coverage, defined as 1 LLIN for every 2 people, has yet to be realised in many areas. An estimated 269 million people at risk of malaria are living in households without an LLIN (WHO, 2016). The most effective way to quickly achieve high coverage has been shown to be through mass distribution campaigns, which target the entire population (Willey *et al.*, 2012). However, these campaigns take place only every 3 to 5 years (depending on the country and financing) and therefore do not take into account new children being born, new sleeping spaces being created and nets wearing out faster than their average lifespan of 2 to 3 years (Gnanguenon *et al.*, 2014, Hakizimana *et al.*, 2014). Continuous distribution strategies are therefore required so that families can replace nets when needed. These include already established channels such as antenatal clinics (ANC), Expanded Programme on Immunisation (EPI), the private sector and schools.

Ensuring everybody at risk of malaria has access to an LLIN in their household does not necessarily equate to everybody at risk sleeping under the net every night. This gap between LLIN ownership and use has been largely attributed to lack of ability or willingness to hang the LLIN after a campaign (Rickard *et al.*, 2011, Macintyre *et al.*, 2012), although this view has been challenged in recent years (Koenker and Kilian, 2014). In any case, information and education campaigns are

essential to motivate and change the behaviour required to ensure continued and correct use. One approach to improve this during a mass distribution is by using a door-to-door technique that focuses on interpersonal communication activities and includes hanging the nets in each household. This is in contrast to the traditional mass-distribution method where people collect nets from a central location and take them home to suspend the nets themselves. Door-to-door visits and hang-up activities require additional resources and chapter 4 of this thesis will assess the differences between distribution strategies and their outcomes in more detail in the Democratic Republic of Congo.

In contrast to the increasing LLIN coverage, the population in sub-Saharan Africa who were protected by IRS in 2014 was just 6%. IRS is the application of a long-lasting insecticide on the interior walls of homes. While it does not aim to provide individual protection like LLINs, a Cochrane Review concluded that it had a clear protective impact against malaria in both low and high transmission settings; however, there was a lack of randomised control trials to quantify the effect (Pluess *et al.*, 2010). Depending on the insecticide used, material of the wall and transmission patterns, IRS needs to be repeated one to three times per year for it to be effective. It also requires a higher coverage of potential resting places to be effective and is logistically more complex as spray equipment is bulky, needs maintaining and involves huge numbers of people to implement. These challenges mean it is much more expensive than LLINs per child death averted (Yukich *et al.*, 2008).

Additional malaria prevention strategies target the parasite through chemoprevention. As malaria during pregnancy carries many risks to the mother, foetus and then new-born, WHO recommends three or more doses of preventive treatment to pregnant women (IPTp) with sulfadoxine-Pyrimethamine (SP) during routine antenatal care visits regardless of parasite infection. However, while the IPTp strategy has been integrated into the malaria control policy in sub-Saharan Africa, only 52% of all eligible women there received at least one dose of IPTp in 2014 (WHO, 2015c). This does not appear to be associated with low antenatal clinic attendance and therefore increased efforts to scale-up IPTp through health worker training and a SP supply chain is vital. Intermittent preventive treatment in children less than 5 years (IPTc) has additionally been recommended during the peak malaria season in areas of highly seasonal transmission. Now referred to by the WHO as seasonal malaria chemoprevention (SMC), it involves the administration of three single doses of an antimalarial treatment combination (amodiaquine and SP) over three months during the course of the transmission season. A Cochrane review of trials showed SMC

prevented approximately three quarters of clinical malaria episodes, including severe malaria and it has subsequently become recommended policy in 9 countries in the Sahel and sub-Sahelian areas of Africa (Meremikwu *et al.*, 2012, Noor *et al.*, 2015).

1.4.3 Improving access to effective tools

With the effective control tools discussed above, the challenge now becomes delivering them to those who are most affected. In high transmission settings, this means children less than 5 years old, pregnant women, displaced populations and those in areas extremely underserved by the health care system. Increasing attention is therefore being devoted to the issue of how to build supply chains, strengthen health systems and ultimately create a political environment capable of improving access to malaria prevention and treatment (Barnes, 2007).

It is well known that there is inequitable geographic distribution of financial resources, heath workforces and ultimately access to health care in sub-Saharan Africa. Studies have shown that patients living farther from health facilities wait longer before seeking treatment (Feikin *et al.*, 2009, Rutebemberwa *et al.*, 2009, Getahun *et al.*, 2010) and often seek initial care from informal health structures (such as pharmacies or traditional healers) closer to home (Littrell *et al.*, 2011). Therefore, a vital step towards linking the community to the health system is by decentralising the medical services to the community level through the use of community health workers (CHWs). This widely accepted strategy for facilitating early malaria treatment for the hardest to access communities will be explored further in chapter 5 of this thesis.

Distance is not the only component that impacts access to health care and health seeking behaviour. There have been five dimensions identified that influence access of the patient to the health care system (Table 1.2).

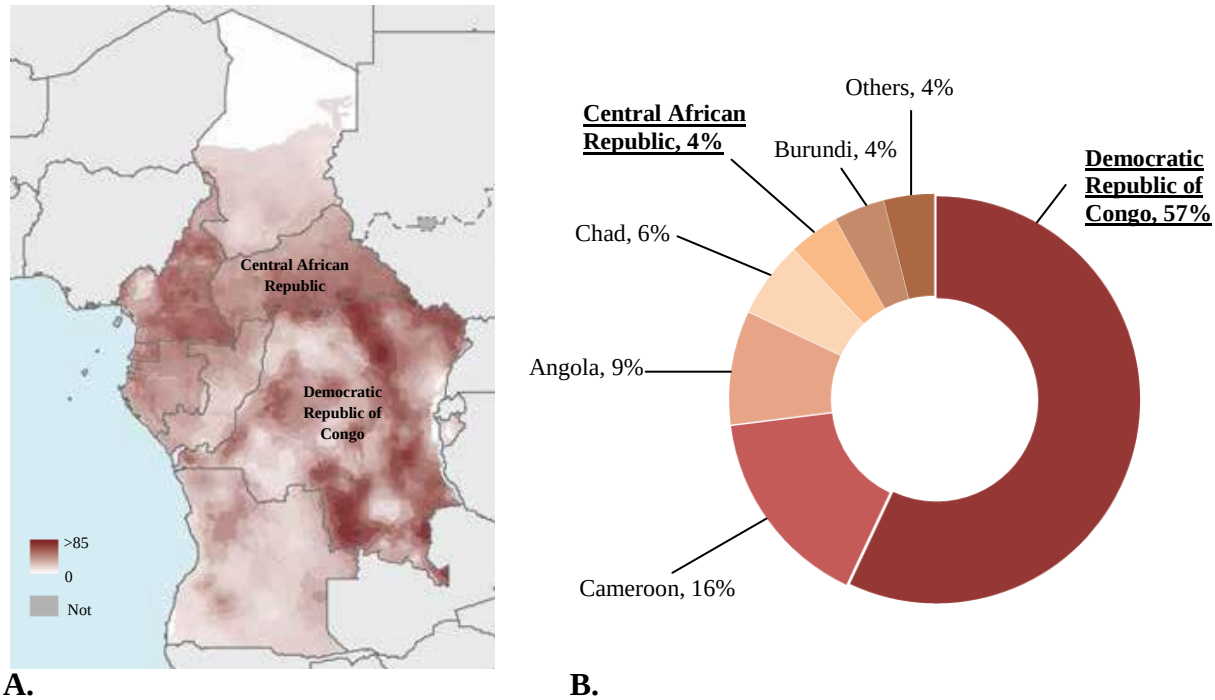
Table 1.2 Five dimensions of access of health care services considered by (Obrist *et al.*, 2007)

Dimension	Definition
Availability	Existing health services and goods meet patients' needs
Accessibility	Location of supply is in line with the location of patients
Affordability	Prices of services fit the patients income and ability to pay
Adequacy	Organisation of health care meets the patients expectations
Acceptability	Characteristics of providers match those of the patients

Improving each of these five dimensions is needed to increase access and ensure acceleration in the reduction of incidence rates in countries with the highest burden. This is essential if the GTS milestone of a 40% reduction in case incidence rates by 2020 is to be achieved in all countries.

1.5 Epidemiology of malaria in Central Africa

Central Africa is home to some of the poorest countries in the world that carry some of the highest malaria burdens. In 2015, in the 10 countries that make up this region, about 174 million people were at risk of malaria with 161 million of these at high risk (Figure 1.3) (WHO, 2015c). Cases are almost exclusively due to *P. falciparum*. Two of the countries with some of the highest burdens in this area are DRC and the Central African Republic (CAR) where the research for this thesis was conducted.



A. **B.**

Figure 1.3. A. Confirmed malaria cases per 1,000 population / Parasite prevalence in the Central African region. B. Share of estimated malaria cases in Central African countries in 2015. Source: (WHO, 2016)**.**

1.5.1 Malaria epidemiology in the Democratic Republic of the Congo (DRC)

The DRC is Africa's second largest country spanning an area of approximately 2.3 million km^2. It is also the third most populated country in Africa with an estimated 71 million inhabitants, 50% of whom are under 16 years old. While the majority (61%) of the population are believed to reside in rural areas, 11.7% of the entire population live in the capital city, Kinshasa. The last census was

conducted in 1984 and therefore current demographic estimates are unreliable. Politically, DRC has had a long period of regional and inter-ethnic conflicts, particularly in the Eastern provinces where tensions and insecurity still continue. It remains a fragile country characterised by political uncertainty and military instability and has consequently experienced mass population displacement over the last decades.

DRC shares borders with nine countries and the Atlantic Ocean to the West (Figure 1.4). The port town of Boma is accessible to sea-going vessels and was originally established as a port for the slave trade. It is a richly diverse country with a mountainous region to the east, the largest rainforest outside the Amazon (representing 6% of the world's forests), an extensive network of rivers that feed the Congo River and regions rich in mineral deposits. It is the vast expanse of rainforest that governs the distribution of populations and this subsequently impacts access to health services. Despite its rich mineral resources, the DRC remains one of the poorest countries in the world, ranking 178 out of 188 countries on the Human Development Index (HDI) (UNDP, 2016) and with an estimated 80 per cent of its population living on less than 1 USD a day (World Bank, 2013).

Figure 1.4 Map of the Democratic Republic of Congo.

DRC is organised into 26 administrative provinces. The 26 health divisions correspond accordingly and are further divided into Health Zones (HZ), of which there are 515 in total. These are the main operational units of the health system, acting as decentralised entities with their own management.

Generally a HZ should contain one General Reference Hospital (GRH) serving an average population of 100,000 to 150,000 people in rural areas and 200,000 to 250,000 people in urban areas, as well as about 15 to 20 health facilities. However, there are currently only 393 functioning GRHs. The HZ are further divided into 8,504 Health Areas (HA) that each serve between 5,000 and 10,000 people. Rural health centres or posts in each health area serve as the first point of healthcare contact for the majority of the Congolese population. They generally provide basic outpatient and curative services while complicated cases are referred to referral health centres, which are often under-staffed and underequipped. Mortality rates are still high with 104 out of every 1,000 children not reaching their 5th birthday (Ministère du Plan *et al.*, 2014). Encouragingly this represents a considerable reduction from the previous rate of 158/1,000 in 2010 (UNICEF, 2010).

DRC has two distinct seasons: the dry season from June to August and the rainy season from September to May. It experiences predominantly hyper-endemic to holoendemic malaria transmission, with 97% of the population living in high transmission areas. DRC saw a large decline in the estimated rate of malaria deaths per 10,000 population per year from 24.8 in 2000 to 10.3 in 2015 (Gething *et al.*, 2016). Despite this dramatic reduction, DRC remains second only to Nigeria in terms of highest global malaria burden. In 2015 the WHO estimates that over 16 million cases and nearly 40,000 deaths occurred in DRC, equalling to 12% of all malaria associated deaths in sub-Saharan Africa (Gething *et al.*, 2016, WHO, 2016).

1.5.2 Malaria epidemiology in the Central African Republic (CAR)

The Central African Republic (CAR) is a vast, sparsely populated country, covering approximately 623,000 km^2 with a population in 2009 of only 4.7 million inhabitants (WHO, 2015a). It is a landlocked country and shares borders with six countries (Figure 1.5). The Ubangi and Mbomou Rivers form most of the southern border dividing it from DRC. Administratively it is divided into 16 Prefectures and further divided into 71 sub-Prefectures. CAR has a subequatorial climate with a rainy season from May to October (Ndiath *et al*., 2016).

Figure 1.5 Map of the Central African Republic.

CAR is one of the poorest countries in the world with two thirds of the population living on less than 1 USD a day (Caleo *et al.*, 2012) and it is currently ranked lowest in the world (188/188 countries) on the HDI (UNDP, 2016). It has been plagued by violence for more than a decade, which increased in 2013 when President Bozizé was overthrown by the Seleka rebel coalition. Rebel groups, government soldiers and armed bandits have all targeted civilians and this has resulted in the displacement of an estimated half a million people to-date. This violence makes it impossible in many places to access basic social services, including health. Consequently, health indicators are among the worst in the world and the urgent needs are far greater than current support available.

Even before this recent crisis, the existing health system was weak and CAR had some of the worst global indicators including the 6th highest child mortality rate in the world (129 per 1,000 live births in 2012) and the second lowest life expectancy (48 years). Since the political and military events in 2013, numerous health centres closed, many health workers were forced to flee and drug supply chains within the country stopped. This resulted in the complete absence of public services in many areas. Subsequently, WHO categorised CARs health crisis as a Level 3 Humanitarian Emergency – its highest grade. Most health care services are now being provided through international aid but innumerable factors still hinder access even for people living nearby. Many health facilities have been looted and there are severe logistical constraints to reach the facilities due to bad road

conditions, especially during the rainy season. Furthermore, the presence of bandits and road blocks pose a constant threat. The lack of resources and the on-going political conflict means insufficient health data are available and thus precise causes of morbidity and mortality are difficult to ascertain. Though health data is imprecise, malaria is known to be a major public health problem in CAR and the leading cause of under-five mortality. In the majority of the country, malaria appears to be hyperendemic, however there is little surveillance outside the capital Bangui and therefore epidemiological variations within the country are unknown (Sangba *et al.*, 2016). In 2015, Doctors Without Borders (MSF) teams treated more than 580,000 malaria cases (12% of the total population) out of just over 1 million outpatients consulted (MSF, 2015).

1.6 Malaria surveillance

Malaria surveillance is an essential component of control programmes, yet the WHO took 50 years to launch the first updated surveillance guidelines for malaria since the GMEP. Without data on the prevalence, mortality and severity of malaria at sub-national level, strategies cannot be effectively tailored to different populations according to their specific needs. When implemented correctly, surveillance guides public health policy and can ensure effective allocation of resources even in emergency situations (Hay *et al.*, 2010).

While deployment of mRDTs over the last decade enabled the move from general fever surveillance to malaria specific surveillance, there are many challenges to overcome between a person being infected with malaria to them being tested, treated and their data recorded. Understanding the complexities of the health systems plays a vital role in this to identify at what stage in the case management process a malaria case is dropped from the system. For example, before the patient can be tested with an mRDT, they must first attend a facility providing this service, yet the proportion of febrile patients that come into contact with formal care facilities remains low (about 30%) (Iwamoto *et al.*, 2017).

Surveillance in sub-Saharan Africa typically relies on routinely collected health facility-based data available as part of a Health Management Information System (HMIS) (Yukich *et al.*, 2014). Obtaining quality data on changing malaria transmission patterns through this channel at sub-national level is extremely challenging. Many parts of the population are simply not having access to formal systems of medical care, this routine system provides non-exhaustive data (limited number of indicators due to the integration of other diseases and health system components), and

the transmission of the data is far from perfect. Furthermore, there are concerns over data validity, representativeness and completeness (partial reporting of integrated structures and not taking into account non-integrated structures). Current efforts to improve this system can be seen in the launch of the web-based District Health Information System 2 (DHIS2) across many sub-Saharan African countries. This has been adopted by DRC (but not CAR) and provides an integrated platform to collect, validate, analyse and visualise patient-based data.

In light of these limitations of the passive data collected from health facilities, countries must also rely on community-based cross-sectional surveys to provide vital information on intervention coverage, mortality, and biomarkers such as parasite prevalence and anaemia. Population-based national surveys, such as Multiple Indicator Cluster Surveys (MICS), Malaria Indicator Survey (MIS) and Demographic and Health Surveys (DHS) typically collect data on a wide range of outcome indicators, permitting the assessment of program coverage across the country or over time using well-tested instruments with built-in systems for data quality control. These surveys can yield national or regional estimates, but rarely have the statistical power to provide estimates at lower administrative levels.

While typically representative of the general population, population-based surveys are geographically representative only at the level at which the sample is drawn and due to cost issues (the larger the sample size, the more expensive the survey), it is often not possible to draw samples that are representative at the district level. The expensive and time consuming nature of these surveys means the information collected is quickly out-dated and causation between predictors and outcomes using the cross-sectional data is difficult to establish.

In DRC there have been two DHS (2007 and 2013) and three MICS (1995, 2001 and 2010). In CAR there has been only one DHS (1994) but four MICS (1996, 2000, 2006 and 2010). Both countries have plans for a MICS in 2017. The long period of time between these surveys highlights the logistical issues of large scale surveys in challenging and fragile contexts. Furthermore, no Malaria Indicator Surveys have been conducted in either DRC or CAR.

One strategy to improve surveillance and offer integrated research capacity is using a sentinel site surveillance system. A sentinel system usually contains a limited number of fixed locations from which high-quality data is collected that is not available through routine surveillance systems. For malaria, this means including data on entomology, programme coverage as well as antimalarial and

insecticide resistance. The assumption is that it is easier to improve the quality of data collection in a small number of facilities and estimate trends rather than improve immediately an entire system. Sentinel sites implemented in remote settings have been shown to effectively measure mortality and malnutrition in the Central African Republic (Caleo *et al.*, 2012). A similar sentinel surveillance programme has been initiated by the Congolese NMCP to provide readily accessible data on the trends of defined malaria indicators that are not collected by the routine health information systems (discussed in further detail in Chapter 6).

1.7 Impact of conflict on malaria control

Sub-Saharan Africa continues to experience a huge amount of social unrest, conflict and humanitarian disasters, which are major obstacles to progress. The Global Peace Index report puts the DRC and CAR among the worst performing countries in terms of 'state of peace' (ranked 152 and 157 out of 163, respectively). Parallel to this, the fragile states index 2016 classifies CAR and DRC as having the 3rd and 8th highest rankings (classified very high alert) of risk indicators. Being classified as a 'fragile state' means the countries face particularly difficult political, social and economic conditions. They have weak institutions and governance systems, and lack effective political processes to influence the state to meet social welfare expectations. DRC and CAR rank 156th and 159th respectively out of 176 countries on the Corruption Perceptions Index which further compounds the fragility of these states.

Access to health care is one of the first things to breakdown during a humanitarian crisis. There are often attacks against patients, against providers, against the facilities, placement of road blocks preventing people getting to and from clinics, as well as interruptions in supply of diagnostic tools and drugs. Consequently, the impact on a country's health indicators is tangible. For example, a global study conducted in 2007 found that the median basic immunisation coverage rates in 19 fragile states were roughly half that of comparable 37 non-fragile developing countries (Gwatkin *et al.*, 2007).

In terms of malaria, it is well known that it is a disease that flourishes in conditions of poverty and unrest. Almost two-thirds of refugees, internally displaced persons, returnees and other persons affected by humanitarian emergencies live in malaria endemic regions, and it therefore poses a significant threat to their health. One study in DRC showed population displacement due to violent conflict appeared to be a risk factor for malaria and a major cause of child mortality (Charchuk *et*

al., 2016). Furthermore, most cases and deaths due to malaria in emergency situations go unreported.

Even after a conflict has ended, such as is the case in DRC, countries face challenges in recovering and strengthening their health systems in the light of often fragile governments. In addition to designing flexible malaria control programmes that can adapt their strategies to changing political contexts, the programmes must strive for peace as recognised in the SDG 16 to 'Promote peace, justice and inclusive societies'. This is an essential step before sustainable gains in reducing the malaria burden can be hoped for in many countries.

1.8 Thesis rational and structure

Long periods of political instability have resulted in a lack of scientific research over the past decades in both DRC and CAR. This thesis will offer a new perspective into how malaria programmes can overcome the issue of access to health care and malaria control interventions in isolated or conflict-affected communities. It will focus on practical ways of tailoring control and surveillance strategies in such settings.

It aims to provide new insights into best strategies for malaria interventions in high endemic, isolated or emergency situations that have a history of political instability. Chapter 3 of this thesis will explore the country specific history of malaria control in DRC to ask how do we build on past successes and learn from failures during a time that was rife with political turmoil. It will then go on to explore current control programmes with Chapter 4 assessing how to maximise use of LLINs (in remote areas of DRC) and Chapter 5 explores a strategy to improve access to essential case management during the on-going conflict in CAR. Chapters 6 and 7 then conclude by investigating the vital role surveillance must play to improve targeted control programmes in these two countries and potential strategies that could be used.

2. Goals and Objectives

Study goal

The overarching goal of this PhD was to describe, characterise and evaluate evidence related to the effectiveness of malaria control and surveillance strategies in areas of extremely limited access to health care and instability. It aimed to contribute quality evidence to better the understanding of how malaria control activities can be tailored to unique settings in the DRC and CAR.

Specific objectives

In order to achieve this goal, the following five specific objectives were pursued:

1. Assemble the historical evidence base of malaria control activities in 20th Century DRC to apply lessons learned for a more targeted approach today.
2. Evaluate the differences in the outcome indicators of LLIN ownership, usage and cost between two distribution strategies used during a mass distribution campaign in Kasaï Province in the DRC.
3. Assess the feasibility and sustainability of using CHWs for malaria case management during on-going conflict in CAR.
4. Measure the community-level indicators related to malaria burden, access and use of control interventions and health care seeking behaviour to assess the representativeness of the routine malaria data collected at sentinel sites.
5. Determine the extent to which malaria infections are underestimated by the Health Management Information System in DRC

3. Assessing the impact of twentieth century malaria control measures in the Democratic Republic of Congo: A historical epidemiological perspective

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Working paper

3.1 Abstract

Background

The Democratic Republic of Congo (DRC) has a long history of dealing with the complexities of malaria. Control efforts faced countless unique challenges through colonialism, including a fragmented health care system, political instability and unrest, corruption, and large numbers of displaced or inaccessible communities. The result is that while scale-up of malaria control interventions have seen an overall reduction in malaria transmission in DRC, it remains one of the most intense transmission settings in Africa.

Method

A review of published and unpublished reports of malaria control in DRC was conducted for the period 1890 to 2000. It compiled evidence of historic malaria control interventions, transmission patterns, prevalence and clinical morbidity and mortality to monitor epidemiological changes and effectiveness of interventions over time.

Results

Review findings give a comprehensive overview of the multiple efforts that targeted malaria in DRC during the 20th Century. Evidence shows that vector control efforts and personal protection measures were largely focussed on the urban centres and European communities residing in DRC. Consequently, malaria burden generally decreased in the European population over time with the exception of during the Second World War and in the years preceding the Global Malaria Eradication Programme. In the Congolese population, malaria burden appeared to increase but this may be more linked to an increase in population in the urban centres from which the data was collected.

Conclusion

Examining the historical malaria control approaches, as well as struggles faced and successes achieved throughout the 20th Century has revealed a great deal about the complex nature of controlling malaria. It has the potential to help understanding of how today's political situation continues to threaten the future of malaria control in the same way it has for decades. Health system authorities must learn from the efforts made in the past to be prepared for effective prevention and case-management in such a diverse and vast country that DRC remains today. The strategies will require a major investment in improved quality of diagnosis and case management, health system

strengthening and case reporting and this must go hand in hand with surveillance to ensure appropriate analysis of the collated data can continue to fill important gaps in today's malaria epidemiology.

Keywords: malaria, Democratic Republic of Congo, history, control

3.2 Introduction

As one of Africa's largest and most resource rich countries, the Democratic Republic of Congo (DRC) has been rocked by world history since the arrival of the first Europeans in 1482. It has endured the consequences of slavery, colonisation from 1908 to 1960, industrial revolution, world wars, expansion of mining, rapid urbanisation and a post-colonial era plagued with civil war. All of these events have had a major effect on the development of the country. So in spite of its immense natural resources, DRC remains one of the poorest countries in the world with a very low standing on the Human Development Index, a life expectancy of only 48 years and the second highest malaria burden in the world.

This lack of development is particularly evident in the highly fragmented health system which has been continuously eroded by conflict. This in turn has meant DRC struggled to keep up with the shifting global agendas for malaria control. While available malaria data from the twentieth century are often either incomplete or of questionable quality, the importance of malaria during this time on the human development in DRC cannot be mistaken. In particular, it was one of the major obstacles to the colonial conquest, and it was found to be the principle disease affecting Europeans as well as the Congolese workforce (Van Campenhout and Dryepondt, 1901). As a result, the colonisation of DRC brought new urgency to European efforts resulting in implementation of mass prophylaxis and vector control measures with varying degrees of success.

In spite of the fact that the twentieth century saw DRC plagued by power struggles and conflict, it also was a period of great scientific discovery. Coinciding with the identification of the *Plasmodium* parasite as the causative agent of malaria and the *Anopheles* mosquito as its vector in the late 19th century, international scientists began opening research laboratories in the DRC. As a result, during the first half of the 20th Century, DRC became a source of abundant data on how science, discovery and reconnaissance shaped malaria control interventions albeit mainly in urban settings where the government and colonial administration were most present. The problem is that most of this data remains largely unknown to contemporary malaria specialists and policy makers because few modern resources are devoted to the field of historical epidemiology (Webb, 2015). Furthermore, most historical resources on malaria in DRC are in French, further limiting its audience.

This manuscript explores the historical malaria research in DRC during the 20th Century. It will produce a timeline of information on how changes in political climate and medical service

initiatives influenced malaria control and what effect these interactions had on disease distribution and burden over time in both the European and Congolese populations. It is thought that understanding the historical evolution of malaria control, its level of prioritisation in the political agenda and its impact on a nation's development can offer a unique insight for todays targeted efforts to reduce the associated burden.

3.3 Methods

A systematic search of published and unpublished literature on malaria control in DRC between 1890 and 2013 was conducted from a wide variety of sources. Grey literature (technical reports and government documents), published peer review journals, abstracts, relevant books and internet articles were reviewed.

The main reference centre was the Institute of Tropical Medicine library in Antwerp whose archives were systematically consulted for malaria data from DRC during the twentieth century. The two principal resources from these archives were the annual reports from the colonial administration (from 1909 – 1958) and the annual reports on public hygiene (from 1925 to 1958). These reports provide analysis and official indicators of all activities of the colonial administration. More specifically, they compiled data on the morbidity and mortality of endemic diseases (including malaria) from all government hospitals and dispensaries in DRC in both the European and Congolese populations in the major urban centres, industrial zones and some rural areas. In addition these reports contain information on the public malaria control activities, research, medical training and education as well as official instructions of the medical service initiatives.

Other valuable resources from this library included the annual reports of the Queen Elizabeth fund for medical assistance to the local population (FOREAMI)[1] which provided detailed malaria data from their intervention zones and the Annals of the Belgian Society of Tropical Medicine[2] where most early medical research from DRC was published.

Online electronic literature databases were also searched to identify peer-reviewed published papers. PubMed, World Health Organisation Library and ITM's specialised 'Medical Literature on Central Africa' database were used to search for relevant literature using free text words 'malaria',

[1] Fondation Reine Elisabeth pour l'Assistance Médicale aux Indigènes
[2] Annales de la Société Belge et Médecine Tropicale

'Congo', 'Zaire' and 'Epidemiology'. Studies published in English and French were included and reference lists of original articles were reviewed.

Malaria data for European and Congolese populations between 1925 and 1958 were assembled from annual medical reports to define reported malaria cases and mortality. After this time the accuracy and completeness of health information reporting on malaria began to decline and routine Health Management Information Systems (HMIS) data were hard to locate.

3.4 Summary of malaria burden results

Malaria burden among the European population

The colonial public hygiene report of 1925 states that between 1918 and 1925 there was a large increase in malaria cases among the European population (Colonie du Congo Belge, 1925). Conversely, repatriation of Europeans due to malaria decreased during this same time period from 43% of those returning in 1919 being due to malaria to 27% of those returning in 1925, although total repatriation also decreased (Table 3.1).

Table 3.1 Repatriation of Europeans due to malaria between 1919 and 1925. Source: (Colonie du Congo Belge, 1925)

Year	Total repatriated	Total repatriated due to malaria (%)
1919	249	106 (43%)
1920	120	31 (26%)
1921	62	12 (19%)
1922	89	29 (32%)
1923	37	10 (27%)
1924	53	6 (11%)
1925	41	11 (27%)

Figure 3.1 shows the proportion of malaria cases (out of all causes of illness) for each year between 1925 and 1958, as well as the proportion of deaths (out of all reported cases). The most notable increase was observed during the Second World War, a time characterised by decreased medical personnel and difficulty procuring medical supplies and equipment, particularly Quinine (Wéry and Janssens, 1992). A decrease in the malaria burden can be seen after the war (1945 – 1952) when synthetic antimalarials became widely available (Duren, 1951b).

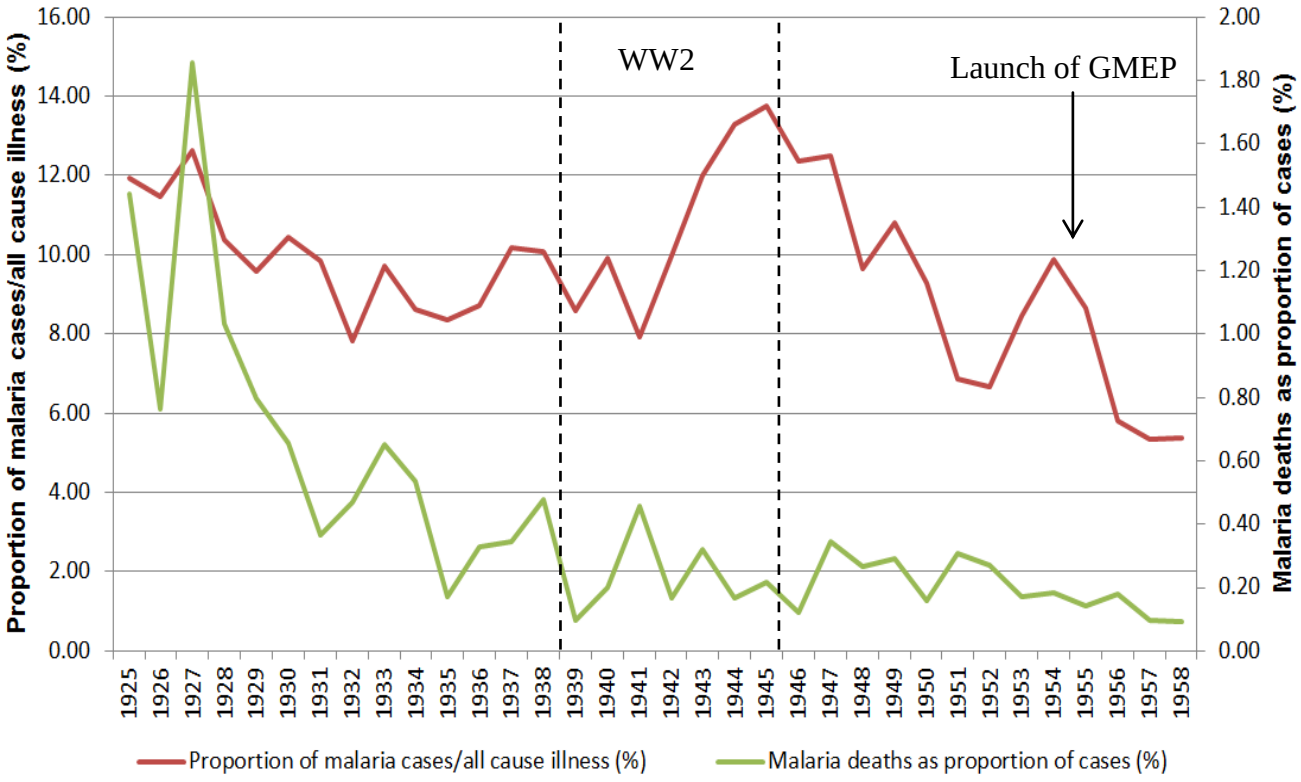

Figure 3.1 Proportion of malaria cases out of all cause illness and proportion of malaria deaths out of the number of malaria cases among the European population between 1925 and 1958. Malaria case data assembled from annual colonial medical reports in the Belgian Congo and the colonial administration reports published 1925 - 1958[3,4].

Malaria burden among the Congolese population

Unlike the European population who were all at risk of the clinical effects of malaria, in the Congolese population it is the children who were the primary victims of malaria. In the holo-endemic region of the gold mines of Kilo, Janssens and colleagues carried out 1,873 autopsies on children between 1940 and 1949 and found that malaria was responsible for 12.3% of their deaths (Janssens *et al.*, 1966). Duren reported infant mortality to be 7.2% in Kwango and 28% in Mayombe (Duren, 1951a).

Malaria cases among Congolese population treated in government facilities increased steadily throughout the colonisation period (Figure 3.2). During the 1950's, reported malaria cases increased at a much higher rate from about 300,000 cases in 1952 to almost 700,000 in 1953 to over 900,000 by 1958. However, looking at these figures as a proportion of the overall morbidity, Figure 3.2 shows that before the 1930s, malaria was present but according to the government reports

[3] Rapports sur l'Administration de la colonie du Congo Belge
[4] Rapports sur l'Hygiène Publique au Congo Belge

contributed less than 4% of the all-cause morbidity. During this time, the primary illnesses were reported to be sleeping sickness, pneumonia and dysentery (Lukwikilu, 2011). The annual public hygiene report of 1934 stated that the increase in the number of malaria cases seen compared to the previous years reflects the expansion of Medical Assistance to the Indigenous population (Colonie du Congo Belge, 1934). This trend continued annually through to 1958, with a much larger rate of increase from 1952 onwards. It is important to note that these figures are just an approximation, and this coincided with an improved access to medical services for the Congolese population. With many Congolese people self-medicating or not accessing facilities, the burden is likely to be greatly underestimated (Wéry and Janssens, 1992). Another factor to consider was that the colonial public health reports suggest that only government doctors regularly reported their data, while private doctors and other societies reported very rarely. Finally, it is thought that malaria is often mixed with other febrile illnesses (Droogmans, 1928).

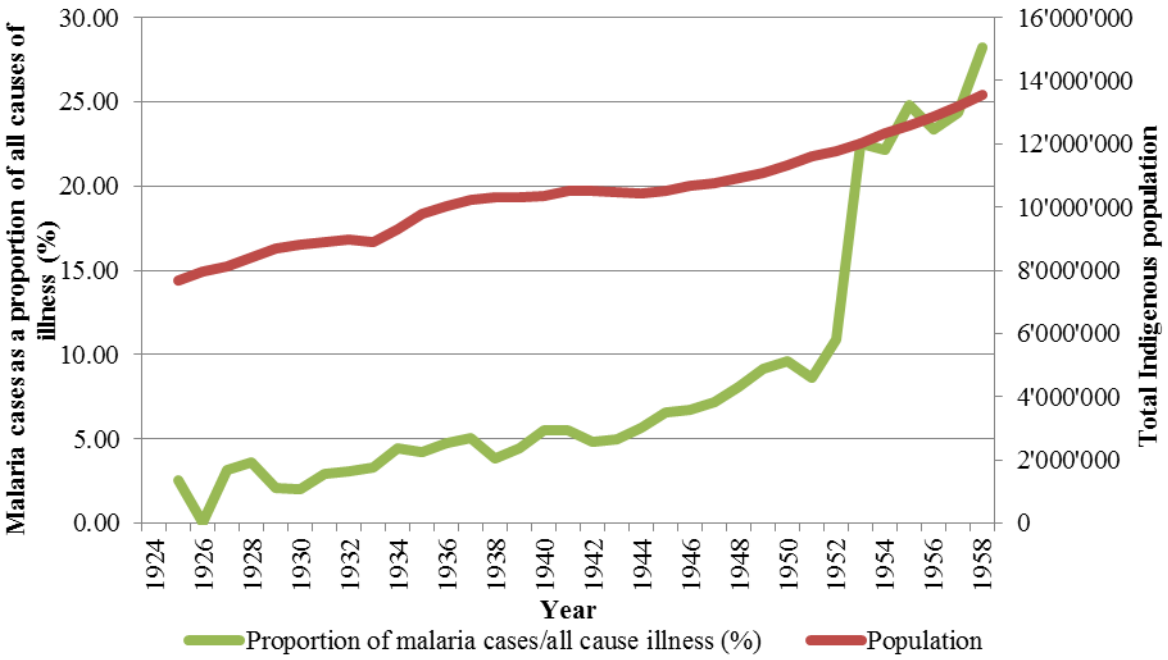

Figure 3.2 Number of malaria cases among the Congolese population between 1925 and 1958 as well as total Congolese population. Malaria case data assembled from annual colonial medical reports in the Belgian Congo and the colonial administration reports published1925 - 1958[5] [6].

The rest of this manuscript will refer to the potential impact specific interventions had on the trends seen here.

3.5 Timeline

[5] *Rapports sur l'Administration de la colonie du Congo Belge*
[6] *Rapports sur l'Hygiène Publique au Congo Belge*

***1890 – 1907**: Malaria research and control pre-colonisation*

Prompted by the need to investigate the causes of mortality among both Europeans and Africans in the then Congo Free State, Henri De Marbaix founded the Boma (then the capital of Congo) laboratory in 1894. This gave scientists in the Congo an opportunity to make contributions at a time of key malaria discoveries, including identification of the mosquito as the vector and the observation of the malaria blood stage parasite. However, after only two years De Marbaix was repatriated and later died, halting progress. Then the Belgian Society of Colonial Studies took over and in 1899 created the Léopoldville (now Kinshasa) Medical laboratory, appointing Dr. Jean Emile Van Campenhout in charge (Dubois and Duren, 1947, Bosmans and Janssens, 1997). In the first two years of its creation, Van Campenhout and Dryepondt conducted the first studies on malaria in the Congo, concluding that of all diseases affecting Europeans in Congo, malaria was the most prominent (Van Campenhout and Dryepondt, 1901). In 1900, Dr A. Broden took over management of the laboratory where he continued to work on malaria and blackwater fever for some years. He confirmed that hemoglobinuria is a complication of malaria and its prevention is therefore the same as that of malaria (Broden, 1906). Complementing this early research, several medical missions made many important discoveries. From 1903 to 1906, J.E Dutton and J.L Todd from the Liverpool School of Tropical Medicine visited the then Congo Free State to report on the state of malaria in the towns of Boma, Matadi, Léopoldville, Coquilhatville and Lusambo (Dutton and Todd, 1906, Lechat, 1964). They recommended vector control through managing mosquito breeding sites and individual protection with nets, window/door screening and quinine prophylaxis. These key approaches reflected international opinions on malaria control at the time.

***1908 – 1919**: Early malaria control initiatives following colonisation*

In 1908, when the Congo Free State was transferred to the Belgian State, malaria continued to arouse great interest from colonial authorities. Furthermore, the urgent need to develop a solid health policy led to the establishment of the colonial Medical Service in 1909 (Porter, 1994). This service was responsible for centralising data and coordinating medical activities. In contrast to earlier public health initiatives, this policy was not only to preserve the health of Europeans, but it also sought to ensure better health conditions for the Congolese people whose work was necessary for the development of the colonial enterprise (Dubois and Duren, 1947).

In spite of this, fear of contagion resulting from the mixing of races was still a popular opinion, leading to high demand for race segregation. This had been seen as early as 1887 in the first of

many public health decrees in Congo, but separation of European and Congolese residential zones was more firmly established in the decree of September 1898 (Porter, 1994).

This opinion was partly founded on the belief that the Congolese children were continual reservoirs from which the *Anopheles* mosquitoes became infected. Dutton and Todd reinforced this belief when they reported considerably higher *Anopheles* densities present in Congolese communities than in European areas, with on average 5 to 10 % and even as much as 20% of those captured in Congolese houses being infected with malaria. Furthermore, blood drawn from Congolese children less than 10 years old in Boma, Matadi, Léopoldville and Lusambo showed malaria infection rates of 70-100% in all but one group living in contaminated areas (Dutton and Todd, 1906).

In reality, race segregation had mainly been attempted in administrative posts until the rapid urbanisation, after which town planning actually incorporated separate living quarters for Congolese and European communities with a separation zone planted with trees and public parks. The width of this zone was generally 250-500 meters to take into account the flight distance of the *Anopheles* whilst minimising disadvantages from the point of urban and economic life (Duren, 1937b). In Leopoldville the original European quarter was separated by a sanitary cordon consisting of a golf course, botanical garden and a zoo making it one of the most extreme examples of racial segregation in colonialized Africa. Governments hoped that the people of the European district would thus be less exposed to the bites of infected *Anopheles* mosquitoes demonstrating that as in other African colonies, the health priority remained the Europeans (Broden, 1922).

During this time of urbanisation, the Belgian's vast public work projects also extended the water, sewage and road systems to create urban sites suitable for new construction (Duren, 1937b). While these public work projects were not essentially undertaken for reasons of public health, the advantages for vector control were well understood and medical services increasingly recognised that mosquito transmitted diseases (including malaria) presented a huge burden on health in the Congo. Consequently, in 1913 to also encourage personal protection against the mosquitoes and the diseases they transmit, the Belgian public health officials passed a legislation that required all European houses in the Belgian Congo to be fitted with metal screens on all windows and doors. In practice, most European houses only came into compliance by the late 1930s (by which time most had also adopted the use of the bed net) (Duren, 1937b). Furthermore, supported by the knowledge that the methodological and conscientious destruction of mosquitoes in the early 1900s had already seen great success in the reduction of malaria cases in towns in Egypt, Malaysia and France as well

as other places, mosquito destruction entered the agenda of the local government. At this time, vector control in the Congo was part of the duties of the health services and was mainly directed against the larval breeding sites (Vincke, 1950). Methods included filling ponds, draining marshes, evacuating rain water and waste, regulating rivers, clearing blockages and mowing banks. The government undertook extensive drainage works channelling water from swamps in Boma, Matadi, Léopoldville, Coquilhatville and Elisabethville. They drained waters from the European residential blocs and from industrial and commercial centres benefitting about one-third of the Europeans living in the Belgian Congo as well as approximately 100,000 Africans who lived in their immediate vicinity (Duren, 1937b). The cost of these works to improve general sanitation on top of vector control efforts meant that it was not possible to extend these measures to the vast rural areas of Congo (Vincke, 1950). While there is no data available for Matadi before the drainage works and fight against mosquitoes by Duren between 1928 and 1933, mosquito density was decreased and sustained at a very low rate for a few years. These works had been primarily to prevent the reoccurrence of the yellow fever epidemic of 1928 – 1929, but it had also remarkable results for malaria. The malaria rate was 2% compared to 14% observed by Duren in the rest of the colony that year, out of 8,051 Congolese, only 57 malaria cases were observed and out of 430 European residents, there were only 9 cases (Zanetti, 1934).

In addition to drainage works, the authorities also attempted larviciding, which required prior determination of the *Anopheles* type and the exact location of its breeding sites. In March 1911, anti-malarial teams were created to monitor stagnant water and collect specimens of larvae in high risk zones (Lukwikilu, 2011). While larvicide powders were rarely used in the Congo, means such as the spreading of diesel oil, walking a cloth soaked in larvicide along the surface of ponds, or by means similar to those used in the vineyard sprayers were used. In the urban centres, regular ‘pétroleur’ teams were established but the lush vegetation of ponds and marshes, the vast expanse of water bodies and the frequency of rainfall made the task difficult and unreliable. At Stanleyville (now Kisangani), methodical larviciding with fuel oil within a radius of several kilometres reduced anopheles populations (mainly *An. gambiae*) by about 90% between 1935 and 1941. However there was no documented effects on parasite transmission and in fact the sporozoite rate of *An. gambiae* rose from 11% in 1940 (based on 30,780 examinations between 1935-1940) to 15% (based on 2,343 dissections in 1948). Larviciding conducted by the ‘Union Minière’ at Jadotville (now Likasi) also had little effect (Vincke, 1950).

***1920 – 1931**: Growing concern for African health: Quinine and larval control*

Most diseases that were rampant in the Congo such as sleeping sickness, malaria or dysentery were not yet well known by European doctors and knowledge about the spread and mode of transmission was still limited. Scientific and biomedical research was therefore assigned a high priority by colonial powers and under the direction of the services of the general Government, further research was done on malaria (Lukwikilu, 2011). This effort produced a richness of data with 331 papers dedicated to malaria being published in the *Annales de la Société Belge de Médecine Tropicale* between 1920 and 1969 (Bosmans and Janssens, 1997). One noteworthy discovery during this time was by Vincke and colleagues who discovered *Plasmodium berghei* in wild rats in Katanga (1948) and were able to infect mice (Vincke and Lips, 1948). This discovery provided a valuable *in vivo* model for the testing of candidate antimalarial drugs (Gillet, 1953b). Duren(1937a, 1951a), Gillet (1953a) and Janssens (1992) attempted to summarise these different studies to give a comprehensive review of malaria in the Belgian Congo, providing valuable references for morbidity and mortality data. Another summary report was done by the Superior Council of colonial Hygiene who was responsible for the coordination of malaria control methods (Rodhain, 1951).

In the 1920s, in the mining town of Elisabethville (now Lubumbashi) in Katanga Province, both the colonial state and the mining companies dispensed free quinine and mosquito nets to their European employees. Due to the high costs of quinine its use was largely restricted to the European administration and their families. To avoid the adverse effects of malaria within the Congolese population and thus the country's workforce, the necessity to implement measures to protect the Congolese people against malaria was recognised. Therefore whilst not centrally organised, quinine use was increasingly found among the natives too and by 1922 African children from selected schools in Léopoldville (now Kinshasa) were receiving preventative quinine treatment twice a week (Van den Branden and Van Hoof, 1923).

In 1922 a Colonial Hygiene Service was established, marking a new direction in public health in the Congo. Independent of the colonial Medical Service, the Hygiene Service was responsible for urban sanitation, potable water supplies, port hygiene, vector control campaigns and overall health of African labourers. Laboratories were opened and posts for medical hygienists established in the provincial capitals, Léopoldville, Elisabethville and Bukavu as well as the ports of Banana, Boma, Matadi, Jadotville and Albertville (Porter, 1994).

Malaria still caused around 10 – 13% of Europeans illnesses diagnosed at government facilities during the first two years of colonisation. This high burden has been argued to be due to the poor

adherence to basic malaria prevention suggesting that the large scale Quininisation campaigns were not being effective. Conversely, a 1931 survey found 84% of the European population took quinine as prophylaxis regularly and had lower malaria incidence compared to those that either took it irregularly or not at all. However, mosquito net usage was also highly correlated with regular quinine usage therefore possibly biasing results (Colombo, 1931). Other studies during this time demonstrated the benefits of quinine and plasmochine as prophylaxis, including one showing reduced malaria transmission among a group of agricultural workers in a plantation near Léopoldville (Henrard and Van Hoof, 1933).

In this early colonisation period, sleeping sickness was taking its toll on the Congo leading to the formation of other organisations whose general health activities also covered malaria (Lukwikilu, 2011). The FOREAMI, established in 1930, worked on the basis that if a specific area was cleaned up by a few years of extraordinarily costly medical service, it then becomes feasible for a smaller team to maintain the improved position (Mouchet, 1951, Porter, 1994). They focused on rural areas starting in the Bas-Congo Province in 1931, and by 1935 encouraging results meant the government could take over the service, enabling FOREAMI to move their activities to Kwango. The new territory had a population of over 600,000 and was characterised by poor land, malnutrition and slow economic development. Medical installations were scarce so FOREAMI had to build hospitals and dispensaries (Mouchet, 1951). In 1958, after decades of concentrating on the Western districts of the colony, FOREAMI began a new project in Uele District in Northern Congo (Porter, 1994). Their annual reports provide an excellent source of data on all epidemic and endemic diseases in the zones covered by their activities (Mouchet, 1951).

***1932 – 1950**: Malaria control at the time of the Second World War*

To promote individual protection against malaria, the Brussels School of Tropical Medicine, established in 1906, led a public health campaign to encourage the use of quinine for malaria prophylaxis. This was strongly supported by a group of Italian doctors, who had an active presence in the Congo medical service and had experienced the positive impact of quinine in Italy (Duren, 1937b). As a result, the government began routine distribution of quinine to Europeans residing in the Congo, particularly to Government employees and officials and their families as well as missionaries (Colonie du Congo Belge, 1934). Private organisations also distributed quinine freely to their employees (Duren, 1937b).

Global quinine production was concentrated on the island of Java in the Dutch East Indies. In 1932, the Belgian Congo colonial administration negotiated a deal with the Department of Agriculture of the Dutch East Indies to deliver large quantities of quinine for lower than the market price to allow medical services to combat malaria adequately. But buying large quantities of quinine still caused a huge financial burden, making it difficult for the administration to significantly improve the situation. So they took the advice of Rodhain (who chaired the colonial health council) and the medical services, to attempt to plant *Cinchona* plantations in several parts of the Congo (Duren, 1937b).

Their greatest success came from the red bark of the *Cinchona succirubra* in an almost equatorial climate above 1500m in the Ituri highland region (Fataki) (Duren, 1937b, Janssens, 1997). Workers planted several thousand seedlings in 1934 and 1935 and it was hoped that within a few years, infusions of the bark could be used among local populations (Webb, 2014).

In 1942, during the Second World War, the cinchona plantations, located in Java, fell under the control of the Japanese troops, which paralysed the export of quinine. The colonial administration was forced to ration its distribution of quinine resulting in an increase in malaria mortality among Europeans and Congolese (see Figure 3.1 and Figure 3.2). This gave even more incentive for colonial authorities to expand their own plantations of *Cinchona* (Duren, 1937b). In 1944, a quinine factory opened in Bukavu allowing the authorities to consider chemoprophylaxis on a larger scale for Congo and other African territories.

The shortage of quinine during the Second World War also led to greater use of synthetic antimalarial products such as Atebrine and Pamaquine and the introduction of new synthetic antimalarials chloroquine, proguanil, pyrimethamine (Lukwikilu, 2011). These products radically changed the malaria control strategy and their distribution became the responsibility of medical services. They distributed them to their staff, children during consultations, antenatal clinics and schools. Again studies in the Congo showed the efficacy of these synthetic drugs in reducing malaria incidence and associated morbidity and mortality. One such study was to test weekly doses of chloroquine dihydrochloride (Aralen) on 30 children who were repeatedly being treated for severe malaria in a mission post of Bibanga, Kasai Province (Rule, 1951). Another study by Delannoy and Hugon in 1954 showed a reduction from 62% participants with malaria positive blood slides to 0.7% positive 6 months after the start of pyrimethamine distribution (Delannoy and Hugon, 1954). In 1955, a 5-year project on the use of mass chemoprophylaxis with pyrimethamine

in over 5,500 children was initiated in Yangambi, in the Isangi territory of Tshopo District. Parasite prevalence was reduced from 30-50% in 1954 to 4.5% in 1959 (Lahon *et al.*, 1960). All authors of such studies were in agreement with Duren's conclusion in his 1937 review that "Regular and on-going preventive treatment is effective; it acts without question to reduce overall morbidity and mortality and has a beneficial influence on endemic infections; it does not seem to prevent acquisition of acquired immunity" (Duren, 1937b).

After the war, the Belgian government created a Welfare Fund in recognition of the war effort provided by Congolese. The fight against malaria entered the agenda of key international actors, in particular the World Health Organisation (WHO). Since its creation in 1948, it became leader of international health action, and the fight against malaria was among its top priorities. In 1950, the WHO convened the first malaria conference in Equatorial Africa to present and assess available information on the epidemiological aspects of malaria, and to coordinate the various methods of research and control of the disease (WHO, 1951, Dobson *et al.*, 2000).

The end of the Second World War also marked by the discovery of powerful residual insecticides, most notably dichlorodiphenyltrichloroethane (DDT) which contributed to the eradication of malaria in many Western countries. Hence, malaria control efforts improved in the years following the Second World War as anti-mosquito campaigns were intensified and various public health services were improved in many urban areas (Lukwikilu, 2011).

The first DDT Indoor Residual Spraying (IRS) campaign in the Belgian Congo took place in 1947 in Katanga Province. Supported by WHO and coordinated by Dr I.H Vincke, Director of the Malaria Control Research and Investigation Section in Elisabethville (Vincke, 1950), the initial phase was concentrated in the urban areas of Elisabethville, Manono, Albertville, Kasenga, Bukama, Kongolo and Kamina. Elisabethville and surrounding area within a radius of 30 km were quickly cleared of Anopheles, which was reflected by a remarkable drop in parasite rates (Janssens, 1997). The "Union Minière du Haut Katanga" (UMHK) also conducted DDT spraying in Jadotoville in 1947, expanding to all its mining centres by 1948 (Vincke, 1950). FOREAMI also conducted four DDT spraying campaigns in 10 posts and villages within a 50km radius of Kwango between 1948 and 1949. Results showed a decrease in malaria by 31% between April 1948 and April 1949, and by 17% between May 1948 and May 1949 (Himpe, 1949).

A study on the effect of house-spraying with the insecticide Gammexane in a water dispersible powder form in Yaligimba, showed that contrary to other studies with Gammexane, untreated houses within a treated village did not see a decrease in mosquito densities concluding that all houses need to be sprayed. Results did however show that the spraying campaign reduced the overall age of the mosquito population and that infection rates in the mosquitoes were very low. There was no significant difference in parasite rates of children in treated and untreated villages, although there was a decrease in intensity of infection in the children from treated villages. The author concluded that these negative results were likely due to the large amount of population movement which had already been seen to affect malaria burden in the Congo (Davidson, 1949). As early as 1917, a decree forbid Congolese from settling in swampy regions because they were deemed Tsetse fly environments, giving colonial officials a pretext to redistribute the Congolese populations responding to the need of labour for private companies. For example, by the 1920s, Kilo Moto Gold Mines had exhausted local labour supply and began recruiting from distant towns in Uele, Kivu, Rwanda and Burundi bringing in workers who were susceptible to new diseases to which they lacked resistance. Consequently, at Kilo-Moto, a public health scheme gradually evolved which by the 1950s included free medical care, maternity and outpatient services for the surrounding villages and the workers inside the mines, as well as malaria control (Porter, 1994). Introduction of malaria from the lowlands also had devastating effects on the highland communities. At the Belgian mission at Fataki in the Ituri region of the Eastern Belgian Congo, situated at 1500 – 2000m above sea level, a small epidemic erupted in 1933 – 1934 and some 60 Africans were hospitalised of which 2 died (Calonne, 1935). This highland region had been previously malaria free but when the Belgian coffee planters arrived earlier in the century they built small dams to enable the processing of coffee beans, creating new breeding ground for mosquitoes (Duren, 1937b).

In the early 1950s aircraft spraying with insecticides was introduced (Lebrun and Ruzette, 1956). Several campaigns of helicopter spraying with insecticides were carried out between May and November 1953 in Léopoldville, resulting in a 90% reduction of the mosquito population at 1,000 breeding sites visited. There was also a reported decrease in parasite rate to 35% compared to 64% in 1950 (Lebrun and Ruzette, 1956). However, reinvasion from untreated zones soon occurred and the eradication campaign was abandoned and replaced in 1954 with “reduction campaigns” through monthly household spraying. Furthermore, the reinvasion that occurred saw higher numbers of mosquitos than previously recorded, leading to researchers hypothesising that the insecticides could

have destroyed larva-eating fish such as small cyprinodontes that can be found in large numbers in the marshes around Leopoldville.

***1951 – 1959**: Early global collaboration to combat malaria*

In 1951, a malaria committee of the Higher Colonial Health Council, chaired by J. Rodhain studied the issue of malaria and highlighted the importance of malaria mortality in the Belgian Congo. It emphasised the need for chemical prophylaxis against malaria and insecticides in the fight against vectors (Rodhain, 1951). They considered that the total eradication of vectors using insecticides is not possible under the current conditions of the Congo, particularly due to the vast territory that would require extensive resources in terms of finance, staff, and materials (Mouchet, 1951). In 1957, following the 1951 commission recommendations, a central body was established, the *Service d'Etude et Coordination de la Lutte Antipaludique* au Congo (SECLA), to coordinate malaria control activities under the Directorate of Medical Services (Lukwikilu, 2011).

Two years earlier in 1955, the WHO had set up the Global Malaria Eradication Programme (GMEP), with the main objective to eradicate malaria around the world. Unfortunately this did not bring progress in the most intense malaria areas in Africa and Asia and in 1969 the effort was discontinued. It had very little success in DRC (Lukwikilu, 2011).

***1960 – 1970**: Malaria control post-independence*

In June 1960 the Belgian Congo gained its independence after 75 years of domination and was renamed Congo. Between 1960 and 1965, the Congo experienced a series of violent upheavals and civil wars culminating in the coup which brought power to Field Marshall Mobutu. There was an almost complete destruction of the health infrastructure in the immediate post-independence period and its slow redevelopment, coupled with a rapid population increase, significantly impeded adequate health care coverage (Porter, 1994).

In 1971 the *Programme de Lutte Antipaludique* was launched by an agreement between the United States Agency for International Development (USAID) and the Congolese Government with an aim to implement and evaluate malaria vector control measures in Kinshasa. The primary anopheline mosquito control measure was intra-domiciliary spraying with DDT (Kazadi *et al.*, 2004). This programme was integrated into the Expanded Programme on Immunisation and the Fight against Childhood Diseases (EPI/MITA).

In spite of some localised efforts from these organisations and some research into chloroquine resistance which was first detected in Congo in Katana on the Western shore of Lake Kivu (Delacollette *et al.*, 1983), few notable efforts to control the disease took place after 1990.Therefore, there is a severe lack of data available describing this period.

Malaria mortality and morbidity began to increase again globally in the 1970s and 1980s due to a combination of factors such as the increase in parasite and vector resistance to the current anti-malarial drugs and insecticides, the weakening of traditional malaria control programs, rapid decentralisation and integration into deteriorating primary health services, and the development of a major humanitarian crisis in some malaria-endemic areas such as Congo. This dramatic increase led to the creation, in 1998, of the Roll Back Malaria Partnership to re-energise global efforts in combating malaria.

3.6 Discussion

The size of the entire Western Europe, DRC has a diverse range of malaria epidemiology and a great diversity of human populations. Looking at the history of malaria control clearly showed that interventions that may have worked in one region failed in another. This confirmed the widely accepted view that the knowledge of the malaria epidemiological profile in a specific area can determine the success or failure of an intervention (Snow, 2015). History also highlights the challenges of controlling malaria during a time when the health system was continually changing and far from adequate to meet the needs of its population. This remains a challenge today in the DRC as in many other African settings. Therefore re-examining historic records could have important implications on malaria control today in specific settings.

The journey of malaria control in the DRC has been mirrored by the social and political struggles the country has faced over the last hundred years. However, in the midst of the political turmoil's of the twentieth century, the Congo produced a plethora of scientific and medical research on malaria. These studies greatly contributed to the global body of malaria knowledge, informing policy makers, public health officials and health professionals to shape the health policies of the time. Such research helped develop an understanding of disease burden and distribution in a given population as well as the effectiveness of different preventive, diagnostic and curative interventions.

The data from government records on the overall county wide malaria burden for both European and the Congolese populations (Figure 3.1 and Figure 3.2) give an indication of the changing malaria burden over time. Figure 3.1 shows there was an increased malaria burden between 1932 and 1933 which the colonial public hygiene report of 1938 related to the fact that quinine was not enough to prevent malaria if people continued to live near malaria mosquito breeding. It emphasised the need to employ larval control measures alongside personal protection methods. However, there are limitations in this data as even amongst the Europeans, only an estimated 50% used the public doctors whose data were reported in the government records (Duren, 1937b). Historic malaria data from the Congolese population is certain to be an even greater underestimation of the actual burden of the time as they had much more limited access to health care compared to the Europeans at the time. Another reason the data is likely to be a gross underestimation is that most data came from urban centres which had lower malaria rates than their rural surroundings. Furthermore, where malaria was highly endemic other diseases with overlapping symptoms were also widespread. While this remains a problem today, the period examined in this paper was one before improved diagnostics, and it was therefore even more difficult to diagnose with precision the causes of morbidity and mortality.

The challenges in such a historic approach is finding the balance between compiling and interpreting data from reliable scientific research and captivating the unique insights available through individual stories and reports from physicians and pioneers in DRC at that time.

Exploring the historical changes in malaria prevalence over time, taking into account the various control efforts being made and the level of political turmoil, has been shown to highlight aspects that could help predict the success of specific malaria control interventions in defined regions. A review of the history in Congo has the potential to provide valuable insight to strengthen expertise and develop flexible strategies most appropriate for each setting. But this long and complex history has not yet produced the fruits desired and in spite of all the attempts to control malaria, it remains a huge public health challenge in DRC today.

4. Long-Lasting Insecticidal Net (LLIN) ownership, use and cost of implementation after a mass distribution campaign in Kasaï Occidental Province, Democratic Republic of Congo

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Published in
Malaria Journal, 2017, **16**: 22

4.1 Abstract

Background

Long-lasting insecticidal nets (LLIN) are a highly effective means for preventing malaria infection and reducing associated morbidity and mortality. Mass free distribution campaigns have been shown to rapidly increase LLIN ownership and use. Around 3.5 million LLINs were distributed free of charge in the Kasaï Occidental Province in the Democratic Republic of Congo (DRC) in September-October 2014, using two different approaches, a fixed delivery strategy and a door-to-door strategy including hang-up activities.

Methods

Repeated community-based cross-sectional surveys were conducted two months before and six months after the mass distribution. Descriptive statistics were used to measure changes in key malaria household indicators. LLIN ownership and use were compared between delivery strategies. Univariate and multivariate logistic regression analyses were used to identify factors associated with LLIN use before and after the mass distribution. A comparative financial cost analysis between the fixed delivery and door-to-door distribution strategies was carried out from the provider's perspective.

Results

Household ownership of at least one LLIN increased from 39.4% pre-campaign to 91.4% post-campaign and LLIN universal coverage, measured as the proportion of households with at least one LLIN for every two people increased from 4.1% to 41.1%. Population access to LLIN within the household increased from 22.2% to 80.7%, while overall LLIN use increased from 18.0% to 68.3%. Higher LLIN ownership was achieved with the fixed delivery strategy compared with the door-to-door (92.5% [95% CI: 90.2%-94.4%] versus 85.2% [95% CI: 78.5%-90.0%]), while distribution strategy did not have a significant impact on LLIN use (69.6% [95% CI: 63.1%-75.5%] versus 65.7% [95% CI: 52.7%-76.7%]). Malaria prevalence among children aged 6-59 months was 44.8% post-campaign. Living in a household with sufficient numbers of LLIN to cover all members was the strongest determinant of LLIN use. The total financial cost per LLIN distributed was 6.58 USD for the fixed distribution strategy and 6.61USD for the door-to-door strategy.

Conclusions

The mass distribution campaign was effective for rapidly increasing LLIN ownership and use. These gains need to be sustained for long-term reduction in malaria burden. The fixed delivery

strategy achieved a higher LLIN coverage at lower delivery cost compared with the door-to-door strategy and seems to be a better distribution strategy in the context of the present study setting.

Keywords: Malaria, LLIN ownership, LLIN use, mass distribution campaign, LLIN cost, delivery strategy, malaria prevalence, Democratic Republic of Congo.

4.2 Background

Long-lasting insecticidal nets (LLIN) are a highly effective means of preventing malaria infection and reducing associated morbidity and mortality, particularly in endemic areas (Lengeler, 2004, Lim *et al.*, 2011). Across sub-Saharan Africa, the use of LLIN has been shown to be associated with an average parasite prevalence reduction of 20% (Lim *et al.*, 2011). Sustained high coverage of LLIN and other effective interventions is essential to achieve and maintain such gains in reduction of malaria burden, and therefore achieve the joint target of the new action and investment to defeat malaria (AIM) and the global technical strategy for malaria (WHO, 2015b, RBM, 2015). Mass free distribution campaigns have been shown to rapidly increase LLIN ownership and use in several countries (Bonner *et al.*, 2011, Bennett *et al.*, 2012, Larson *et al.*, 2014). Across Africa, different distribution strategies such as fixed or door-to-door delivery have been used with varying effects on LLIN coverage and use. Furthermore, despite overall LLIN scale-up, several other factors still influence LLIN use including demographic characteristics; individual's knowledge and beliefs related to malaria and LLIN; dwelling construction, family size, sleeping arrangements; LLIN characteristics; environmental factors; community and cultural characteristics; distribution strategy and household net density (Thwing *et al.*, 2008, Atieli *et al.*, 2011, Bennett *et al.*, 2012, Macintyre *et al.*, 2012, Auta, 2012, Larson *et al.*, 2014).

The Democratic Republic of Congo (DRC), through its National Malaria Control Programme (NMCP) is in the midst of unprecedented efforts to rapidly scale up coverage of malaria interventions. As recommended by the World Health Organization (WHO) to achieve universal coverage of LLIN, the NMCP has adopted a combined strategy of: free mass distribution campaigns every three years and routine distribution through antenatal care visits and immunisation services (WHO, 2014a). While the mass distribution has been shown to be the best approach to achieve rapid scale up (aiming to achieve at least 80% of people sleeping under a LLIN), routine distribution is important for maintaining high levels (WHO, 2013a, PNLP, 2013a).

Since the adoption of free of charge LLIN policy in 2006, over 75 million LLINs have been distributed across the country, leading to a tremendous increase in ownership and use (PNLP, 2013b). For example, the overall proportion of households with at least one LLIN increased from 9% in 2007 to 70% in 2014 (Ministère du Plan *et al.*, 2007, Ministère du Plan *et al.*, 2014). However, the scale-up of these interventions has not been achieved across all geographic areas of the DRC. Results of the 2013-2014 Demographic and Health Survey (DHS) showed a strong coverage gradient between provinces with Orientale and Kasaï Occidental Provinces having the

lowest ownership rate at 47% and 58%, respectively. Furthermore, the lowest LLIN use in children less than five years of age was reported in Kasaï Occidental at 36% (Ministère du Plan *et al.*, 2014).

Consequently, as part of a larger effort by many partners to accelerate the progress towards the goal of increasing coverage and use of LLIN, a mass distribution campaign was organised in 2014, distributing approximately 3.5 million LLINs in Kasaï Occidental using two different approaches, a fixed strategy and a door-to-door strategy with hang up activities. The aim of this research was to measure changes in key malaria household indicators before and after the LLIN mass distribution campaign, as well as malaria morbidity after mass distribution and to identify factors associated with LLIN use. This study also compared the two distribution strategies in terms of LLIN ownership, use and associated cost.

4.3 Methods

Study site

This study was conducted in the Kasaï Occidental Province, located in the centre of the Southern part of the DRC (Figure 4.1). Kasaï Occidental spans over 170,000 square kilometres and has an estimated 7.3 million inhabitants. The province has two districts (Lulua and Kasaï) and one large city in each - Kananga and Tshikapa respectively. On the health front it is divided into 44 Health Zones (HZ) grouped into five Health Districts. The HZ represents the primary operational unit of the health system in DRC. It usually covers a population of 100,000–150,000 in rural areas and 200,000–250,000 in urban centres. It includes a general referral hospital, some health centres and about a dozen lower level health facilities. Each HZ is further divided into 15 health areas (HAs) on average, which represent the lowest level of the health system. Each HA is clearly delimited and defined by the Ministry of Health and usually has 10,000–15,000 inhabitants. In Kasaï Occidental Province, malaria is endemic with stable transmission throughout the year. The DHS 2014 reported an average malaria prevalence of 45% in children less than five years (Ministère du Plan *et al.*, 2014), one of the highest in the world. A previous mass distribution campaign in the province was organised in 2011.

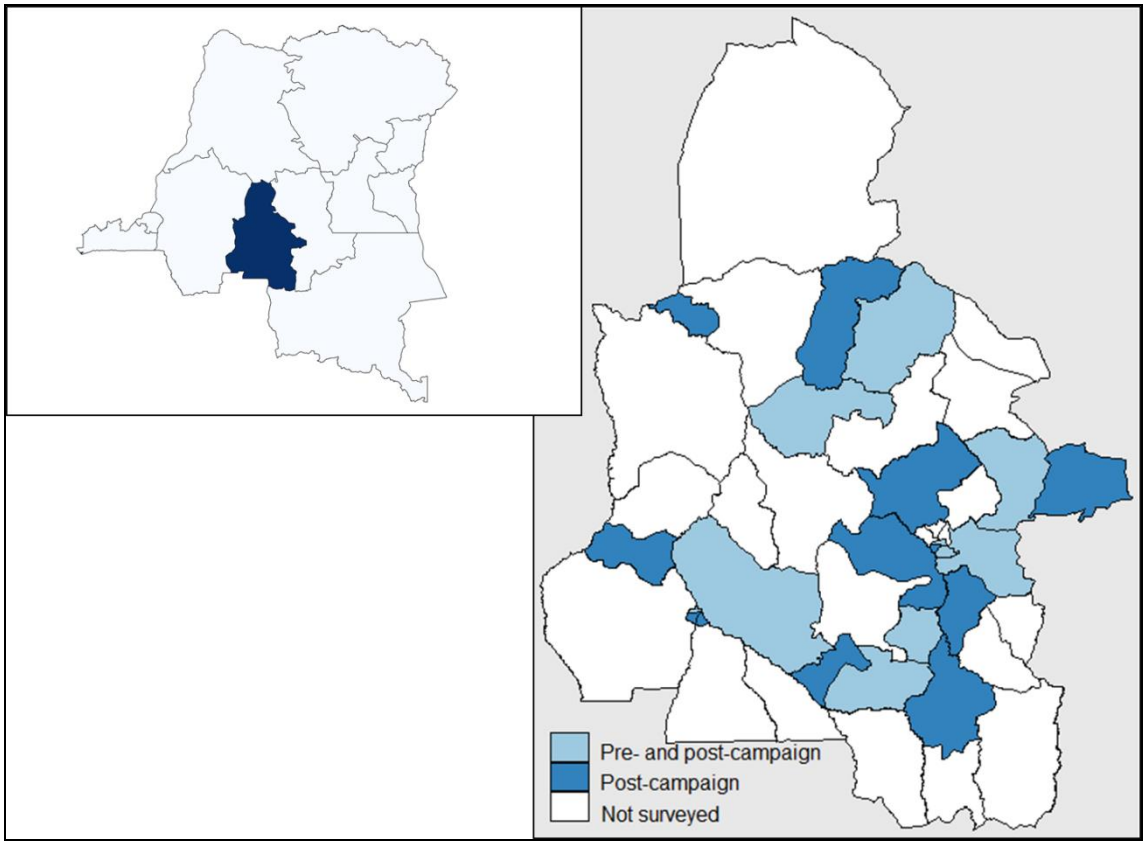

Figure 4.1 Map showing the location of the study sites.

Mass distribution campaign

A free LLIN distribution campaign took place in all HZ of Kasaï Occidental Province in 2014 using two different strategies: a) Fixed delivery strategy; b) door-to-door (hang up) strategy.

- *Fixed strategy*: This strategy was used to distribute nets in 35 of the 44 HZ in Kasaï Occidental Province. Specially selected community volunteers were mobilised and trained to visit each household before the campaign. The volunteers registered the number of residents per household, issued a numbered coupon to be exchanged for LLIN on distribution day, and delivered educational messages on malaria and the importance of sleeping under a treated net. LLIN distribution was done at fixed sites at the 'health area' level and each household presented their coupon in exchange for LLINs. The number of LLINs to be allocated per household was calculated according to household size as follows: 1–2 persons=1 LLIN; 3–5 persons=2 LLINs; 6-8 persons=3LLINs; 9 and more persons=4 LLINs.

- *Door-to-door (hang up) strategy*: This strategy was used to distribute nets in 9 of the 44 HZ in Kasaï Occidental Province. Teams of 3 to 4 community volunteers visited each household sequentially at the moment of distribution. They were responsible for household registration (recording number of people, sleeping spaces, nets, etc.), giving nets and hanging them with the head of the household or another household member. The household registration and the

delivery/hanging of nets were conducted in one visit. Community volunteers were provided hammers, string and nails for this purpose. Contrary to the fixed strategy, the number of LLIN per household here was calculated based on the number of sleeping spaces, with a ratio of one LLIN per sleeping space. Community volunteers were also trained in the use of smartphones to collect household data (socio-demographic, health seeking behaviour, use of malaria prevention measures, etc.) and delivered educational messages about malaria and the importance of net use.

Study design and sample size

A cross-sectional household based survey was conducted two months before and repeated six months after the mass LLIN distribution campaign. The pre-campaign survey took place in October 2014 and the post-campaign survey was conducted in July 2015. Sample size calculation was based on LLIN coverage of 55% before the campaign (Kinshasa School of Public Health 2012, unpublished report) and 85% after the campaign, a precision of 5% and 80% power. The resulting number of HZ to be sampled was calculated as 10 for the pre-campaign survey and 22 for the post-campaign survey (of which the 10 HZ from the pre-campaign survey were kept). In both surveys, 51 households were sampled per HZ.

A multi-stage cluster sampling method was used to select households. Health Zones were randomly selected from a complete list. To ensure sufficient representation from the door-to-door strategy (conducted in 9 of the 44 HZ), two of the 10 pre-campaign HZ and five of the 22 post-campaign HZ were randomly selected from those nine that received the door-to-door strategy. In each selected HZ, three HA were randomly selected from a complete list. In each HA, an exhaustive list of streets (for urban areas) and villages (for rural areas) with their corresponding populations was drawn up and three streets or villages were randomly selected from this list. A total of 17 households were sampled in each HA (to give a total of 51 households per HZ) and the number of households to be surveyed in each of the three selected villages/streets from the HA was proportional to the size of the street or village. Households were identified by systematic random sampling. A total of 509 households were surveyed in the pre-campaign and 1,121 in the post-campaign.

Data collection

Household survey questionnaire

In all selected households the head or another responsible member of the household was interviewed after written informed consent was obtained. Interviewees were asked questions on all household members (sex, education level, occupation, whether they slept under net previous night),

on all nets in the household (type, source, location and if it was slept under the previous night) as well as general information about the house including number of sleeping spaces and malaria knowledge. LLIN ownership and use were established by respondent self-report, however data collectors also requested to observe all nets available in the household at the time of the visit. The survey teams recorded the presence of material goods in the household such as radios, electricity and various types of livestock, and also noted types of toilets, types of roof and wall construction. From this, a composite household wealth index was created using a principal components analysis (PCA) to determine households' socioeconomic status (Vyas and Kumaranayake, 2006).Longitude and latitude coordinates of all surveyed households were recorded on-site using the integrated Global Positioning System (GPS) of the data collection devices. Data were collected using a standardised questionnaire electronically programmed on tablets (Samsung Tab 3) running Google Android operating system and equipped with Open Data Kit software (ODK, University of Washington & Google Foundation). This questionnaire was adapted from the standard Malaria Indicator Survey household questionnaire from the Roll Back Malaria (RBM) partnership (RBM, 2013). It was developed in French with oral translation into local language and dialects, and pre-tested prior to use in the field. After daily quality control checks by field supervisors, completed data were sent regularly to the central server housed at the Swiss Tropical and Public Health Institute (Swiss TPH) for distant access and verification by members of the coordination team.

Blood testing

During the post-survey only, all eligible children aged 6 to 59 months present in surveyed households were tested for malaria using the SD Bioline three bands *Plasmodium falciparum/*Pan malaria Rapid Diagnostic Test (mRDT) (Standard Diagnostics, Kyonggi, Republic of Korea) and had haemoglobin levels measured using a blood haemoglobin photometer (HemoCueHb201+ Ängelholm, Sweden). Children with positive malaria tests were given free treatment with an artemisinin-based combination therapy (ACT), in particular artesunate-amodiaquine (AS-AQ), the official first-line malaria treatment at the time of the survey in the DRC. For children with signs of complicated malaria or low haemoglobin levels, parents were advised to visit the nearest health facility.

Collection of cost data

A comparative financial cost analysis between the fixed delivery and door-to-door distribution strategies was carried out from the provider's perspective, which was defined as the cost incurred by implementation agencies. All the distribution activities including LLIN procurement and

delivery were conducted separately by the two implementation agencies. Cost components of each distribution strategy were identified using the ingredients approach. Costs were collected retrospectively using financial expenditure records to capture financial costs from the accountant service of the implementing agencies using a standardised spread sheet developed by the NMCP. Costs related to research activities were excluded. The procurement cost of LLIN including purchase cost, shipment and custom clearance were included in the analysis. For the fixed delivery strategy, some of the costs were collected in Great British Pound (GBP) and converted into US Dollars (USD) applying the 2015 –year of expenditure- average exchange rate of USD 1,5283 to the GBP (OANDA, 2013). For the door-to-door strategy, costs were collected in USD. For each distribution strategy the delivery cost per LLIN (i.e. total cost per net delivered) was calculated. Calculations of 'per LLIN' costs under each distribution strategy were based on the total number of LLINs recorded as distributed per strategy. Costs are presented in 2015 USD.

Measurements and indicators' definition

Standard malaria household survey indicators were measured as recommended by the RBM Monitoring and Evaluation Reference Group (MERG) (RBM, 2013) as follows: Prevention indicators: 1) Proportion of households with at least one LLIN; 2) Proportion of households with at least one LLIN for every two people; 3) Proportion of population with access to a LLIN within their household. This indicator estimates the proportion of the population that could potentially be covered by existing LLIN, assuming each LLIN can be used by two people within a household. The calculation used took into account those household members who actually slept under an LLIN the previous night considered as having access to a LLIN within the household. The indicator needs an intermediate variable which is "potential users" calculated by multiplying the number of LLIN in each household by two. The indicator is then calculated by dividing the sum of all potential and actual LLIN users in the sample by the total number of individuals who spent the previous night in surveyed households. Full details are described by Kilian *et al. (Kilian et al., 2013)*; 4) Proportion of population that slept under a LLIN the previous night; 5) Proportion of children under five years old who slept under a LLIN the previous night; 6) Proportion of pregnant women who slept under a LLIN the previous night; 7) Proportion of existing LLINs used the previous night. Case management indicators: 8) Proportion of children less than five years old with fever in the last two weeks who had a finger or heel stick; 9) Proportion of children less than five years old with fever in the last two weeks for whom advice or treatment was sought; 10) Proportion receiving an ACT (or other appropriate treatment), among children less than five years old with fever in the last two weeks who received any anti-malarial drugs. Morbidity indicators: 11) Malaria prevalence, defined

as the proportion of children aged 6-59 months with a positive mRDT; 12) Anaemia prevalence, defined as the proportion of children aged 6-59 months with haemoglobin rate <8g/dl.

Data management and analysis

Data were extracted from the ODK aggregate server using the ODK Briefcase in the CSV format and imported into STATA version 13 (Stata Corporation College Station, TX, USA) for statistical analysis. Dichotomous outcomes were summarised as proportions with 95% confident intervals. Continuous outcomes were described using their mean and standard deviation, or median and 90% central range if the distribution was skewed. The Pearson chi square was used to compare proportions. Bivariate associations between the primary outcome and hypothesised explanatory variables were first done to guide subsequent model building; odds ratios and 95% confidence intervals were produced using logistic regression. After testing individual bivariate associations, a backward selection procedure was used to create an optimal multivariate model while adjusting for potential confounders. To take into account clustering by HZ and HA, a multi-level mixed effects logistic regression model was used to assess the association between the outcome and explanatory variables. Clustering at street/village level was not accounted for in the analysis; clustering by HZ and HA explains most of the variability in the sample. Results are presented as adjusted odds ratios with their 95% confidence intervals.

4.4 Results

Households characteristics

Table 4.1 displays the characteristics of all surveyed households. During the pre-campaign survey, a total of 509 households were visited across 10 HZ including 3,227 people of which 51.5% were female. The median (90% central range) number of persons per household was 6 (2-12); the median number of children less than five years of age per household was 1 (0-3). In the post-distribution survey, 1,121 households were sampled of which 868 were from HZ that received LLIN through the fixed delivery strategy and 253were from HZ that received LLIN through the door-to-door strategy. In total, 6,157 people lived in the households surveyed, 4,886 in HZ with fixed strategy and 1,271 in HZ with door-to-door strategy and in both strategies, about half (50.5%)of the survey population were female (fixed: 50%; door-to-door:52.5%). The median number of persons per household was 5 (2-10) [fixed: 5 (2-10); door-to-door: 5 (2-9)] and the median number of children less than five years of age per household was 1 (0-3) [fixed: 1 (0-3); door-to-door: 1 (0-2)].

Table 4.1 Characteristics of surveyed households.

Characteristics	Survey		Post survey by delivery strategy	
	Pre	Post	Fixed	Door-to-door
Number of households	509	1121	868	253
Number of individuals in sampled households	3227	6157	4886	1271
Percent female	51.5	50.5	50.0	52.5
Median (90% central range) number of people per household	6 (2-12)	5 (2-10)	5 (2-10)	5 (2-9)
Median (90% central range) number of children under 5 per household	1 (0-3)	1 (0-3)	1 (0-3)	1 (0-2)
Median (90% central range) number of nets per household	0 (0-2)	2 (0-4)	2 (2-4)	2 (2-4)

Households' LLIN ownership and intra household access to LLIN

Table 4.2 shows key malaria household indicators before and after the campaign. Table 4.3 shows post-distribution indicators by distribution strategy. The proportion of households owning at least one LLIN increased from 39.4% [95% CI: 32.2%-47.0%] before the distribution to 91.4% [95% CI: 88.8%-93.4%] after the distribution (Table 4.2). Household ownership of at least one LLIN after the distribution was significantly higher in HZ with fixed delivery strategy compared to those with door-to-door strategy with a mean of 92.5% [95% CI: 90.2%-94.4%] versus 85.2% [95% CI: 78.5%-90.0%],respectively ($\chi 2$=5.71 p=0.026) (Table 4.3).

LLIN universal coverage, measured as the proportion of households with at least one LLIN for every two people increased from 4.1% [95% CI: 2.5%-6.5%] in the pre-campaign to 41.1% [95% CI: 36.1%-46.2%] in the post-campaign (Table 4.2). After the distribution, the proportion of households owning at least one LLIN for every two people was significantly higher in HZ with fixed delivery strategy compared to HZ with door-to-door strategy with a mean of 44.1% [95% CI: 38.7%-49.7%]versus 30.9% [95% CI: 22.7%-40.6%], respectively($\chi 2$=5.14 p=0.034) (Table 4.3).The average number of LLIN in the surveyed households was approximately one for every 2.5 people (Fixed:1 LLIN:2.4; door-to-door: 1 LLIN:3).

To assess the performance of each delivery strategy, the proportion of households reached during the campaign (proportion of households with at least 1 LLIN from the campaign) was calculated while the proportion of households with sufficient LLIN (1 LLIN for every two people) was calculated among those households that received at least 1 LLIN from the campaign to assess the

efficiency of each allocation method. The proportion of households with at least 1 LLIN from the campaign (households reached) was significantly higher in HZ that received LLIN through fixed delivery strategy compared to those that received LLIN through the door-to-door strategy with a mean of 91.4% [95% CI: 89.1%-93.7%] *versus* 79.0% [95% CI: 70.2%-87.8%],respectively ($\chi 2$=13.87 p<0.001). Among households reached, the proportion of those that received enough LLIN (1 LLIN for 2 people) did not significantly vary by net allocation method (net per person: 50.0% [95% CI: 45.6%-54.5%]; net per sleeping space: 42.7% [95% CI: 29.2%-56.2%]; $\chi 2$=1.90p=0.186).

In households containing more than four people, regardless of the delivery strategy, the mean number of LLIN received from the campaign was consistently lower than the WHO recommendation of one LLIN for every two people (Figure 4.2). Population access to LLIN within the household increased from 22.2% [95% CI: 17.9%-27.3%] pre-campaign to 80.7% [95% CI: 76.8%-84.6%] post campaign (Table 4.2). The post distribution access to a LLIN within the household did not vary by distribution strategy (fixed: 85.0% [95% CI: 81.1%-88.2%]; door-to-door: 75.8% [95% CI: 65.3%-83.9%]; $\chi 2$=2.45 p=0.131) (Table 4.3).

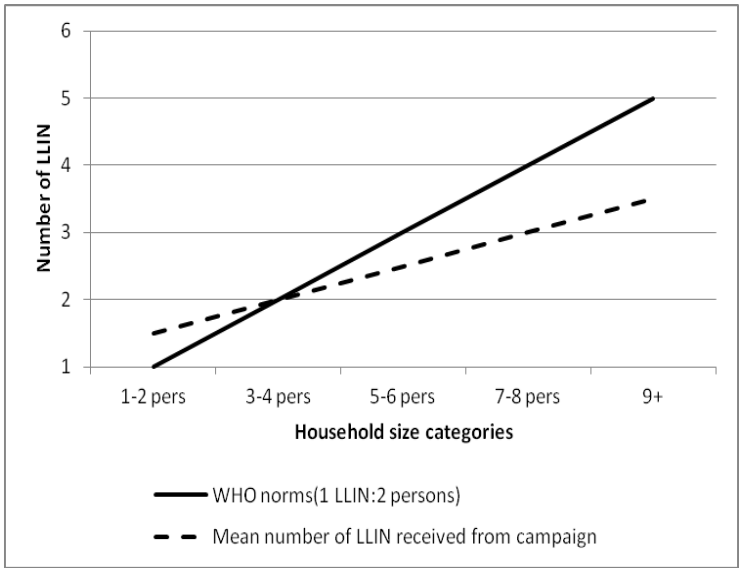

Figure 4.2 Number of LLINs received from the mass distribution campaign, by household.

LLIN use

Overall LLIN use increased from 18.0% [95% CI: 14.5%-22.2%] in the pre-distribution survey to 68.3% [95% CI: 62.9%-73.3%] after distribution. The overall use of LLIN was not statistically different between HZ with different distribution strategies (fixed: 69.60% [95% CI: 63.1%-75.5%]; door-to-door: 65.7% [95% CI: 52.7%-76.7%]; $\chi 2$=0.07p=0.791) (Table 4.3).

Before the mass distribution campaign, LLIN use was lowest among the poorest wealth quintile and progressively increased with increasing wealth with a concentration index of 0.12 [95% CI:0.02-0.22]. After the distribution no specific pattern was observed in the LLIN use with regard to the socio economic status of the household with a concentration index of 0.02 [95% CI:0.00-0.02]. Figure 4.3 presents the Lorenz concentration curve describing the equity in LLIN use before and after the campaign.

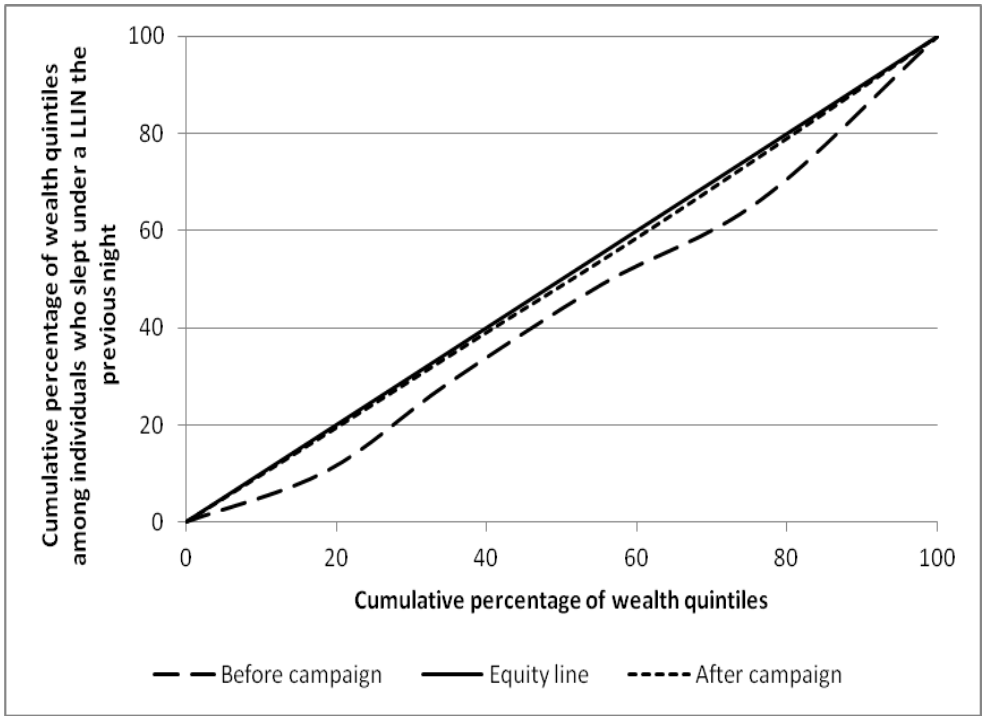

Figure 4.3 Lorenz concentration curve showing equity in LLIN use before and after the campaign.

After the mass distribution, LLIN use was significantly higher in households with universal coverage (1 LLIN for 2 people) with a mean of 82.0% [95% CI: 76.6%-87.4%] *versus* 58.4% [95% CI: 52.2%-64.6%] ($\chi 2$=44.70 p<0.001). During both pre- and post-distribution surveys, at least 80 %(pre: 81.1%; post: 84.6%) of the population with access to a LLIN within their household slept under it the previous night (Figure 4.4).

Approximately one quarter (23.8%) of children less than five years of age slept under a LLIN before the distribution while there were three quarters (73.7%) after the distribution (Table 4.2). The post-distribution use of LLIN by children less than five years of age did not vary by distribution strategy (Fixed: 74.8% [95% CI: 67.9%-80.7%]; door-to-door: 71.6% [95% CI: 57.2%-82.6%]) (Table 4.3).

In both pre- and post-distribution surveys, the use of LLIN varied strongly across different age groups, with the lowest use rate observed in the age group of 5-19 years old (Figure 4.5A). Even in households with universal coverage (1 LLIN for 2 people), age specific use of LLIN consistently showed the same pattern (Figure 4.5B).

Use of LLIN by pregnant women increased from 20.9% [95% CI: 12.7%-32.4%] to 74.0% [95% CI: 63.9%-82.2%] before and after the distribution respectively (Table 4.2). The latter did not vary by distribution strategy (Fixed: 79.6% [95% CI: 64.0%-89.6%]; door-to-door: 65.0% [95% CI: 34.4%-86.9%]) (Table 4.3).

After the distribution campaign, on average 66.7% [95% CI: 61.5%-71.5%] of existing LLIN were used the previous night. This proportion was slightly higher in HZ with door-to-door strategy compared to those with fixed strategy with a mean of 76.9% [95% CI: 68.0%-83.9%] versus 63.7% [95% CI: 58.3%-68.8%] ($\chi 2$=9.01 p=0.007) (Table 4.3). On average, 2.4 sleepers shared the same LLIN the previous night. Overall, around 60% of existing LLIN used the previous night had one or two sleepers, considered as appropriate coverage while the rest had more than two sleepers.

During the post-distribution survey, about 60% of interviewed household members reported to have heard or seen a message on malaria or LLIN in the last thirty days. The most commonly mentioned sources of messages were community health workers (46.2%), health centres (33.7%) and radio (32.3%), TV and other mass media channels were mentioned by about 10 % of respondents. The most commonly recalled message content were “nets prevent malaria” (66.6%) and “use a net every night” (67.6%).

LLIN characteristics

During the post-distribution survey, a total of 2,479 LLINs were recorded in surveyed households; 2,121 (85.6%) of which were observed. Of the 2,121 LLIN observed, 70.6% [95% CI: 64.7%-76.4%] were hung at the time of the interview. The proportion of LLIN hung per strategy was significantly higher in HZ with door-to-door strategy compared to the fixed delivery strategy with a mean of 90.1% [95% CI: 86.0%-94.2%] versus67.5% [95% CI: 61.6%-73.3%] respectively ($\chi 2$=8.56 p=0.008). Nearly all (98%) of the LLINs observed in households during the post-distribution survey were marked Permanet® and were obtained from the mass distribution campaign.

Overall, 60% of households reported to have hung their LLINs the same day or the day following its reception but this proportion was higher in HZ with door-to-door strategy than in HZ with fixed delivery strategy (90.1% *versus* 52.6%).In HZ with fixed strategy, nearly all households (98.7%) reported their LLINs were hung by a household member, whereas in HZ with door-to-door strategy, over half of the households (56.5%) reported their LLINs were hung by a member of the distribution team and 43.5% by a household member. Nearly all households (97.7%) encountered no problems hanging their LLIN in both strategies.

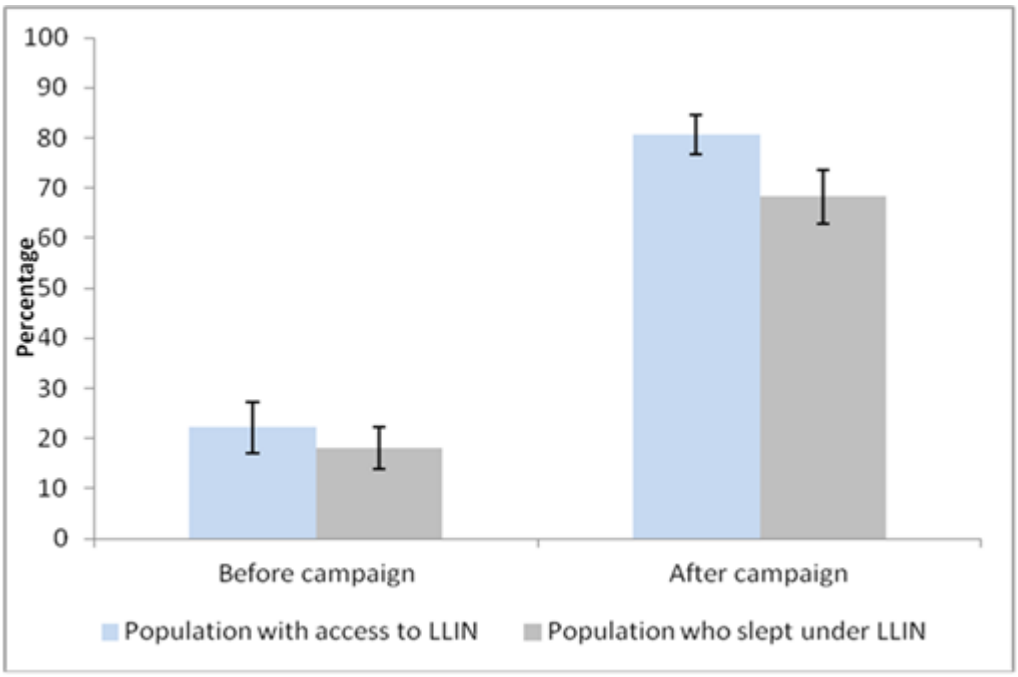

Figure 4.4 Population access and use before and after the mass distribution campaign.

Health seeking behaviour and malaria morbidity

Data on health-seeking behaviour and malaria morbidity were collected only during the post-distribution survey. More than one third (37.7% [95% CI: 29.5%-46.0%]) of children less than5 years old had fever in the two weeks preceding the survey. Advice or treatment was sought for 31.0% [95% CI: 23.1%-38.9%] of them and a quarter (26.1%; [95% CI: 20.5%-31.6%]) had a finger or heel prick. Among these children less than5 years of age who had fever in the two weeks before the survey and who received any anti-malarials, 32.6 % [95% CI: 15.7%-49.4%] received ACT (Table 4.2).

Malaria prevalence among children less than5 years old was 44.8 % (95% CI: 34.7%-55.0%) and the proportion of children aged 6-59 months with a haemoglobin measurement of <8 g/dl was

37.7% [95% CI: 29.5%-46.0%] (Table 4.2). Malaria and anaemia prevalence was not significantly different between distribution strategies (Table 4.3).

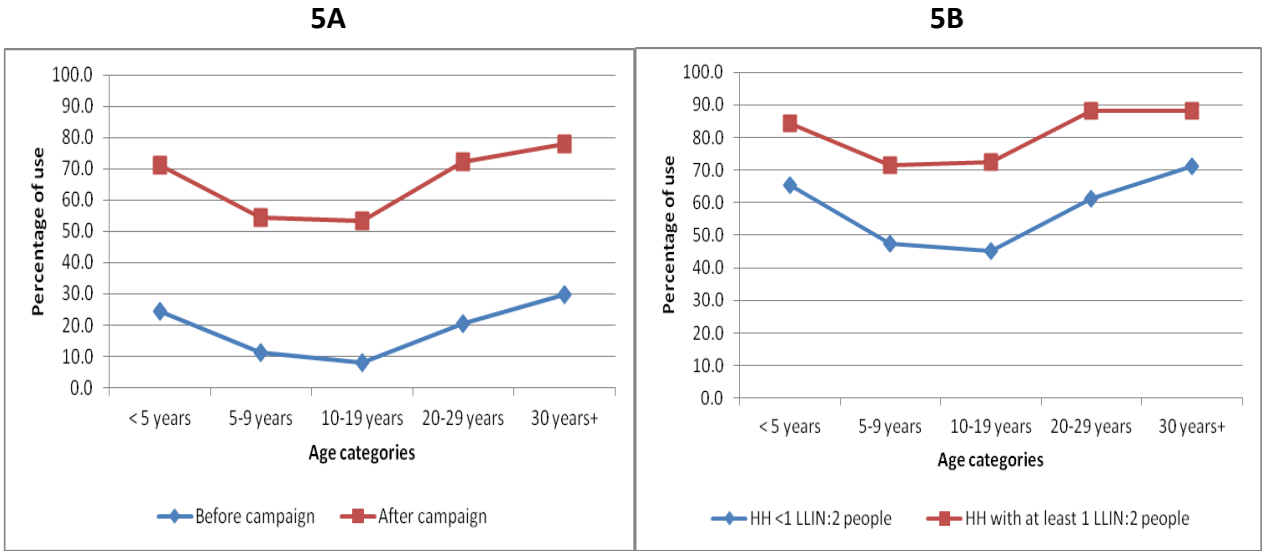

Figure 4.5 Age specific use of LLIN. 5A: Before and after the mass distribution campaign. 5B: By coverage level after the mass distribution campaign.

Table 4.2 Key malaria household survey indicators before and after the mass distribution campaign.

Indicators	Pre (% CI)	Post (% CI)	p-value
Proportion of households with at least one ITN	39.4 [32.2-47.0]	91.4 [88.8-93.4]	<0.001
Proportion of households with at least one ITN for every two people	4.1 [2.5-6.5]	41.1 [36.1-46.2]	<0.001
Proportion of population with access to an ITN in their household	22.2 [17.9-27.3]	80.7 [76.8-84.6]	<0.001
Proportion of the population that slept under an ITN the previous night	18.0 [14.5-22.2]	68.3 [62.9-73.3]	<0.001
Proportion of children <5 y who slept under an ITN the previous night	23.8 [18.0-30.6]	73.7 [67.8-78.9]	<0.001
Proportion of pregnant women who slept under an ITN the previous night	20.9 [12.7-32.4]	74.0 [63.9-82.2]	<0.001
Proportion of existing ITNs used the previous night	82.2 [75.9-87.2]	66.7 [61.5-71.5]	<0.001
Proportion of children <5 y with fever in the last two weeks		37.7 [29.5-46.0]	
Proportion of children <5 y with fever in last two weeks who had a finger or heel stick		26.1 [20.5-31.6]	
Proportion of children <5 y with fever in the last two weeks for whom advice or treatment was sought		31.0 [23.1-38.9]	
Proportion receiving an ACT (or other appropriate treatment), among children under five years old with fever in the last two weeks who received any anti-malarial drugs		32.6 [15.7-49.4]	
Proportion of children aged 6-59 months with malaria infection		44.8 [34.7-55.0]	
Proportion of children aged 6-59 months with a hemoglobin measurement of <8 g/dl		14.6 [11.0-18.3]	

Table 4.3 Key malaria household survey indicators by distribution strategy.

Indicators	Fixed (% CI)	Door-to-door (% CI)	$\chi 2$	p-value
Proportion of households with at least one ITN	92.5 [90.2-94.4]	85.2 [78.5-90.0]	5.71	0.026
Proportion of households with at least one ITN for every two people	44.1 [38.7-49.7]	30.9 [22.7-40.6]	5.14	0.034
Proportion of population with access to an ITN in their household	85.0 [81.1-88.2]	75.8 [65.3-83.9]	2.45	0.131
Proportion of the population that slept under an ITN the previous night	69.6 [63.1-75.5]	65.7 [52.7-76.7]	0.07	0.791
Proportion of children under five years old who slept under an ITN the previous night	74.8 [67.9-80.7]	71.6 [57.2-82.6]	0.12	0.729
Proportion of pregnant women who slept under an ITN the previous night	79.6 [64.0-89.6]	65.0 [34.4-86.9]	1.08	0.310
Proportion of existing ITNs used the previous night	63.7 [58.3-68.8]	76.9 [68.0-83.9]	9.01	0.007
Proportion of Children Aged 6-59 Months with Malaria Infection	37.8 [25.9-51.5]	64.9 [39.6-83.9]	2.78	0.110
Proportion of Children Aged 6-59 Months with a Hemoglobin Measurement of <8 g/dL	13.4 [10.1-17.6]	11.6 [6.6-19.6]	0.29	0.597

Determinants of LLIN use

The contribution of different factors associated with LLIN use before and after the distribution is shown in Table 4.4Table 4.5. During the pre-distribution survey, there was no evidence of association between use of LLIN and gender, while significant heterogeneities were observed in LLIN use among age groups. Compared to children less than5 years of age, individuals aged 5-19 years were significantly less likely to sleep under a LLIN (OR = 0.26 [95% CI: 0.19, 0.34])and those aged 30 years and above were significantly more likely to use a LLIN (OR = 1.40[95% CI: 1.06, 1.86]).A higher educational level of the head of the household was associated with increased odds of sleeping under a LLIN (OR = 2.67 [95% CI: 1.15, 6.19]). Individuals living in households whose head was employed were also significantly more likely to use a LLIN than those of other occupations (OR = 1.81 [95% CI: 1.06, 3.09]).There was no evidence of an association between LLIN use and the number of persons per sleeping space, the knowledge of malaria transmission or the exposition to a sensitisation message on malaria/LLIN. The least poor socio-economic quintile (compared with the poorest) was associated with significant increased odds of sleeping under a LLIN (OR = 2.79 [95% CI: 1.54, 5.07]).

Following the mass distribution, no association was found between gender and the use of LLIN as before. The age specific use of LLIN showed the same pattern as before the distribution, with the 5-19 years olds having the lowest odds of LLIN use (OR = 0.39 [95% CI: 0.33, 0.46]) and the 30 years and above being more likely to use a LLIN (OR = 1.46 [95% CI:1.21, 1.78]) compared with children less than 5 years. As before the distribution, occupation and educational level of the head of the household were significantly associated with the use of LLIN. There was no evidence of association between the use of LLIN and the distribution strategy. Individuals living in households whose head knew the cause of malaria (OR = 1.39 [95%CI: 1.16, 1.68]) or have heard about malaria or LLIN in the last month (OR = 1.57[95%CI: 1.34, 1.84]) were more likely to sleep under a LLIN. The socio-economic status of the household was not associated with LLIN use. Individuals living in households owning at least one LLIN for every two people had the highest odds of sleeping under a LLIN (OR = 3.79 [95%CI: 3.21, 4.49]).

Table 4.4 Logistic regression model showing determinants of LLIN use before the mass distribution campaign.

			Univariate analysis			Multivariate analysis		
Variable	***n***	**(%)**	**OR**	**95% CI**	***P*-value**	**OR**	**95% CI**	***P*-value**
Sex								
Male	1413	17.7	1			1		
Female	1582	19.1	1.17	0.96-1.43	0.118	1.15	0.93-1.42	0.190
Age								
<5 years	576	24.3	1			1		
5-19 years	1328	9.3	0.26	0.19-0.35		0.26	0.19-0.34	
20-29 years	383	20.6	0.73	0.52-1.02		0.80	0.56-1.13	
>=30 years	708	29.5	1.2	0.92-1.57	<0.001	1.40	1.06-1.86	<0.001
Education of the head of the								
No education	73	15.1	1			1		
Primary	640	11.3	1.06	0.50-2.22		1.20	0.55-2.63	
Secondary	2,066	18.2	1.8	0.89-3.64		1.59	0.74-3.42	
Superior and above	216	43.1	3.8	1.78-8.13	<0.001	2.67	1.15-6.19	0.010
Occupation of the head of the								
Without occupation	187	13.4	1			1		
Farmer	1,160	12.4	0.87	0.53-1.42		0.83	0.49-1.41	
Merchant	927	15.3	1.14	0.70-1.85		0.93	0.54-1.60	
Employed	721	33.4	2.42	1.51-3.90	<0.001	1.81	1.06-3.09	<0.001
Persons per sleeping space								
2 or less	1,752	19.18	1			1		
More than 2	1,243	17.38	0.79	0.64-0.97	0.025	1.04	0.58-1.88	0.889
Wealth quintile								
Poorest	558	10.6	1			1		
Second	496	20.4	2.67	1.78-4.00		2.38	1.54-3.68	
Middle	624	17.8	2.54	1.66-3.88		2.23	1.40-3.54	
Fourth	637	15.2	1.93	1.23-3.02		1.82	1.06-3.11	
Wealthiest	680	27.1	3.23	2.00-5.23	<0.001	2.79	1.54-5.07	<0.001
Knowledge transmission								
No	775	13.7	1			1		
Yes	2,220	20.1	1.29	0.98-1.29	0.064	1.20	0.89-1.60	0.226
Heard a message on malaria/ITN last								
No	1,113	16.4	1			1		
Yes	1,882	19.6	1.14	0.90-1.45	0.274	0.97	0.74-1.26	0.798

Table 4.5 Logistic regression showing determinants of LLIN use after the mass distribution campaign.

			Post distribution					
			Univariate analysis			Multivariate analysis		
Variable	***n***	**(%)**	**OR**	**95% CI**	***P*-value**	**AOR**	**95% CI**	***P*-value**
Sex								
Male	2746	66.4	1			1		
Female	2913	67.2	1.05	0.93-1.18	0.458	1.05	0.93-1.20	0.422
Age								
<5 years	1308	71.6	1			1		
5-19 years	2164	54.1	0.41	0.35-0.49		0.39	0.33-0.46	
20-29 years	706	72.5	1.03	0.83-1.28		0.97	0.77-1.23	
>=30 years	1481	78.4	1.49	1.24-1.79	<0.001	1.46	1.21-1.78	<0.001
Education of the head of the household								
No education	397	58.2	1			1		
Primary	1599	62	1.35	1.04-1.74		1.28	0.97-1.69	
Secondary	3265	68.8	2.08	1.63-2.66		1.92	1.46-2.52	
Superior and above	398	78.1	2.95	2.06-4.23	<0.001	2.29	1.52-3.45	<0.001
Occupation of the head of the household								
Without occupation	355	63.9	1			1		
Farmer	2748	63.8	0.91	0.70-1.19		1.40	0.94-2.09	
Merchant	1397	64.3	1.06	0.81-1.39		1.62	0.94-2.79	
Employed	1159	77.8	1.95	1.47-2.59	<0.001	3.73	1.75-8.38	<0.001
Persons per sleeping space								
2 or less	3722	70.0	1			1		
More than 2	1937	65.2	0.84	0.74-0.96	0.010	0.97	0.66-1.41	0.862
Distribution strategy								
Fixed	4577	67.2	1			1		
Door-to-door	1082	65.3	0.87	0.47-1.61	0.655	0.80	0.40-1.62	0.538
Wealth quintile								
Poorest	1114	63.6	1			1		
Second	1081	66.2	1.04	0.84-1.27		0.94	0.71-1.25	
Middle	1137	64.6	1.47	1.14-1.88		1.51	0.98-2.33	
Fourth	1105	68.3	1.72	1.33-2.23		1.84	0.98-3.37	
Wealthiest	1222	70.8	1.49	1.12-2.00	<0.001	1.53	0.67-3.46	0.061
Knowledge transmission								
No	1,121	62.1	1			1		
Yes	4,538	68.0	1.47	1.25-1.73	<0.001	1.39	1.16-1.68	<0.001
Heard a message on malaria/ITN last month								
No	2,110	61.4	1			1		
Yes	3,549	70.0	1.74	1.51-2.00	<0.001	1.57	1.34-1.84	<0.001
At least 1 LLIN/2 people								
No	3,730	58.79	1			1		
Yes	1,929	82.27	3.35	2.89-3.88		3.79	3.21-4.49	<0.001

Cost analysis

Costing details for both strategies are shown in Table 4.6. The total financial cost of the campaign from the provider perspective was USD 22.84 million (USD 18.71 million for the fixed delivery strategy and USD 4.13 million for the door-to-door strategy). The total financial cost per LLIN distributed was USD 6.59 (USD 6.58 for the fixed distribution strategy and USD 6.61 for the door-to-door strategy) of which USD 4.08 were used for LLIN purchase and custom clearance and USD 2.51 were for LLIN transport, storage, training, mobilisation/IEC, management and M&E. Overall, LLIN cost, transport and storage comprise around 80% (87.3% for the fixed delivery strategy and 70.3% for the door-to-door strategy) of the total financial cost. The cost of LLIN purchase was higher for the fixed strategy compared to the door-to-door strategy (USD 4.17 *versus* USD 3.66) while the non-LLIN costs were lower for the fixed strategy compared to the door-to-door strategy (USD 2.41 *versus* USD 2.95).

Table 4.6 Financial costs of the LLIN distribution by cost category and delivery strategy.

	Door-to-door			Fixed			Combined		
Number of LLIN distributed	624,532			2,843,442			3,467,974		
Total financial cost (2015 USD)	4,130,050			18,706,824			22,836,874		
Financial cost per LLIN delivered	6.61			6.58			6.59		
Cost of LLIN Campaign (2015 USD) per category	**Cost**	**Cost per LLIN**	**% of cost**	**Cost**	**Cost per LLIN**	**% of cost**	**Cost**	**Cost per LLIN**	**% of cost**
LLINs	2,287,500	3.66	55.4	11,858,176	4.17	63.4	14,145,676	4.08	**61.9**
Transport and storage	613,920	0.98	14.9	4,477,243	1.57	23.9	5,091,163	1.47	**22.3**
Personnel	567,484	0.91	13.7	555,023	0.20	3	1,122,507	0.32	**4.9**
Trainings	140,997	0.23	3.4	660,994	0.23	3.5	801,991	0.23	**3.5**
Office, supplies and equipment	438,654	0.70	10.6	566,167	0.20	3	1,004,821	0.29	**4.4**
IEC	20,995	0.03	0.5	469,300	0.17	2.5	490,295	0.14	**2.1**
M&E	60,500	0.10	1.5	119,921	0.04	0.6	180,421	0.05	**0.8**

4.5 Discussion

Concerted efforts to scale up LLIN coverage through a free mass distribution campaign in the Kasaï Occidental province have rapidly increased ownership and use of LLIN. In terms of coverage, RBM targets of 80% of households owning at least one LLIN and 80% of population having access within their household have been achieved. Universal coverage (defined as households with at least one LLIN for every two people) though below the 80% target, has shown a remarkable tenfold increase from 4% to 41%. These findings are consistent with what is known about the effectiveness of mass distribution campaigns to quickly scale-up LLIN coverage in low coverage areas (Bonner *et al.*, 2011, Bennett *et al.*, 2012, Renggli *et al.*, 2013, Larson *et al.*, 2014). However, considering there had been a previous mass distribution campaign in 2011 with high coverage values, the ownership and use indicators found in the pre-distribution survey were surprisingly low.

Following a universal free mass distribution campaign, the fact that less than half of surveyed households had at least one LLIN for every two people can be surprising. This highlights a limitation of the distribution campaign in quantifying the number of LLIN allocated per household, in particular for households of more than four members. A study conducted in Sierra Leone six months after a mass distribution campaign also showed that when limiting the maximum number of LLIN one household can receive, households with more than five residents were less likely to have sufficient LLIN to cover all occupants (Bennett *et al.*, 2012).

Despite a dramatic increase in LLIN access and use overall, significant heterogeneities were observed in LLIN use among age groups, with the lowest use rate observed in the age group of 5-19 years old. The age specific pattern we observed has been reported by other researchers in different contexts including DRC, (Auta, 2012, Loha *et al.*, 2013, Kateera *et al.*, 2015, Ferrari *et al.*, 2016a).Interestingly, in this study, the same pattern was observed even in households possessing sufficient numbers of LLIN to cover all residents, suggesting a behavioural gap in LLIN use among older children and adolescents. The lower LLIN use rate obviously put this age group at higher risk of malaria prevalence as reported in other studies (Ferrari *et al.*, 2016b, Nankabirwa *et al.*, 2014).

Findings from this study also showed that both before and after the campaign, at least 80% of those with access to a LLIN used it the previous night. While remarkable efforts are made to increase access to LLIN, it is also important that the NMCP focus on developing behaviour change

communications strategy and plan to promote LLIN use in the general population as well as in specific group such as older children and adolescents.

Contrary to what could be expected, results of this study showed that the fixed delivery strategy reached a much higher proportion of households compared to the door-to-door strategy with 91.4% of households with at least 1 LLIN from the campaign *versus* 79.0% respectively. However, among those households reached by either strategy, the net allocation method (which differed by strategy) did not influence whether a household had sufficient LLIN for one per two people. A multi country comparison of LLIN delivery strategies based on 14 surveys from five African countries did not find a significant association between delivery strategy and ownership of a net from the campaign but found a positive association between sleeping space allocation and enough LLIN in the household (Zegers de Beyl *et al.*, 2016).

Only half of surveyed households in areas where the hang up approach was implemented reported their LLIN was hung by a member of the distribution team. However, of those that were hung by a member of the distribution team, a higher proportion were still hung and used the previous night compared to those not hung by a member of the distribution team as also noted by other researchers (Bennett *et al.*, 2012, Macintyre *et al.*, 2012). However this did not necessarily result in higher LLIN use rates among the population, indicating that the distribution strategy has no influence on LLIN use. A cluster randomised controlled trial conducted in Uganda showed that additional hang up activities following a mass distribution campaign did not provide any additional impact on net use (Kilian *et al.*, 2015a). In this study, the strongest determinant of LLIN use – having sufficient LLIN to cover all households' residents – did not differ significantly by distribution strategy.

As could be expected after a free LLIN mass distribution campaign that targeted the entire population at risk for malaria, equity in household LLIN coverage and individual use of LLIN has been improved as demonstrated by the Lorenz curve meeting the equity line as well as the concentration index shifting from positive to close to zero values. These findings corroborate results from other mass distribution campaigns showing equitable LLIN ownership and use (Noor *et al.*, 2007, Thwing *et al.*, 2008, Ye *et al.*, 2012, Renggli *et al.*, 2013).

Despite higher coverage and reported use of LLIN six months after a free mass distribution of LLIN, malaria prevalence among under-fives remains high in the province. The overall malaria prevalence among children aged 6-59 months found in this study was higher than the national

average of 31% prevalence reported by the DHS (Ministère du Plan *et al.*, 2014). This high malaria prevalence rate calls for further investigation of possible contributors. As an attempt to identify factors explaining high malaria rates in northern Ghana, Monroe *et al.* found that under-usage of LLINs at times when they could confer maximum protection as well as a variety of outdoor night-time activities, including outdoor sleeping were factors that could have potentially contributed to high rates of malaria in that setting (Monroe *et al.*, 2015).In this study, the prevalence of anaemia was high and consistent with findings of other researchers (Ferrari *et al.*, 2016b), however additional factors common in this setting such as malnutrition (Ministère du Plan *et al*., 2014) and sickle cell anaemia (Tshilolo *et al*., 2009) play a role in the occurrence of this condition.

Access to diagnostic testing and malaria treatment is very low; efforts should be made to increase availability of mRDT and ACT in both public and private sectors. To estimate the cost of implementation, a comparative financial cost analysis providing the cost per LLIN delivered was more suitable than a cost effectiveness analysis. For both fixed delivery distribution and door-to-door strategies, the average cost per LLIN distributed was consistent with findings of other researchers (White *et al.*, 2011). As expected, the highest proportion of cost was attributable to the purchase cost of the LLIN. Compared to the fixed strategy, the average cost per LLIN distributed was slightly higher in the door-to-door strategy with the personnel cost being the second highest single cost position after LLINs. This is consistent with the additional cost associated with hang up activities as reported by other researchers (Kilian *et al*., 2015a, Smith Paintain *et al.*, 2014). While the overall non-LLIN cost was lower for the fixed delivery strategy, the costs of transportation and storage were higher for the fixed delivery strategy compared to the door-to-door strategy. The fact that the 35 HZ with fixed delivery strategy were spread over 4 districts whereas the 9 HZ with door-to-door strategy are all in 1 district might have resulted in higher logistics costs in fixed delivery strategy.

This study has limitations. Although interviewers were required to observe LLINs owned by households, most net results reported in this study relies on data reported by respondents, thus they are prone to recall and information bias. LLIN may be more subject to over-reporting due to social desirability bias. As mRDTs were used for malaria diagnostic and parasite antigens (detected by the test) often persist up to two weeks post-treatment, some children previously treated for malaria might have tested positive within 14 days after treatment.

4.6 Conclusions

This study demonstrates substantial improvements in LLIN coverage, use and equity. Although all RBM targets were not met, much progress has been made. In addition to antenatal and vaccination clinic programmes, other LLIN distribution strategies should be explored as part of a keep-up strategy in order to maintain high and equitable coverage over time. The very low ownership and use levels observed before the campaign in this study despite a previous mass distribution campaign in 2011 is a stark reminder of the need for a keep-up mechanism.

These results also suggest a revision of distribution guidelines especially with regard to LLIN quantification to better cover larger households and those not reached by the mass distribution campaign. Having sufficient numbers of LLIN to cover all residents in the household was the strongest determinant of LLIN use. As access to LLIN is increasing, results of this study suggest that behaviour change strategies should focus on interpersonal interventions to promote LLIN use in the general population and specific groups such as older children and adolescents. In the context of the present study setting, a fixed delivery strategy seems to be a better LLIN delivery option, as it was shown to be associated with higher levels of LLIN coverage and use indicators as well as lower delivery cost.

5. Malaria case management by Community Health Workers in the Central African Republic from 2009-2014: overcoming challenges of access and instability due to conflict

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Published in
Malaria Journal, 2017, **16**: 388

5.1 Abstract

Background

In the Central African Republic (CAR), decades of armed conflict have crippled the public health system. This has left the population without timely access to life-saving services and therefore vulnerable to the numerous consequences of infectious diseases, including malaria. As a response, in 2008 an international non-governmental organization started a network of community health workers (CHWs) in the highly malaria-endemic region of northwest CAR. The area has experienced years of violent clashes between rebel groups and seen hundreds of thousands of people displaced.

Methods

Data from routine patient registers from 80 CHWs working in Paoua and Markounda sub-prefectures were entered and retrospectively reviewed. The time period covered December 2009–April 2014 and hence different stages of conflict and unrest. Several indicators were measured over time, including malaria rapid diagnostic test (RDT) positivity rates, CHW reporting rates, and malnutrition indicators.

Results

Among nearly 200,000 people who consulted a CHW during this period, 81% were found to be positive for malaria parasites by RDT. In total, 98.9% of these positive cases were appropriately treated with artemisinin-based combination therapy (ACT). Only 1.2% of RDT negative cases were incorrectly treated with an ACT. Monthly data from each CHW were regularly reported, with more than 96% of CHWs reporting each month in the first 3 years of the project. However, since the coup d'état in March 2013, the number of CHWs reporting each month decreased as the programme battled the additional constraints of civil war.

Conclusions

Although the political crisis affected the CHWs, the programme showed that it could reach those most vulnerable and continue some level of care at all times. In addition, this programme revealed that surveillance could be maintained in conflict zones. This paper fills a significant gap in the knowledge of malaria control in CAR and this is especially important for agencies which must often decide in a short space of time how to respond effectively to complex emergencies.

Key words: Malaria, Central African Republic, Conflict, Community Health Worker, Emergencies.

5.2 Introduction

The disruptive impact of armed conflict on a country's health system has been well documented. It destroys infrastructure, impedes delivery of essential medical supplies, causes large-scale flight of qualified medical staff, and displaces populations; this leads to deterioration in living conditions and increased exposure to infectious diseases (Connolly *et al.*, 2004, Gayer *et al.*, 2007). It also leads to decreased access to fundamental health care, resulting in excess morbidity and mortality, which in sub-Saharan Africa are predominantly due to infectious diseases, such as malaria (Anderson *et al.*, 2011).

Geostatistical analysis using a mixed model approach found that the distance from armed conflicts as well as the duration and violence have been shown to have significant influence on malaria parasite rates (Sedda *et al.*, 2015). This is not surprising when considering that conflict is synonymous with multiple risk factors that are known to increase malaria transmission, including the disruption of control programmes (Fürst *et al.*, 2009). Unfortunately, evidence today suggests that such emergencies in sub-Saharan Africa are not only increasing but also becoming more complex (IEP, 2016). Therefore, as conflicts play a crucial role in the operational feasibility of malaria control programmes, it is essential to adapt the strategies used during peace time to emergency conditions and document their implementation (Rowland and Nosten, 2001).

The Central African Republic (CAR) is a country that has been plagued by violence and political instability since its independence from France in 1960 (Berman and Lombard, 2008). Frequent and violent clashes between rebel groups regularly force people to flee their homes. The fragile political situation has seen five *coup d'états* since independence (IOM, 2014). The most recent, in March 2013, saw the country descend into chaos once more, displacing hundreds of thousands of people. The impact on the health system has been dramatic. Essential medicines have been looted from hospitals all over the country, resulting in an inability for the state to provide care (WHO, 2014).

Difficulty to access care combined with a lack of quality data within the health sector in CAR means national health facility-based surveillance is almost non-existent. Such surveillance data are vital to improve knowledge about how the epidemiology of malaria changes as the political, social and population displacement conditions evolve at both local and national level. Data are required to guide future policies and plans adapted to fragile settings.

As a result of this lack of surveillance, very little is known about the epidemiology of malaria in CAR, except reports suggest that it is the leading cause of under-five mortality and accounts for approximately 40% of hospitalizations across the country (MSF, 2011). In 2008, the international non-governmental organisation (NGO) called The MENTOR Initiative launched a community health worker (CHW) programme in two sub-prefectures of northwest CAR as a way to improve access to malaria case management for vulnerable populations, including children under 5 years, pregnant women and displaced persons. The NGO worked on the assumption that trained CHWs continue to provide basic care to their communities even when these are on the move or in new settlements. The programme began during a time of instability, when clashes between local rebel groups were the main cause of displacement.

Extensive evidence has demonstrated the effectiveness of CHWs for malaria control. As a result, decentralizing medical services from health facilities to the community has become a widely accepted strategy for facilitating early malaria treatment. Studies have shown that CHWs are capable of safely and accurately diagnosing malaria with rapid diagnostic tests (RDTs) if sufficient training and job aids are provided (Harvey *et al.*, 2008, Khalid *et al*., 2009). Furthermore, training CHWs to administer artemisinin-based combination therapy (ACT) to malaria-confirmed patients significantly decreases inappropriate anti-malarial use (provided that ACT supply is maintained). This is an effective way of improving overall child health and reducing patient burden in health facilities (Sievers *et al.*, 2008, Yeboah-Antwi *et al.*, 2010). However, these studies have been conducted in politically stable settings, where some form of health system is in place to manage the supply chain and supervise the CHW work. A search of available literature revealed no prior evidence on the impact of a CHW approach in conflict settings.

This study assesses the feasibility and sustainability of a CHW strategy during an ongoing conflict in CAR. The programme in CAR continued running and collecting data from 2009 to 2014, offering a unique opportunity to observe malaria trends during conflict as well as across seasons. It reports on the achievements of the CHW project, its ability to conduct surveillance as well as its challenges and limitations. As the security situation in CAR remains fragile, this analysis is essential to guide the next steps in malaria control in CAR and similar settings and to minimise the consequences of reduced access for those most vulnerable to malaria.

5.3 Methods

Study site

The CAR is a vast but sparsely populated country of about 623,000 sq km with an estimated population of 4.9 million (WHO, 2015a). It is bordered by Cameroon to the west, Chad to the north, Sudan and Southern Sudan to the east, and the Democratic Republic of Congo (DRC) and the Republic of Congo to the south.

The intervention and study site is located in Ouham and Ouham-Pendé Prefectures in northwest CAR, where it is estimated that over 200,000 persons are displaced. More specifically, the community-based malaria control programme is located in Paoua sub-prefecture (Ouham-Pendé) and Markounda sub-Prefecture (Ouham) (Figure 5.1). The total population in these sub-prefectures is an estimated at 222,000 (200,000 in Paoua and 22,000 in Markounda). While it is difficult to have a clear picture of the number and exact locations of internally displaced persons, many are thought to be in the programme areas. The region is holo-endemic for malaria, with peaks during the rainy season (May–October).

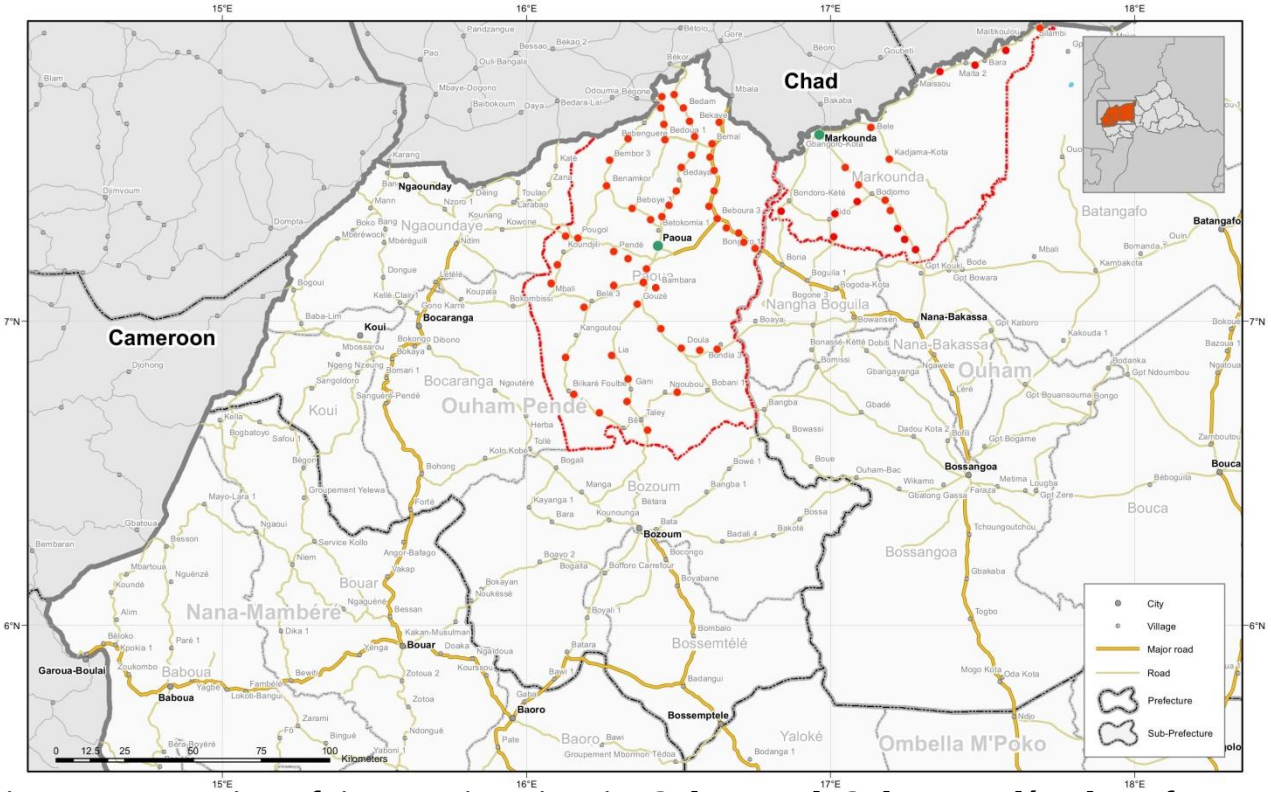

Figure 5.1 Location of intervention sites in Ouham and Ouham-Pendé sub-Prefectures (*outlined in red*) in North-West CAR. Each *red dot* represents the location of a CHW. Adapted from a UNDP map produced by the Office of the UN Resident and Humanitarian Coordinator 2008.

Description of the intervention

The CHW intervention was designed to target the most vulnerable displaced and host populations with the aim of reducing morbidity and mortality by improving access to quality health care at community level. It began in 2008 in Paoua and in 2011 in Markounda. It is ongoing in both areas. The focus is on malaria case management for children under 5 years and pregnant women, the groups most vulnerable to severe forms of the disease if they are not treated immediately. The programme began with 30 CHWs, known locally as malaria agents, in Paoua and expanded to 60 by 2011, with an additional 20 CHWs that began activities in Markounda in December 2011. In these 80 villages, literate volunteers were selected by the NGO programme management in close collaboration with community leaders. The CHWs were then trained by NGO-employed nurses or physicians over 5 days to implement basic health interventions in their homes, and sensitise their community members on prevention and treatment against infectious diseases. A 3 day refresher training took place every 6 months. Priority of the essential health services was given to malaria diagnosis and treatment. Every patient visiting a CHW from the surrounding area was tested with an RDT (SD Bioline Ag Pf®, Standard Diagnostics, Kyonggi, Republic of Korea) and all positive cases were treated with artemether–lumefantrine (AL). For patients with signs of severe malaria, according to the WHO severe malaria management guidelines, CHWs administered rectal artesunate (Artesiane® Suppogel Artemether 40 mg (Dafra Pharma GmbH, Basel, Switzerland)) before referring them to the nearest health facility. The CHWs also conducted malnutrition screening using the mid-upper arm circumference measurement (MUAC) for all children from 6 to 59 months, classifying them into four categories: well-nourished (>135 mm); at risk of acute malnutrition (125–135 mm); moderate acute malnutrition (110–125 mm); severe acute malnutrition (<110 mm). All children identified as severely malnourished were referred to the nearest NGO-supported treatment centre.

Additional components of the intervention for children under 5 included de-worming with mebendalzole every 6 months, rehydration treatment with oral rehydration solution in case of diarrhoea and administration of vitamin A. For pregnant women, additional interventions included intermittent preventive treatment with sulfadoxine-pyrimethamine, and folic acid supplements, and when available, provision of home delivery kits. Limited prevention campaigns were conducted in this area throughout the study period. In 2010, CHWs distributed 41,194 long-lasting, insecticidal bed nets (LLINs) in Paoua and 4458 in Markounda (totalling approximately one LLIN per household). Additionally, 3830 LLINs were distributed to pregnant women consulting with CHWs

in 2010. No LLINs or indoor residual spraying (IRS) campaigns took place in the project area during 2011 and 2012. In the second half of 2013, CHWs distributed 32,900 LLINs in Paoua and Markounda.

All necessary materials and supplies were delivered every month to the CHWs at their homes. Trained staff employed by the NGO supervised each CHW two times per month, enabling quality control and stock replenishment. During these visits, the CHWs received 1 month of anti-malarial stock (based on the consumption from the previous month) plus 2 weeks of buffer stock. During times of increasing insecurity when supervisory visits were sometimes less frequent, the CHWs received 1 full month of buffer stock. To deter falsification of RDT results by CHWs, supervisors cross checked all RDTs during these supervision visits with the number of ACTs given out each month. CHWs were required to pay a financial penalty for any ACTs distributed without a corresponding positive RDT. As additional CHWs were recruited for new villages, the numbers of supervisors also increased proportionally. Each CHW was also responsible for conducting regular information education communication/behaviour change communication sessions on communicable diseases in their villages, as well as being available for specific campaigns, such as distribution of LLINs.

CHWs were responsible for keeping daily registers to record each patient consultation, including basic demographic information, symptoms, test results, and treatment given. The NGO-employed nurses were responsible for collecting the records during their supervision visits and then entering them into a database for basic analysis and reporting. CHWs received a financial stipend for their work, equalling an estimated US$30/month (20,000 CFA) to encourage them to be available for their community without need for additional employment. This amount was decreased from approximately US$50 (30,000 CFA)/month in May 2012 to align with the few *Médecins Sans Frontières* and International Committee of the Red Cross supported CHWs in other areas of the country.

Study design and population

To assess the ability of this community-based malaria control programme to provide malaria case management services and surveillance in a crisis setting, a retrospective descriptive study was done based on malaria case management data routinely collected by CHWs between December 2009 and April 2014 (53 months). Whilst the programme was launched in Paoua in 2008, reliable data recording tools were only fully established and implemented in December 2009. Therefore, only

data after this date were included in the analysis. The programme in Markounda began activities in December 2011. After April 2014 activities and monthly summary data analysis continued but the detailed data entry of individual patient data stopped due to decrease in funding.

The study population consisted of all suspected malaria cases (defined as patients presenting with fever >37.5 °C or having a history of fever in the last 24 h) as recorded by a CHW as well as pregnant women attending for intermittent preventive treatment. Patients of all ages and from any location were included in the study.

Data management and analysis

The routinely collected data recorded by CHWs were the basis for this analysis. The CHW registers were collected during monthly supervision sessions and the data were entered into EpiInfo (version 7, CDC, Atlanta, GA, USA) and retrospectively reviewed. Basic clinical and demographic data were recorded (age, gender, village of residence, symptoms, temperature), as well as diagnostic test results, any treatment given and whether the patient was referred to the nearest NGO-supported facility (for example in the case of signs of severe malaria). Data were analysed using STATA 11 (STATA Corp, College Station, TX, USA) to observe trends in malaria incidence during different stages of conflict, to assess the ability of the CHWs to manage uncomplicated malaria cases, and to evaluate the ability of such a programme to continue activities and conduct surveillance during conflict. Annual rainfall data were obtained from The World Bank Group (World Bank Group, 2012).

Malaria incidence rate was calculated as the number of RDT-confirmed cases per month divided by the total population at risk in the area covered by the CHW. Average RDT positivity rates were calculated per CHW instead of exact numbers of cases to take into account the increasing number of CHWs covering a larger area and therefore seeing more patients. The denominator of each monthly calculation also excluded the CHWs that did not report data for that month.

5.4 Results

Study population

A total of 198,382 people consulted with a trained CHW between December 2009 and April 2014 across both study sites. In total, 68.7% (136,265) were children under 5 years old and 8.9% (17,658) were pregnant women. The ages of patients ranged from newborn to 89 years, and 52.5% were

female. In total, 90.3% of these patients presented to CHWs in Paoua sub-prefecture where data were included since December 2009. Only 9.7% presented to CHWs in Markounda which has a much smaller population size and where activities did not begin until December 2011.

Malaria burden

Each person visiting a CHW was tested for malaria using an RDT. The overall test positivity rate from both study sites was 81.2% (161,052/198,382). Test positivity was higher in children <5 years [83.6% (113,875/136,266)] compared to pregnant women [64.9% (11,463/17,658)] (Table 5.1).

Table 5.1 Summary of treatment practices for malaria RDT-positive and -negative cases in the total population, as well as for children <5 years and pregnant women.

	Total population		Children <5		Pregnant women	
Total tested with mRDT	198,382		136,266		17,658	
mRDT positive	161,052	(81.2%)	113,875	(83.6%)	11,463	(64.9%)
mRDT positive treated with ACT	159,279	(98.9%)	112,490	(98.8%)	11,372	(99.2%)
mRDT positive treated with rectal artesunate	2,378	(1.5%)	2,165	(1.9%)	14	(0.1%)
mRDT positive treated with ACT/rectal artesunate	159,695	(99.2%)	112,864	(99.1%)	11,378	(99.3%)
	37,330	(18.8%)	22,391	(16.4%)	6,195	(35.1%)
mRDT negative	439	(1.2%)	263	(1.2%)	59	(1.0%)
mRDT negative treated with ACT	299	(0.8%)	252	(1.1%)	2	(0.03%)
mRDT negative treated with rectal artesunate	737	(2.0%)	514	(2.3%)	61	(1.0%)
mRDT negative treated with ACT/rectal artesunate						

Malaria incidence rates calculated separately for Paoua and Markounda populations are plotted in Figure 5.2. Data collected during the first year of the programme activities in Markounda (which began 4 years after Paoua) saw higher incidences than in Paoua, which decreased over time from an average of 314 per 1000 population per month in 2012 to 273 per 1000 population per month in 2013. Conversely, the annual incidence in Paoua increased from 140 per 1000 population in 2010 to 197 per 1000 population in 2013. There was also a distinct seasonality in the malaria incidence rate at both sites with a peak occurring every year during the rainy season (May–October). Rainfall did not significantly differ between years, although the data are nationwide and not specific to the study sites.

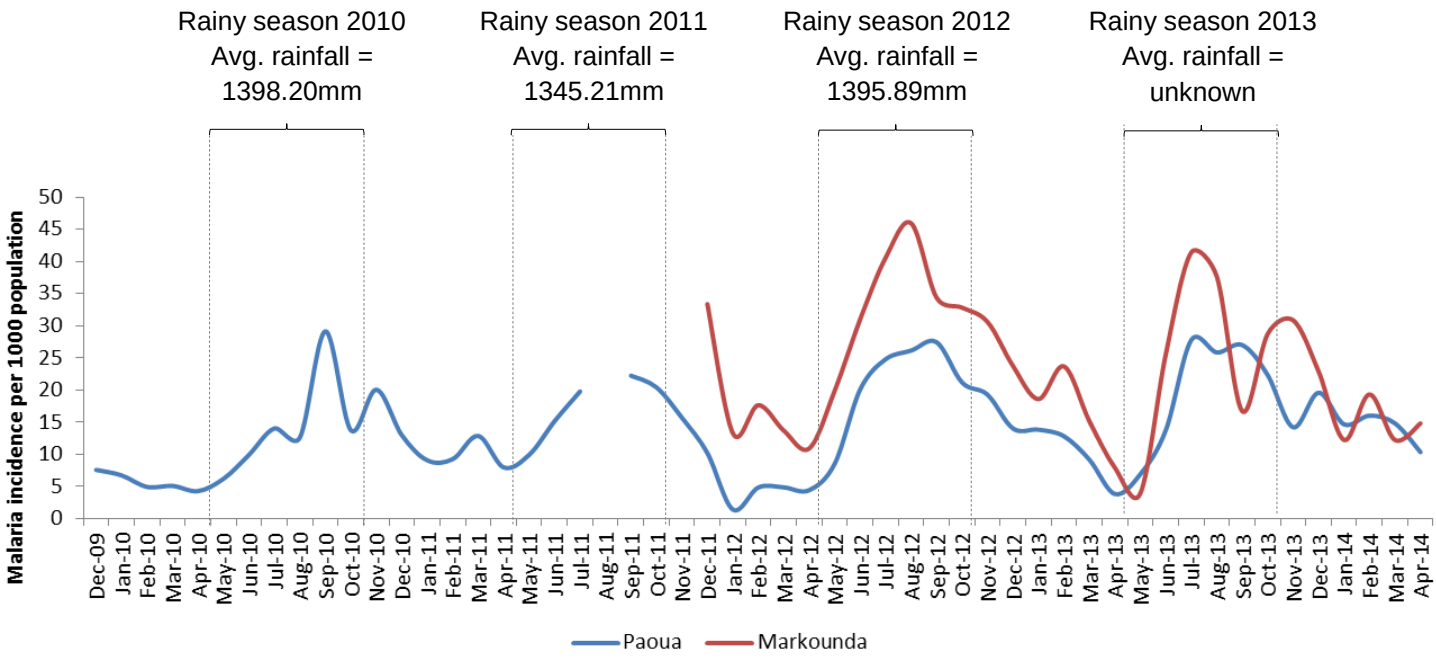

Figure 5.2 Monthly malaria incidence rate for Paoua and Markounda populations over time. Rainy seasons of each year have been *outlined* with the average annual rainfall where known. Data for August 2011 were lost in the field and therefore this month has been excluded.

Figure 5.3 shows the average number of patients consulting with a CHW by their RDT test result. It shows a reduction in the proportion of RDT negative cases over time from 25.6% in 2010 to 11.9% in 2013. It also shows that on average, CHW consulted the most patients per month in the first year of data collection.

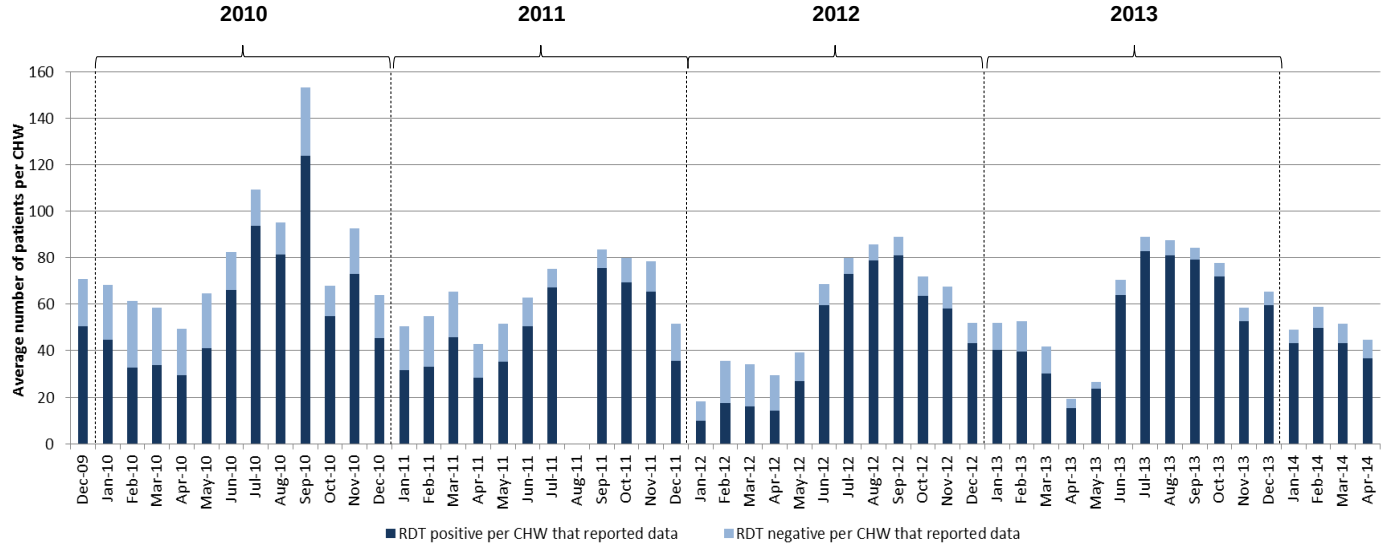

Figure 5.3 The average number of patient visitis per CHW who received a RDT each month according to test result. Data for August 2011 were lost in the field and therefore this month has been excluded.

Malaria diagnosis and treatment (with ACT and rectal artesunate)

In total, 99.2% of RDT-positive cases received either ACT or rectal artesunate (Table 5.1). Most [98.9% (159,279/161,052)] RDT-positive cases were appropriately treated with an ACT. Furthermore, 416 RDT-positive cases that showed signs of complicated malaria received rectal artesunate instead of ACT before referral to the nearest health facility. There were 1962 RDT-positive cases that received both ACT and rectal artesunate, giving a total of 99.2% of RDT-positive cases that received either ACT or rectal artesunate.

Very few RDT-negative cases [1.2% (439/37,330)] were treated with an ACT. However, 298 RDT-negative cases (0.8%) received rectal artesunate resulting in a total of 2% (n = 737) of RDT negative cases receiving either ACT or rectal artesunate. There was only one RDT negative case that received both ACT and rectal artesunate. Paracetamol was administered to 70.0% (26,125/37,330) of RDT negative cases and 1.3% (2125/158,927) of RDT positive cases.

Malnutrition indicators for children 6 to 59 months

In total 94.1% (127,654/135,595) of children 6–59 months old were tested for malnutrition using MUAC during the data collection period (Table 5.2). Despite the conflict situation, the majority of children (84.4%) were well nourished. However, 364 children (0.3%) were classified as severely malnourished, 54.5% of whom were female. The proportion of severely malnourished children was not significantly different across the study period, including during the most severe times of conflict. In total, 301 of these severely malnourished children were referred to the nearest health facility.

Table 5.2 Summary of Mid-Upper Arm Circumference (MUAC) results for children aged 6-59 months.

Malnutrition measurement indicator	TOTAL	
Children 6 – 59 months		
Total measured (mid upper arm circumference)	127,654	
Well-nourished (>135mm)	114,443	(84.4%)
At risk of acute malnutrition (125 – 135mm)	9,508	(7.0%)
Moderate acute malnutrition (110 – 125mm)	3,339	(2.5%)
Severe acute malnutrition (<110mm)	364	(0.3%)

Non-malaria indicators

Of those who had diarrhoea (34,379), 88.0% (30,358) received oral rehydration solution. In total 57,276 doses of mebendazole were given for deworming to children under 5 years, and 704 doses were given to pregnant women. In total, 15,797 people were referred to a health facility for additional follow-up but compliance with this advice to proceed to the nearest health facility was not measured.

CHW reporting rate

During the first year of the study period (2010), 100% of CHWs reported their data each month with the exception of April, October and November when 4% of CHWs did not report. During 2011 and 2012, less than 4% of CHWs consistently did not report their data monthly and in general it was the same CHWs who did not report. Some peaks in non-reporting can be seen in Figure 5.4. From the beginning of 2013 when the insecurity increased and political violence peaked, reporting decreased. The most notable increase in non-reporting is seen in the months immediately following March 2013, when the coup d'état occurred.

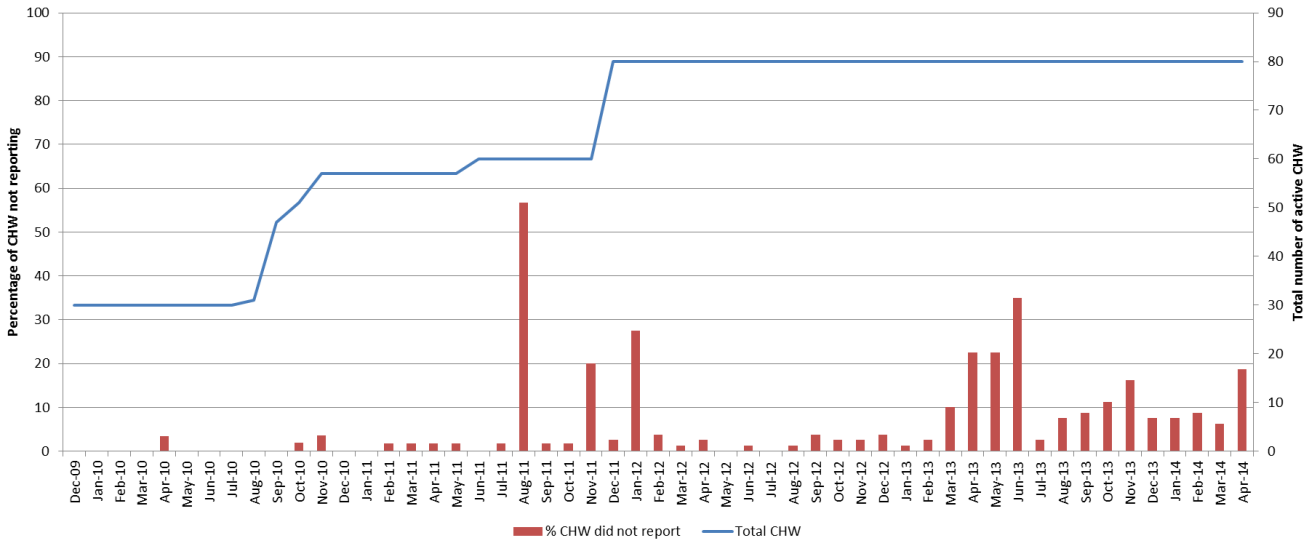

Figure 5.4 Proportion of CHW that did not report data, by month. Data for August 2011 was lost in the field and therefore this month has been excluded.

5.5 Discussion

The CHW programme in northwest CAR plays a pivotal role in ensuring communities have access to effective malaria treatment. It is well targeted to those most vulnerable to severe effects of the disease as 77.6% of those consulting with a CHW were children under five and pregnant women.

Analysis of the routinely collected data from this programme highlights that one of its successes was that it has continued, undisrupted, over many years of conflict and instability. The numbers of CHWs even increased over time to access harder-to-reach populations. The programme recruited CHWs from the local population, with the help of the community leaders, which facilitated development of excellent community relations. This in turn led to a deeper understanding of the needs of specific communities. Knowledge of these differences enabled operational adaptations to the intervention to be made over time in order to maximise its effectiveness. For example, the CHW data were used to target IRS campaigns to areas known to experience higher burdens of disease. However, these campaigns took place before the timeframe covered by these data because by the end of 2009 there was a recommendation to shift from conducting IRS towards LLIN distribution. These relationships also meant that the CHW network could be utilised for other activities, including prevention campaigns or special surveys.

The results presented here cover more than 4 years of routine data collection, allowing patterns of malaria seasonality to be monitored while also capturing trends over time during the changing political situations and rebel clashes. Annual malaria incidence rates were extremely high throughout the study period and actually increased over time in Paoua (Figure 5.2). This was expected because with little prevention, the programme was managing cases rather than reducing transmission. The assumption when calculating this incidence rate was that the denominator (population at risk in the catchment area of the CHWs) for Paoua and Markounda was constant over time. While the area suffered a high degree of displacement, most is believed to have been local displacement within the same catchment area. People fled into the bush, often for relatively short periods of time, and returned when the situation calmed down. Furthermore, the CHW programme was designed with this in mind so that the CHWs would either flee with the villagers or be able to track people from their community and continue care.

The RDT data showed that there was a decrease in the proportion of RDT-negative cases over time (Figure 5.3). This could be because the communities realised with time that the CHW mainly diagnosed and treated malaria. Therefore, community members were maybe less inclined to present themselves to a CHW when they had something that they did not expect to be malaria. This phenomenon was observed when the programme was expanded to a new area in 2014. A high ‘caseload’ was seen in the initial 6 months–1 year when people sought general primary health care for many illnesses, followed by a steady decrease once the limited care capacity of CHWs was understood by the population. Alternatively, when insecurity was higher, people may have waited

before seeking care during which time self-limiting viruses causing fever may have resolved. Malnutrition rates did not significantly change over time (trend data not reported) with a low level of severe acute malnutrition diagnosed (0.3%). This level is lower than that measured in southern CAR (Caleo *et al.*, 2012).

The data also showed that during the first and relatively peaceful year of data collection, the CHWs were on average seeing more patients per month than in subsequent years. The most likely explanation for this decrease is that the number of villages with CHWs increased over the years, giving more villages access to their own CHW, therefore sharing the burden of patients. Furthermore, all patients were included in this study even if they travelled from outside the catchment area, something which may have happened more often during more peaceful times. Looking into patient origins and distances travelled would enable this to be explored further. An additional factor which may have contributed to the observed decrease is that CHW motivation may have decreased over time. However, this does not seem likely because even when there was a decrease in the remuneration amount paid in May 2012, the number of patients seen per CHW did not change, suggesting their motivation was not only financial.

Another key strength of this programme was its ability to overcome issues of inaccessibility due to insecurity and extremely poor road conditions, especially during the rainy season. The NGO-supported nurses were able to provide regular extensive training and on-site supervision during which they also maintained the supply chain of essential medicines and materials throughout the periods of highest instability. These factors facilitated the implementation and use of RDTs and led to a very high percentage of RDT-positive cases receiving appropriate ACT treatment (98%). The benefits of intensive supervision and coaching may also explain why such a low proportion of RDT-negative cases were incorrectly treated with ACT (1.2%). This rate is comparable with a recent study in three stable malaria-endemic sub-Saharan African countries that found that CHWs treated 1.03% of RDT-negative cases with ACT (Singlovic *et al*., 2016). Most cases of incorrect treatment of RDT negative cases with ACT seemed to be by a few individual CHWs. In particular, one CHW treated 111 negative RDT with both ACT and rectal artesunate during the course of 2011. It is unclear why this incorrect treatment practice took so long to be corrected.

The ability to treat such a high proportion of RDT-positive cases is also testimony to the regular stock replenishment with ACT. It is unknown whether there were stock outs of both RDTs and ACT at individual CHW level, but the high treatment rates suggest that this could not have been

very often. A drawback of two supervision visits per month and repeated training every 6 months is the expense involved. This brings into question the sustainability of maintaining the quality care without the support given by an international NGO.

One of the main limitations of the programme was the handling of malaria-negative cases. CHWs have restricted options when faced with an RDT-negative patient whose symptoms persist but who does not have the means to travel to a health centre. While the programme made attempts to provide training to recognise the warning signs of other causes of fever, such as respiratory tract infections, dealing with negative cases in the absence of an effective referral and transport system is challenging. It is important to note that this limitation is not just experienced in this CHW programme but is a general problem within the healthcare system in many other sub-Saharan African countries (D'Acremont *et al.,* 2014). Even trained nurses in health facilities often default to malaria treatment when another clinical diagnosis cannot be made or other treatments are not available. An important next research step to better understand the overall healthcare system would be to follow up referred patients to assess the proportion reaching a referral centre and the quality of care they receive there according to their final diagnosis.

The results presented here show that the overall reporting rate was extremely high. However, this did decrease over time as the project expanded. While the number of supervisors also increased, the larger distances covered could have put an additional strain on their ability to maintain regular supervision visits. This was most evident during the 2013 crisis when the proportion of CHWs not reporting each month increased from less than 5% in February 2013 to over 30% in April 2013. While the project location is almost 500 km from the capital Bangui, the events in the capital triggered a countrywide increase in fragility and attacks and thus the impact was felt in the programme area. During that time, all international staff were evacuated and therefore the flow of money was temporarily slowed as access to banks in Bangui became difficult. This meant that fewer supervision sessions could take place and fewer RDTs and ACT could be delivered. While the initial crisis calmed after several months and relatively normal activities could be resumed, a general insecurity remained. There was very little state authority present in the programme area and NGO teams met increasing difficulties in accessing the communities as a result. This might explain why the proportion of CHWs not reporting remained significantly higher after the crisis (around 10% of CHWs not reporting each month). In spite of the challenges, the timely recording and reporting of data by these CHWs on malaria, nutrition status and diarrhoea was impressive and it was the only efficient surveillance system in the area. The same system has the potential for

including other key indicators of diseases found to be affecting the population, e.g., neglected tropical diseases. Through consistent timely analysis and monitoring of these data, the programme was able to continually re-assess and adapt as political and epidemiological conditions evolved.

Data and experience from this study have the potential to serve as an example of effective malaria control intervention in similar environments. In CAR the internally displaced persons are not organised into camps as is often experienced elsewhere, but rather flee into the bush. These displacements, although usually temporary, are frequent and mean that communities are often scattered and consequently very difficult to reach through a conventional health care approach.

This approach has become an integral strategy of the national malaria control programme in CAR since 2012. Unfortunately, implementation has yet to be realised beyond the project area, mainly due to lack of funding. In addition to building this community-based approach into national policies, solid commitment from governments, key international stakeholders and donors must be realised. But ultimately, without peace, health cannot thrive as the State cannot begin to rebuild infrastructure or pay health staff salaries, and trained health staff will not have renewed motivation to return to the most insecure areas. This has been recognised in the Sustainable Development Goal 16, which strives to promote peaceful and inclusive societies to see poverty eradicated and sustainable development thrive which must include health goals (UN General Assembly 2015). Therefore, the next steps must be to not only continue treating malaria cases and implement prevention, but to also promote peace, without which a sustainable health system cannot be built and the catastrophic impact of the silent yet deadly ongoing epidemic of health system failure will continue.

5.6 Conclusion

Overall, this study demonstrated that decentralizing basic health care to community level during times of instability and unrest through a network of CHWs can be an effective way to manage malaria in hard-to-reach, conflict-affected populations suffering frequent displacements. It showed that supply chains, surveillance systems and continuous capacity building can be maintained in spite of security challenges. However, these humanitarian interventions require extensive resources and do not result in long-term health system development. Peace and good governance are required for strengthening the health care system.

6. Malaria sentinel site surveillance in the Democratic Republic of Congo: Key to understanding real burden and improving targeted control?

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Working paper

6.1 Abstract

Background

Malaria surveillance is an essential component of control programmes. It ensures interventions are tailored at the sub-national level to reach the most vulnerable people. In the Democratic Republic of Congo, a network of sentinel sites have been established to improve the quality, scope and representativeness compared to that currently collected through the routine Health Management Information System and population based surveys.

Methods

A community-based cross-sectional survey was conducted in two sentinel sites (Kimpese and Vanga) during the rainy season in 2016. A structured household questionnaire was administered to households in the catchment area of the sentinel site health facilities to collect data on basic demographics, treatment seeking behaviour and use of prevention tools. Each member of the household was tested for malaria and anaemia. Health facility registers were also analysed and the estimated incidence compared to a model predicted incidence to assess the proportion of the community accessing health services.

Results

During the community survey, data were collected from 271 households including 2,116 people across the two sentinel sites. Malaria prevalence in children aged 6 to 59 months was 39.4%. Of those children 6 to 59 months who had a fever in the two weeks preceding the community survey, 81.4% in Kimpese and 34.8% in Vanga visited a pharmacy first to seek treatment. Only 6.6% and 12.9% in Kimpese and Vanga respectively visited a formal health facility. Of the 4 Kimpese health facilities, 57.1% of malaria diagnosed patients (with or without a confirmed diagnosis) received an ACT.

Conclusions

This study will be the baseline for assessing the functioning of the sentinel site system. The low proportion of people seeking care at the formal health facilities suggests the data collected by this system is only capturing a fraction of the actual burden experienced by the community.

Keywords: malaria, malaria surveillance, health facility data, sentinel site, Democratic Republic of Congo

6.2 Background

Malaria surveillance is a vital component of control programmes. When executed well, it enables understanding of the epidemiological profile at sub-national level, as well as the unique challenges affecting communities. This is essential for planning responses and targeting interventions at the sub-national level to ensure they reach the most vulnerable people.

The importance of surveillance is clearly evident in the Democratic Republic of Congo (DRC), which not only battles with health system limitations common in sub-Saharan Africa, but as the second largest country in Africa, implementation of an extensive surveillance system is almost impossible with currently available resources.

As in many country programmes, DRC relies largely on a combination of routinely collected health facility-based data available as part of a Health Management Information System (HMIS), and national population based surveys to evaluate the impact of malaria control interventions and health impact (Yukich *et al.*, 2014). However, the disease-reporting systems that are at the core of malaria surveillance in sub-Saharan Africa today, are simply unable to capture all cases or deaths due to malaria (WHO, 2016).

This is firstly because the infrastructures in place to collect data are not accessible to the entire population. Secondly, large proportions of febrile cases never seek treatment at formal facilities. In fact, previous research has shown that across sub-Saharan Africa, only between 20-36% of febrile patients come into contact with the formal health infrastructure (Agyepong and Kangeya-Kayonda, 2004, Rowe *et al*., 2009, Iwamoto *et al.*, 2017). Thirdly, not all health care structures report their data consistently to the central system. Fourthly, these sources of data are non-exhaustive since they only include a limited number of indicators. And fifthly, the collected data are of variable quality. While national surveys can complement the routine data by assessing demographic trends and levels of coverage and household characteristics to evaluate programmes and risk factors, they rarely have the statistical power to provide estimates at lower administrative levels.

Sentinel surveillance sites are one strategy proposed to overcome the limitations listed above. Studies have already shown their ability to be reliably implemented to monitor trends (Sserwanga *et al*., 2011, Caleo *et al.*, 2012). The term ‘sentinel’ refers to the fact that the system is limited to a fixed location but is meant to operate continuously over a long time period. This facilitates

improving the quality of the care and surveillance over time because it is easier to improve data collection and collation in a small number of facilities rather than the entire system. Sentinel surveillance sites in DRC have been undertaken in a limited number of health facilities as part of a comprehensive strategy to improve the quality of malaria surveillance and strengthen the HMIS. A network of 26 sentinel sites has been established in DRC, one per Provincial health unit.

The overall goal of the sentinel site system studied here is to deliver faster, more complete, quality malaria surveillance data through both (1) active community based studies and (2) passive routinely collected health facility records. In addition, sentinel sites offer the opportunity to provide information on the trends of indicators not collected by other systems or surveys (e.g. entomological data, parasitological data, pharmacology etc.) (Sserwanga *et al*., 2011). Sentinel site programmes also place a strong emphasis on local training and capacity building, the transfer of technology, and building strong relationships between researchers and policymakers.

As these sentinel site systems still heavily rely on data collected at health facility level, it is important to understand how this reflects the true burden of malaria in the surrounding communities. Accounting for prevalence, testing and positivity rates, as well as quantifying the proportion of the population accessing care, could enable a correction factor to be applied to health facility data to better estimate the actual malaria burden. Historically, the WHO estimates national levels of incidence by adjusting the number of reported cases to take into account the estimated proportion of cases that are not captured by a surveillance system (WHO, 2008). More recently, cartographic approaches utilised several models, calibrated to extensive datasets, to estimate relationships between incidence and prevalence (Cameron *et al.*, 2015). Coupled with geospatial models of prevalence and intervention coverage, geographic and temporal patterns of malaria incidence were constructed (Bhatt *et al.*, 2015, WHO, 2016). One of these microsimulation models, OpenMalaria (OpenMalaria, Smith *et al*., 2012b) has been used to estimate national levels of incidence given access to care (Penny *et al*., 2015), as well as national levels of access to severe treatment (Camponovo *et al.*, 2017). In addition, several authors have produced national estimates of treatment seeking rates or coverage of access to effective treatment from multiple health and indicator surveys such as the Demographic and Health Surveys (DHS), Multiple Indicator Cluster Survey (MICS) and Malaria Indicator Survey (MIS) (Battle *et al.*, 2016, Galactionova *et al.*, 2015), as well as geospatial models of treatment coverage (Gething *et al.*, 2016, Bennett *et al.*, 2017). However, the subnational estimates rely on geospatial models for inference and extrapolation and do not take into account many of the contextual and local factors needed for local decision making.

The ultimate goal of this community survey and its analysis is to understand and quantify the true malaria burden at health area level, and quantify how much is captured by the routine health facility data. This should help to address what improvements can be made to the sentinel systems and apply correction factors to the recorded incidence data.

6.3 Methods

Overview of the sentinel site surveillance programme

The DRC is divided into 26 provincial health divisions. Each Province is broken down into Health Zones (HZ), the main operational unit of the national health system which conventionally includes a general reference hospital and 15-20 health centres. These HZ are further divided into Health Areas (HA) comprising several villages with an estimated 5,000 to 10,000 inhabitants, all serviced by a health facility. A total of 26 sentinel sites have been established in DRC to correspond with the number of provincial health districts. The National Malaria Control Programme defined a sentinel site as the geographical area within a HZ comprising the general reference hospital and three medical centres from three different Health Areas (2 public and 1 private) (PNLP, 2014). The system was designed to assess an extensive list of indicators going beyond those collected by the routine system and including parasitaemia, entomology, drug and insecticide resistance, pharmacology and climate.

Study site and population

The present study was conducted in two sentinel sites in Kimpese and Vanga HZ located in the Provinces of Kongo Central and Kwilu, respectively (Figure 6.1). Situated in the West of the DRC, these two rural Health Zones are endemic for malaria with stable transmission throughout the year.

For both Kimpese and Vanga Health Zones, each of the 3 Health Areas possessing a health centre under the sentinel surveillance site project was selected for sampling. The target population were people of all ages and genders residing in these health areas stratified into two age groups (<5 and ≥5 years of age). The study took place before the planned rehabilitation of these sites, thus providing baseline data.

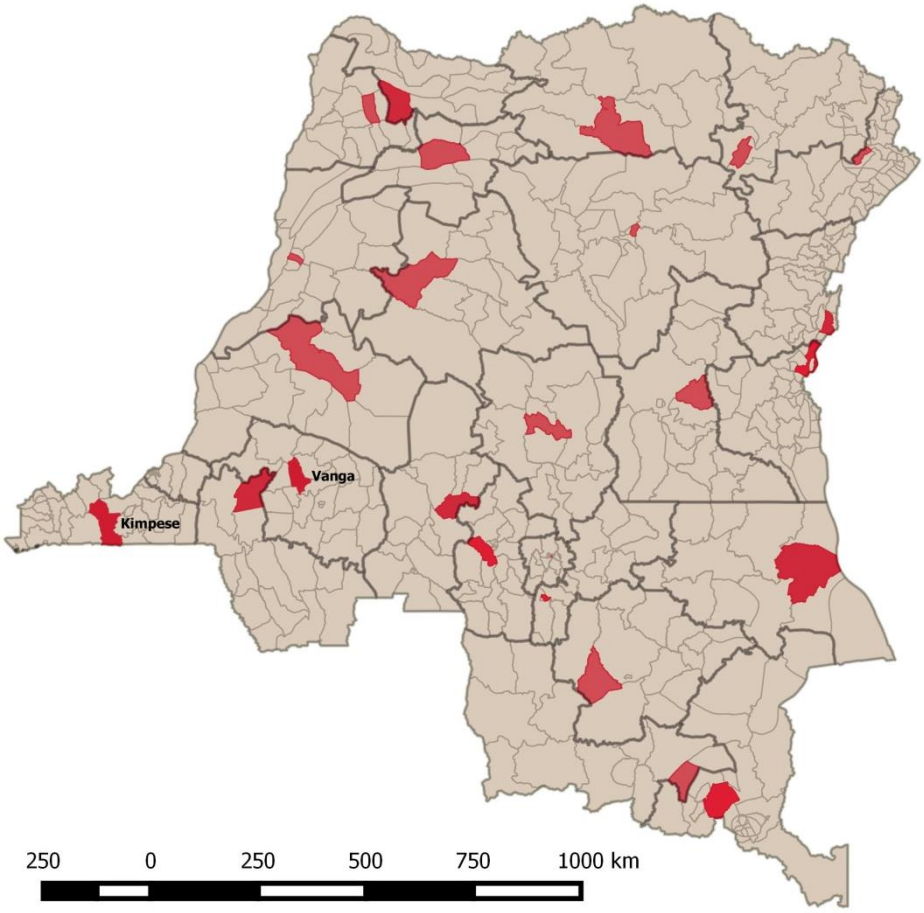

Figure 6.1 Map of DRC showing the location of the sentinel sites (red). The borders of the 26 provincial health divisions are also outlined with their respective Health Zones.

Study design and data collection

A community-based cross-sectional survey was conducted in Kimpese and Vanga sites in January and February 2016 (during the rainy season) using a multi-stage cluster random sampling. The sample size was calculated separately for the two age categories and was based on estimating the primary indicator (parasitaemia as measured by a mRDT) (Ntuku *et al.*, 2017). The sample size calculation was based on a precision of ±10 absolute percent and a design effect of 1. The cluster effect of selecting villages and then households within each health area was also taken into consideration and the resulting number of individuals to be sampled was 104 children less than 5 years and 144 individuals over 5 years per Health Area.

After obtaining the approval of local authorities at each HZ, three villages were randomly selected from a complete list of all streets/villages with their corresponding populations in each Health Area.

Households were then randomly selected using the random walk method. Teams of two trained field workers visited each selected household:

- **An interviewer** to explain the study to the head of household or their delegate, obtain informed consent and then administer a structured questionnaire. The questionnaire collected data on the demographics of all household member's, household facilities such as latrine access and goods owned such as a bicycle (for socioeconomic calculations), health seeking behaviour and malaria prevention practices such as LLIN usage.
- **A field lab technician** to test for malaria using the SD Bioline three bands *P. falciparum/*Pan malaria Rapid Diagnostic Test (RDT) (Standard Diagnostics, Kyonggi, Republic of Korea) and measure haemoglobin levels using a blood haemoglobin photometer (HemoCueHb201+ Ängelholm, Sweden). In addition, dry blood spots on filter paper were taken for a later analysis of the gametocyte index.

Random selection of households continued until the sample size for each category was reached. Parallel to the community-based survey, patient registers from all sentinel site health facilities were scanned and entered into a data base for triangulation with other sources of data. Socioeconomic status was calculated by using a principal components analysis (PCA) to create a composite household wealth index (classified into 5 classes) (Vyas and Kumaranayake, 2006).

In addition to the community survey in Kimpese, Health facility records for the two months preceding the community survey (December 2015 and January 2016) were entered into an electronic database using EpiData. Data collated for febrile patients included age, malaria diagnostic test result, diagnosis and treatment. Unfortunately, registers from the Vanga sentinel site facilities are not available at this time because the diagnostic test results are recorded in the laboratory yet patient information including final diagnosis and treatment are recorded in the outpatient registers and these two sources have not yet been consolidated.

Estimations of case incidence

Estimates of Health facility case incidence were calculated from the health facility data by multiplying the total patients diagnosed with malaria at each facility over the 2 months of data collection (regardless of test result) by 6 to get an annual estimate (assuming little seasonal variation). Incidence was then calculated by dividing the resulting estimates of new cases per year by the catchment population of the health facility and multiplying by 1,000 to get an estimate of the

number of new cases per year per 1,000 population. Children less than 5 years were estimated to make up 18.9% of the population in DRC.

To estimate the likely incidence in each sentinel site, prevalence data from the surveys were modelled. Prevalence - incidence (per 1,000 persons per year) relationships for different ages and different levels of access to effective treatment were constructed using OpenMalaria, a microsimulation model of malaria epidemiology and transmission, calibrated to historical data (Smith *et al.,* 2012b). Similar to previous modelling studies, an ensemble of six models covering different assumptions concerning immunity decay, heterogeneity in transmission and heterogeneities in comorbidities was simulated. Assuming coverage of vector control held constant, a range of entomological inoculation rates (EIR) (0-512) and levels of access to effective treatment (0 to 55%) was used, with all other epidemiological inputs the same. Ten stochastic realisations were used to account for stochastic variation, and the ensemble accounted for epidemiological parameter variation. A nonlinear model was fitted to the predicted prevalence and predicted incidence using nonlinear least-squares. Incidence as uncomplicated cases per 1,000 per year, for all ages or under 5 years of age, was predicted from the non-linear model for prevalence at each site from the survey, for access levels of 0 and 5%. This was compared with the health facility estimates of incidence in Kimpese to estimate the likely proportion of total malaria cases receiving an ACT.

There was no community survey completed in the catchment area of the general reference hospital because it covers the entire Health Zone and therefore sampling from only the health area where the hospital is located would not be representative of the catchment population.

6.4 Results

Community survey

Characteristics of the study population

During the two community surveys, data were collected from 271 households and included 2116 people across the two sentinel sites (149 and 122 households in Kimpese and Vanga sentinel sites and 1,136 and 980 individuals, respectively). Table 6.1 presents a description of the sample characteristics. Household characteristics differed between the two sites as Vanga is a very rural and geographically isolated area compared to Kimpese. where only 11.4% of households were classed as rural. Furthermore, socioeconomic status analysis across both sites combined indicated

that 99% of households from Vanga were categorised into the two poorest quintiles and, in contrast, 71.8% of Kimpese selected households were categorised into the two least poor quintiles. Education levels were higher in Kimpese than in Vanga, and the primary source of income differed slightly with 59% being into agriculture in Vanga compared to 26% in Kimpese.

Table 6.1 Demographic of household survey participants

Households		**Kimpese**	**Vanga**
Number of households		149	122
Number of residents normally residing in the house	n Female Mean Range Standard deviation	1,136 641 (56.4%) 7.62 2 - 21 3.69	980 521 (53.2%) 8.03 2 - 18 3.20
Sex of head of household	Men Women	97 (65.1%) 52 (34.9%)	108 (88.5%) 14 (11.5%)
Education level of head of household	Never attended Primary Secondary Superior	3 (2.1%) 36 (24.8%) 81 (55.9%) 25 (17.2%)	23 (19.5%) 44 (37.3%) 47 (39.8%) 4 (3.4%)
Main activity of head of household	School Agriculture Unemployed Merchant/Trader Employed Civil servant Informal	1 (0.7%) 38 (25.5%) 17 (11.4%) 6 (4.0%) 33 (22.2%) 16 (10.7%) 38 (25.5%)	3 (2.5%) 72 (59.0%) 11 (9.0%) 3 (2.5%) 2 (1.6%) 16 (13.1%) 15 (12.3%)
Environment (n=149)	Rural Urban-rural	17 (11.4%) 132 (88.6%)	122 (100%) 0
Socioeconomic status	(poorest) 1 2 3 4 (least poor) 5	0 (0%) 0 (0%) 42 (28.2%) 53 (35.6%) 54 (36.2%)	55 (45.1%) 54 (44.3%) 12 (9.8%) 1 (0.8%) 0 (0%)
Individuals			
Sex	Men Women	495 (43.6%) 641 (56.4%)	459 (46.8%) 521 (53.2%)
Education level (age>5years)	Never attended Primary Secondary Superior Don’t know	25 (3.4%) 341 (47.0%) 301 (41.5%) 48 (6.6%) 11 (1.5%)	135 (22.5%) 279 (46.4%) 177 (29.5%) 5 (0.8%) 5 (0.8%)

Malaria prevalence and anaemia

Out of the 713 children 6 to 59 months tested with an mRDT, 281 (39.4%) were positive. In total 50.5% of infections (142/281) were due to *Plasmodium falciparum* with the remaining due to mixed infections including *P. falciparum*. The malaria prevalence was not significantly different between Kimpese and Vanga (36.7% [95% CI 31.7 – 41.8] and 42.1% [95% CI 36.9 – 47.2]).
In contrast, within the two sentinel sites, the malaria prevalence was significantly higher (p<0.000) in Yanga dia Songa Health Area compared to the others (Figure 6.2). Furthermore, in Vanga sentinel site, Mayoko Health Area had a significantly lower malaria prevalence (p<0.000) compared to the other Health Areas. The same pattern was observed for all ages between Health Areas (Figure 6.2 plots data for children age 6-59month).

For the participants ≥5 years old, 1779 were tested using an RDT of which 38.9% (692) were positive. In total, 58.1% of infections (402/692) were due to *Plasmodium falciparum.* The prevalence was also not significantly different between the two sites in Kimpese and Vanga (39.7% [95% CI 36.5 – 42.8] and 38.1% [95% CI 34.8 – 41.3]).

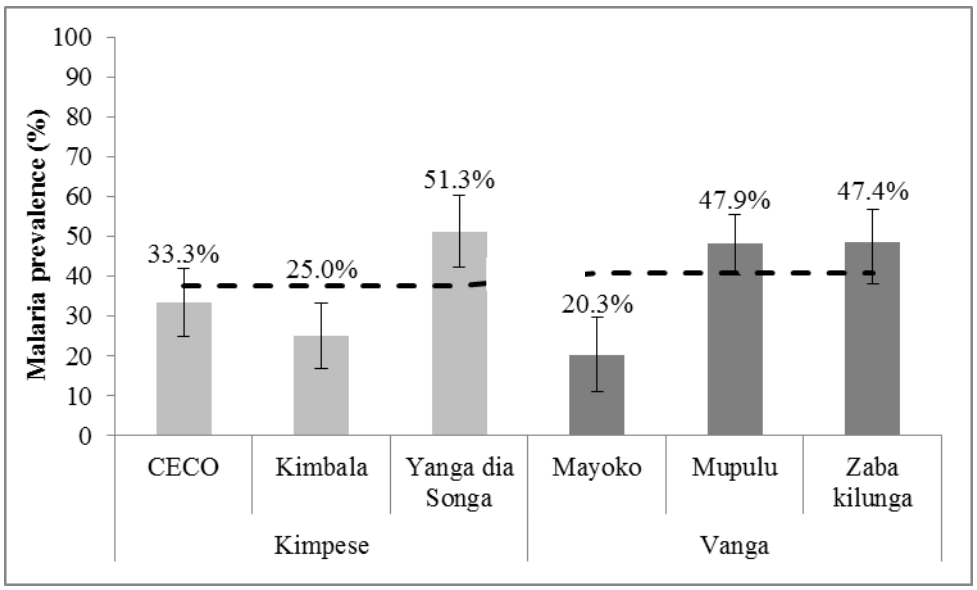

Figure 6.2 Malaria prevalence (measured with mRDT) in each Health Area in Kimpese and Vanga. The dotted line shows the weighted average malaria prevalence for Kimpese HZ (38%) and Vanga HZ (40%).

Out of the 579 children aged 6 to 59 months who had their haemoglobin levels measured, the average haemoglobin levels were 10.4g/dl in Kimpese and 9.3g/dl in Vanga. There was a significant difference (p<0.0001) in the levels of severely anaemic children (<8g/dl) between the two Health Zones with 3.5% in Kimpese (10/287) and 14.4% in Vanga (42/292). While differences

within the Health Areas were not evident in Kimpese (due to the small sample size), Mupulu Health Area had a significantly higher (p=0.001) burden of severe malaria compared to the other Health Areas in Vanga (Mayoko and Zabakilunga) (Table 6.2).

Table 6.2 Malaria prevalence (measured with RDT) and anaemia levels (measured with Haemocue) in Kimpese and Vanga.

Malaria prevalence			**Kimpese**	**Vanga**
Overall			368/955 (38.5%)	325/854 (38.1%)
By sex	Male		169/397 (42.6%)	152/393 (38.7%)
	Female		199/558 (35.7%)	173/461 (37.5%)
By age group	6 to 59 months		130/354 (36.7%)	151/355 (42.5%)
	≥5 years		237/571 (41.5%)	174/495 (35.2%)
By Health Area	Kimpese:	Vanga:		
	CECO	Mayoko	118/341 (34.6%)	43/173 (24.3%)
	Kimbala	Mupulu	75/281 (26.7%)	176/408 (43.1%)
	Yanga dia Songa	Zaba Kilunga	175/333 (52.6%)	107/273 (39.2%)
By species	*Plasmodium falciparum*		195/368 (53.0%)	207/325 (63.7%)
	P.f. and other		170/368 (46.2%)	118/325 (36.3%)
	Only non-P.f.		3/368 (0.8%)	0
Anaemia (age 6 to 59 months)				
Overall anaemia (<8g/dl)			10/287 (3.5%)	42/292 (14.1%)
By Health Area	Kimpese:	Vanga:		
	CECO	Mayoko	4/86 (4.7%)	4/54 (7.4%)
	Kimbala	Mupulu	4/109 (3.7%)	35/169 (20.7%)
	Yanga dia Songa	Zaba Kilunga	2/92 (2.2%)	3/69 (4.3%)

Coverage and use of LLINs

It is important to note when interpreting these results that data collection occurred 1 month after a mass distribution campaign of Long-Lasting Insecticidal Nets (LLINs) in Vanga and 1 year after a mass distribution campaign in Kimpese. Such factors are impossible to avoid in a sentinel site and need to be considered in the analysis.

Across both sentinel sites, there were only 5 households that did not own at least 1 LLIN (all 5 were in Kimpese HZ). However, there was a significant difference between Health Zones in terms of universal coverage (1 LLIN per 2 people) as 32.9% and 82.8% of households in Kimpese and Vanga respectively possessed at least 1 LLIN for every 2 household members. Consequently, the proportion of people who had access to an LLIN 23.6% (268/1,136) in Kimpese compared to 78.3% (767/980) in Vanga.

Despite this difference, the reported proportion of people who slept under a LLIN the night before the survey was above 90% in both Kimpese and Vanga, and this for both age groups.

Health seeking behaviour

Out of 737 people who reported having a fever during the 2 weeks preceding the survey, the majority sought heath care initially from a pharmacy. This was much higher in Kimpese (81.4%) compared to Vanga (34.8%). Only 7.4% of people with a fever in Kimpese presented to a formal health care facility or community health worker compared to 12.9% in Vanga. The other places people sought treatment for their fever are summarised in Table 6.3. They include traditional medicine and use of medicine at home.

Table 6.3 Kimpese and Vanga: Treatment seeking behaviour of people with fever in the two weeks preceding the survey.

Health seeking behaviour	**Kimpese**	**Vanga**
No action taken	11 (3.01%)	66 (17.8%)
Took traditional medicine already available at home	7 (1.9%)	51 (13.8%)
Took modern medicine already available at home	18 (4.9%)	72 (19.4%)
Visit pharmacy	298 (81.4%)	129 (34.8%)
Visit health facility	24 (6.6%)	48 (12.9%)
Visit community health worker	3 (0.8%)	0
Did not know	5 (1.4%)	5 (1.4%)

Malaria case management at health facilities

Figure 6.3 shows the step wise progression of fever cases in the community. It is clear that the biggest ‘drop out’ of the system is those not attending the health facility. Of those patients who did visit, most reported being tested for malaria (63.4% in Kimpese and 60.0% in Vanga). However, out of the 9 people who reported having a positive test result in Kimpese, only 3 reported receiving ACT and in Vanga, none of the 15 people who reported receiving a positive test result received ACT. The surveys did not include any further information to capture the reasons why ACT was not received.

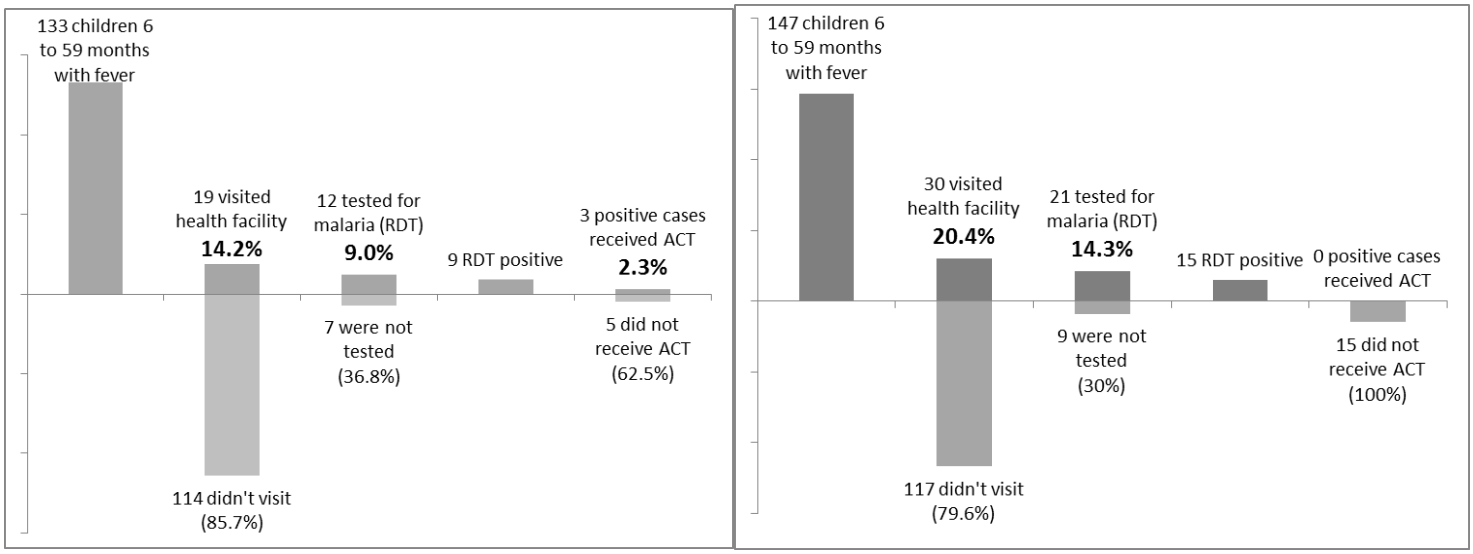

Figure 6.3 Self-reported diagnosis and treatment practices at health facilities of those who reported having a fever in the two weeks preceding the community survey in Kimpese and Vanga.

Health facility register data

Health facility data was only available for Kimpese sentinel site facilities and the summary results from the patient registers at each facility are presented in Table 6.4.

Across all 4 facilities, 51.1% of patients visiting a health facility were tested for malaria. The average test positivity rate was 65.3%. Out of those diagnosed with malaria, 79.3% tested positive with either an RDT or microscopy, the rest being diagnosed on clinical grounds alone. A further 16 people who had a negative RDT result and 18 people who had a negative blood slide were also diagnosed with malaria. On average, 57.1% of malaria diagnosed patients (with or without a confirmed diagnosis) received an ACT which is considerably higher than that reported during the community survey. However, this differed greatly between health facilities from 23.6% in CECO health centre to 88.4% in Yanga dia Songa health centre.

Comparison of incidence estimates

Model based estimates of incidence of uncomplicated malaria (per 1,000 persons per a year) assuming low levels of treatment are shown in Table 6.5.

Across the three sites in Kimpese, incidence rates are predicted to range from 1,289 to 1,500 for all ages and from 2,006 to 3,368 in children less than 5 years old. The highest incidence rates predicted

by the model were in Yanga dia Songa. However, this site had the lowest recorded incidence rate according to the health facility register from our survey. The recorded incidence rates in health facilities for all ages, represented the following percentages of the modelled predicted incidence rates: 12.4% for Kimbala, 16.4% for CECO, and only 4.4% in Yanga dia Songa. In children less than 5 years old, these proportions were similar with 12.1% for Kimbala, 22.6% for CECO and 3.8% for Yanga dia Songa.

Table 6.4 A summary of data from the patient registers in the two months preceding the community survey from the four sentinel site health facilities in Kimpese

Patient data Dec 2015 and Jan 2016		**'CECO' health centre**	**'La Famille' health centre (Kimbala)**	**'Yanga dia Songa' health centre**	**'IME' General Reference Hospital**
Catchment area of facility		13,289	15,924	18,694	
Total patients recorded	n	850	772	576	955
	Male	392 (46.1%)	295 (38.2%)	255 (44.3%)	502 (52.6%)
	Female	458 (53.9%)	477 (61.8%)	321 (55.7%)	453 (47.4%)
Malaria test performed	Total tested	446 (52.5%)	504 (65.3%)	281 (48.8%)	217 (22.7%)
	RDT	143 (32.1%)	320 (63.5%)	276 (98.2%)	111 (51.2%)
Type of test used	Microscopy	301 (67.5%)	180 (35.7%)	5 (1.8%)	93 (42.9%)
	RDT and microscopy	3 (0.5%)	4 (0.8%)	0	13 (6.0%)
Malaria test positivity	Total tested positive	341 (76.5%)	416 (82.5%)	208 (74.0%)	105 (48.4%)
	RDT positive rates*	85 (76.6%)	258 (79.9%)	205 (74.5%)	59 (54.1%)
	Microscopy positive rates	256 (94.8%)	158 (89.3%)	3 (60.0%)	46 (57.5%)
Malaria Diagnosis	Total diagnosed with malaria	523 (61.5%)	425 (55.1%)	207 (35.9%)	186 (19.5%)
	Uncomplicated malaria	169	323	186	174
	Severe malaria	201	81	19	6
	Severe malaria with anaemia	150	5	2	4
	Malaria during pregnancy	3	16	0	2
Malaria Treatment	Total treated with antimalarial	508 (97.1%)	423 (99.5%)	204 (98.6%)	122 (65.6%)
	ACT	123 (23.6%)	301 (70.8%)	183 (88.4%)	85 (45.7%)
	Quinine	298 (57.0%)	38 (8.9%)	20 (9.7%)	6 (3.2%)
	Artesunate	49 (0.2%)	69 (16.2%)	0	2 (1.1%)
	Other antimalarial	38 (7.3%)	15 (3.5%)	1 (0.5%)	29 (15.6%)

* Test results of patients tested with RDT and microscopy were counted in the RDT result

Comparison of survey Incidence from sentinel sites with model based predictions

Table 6.5 Comparison of observed and estimated incidence from the community survey from sentinel site health facilities in Kimpese HZ.

Health Area(in Kimpese)	Incidence from survey (converted to cases per1,000 per year) all cases [uncomplicated only]	Prevalence from Survey (RDT)	Median Model predictions of incidence 0% access (Cases per 1,000 per year) [range]	Median Model predictions of incidence 5% access (Cases per 1,000 per year) [range]
Under 5				
CECO	571 [124]	41/123 (33.3%)	2455 [2325-2590]	2523 [2423-2631]
Kimbala	243 [179]	28/112 (25.0%)	1964 [1848- 2084]	2006 [1917- 2100]
Yanga dia Songa	129 [110]	61/119 (51.3%)	3244 [3126- 3372]	3368[3283-3461]
All ages				
CECO	236 [76]	118/341 (34.6%)	1453 [1385- 1510]	1438 [1374-1494]
Kimbala	160 [122]	75/281 (26.7%)	1297 [1235- 1352]	1289 [1229- 1343]
Yanga dia Songa	66 [60]	175/333 (52.6%)	1533 [1471- 1587]	1500 [1443- 1546]

6.5 Discussion

The results presented here from a cross-sectional community survey at two sentinel sites will act as a baseline for monitoring the reporting rates of the sentinel site system over time. As the programme focuses on improving the quality of reporting at these sentinel sites, it will be important to track how the proportion of detected cases is changing over time. Hopefully, improved quality of care will also draw more patients to the health facilities and improve the percentage of malaria patients attending health facilities and showing up in the statistics.

Conducted during the rainy season, our surveys showed high malaria prevalence rates despite a reported LLIN usage of over 90% in all health areas. In the future, entomological research may be able to explain this high prevalence rate despite a high rate of net usage. Mosquito populations may be extremely dense or species may be present that are behaviourally adapting to bite earlier or outdoors before people go to sleep (Pates and Curtis, 2005, Gatton *et al.*, 2013). Furthermore, rates of severe anaemia are alarmingly high in Vanga, suggesting a more endemic health problem and

pointing to the underlying poverty that needs to be addressed. Investigation into which risk factors are present in Vanga but maybe absent in Kimpese is vital for targeting of health interventions to improve haemoglobin levels. The difference between the severe anaemia level between these two sites once again highlights that programmes must be adapted to the local setting.

Treatment seeking behaviours of communities highlights that children who are most vulnerable to the severe consequences of malaria when not diagnosed and treated promptly, continue to not access appropriate care from health facilities. Only 7.4% and 12.9% of children less than 5 years old sought care from formal facilities in Kimpese and Vanga, respectively. This is similar to what has been seen elsewhere, for example in Ghana (Agyepong and Kangeya-Kayonda, 2004). The staircase effect (Figure 3), as described elsewhere (Tugwell *et al.*, 2006), showed that this low proportion of people seeking care at the health facility was by far the biggest bottleneck in preventing case detection and appropriate treatment of malaria cases. Instead, the majority of febrile cases in the community continue to seek care from private pharmacies, with as high as 81.4% reporting this in Kimpese. Programmes to try to improve the quality of the malaria case management at pharmacies are underway in Kinshasa, the capital of DRC, but challenges are immense and rolling out such a programme in rural and isolated locations such as Vanga, where pharmacies are highly unregulated, would not be operationally feasible.

Reported fever treatment with an ACT at health facilities was low at only 2.3% in Kimpese. A previous study in DRC found similarly very low proportions of 5% (Littrell *et al.*, 2011). Interestingly, a much higher proportion of malaria cases (57%) received an ACT according the health facility registers; however, this was only 23.6% in CECO health facility. This difference suggests that household surveys are not giving an accurate representation of ACT use possibly due to the recall bias and people simply not knowing what treatment they received. This raises the question of whether using retrospective studies are a reliable source for this indicator. For example, DHS surveys systematically report low ACT use but the methodology used to collect this information may explain some of these low reported rates. Further investigation comparing the methods used to assess treatment with ACT in retrospective surveys compared to health facility records of patients will be important to improve household surveys.

A surprising result from the CECO health facility was that a higher proportion of patients were diagnosed with complicated malaria than with simple malaria. There is no obvious explanation for

this and clearly points towards an error in data recording. This kind of gross inaccuracy is worrying in a sentinel site and shows that the way towards good and representative data is still very long. Furthermore, the issue with the Vanga outpatient and laboratory registers not being consolidated illustrates the reality of surveillance in rural sub-Saharan Africa. This challenge can only be overcome with an improved data recording system and collaboration between different departments of a health facility.

It is important that future routine surveillance visits of the sentinel sites investigate both why some suspected cases are not tested, and then why some diagnosed cases are not treated with ACT. Evidence from this survey suggests that it is not due to stock outs of diagnostics or treatment, because assessing case-management at these facilities over time showed that there is no point at which diagnosis or treatment stopped. Therefore, those suspected cases that are not diagnosed, and the diagnosed cases not treated seemed to be more randomly distributed. The health worker conducting the consultation was not recorded in the registers and therefore there may be a difference in practice between individuals which should be assessed.

Using a simulation model for comparing the observed and expected incidence rates we expected that both values would be higher where the measured prevalence rate was the highest. In Yanga dia Songa health area, in spite of it having the highest prevalence (52.6%), the recorded health facility incidence rate was very low. This implies that the health facility is an outlier in terms of reporting the malaria disease burden, illustrating the quality issues faced by the sentinel site system.
A third source of estimation to triangulate with both the observed data and our current model will be interesting to explore in order to obtain a better idea of how well we can measure the actual burden of disease. The next step in this analysis will be to explore the methodology used by WHO and collaborators at the malaria Atlas Project, extracting their model based estimates of prevalence and incidence from the 2015 geospatial inference models.

7. Malaria morbidity in the Democratic Republic of Congo from 2010 to 2014: What is really captured by the surveillance system?

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Working paper

7.1 Abstract

Background

Despite inherent challenges, health facility-based data remain the only consistent and readily available source of information on malaria in many endemic areas. In the Democratic Republic of Congo (DRC), the use of malaria rapid diagnostic tests (mRDT) has been expanded since 2010, leading to a marked increase in suspected malaria cases receiving a diagnostic test. Together with other management measures, this should improve the quality of the incidence rates obtained through the Health Management Information System (HMIS). Based on household survey data, the Malaria Atlas Project (MAP) has produced estimates of clinical incidence of malaria for the years 2000-2015 for all African countries. Here we assess how well the two data sources (routine versus modelled) correlate.

Methods

Validated HMIS data from 2010 to 2014 were obtained through the National Malaria Control Programme (NMCP). Data on incidence cases of clinical malaria by province were downloaded from the MAP website. Trends in surveillance indicators were examined over a 5-year period. The number of reported confirmed malaria cases was compared to the MAP predicted incidence counts to determine the relative reporting of the HMIS system.

Results

While the incident cases predicted by the MAP model progressively decreased (from 27.7 million cases in 2010 to 20.1 million cases in 2014), the reported confirmed malaria cases increased from 2.4 million in 2010 to 9.8 million in 2014. As a result, the percentage of suspected malaria cases receiving a diagnostic test increased from 37.4% in 2010 to 90.1% in 2013. Over this time period the slide and mRDT positivity rates have remained almost constant, with an average of 62.7% and 68.9%, and the reporting completeness rate as well as the total number of outpatients and the number of suspected cases have not shown marked changes either. When compared to the MAP predicted incidence cases, the fraction of incidence cases reported by the HMIS has been progressively increasing from 8.7% in 2010 to 48.7% in 2014.

Conclusions

Due to the expansion of parasitological diagnosis, the number of confirmed malaria cases reported and hence the fraction of incident cases captured by the HMIS data is increasing over time. Because of inconsistencies in reporting, it has been difficult to establish trends in malaria morbidity from

nationally aggregated data, but the unchanged test positivity rates suggest malaria transmission remained high and stable over that time period.

7.2 Background

Information on the number and distribution of malaria cases and deaths is fundamental for the design, implementation and evaluation of malaria control programmes (WHO, 2011). As in many sub-Saharan African countries, the decision makers in the Democratic Republic of Congo (DRC) rely on two main sources of data: (1) routinely collected health facility-based data available through the Health Management Information System (HMIS); and (2) nationally representative surveys such as the Demographic and Health Survey (DHS), Multiple Indicator Cluster Survey (MICS), and Malaria Indicator Survey (MIS) (PNLP, 2013a). These nationally representative surveys provide reliable estimates for key malaria indicators that are important for: (1) planning control interventions, (2) monitoring trends in population intervention coverage, and (3) evaluating impact on malaria burden. They also provide valuable information for interpreting data from other sources (Cibulskis *et al.*, 2007). Recent collaborative work by the Information For Malaria (INFORM) project assembled data from household surveys to produce an epidemiological profile of malaria in the DRC (Figure 7.1) (PNLP *et al.*, 2014). However, nationally representative surveys are designed to produce precise estimates at national and at best at regional level. Using these data to provide sub-regional level estimates of outcome will therefore lead to low precision in the estimates. Furthermore, since un-sampled areas get an estimate on the basis of neighbouring sampled areas, the validity of such estimates also becomes an issue. DRC is the size of Western Europe and has a highly decentralised health system (Figure 7.2). The operational unit of the health system is the health zone (sub-provincial level). Given the low total number of parasite prevalence surveys done in the country (1400 time-space surveys since 1980), the validity and precision of the estimates at the level of the health zone is low. This, along with the long interval between surveys (usually 3-4 years) and their high cost constitute a clear limitation of such data sources for monitoring and planning purposes.

HMIS data have the advantage of being collected continuously from every health facility in the country. When such a system is working well, it can continuously monitor, with a high time-space resolution, the evolution of malaria cases (Gething *et al*., 2007, Bennett *et al.*, 2014). However, HMIS data also have limitations. Firstly, varying degrees of data quality and completeness are observed across the HMIS system and therefore trends in morbidity and mortality can vary over time for reasons that have nothing to do with the epidemiology of disease. Secondly, the reported cases in a HMIS are influenced by changes in use of health services, diagnostic technologies, medical procedures, and changes of regulations within the HMIS itself. Thirdly, the HMIS only

captures those members of the population that seek care at a formal health facility and represents therefore an incomplete sample of the morbidity and mortality experienced by communities. As a result of these limitations, a HMIS can underestimate the total burden of disease by a considerable fraction (Chilundo *et al.*, 2004, Rowe *et al.*, 2009). The World Health organisation (WHO) estimates that routine health information systems detect only 14% of the malaria cases estimated to occur globally. Furthermore, case detection rates and the proportion of deaths reported are lowest in countries with the highest malaria disease burden As a result of this weak information system, it is not possible to reliably assess malaria trends using the data submitted to the WHO in 32 highly endemic countries, including DRC (WHO, 2013b, WHO, 2014b) Despite these inherent challenges, in many settings the HMIS data remain the only consistent and readily available source of information on malaria.

Due to an increase in the use of rapid diagnostic tests, there has been a marked increase in the proportion of suspected malaria cases receiving a malaria diagnostic test. Substantial improvements have also been observed in treatment seeking rates for malaria (Ministère du Plan *et al.*, 2007, UNICEF, 2010, WHO, 2013b, Ministère du Plan *et al*., 2014, WHO, 2015c, Battle *et al*., 2016), often thanks to donor-supported programmes. These trends have the potential to improve the case detection rate of HMIS data and hence the fraction of the actual community malaria incidence that is captured.

Based on parasite rate household surveys, the Malaria Atlas Project (MAP) has produced modelled estimates of clinical incidence of *Plasmodium falciparum* malaria for the years 2000-2015 for all African countries (Bhatt *et al.*, 2015). Although these estimates come with uncertainties and some limitations, they constitute probably the best estimates of clinical malaria incident cases at present for countries with incomplete reporting systems. Even though they do not constitute a Gold Standard, these modelled numbers provide at least a reference value to allow an estimation of how well the HMIS is reporting incidence rates. This study assesses the malaria incidence rates obtained from the HMIS data in the DRC from 2010 to 2014, and compares them to the modelled incidence rates from the MAP project for the same time period.

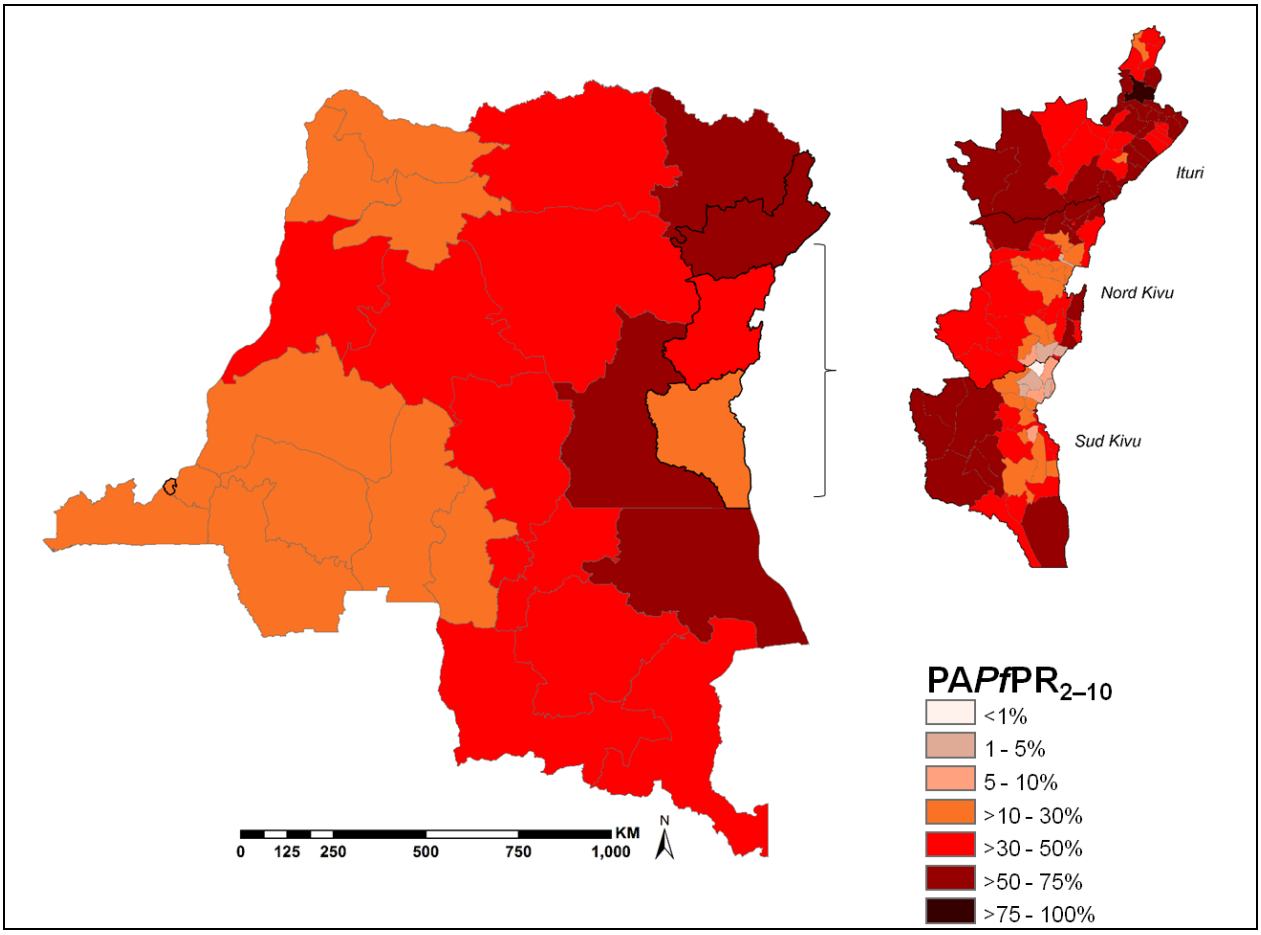

Figure 7.1 Population-adjusted *P. falciparum* parasite rate in 2-10 year olds, by region (large map) and by Health Zone for three regions (detailed map for Ituri, North Kivu and South Kivu), 2013. Source: INFORM Project.

7.3 Methods

Study site

The DRC is one of the most malarious countries in the world. Together with Nigeria, DRC accounts for about 40% of the total of estimated malaria cases worldwide, and for more than 35% of the total estimated malaria deaths (WHO, 2015c). In total, 97% of the estimated 72 million inhabitants live in high malaria transmission areas. In 2014, the DHS reported an average malaria prevalence (using microscopy) of 23% in children less than 5 years (Ministère du Plan *et al.*, 2014).

The health system in DRC has a pyramidal structure with three levels (Figure 7.2): central, intermediate and peripheral level. The central level includes the office of the minister of health (MoH), the general secretary of the MoH, and the directorates of national disease-specific programs. The intermediate level is composed of 26 provincial health divisions (previously 11 until 2013). The peripheral level comprises 516 Health Zones (HZ). The HZ is the actual operational unit

of the health system and includes a general referral hospital and 15-20 health centres. A HZ is further divided into 15 Health Areas (HA) on average. The health system also includes community health workers providing treatment at community level in the framework of the integrated community case management (iCCM). The national guidelines for the management of malaria recommend parasitological confirmation for all malaria suspected cases seen at all levels of the health system using malaria Rapid Diagnostic Test (mRDT) or microscopy.

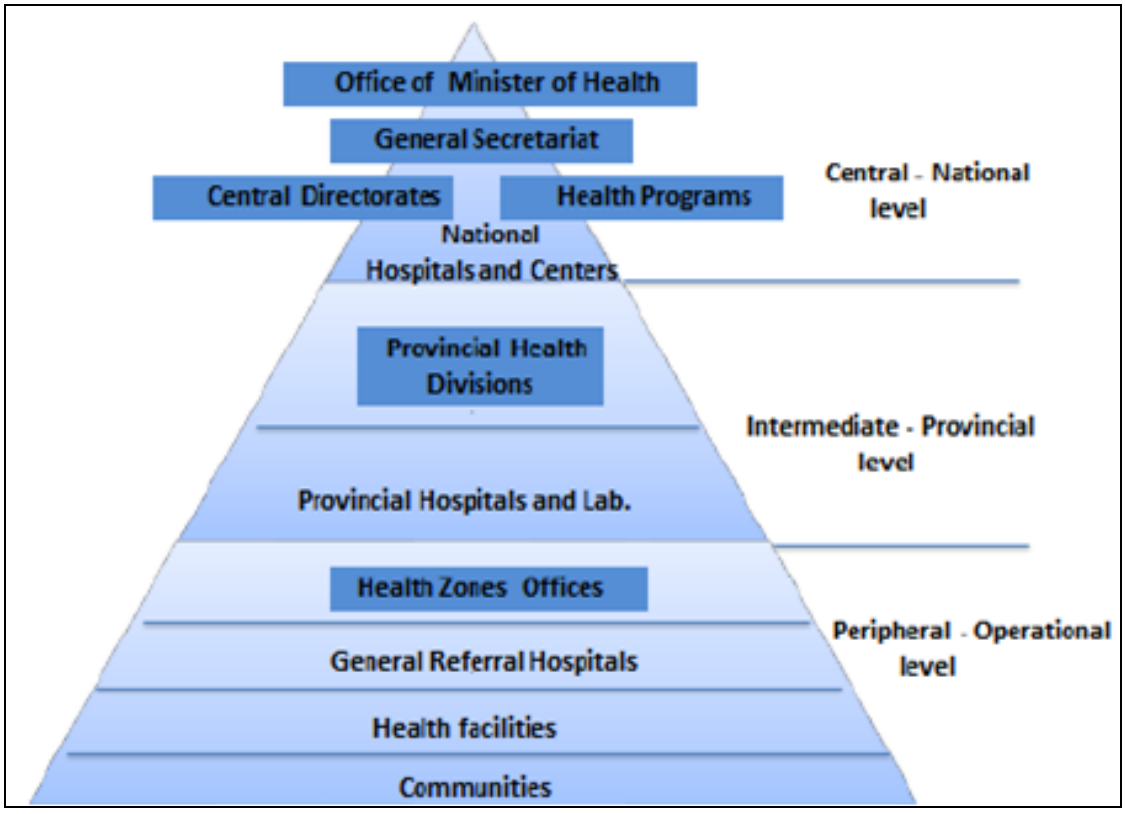

Figure 7.2 Health system structure in the DRC

Data assembly

HMIS data from 2010 to 2014 were obtained from the Monitoring and Evaluation division of the National Malaria Control Programme (NMCP). Monthly data from iCCM sites and health facilities as well as data from the general referral hospitals are transmitted to the HZ office, where they are analysed and validated during a monitoring meeting with nurses responsible for the different HA. The data are then transmitted to the provincial level, which compile, analyse, validate, and transmit the consolidated data to the central level, where they are further consolidated, verified, analysed and validated. Aggregated data at country level are then used to produce the NMCP annual report and these data are transmitted to the WHO. While the entire system is progressively being made electronic by the scaling up of the District Health Information Software 2 (DHIS2), many HZ

continue to use paper forms for the collection of routine malaria data. In these cases the data are then entered into an electronic database at the provincial level.

Data on modelled incident cases of clinical malaria were downloaded from the MAP website (http://www.map.ox.ac.uk). These data are available for use on an open access basis. For the DRC, the modelled clinical incident cases of *Plasmodium falciparum* malaria are derived from a cartographic method based on parasite rate surveys, including the DHS 2014. Firstly, parasite prevalence data from 1995 to 2014 were assembled within a spatiotemporal Bayesian model, taking into account environmental and socio-demographic covariates, as well as data on use of insecticide treated nets (ITN) and access to treatment. The model predicted *P. falciparum* prevalence at a resolution of 5x5km^2. Secondly, an ensemble model was developed to predict malaria incidences as a function of parasite prevalence, and then applied to obtain estimates of malaria incidence cases at 5x5km^2. Data for each 5x5km^2 grid were then aggregated to obtain national and regional estimates of malaria cases (Bhatt *et al.* 2015). Data on predicted malaria clinical incidence are available as annual incidence counts (total number of malaria cases) and annual incidence rates (cases per 1,000 people per annum), for both country and provincial levels.

Analysis

National HMIS case data were obtained in XLS format from the NMCP and converted into STATA version 13 (Stata Corporation College Station, TX, USA) for analysis at both national and provincial levels. Overall trends at national and provincial level were produced over a 5-year period for the following key surveillance indicators: (1) number of confirmed malaria cases per 1,000 population per year; (2) percentage of suspected malaria cases receiving a diagnostic test; (3) malaria test positivity rate (mRDT and slide positivity rate) and (4) completeness of reporting (i.e. number of monthly reports received out of the total expected). Incidence rates were calculated using the population data from the National Health Development Plan as the denominator. Unfortunately, these data are based on the 1984 census to which a yearly growth rate of 3% is applied (Ministère de la Santé, 2011), and the numbers are likely to be subject to some (unknown) error.

To assess variation by geographical area, the incidence of reported confirmed malaria cases and test positivity rates were mapped at provincial level using quantum GIS version 2.0 (Quantum GIS Development Team, Open Source Geospatial Foundation).

Finally, the number of reported confirmed malaria cases was compared to the predicted incidence count to determine the representative fraction of HMIS data. Trends in this fraction were examined over the same time period.

Given large numbers of reported cases and hence large numerators and denominators, confidence intervals were very small; therefore they are not shown in the text.

7.4 Results

The HMIS dataset was collected from the NMCP for the period 2010 to 2014. For each year, data were available for all 11 provinces; 2014 data were also presented for the 26 new provinces. Available data included, amongst others, the total population, the number of suspected cases, the number of microscopy slides performed with the number of positive slides, the number of mRDTs performed with the number of positive mRDTs, and the report completeness.

Completeness of reporting

Over the period considered, the completeness of reporting has been fluctuating with the highest value (94%) reported in 2010 and the lowest value (84%) reported in 2014 (Table 7.1).
The provinces of Equateur, Kasai Occidental and Katanga have reported the lowest rates of reporting completeness for the year 2014, with 57%; 72% and 79% respectively. Moreover, during the past five years, the provinces of Equateur and Katanga have reported some of the lowest rates of reporting completeness with 73% in 2013 and 2012 for Equateur and 67% in 2012 and 55% in 2011 for Katanga. The provinces of Bas Congo and Nord Kivu have reported consistently over 90% during the five-year period.

Reported suspected malaria cases

From 2010 to 2014, the total number of outpatients did not show any particular trend. The same was found for the number of suspected malaria cases reported nationally, which ranged between 129 and 148 cases per 1,000 population, with the highest value observed in 2013 and the lowest observed in 2014 (Table 7.1). Higher numbers of suspected malaria cases per 1,000 population were reported in provinces with higher reporting completeness rate. The province of Bas Congo, with the highest reporting completeness (average 97% over the period considered), reported the highest number of suspected cases, showing a peak of 266 cases per 1,000 population in 2013 (Figure 7.3).

Percentage of suspected malaria cases receiving a diagnostic test

Overall, the proportion of suspected malaria cases receiving a diagnostic test has been progressively increasing. From 37.4% in 2010, this percentage increased to 69.4% in 2011; 76.9% in 2012; 90.1% in 2013 and it was reported to be 147.6% in 2014 (Table 7.1). The observed increase in percentage of suspected malaria cases tested was seen across all provinces. When split by the types of diagnostic test used, the results showed that while the proportion of suspected cases tested by microscopy has remained almost constant throughout the study period with a slight decline during the past 3 years (36.8% in 2010; 41.0% in 2011; 43.5% in 2012; 36.4% in 2013 and 35.7% in 2014), the proportion of cases tested by mRDT has progressively increased from 0.005% in 2010 to 53.7% in 2013 and 111.9% in 2014. A possible explanation for the proportion of suspected cases tested being more than 100% might be a misclassification of patients resulting in fewer reported suspected cases compared to the number of tests performed or due to double testing with both mRDT and microscopy. At provincial level, the data showed the same patterns with constant or decreasing percentage of cases tested by microscopy, and increasing percentages of cases tested by mRDT. The province of Equateur showed one of the lowest testing rates, increasing from 16.9% in 2010 to only 51.8% in 2013. For almost all provinces, the percentage of suspected cases tested by mRDT in 2014 was above 90%, except Maniema (83%) and Kasai Oriental (82%). The lowest percentage of cases tested by microscopy was reported in Maniema Province (from 19% in 2010 to 10% in 2014), while the province of Bas Congo reported the highest percentage of cases tested by microscopy: 80% in 2010 and 2011; 87% in 2012; 88% in 2013 and 67% in 2014.

Table 7.1 Summary of malaria surveillance indicators at national level from 2010 to 2014

NATIONAL	2010	2011	2012	2013	2014
Population	64,420,000	66,352,600	68,343,178	70,393,473	72,505,278
Reporting completeness (%)	94	86	87	88	84
OPD	24,631,423	26,189,657	24,225,892	27,167,148	27,370,003
Suspected cases	9,252,959	9,442,144	9,128,398	10,408,506	9,378,589
Suspected /1,000 population	143.6	142.3	133.6	147.9	129.4
Tested/Suspected (%)	37.4	69.4	76.9	90.1	147.6
Slide positivity rate (%)	64.6	63.9	61.4	63.3	60.2
mRDT positivity rate (%)	78.3	63.9	64.2	67.3	70.8
Confirmed cases	2,417,780	4,561,981	4,791,598	6,715,223	9,823,673
Incidence rate/1,000 population	37.5	68.8	70.1	95.4	135.5
MAP predicted number of cases	27,732,836	25,687,991	22,446,366	21,083,796	20,170,486
Fraction captured (%)	8.7	17.8	21.3	31.9	48.7

Malaria test positivity rate

Neither the slide positivity rate nor the mRDT positivity rate has shown marked changes over time during the period considered. The slide positivity rate has remained almost constant, with an average of 62.7% (64.6% in 2010; 63.9% in 2011; 61.4% in 2012; 63.3% in 2013 and 60.2% in 2014). The mRDT positivity rate has shown a slight increase of 7 points from 2011 to 2014. The average mRDT positivity rate was 68.9% (78.3% in 2010; 63.9% in 2011; 64.2% in 2012; 67.3% in 2013 and 70.8% in 2014) (Table 7.1).

The provinces of Nord Kivu and Sud Kivu in the eastern part of the country reported the lowest slide positivity rates, with respectively an average of 50.0% (46.2% in 2010; 53.1% in 2011; 51.6% in 2012; 51.7% in 2013 and 47.6% in 2014) and 42.6% (44.7% in 2010; 45.5% in 2011; 42.1% in 2012; 40.4% in 2013 and 40.2% in 2014). These provinces also reported the lowest mRDT positivity rates with respectively an average of 45.0% (46.1% in 2011; 45.5% in 2012; 43.4% in 2013) and 38.6 %(29.6% in 2011; 37.8% in 2012; 48.6% in 2013). The highest slide positivity rates were reported in the provinces of Bas Congo and Katanga with respectively an average of 69.2% (67.6% in 2010; 69.4% in 2011; 69.1% in 2012; 68.7% in 2013 and 70.9% in 2014) and 68.6% (71.6% in 2010; 68.5% in 2011; 67.7% in 2012; 64.2% in 2013 and 71.1% in 2014) (Figure 7.5A). Whereas the highest mRDT positivity rates were reported in the provinces of Katanga and Orientale, with respectively an average of 77.1% (86.6% in 2010; 75.5% in 2011; 75.8% in 2012; 78.3% in 2013 and 69.1 in 2014) and 75.6% (73.8% in 2010; 72.8% in 2011; 70.9% in 2012; 73.2% in 2013 and 87.6% in 2014) (Figure 7.5B).

When compared at national and provincial levels, the mRDT positivity rates were consistently higher than the slide positivity rates over time, except for the provinces of Kinshasa and Nord Kivu (Figure 7.4). The greatest differences were observed in the provinces of Orientale, Equateur and Maniema. In most provinces, the slide positivity rate curves seem flatter and thus more constant than the mRDT positivity rate curves.

Reported confirmed malaria cases

Overall, the number of reported confirmed malaria cases has been increasing over time. The reported malaria incidence rate has shown a 100% increase from 37.5 per 1,000 population in 2010 to 135.5 per 1,000 population in 2014. The biggest increases have been observed from 2010 to 2012, with a 30% increase, and from 2013 to 2014 with an increase of 40% (Table 7.1, Figure 7.3). Much of this increase in confirmed cases is linked to the much higher testing rates. For the year

2014, the highest confirmed malaria incidence rates have been reported in the provinces of Bas Congo with 319 cases per 1,000 population and Kasai Oriental with 258 cases per 1,000 population (Figure 7.3), whereas the lowest confirmed incidence rates have been reported in the provinces of Katanga with 118 cases per 1,000 population and Equateur with 124 cases per 1,000 population (Figure 7.3).

Except for the province of Bandundu, where an apparent decrease in confirmed malaria incidence was reported between 2011 and 2013 (82.7 per 1,000 in 2011; 78.9 per 1,000 in 2012 and 64.4 per 1,000 in 2013) followed by an increase in 2014 (175.5 per 1,000), in all provinces the data showed the same patterns as the national level: reported confirmed malaria incidence progressively increased over the period considered. The ascending curve was interrupted by a small drop in 2012 in four provinces (Bas Congo, Nord Kivu, Equateur and Kasai Oriental) and in 2013 in two provinces (Kinshasa and Maniema).

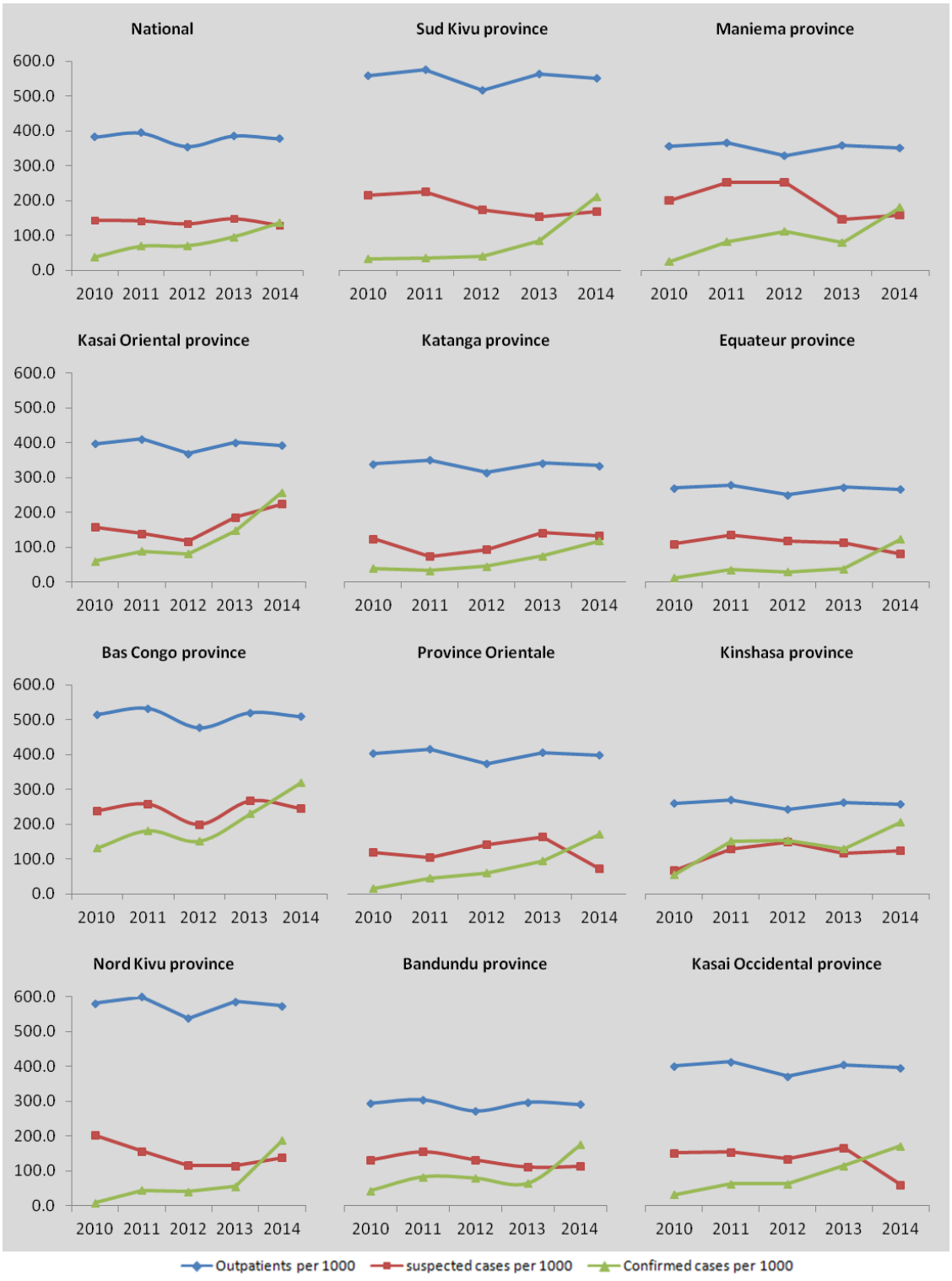

Figure 7.3 Total all-cause outpatient incidence, total suspected and confirmed malaria case incidence, per 10,000 population, by Province and year, 2010-2014, DRC

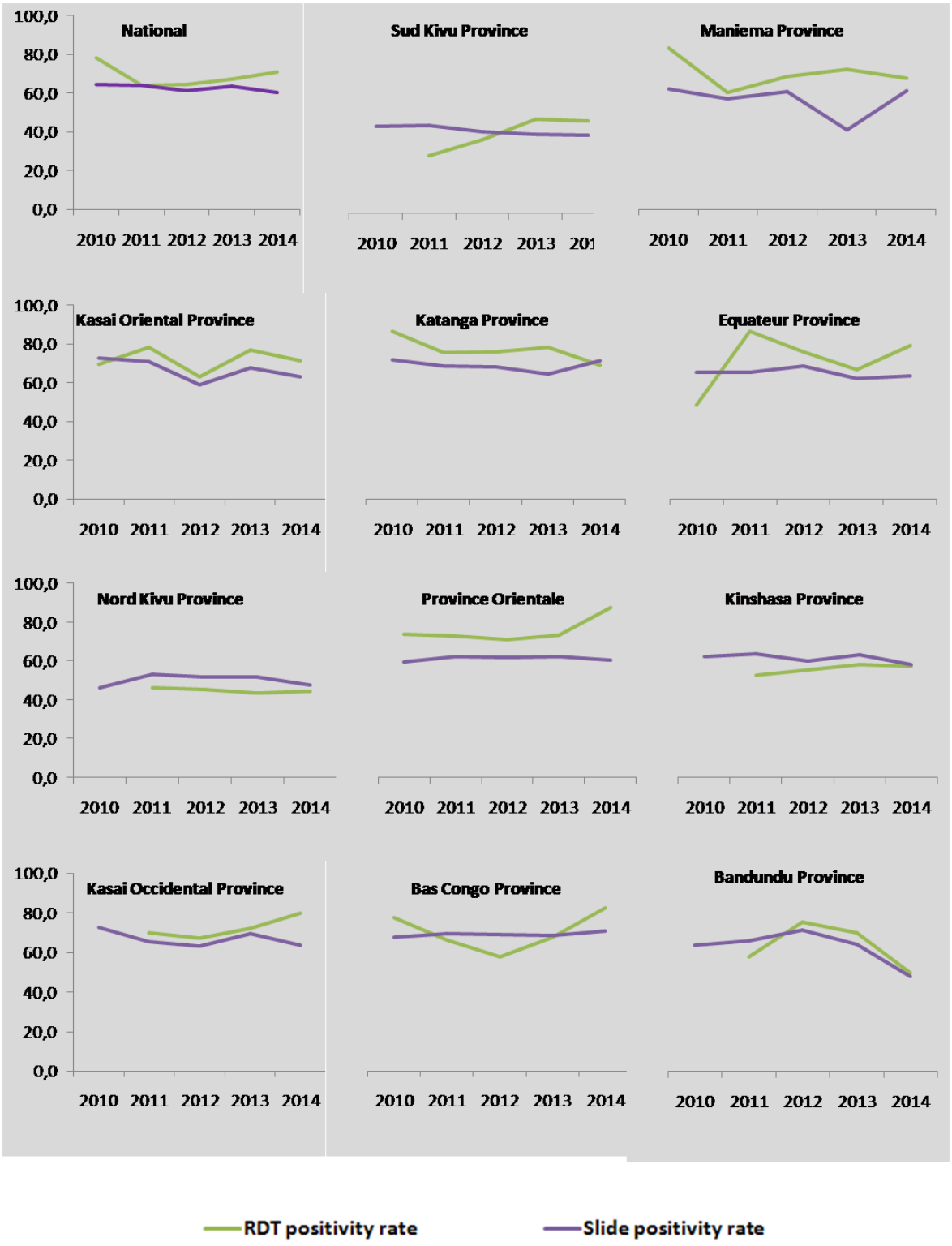

Figure 7.4 mRDT and slide positivity rates, by Province and year, 2010-2014, DRC

Relative fraction of malaria cases reported by the HMIS data

The number of reported confirmed malaria cases was compared to the predicted incidence counts estimated by the MAP project, to determine the fraction of all malaria cases reported by the HMIS.

The MAP predicted numbers of malaria cases for the period 2010 to 2014 were 27.7 million cases in 2010, 25.7 million cases in 2011, 22.4 million cases in 2012, 21.1 million cases in 2013 and 20.1 million cases in 2014 (Table 7.1).

Over the period considered, trends in malaria incidence using the two different sources of data showed opposite patterns. While the MAP predicted incidence of cases progressively declined from 27.7 million predicted cases in 2010 to 20.1 million predicted cases in 2014 (mainly as a result of the predicted effect of key interventions such as Long Lasting Insecticidal Nets), the reported confirmed HMIS number of malaria cases increased over time (from 2.4 million cases in 2010 to 9.8 million cases in 2014 (Table 7.1). Obviously, as more cases were tested, the number of confirmed cases increased. The same pattern was observed across all provinces (data not shown).

When compared to the MAP predicted incident cases, the reported confirmed cases by the HMIS data in 2014 represented 48.7%. This fraction has been progressively increasing since 2010: it was only 8.7% in 2010, 17.8% in 2011, 21.3% in 2012 and 31.9% in 2013. The biggest increase in the fraction reported by the HMIS was observed from 2013 to 2014, with an increase of 17 points (Table 7.1).

The same pattern of increasing representative fraction was observed in all provinces. The lowest representative fractions were observed in the provinces of Province Orientale (1.8% in 2010; 5.6% in 2011; 8.5% in 2012; 14.9% in 2012 and 29.2% in 2014) and Katanga (9.8% in 2010; 8.9% in 2011; 13.3% in 2012; 23.2% in 2013 and 38.3% in 2014). In the majority of provinces the number of confirmed malaria cases reported has markedly increased in the last year (2014), with a representative fraction of over 90% in two provinces; Kinshasa (93.3%) and Bandundu (90.4%). In four provinces, there were more confirmed malaria cases reported in the HMIS than those predicted by the MAP, leading a representative fraction over 100%; Bas Congo (126%), Nord Kivu (209.3%), Kasai Oriental (100.6%) and Sud kivu (176.1%).

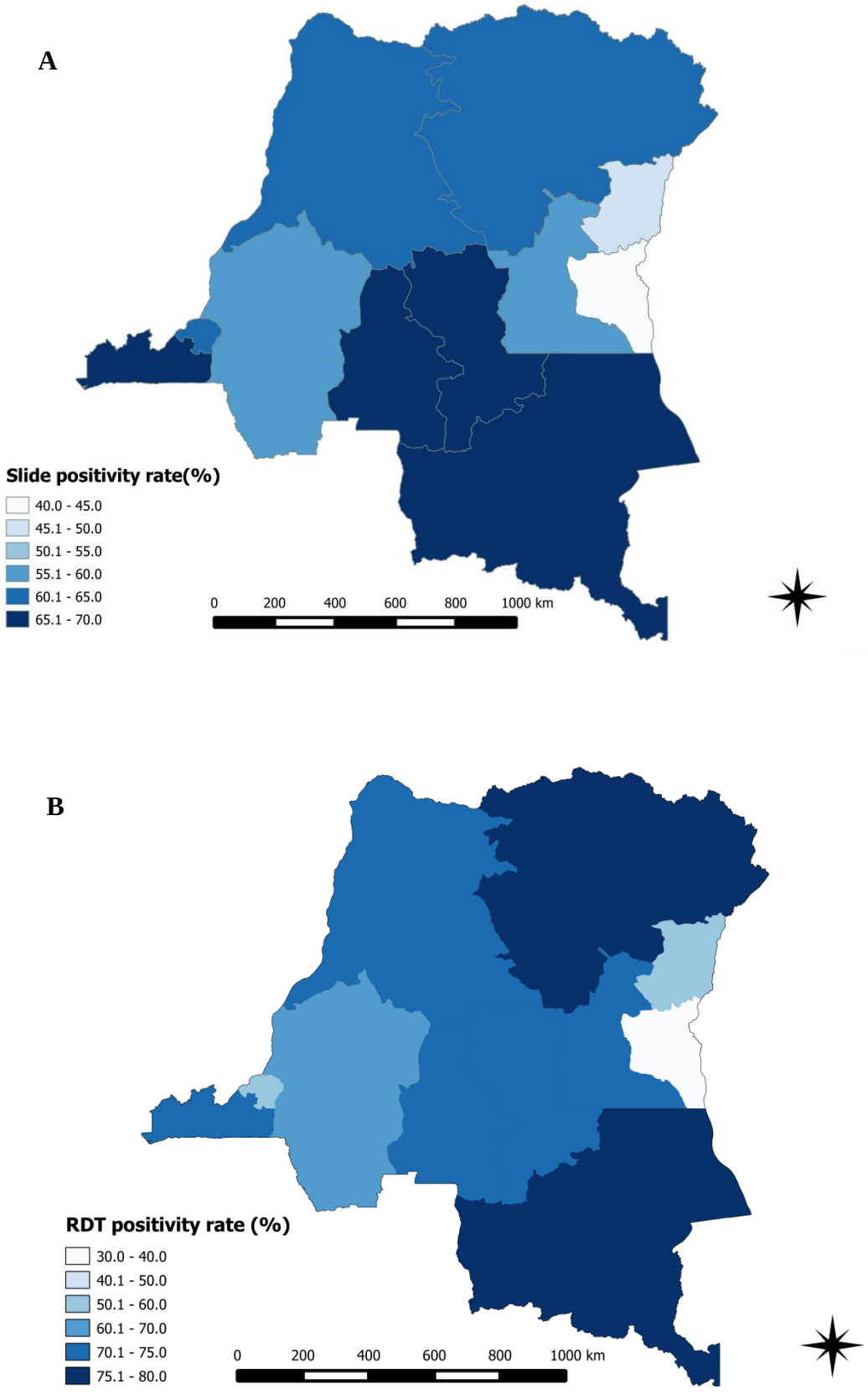

Figure 7.5 A. Average slide positivity rate, B. Average mRDT positivity rate, 2010-2014, DRC.

7.5 Discussion

The two principal objectives of malaria surveillance systems are to provide programme managers with accurate and timely spatio-temporal information on malaria incidence trends to (1) track the epidemiological situation, and (2) guide interventions. Due to known biases and confounders in HMIS data, different methodological approaches have been used to improve the use of routine health system data for rigorous programme evaluations (Graves *et al.*, 2008, Rowe *et al*., 2009, Bennett *et al.,* 2014). Using a simple analysis of HMIS datasets, results of this study showed that over the period considered, the percentage of suspected malaria cases receiving a diagnostic test and subsequently the number of confirmed malaria cases were increasing. At the same time the malaria test positivity rates remained almost constant at a very high level (62% for microscopy and 68% for mRDT) and the representative fraction of HMIS increased.

The number of confirmed malaria cases reported by the surveillance system is obviously highly sensitive to changes in a number of operational factors such as reporting rates, diagnostic practices and health facility usage rates. The period considered in this study coincided with changes in diagnostic practices, especially the introduction of mRDTs in 2010. This translated directly in an increasing proportion of suspected cases receiving a diagnostic test, hence leading to increasing numbers of reported confirmed malaria cases.

With the introduction of mRDT, it could be expected that the proportion of suspected cases tested with microscopy would be decreasing, but this proportion remained almost constant. This, along with the fact that the proportion of suspected cases receiving a diagnostic test was over 100% in some provinces, might suggest the use of both mRDT and microscopy for malaria diagnostic in many health facilities. Economic incentives work in favour of doing blood slides (paid for by patients) in addition to mRDTs (provided for free to health facilities and hence in principle also free to the patient).

In contrast to trends in confirmed malaria cases, the malaria test positivity rate is less sensitive to factors such as changes in reporting rates, diagnostic practices and health facility usage rates, and may therefore provide more reliable information on trends in malaria burden. In this study, both slide and mRDT positivity rates have remained stable at high values over the study period. The stable and high test positivity rates despite scaling up of control measures are rather surprising. For example, during the same period, the household ownership of at least 1 ITN increased from 51% in

2010 to 70% in 2013-2014 (UNICEF, 2010, Ministère du Plan *et al.*, 2014). In other settings the malaria test positivity rate has been used to estimate changes in malaria incidence following the scaling up of malaria interventions (Jensen *et al*., 2009, Karema *et al.*, 2012, Bi *et al.*, 2012, Assele *et al*., 2015). It has been shown in a recent study to be a valuable surveillance indicator especially in high transmission settings (Boyce *et al*., 2016). Although the test positivity rates are not immune to distortions due to bias and/or confounding (Francis *et al.* 2012), the consistency and stability observed here in both mRDT and slide positivity rates are less likely to be explained solely by the poor quality of data. If true, these estimates suggest that the DR Congo remains one of the most endemic settings in the world.

While the routine surveillance system cannot be expected to detect all malaria cases in the community, it should be expected to reflect at least the relative changes in incidence over time, and between areas. Based on parasite prevalence data from nationally representative household surveys (Ministère du Plan *et al*., 2014), the current malaria stratification used for planning interventions in the new malaria strategic plan 2016-2020 (PNLP, 2016) defines essentially two zones in the DRC: (1) the pre-elimination zone in the province of North Kivu (prevalence <5%) and (2) highly endemic zones in the rest of the country (prevalence 6-45%). However, the number of HMIS confirmed malaria cases per 1,000 population reported in 2014 does not reflect the malaria distribution in the country on the basis of prevalence data. The highest malaria incidence rates were reported in the province of Bas Congo in the western part of the country. The lowest values of malaria incidence were reported in the provinces of Katanga and Equateur – where conversely some of the highest parasite prevalence rates were reported by the DHS. So this is clearly pointing towards under-reporting of cases by routine statistics.

By contrast, the test positivity rates followed the malaria distribution in the country rather well. Both mRDT and slide positivity rates were consistent with the two zones defined by parasite prevalence data, with the Eastern part (Nord Kivu and Sud Kivu) having the lowest rates (<=50%) and the rest of the country having higher rates (>=50%).

The higher mRDT positivity rates compared to microscopy positivity rates are consistent with reports from other researchers in similar transmission setting (Francis *et al*., 2012). A further analysis of the DRC DHS 2013-2014 suggested that mRDTs, in particular Histadine-rich protein 2 (HRP-2) based mRDTs (the ones most used in DRC) generate frequent false-positive results which

are likely due to the persistence of HRP-2 in the circulation after parasites had been cleared (Ministère du Plan *et al*., 2014).

With the progressive increase in the number of confirmed malaria cases reported by the HMIS data and the progressive decrease in the number of malaria cases predicted by the MAP, the fraction of incidence captured by the HMIS data is increasing. This is likely to be due primarily to the improvement in diagnostic practices with the introduction of mRDTs. But the fact that in some provinces the total number of reported confirmed cases is higher than the total number of predicted cases points towards a low quality in HMIS reporting, hence also contributing to the observed trend. Furthermore, for a country of the size of DRC with a very low number of parasite prevalence surveys available, it would be appropriate to hypothesise that the small sample size and the low spatiotemporal density of prevalence surveys might have been contributing to uncertainty in outputs and hence a low precision in MAP estimates.

This study took a rather simple analysis approach and did not include trends in other factors that could influence trends in malaria cases seen at health facilities, such as health services usage rates and rainfall.

7.6 Conclusion

This study showed that due to the expansion of parasitological diagnosis, the number of confirmed malaria cases reported and hence the fraction of incident cases captured by the HMIS data has been increasing over time. Because of inconsistencies in reporting, it has been difficult to establish trends in malaria morbidity from nationally aggregated data. The test positivity rates suggest malaria transmission remained high and stable over time, despite a substantial increase in coverage of control interventions. Hence, health facility based data do not seem to reflect adequately the malaria distribution in the country at present, and the HMIS has not yet reached its full potential in monitoring disease trends. Improving the routine data system to provide robust, geographically detailed and timely data remains crucial for supporting the current malaria control efforts.

8. Discussion

The present thesis investigated diverse aspects pertaining to the implementation of malaria control interventions in holo- and hyper-endemic regions of Central Africa where populations are often isolated by geography or violence. It aimed to provide a locally-relevant evidence base to inform national policy about how quality malaria prevention, case management and surveillance interventions can be tailored to specific settings in DRC and CAR.

Based on the objectives defined in Chapter 2, these concluding remarks will review the lessons learnt from the research conducted for this thesis. Contributions it has made to understanding the challenges of combatting malaria and improving access to health care services in challenging settings will be considered. It will conclude with recommendations for policy makers as well as for further research.

8.1 Improving access to health care in isolated communities

As introduced in chapter 1, there are five key components that influence an individual's access to health care (Table 1.2). Generally, the findings presented here addressed two of these dimensions: availability and accessibility, specifically related to malaria control tools. The results showed how improvements to LLIN distribution strategies can increase availability of LLINs in rural communities of the DRC that are often completely isolated during the rainy season. This in turn accelerates progress towards universal coverage (defined as 1 LLIN for 2 persons). Results also showed how a network of CHWs can provide essential malaria diagnostic and treatment facilities to conflict-affected communities in the CAR in spite of chronic instability and the absence of a formal health care system. Finally, the results highlight the role a sentinel site surveillance system can play in improving a community's access to appropriate malaria diagnosis and treatment as well as ensuring the timely reporting of these cases.

8.1.1 Availability of malaria control tools

Vector control tools

The distribution of LLINs is the key component of malaria prevention in sub-Saharan Africa. There have been two rounds of mass LLIN distribution in DRC since the NMCP adopted a free-of-charge LLIN policy in 2006. The first took place between 2008 and 2012, during which over 35 million

LLINs were distributed across all Provinces (11 in total at the time). The second round of mass distribution was between 2013 and 2016, during which time over 47 million LLINs were distributed (NMCP unpublished data, 2016).

The impact of such mass LLIN distribution campaigns on reducing malaria burden has been well documented (Lengeler, 2004). However, there remains a lack of understanding of how specific demographics, culture and beliefs at the local level can influence the acceptability and use of LLINs. The cross-sectional study described in chapter 4, contributed to filling this gap by assessing the effect of two different mass distribution strategies on the outcome indicators of LLIN ownership and use as well as the cost of these distribution strategies within the rural Province of Kasai Occidental in DRC.

Results found that the strongest predictor of net use was having sufficient numbers of LLINs in the household to cover all residents. The fixed-distribution strategy achieved higher universal LLIN coverage and at a lower cost per LLIN delivered compared to the door-to door strategy as noted by others (Smith Paintain *et al*., 2014, Kilian *et al*., 2015a). As LLIN usage did not significantly differ between strategies the fixed distribution strategy is recommended for future mass campaigns in DRC. This recommendation is likely to be appropriate for other settings with extremely remote and rural populations because the door-to-door approach may miss the most remote people while with enough awareness raising, the mass campaigns are likely to attract even the most remote communities to come to fixed centres.

It is not only the net allocation strategy that determines the household's likelihood of having enough LLINs for all residents, but also the means of calculating how many nets each household receives during distribution. This was one of the methodological issues with this study, because not only were two different mass distribution methods compared, but each method used a different definition to calculate the number of LLINs to be distributed. The fixed strategy distributed 1 LLIN for 2 people, whereas the door-to-door strategy distributed 1 LLIN per sleeping space. It is common in DRC (and many other sub-Saharan African countries) for more than two people to sleep in one space covered by a LLIN. Therefore, assigning LLINs based on this would often fail to reach the RBM definition of universal coverage. While it may be more economical, as an extra LLIN cannot be used if there are no spare sleeping spaces to be covered, it doesn't allow for replenishing damaged LLINs within the household before another campaign. However, the calculation method of 1 LLIN per 2 persons used in DRC was also not sufficient for universal coverage because

number of LLINs were rounded down in case of an odd number of residents, instead of rounding up. Furthermore, there was a cap set at a maximum of 4 LLINs per household, regardless of how many more people there were. These factors may explain why only 6 months after distribution, less than 50% of households had enough LLINs to cover all residents. Therefore net allocation in future campaigns should be improved to strictly respect the criteria required for reaching universal coverage and not place a maximum cap on number of LLINs received.

It is also important to reduce the interval between mass campaigns to ensure LLINs are replaced by new rounds of mass distribution before their average life span of 2 to 3 years (Gnanguenon *et al.*, 2014). The two mass distribution campaigns in DRC took about 4 years to be completed. Additionally, while waiting for the next round of mass distribution it is important to improve the routine distribution strategies which currently only target pregnant women through ANC and children through vaccination campaigns and more recently schools (the first pilot school distribution was conducted in Kasai Occidental). Therefore additional avenues need to be explored that reach the whole population if high coverage levels are to be sustained over time. Finally, as discussed in chapter 1, by not only focussing on the vector control tools, but by also improving education and quality of living through improving housing conditions, sanitation etc., substantial gains can be made in LLIN lifespan (Kilian *et al.*, 2015b).

ACT availability

In addition to ensuring availability of LLINs for rural communities to prevent malaria, it is vital that effective ACT is available for the treatment of malaria when it arises. While ACT availability is a problem experienced across many sub-Saharan African countries, especially in rural areas, the reasons behind the limited availability differ and therefore the solution cannot be the same. For example, in the CAR, due to the absence of a state health system, availability of ACT is almost exclusively through international NGOs. The fragility here stems from the reliance on continued donor funding for ACT provisioning. While this is also a factor in the DRC, the historical review of malaria control (detailed in chapter 3) points to a more unique challenge in increasing availability in ACT (as well as acceptability by health care workers). An important event in DRCs history of malaria control was how it was able to start quinine production when importing it became impossible during the Second World War. At the time, it was a vital anti-malarial drug that reduced the malaria burden and producing it in-country also meant that it became an important economic activity. This has important implications today because while quinine may still have some role to play in treating malaria during the first trimester of pregnancy, it threatens effective management of

uncomplicated malaria with ACT and has been shown to be more expensive and harder to use for severe malaria compared to injectable artesunate (Achan *et al*., 2011, Ferrari *et al*., 2015, Ntuku *et al*., 2016). The production of quinine in DRC retains its economic value today and it is still widely accepted as the preferred anti-malarial by many health care professionals in DRC as well as in many other sub-Saharan African countries. Therefore it is vital to continue to educate providers and patients about the benefits of ACT for uncomplicated malaria, and the value of injectable artesunate for severe malaria.

The barriers to access mentioned above can prevent an intervention with the highest efficacy under controlled conditions from being effective in reality (Tugwell *et al.,* 2006). Studies (including the one presented in Chapter 6) have shown that the main drop from efficacy to effectiveness is due to the health seeking behaviour of individuals. It is influenced by a person's perception of the nature of the disease, its potential severity, as well as the costs and potential benefits of accessing care. This behaviour subsequently influences the proportion of the population within a given community that present to health facilities and therefore affects the representativeness and completeness of facility-based data.

The importance of the private sector

An important aspect in treatment seeking behaviour discussed in chapter 6, as has been reported elsewhere, is the important role the private sector plays in delivering malaria treatment in DRC. Findings presented here show that private pharmacies were the most common providers of treatment amongst those who sought care for a fever. This was higher in the semi-rural areas of Kimpese Health Zone compared to rural areas of Vanga Health Zone. Increasing access to health care therefore needs to include the private sector and focus on where the people actually go. There is a need to better understand the care received at pharmacies in terms of whether there are quality medicines available, if it is feasible to introduce any data collection (HMIS or other) or diagnostic testing and if so, what additional incentives would be needed and would it be sustainable.

To overcome the fact that most people with fever seek treatment in private drug outlets in DRC, which usually stock cheap but ineffective monotherapies including quinine, Population Services International (PSI) and Association de Santé Familiale (ASF) have created the 'ACT access programme'. This is part of the 'ACTwatch' research project which launched in 2008 to conduct research on the anti-malaria market across 7 sub-Saharan African malaria-endemic countries including DRC (ACTwatch Group *et a*l., 2017). The ACT access programme aims to transform the

private sector anti-malarial market through increasing consumer demand of ACT and fostering private sector case management (Lussiana, 2016).

8.1.2 Accessibility of health care services

The historical review of malaria control in the DRC also highlighted that malaria control programmes have always been largely focussed on the urban centres that are more densely populated, where infrastructure is often better, and therefore populations are easier to access with interventions. This issue remains today as the most remote populations receive the least investment and attention and consequently carry the highest burden of disease. For example, the ACT access programme discussed in the above section is being rolled out only in the DRC's capital, Kinshasa, meaning that peripheral services continue to rely heavily on quinine and other ineffective antimalarials. This was even seen in the sentinel site surveillance survey presented in Chapter 6 in which for largely logistical reasons, two of the three sites nearest to the capital Kinshasa and therefore accessible by road were selected for the pilot community survey. If these surveys are to be repeated in the more distant or rural sentinel sites, considerably more financial and logistical resources will be required.

A well-known strategy to increase accessibility of health care services, particularly for malaria case management in rural areas is through the use of CHWs. This allows health care to be effectively decentralised to remote areas far from health facilities where the need is often great as a consequence. However, there is a gap in knowledge of how this system which is effective in peaceful areas could also be effective in conflict-affected communities. The results presented in chapter 5 contributed to filling this gap in knowledge and showed that CHWs can provide access to health care where insecurity is rife and there is no other source of care. The research for this study was carried out within two rural sub-Prefectures in North West CAR where on-going civil war has resulted in a near total collapse of the health system. Consequently, existing levels of medical assistance, including malaria case management are simply insufficient for the scale of the needs and there are very few malaria prevention interventions available.

This study was the first to assess the feasibility and sustainability of a CHW project in a conflict zone of Central Africa. One of its main strengths is that the data covered a period of over four years, capturing seasonality trends as well as changes during different stages of conflict. As it also assessed two different areas where the CHWs began operating at different times, it enabled

comparisons to be made between a site where the intervention had been running for several years and where it had been newly implemented. The results showed that in emergency situations community-based case management and surveillance can help fill the gaps left by inexistent health systems and inform operational decisions to target those most vulnerable. CHWs maintained high levels of data reporting and while the programme largely focussed on case management (and not prevention) the impact on reducing malaria associated morbidity in the absence of alternative care is undeniable.

The historical review of DRC also highlighted the importance of understanding how changes in the political climate influenced health care and ultimately disease burden. It showed that unstable governments and conflicting agendas disrupted medical services and malaria control programmes leading to a devastating increase in malaria. Strategies, such as the CHW programme described here, that can access displaced populations will be essential for the future of malaria control in both DRC and CAR, where the effects of internal conflict have continuously resulted in massive numbers of displaced populations.

While these CHWs have treated about 200,000 malaria patients over a four year period in CAR, the results presented highlight that peace is essential for sustainable health care and particularly malaria control. While civil disruption doesn't have to cause malaria control programmes to fail, as seen in Sri Lanka's ability to eliminate malaria in spite of 30 years of civil war, conflicts in sub-Saharan Africa have brought a much higher level of destruction to the health system and therefore are somewhat incomparable. A striking feature of sub-Saharan African conflicts is also the atrophy of the state, which often begins even before violent conflict, as was the case in CAR. Ample evidence from sub-Saharan Africa suggests that conflicts along with large-scale population movements have contributed to dramatic declines in health sector functions and delivery. As a result, armed conflict is arguably the most important determinant of poverty in such countries in sub-Saharan Africa.

8.2 Prospects for malaria surveillance in low resource settings

Overall, the evidence shows that malaria control in both the DRC and CAR is a complex problem requiring multiple layers of information to target and tailor resources, partnerships and approaches to reaching inaccessible and vulnerable communities. Chapter 6 and 7 highlighted how the malaria surveillance system in DRC is currently insufficient to identify locations where the incidence of malaria is greatest. With this in mind, chapter 6 described the implementation of a community-

based sentinel surveillance site and its ability to capture malaria cases. A community-based survey was conducted at two sentinel surveillance sites, one rural and one semi-rural, to investigate the representativeness of the sentinel surveillance site. It showed that a key strength of this sentinel site programme in a country as vast as DRC is that concentrating efforts on one sentinel site per province ensures the differing climates and malaria transmission dynamics seen across this vast country are captured.

While it cannot ensure improved data management across the health system in general, it can enhance supervision and reporting mechanisms in a selected number of sites to complement HMIS data and possibly act as a quality-control mechanism. Also, by encompassing many different aspects of malaria transmission, this surveillance system reflects the complex nature of the relationship between the malaria parasite, mosquito vectors and human hosts, as outlined in Figure 1.1, much more than the information taken from routine data. With time and the relevant investments, it should become easier to obtain high quality data from the selected health facilities, rather than trying to improve the whole system. Then, the biggest challenge in the long-term will be that these sentinel sites remain representative of the Health Zone as a whole and ultimately the Province.

Low quality data was one of the major limitations of the sentinel site health facility records during the baseline community survey. When incorporated into the HMIS system as a whole, this leads to inaccurate evidence which in turn results in poor decision making that does not reflect the reality of the needs of the population. WHO identifies 7 components of quality data: accurate/valid; reliable; complete; legible; timely, accessible and useful. In reality, few of these conditions are met and therefore the interpretation may not accurately reflect reality. Part of the problem is that patient registers are not harmonised and there is a lack of reconciliation between laboratory and outpatient registers risking misclassification of patients. Improving these components will be a focus of sentinel surveillance supervision. Another issue with data quality is in the reconciliation of routine health facility data and community survey data. Comparison between the health facility routine data and the community survey in DRC (chapter 6) showed large differences. This brings into question the ability of retrospective community surveys to accurately capture the treatment patients received from facilities. In light of this poor quality of quantitative data currently collected at the sentinel sites, qualitative components (such as focus group discussions or key informant interviews with health workers, possibly as a part of routine supervision), could complement the quantitative data.

For example, it could provide further insight into reasons behind treatment seeking behaviour or health care practice.

Not only should the quality of data collected and entered into the HMIS be improved as discussed above, but reporting rates must be increased. In order to strengthen the routine health data systems in this way, the District Health System 2 (DHIS2), which has already been adopted as DRC's national HMIS database, has the potential to substantially improve data recording. Its automatic consistency checks integrated into the software have already been used in countries further along the implementation process of this platform. The DHIS2 system needs to be expanded to increase the proportion of facilities (especially private) submitting monthly reports.

In summary, data driven decision making and improved surveillance are essential to address technical, operational and financial challenges. It is critical that good quality and relevant data are available and accessible to programme managers and policy makers and that they are encouraged to use this data to inform policy and implementation decisions. To keep up motivation and continue generating data it is important that people witness policy makers reviewing and analysing this data and using them to make informed decisions.

8.3 Methodological issues and limitations of the thesis

In DRC, the sampling method we used for the sentinel site community survey was problematic. The health areas were selected so that the sample population were representative of those attending the sentinel site facilities as it was assumed that the majority of patients will be from the surrounding area. This was based on assumptions we could not test. It was also not known if the area surrounding the sentinel site was representative of the rest of the Health Zone and therefore how representative the data is. Furthermore, the sample of individuals from the households was stratified into children less than 5 years old and then individuals 5 years or older. In each randomly selected household, all residents were sampled until the sample size was reached. The older age category was completed much sooner than the younger age group and therefore in the remaining selected households we sampled only those under 5s. This caused some confusion for the interviewers and also the households in the communities who saw other adults were tested and therefore couldn't understand why they were not. If the study is to be repeated in the future, then this should be modified so that in each household, the persons 5 years or older are matched to a child less than 5.

More broadly, carrying out research in the study area of the CAR in particular was operationally extremely challenging which resulted in some methodological limitations. Civil unrest, rebel activity and the on-going political conflict greatly restricted movements of data collection teams. Therefore the analysis was based on historic data alone. A major limitation of estimating incidence trends from this data was that demographic data was unavailable on the population who were affected by regular displacement and assumptions had to be made to calculate the denominators for the community-level indicators. Furthermore, it was difficult to disentangle the effects of conflict on the programme compared to other forces at play at the same time. Further studies, both quantitative and qualitative would be important to better understand the epidemiological situation at sub-national level, but this will require sustained peace to implement effectively and maintain a high level of scientific quality. Ideally a comparative trial to compare access to health care in areas covered by CHWs compared to areas without would offer statistically stronger evidence of their impact, but this was simply not feasible due to numerous constraints.

8.4 Operational research to guide malaria interventions: The past, present and future

Historically, researchers in the DRC were able to overcome issues of poverty and instability to be at the forefront of malaria research in sub-Saharan Africa (as detailed in chapter 3). This contrasts with the last decade which has seen a scarcity of malaria research from DRC published in peer-review journals. While this is being improved by the collective efforts of institutions including the NMCP, the Kinshasa School of Public Health, the National Institute of Biomedical Research and the University of Kinshasa, much more still needs to be done. As for most components of malaria control in sub-Saharan Africa, one of the main constraints to increasing quality research is funding restrictions. During the major efforts in the beginning of the 20th Century, funding came from the colonial powers who also had an interest in controlling the disease that was affecting colonialists and their workforce. Fortunately, more funds are available today for malaria through donors including the Global Fund to fight AIDS TB and Malaria, the Department for International Development (DfID), UNICEF and other research donors. Realising high quality research data on malaria transmission and vector ecology to directly support control should undoubtedly be of high priority.

The following operational research ideas should be prioritised:

- **Investigate the appropriate timing and mechanisms of continuous LLIN distribution strategies in DRC.** This will be essential to prevent oversupply of LLINs to some communities, while not reaching target coverage levels in others.
- **Investigate care at pharmacies in DRC.** Assess what is currently offered in terms of anti-malarials and the feasibility of introducing mRDTs as well as collecting data in the most rural and informal pharmacies. Also, assess role of the private sector in conflict settings such as CAR.
- **Repeat the community surveys in the sentinel sites in DRC.** This will be vital to monitoring progress on the impact of these sites in the communities. They should also be conducted at the other sentinel sites.
- **Analyse the GPS data to map distance travelled to health facilities and CHW in DRC and CAR.** This could help identify areas in need of CHW (if many people travel far and from the same area) and also allows comparison of indicators such as incidence, treatment seeking behaviour etc. by distance travelled or region travelled from.
- **Investigate the feasibility of using CHWs in conflict areas for prevention and other forms of work.**
- **Follow up patients referred by CHWs.** Assess the proportion of patients that reach the referral centre and the quality of care they receive according to their final diagnosis. Assess the impact of the referral system on severe malaria treatment.
- **Review how emergency and development donors can better coordinate and finance programmes and research in conflict areas in sub-Saharan Africa.**

8.5 Policy implications and recommendations

The following recommendations are for donors, health authorities, policy makers and control programmes in DRC and CAR:

LLIN distribution in DRC

- **Increase the frequency of mass distribution strategies (every 2 years) using a fixed distribution strategy.** This should be combined with effective Behaviour Change Communication campaigns to ensure the most remote communities are informed of the campaign and can access the distribution site.

- **Quantify the number of LLINs distributed per household to allow for universal coverage.** In case of odd number of residents in a household, round up the number of LLINs allocated (e.g. for 3 persons distribute 2 LLINs). Furthermore, do not limit the number of LLINs distributed to each household. This will have high cost implications on the budget and therefore additional financing would need to be secured but it allows for more LLINs to be available between campaigns and capitalises on the logistical costs of delivering during a mass campaign.
- **Remove LLINs from the packaging when distributed from fixed location.** Many LLINs were found still unused in their bags while old damaged LLINs were slept under. Removing the packaging may encourage use of a more effective/newer LLIN sooner.

Minimising the effect of conflict on health systems and malaria control in CAR

- **Increased priority should be given to malaria prevention and not only case management.** In CAR, the donor community must begin to exploit the CHW network and other channels for distribution of LLINs and regular IRS where appropriate.
- **Peace building should be built into aid operations.** This will require additional expertise and coordination but is essential to ensure that in addition to addressing the health needs of the most vulnerable groups, their policies and programmes also build peace.
- **Greater international coordination is required between donors and international agencies.** Continuum of funding and greater dialogue between development and emergency donors as well as development and emergency implementers is essential. They will also need to be proactive in their relations with potentially obstructive governments and warring groups.

Surveillance in DRC and CAR

- **Conduct a national census of the population and track population movement.** Planning targeted resources requires a clear definition of where people live. The lack of census data restricts any accurate predictions of populations at risk or needs assessments. There is a need to reduce the inaccuracies in population denominators. Mapping population moving between areas with different transmission levels is particularly important, e.g. from low to high transmission potentially causing epidemics due to lack of immunity.
- **Entomological surveillance of the distribution, density and susceptibility of vector species.** To ensure the appropriate prevention tools are chosen.
- **Map state-based, private, NGO and faith-based health services including CHWs.** The absence of a geo-coded health service inventory covering the multiple service providers across

the DRC and CAR is a major rate limiting factor in designing broad health sector initiatives (including for malaria).

- **Improve uniformity and simplicity of health facility registers.** Ensure laboratory results are reconciled with patient records and where possible standardise the register format. It is important to keep the surveillance systems simple and small enough to be understood and managed and not to burden data collectors. Where possible, integrate private facilities and pharmacies into the recording of data.

9. Conclusions

In conclusion, this thesis demonstrates that important actions can be taken to ensure the malaria control tools currently at our disposal can be effectively adapted to the local setting to ensure maximum impact. It has shown that integration of research within malaria prevention, case management and surveillance programmes is an effective and dynamic mode of working that can lead to innovation and hopefully sustainable malaria control, reaching the most vulnerable populations.

Research covered in this thesis provides detailed insight into how best to distribute LLINs to remote communities in DRC and ensure access to malaria case management in conflict-affected communities in CAR. The recommendations presented have direct implications for programmes and take into account the bigger picture of malaria control within challenging political and social environments. It contributes to a better understanding of how sentinel sites can play an important role in improving representativeness of routinely collected data, and identified areas where more research is needed to complete our epidemiological understanding in different settings.

The interconnectedness between malaria-specific programmes such as those discussed throughout this thesis and health systems has become one of the most prominent issues within global health debates today. It is recognised that vertical programmes focussing solely on attacking the malaria parasite and mosquito vector are no longer a sustainable solution and that programmes need to incorporate general health systems strengthening, improved quality of life as well as peace and good governance to see lasting impact on reducing the unacceptable consequences of malaria.

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