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Feasibility, cost and effectiveness of using mobile health clinics to provide antenatal care interventions in Tanzania

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1.1 Background and literature review

The Mobile Health Clinic (MHC) is an innovative service delivery approach that uses moving vehicles to deliver health care services in areas that lack services aiming at improving the health outcomes of the population. Targeting remote and geographically displaced populations with effective health interventions such as family planning(Coeytaux et al. 1989), disease screening(Bassett et al. 2014, Liang et al. 2005, Lindgren et al. 2011, Lipsitz et al. 2014, Patten and Susanti 2001, Schnippel et al. 2015), immunization(Creese et al. 1982) and other effective interventions. MHC has continued to be part of the health systems of many countries across the globe(Roodenbeke et al. 2011).

While the MHC approach is an old one in the areas of health care delivery in Tanzania, it has drawn significant attention in the healthcare community in recent years(Roodenbeke et al. 2011). The comeback of this mode of service delivery is mainly due to the chronic problem of health care access and its associated disparities. MHC could tackle some barriers to access proposed by various frameworks, especially reducing the distance to where health interventions are provided (Jacobs et al. 2012). Countries have adopted this mode of service delivery to ensure to tackle inequalities in health by ensuring that essential interventions reach the need regardless of where they reside.

Literature Review on the impact of MHC on antenatal interventions

MHC, as opposed to outreach services, is the concept of using moving vehicles that can provide equipment like diagnostic tests and medicine, and health workers like nurses and doctors to send health care services where the people are(Abdel-Aleem et al. 2016). The World Health Organisation(Roodenbeke et al. 2011) documents up to around ten outreach programs that offer medical interventions to remote populations. Large programs exist in the USA and Australia, with small-scale programs reported in Sub Saharan Africa and South East Asia. The impact of these clinics on improving access to health care within and between countries has acknowledged by various health actors including WHO(Roodenbeke et al. 2011) and UNFPA(UNFPA 2016). A recent review from the USA Mobile Health Map, for example, documents how MHC has reached over five million clients per year through 2000 operating MHC nationwide(Hanson 2017). In Australia, over outreach services operated by the Aboriginal Community-controlled Health Services served between a third to a half of the Aboriginal and Torres Strait Islander population(Robinson et al. 2017).

Effects on the uptake of essential antenatal interventions

The significant impact of MHC on maternal health services is on its role in increasing access to maternal health (Edgerley et al. 2007, Fox-Rushby and Foord 1996, Peters et al. 2014). MHC activities reported in the studies reviewed examined the effect of MHC on access including primary preventive care and secondary preventive measures on pregnant women. These measures included essential antenatal care that offers effective interventions to improve the outcome of the mothers and their children. A UNFPA supported MHC in Myanmar(UNFPA 2016) is reported to have reached more than 3000 pregnant women in the year 2016, out of which 13% are adolescents. These women are living in displaced environments, which they would not have reached by the traditional healthcare provision platform. Essential screening services for pregnant women during their antenatal period were increased in rural Guatemala through the MHC. In their study(Smith et al. 2015), Smith et al. reported a significant increase in antenatal care coverage to 99.6% which accounts for 32.5% increase ($p < 0.001$). Specifically, uptake of HIV counselling and testing services increased to 50.3 %(p-value >0.001); uptake of syphilis screening increased by 1.3%, and HBV testing increased from 0 to 42.2%. In Zimbabwe, for four months, an MHC reached a total of 93 pregnant women who live in the farming areas where no health facility is available(Vos et al. 1990).

Evidence shows that many pregnant women tend to book late into antenatal care. Late or delay in booking leads to a series of delays in care during pregnancy, for instance, delay in the screening of diseases that may affect the mother as well as a delay in initiation of essential interventions. Several evaluations done on MHC indicate that this portal can significantly increase the number of women who book early into care. A quasi-experimental study in the Gambia(Fox-Rushby and Foord 1996) indicates that in areas where the MHC were implemented, by the end of the 23rd week, all women had registered to the clinic for their first visit, as compared to the 24% in the areas with no MHC. Similar findings are reported from a study in the USA(Edgerley et al. 2007), which shows that underserved women utilising the van services for prenatal care initiated care three weeks earlier than women using other services (10.2 +/- 6.9 weeks vs 13.2 +/- 6.9 weeks, $P = 0.001$). Another study also conducted in the USA showed a significant difference ($P = 0.0006$) in the trimester in which mothers began prenatal care(O'Connell et al. 2010). Eighty-one per cent of mothers in the mobile group started prenatal care in the first trimester compared to 63.2% in the comparison group. Only one mother (0.55%) in the mobile group had late or no care while there were three mothers (1.7%) in the comparison group although this is not a significant difference.

Improving access to antenatal care interventions for hard-to-reach population

Almost all MHC have a primary goal of providing services to populations that are hard to reach. Hard to reach pregnant women are reported to have less mobility and less access to care. These include women who are migrants, women who live in difficult and oppressed circumstances, or women who live in a displaced environment. In the UNFPA report(UNFPA 2016), pregnant women reached with services almost all live in areas with no health facilities. Similar to Plan International report from Tanzania(International 2016), in which all women attending the MHC live more than ten kilometres from the functioning health facility. "Hard to reach" can be a result of not having insurance as it is the case in the USA. Studies in the USA have shown that many of the women using the MHC services are uninsured immigrants (Edgerley et al. 2007, O'Connell et al. 2010).

Effects of MHC on consequences and pregnancy outcome

Although this review found no grounds to conclude on the effect of MHC on maternal mortality because of limited information, it is worth to report some findings which were observed on this indicator. According to a quasi-experimental study in the Gambia, only one maternal death occurred in the areas where MHC was implemented as compared to 5 maternal deaths in the areas with no MHC(Fox-Rushby and Foord 1996). Another outcome reported was on the area of case finding in which the study in Guatemala reported that out of 901 pregnant women who screened for syphilis, eight tested positive and treatment was initiated accordingly(Smith et al. 2015).

Cost and effectiveness of MHC

Data on costs and effectiveness were more limited than the evidence on the utilisation of MHC for antenatal care interventions. Three studies reported on the costs of MHC, while only one reported a comprehensive cost and effectiveness of MHC. In Kenya, an AMREF MHC held many clinics in the Kibwenzi region serving nine sub locations ranging from 15 to 55 km from the health centre. This study does provide utilisation data; however, the estimated costs of running an MHC per visit, which amounted to 16.45 Ksh in 1987, were not compared with the effects of the intervention provided(Johnson et al. 1989). The study in the Gambia reported the incremental costs effectiveness that ranged between US$42.9 and US$ 206.3 per averted DALYs(Fox-Rushby and Foord 1996). Probably the primary concern with MHC has been its efficiency. A study from 1987 comparing the cost per patient attending the MHC, with similar costs at the health centre, found the mobile unit cost per patient to be approximately 26% higher(Johnson et al. 1989). Although MHC services were reported to be more expensive to providers, they were significantly less costly to the user.

The decision to continue or halt MHC depends very much on the use of appropriate value assessment methods and the economic viability of such approaches in the healthcare settings. Like any healthcare service delivery strategy, MHC services have costs and consequences requiring considerations by health systems that seek to derive maximum value from limited resources. Economic evaluation provides healthcare decision makers with a powerful tool for resource allocation decisions because it offers a framework for comparing costs and benefits of available options(Hutubessy et al. 2003). In developed countries, cost-effectiveness analyses have become a central part of decision-making processes to support a "value for money" argument, examining the incremental costs and health gains of various health care interventions given limited resources. Similarly, in developing countries, the practice is starting to gain momentum. However, and to our knowledge, little documentation exists on an economic evaluation of MHC.

1.2 Policy environment influencing MHC activities

Dissecting the feasibility and practicability of MHC activities within the broader policy environment is vital as international and national health policy, and guidelines around health service provision are relevant across all tiers of service provision. From the international policy perspective, implementation of MHC continues to be in the spotlight with emphasis on ensuring that it is used in particular situations like reaching the marginalised, providing care to the disenfranchised population and improving access to the high-risk populations(Roodenbeke et al. 2011). Historically MHC gained their popularity almost 39 years ago when countries agreed to embrace and promote the idea of primary health care through the Alma Ata Declaration(WHO 1978). After the 90s and the awakening of the 2000s(Van Lerberghe 2008), the Universal Health Coverage campaign rejuvenated the armour of their existence, and the current agenda of promoting community health services brought MHC back to the international debates.

The policy frameworks guiding and influencing MHC and outreach services vary from region to region and from country to country. In Tanzania, most notably in the Tanzania health service provision, maternal health is influenced by a mix of policies which includes policies that address service provision and those that address poverty or diminish disparities in access and those that result in increased equity. At different points in its history, Tanzania has created policy tools that explicitly aimed at reducing bad maternal outcomes through increasing coverage of effective interventions. The prime example is the introduction of the MHC in the 1990(MoHSW 2003), in which the National Health Policy put special efforts towards areas with low coverage of interventions in an integrated approach to improve efficiency and reduce costs. In that time around the national health policy was geared toward

supporting MHC and outreach services in underprivileged and hard to reach areas. More specifically, the policy instructs on the need for stratification and mentions that MHC should target vulnerable populations like pregnant women and their children as well as nomadic populations, it also provides guidelines for implementation of these services(MoHSW 2008).

Policies that might be said to have moved the country in the directions that are favourable for MHC activities have increased during this time. For instance, the Maternal and New-born Strategic Plan of 2000(MoHSW 2008), instructed districts to conduct MHC on a monthly basis in all villages that are very hard to reach, or in those who do have health facilities that lack health providers. The recent National Community Based Health Policy of 2015(MoHSW 2015) pushed for the formalisation of the Community Health Care carder to support the workload at the MHC. It further pushed for the local government authorities to ensure resource mobilisation that will support MHC. The Human Resource for Health and Social Welfare strategic plan developed in 2014 also influenced the contours of MHC activities by strategising to improve health care providers at community levels to support all health-related activities that are happening at that level(MoHSW 2014). Notably, most of the policies and strategic plans starting in the year 2000 are a result of the challenges that the health system has been facing for many years, including those reported on MHC.

Nevertheless, policies that affect the other sectors like roads and infrastructure, finance, rural energy policies and education are perhaps the most important ones, although their indirect nature concerning health service provision makes them appear less prominent. For instance, in recent years the MHC activities have mainly been affected by heavy rains which destroyed roads(International 2016). That led to inefficiency in service provision because of too much time wasted on the roads as well as the possibility of MHC workers to work in the dark in case they start the clinic late. These policies might be said to have moved the country's MHC initiatives in the opposite direction—making it difficult for the workers to deliver the expected care and increasing waiting time for the clients, among other things.

1.3 Rationale, significance and objectives of this thesis

The disparity in access to maternal health intervention remains to be a problem, which in turn delays efforts geared to improve maternal and neonatal outcomes in impoverished settings. MHC has potential in reducing these disparities by improving access to intervention to isolated residing populations. Research reported on how they have improved access to interventions and reached the vulnerable and hard to reach populations (Bassett et al. 2014, Grabbe et al. 2010, Larson et al. 2012, Liang et al. 2005, Lindgren et al. 2011). Additionally, they have provided an avenue for referring clients who need specialised care to the next level of health care system. Specifically for maternal health, MHC has enabled a significant

number of pregnant women to attend ANC early which may mean access to available interventions, and this, in turn, has led to an increase in women who gave birth at the health facilities (Edgerley et al. 2007, O'Connell et al. 2010).

The MoHSW considers pregnant women to be vulnerable and high-risk groups which may be a barrier to accessing health services due to their limited mobility. That is why the government exempt pregnant women and children from sharing the cost of interventions as well as implementing MHC to provide essential maternal health interventions closer to them. While it is unarguable that bringing the service to them may have a more significant impact on their health than on the health of other population groups, such as men(Abdel-Aleem et al. 2016), evidence on how this can be achieved and at what cost remains patchy. Existing data in the region are mainly on utilisation, return of investment and cost and effectiveness of MHC in providing other health intervention like male medical circumcision, HIV counselling and testing with limited information on their impact on maternal health services. One evaluation did the Gambia in the 90sgave a cost-effectiveness snapshot of MHC in providing maternal health services, but they compared strategies of the static health facilities which do not provide information about the "do nothing" approach which is crucial in this context.

Until recently, the MoHSW is still at a crossroads regarding this matter. In the current strategic plan, the MOHSW had called for evaluations of all strategies that are currently implemented within the country on areas of maternal health service provision [49]. At the same time, the challenge exists in advocating for the MHC to the central budgeting committees because of lack of information that will describe the significance of these services. Therefore, to be able to answer those questions, it is crucial to quantify the value of the contributions of the MHC and to demonstrate the potential benefit of increased investment in this system of healthcare delivery when compared to no service. Such data would help and guide the MoHSW in the implementation and plans of scaling them up to other parts of the country.

Objectives of this thesis

General Objectives

Overall, this thesis investigates the cost-effectiveness, challenges and opportunities of continued use of MHC to deliver health care while using intermittent preventive treatment for malaria in pregnancy as an example.

Specific Objectives

1. To determine the perception and attitude of policy makers towards the use of MHC to provide maternal health interventions in Tanzania (Chapter three)
2. To estimate the cost of providing and receiving IPTp-SP3 at the MHC in Kisarawe Tanzania (Chapter four and six)
3. To estimate the effectiveness of IPTp-SP3 on preventing maternal parasitaemia and severe maternal anaemia compared to placebo or no drug (Chapter five).
4. To estimate the incremental cost-effectiveness of using MHC providing IPTp-SP3 via mobile health clinic compared to wait to treat the consequences (Chapter six).
5. To estimate the incremental net health benefits (INHB) of using MHC to provide IPTp-SP3 compared to wait to treat according to parity and HIV status (Chapter seven).

1.4 Organisation of this thesis

This thesis consists of a series of chapters which sought to close in on the information gaps highlighted in the paragraphs above.

Chapter one has provided the background information on MHC, highlighting their significance in health provision, showing which policies support their implementation while pointing out existing research gaps. In recent times data on MHC are required to guide decision making. Although evidence on increasing utilisation of services is reported in some countries, there is only limited documentation of such evaluations in low resource settings which are facing the dilemma of deciding while in darkness. Chapter two describes the setting that this study was conducted and gives a summary of the methodologies adopted by the five sub-studies.

Chapter three presents the decision makers' perspective of MHC in the country while giving an overview of issues related to implementation, challenges and opportunities of providing services through mobile clinics. It builds on the availability of policy guidelines that guide the provision of care, monitoring and evaluation of services. It highlights the mixed perceptions and attitudes of decision makers at different levels of the health systems in Tanzania toward MHC, while giving insight into what they considered significant when they make decisions.

Chapter four provides results on the costs borne by clients when they visit MHC for ANC. It also includes information on their sociodemographic, gynecologic and obstetric status. It shows how MHC achieved in fulfilling the "not more than 5km" policy as well as how it had reduced the distance of travel, time and costs for the pregnant women. It, however, suggests that women are still incurring costs which can be avoided by the strategic planning of service provision - for instance, by adopting task shifting policies. It also suggests that increase in

uptake of family planning can reduce the time costs for relatives who help these women when they attend ANC clinics.

Chapter five is a systematic review which aims at gathering information on the effect of three or more doses of SP compared to placebo, or no drug or case management. Data on interventions that had compared an intervention with placebo especially for essential, effective interventions is limited. That is because of ethical issues surrounding denying an already effective intervention to one group. However, that information is always useful in assessing the impact of interventions when the decision question involves stopping the intervention among the considered options.

Chapter six addresses an economic assessment in which the potential added value of MHC in clinical practice is examined. For this purpose, a Markov decision model was created to assess the costs and effects of the interventions comparing with no intervention. It illustrates costs of the intervention and costs of the consequences as well as the incremental effects associated with using MHC to deliver IPTp-SP3 to pregnant women with the aim of preventing them from malaria and severe anaemia. This includes possible costs of intervention and the costs of consequences as well as taking into account the recurrent nature of malaria by using the Markov model that can capture recurring events. Chapter seven explore the net benefits associated with acknowledging differences in the baseline characteristics of the women according to parity and HIV status.

Chapter eight provides a general discussion of the matters that arose from the study and gives recommendations based on the evidence presented. It emphasizes the importance of MHC especially on its role in preventive care and the potential that it demonstrated in reducing the cost of the consequences.

Methodologies and ethical considerations

Detailed methodologies adopted for the sub-studies in this thesis are presented in their respective chapters. In this section study setting and ethical considerations are presented

2.1 Study Setting and Study Area

The United Republic of Tanzania is projected to have a population of 45 million people according to the 2012 census. The country is diverse, with more than 200 ethnic groups and languages. However, the country has two official languages namely English and Swahili, but the majority of Tanzanians speaks Swahili. According to the 2012 estimates, the gross domestic product per capita was US$637, life expectancy at birth was 65.49(66 for women and 64 for men), the fertility rate in Tanzania stand at 5.2 children per woman(NBS 2016).

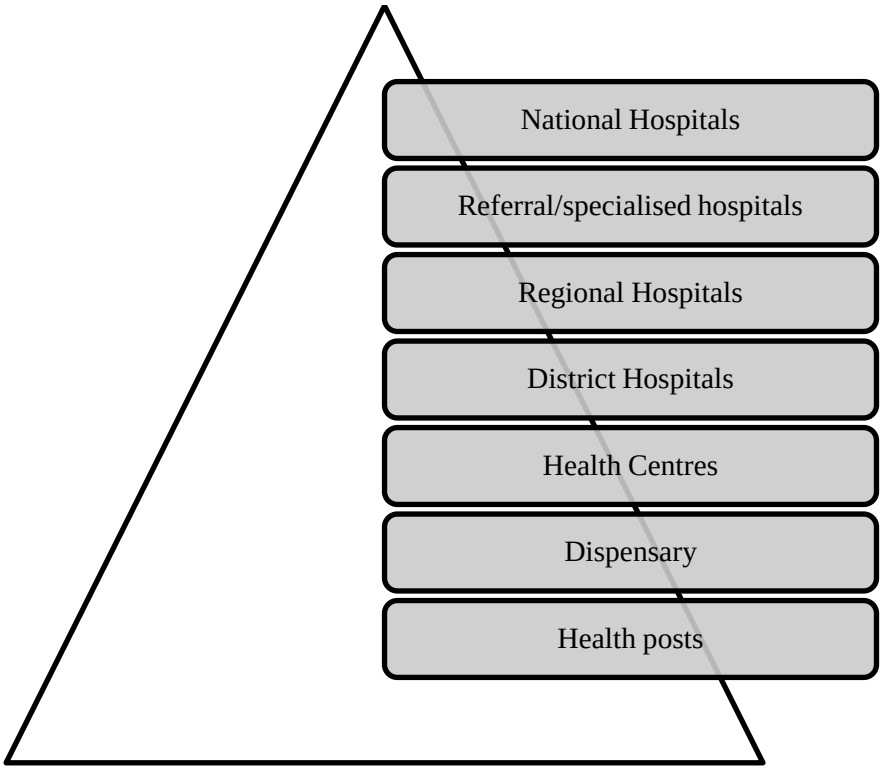
Tanzania service delivery system follows the pattern of government structures of leadership in the form of hierarchy(MoHSW 2003). Hence it is worth to describe the government administrative system first. The country is divided into six zones namely– central, eastern, and coastal, lake, northern, southern highlands and Zanzibar. The six zones comprise 30 regions, each having urban and rural settings. In rural settings, regions are divided into the district; then the district is divided into wards and wards are divided into villages. On the other hand, urban setting regions are divided into the city, or municipal council or city council, which are later divided into wards and wards are divided into streets.

With that background, the health system begins at a lower level with the primary health care which serves villages to the district. Village health workers are responsible for providing essential health service at the village level through the community health post, advanced medical officers provide primary health care at the ward level through the dispensaries and health centres, and medical officers provides care to the district. The referral system at this level begins from the community health posts to the dispensary, then to the health centre. The district hospitals have a role of supervising the health centres while health centres provide technical supervision to the dispensaries and the dispensary supervise the community health posts. It is at this level implementation and monitoring of MHC occurs(MoHSW 2003).

The next level comprises regional hospitals, and it provides secondary care. Regional hospitals offer health care similar to the district hospital, but they differ from the later regarding the quantity of service provided and some extent of specialised care available. According to the policy, this level should have health workers with medical specialties to allow the provision of specialized care. The regional hospitals receive supervision from the tertiary hospitals, and it provides supervision to the district hospitals within their jurisdiction.

The third level comprises tertiary hospitals which provide tertiary care. Tertiary hospitals include teaching and national hospitals, in which advanced technology and highly skilled health workers are based(MoHSW 2003).

Figure 1: Health service provision levels in Tanzania

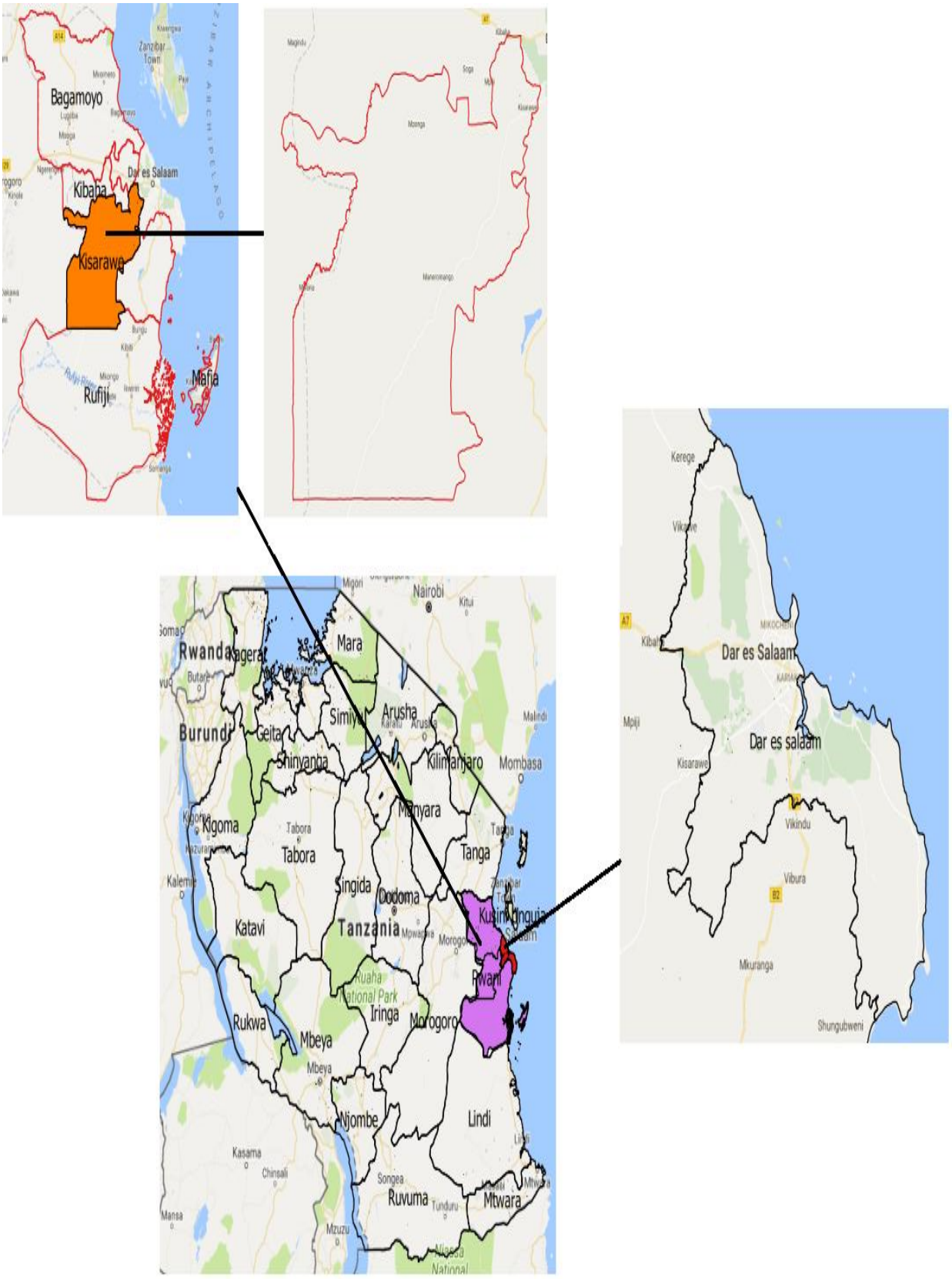


Source (MoHSW 2003)

Data collection for the sub-studies in this thesis were collected in Dar es Salaam region and Kisarawe District of Pwani Region. Both Dar es Salaam and Pwani regions are located in the eastern zone (see maps in figure 3 below).

Kisarawe district is one of the 6 districts of the Pwani Region of Tanzania. According to the 2012 Tanzania National Census, the population of the Kisarawe District was 101,598 out of which 50,967 being women of reproductive age. The district has four administrative divisions, namely—Mzenga, Chole, Sungwi and Maneromango. In these divisions, there are a total of 15 wards with 76 registered villages and 226 hamlets(NBS 2016). Kisarawe was identified as an appropriate area for this study because of its poor health outcomes mainly related to low rates of immunisation to children under-fives and low utilisation of antenatal care among pregnant women. Nevertheless, the districts have a weak health system characterized by poor geographical accessibility of health (International 2016).

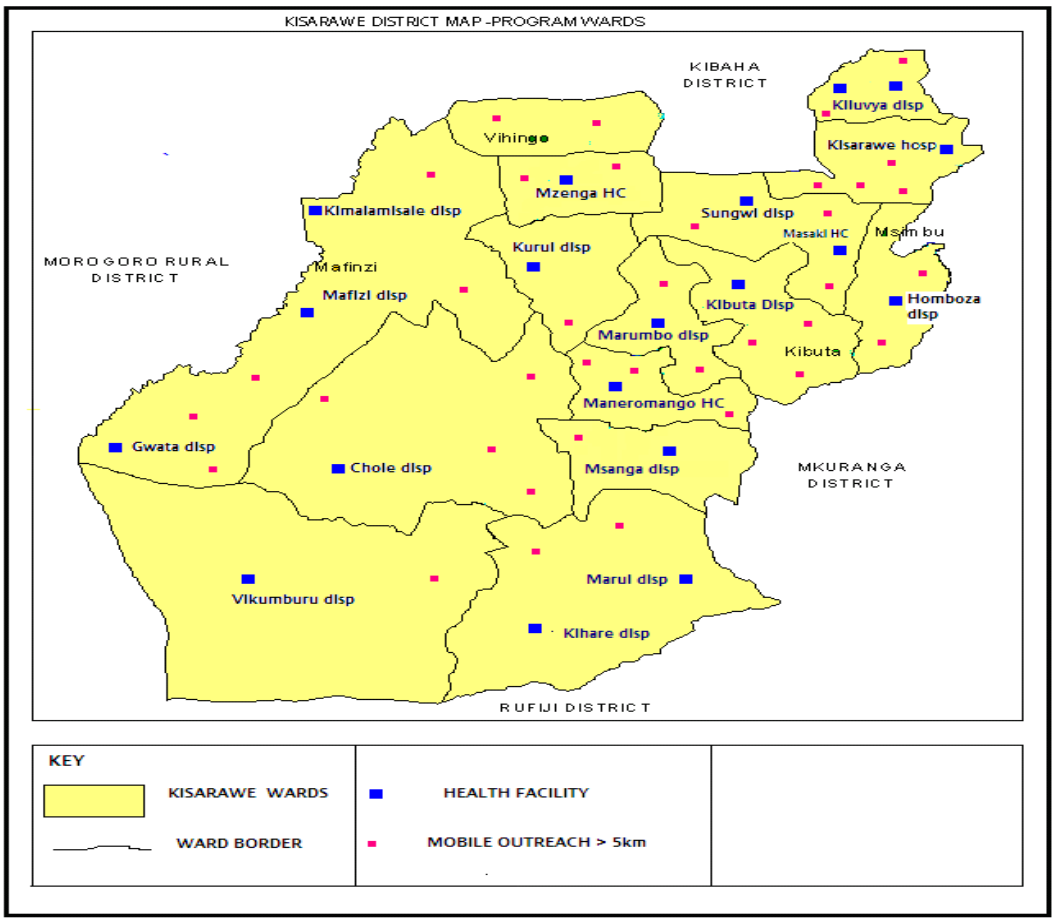
Figure 2: Map of study areas in the coastal zones of Tanzania



Source: (Hashim 2017)

Figure 3 below depicts the distribution of health facilities and mobile clinic centres in 15 wards of Kisarawe district were data for sub-study II, and IV were collected. Client and provider cost data were collected from all MHC at each ward from November 2015 to June 2016.

Figure 3: Study area with mobile clinic outreach centre



Source: (International 2016)

2.2 Summary of the Study Design

This thesis employed a mixed method approach as summarised in Table 1 below. Detailed methodologies are presented at their respective chapters.

Table 1 Summary descriptions of methodologies used in this thesis

Study	Approaches	Source of data
Sub-study I	Qualitative case-study	Data collected through in-depth interviews. Thematic data analysis was done using Nvivo qualitative data analysis software.
Sub-study II	Cost analysis	Client data on demographic, resource use when they access to care regarding time and out of pocket payments were collected by interviewing pregnant women who came out of the nurse's room after consultation. Data was entered in Epidata and later exported in STATA for analysis.
Sub-study III	Systematic Review	Articles were searched from databases and reference lists from 1970 to July 2017 followed by screening and assessment or risk of bias of eligible RCTs. Meta-analysis was conducted whenever feasible, and findings reported.
Sub-study IV	Cost-effectiveness analysis	Cost data were primarily collected at the district level in Tanzania while effectiveness data were collected from the systematic review in sub-study III. The analysis was done from the provider perspective using the Markov decision analytic model In Microsoft Excel. The PSA was done with 1,000 Monte Carlo simulations. The model had a time horizon of 33 weeks.
Sub-study V	Subgroup analysis	The model in sub-study IV was analysed while changing effectiveness data according to parity and HIV status. ICER, NHB and the INHB were calculated accordingly.

Source: Author's own summary

2.3 Ethical Considerations

The study was granted ethical approval by the National Research Ethics committee in Tanzania (reference number NIMR/HQ/R.8a/Vol. IX/2061) and the Ethics Committees of the Faculty of Medicine of the University of Duisburg-Essen in Germany (reference number 15-6512-BO). All approvals are attached in the appendices 3.

Potential risks and benefits

No direct risk and benefit of this study were noted; however, the result of the study will provide policymakers with evidence-based information that they can use to improve the implementation of the MHC services in the country.

Ethical Approval

This study received approval from the National Institute for Medical Research review board with approval with the reference number and the Duisburg Essen University ethical approval with the approval reference number. The two approvals were presented at the district level and at the partner organization which were involved in the interview before the interviews.

Informed Consent

We obtained signed informed consent for each of the participants who were involved in the interview using the informed consent form in Appendix 4 and 5. None of the interviews was conducted before the informed consent was sought. Participants were given the opportunity to ask the question, and, the interviewer answered the raised question to the best of her ability. The right of the participant to refuse to participate without giving reasons will be respected. All participants were free to withdraw at any time from the formative research without giving reasons.

Confidentiality

All procedures in this study were done in the manner that ensured confidentiality. Interviews were all conducted in private as well as all information gathered did not have any quotations that link the information to the informer.

3.1 Introducing sub study I

Accessibility to maternal and child health (MCH) services continues to be an intractable problem in the developing world. To date over a third of all pregnant women in developing countries attend the recommended four ANC visits with only 46% of women benefiting from skilled care during childbirth(Gabrysch and Campbell 2009). This signifies an existence of millions of births that are not assisted by a midwife, a doctor or a trained nurse. Tanzania, which is a predominantly rural, low-income country in the eastern part of Africa, has a maternal mortality ratio of 454 per 100000 live births, and only 35% of women living in rural areas delivered their last child in the hospital. According to the National Bureau of Statistics' recent report, 43% of women attended the recommended ANC, with only 15% were attending their first visit during their first trimester(NBS 2016). Large proportions of those pregnant women who lack access to care with an increased risk of maternal mortality live in remote, hard to reach settings(Gupta et al. 2014). Women in Tanzania and similar low-income settings frequently identified multiple barriers that prevent them to access health care for themselves or for their children, which includes the distance from their village to the hospital(Gabrysch and Campbell 2009, Gupta et al. 2014).

For the past four decades, Tanzania has been implementing and adopting different strategies aiming at improving MCH services utilization. However, utilization had remained at a level that is not satisfactory and declining in some areas due to many factors including a limited number of health facilities and great distances from health facilities to the villages(Gupta et al. 2014). To overcome these difficulties, a variety of measures have been developed to improve access to and utilisation of MCH services, and to increase contact with clients to provide health education (Byrne et al. 2014). These include, but are not limited to the use of community health providers, use of mothers as peer educators, MHC and outreach program – often using a mobile van or bus, and sometimes home-visits. One goal of the mobile clinics is to improve access to antenatal care, postnatal care and childhood immunization.

Despite their usefulness, little is documented regarding the what promotes this mode of service delivery, what are the challenges both regarding policy and implementation barriers as well as what can be done to improve them. Our objectives for this chapter were to use a qualitative approach to explore the feasibility and practicability of using MHC to provide maternal and child health services in remote parts of Tanzania. Conducting a qualitative study is essential to better understand the essential details of the implementation of this model of service delivery.

3.2 Methodology adopted

Study design, sampling and sample size

We used the qualitative study design. This design is useful for the understanding of the specific situation surrounding provision of MCH services through mobile clinics in Tanzania(Baxter and Jack 2008). This study also follows the consolidated criteria for reporting qualitative research (Tong et al. 2007). We selected a total of eighteen key informants using purposive sampling methods. We included five participants from the Safe Motherhood Unit of the Reproductive and Child Health Department at the Ministry of Health and Social Welfare and five members of the Council Health Management Team. We also included three health providers who are part of the team that provides services at the mobile health clinic and three informants from the international non-governmental organisations which provide MCH services through mobile clinics. We first contacted the Safe Motherhood Unit of the Ministry of Health and Social Welfare, which provided us with the organizational structure of the service provider. We later on selected the informants according to their role and responsibility in the service provision. In the end, we managed to interview 15 out of the 18 key informants we selected.

Description of the study participants

The criteria for selecting the key informants were based on three things: Informant experience and involvement in the subject area, institutional and professional reputation in issues related to MCH services provision. Our informants from the ministry of health and social welfare were senior officials from the ministry of health with the background of obstetrics and gynaecology (3). At the council levels, there was a clinician (1); a pharmacist (1); health planners (2); nurses (3) and health officers (3); while at the international organization there were social scientists (2) and a clinician (1). Apart from the two social scientists and one health officer who had a work experience of 6 to 10 years, all other participants had more than 10 years of experience in the area of MCH services.

Data collection methods

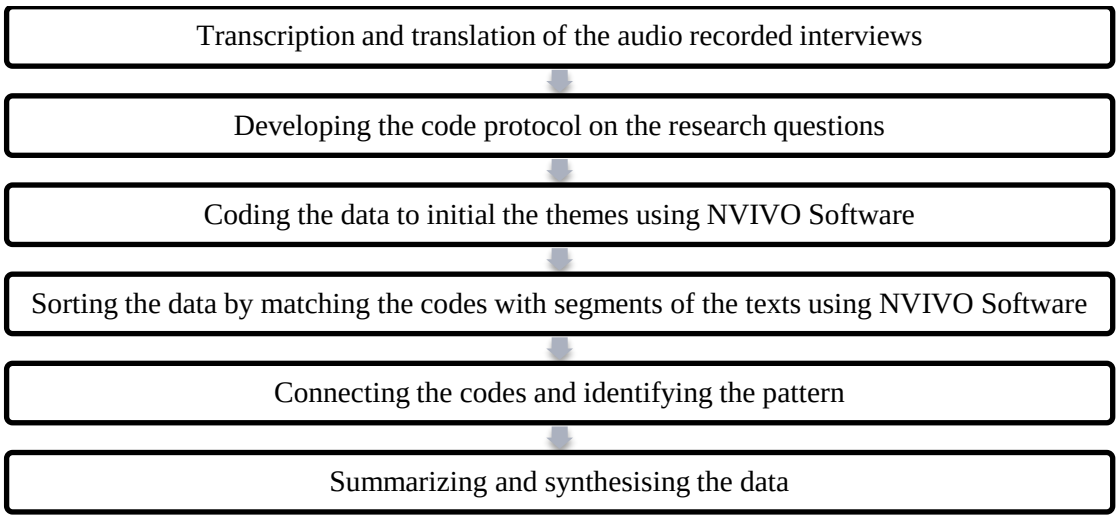
Key informants interviews were conducted as a face-to-face encounter at the offices of the key informants. Only the interviewer and the key informants were available during the interviews. 12 out of 15 key informants accepted to be digitally recorded during the interview while the other three were not comfortable to be recorded hence their interview was noted on shorthand and notice expanded immediately after the interview. Recorded interviews lasted for 25-45 minutes. Interviews were conducted in Swahili guided by a pre-tested, semi-

structured interview guide. The guide was pre-tested on five participants and fine-tuned accordingly. During the discussion, the flow of the discussion varied from one informant to the other, depending on the way the discussion unfolded.

Data Management and Analysis

We transcribed the audio-recorded data following the standardised transcription protocol(McLellan et al. 2003, Tong et al. 2007). One translator translated the Swahili transcript into English, and then two research scientists read the transcript and made edits. The English version of the transcripts was then uploaded into NVivo Software QRS 2011. We used the thematic content approach(Baxter and Jack 2008, Green and Thorogood 2013) in which we read each transcript carefully and repeatedly to identify relevant text. After that, we developed a data-coding scheme by organising similar codes into categories and used it to code all the data. We read the quotations that were attached to the codes and summarised the main description in the memos.

Figure 4: Steps followed during data management and analysis



Source: Author own drawings

3.3 Results from sub study I

We conducted 15 key informant interviews and identified six themes as follows:

- Organization, coordination and implementation of mobile clinics activities
- Perception of respondents on mobile clinics activities
- Guideline use in the provision of services in mobile clinics
- Perceived impacts of using mobile clinics to support MCH
- Strategies used to increase uptake of MCH services at the mobile clinics

- Challenges facing mobile clinics

Organization, coordination and implementation of mobile clinics

The President Office-Regional Administration and Local Government Authority (PO-RLGA) and the Ministry of Health and Social Welfare (MoHSW) through council health department are responsible for coordinating and overseeing mobile clinics and other outreach services that deliver MCH services. Mobile clinics were established in the 70s as part of the government initiatives to increase access to health care. Ideally, the mobile van with health providers and a driver visit each village once per month and offer MCH services. They are offered in areas which are located more than 7 kilometres from the health facilities, while outreach services are conducted in areas that are more than five kilometres from the health facilities. The difference between the two lies not only in the distance travelled but also in the number of health providers who will provide services. The mobile clinics have approximately 4-5 health providers in one team, while only one health provider does outreach services. A wide range of MCH services is provided in mobile clinics including immunisation, family planning, antenatal care, child growth monitoring and HIV/AIDS interventions like PMTCT services and counselling and testing. Although this study confirmed the existence of mobile activities in one council only, it appeared from the data collection and KII that mobile clinics are conducted nationwide.

Perception of respondents on mobile clinics activities

Respondents agreed to the idea of providing MCH services through mobile clinics. They support the idea given the fact that it increases the coverage of interventions and reaches remote areas. Different views arose when they were asked which MCH interventions should be ideally provided at the mobile clinics. Few (2) said that mobile clinics are ideal for interventions like family planning, immunisation, growth monitoring, HIV counselling and testing and health education specific for MCH interventions. The majority of the respondents said that all MCH interventions could be delivered at the mobile clinics in an integrated manner which means women and children can come and receive more than one intervention at once and reduce the distance travelled by the clients.

Specifically, for antenatal care service provision, respondents gave different perceptions of mobile clinics providing MCH services. Few (2) were sceptical about the whole situation of using mobile clinics to provide MCH services, arguing that they do not uphold the principle of a continuum of care. A respondent from the MoHSW said:

> "[The concept of] *Mobile clinic is a good idea because this is going where the demand is, but it will not be able to provide services in a manner that will fulfil the continuum of care…."* Senior official at the MoHSW

On the other hand, 13 participants supported the idea of giving the reasons that the country will continue to have people who live in areas that do not have health facilities. When asked about the policy of "each village one dispensary", they argued that it would take long for each village to have a dispensary and so mobile clinic are significant.

> "*There are people who live in unimaginably remote areas, others move from one place to another, and others refuse to get out of the wild, that is where your study comes in, the one that uses mobile clinics so that we can reach people in remote areas. The country's behaviour is changing slowly regarding customs and traditions, and that is where the problem begins, we will get to that point of having a dispensary in each village, but in the meantime, because they also need services and life must continue, we are sending those mobile clinics"*. Senior Officer at the MoHSW.

They, however, acknowledge that services should be provided in a manner that will promote the continuum of care, and it is for that reason that they have long ago advised the councils to establish maternity homes in which pregnant women will live to wait for their time of delivery. These homes are in close proximities to the health facilities, so women who are attending antenatal care at the mobile clinics can live there when the time of delivery is approaching.

> *"…Labour does not tell you when it will start, so what we do and our aim is when we go there we provide them with health education that when it reaches the EDD, they should go and give birth at the health facility. As a ministry of health, we have recommended that in each facility where they provide delivery services, then they should have what we call maternity waiting homes or a house of waiting*". Senior Officer at the MoHSW

These homes are already available and operating in some council. Councils are the ones responsible for managing these homes in collaboration with the clients. The clients are responsible for buying their food while they are there, and the council covers electricity and water bills. The respondents feel that these homes provide an opportunity for all those women who live far away from the facilities to deliver their baby in the hospital.

There were different perceptions about the practicability of providing services in the mobile vans especially on issues related to privacy and confidentiality:

> '*…In that car, there is a space like a room, on the back of the car, and inside that small space there is a bed, chair, and you can sit inside with a woman, and you can provide services to her without people outside hearing what is being discussed or done in that room. Alternatively, sometimes we go to the office of the village or the school, and they give us a room which we can use for that day. Therefore these services are provided confidentially and privately'.* (Nurse-midwifery at the Council)

A similar view was also echoed at council level:

> '*I do not see any problem because in the mobile van there is privacy when a client enters the van no one will know what service is provided apart from the client and the provider. Because people go in for different services, some go for family planning, some for HIV/AIDS services; some came only for routine antenatal care. So a client enters and comes out, and I do not see it is a problem because she is in there with her doctor only… also, it is not that different from our rooms in the facilities… Moreover, in other places, we have normally given a classroom if we conduct those services in a school or village office....*' (District Medical Officer).

On the contrary, a senior official at the international NGO stated:

> '… *You must also look at issues of privacy, and space and whether after taking care of the clients there is a place for them to rest for a while...*'(Senior Official at Marie Stopes International).

Despite different opinions about privacy and confidentiality, there was a general recognition that mobile clinics activities need to be improved. Highlighted was the importance of ensuring that medical supplies and laboratory equipment are sufficient to allow them to offer standardised care and to make services more attractive.

> '*I mean, if we have simple and easy to carry laboratory machines for simple but very significant investigations like MRTD for Malaria, haemoglobin testing, urinalysis for UTI and protein in the urine, our services will be much better and more attractive*.'

The issue of incentive came up in all interviews. Senior officials both at the Ministry, Council and International NGO insisted on having a plan to reimburse the health providers who travel to provide care in the mobile van. Reason for that being the fact that these providers sometimes find themselves stuck in the village and they have to spend a night there in case the car breaks down or when there are too many clients. Hence they felt that giving them something small to compensate for the hours that they work overtime would motivate the workers.

> '*Health providers are motivated because of the incentives that they receive, and they can take the risk of going there, and, even sometimes sleeping over there to provide services, you find someone has a family but she will sleepover in the site because there is an incentive*'. Senior official at the Council

Coinciding with those views were the statements from the health providers although they did not attach too much importance to incentives; instead, they insisted more on the availability of equipment and tools.

> *'For us, because it is our responsibility, incentives or money is not a problem although in the past we used to get an incentive when we came from mobile clinics. That was nice since you get something to send home to your children after a long day of work, but even now when that is not happening, we still see it as our responsibility… It is the job that I would have done here if I will not go to the field, so it is not a problem'* Nurse-Midwifery at the Council.

Guideline Use in the provision of services in Mobile clinics

Respondents were aware of the available guidelines for the provision of MCH services. They were also able to describe key aspects that are in those guidelines and affirmed their availability at each mobile clinic. However, the mere fact that these guidelines existed did not mean that they are applied as desired because of existing barriers. For instance, shortage of resources - both human and supplies - was mentioned to be among the barricades that hinder guidelines implementation. A respondent described that:

> "*…The team that goes to the field normally is not complete because of shortage of staff, because we cannot leave the health facility without health providers, so we find that the team that goes to the field has to go with few people; sometimes, only a person who is needed to assess the mother and the child are the ones going. In many cases, you may find that the clinical officer and the health officers are missing, so those kinds of shortage*". District Nurse Officer

So that makes them provide services using the number of health providers they have and not what the guidelines say. Describing what the ideal service provision at the mobile clinic should be, the DNO illustrated that the team should be complete for all services to be provided within standards. Lack of reagent and other medical supplies was also another obstacle to providing services according to the guidelines. A senior nurse at the council pointed it out by saying that:

> "…. *Guideline for the provision of antenatal care, for instance, states that women should be screened for STI infections like Syphilis and HIV, but that is not always happening because of lack of reagen*t". District Nurse Officer

Those barriers are known from all levels of the health systems. A respondent from the ministry level which is responsible for guideline formulation and translation echoed similar concern as those raised by the respondent at the council level:

> "*In other time you find that we do not have needed supplies and equipment to be used according to how we taught them. Shortage and lack of supplies and equipment is a challenge*". Senior Official-MOHSW

Perceived impact of using mobile clinics to support provision of MCH services

The perceived impact of mobile clinics in terms of increasing coverage of MCH interventions came prominently during the discussions. All respondents reported that without doubt mobile clinics had changed the picture of the coverage of all MCH interventions. One respondent reported that mobile clinics had increased the coverage of immunization of all antigens in a significant amount.

> "*The immunisation coverage was meagre; we had only 70% and in other antigens only 60% coverage. The only antigen that was doing better was just 80% coverage while the country's target is 90% and more* ". District Immunization and Vaccine Development Officer.

Another informant, who works specifically in family planning interventions, added how mobile clinics have contributed to the reduction of maternal and child death. He highlighted that:

> *".... Through mobile clinics we have managed to increase the CYP (Couple Years of Protection); CYP is very large. Moreover, then the amount is also consistent with the clients, the number of clients has increased…. that gives us, or it tells us that we have a huge contribution in the provision of family planning services of all methods in the nation. Therefore, we have contributed largely to reducing maternal and child death".*

Participants at the council level also discussed how mobile clinics had raised awareness of the importance of MCH among the community that they visit. Both supervisors and the frontline health providers agreed that the level of awareness that is seen now is a result of mobile

clinics activities that are sent to their village. Personnel responsible for overseeing immunisation activities in the council described a similar scenario:

> *"People have been so receptive and even, for instance, when it happens that we cancel the route, they will call to ask why we have not visited them, and when we will go again…Therefore the people now understand the importance of vaccination and antenatal care…"* District Immunization and Vaccination Officer

Participants specified further that the level of awareness which is now seen is perceived to have broken the barrier of men not wanting anything to do with their wives' and children's' health. They also suggested that men are now seen more often escorting their wives to the clinics or even bringing their children for vaccination - even in areas where that was previously impossible. A program manager in one of the organisations that implement clinics in Pemba said:

> "…*Moreover, even now, if you go to those areas, many men come with their wives to the clinics, and it was through mobile clinics that they got sensitised*". VSO Programme Manager for Maternal and Neonatal Health

Another informant added:

> "…*The number of men participating in the mother and child health issues has also increased as compared to the past…moreover, we see quite some men now escorting their partners to the clinic, and others they bring their children to get vaccinated".* Mobile Clinic Coordinator

Strategies used to increase uptake of MCH services at the mobile clinics

Many informants reported that they used health education and promotion strategies to encourage women and children to use services that were provided at the mobile clinic. Educating the people about the importance of the interventions was the most cited approach to have been used by different informants. Two informants said:

> "*We started by giving education to village leaders, and we told them about the importance of reproductive health*…" District Reproductive and Child Health Coordinator

Regarding the question of whom to use in sending the information to the people, all informants acknowledged that influential community members are the best ones to use. These are perceived to understand their communities more hence making it easy for them to reach the people with information. An informant said:

> "…*The strategy that we used was to engage influential people who are in those villages. Those people are the village health workers and the village leaders. That is the first strategy which we use, those people are near to the communities we want to reach, so we communicate with them, and then they share the news with the community…*" Mobile Clinic Nurse-Midwifery

Use of adverts is also mentioned as a possible way to spread the news about availability of services in the villages. An informant described this by saying:

> *"…. We send advertisements in collaboration with the districts' and councils' authorities that we want to provide services. In other areas we use messengers, in which a person is hired to pass through the streets with the microphone in the car, and he will pass in streets and announce that we will be providing reproductive health services together with family planning at a certain place and on a certain date, and, so people should come forward…"* Head of Clinical Services Marie Stopes International

Challenges facing delivery of MCH services at the mobile clinics

Poor road infrastructure, funding, shortage of medical supplies and human resources were mentioned as among the challenges that mobile clinics are facing. These challenges together are said to threaten not only the sustainability of these services but also the quality of care. All informants acknowledged that running mobile clinics is a resource consuming undertaking. They said that the existing policy requires all MCH services to be provided free of charge to all who need it because of the vulnerability of this group. They also agree that providing these services at static facilities would have been a cheaper option to the government but ensuring that every village has a facility needs heavy investment. One informant said:

> "…*Mobile and outreach services are very expensive. I can't give you figures but it is expensive because of a lot of things. You must pay for the car and maintain it; you have to factor in supplies...*" Head of Clinical Services Marie Stopes International

Despite the cost implications, a number of informants cautioned that the concept of mobile clinics is something that the country cannot simply terminate due to many reasons. One being that maternal death should not be allowed to happen at any cost. Describing this, a senior official at the MOHSW said:

> *"...Normally I tell people in order to improve health care services, you need heavy investment, and the outcome will be seen later… and now try to look at the life of a woman, when she dies because of not receiving these interventions, how costly it is*

> *there… so if you see that going for outreach services is expensive, then try maternal death and you will know what is costly".* Senior Official MOHSW

They rather recommend and advice that councils should make a good and sustainable plan of reaching these women and children since they believe it is not an issue of funding, but rather a priority setting problem. One official explained:

> *"…. They should add it on the CCHP, so that it can be something that must be done given its significance, and it has a play in improving maternal and child health..."* Senior Official MOHSW

On the other hand, informants working with the development partners said that the council's health department has assured them that these services will continue and plans to mobilize funds are already in place.

> "…. *We had a meeting with DMO and CHMT, they have assured us that the activities of this project are in the budget and they have shared with us that budget; therefore, the issue is to execute that budget and to implement as it was planned...*" Mobile Clinic Coordinator Plan International

Conversely, informants from the council agreed that these activities are included in the Council Comprehensive Health Plans (CCHP), however, in many cases the activities get into the plan either in a piecemeal or not in time hence rendered it difficult to be executed as expected;

> *"…You might convince them, and it can get into the plan, but it will not happen in the way it was requested*." District Reproductive and Child Health Coordinator

When confirming this with the member of the CHMT, they agreed that they had made plans to ensure that MCH services continue in villages where there is no hospital, but they are always caught up in the situation that they receive less money in contrary to what they have budgeted.

> *"….We have tried to incorporate mobile clinics and outreach services into our health plans, but even if you put in that health plan, the challenge is that we have minimal budget, for example, the year before last year we had 275 million for the whole district, last the budget was reduced from 275 to 250 million…. and in this year it was reduced from 250 to about 205 million. Therefore each year the budget decreases and the prices for equipment and supplies do increase..."* District Health Secretary

Additionally, mobile clinics were said by all respondents to create a shortage of health providers in the facilities. Demonstrating this, one respondent said:

> "…*Because whenever we take a health worker from one facility to the mobile clinic, it means that a particular facility will have a shortage from that outsourcing*…" Senior Official MOHSW

Finally, the impact on the quality of care when health workers carry out additional tasks like collecting medical information during mobile clinics activities, work was raised by some KIs including a senior MoHSW representative:

> *"…Collecting information is not very hard if you have time and enough human resources… Also, if we are going to rely on the same person who is providing the service and then collects the information, we will be either compromising the quality of the services and the data collected".* Senior Official MoHSW

3.4 Discussion of findings from sub study I

This sub-study explored the feasibility and applicability of providing MCH services through mobile clinics from the perspective of the policymakers, CHMT members, health workers and non-governmental representatives. The outlook of the views that emerged from the respondents was, overall, a positive one. Mobile clinic service delivery is an essential opportunity that had managed to improve access to MCH services. Foremost, all respondents shared the opinion that mobile clinics are at this time the only way that can allow women and children who live in remote, hard to reach villages to access life-saving interventions. Thus this may, in the end, improve their knowledge of the importance of coming to the hospitals during delivery, and bringing their children to the hospital when they detect danger signs. This is confirmed in studies that have been done in other settings both developed and developing countries(Edgerley et al. 2007, Fox-Rushby and Foord 1996, LeBaron et al. 1998). In those studies, it is reported that the mobile clinic's concept has the potential to increase early access to antenatal care among other MCH interventions, improve knowledge and awareness of the client on issues relevant to MCH services, and in turn improved hospital deliveries in the areas where mobile clinics were conducted.

Despite the general views in favour of MHC, our participants also recognised that MHC is resource intensive, both concerning supplies and time. The journey to and from the site was said to be a long one and insecure. In line with that they were also noted to create the gap of resources at the health facilities since in most of the cases resources that are used at the facilities are limited, and when the mobile team takes medical equipment, it leaves the clinic

with little resources. The same was reported for human resources. Researchers who evaluated mobile clinics which provide immunisation services(Creese et al. 1982, LeBaron et al. 1998) and other curative health care(Walker and Gish 1977) affirmed that this mode of services delivery requires a large number of resources concerning fuel and vehicle maintenance. On the contrary, albeit few, studies on cost and effectiveness of mobile clinics reported that this mode of service delivery could provide a significant return on investment. In that study, they modelled the quality adjusted life-years gained by the prevention activities conducted and the savings from unnecessary emergency department visits and found that their services resulted in a $30 return on investment for every $1 invested(Oriol et al. 2009).

Notwithstanding, a few aspects of the mobile clinic's service provision could benefit from some improvement. First, all respondents were of the opinion that that services provided at the mobile clinics do in many cases not follow standardised guidelines due to limitations of resources. They argued that the council through the Local Government Authority should consider allocating more resources in the area of reproductive and child health, which will help services to be delivered in a manner that is according to standard procedures. Secondly, they echoed that portable and simple to use laboratory equipment should be made available in the mobile clinics to make it easy for them to serve the clients sustainably. Similarly, previous studies and reviews reported that provision of health care in mobile clinics needs to be reviewed and strengthened by ensuring that resources are available(Edgerley et al. 2007, Nuttbrock et al. 2003, Walker and Gish 1977).

Closely related to that, shortage of human resources hinders collection of essential health information during the mobile clinic's activities. Our findings show that an overworked health provider would not regard recording health information as a priority when she or he has many clients to see and is alone at the mobile clinics. That may imply that health information collected in the mobile clinics may be of questionable quality and they may be unreliable for planning. For instance, an evaluation from the mobile clinic in Malawi indicated that collection of health information at the mobile clinics was compromised because of a high volume of patients and few health providers, which makes health providers allocate their time in care provision, and ignore recording of health information(Lindgren et al. 2011). Similar challenges were reported elsewhere, in which absence of patient outcome data due to lack of resources to gather information was seen as a fundamental challenge of mobile clinics (Song et al. 2013).

Our findings emphasise the need for councils to ensure that they have proper planning and adhere to budget allocations. This came about when respondents who are also members of the CHMT raised concerns that their plans are either not being approved according to how they

see the situation or they get approved in piecemeal, which prevents them from providing care smoothly. In line with that our findings show that in many cases budgets are not allocated as they have been planned and often re-allocation of funds occurs. That poses a barrier to the implementation of activities, irrespective of those activities being in the plan. Other studies carried out in Tanzania have also found that district health plans are rarely implemented as planned, and lots of re-allocation and re-setting happens throughout the year(Maluka et al. 2010). It can, therefore, be argued that the councils will benefit from proper planning and priority settings to address those challenges, which seems to be rooted in the health of the priority setting.

Finally, some respondents were sceptical about the use of these services to provide antenatal care since they argued that the model does not uphold principles of a continuum of care despite the existence of the maternity homes that are linked with these services. In the council where we did the interviews we did not find the maternity homes as we were informed at the ministry level; however, this does not mean that those homes are not in operation in other councils. Noted is the possibility of linking ANC services provided at the mobile clinics with the existing waiting homes to bridge the gap and ensuring that these women deliver at a health facility. Studies that investigated the impact of mobile health vans specifically for antenatal care affirmed that mobile health vans enabled women who live in remote, underserved populations to start ANC during their first trimesters(Edgerley et al. 2007, Fox-Rushby and Foord 1996, O'Connell et al. 2010). Nevertheless, the authors concluded that there is a need to explore this further to improve these services.

4.1 Introduction for sub-study II

News has it, that ANC coverage in Africa is promisingly increasing. Yet, this promise continues to be missed by the marginalised and displaced populations. Evidence shows a considerable discrepancy in the utilisation of services between women who live in remote areas as compared to those living closer to health facilities(O'Donnell 2007, Simkhada et al. 2008). Many factors contribute to underutilization of ANC services in developing countries(Simkhada et al. 2008). According to the economic model, a perceived lower quality regarding the unavailability of medical supplies and higher costs of ANC, including both time and financial costs of treatment and travel would reduce its use. Indeed, distance to the health facilities hinders service utilisation by imposing both actual travel costs and time costs due to travel (Acharya and Cleland 2000, Magadi et al. 2000, Raghupathy 1996, Simkhada et al. 2008).

MHC is among the approaches that have for the long time being implemented to break the barrier of physical availability of health interventions. Their use has been documented well in the areas of vaccination(Creese et al. 1982), cancer screening(Naeim et al. 2009, Reuben et al. 2002), and HIV counselling and testing services(Larson et al. 2012) to name a few. Although they have been implemented for more than 20 years, the debate on these approaches has also been going on for ages with questions raised on their sustainability(El-Zanatay and Hamed 2001), quality(El-Gibaly OMH 2008) and costs(Mercer et al. 2005). Recent work on MHC has included cost estimation using a provider perspective with the aim of demonstrating the cost-saving ability of this approach, estimating the return for investment per avoided admissions(Oriol et al. 2009) and lowering hypertension(Song et al. 2013).

Although some light has been shed regarding the cost of providing services at the MHC, yet, poorly is known on how much clients spend concerning time and direct costs. One can argue that health care for pregnant women in Tanzania is free of charge(MoHSW 2008). However, evidence from previous studies indicates that pregnant women still pay for essential health services(Kowalewski et al. 2002, Levin et al. 2003). A recent systematic review(Abdel-Aleem et al. 2016) on MHC for women and children health found only two studies that had systematically reported on the impact of MHC. Concluding remarks from that systematic review echoed the need for more studies, specifically those who will measure the effect of mobile clinics on cost and people's access to healthcare, their satisfaction, health, and well-being. This sub-study is set to respond to the call as mentioned above, in which it estimates the hidden costs in using apparently 'free' ANC services among women residing in remote areas of Kisarawe District in the Pwani Region of Tanzania. We also assessed whether MHCs had reduced the cost of travel as well as time consumed in utilising ANC.

4.2 Methodology adopted for sub-study II

Study Setting and study subject

The study was carried out in Kisarawe District in the Coast Region of Tanzania as detailed in chapter two of this thesis. From November 2015 to June 2016, 293 pregnant women who attended the MHC were interviewed. Sampling was incidental, and all mothers were included who had no medical or obstetric complications and were willing to be interviewed.

Study Design

The study used quantitative methods. Because the primary aim of this part of the study was to estimate the resource use by pregnant women when seeking a free health care services, it was justified to concentrate on service users only rather than doing a household survey(Creese et al. 1982, Kowalewski et al. 2002). All cost data were collected in Tanzanian shillings and converted to US$ for the exchange rate of the year 2016 (US$1=2200 TZS)(BoT 2017).

Measurement of direct costs and time

Type, amount and extent of the cost incurred by women were established by conducting key informant interviews with ten pregnant women before the design of the interview guide. The information gathered from the key informant interviews together with that found in the literature was used to create the interview guide. The structured interview questionnaire was administered to a total of 293 pregnant women attending the MHC from November 2015 to June 2016. The questions were on time spent on travelling; waiting and consultation at the MHC. That information was used to calculate total time cost which was calculated by adding consultation, waiting time and travel time. We also asked about cash payments for services, travel, drugs and supply cost; and those were added to create the variable direct total cost or direct out of pocket cost. Other information collected was on the woman social demographic characteristics as well as the woman demographic history.

Interview data on time spent on services was compared and verified by observing waiting and consultation time at the MHC. Information on travel costs was verified by comparing them with the government transport rates in the rural areas, while information on costs of prescribed medicines was compared with the Tanzania MSD drug cost lists. To estimate distances travelled, women were asked to account for the distance, but they were probed on the name of their neighbourhood (*kitongoji*) as well as the village in which they live, then as part of an incentive, each woman interviewed was returned to their household by the rented motorcycle in which the distance in kilometre from the woman's residence to the point of care (mobile clinic) was recorded

Data entry and analysis

Double data entry was done using EpiData software version 3.1. Data were cleaned and extracted in STATA version 12 where descriptive and regression analyses were performed. The summary statistics like mean, and their standard deviations were estimated. Although the cost data was skewed, we computed the mean cost and time because this analysis aimed to inform policymakers of the total direct cost spent by women when they utilise health care services. We also compared the mean cost and time variables for women who indicated to have travelled more than 5 kilometres and those who travelled less than 5 kilometres by performing a non-parametric statistical test (Wilcoxon–Mann–Whitney rank-sum test).

Multiple linear regression was conducted, with the outcome variables of choice being those total costs, total time and helper time. Since ANC at the public health outlets is free of charge, we hypothesised that the direct client cost of accessing ANC care depends on the distance from the household to the mobile clinic location, frequencies of out of stock of needed medicine and laboratory investigations. These were therefore examined as explanatory variables. Our descriptive regression analysis started by examining the statistical association of each independent variable on the outcome variables and later on the model was fitted to exclude explanatory variables, which were not significant like waiting time. The second hypothesis was regarding the helper time, in which we hypothesised that the need for helper time is dependent on distance to the MHC, age of her last child and number of living children.

4.3 Results of client costs analysis

Characteristics of respondents

From January to December 2015, a total of 513 pregnant women attended the mobile clinic. Exit interview using the questionnaire available in Appendix 5 of this thesis, was done with 293 women between October 2015 and March 2016. The mean age of women attending the mobile clinic is 25 years with the range of 15-40 years. 75% of the women were married, 18.8% were cohabiting, and 5% were single mothers. The majority (70%) had no formal education, while 27% had a primary school education and only 2% had a secondary school education. These women mostly engage themselves in livestock keeping and farming (35%), food vending (28%), livestock keeping alone (16%), housewives (11%), farming alone (7%), formal employed (2%), with 1% who cannot work because of sickness. With regards to obstetric and gynaecological history, the mean gravidity was estimated to be 3 (ranging from 0-9 pregnancy), at least 6% of the women had a history of at least one neonatal death and home delivery of the last child was reported by at least 48% of the women.

Types of ANC interventions provision at the MHC

During the time of the study, no HIV, Syphilis and screening for the possibility of protein in urine was done. Due to lack of reagent at the MHC, only 27% and 8.87% of pregnant women were screened for anaemia and malaria according to the recommendations. Out of stock reagents were reported by 94% of the pregnant women who did not receive diagnostic services at the MHC. It was observed that 87% of the women had their first dose of sulfadoxine-pyrimethamine, 78.6% had two doses, and 78% had three doses of pregnant women had two doses. A complete course of iron sulphate and folic acid supplementation to prevent anaemia in pregnancy were provided as scheduled to 71.6%, with 80.9% receiving only three courses, 85% received only two courses while 97.74 had received their first course. Provision of dose one, two and three of tetanus toxoid was done to 99%, 85% and 85.5% respectively.

Distance travelled and time used to access ANC at the mobile health clinic

Women attending the MHC have to travel a mean distance of 6.64 kilometres [95% CI: 6.15-7.14] as presented in Table 2. The mean estimated time used for travel was 83.51 minutes [95% CI: 76.61-90.41]. The majority of those women walk to the MHC (78.8%), while 11 % use private transport, 5.5 % commute using a bicycle, 3.71 % use public transport in the form of a bus or rented motorcycles to reach the clinic. Of the 15% who had to pay for transport, the mean cost of travel was estimated to be US$0.70(0.49-0.90).

Table 2. Time spent utilising ANC services (n=293)

	Mean (SD)	Minimum	Maximum
Waiting time in minutes	113(78)	3	360
Consultation time in minutes	29(6.22)	15	45
Travel time in minutes	83(60)	1	255
Total time cost in minutes	225(109)	39	539
Helper time in minutes	250(147)	30	607
Distance to Health Centre in kilometres	16(7.83)	5.25	31
Distance to Mobile Clinic in kilometres	6.57(4.24)	0.1	16

NB: n= Sample size

There was a significant difference in waiting time and helper time according to the distance of residence as presented in Table 3. Those who live more than 5 km away from the MHC incur large costs as compared to those living less than 5 km.

Table 3. Differences of time used according to the distance travelled

	Distance to the Mobile Health Clinic		
Variable	<5km, n(142)	>5km,n(151)	p-value*
Mean helper time in hours, [95% CI]	2.23[2.01-2.44]	5.97[5.68-6.27]	0.000
Mean waiting time in hours, [95% CI]	1.56[1.40-1.72]	2.19[1.95- 2.43]	0.002

*Wilcoxon rank-sum (Mann-Whitney)

Out of pocket payments

Table 4 presents direct costs spent by women when they utilise health care at the MHC. Due to out of stock situations, reported by 84.98% of the respondent, women had to buy medicines and pay for laboratory services at the private outlets. The mean costs of prescribed drugs and laboratory services were US$0.34(SD=0.28) and US$3.98(SD=1.46), respectively. Women reported the costs that they expect to incur which are related to delivery. The mean cost reported was US$3.48(SD=0.01). For those who paid for transport (15%) and a helper (0.69%), the estimated mean costs were US$0.75(SD=2.03) per one-way trip and US$0.05(SD=0.56). No informal payments to the health worker were reported.

Table 4. Patient hidden costs (in US$) of utilising ANC services (N=293)

	Mean (SD)	Minimum	Maximum
Laboratory costs	3.98(1.46)	1.36	8.12
Medicine costs	0.34(0 .28)	0	1.18
Travel costs (one way)*	0 .75(2.03)	0	8.12
Helper costs	0.05(0.56)	0	7.27
Total direct cost**	5.12(2.59)	1.86	13.32

Note

*Only 0.69% and 15% of the participants reported incurring helper and travel costs,

**Total costs will be US4 4.32 when helper and travel cost are excluded in the calculation

Relative's (household helper) time spent to cover the absence of the client at home

In this study, almost 96.6% of women had someone to help them with house chores, which ranged from helping out with the children during the time of which they come to access care. On average, the mean total time estimated for a helper for one visit was 250 minutes [CI: 233 -267]. Only 0.69% reported paying the helpers for their services, in which they reported to pay around US$ 0.02(SD=0.28) per visit.

Regression analysis results

Table 5 shows results of the stepwise regression looking at the drivers of helper time; opportunity costs (total time cost) and direct out-of-pocket costs per visit made. Helper time was positively driven by the distance from the MHC to the household (β coefficient =24[95% CI: 22-28]) and consultation time (β coefficient =2[95% CI: 0.51-3.68]). On the other hand, the age of the last child (β coefficient=-37[95% CI: -50 to -23] and a number of living children (β coefficient=-8[95% CI: -16 to -2]) had a negative effect on helper time. That means that there will be an increase in helper time by 24 minutes for every kilometre that a woman travels to seek health care. Similarly, for every minute increase in consultation time, a woman will need a helper for two more minutes. An increase in age of the last child will favour reduction of helper time by 37 minutes, while the increase in a number of living children will also favour reduction of helper time by 8 minutes. To our surprise waiting time, marriage type and occupation were not significant drivers of helper time.

Table 5 Drivers of client total direct costs and total time costs

Explanatory variables	β Coefficient	P value	95% Conf. interval
Helper time in minutes per visit			
Distance travelled per visit in km	24	0.000	22 to 28
Age of the last child in years	-37	0.000	-50 to -23
Number of living children	-8	0.016	-16 to -2
Consultation time	2	0.010	0.51to 3.68
Direct out-of-pocket payment			
The frequency of out of stock reagents	1.22	0.000	0.32 to 2.12
Frequency of prescription	7.39	0.000	6.98 to 7.80
Total time cost			
Gravidity	2.25	0.004	0.74 to 3.75
History of miscarriage*	2.73	0.013	0.59 to 4.87
Number of living children	-2.22	0.005	- 0.3.77 to -0.67
Age of the last child	-0.33	0.001	-0.52 to -0.13

NB: *No history of miscarriage was the reference group

Direct out-of-pocket costs incurred by women were increasing by US$1.22 and US$7.39 as the frequency of out of stock reagents and medicine increase. Number of pregnancy a woman has had and whether a woman has had a history of miscarriage positively influenced total time costs. On the other hand, as the age of the last-born child as well as the number of living children of a woman increase, the total time cost per visit was predicted to decrease.

4.5 Discussion of the patient cost analysis

This study analysed data from exit interviews to estimates cost incurred by pregnant women when utilising ANC at the MHC. This client cost analysis accounts for distance travelled, time and money spent directly for services and impact of service utilisation on relatives' time. The results indicated that MHC reaches women at a distance slightly lower than the recommended with much waiting and consultation time. The cost attributed to not having medicine and supplies at the MHC may jeopardise the significance of the MHC. These results provided evidence that supports MHC activities regarding its potential in reducing distance and travel time and proposing for service provision design that may reduce consultation and wait time. To some extent, our results extend those reported in previous studies(Kowalewski et al. 2002, Sauerborn et al. 1995) by documenting time for both clients and their relatives while determining the drivers of both.

Although there were more than half of the women who travelled more than five kilometres, our findings show a significant saving in travel distance to women who utilise services at the MHC as compared to the scenario of having no MHC. On average women saved an approximate of a ten kilometres journey when they utilised the MHC as compared to situations in which these services were not available. Our findings resonate similarly to findings from the study in Bangladesh, in which they estimated an average distance travelled by women to the maternity waiting homes which are designed to bring women closer to care to be six kilometres with more than 50% of women traveling more than ten kilometres to the point of care(Keya et al. 2013). The findings from this work on travel costs were slightly higher than those reported by a multi-country study done in three African countries in 2000. The estimated travel costs for Uganda, Malawi and Ghana were USD$ 0.56, US$ 0.12 and US$ 0.15 respectively(Levin et al. 2003). However, it should be noted that our travel costs account only for the 5% since the other came to the clinic by foot regardless of whether they lived far or near.

Proximity as a strong determinant of utilisation of services cannot be over-emphasised; this implies that women may not utilise these services if they are located far away. For instance, 15 per cent our participants reported having missed their scheduled appointment because of distance and long hours of travel, while 16 per cent had ignored some of the emergency symptoms because of the long distance they would have travelled. These findings agree with what has for long been postulated in several conceptual frameworks that distance to the point of care is associated with reduced utilisation of maternal health care(Ensor and Cooper 2004, Jacobs et al. 2012).

Private costs for medication and laboratory investigations that were not available at the MHC contributed to a 97% of the total costs. Those costs will go up further if there is an increase in out of stock reagents at the MHC. In the study done in Tanzania(Ngalesoni et al. 2015), it was reported that private payments for medication in case of out of stock situations are the primary driver of the direct cost of the client, even to the clients who utilise free services in public facilities. Reasons for unavailability of essential medicine and supplies during our study are also similar to those reported in other studies, which mostly are due to out of stock situations and lack of reliable information that can aid evidence-based planning and budgeting(Ensor and Cooper 2004). Lack of essential drugs and reagents in public facilities is reported not only to have cost implications to the users of free services but also to discourage women from utilising available health services(Kruk et al. 2009).

In the context of free services for maternal health care, the problem of out of stock reagents and needed medicines may nullify the whole point of free services. In our study, out of stock situations were reported by almost 94% of respondents, and the mean number of the frequency of out of stock situations was estimated to be 2.18(CI: 2.10- 2.30). The significant impact that frequency of out of stock medicine has on costs suggests the perceived issues of inadequate health care quality in rural areas(Kruk et al. 2009) and problems that are reported on the implementation of decentralization in Tanzania's health sector(Maluka et al. 2010, Maluka et al. 2011, Munga et al. 2009) as well as the raised challenge of competing for resources between MHC and static health facilities as presented in sub-study I in chapter three of this thesis. The problem of out of stock situations arises due to many factors in the operation of the health systems, like poor supply chain management and lack of reliable information to guide budgeting and planning, all of which cannot be addressed at the district level.

The extent to which health care utilisation imposes on time cost goes beyond the woman to involve the family and relatives. On visit day a client does not only forsake time that she would have spent on other productive activities but also needs help from relatives to take over her responsibilities when she is not around. Helper time in our study was almost the same as the total time that a woman used, and it varies considerably depending on several socio-demographic characteristics. However, helper time can be reduced by ensuring uptake of other reproductive health interventions. For instances, we found that the number of living children and age of the last child considerably drove helper time. This implies that having women abiding by family planning policies, which can translate to large child space and few children per woman, could reduce helper time costs.

On the other hand, rearranging the way services are provided by ensuring that not everything is done by the nurse or clinical officer will lower consultation time which also is suggested to drive helper time in this study. For instance, provision of iron and folic acid supplementation represents one of the simplest and cheapest 'safe motherhood' interventions in this context which community health workers can do. This indicates that if task shifting strategies are effectively adopted in this context, they will not only reduce time cost for clients and their relatives but also ensure that nurses are not overworked. Task shifting is an effective strategy for addressing shortages of HRH since it offers cost-effective care to more patients than a physician-centred model (Braitstein et al. 2012, Callaghan et al. 2010).

The current gross domestic product per capita for Pwani region in which the Kisarawe district is located is US$470(Region 2016), implying that women in this study spend on average 1% of their annual income on utilising ANC services. Our estimates present the value that is close to the reported health expenditure per capita for the Tanzanian as a general population, which is 5% of the total expenditure per capita. However, for a rural woman to spend 1% of their annual per capita on ANC care is alarming. Such a high financial burden on clients for preventive services patients might have an impact on their health-seeking behaviour and hence lead to low utilisation of health services as reported elsewhere(Ensor and Cooper 2004, O'Donnell 2007).

ANC services are a gateway to the prevention of any misfortunes associated with pregnancies. This provides entrance to effective interventions, which may prevent the adverse outcomes to the woman and her unborn baby. That means its outlook on all aspects of the quality of care to costs should not be an obstacle. When women have to deal with opportunity costs of time and other direct payments, they may refrain from utilising services or choose to utilise services in a non-continuous manner(Kruk et al. 2009). It is not surprising that 48% of women in this study reported that delivery of their last child was at home despite a positive indicator of utilising ANC from the first trimester of their pregnancy. That can be explained by the long distance that they have to travel when it comes to delivery and bearing in mind that they are already informed about the delivery kit costs. Aligning MHC with the maternity homes will aid in improving the current situation by ensuring that all women attending the MHC are linked with the maternity homes.

Strengths and limitations

This study had several strengths. First, we accounted for a time as a resource, which goes beyond estimating resources exploited by users by monetary means alone. Most of the women in this setting and other settings like this one do not work in formal sectors, but rather in informal sectors in which they contribute their time and do not get paid in monetary terms.

Second, the study avoided double counting of the cost of medicine and diagnostic services since pregnant women do not pay anything at the public health services; hence all of the reported payment was made at the private drug stores of health diagnostic outlets.

Despite the strengths mentioned above, this study, however, is not immune to limitations. MHC is implemented in different contexts, and this particular MHC had an advantage of having a local non-governmental organisation which assists in providing technical support, funding when needed, as well as advocacy services, that may explain, for instance, an increase in coverage and reach much more remote settings, hence these results cannot be used to make broad generalizations on how MHC can reduce, for example, opportunity costs. More research is needed to predict better the cost implications of utilising ANC in MHC.

Third, the study was conducted in the year that the country was preparing for election; this can affect, for instance, the estimation of time costs because in most of the cases and during campaigning time road infrastructures are generally at their best. Hence, running of the MHC is much better regarding travel to the centres as compared to other times. That can influence the waiting time - which is among the driver of time costs - because the MHC will reach the village early and services will start early as compared to other times. The same can be said about different seasons of the year; rainy seasons are associated with difficulties in road infrastructures; hence, cost of using MHC is subject to changes in road and transport infrastructure. Evidence shows that peoples' walking pace is season dependent, in which people tend to walk faster during the dry season and slower during the rainy season (Stock et al. 1983); hence, that can lead to differences in travel time in this study.

5.1 Introduction of sub-study III

Pregnant women living in malaria-endemic areas continue to be at risk of acquiring the disease which contributes to antenatal anaemia(Brabin et al. 2001). About 0.8 million pregnant women globally suffer from severe anaemia (WHO 2015), and that is associated with an increased risk of maternal and infant mortality(Benoist et al. 2008). Hospital-based studies in Africa suggest that severe anaemia is a leading cause of indirect maternal deaths (Ngwan and Swende 2011, Pembe et al. 2014, Ujah et al. 2005, Yego et al. 2013). Although it is estimated that about 50% of anaemia cases in pregnant women is amenable to iron supplementation(Benoist et al. 2008), these estimates are likely to be much lower in malaria-endemic areas. For a holoendemic malarious area with a 5% severe anaemia prevalence, it was estimated that in primigravidae there would be nine severe-malaria anaemia-related deaths and 41 non-malarial anaemia-related deaths per 100,000 live births(Brabin et al. 2001). Therefore antimalarial drugs have been widely used with the aim of preventing, suppressing or eradicating the infection or its consequences. The recent WHO guideline recommends provision of three or more doses of sulfadoxine-pyrimethamine(WHO 2016).

Three systematic reviews (Kayentao et al. 2013, McClure et al. 2013, Radeva-Petrova et al. 2014) have been conducted to assess the efficacy of SP on adverse effects of malaria in pregnant women. Radeva-Petrova and his colleagues indicated that the intervention has a significant impact on preventing parasitaemia, low birth weight (LBW), preterm delivery and severe anaemia compared to no therapy(Radeva-Petrova et al. 2014). Similar results were echoed by another review focusing on LBW and maternal anaemia as the outcome of interest(McClure et al. 2013). However, the two reviews did not explore the impact of the intervention on severe anaemia according to the woman' HIV (Human Immunosuppression Virus) status. HIV, just like any other chronic infection, may affect severe anaemia and other complications in pregnancy outcomes like LBW and preterm delivery(Ayisi et al. 2003). HIV also leads to immunosuppression, making the already vulnerable population of pregnant women more susceptible to other infections. Chico et al. showed HIV-infected women being at a higher risk of co-infection with malaria than HIV-uninfected women (Chico et al. 2017).

This sub-study aimed at synthesising effectiveness data that will be used in the decision analytic model. It estimates the impact of three or more doses of SP compared to no drug or case management or placebo on preventing antenatal parasitaemia and severe anaemia. It considers estimates the heterogeneity in the effect of intervention concerning woman parity and HIV status.

5.2 Methodology adopted for sub-study III

We conducted a systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline (Moher et al. 2015). Randomized and quasi-randomised trials that recruited pregnant women residing in malaria-endemic areas of SSA were included. We defined the population as pregnant women regardless of age, parity and HIV status. Only those studies whose intervention provided three or more doses of SP from the beginning of the second trimester were eligible for inclusion. The comparison groups consisted of pregnant women with similar characteristics without provision of SP or any other malaria chemoprophylaxis. The primary outcome was maternal parasitaemia defined as the presence of asexual stage parasites in maternal peripheral blood as seen in thick smears and severe anaemia defined as haemoglobin of less than 8g/dl. We excluded studies on other malaria chemotherapies and studies which did not provide at least three doses of SP (IPT-SP3).

Search methods for identification of studies

We searched the following databases: Central Register of Controlled Trials (CENTRAL), published in *The Cochrane Library* (2016, Issue 1); MEDLINE (1966 to March 2017); EMBASE (1974 to March 2017) and CINAHLS (1974- March 2017) using a search strategy comprising terms for malaria and pregnancy. We aimed to identify the whole body of evidence documented in the English language regardless of its publication status, and therefore contacted researchers working in the field asking for unpublished data, confidential reports, and raw data of published and unpublished trials, work in the press, and work in progress. Also, we checked the reference lists of literature reviews (Brabin et al. 2001, Kayentao et al. 2013, Radeva-Petrova et al. 2014), and the references to all trials included. The search strategy used is available in Table 6 on the next page.

Exclusion and Inclusion criteria

The study included studies done in SSA targeting pregnant women of all age regardless of their parity, marital status and HIV status. In case a study had provided different dosages, only those results for three or more doses were taken. The comparison was either placebo or no drug given or case management. A summarised detail of criteria for inclusion and exclusion is tabulated in Table 7 in the next page**.**

Table 6. Detailed search methods and search strategies

Set	CENTRAL	MEDLINE via OVID	EMBASE via Elsevier	CINAHLS via EBSCOhost
1	MALARIA	MALARIA	MALARIA	MALARIA
2	malaria	malaria	Malaria	malaria
3	1 or 2	1 or 2	1 or 2	1 or 2
4	PREGNANCY	PREGNANCY	PREGNANCY	PREGNANCY
5	pregnan*	Pregnan*	pregnan*	pregnan*
6	4 or 5	4 or 5	4 or 5	4 or 5
7	3 AND 6	3 AND 6	3 AND 6	3 AND 6
8		limit 7 to humans	limit 7 to humans	limit 7 to humans
9		limit 8 to English language	limit 8 to English language	limit 8 to English language
10		limit 9 to clinical trial, all	limit 9 to controlled clinical trial	limit 9 to Evidence-Based Practice

Source: Author's own

Table 7. Summary Inclusion and Exclusion criteria

Criteria	Inclusion	Exclusion
Study design	Randomized control trials, Quasi controlled trials	Other study designs
Population	Any pregnant women regardless of their age, parity and HIV status	Not pregnant
Study setting	Sub Saharan Africa	Not done in SSA
Intervention	Three or more doses of SP for prevention of maternal malaria and severe anaemia	Other antimalarial Studies that provided SP for treatment of malaria or other condition and not for preventive purposes A study that compared different doses of SP, for instance, those that compared three doses and two doses
Control	Placebo or case management or no drug	Other antimalarial like metformin, chloroquine, another different dosage of SP
Outcome	Maternal peripheral parasitaemia Maternal severe anaemia (Hb less than 8g per dl)	Other outcomes like LBW, preterm delivery, placental malaria, neonatal death, maternal mortality
Language	English publications only	Non-English publications

Source: Author's own

Data collection and management

Two reviewers independently screened titles, abstracts, and full-texts and decided about the eligibility of articles. Discussion resolved any disagreements. Relevant data were extracted and cross-validated.

Assessment of risk of bias in included studies

Two authors independently assessed the trials' risk of bias using The Cochrane Collaborations' tool for assessing the risk of bias in randomised trials (Higgins et al. 2011).

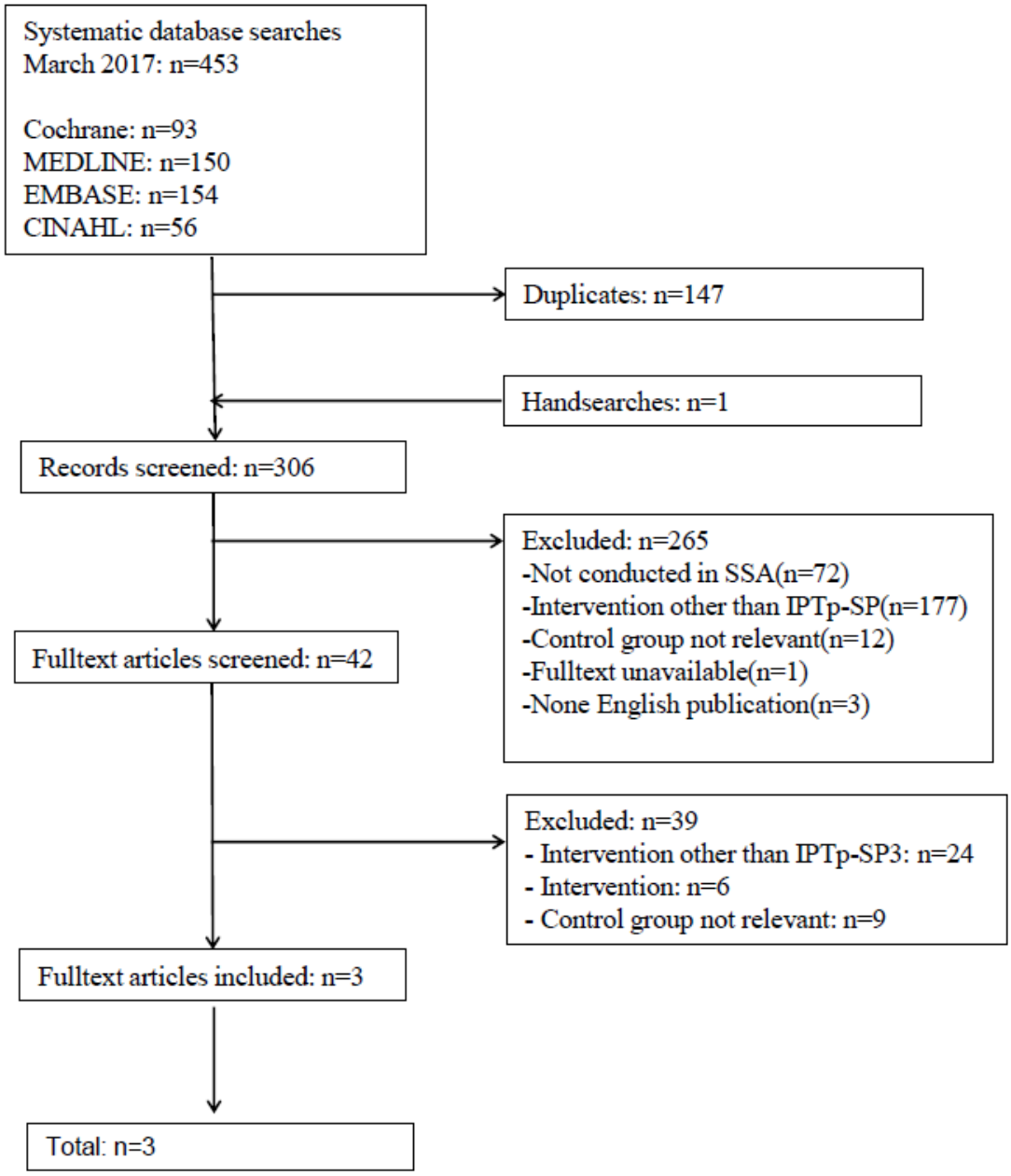
Statistical analysis

The software 'Review Manager (version 5.3) provided by the Cochrane Collaboration was used for statistical analysis. Because the outcomes of interest for this study were dichotomous, we calculated the risk ratios with their corresponding 95% confidence intervals. For meta-analyses, we used a random-effects model similar to the method used in the only previous meta-analysis of the effect of SP on malaria prevention in pregnancy (Kayentao et al. 2013, Radeva-Petrova et al. 2014). This method was used because it takes into account the heterogeneity of the various studies(Higgins and Green 2011). The heterogeneity was assessed by evaluating the chi-squared test on Cochrane's Q statistic (Cochran 1954), and quantified by I-squared values, assuming that I-squared values of 25, 50, and 75% being representative of low, medium, and high heterogeneity, respectively(Higgins and Thompson 2002). If substantial heterogeneity was detected, we performed a subgroup analysis to investigate the possible sources of heterogeneity using the following grouping variables: Parity and HIV status.

5.4 Results of the systematic review and meta-analysis

The results of the systematic searches and screening process are presented by the PRISMA (Moher et al. 2015) diagram in Figure 5 below.

Figure 5 Flow diagram of literature search and study selection



Source: Authors own drawing

Study characteristics, interventions and location

Table 8 presents the characteristics of the included study populations. A total of three trials met the inclusion criteria: Two trials evaluated the intervention in low parity women (Parise et al. 1998, Shulman et al. 1999) while one evaluated the intervention in high parity women (Mbaye et al. 2006). Two trials had two arms and were placebo-controlled (Mbaye et al. 2006, Shulman et al. 1999), while one had three arms, monthly SP, double dose SP, and case management in which women were provided SP only when they presented with a recent

history of fever and parasitaemia(Parise et al. 1998). All interventions were provided as directly observed treatment (DOT). Parise et al. 1998(Parise et al. 1998) provided 200 mg iron sulphate tablets and 5 mg folic acid tablets, Shulman et al.(Shulman et al. 1999) did not indicate at what dose and Mbaye et al. (Mbaye et al. 2006) provided a combination of iron and folic acid 'Fefol' tablets (500 μg of folic acid and 47 mg of ferrous sulphate). Two trials were conducted in areas where insecticide-treated bed nets (ITNs) were used. Seventy-eight per cent of women in the trial of Mbaye et al. (Mbaye et al. 2006) slept under ITNs, 93% of whom stated that they always slept under the ITNs, while Shulman et al. (Shulman et al. 1999) reported that the population used ITNs not stating further details. Trials were done in Kenya (Parise et al. 1998, Shulman et al. 1999) and The Gambia(Mbaye et al. 2006) in regions which are considered as malaria highly endemic areas.

Table 8 Baseline characteristics of the participant in the RCT included in this review

Study	Sample size	Gestation[a]	% with Malaria[b]	Haemoglobin[c]	% with HIV	Age[d] in yrs.	Parity %
Mbaye 2006	Intervention (1346)	15+	15.4%	7-9g/dl=71%	n.a	15-19(81)	1st pregnancy =1.2
				>9g/dl=29%		20-29(852)	2nd pregnancy =20.3
						30-39(378)	3rd pregnancy =18.8
						40-50(28)	>4th pregnancy =59.6
	Control (1342)	15+	14.5%	7-9g/dl=70%	n.a	15-19(79)	1st pregnancy =1
				>9g/dl=30%		20-29(847)	2nd pregnancy =21.8
						30-39(395)	3rd pregnancy =19.1
						40-50(18)	>4th pregnancy =58.4
Shulman 1999	Intervention (640)	23.0	0%	n.a	5.1%	19.6±3	1st pregnancy=100
	Control (623)	23.3	0%	n.a	5.8%	19.7±3	1st pregnancy=100
Parise 1998	Intervention (661)	16-26	45.2%	9.7±1.9	23%	n.a	1st pregnancy=63.6
							2nd pregnancy=36.4
	Control (736)	16-26	44.9%	9.6±1.9	26%	n.a	1st pregnancy=62.3
							2nd pregnancy=37.7

Source: Author's own

[a] at recruitment in weeks

[b] Malaria parasitaemia in the maternal peripheral blood at recruitment

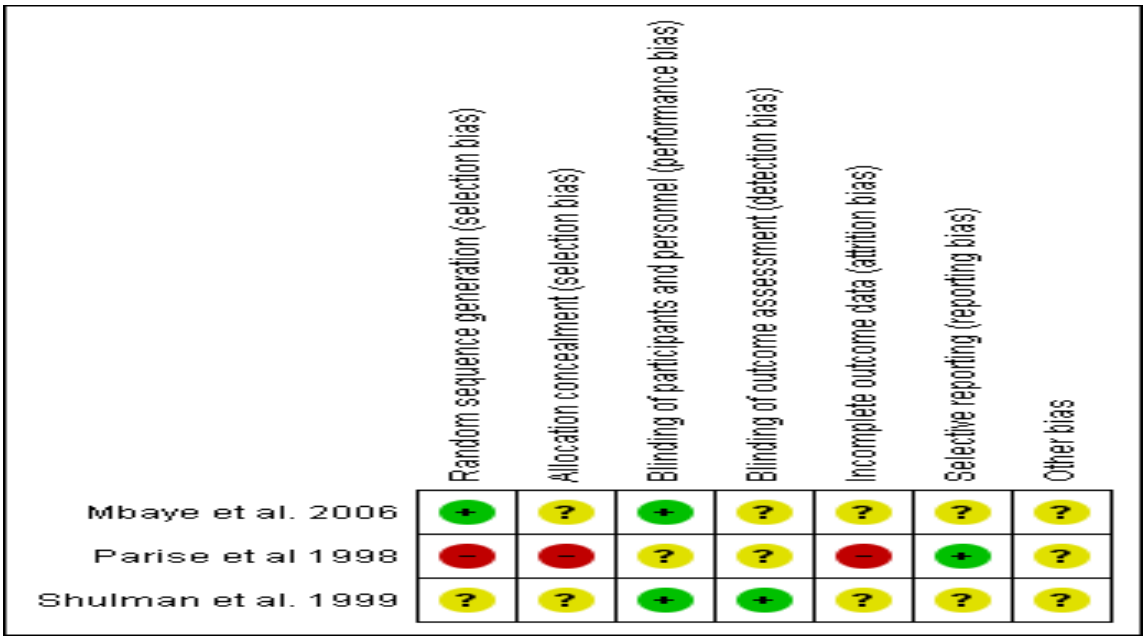
[c]Shulman(Shulman et al. 1999) haemoglobin levels presented as mean value in g/dl, Mbaye(Mbaye et al. 2006) presented as percent

[d]Mbaye(Mbaye et al. 2006) age presented in age groups(n), Shulman(Shulman et al. 1999) presented as mean age

Risk of bias in included studies

Figure 6 presents the risk of bias assessment. In the study by Mbaye et al.(Mbaye et al. 2006), randomization sequence was generated by computer software hence suggesting low risk of bias, while for the trial by Shulman et al. (Shulman et al. 1999), participants were assigned unique identification numbers sequentially but it is unclear how those numbers and sequences were generated indicating unclear risk of bias. The study by Parise et al. (Parise et al. 1998) used a method leading to high risk of bias because they assigned participants to their respective arms systematically without reporting any randomisation method. Concerning allocation concealment, Mbaye et al. (Mbaye et al. 2006) prepared four envelopes for each woman in which tablets were pre-packed,– one for each potential treatment. The envelopes were pre-labelled with the same packet number and placed in a wallet bearing the subject's number and packet number. That method was judged as an unclear risk because it is not sure whether the envelopes used were opaque or not, hence difficult to judge whether participants and recruiter could not visualise what was in the envelopes. Similarly, the study by Shulman et al. (Shulman et al. 1999) used a method that was judged to have an unclear risk of bias because it remained unclear if the allocation of women could be foreseen. On the contrary, allocation concealment methods used by Parise et al. (Parise et al. 1998) were judged as high risk of bias because the allocation of subjects to treatment groups was performed systematically based on clinic day rather than by randomised assignment.

Figure 6 Risk of bias summary: Review authors' judgements about each risk of bias item for each included study



Source: Author's figure

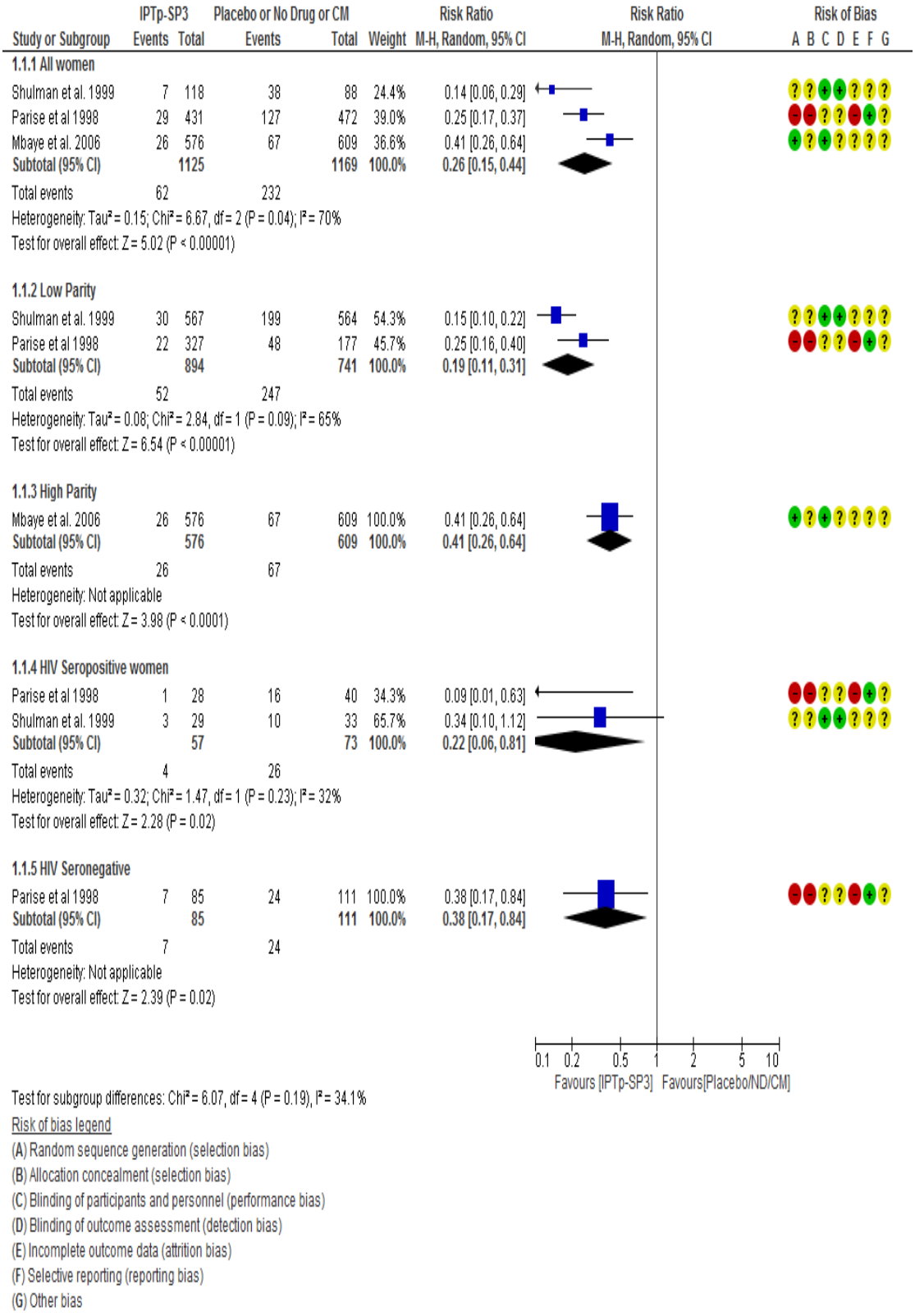
Participants and personnel involved in two studies were adequately blinded (low risk of bias), one indicating that both clients and investigators were not aware of which intervention was assigned to which group(Mbaye et al. 2006), while Shulman et al. (Shulman et al. 1999) specifically reported that a statistician and clinician retained the code relating to bottle numbers to their contents at the research unit, who was not involved in the study. However, blinding of personnel and participants were not reported in the trial by Parise et al. (Parise et al. 1998). While blinding of outcome assessors in the trial by Mbaye et al.(Mbaye et al. 2006) and Shulman et al.(Shulman et al. 1999) was adequately done, the trial by Parise et al.(Parise et al. 1998)did not state whether the investigators who assessed the outcome were unaware of the assigned groups.

All included studies initially indicated that they adopted an intention to treat analysis which would have reduced the risk of attrition bias. However, they reported an exclusion of all data that were missing which contradicts the original analysis plan leading at least to a judgement of unclear risk of bias. Besides, none of the authors described the methods for handling missing participant data (e.g. last observation carried out forward). Parise et al. (Parise et al. 1998) reported the results for 60-70% of participants without providing any reasons, clearly indicating a high drop-out rate leading to attrition bias and judgement of high risk of bias. There was no selective reporting by Parise et al. and Shulman et al. because they described results for all outcomes mentioned, but Mbaye et al. did not define any outcome parameters, leading to the assessment of the unclear risk of bias. There was an unclear risk due to other bias, because none of the authors reported conflicts of interest, or sponsoring of medication.

Effect of IPTp-SP3 versus placebo or no drug or case management on the prevalence of maternal parasitaemia

Figure 7 depicts the results on the effect of IPT-SP3 on antenatal parasitaemia compared to either case management or placebo or no drug. Fewer women in the group receiving IPT-SP3 had antenatal parasitaemia regardless of their parity or HIV status (RR 0.26, 95% CI 0.15 to 0.44). Women in their first or second pregnancy (low parity) who received the intervention were also less likely to have antenatal parasitaemia (RR 0.19, 95% CI 0.11 to 0.31). The intervention had a 59% risk reduction when it was provided to high parity women (RR 0.41, 95% CI 0.26 to 0.64). Aggregated findings for women living with HIV suggested that the intervention offers a 78% risk reduction of having antenatal parasitaemia among HIV positive women (RR 0.22, 95% CI 0.06 to 0.81). The study by Parise showed a 62% risk reduction among women who were HIV negative (RR 0.38, 95% CI 0.17 to 0.84).

Figure 7 Effectiveness of IPTp-SP3 on prevention of antenatal parasitaemia

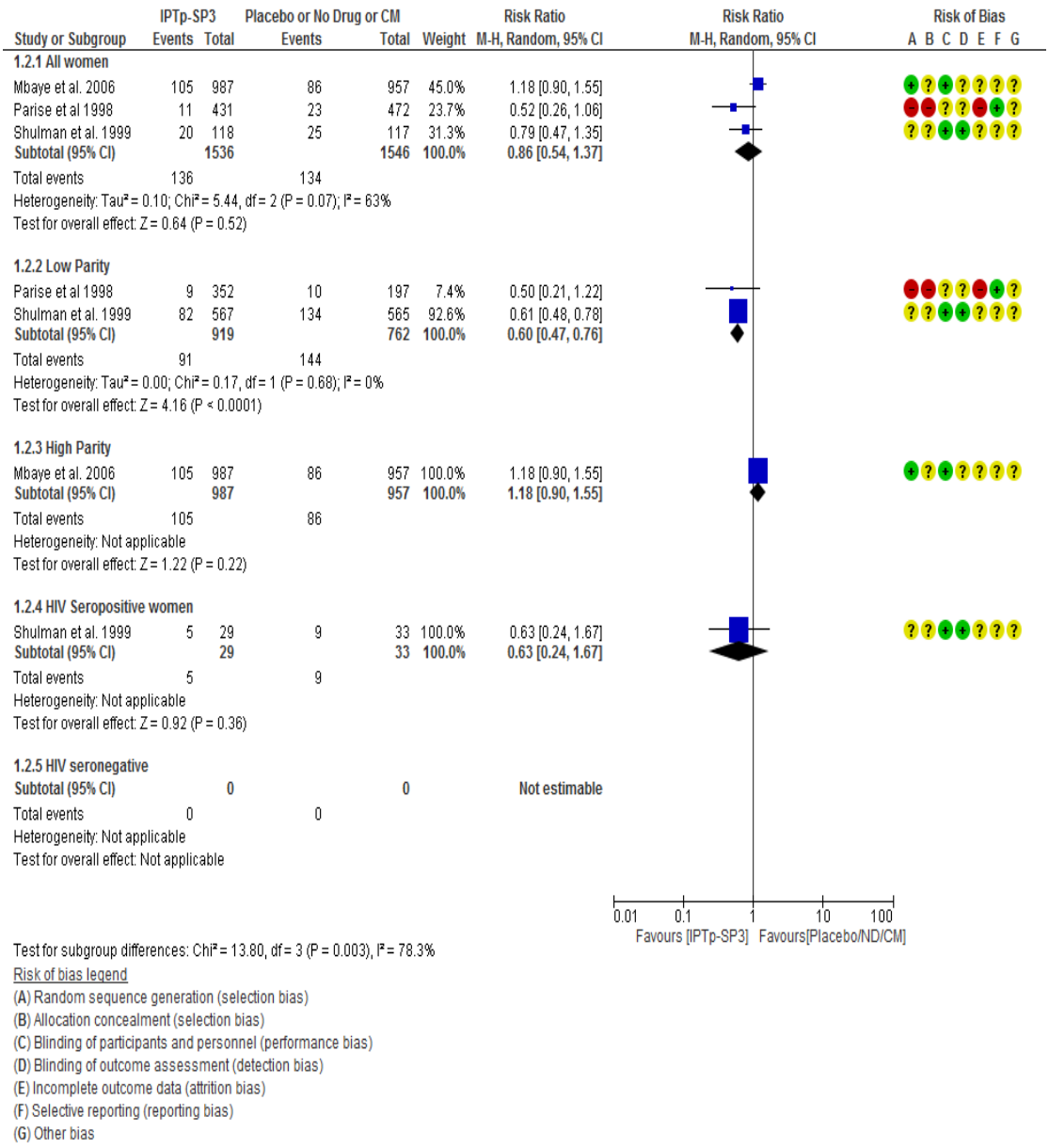


Source: Author's figure

Effect of IPTp-SP3 versus no intervention on the prevalence of severe anaemia

Figure 8 presents the results for the effect of IPTp-SP3 on severe anaemia. There was no data available for HIV seronegative women. Overall, women who received IPTp-SP3 had a 19% reduction in the relative risk of having severe anaemia compared to placebo (RR 0.86, 95% CI 0.54 to 1.37). Among the low parity women, IPTp-SP3 leads to a 40% risk reduction (RR 0.60, 95% CI 0.47 to 0.76) while there were no statistically significant group differences concerning the effect on multigravida women (RR 1.18, 95% CI 0.90 to 1.55) and HIV positive women (RR 0.63, 95% CI 0.24 to 1.67).

Figure 8 Effect of IPT-SP3 in preventing severe maternal anaemia



Source: Author's figure

5.6 Discussion of the results from the systematic review and meta-analysis

This systematic review highlights the role of SP during pregnancy on maternal parasitaemia and severe anaemia compared to placebo. We found IPT-SP3 reducing the risk for maternal parasitaemia and severe anaemia among pregnant women regardless of their parity and HIV status. The summary estimates of the effect of IPT-SP3 on the prevalence of malaria and severe anaemia were 0.26 (95% CI: 0.16-0.41) and 0.81(0.68-0.97), respectively. The risk of bias assessment suggested that included trials were of low to moderate quality with substantial limitations in reporting of outcomes. Studies included showed no evidence of publication bias in the studies included in the review, however significant heterogeneity in the findings was observed: the *I*-squared statistics were 48.7% and 85.5% for maternal parasitaemia and severe anaemia respectively. Even though limited sensitivity analysis could be performed because of differences in the variables recorded in the various studies and few participants in the studies, the results suggest that parity and HIV status may explain the heterogeneity.

Intermittent presumptive treatment therapy with three or more doses of SP during pregnancy is overall beneficial. Its use among women in their first or second pregnancy is associated with fewer women having antenatal parasitaemia as well as severe anaemia. This is similar to what was reported by the previous review which indicated that regardless of the type of drug, any malaria chemotherapy used was beneficial compared to no chemotherapy at all (Radeva-Petrova et al. 2014). However, and to date, evidence on SP resistance is unclear because of mixed results reported by different studies. Some studies suggest that its use in populations with high levels of resistance is associated with worse pregnancy outcomes(Harrington et al. 2009, Roper et al. 2003), while others had indicated that there is still a significant benefit of IPTp in Africa because the significant burden occurs in regions where SP efficacy remains high (Taylor et al. 2012, Walker et al. 2017). Additionally, others have indicated the need to explore further benefits of the intervention suggesting that it may affect reproductive tract infections(Chico et al. 2017).

The present study also showed that severe anaemia was overall not common among women who received IPTp-SP3; however, this protective effect was not seen among women of high parity. Nevertheless, the body of evidence in the current review was too small to conclude on the effect of IPTp-SP3 on severe anaemia confidently. While many studies have assessed the role of IPTp-SP3 on malaria in pregnancy, many have focused on LBW and placental malaria(Radeva-Petrova et al. 2014). Those preoccupations on the two outcomes have overlooked the significance of malaria in pregnancy on severe anaemia(Brabin et al. 2001,

WHO 2015). Hence future studies on interventions on malaria in pregnancy should consider thorough evaluation that includes severe anaemia.

We anticipated that other drugs that are provided during pregnancy might interact with the intervention. Folic acid supplementation is recommended for all pregnant women to reduce the rate of congenital anomalies at a dosage of 5 microgram per day and high doses are said to interfere with the antimalarial efficacy of SP(WHO 2016). Two of the included trials folate was provided at a recommended dosage excluding the possibility that it could have limited the effect of IPT-SP3(Hastings et al. 2002). A similar conclusion cannot be made concerning the third study which did provide folic acid at higher than recommended(Parise et al. 1998). Noteworthy and of policy implication, other malaria interventions that were being implemented in the areas where the trials were conducted could have also affected the results. We expected differences in the protective effect against malaria between women who sleep under ITNs and those who do not because of the existing evidence compiled by Gamble et al. (Gamble et al. 2007) on ITN's protective effect against malaria and its related consequences. In that systematic review which included three clusters randomised trials and two individually randomised trials with a total of 6641 participants, the authors concluded that ITNs, when used throughout pregnancy or from mid-pregnancy onwards, have a beneficial impact on pregnancy outcome in malaria-endemic Africa. Two trials(Mbaye et al. 2006, Shulman et al. 1999) included in the current review reported having participants using ITNs during the trial period, suggesting that IPTp with SP had a significant protective effect against anaemia in women who received SP even if they never slept under ITNs. This study findings agree with findings reported in a systematic review on the effect of ITN use for prevention of malaria adverse effect, concluding that there is a lack of evidence supporting that ITN use alone can protect pregnant women against severe anaemia (OR 0.77 (0.56–1.08, p = 0.13, two trials)(Gamble et al. 2007).

We acknowledge the likelihood that the estimations on maternal parasitaemia from the studies included in this review may be underestimating the true picture due to the timing when the reported values were recorded and its relationship on malaria parasite levels. For instance, the recorded value in Parise et al. (Parise et al. 1998) was measured at the third trimester; Shulman et al. (Shulman et al. 1999) reported values that were measured between 32-35 weeks, while Mbaye et al. (Mbaye et al. 2006) reported values measured at delivery. It may be assumed that the estimate from those measurements is influenced by the total amount of antimalarial drug administered during the antenatal period and by near-to-term therapy increasing the heterogeneity of the pooled data. Brabin et al. reported that maternal parasitaemia is highest between gestational weeks 9 and 16, and then tapers until term(Brabin 1991, Brabin et al. 2001).

We expected our findings to be prone to heterogeneity because studies included had variations in characteristics of their participants regarding parity and HIV status. Subgroup analysis results indicated significant heterogeneity concerning parity and HIV status as indicated in the heterogeneity tests. For instance, IPT-SP3 was beneficial to women of low parity as compared to those with high parity both regarding protection against antenatal malaria and severe anaemia. Unfortunately, and because of limited data, nothing can be concluded regarding the impact of the intervention on severe anaemia among the HIV positive women. This calls for research that will consider the role of other infections like HIV on the impact of the intervention. Further studies should also consider the possibility that other interventions provided to HIV positive pregnant women like antiretroviral therapy (ART) or cotrimoxazole (CMX) therapy for prevention of opportunistic infections may act synergistically to provide protection against susceptibility to malaria and severe anaemia. A recent trial comparing the effect of CMX and SP in preventing maternal malaria among HIV individual suggested that the two drugs have at least similar effect on maternal parasitaemia(Klement et al. 2014).

The current review was limited by three main issues. At first, all trials included had serious weaknesses due to misreporting or misleading reporting of outcomes. Two trials were not clear concerning the HIV status of the included participants. While Mbaye et al.(Mbaye et al. 2006) did not perform an HIV testing to confirm the status of the participants and assumed that they were HIV negative based on the information on the overall HIV prevalence from another study that was done three years prior to the trial, Shulman et al.(Shulman et al. 1999) did not mention if the findings reported in their primary results come from a population of HIV negative or positive. Those problems made it difficult to come to certain conclusions regarding what was reported, and it might have led to understanding the reported findings in the manner that does not portray what happened. A recent systematic review of the methodological problem of RCTs done in sub-Saharan Africa which included 121 RCTs conducted from the year 2014 to 2015 indicated that incomplete reporting is widespread (Diakou et al. 2017).

Secondly, the number of trials was limited including few participants, which made it difficult to draw definite conclusions especially on the impact of IPT-SP3 on severe anaemia according to HIV status. Thirdly, limitations related to protocol violation in the included studies will also be a problem in this review because it is a known fact that protocol violations may affect the outcomes of any intervention. For instance, Shulman et al. (Shulman et al. 1999) reported that six and eight women from the IPT-SP3 arm and placebo arm respectively reported having used their SP on top of the intervention which they received. Chloroquine was reported in the same study to have been used by 69 and 61 in the IPT-SP3 arm and

placebo arm, respectively. This protocol violation may have affected the reported results. Additionally, the large number of women lost or excluded from the final analyses could potentially mean that the more disadvantaged groups were excluded from the results. Although not specific for malaria intervention, evidence from other health intervention in sub-Saharan Africa indicated that clients from the disadvantaged group were more likely to drop out of care as compared to their counterparts (Geng et al. 2010, Koole et al. 2014). Despite the uncertainties in the effect estimates obtained from available RCT on use of IPT-SP3 for mitigating malaria-related severe anaemia in pregnant women, this review compiles the best available evidence comparing the aforementioned intervention with no intervention or placebo.

6.1 Sub study IV Introduction

Malaria in pregnancy is an intractable public health problem. It is responsible for the death of about 10,000 women every year although it can be prevented by already known simple and inexpensive interventions (WHO 2017). For instance, the WHO still recommends a monthly dose of sulfadoxine-pyrimethamine (SP) from the second trimester onwards among the interventions for malaria in pregnancy despite the ongoing debates and fear of resistance (WHO 2016). Recent mathematical models(Walker et al. 2017) and economic evaluations(Fernandes et al. 2016, Fernandes et al. 2015, Sicuri et al. 2010) indicated that even when accounting for SP resistance, extending its coverage to all pregnant women at risk, would have a sizeable impact upon maternal and infant health in almost all malaria-endemic settings in SSA.

However, accomplishing the recommended coverage rates for intermittent preventive treatment with SP has remained elusive for many countries in SSA(van Eijk et al. 2013). That is because access to antenatal clinics—where most of the essential interventions are provided and malaria risk varies substantially. Evidence indicates that pregnant women who live in remote and rural areas do not access effective essential antenatal interventions including malaria interventions due to existing inequities in the distribution of health care (Jacobs et al. 2012, O'Donnell 2007). To date, researchers and policymakers are advocating for continuing research on alternative delivery approaches to increase access to malaria prevention interventions in pregnancy(Simkhada et al. 2008, van Eijk et al. 2013).

In Tanzania, MHC, outreach workers and community health volunteers are mobilised to support delivery of maternal health interventions to increase access and reduce inequalities in access to health care (MoHSW 2008,2008,2008). To date, several studies had indicated an increase of utilisation of maternal health interventions using MHC (Edgerley et al. 2007, International 2016, O'Connell et al. 2010, Schnippel et al. 2015), yet little is known regarding the cost implication associated with this strategy. While we are acknowledging that economic evaluations may be constrained by the need for large sample size, time and the related financial inputs(Walker and Fox-Rushby 2000). However, some country experiences have shown that information on the cost-effectiveness of health strategies can be used to aid different policy decisions(Hutubessy et al. 2003). Policymakers can be guided with such evidence to make the right judgements and address inequities about the pros and cons of the different policies and programs(Oxman et al. 2009).

This, therefore, seeks to evaluate the cost and effectiveness of using MHC to roll out IPTp-SP3 to remote populations by constructing an analytic decision model.

6.2 Methodology adopted for sub-study VI

This was an economic evaluation study. Economic evaluation of health care is the process of systematic identification, measurement and evaluation of the inputs and outcomes of two (or more) alternative activities, and the subsequent comparative analysis of these. The primary purpose was to identify the best course of action, based on the evidence available. Five types of economic evaluation exist, namely, cost-benefit analysis (CBA), cost-effectiveness analysis (CEA), cost-utility analysis (CUA), cost-consequences analysis (CCA), and cost minimisation analysis (CMA), which can be applied depending on the question at hand(Drummond et al. 2015). This sub-study adopted the CEA and used a decision analytic Markov model to estimate the costs and effectiveness in the form of DALYs of providing the IPTp-SP through MHC as compared to not providing the intervention and waiting to treat the consequence when they happen. The Markov model was chosen because of the recurring nature of the disease in which the decision tree analytic model cannot account for recurring events which may lead to underestimation of cost and effect.

Definition of the intervention and target population

The cost-effectiveness analysis is comparing the implications for medical care costs and health-related outcomes of two or more alternative strategies. The first strategy is to use MHC to provide three or more doses of SP for intermittent preventive treatment for malaria and severe anaemia. In this strategy, women will be provided with IPTp-SP3 via the MHC, and, in case it happens that they get malaria or severe anaemia, we assumed that they will be treated at the public health facilities according to the MOHSW guidelines. According to the recent malaria treatment guideline, the first line drug to treat uncomplicated malaria for women in their second trimester onwards is the combination of Arthemether and Lumefrantine (ALU), and first line drug for treatment of severe malaria is Quinine (QN). All women who had malaria (either the severe form or uncomplicated malaria) were assumed to have been treated by the first line drugs accordingly. For simplicity, we will refer to this strategy as mIPTp-SP3. The second strategy will be not to provide IPTp-SP3 through MHC. Here we assumed that woman residing in remote areas with no health facilities would not receive IPTp-SP3 without the availability of MHC. Similar to the first strategy, when women in this second strategy get malaria or severe anaemia, they will be treated at the public health facilities as in the first strategy. For simplicity, we will refer to this second strategy as WTC*n*.

MHC can be defined as a ‘doctor's office and clinic on wheels'. It is a specially outfitted truck, which provides examination rooms, laboratory services, and specialised medical tests to those in remote areas who have access to little or no medical facilities, and to patients who do not have the resources to travel to obtain care(Abdel-Aleem et al. 2016). While we

acknowledge that several maternal interventions are currently delivered through the MHC, notably this study focused only on those costs and effects of delivery of IPTp-SP3 to pregnant women, aiming at preventing them from getting malaria and its complications compared to avoiding prevention but providing treatment when they get the disease.

The perspective of the Evaluation and time horizon

Because in Tanzania all of the maternal health services are free of charge(MoHSW 2008,2008), the health provider perspective was used. In summary, IPTp is usually provided to pregnant from the beginning of the second trimester, and, up to 36 weeks of pregnancy. The evaluation considered all events that occurred from the first week of the second trimester of pregnancy to four weeks after delivery. Hence the time horizon of this study was 34 weeks. Due to the history of malaria, the cycle length was set to one week which was enough to capture all the important events that happen to the pregnant women about malaria, and all of the parameters used were converted to weekly probabilities from their respective initial measurement.

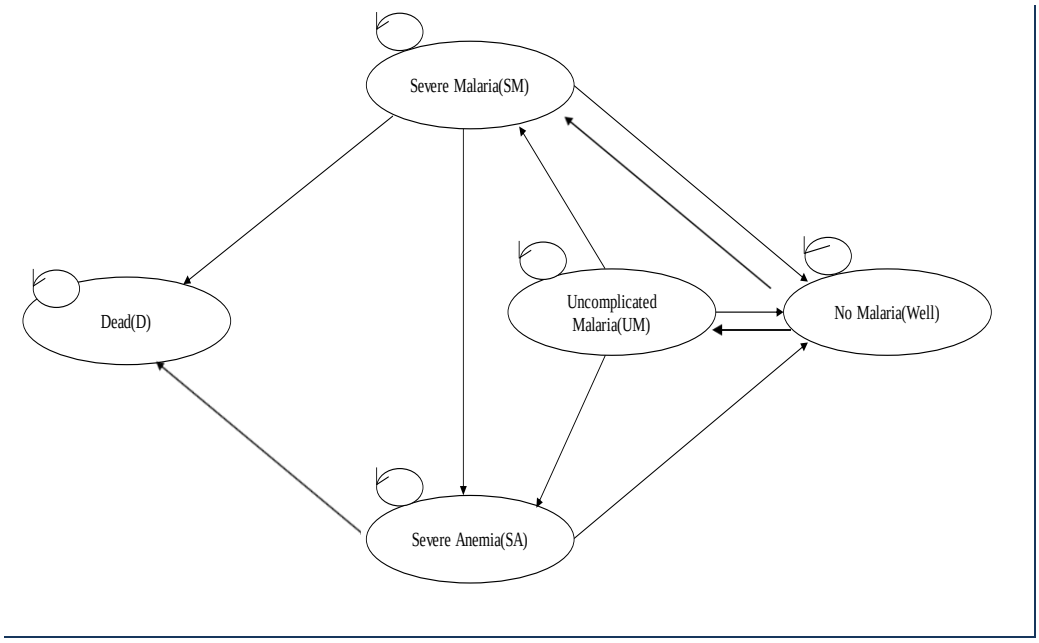
The Structure of the model and simplification

Using a Markov decision analytic model, we followed two hypothetical cohorts, one that used the mIPTp-SP3 strategy and the other which adopted the WTC*n* strategy, through possible health states over a period of 34 weeks. Based on the literature, we specified for each cohort the probabilities of passing through five mutually exclusive health states: uncomplicated malaria, severe malaria, severe anaemia, and normal health without malaria ("Well" state), and death, which was an absorbing state. All pregnant women at any gestation age are at increased risks of malaria, however, due to safety issues malaria chemoprophylaxis is only provided at the beginning of the second trimester (WHO 2012). Therefore, women will enter the model when they reach the13th-week pregnancy in the "Well" state. In the model, they will be tracked until 28 days after delivery.

During each week women face the probability of moving between health states depending on the risks of getting malaria and effectiveness of antimalarial and anti-anaemia drugs. The model was simplified by assuming that uncomplicated malaria is not fatal; hence it did not lead to death, instead malaria-related death may occur when a woman had severe malaria or malaria-related severe anaemia. During each week, each cohort faced a certain probability of uncomplicated malaria depicted in Figure 9 below. Each week the changes in costs and health outcomes within each cohort depended on the proportion that moved between different health states.

Acknowledging that the intervention may affect the overall maternal mortality, this model did not include other maternal causes of death, because we assumed that IPTp-SP does not have any direct effect on other maternal causes of death. For simplicity, and because the effectiveness of treatment of both forms of malaria and severe anaemia was not the primary focus of this study, it was assumed that all women who were clinically diagnosed to have uncomplicated malaria were treated with the first line recommended the drug for pregnant women herein ALU. We also assumed that all pregnant women who were clinically diagnosed to have severe malaria were treated with the first line drug for the treatment of malaria in pregnancy, herein QN.

Figure 9: A dynamic model structure



Source: Author's figure

Transition probabilities

Women enter the model in a "Well" state where they receive the intervention or do not receive the intervention, and they can acquire uncomplicated malaria based on the estimated probability shown in Table 9a-c below. Without the intervention (WTC*n*), about 23.27% of the pregnant women regardless of their parity or HIV status may acquire uncomplicated malaria monthly (Mbaye et al. 2006, Parise et al. 1998, Shulman et al. 1999). This varies according to parity, in which estimates indicate that women on their first or second pregnancy have a monthly probability of 33.3 %(Parise et al. 1998, Shulman et al. 1999) while that of multigravida women is estimated at 11%(Mbaye et al. 2006). Additionally, probability of acquiring malaria varies also according to HIV status, in which HIV positive pregnant women

are estimated to have a monthly probability of 45.1%(Parise et al. 1998), and that of HIV negative was 22.9%(Mbaye et al. 2006, Parise et al. 1998, Shulman et al. 1999). According to the natural history of malaria, almost 1% of untreated cases of uncomplicated malaria regardless of their parity or HIV status may progress direct to severe malaria, and 1% of women who had severe malaria may progress to severe anaemia(Goodman et al. 2000).

The probability of progressing from uncomplicated malaria to severe anaemia also varied according to parity and HIV status. Studies estimate that about 13.6% of women who did not receive SP for prevention and have malaria will develop severe anaemia regardless of their parity or HIV status [6-8]. Regarding parity and HIV status, 18.9% of primigravidae and secundigravidae (Parise et al. 1998, Shulman et al. 1999) and 9% of multigravida(Mbaye et al. 2006) who had a history of malaria stand a chance of getting severe anaemia. Notably chances of getting malaria-related severe anaemia also vary according to HIV status, in which HIV positive pregnant women have a monthly probability of 21.3% (Parise et al. 1998) while that of HIV negative was 13.5 % (Shulman et al. 1999). The model assumes a 3% late treatment failure rate when pregnant women are treated with AL for uncomplicated malaria(D'alessandro 2016, Manyando et al. 2012); hence this 3 % of women were assumed to progress to severe malaria state from uncomplicated malaria.

Pregnant women with uncomplicated malaria or severe malaria or severe anaemia had a chance to recover and bounce back to being well. The transition probability from the aforementioned health states to well were calculated while taking into account the drug effectiveness against, and patient compliance to, malaria treatment. Efficacy rate of AL for treating uncomplicated malaria was 94%, treatment failure rate was 0.3 %(D'alessandro 2016) and of QN for treatment of severe malaria was 95%(Adam et al. 2004). The baseline compliance rates for the two drugs were 51% and 82% for AL and QN, respectively(Bruxvoort et al. 2014). Additionally, the estimated cure rate of women who will not comply with AL was 10-30%(Coleman et al. 2004, Goodman et al. 2000) and that of QN was assumed to be 5-15%. Probabilities of treatment success from severe anaemia were calculated from the estimated efficacy and compliance of the combination therapy of Ferrous Sulphate and Folic acid which is the recommended treatment regime for severe anaemia(WHO 2015). Herein the treatment response rate of Fefol was estimated to be 66% and the compliance ranging between 65-85%(Christian et al. 2009). Then the effectiveness of treatment was calculated using the recommended formula below in which E_{ff} is the effectiveness rate of the drug; E_o is the efficacy; C is the compliance rate, and E_{nc} is the proportion of non-compliers for whom treatment is effective.

$$E_{ff} = E_o \times C + (E_{nc} * 1 - C)$$

It is estimated that 0.26% of pregnant women who had severe malaria and 1% of pregnant women who had severe anaemia due to malaria die annually (Brabin et al. 2001, Pembe et al. 2014). We used those case fatality rates to calculate the transition probabilities from severe malaria and severe anaemia to death. Transition probabilities that were not measured on a weekly basis were converted to rates as recommended(Briggs et al. 2006). The formula below was used to convert those probabilities to rates. –t represents time in weeks or month, and p represents probability.

$$rate(r) = \frac{1-p}{t}$$

Whereby t= time and p=probability

Assuming that rates are constant over a specified time, those rates were then converted to weekly probabilities. Then the rate was then converted back to probability by

$$probability(p) = 1 - e^{(-rt)}$$

Data collection and analysis

Mixed sources of data were used in the costing part of the study. In case of the cost of the intervention, we used primary data collection whereby all steps narrated below were followed to capture all relevant costs. In case of cost of treatment of the consequences, we used the secondary data from the WHO-CHOICE Study(WHO 2010), which provided us with the cost of admission per overnight stay in health centres and outpatient costs in the public health facility at the dispensary level and health facility level. Because we wanted to illustrate the cost incurred by the MHC in delivering the intervention and the consequences of the disease in case of sickness, we decided to use a recommended disease-specific approach(Conteh and Walker 2004) as our unit of cost evaluation. That means our unit of costing was one pregnant woman, and we did value the cost in totality for the total costing period, but in the end, we computed the cost incurred to provide the intervention to one pregnant woman. To support this, we developed the clinical pathway which was based on the Focus Antenatal Clinic Guideline(MoHSW 2012) to guide the costing activity. We identified MHC activities through interviewing the nurses responsible for service provision at the clinic. Specifically cost items, which were found relevant for the intervention in question; staffing, equipment, and utility costs, IEC material, office space, mobile vans and furniture.

Table 9a: Input parameters for the deterministic and probabilistic CEA

Monthly probabilities for no IPTp-SP3	**Mean**	**Lower**	**Upper**	**Distribution**	**Source**
Maternal antenatal parasitaemia(all)	0.175	0.14	0.210	Beta	(Mbaye et al. 2006, Parise et al. 1998, Shulman et al. 1999)
Maternal antenatal parasitaemia (low parity)	0.333	0.267	0.400	Beta	(Parise et al. 1998, Shulman et al. 1999)
Maternal antenatal parasitaemia (high parity)	0.110	0.088	0.132	Beta	(Mbaye et al. 2006)
Maternal antenatal parasitaemia(HIV)	0.451	0.361	0.541	Beta	(Parise et al. 1998, Shulman et al. 1999)
Maternal antenatal parasitaemia (non HIV)	0.229	0.183	0.275	Beta	(Mbaye et al. 2006, Parise et al. 1998, Shulman et al. 1999)
Severe anaemia secondary to malaria(all)	0.136	0.109	0.164	Beta	(Mbaye et al. 2006, Parise et al. 1998, Shulman et al. 1999)
Severe anaemia secondary to malaria (low parity)	0.189	0.151	0.227	Beta	(Parise et al. 1998, Shulman et al. 1999)
Severe anaemia secondary to malaria (high parity)	0.090	0.072	0.108	Beta	(Mbaye et al. 2006)
Severe anaemia secondary to malaria(HIV)	0.213	0.171	0.256	Beta	Assumption
Severe anaemia secondary to malaria (non HIV)	0.135	0.108	0.162	Beta	(Mbaye et al. 2006, Parise et al. 1998, Shulman et al. 1999)
Mortality estimates					
Annual malaria attributable case fatality rate	0.003	0.002	0.003	Beta	(Pembe et al. 2014)
Annual malaria related anaemia case fatality rate	0.010	0.008	0.012	Beta	(Brabin et al. 2001)
RR for Maternal peripheral parasitemia					
All women	0.260	0.150	0.450	Lognormal	(Mbaye et al. 2006, Shulman et al. 1999)
Low parity women	0.190	0.110	0.310	Lognormal	(Mbaye et al. 2006, Parise et al. 1998)
High parity women	0.410	0.260	0.640	Lognormal	(Mbaye et al. 2006)
HIV Seropositive women	0.190	0.120	0.310	Lognormal	Assumption

Note: [1]Low Parity: First and second pregnancy; [2]High parity: More than two pregnancies

Table 9b: Input parameters for the deterministic and probabilistic CEA

The parameter for Efficacy and Compliance Rates	Mean	Lower	Upper	Distribution	Source
Treatment Failure Rate with ALU (measured at day 3)	0.030	3.200	4.800	Beta	(D'alessandro 2016)
Treatment Success Rate with ALU(measured at 3 days)	0.942	0.024	0.036	Beta	(D'alessandro 2016)
Compliance to ALU	0.510	0.380	0.650	Beta	(Bruxvoort et al. 2014)
Non-Compliers with ALU who got cured	0.200	0.100	0.300	Beta	(Coleman et al. 2004)
Treatment Success Rate with Quinine(measure at day 7)	0.950	0.760	1.140	Beta	(Adam et al. 2004)
Compliance of Quinine	0.827	0.6616	0.9924	Beta	(Bruxvoort et al. 2014)
Non-Compliers with Quinine who got cured	0.100	0.050	0.150	Beta	Assumption
Probability of Severe Anaemia secondary to Severe Malaria	0.010	0.642	0.963	Beta	(Adam et al. 2004)
Treatment Success Rate with FeFol (at 28 day)	0.636	0.508	0.763	Beta	(Christian et al. 2009)
Compliance to FeFol	0.765	0.680	0.850	Beta	(Christian et al. 2009)
Average Age (yrs.)	26	25	27	Point estimate	Patient level data
Life Expectancy for women aged 25-29(yrs.)	45	45	55	Point estimate	(WHO 2015)
Disability weight for Uncomplicated Malaria in weeks	0.001	0.001	0.002	Lognormal	(Salomon et al. 2013)
Disability weight for Severe Malaria in weeks	0.004	0.003	0.006	Lognormal	(Salomon et al. 2013)
Disability Weight for Severe Malaria related anaemia	0.003	0.002	0.005	Lognormal	(Salomon et al. 2013)
Length of disability with Severe Malaria in weeks	0.125	0.107	0.179	Lognormal	Assumption
Length of disability with moderate to Severe Anaemia in weeks	0.750	0.600	0.900	Lognormal	(Price et al. 2001)

Table 9c: Input parameters for the deterministic and probabilistic CEA

Parameter	Mean	Lower	Upper	Distribution	Source
Number of tablets of SP per dose	3	2.40	3.60	Gamma	Patient level data
Hospital stay per a case of severe malaria or severe anaemia	4	3.20	4.80	Gamma	Patient level data
Cost of One tablet of SP	0.06	0.05	0.08	Gamma	(MSD 2016)
Mobile health clinic costs in US$ per pregnancy	4.41	3.53	5.30	Gamma	Patient level data
Personnel Costs in US$ per pregnancy	5.57	4.50	6.70	Gamma	Patient level data
Equipment Costs in US$ per pregnancy	0.31	0.25	0.40	Gamma	Patient level data
Information, Education and Communication Materials Costs	0.18	0.15	0.25	Gamma	Patient level data
Utilities Costs in US$ per pregnancy	1.26	1.01	1.51	Gamma	Patient level data
Office space Costs in US$ per pregnancy	0.44	0.35	0.53	Gamma	Patient level data
Furniture Costs in US$ per pregnancy	0.09	0.07	0.11	Gamma	Patient level data
IPTp-SP3 administration costs in US$ per pregnancy	12.87	10.31	15.44	Gamma	Patient level data
Cost of inpatient stay per night in US$	7.81	6.25	9.37	Gamma	(WHO 2010)
Outpatient Cost per day in US$	4.52	3.62	5.42	Gamma	(WHO 2010)
Cost of Treatment of uncomplicated malaria per case in US$	7.20	5.76	8.64	Gamma	Patient level data
Treatment of severe malaria per case in US$	42.99	34.39	51.59	Gamma	Patient level data
Treatment of severe anaemia per case in US$	42.99	34.39	51.59	Gamma	Patient level data
Maximum WTP per averted DALYs in US$	150	120	180	Gamma	(Shillcutt et al. 2009)

Cost measurement and valuation

We applied the principles stated in the 'Cost Analysis in Primary Health Care' and borrowed some from 'Costing Guidelines for HIV Services'(UNAIDS 2000,2011) to guide the provider perspective costing because of no single guideline guides costing in the area of maternal health. We used activity-based costing to identify and measure all providers' resource use. Detailed interviews were conducted with key personnel at the MHC and the district hospital offices as well as the non-governmental organisations (Plan International) that provide financial support to run the clinic. To understand the standard service pathways for selected maternal intervention, we spent time observing the maternal service care provision, documenting time consumed from the first stage where women receive health education to the last stage where they are being provided with the intervention. Additionally, we requested and inspected order books, inventory records, issue vouchers and delivery notes to record all the equipment and supplies consumed.

Consultations with the hospital secretary, district nurse officer, district reproductive and child health coordinator were made to determine resources used at the administrative level and overhead costs. When necessary, physical counting of equipment and supplies deemed was conducted. To estimate utilisation data, we visited the Health Management and Information Systems (HMIS) books and MHC client log book. In those books we collected data on the number of pregnant women seen during the year 2015 and drugs dispensed; in this case, we looked in the tally book which tallied the provision of doses of SP, Fefol and Albendazole for the costing period.

As recommended by Gold et al(Gold et al. 1996), and widely used and advocated in recent costing guidelines(Briggs et al. 2006, Drummond et al. 2015, Gray et al. 2010), we adopted the economic (opportunity) cost valuation approach in which resources were valued at the cost of their best alternative. Cost data for medical supplies and equipment were based on the Tanzania Medical Stores Department (MSD) price catalogue(MSD 2016). To ascertain other non-medical costs like office utilities, IEC materials and others, the Tanzania Government Procurement Services Agency tender price was used. Rental charges for buildings were calculated according to National Housing Corporation (NHC) rates. The actual costs of purchasing the mobile van were used, these costs were available at the Plan International financial accounts. We estimated all costs in Tanzanian Shillings (TZS) and converted them to US$ using a mean exchange rate of 2200 TZS/US$ as published by the Bank of Tanzania on the 10th July 2017(BoT 2017). Drug costs were raised by 15% to account for taxes and an extra 10% to account for possible wastage(Gold et al. 1996).

Cost analysis

Cost analysis was performed using Microsoft Excel version 12.0. All relevant MHC departments were grouped into direct, indirect, supporting and administration service centres depending on whether they had direct patient contact or facilitated, supported or provided services necessary for a facility to function. Resource use was then classified as financial and economic costs and later grouped under capital or recurrent costs. Capital costs consisted of items like buildings and equipment the useful life of which exceeds a year, while recurrent costs include salaries, utilities and supplies. Capital costs were annuitized using a rate of 9.8%, which was the average interest rate for the year 2015/16 reported by the Bank of Tanzania(BoT 2017) and their useful life years were based on WHO assumptions(WHO 2016).

Each service department was allocated a portion of the overhead costs proportional to its percentage contribution to the total allocation base by using the direct-allocation method(Drummond et al. 2015). For instances, cleaning cost was allocated based on the floor space, but difficulties were encountered in allocating some shared expenditures that were paid centrally, and their usage was not specified by department like electricity, phone calls expenses and stationaries. Hence that necessitated distributing equally some of the overhead costs and allocate others based on the estimate weighted allocation factor that was derived from the interviews with health providers. Therefore, the unit costs for the provision of IPTp-SP3 to one pregnant woman was calculated by dividing the total costs of providing IPTp-SP3 for the service centres by the respective number of pregnant women who received the intervention (519 women) during the year. Uncertainties were accounted for by performing sensitivity analysis assuming ±20% change around input prices(Mogyorosy and Smith 2005). In line with variability around drug prices, a scenario analysis was performed to test changes in providers' unit cost when other valuation sources are applied.

Data collection, sources and estimations of effectiveness data

Data on the effectiveness of IPTp-SP3 compared to placebo or case management was taken from RCTs as presented in chapter five. Because none of the eligible RCTs reported on uncomplicated malaria, instead, they all reported on maternal peripheral parasitaemia, we used that as uncomplicated. Similarly, for severe malaria, none of the RCT reported on that; hence we used data from RCT done on the treatment of malaria on pregnant women, which reported failure rates to ALU. The reported failure rate was used to represent the rate of transiting from uncomplicated malaria to severe malaria, and that was used regardless of the parity or HIV status because data on that RCT was not aggregated in subgroups.

We used the Disability Adjusted Life Years (DALYs) as a measure of effect, which is the combination of years of life lost due to disability and years of life lived with the

disability(Fox-Rushby and Hanson 2009). We used the disability weight of 0.05, 0.21 and 0.164 for infectious disease acute episode moderate, infectious disease acute episode severe and severe anaemia, respectively, as presented in the Global Burden of Diseases Study(Salomon et al. 2013). The standard method of DALYs calculation was used, and the DALYs averted calculation followed a similar approach by taking the DALYs lost in the no intervention group minus the DALYs lost in the intervention group(Fox-Rushby and Hanson 2009). No age weighting was in used in the estimates of final DALYs; however, that was used in the sensitivity analysis.

Data analysis and sensitivity analyses

We calculated the incremental cost-effectiveness ratio (ICER) by;

$$ICER = \frac{\text{Incremenatl Cost}}{\text{Averted DALYs}}$$

To ascertain the net benefit of the intervention as compared to no intervention, we used the net benefit framework and calculated the incremental net health benefit (INHB) which allowed presentation of the results in the cost-effectiveness acceptability curve (CEAC). The INHB was calculated by the formula;

$$\text{INHB} = \Delta DALYs - \frac{\Delta Cost}{Threshold}$$

Dealing with variability and parameters uncertainties

Since all cost and effect estimates are subject to variations and uncertainties (Briggs et al. 2006, Drummond et al. 2015, Gray et al. 2010), the Monte Carlo microsimulation was conducted in Microsoft Excel version 15.37 with 10,000 iterations. Later uncertainty in the probabilistic sensitivity analysis results was presented using the CEAC. This was done by assigning the probability distribution to each input parameter according to the characteristic of the parameter. This required availability of maximum and minimum value of the parameters which were taken from the individual data or literature and when not available in the two sources, the recommended deviation of ±20% was applied(Briggs et al. 2006). Assigning appropriate distribution followed the recommended approach (Briggs et al. 2006, Gray et al. 2010). For all probabilities that represent the effectiveness of the therapy, the beta distribution was used because the outcome of the therapy was assumed to be constrained between zero and one.

Additionally, the outcomes of therapy were mutually exclusive events with having an event or no event when IPT was given or not given and having being cured or not when treated for uncomplicated malaria, severe malaria and anaemia. Gamma distribution was used to restrain

costs on the interval of zero to infinity. In both cases, the method of the moment was adopted appropriately to estimate the associated hyper-parameters which are needed to calculate the aforementioned probabilistic mean values (alpha and beta). In case of point estimates, the uniform distribution was applied, and for relative risk, the lognormal distribution was used because it reflects the ratio nature of the relative risks(Briggs et al. 2006, Gray et al. 2010).

Dealing with Heterogeneity and structural uncertainty

Because of differences in the effect of the interventions regarding differences in clients baseline characteristics like gravidity and HIV status(McGready et al. 2011), the subgroup analysis was conducted and ICER for different subgroups were calculated. HIV status was considered because co-infection may not only undermine the effectiveness of the intervention but also because women who have HIV have low immune systems which may predispose them to other infection like malaria(McGready et al. 2011). Input parameters were varied input including decreased efficacy of SP, and the mean follows up at which the prevalence of malaria was estimated in trials, the cost of MHC, and the cost of health provider time per minute.

Discounting and half cycle correction

The half cycle correction was conducted using the algebraic approach (Naimark et al. 2008). That was aimed at relaxing the assumption made by the computer-based Markov models that transitions between states usually occur at the beginning or end of a cycle, which is not the case in real situations whereby transitions may on average occur in the middle of each cycle(Naimark et al. 2008). Although we used the algebraic approach, our estimate would be similar even if the alternative approach was adopted because the outcomes in this model were not discounted due to the short horizon of 34 weeks(Gray et al. 2010).

6.3 Results of the economic evaluation

6.3.1 Cost of providing IPTp-SP3 via MHC

Table 10 below presents results from the itemized costs. The total weighted average cost of rolling out at least three doses of SP to pregnant women residing in remote areas through MHC is US$ 12.87 per woman and pregnancy. Recurrent costs accounted for 60% of the total costs of the intervention, while 40% was contributed by capital costs. In the year 2015, the MHC in Kisarawe spent a total of US$ 6 636 to provide at least three doses of SP to a total of 519 pregnant women excluding drug costs.

Table 10 Total and unit costs (in US$) of delivering IPT-SP3 at the MHC

		Cost Centers				
		Consultation	Pharmacy and Laboratory	Health Education	Total Costs*	Unit Costs**
Recurrent Costs	Drugs	0	311	0	311	0.60
	Personell	2098	132	743	2974	5.73
	Office space	80	119	32	230	0.44
	Utilities	324	163	169	656	1.26
	IEC Material	21	12	55	88	0.17
	Total Recurrent	2523	737	999	4259	8.21
Capital Costs	Equipment	21	93	47	160	0.31
	Mobile vans	1346	305	520	2171	4.18
	Furniture	21	15	10	47	0.09
	Total Capital	1388	413	577	2378	4.58
Total Costs		**3911**	**1150**	**1576**	**6636**	**12.79**

NB: *Total number of women recorded to receive at least three doses at the MHC for the year 2016 was 519

** $Unit\ cost = \frac{\text{Total cost attributable to IPT−SP provision for the service centres}}{Respective\ number\ of\ pregnant\ women\ recorded\ to\ receive\ IPT\ at\ the\ MHC}$

6.3.2 Cost consequences analysis results

Table 11 presents the cost consequences analysis depicting the cost of scaling up SP for malaria prevention in pregnancy through MHC. The cost of scaling up the intervention is estimated to be around US$14,440 per 1,000 women per pregnancy with US$ 8,161 costs of consequences per one woman per pregnancy, making up a total of US$20,526. On the other hand, not scaling up the intervention and waiting to treat the consequences was estimated to incur US$ 12,365 as cost for treating uncomplicated malaria, severe malaria and severe anaemia. Compared to waiting to treat the consequences which was contributed to 460 DALYs lost, scaling up IPTp-SP3 to women living in remote was associated with a loss of about 265 DALYs.

Table 11 Base case cost consequences analysis

	mIPT-SP3	**WTCn**
	Mean [95% CI]	Mean [95% CI]
Estimated costs per 1000 women		
Cost of providing IPTp-SP3	14,440 [9,273 - 21,204]	
Cost of treating the consequences	6,086[4,315 - 8,502]	12,365[8,888- 17,101]
Total costs	20,526[15,414 - 27,293]	12,365[8,888- 17,101]
Incremental Costs	8,161[2,2256 -15,334]	
Outcome contributing to DALYs		
Total DALYs	265[188 - 369]	460[319 - 653]
DALYs from uncomplicated malaria	0.53[0.20 - 1.15]	1.27[0.46 – 2.78]
DALYs from severe malaria	55[37- 79]	95[63 - 137]
DALYs from severe anaemia	210[141 - 300]	364[245 - 530]

Source: Author's own

6.3.3 Cost-effectiveness analysis

Table 12 presents the base case analysis for which the model predicts scaling up provision of SP for prevention of malaria and severe anaemia in 2016 to women regardless of their parity or HIV status is more cost effective than status quo (not providing the intervention). The deterministic results of the model predict scaling up IPTp-SP3 to 1000 women is cost effective with an ICER of US$ 40 per DALYs averted compared to waiting to treat the consequences. Per 1,000 women the incremental costs amounted to US$ 7,902, with scaling up IPTp-SP3 having much cost than not using MHC to scale up the intervention. Probabilistic results on the other hand indicated an average ICER of US$54[95% CI: 7 – 167], and incremental costs amounting to US$ 8,161[95% CI: 2,226 – 15,334].

Table 12 Base case cost-effectiveness analysis

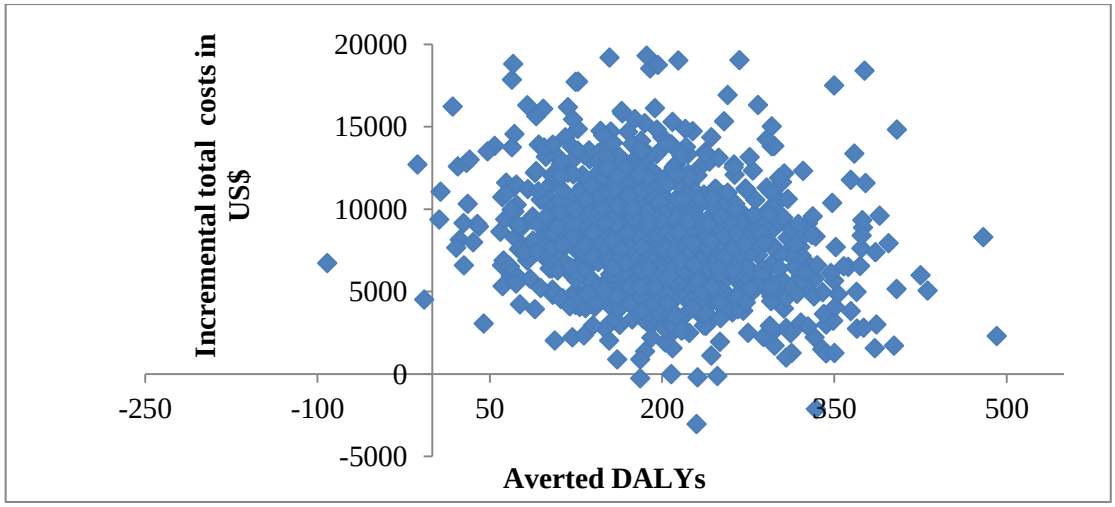
	mIPTp-SP3	**WTC*n***
	Mean [95% CI]	Mean [95% CI]
Deterministic Results		
DALYs lost	263	461
DALYs averted	198	0
Total Costs (US$ 2016)	20,320	12,283
Incremental Costs	7,902	0
ICER per averted DALYs	40	-
Probabilistic Results		
DALYs lost	265[188 - 369]	460[320 - 653]
DALYs averted	195[64 - 362]	0
Total Costs (US$ 2016)	20,526[15,414 - 27,259]	12,365[8,888 – 17,101]
Incremental Costs (US$ 2016)	8,161[2,226 – 15,334]	0
Average ICER (US$/DALYs)	54[7-167]	

Source: Author's own

Incremental cost-effectiveness scatter plot

Figure 10 depicts an incremental cost-effectiveness scatter plot for the base-case analysis when the intervention is provided to all women regardless of their parity or HIV status. When both costs of the intervention and the consequences were included, the model predicts that scaling up IPTp-SP3 using MHC is cost effective in almost 97% of the iterations at a WTP threshold of US$150.

Figure 10: Cost-effectiveness scatter plot (including the cost of the consequences)

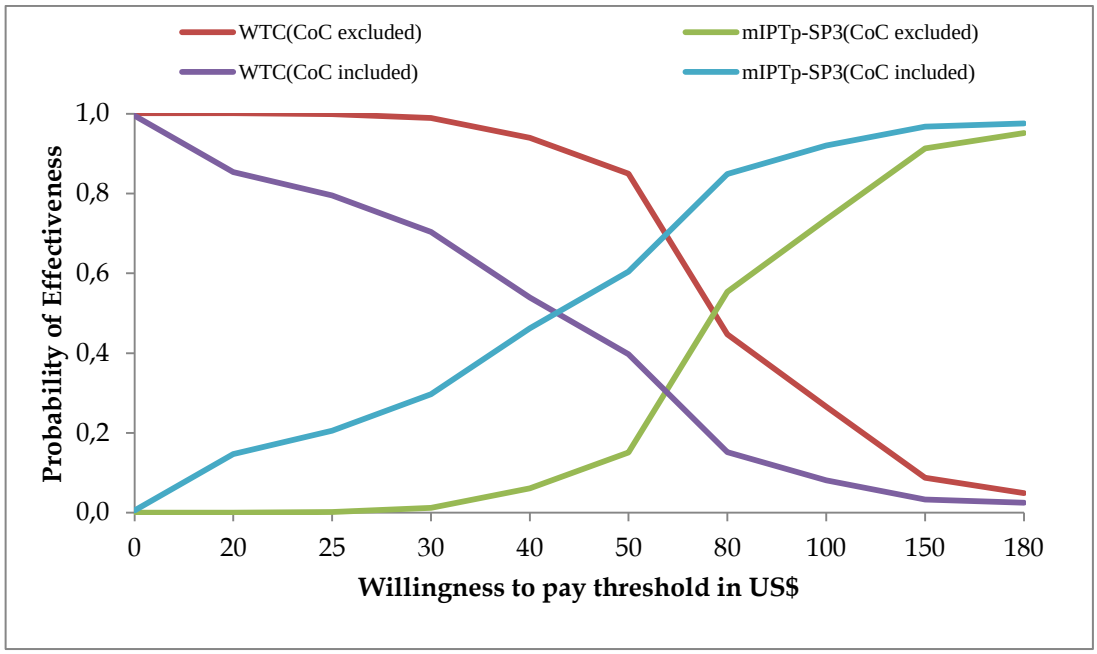


Source: Author's own figure

Cost-effectiveness acceptability curve

We used the net benefit approach to explore the likelihood that the intervention will be cost effective and acceptable to payers at different hypothetical WTP thresholds. As depicted in Figure 11, and including the cost of the consequences, the scaling up of IPTp-SP3 to women had a 97% probability of being cost effective at the WTP threshold of US$ 150 per averted DALY. On the other hand, ignoring the cost of the consequences, the intervention had a probability of effectiveness of 91% at the recommended WTP of US$ 150 per DALY averted.

Figure 11: Cost-effectiveness acceptability curves



Source: Author's own figure

6.3.4 One-way sensitivity and subgroup analysis

Results were sensitive to changes in the size of the population needing services, relative risk of SP on antenatal parasitaemia, service integration and using CHW instead of nurses to provide IPTp-SP3. Table 13 below shows that when the number of pregnant women in need of the intervention increases from 519 to 1,000 the ICER becomes US$7 instead of US$40. Increase in the number of women needing the intervention to as low as 100 will increase the ICER from US$40 to US$327.When the relative risk of IPTp-SP3 on antenatal malaria decreases by 50%, the number of DALYs averted will increase and ICER will be reduced. If RR increases by 100%, averted DALYs will be lowered which will also reduce the ICER making the strategy ineffective compared to wait to treat.

Shifting to using CHW to provide the intervention will reduce the costs of services and reduce ICER to -US$32. When provision of IPTp-SP3 account for only 10% of the activities at the MHC, the ICER will decrease to US$12 as compared to the base case where provision of a full course IPTp-SP3 accounted for 30% of the total cost excluding drugs(ICER=US$40).

Table 13 One way sensitivity analysis results

Variable changed		Incremental Costs	Averted DALYs	ICERs
Relative risks	50% less	7,208	311	23
	50% higher	8,460	115	74
	100% higher	9,526	-32	-299
Integration	10%	2,436	198	12
	50%	13,368	198	68
	100%	27,035	198	137
Number of women	1000	1,372	198	7
	500	8,418	198	43
	100	64,785	198	327
Task shifting from nurses to CMW		-6,274	198	-32
Base case analysis		7,902	198	40

Source: Author's own

Table 14 presents the subgroup analysis results. The strategy was less costly and highly effective when the intervention was provided to HIV positive women and low parity women as compared to other cohorts.

Table 14: Stratified Incremental Costs, averted DALYs and ICERs results

Cohort of 1000 women	Incremental Costs in US$	DALYs averted	ICER
All	7,902	198	40
Low parity	826	167	5
High parity	9,938	75	133
HIV positive[a]	-668	135	-5
HIV negative	5,809	121	48

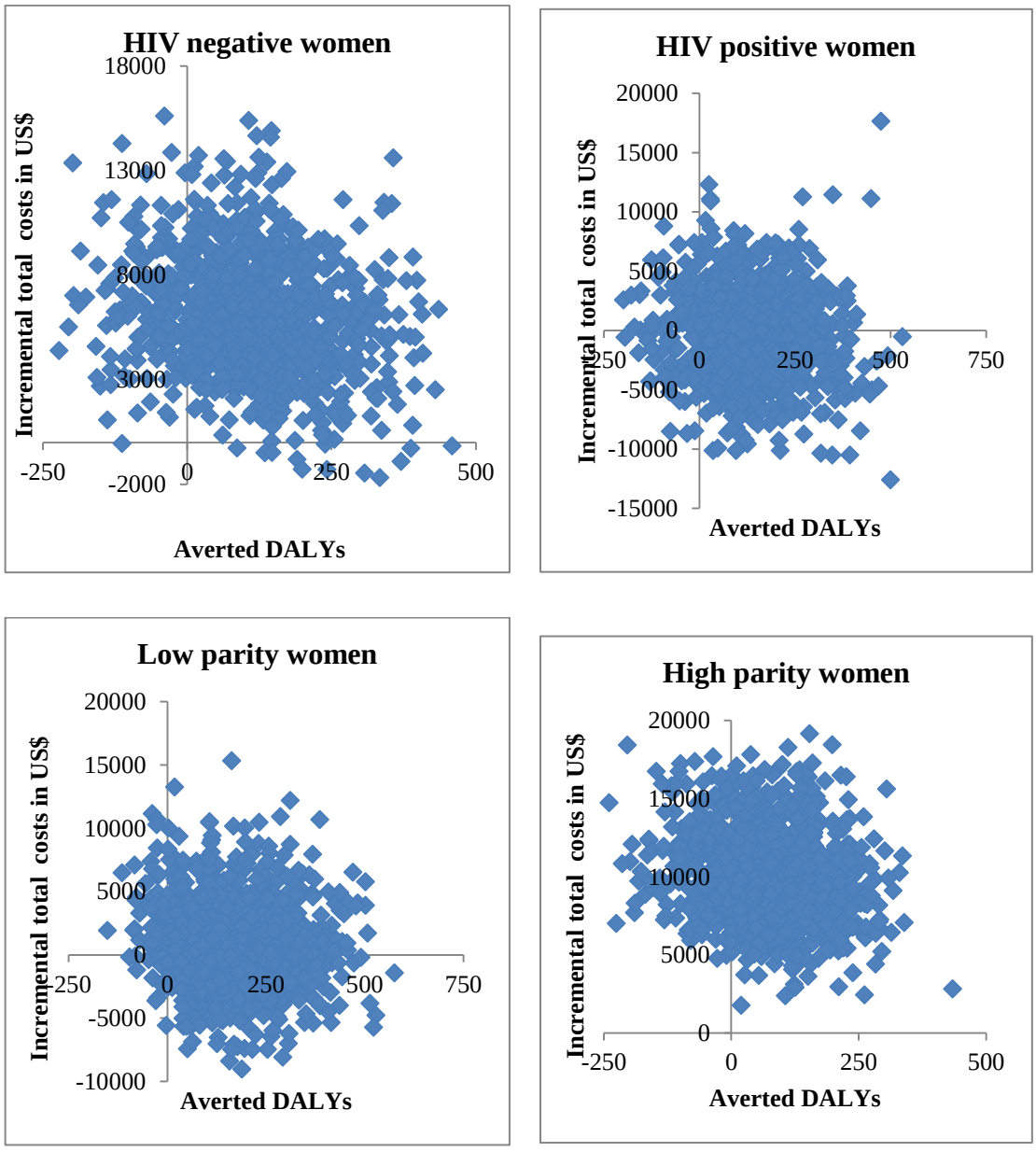
Source: Author's own table; Note [d]Include only low parity women with HIV

Cost effectiveness scatter plots

Figure 12 depicts four scatter plots stratified according to parity and HIV status when considering both intervention and consequence costs. At the WTP of US$150 per averted DALY, the model predicts that the strategy is cost-effective in almost 92%, 54%, 89% and

74% of the iterations for low parity, high parity, HIV positive and HIV negative women, respectively. Excluding consequence costs, the probability of effectiveness declined to 78%, 46%, 69% and 63% for the aforementioned groups, respectively (figure not shown here).

Figure 12: Cost-effectiveness scatter plot (including cost of the consequences)



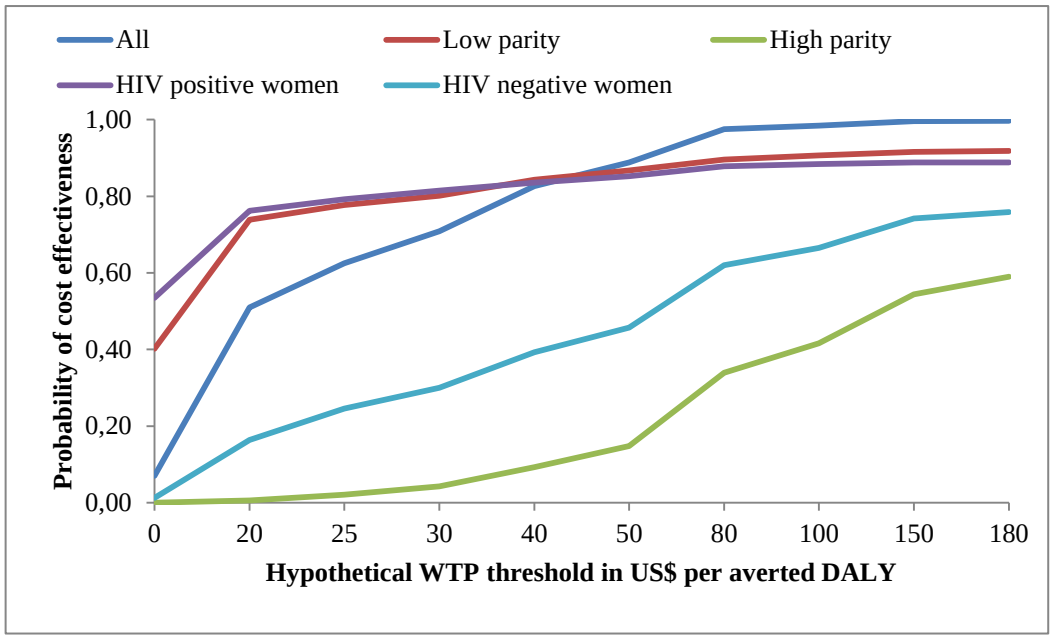
Source: Author's own figure

Cost-effectiveness acceptability curves

Figures13 and 14 depict the cost-effectiveness acceptability curves for the four subgroups. At a WTP threshold of US$150 per DALYs averted, mIPTp-SP3 had approximately 92% probability of being cost effective if low parity women are targeted, unlike 54% when high

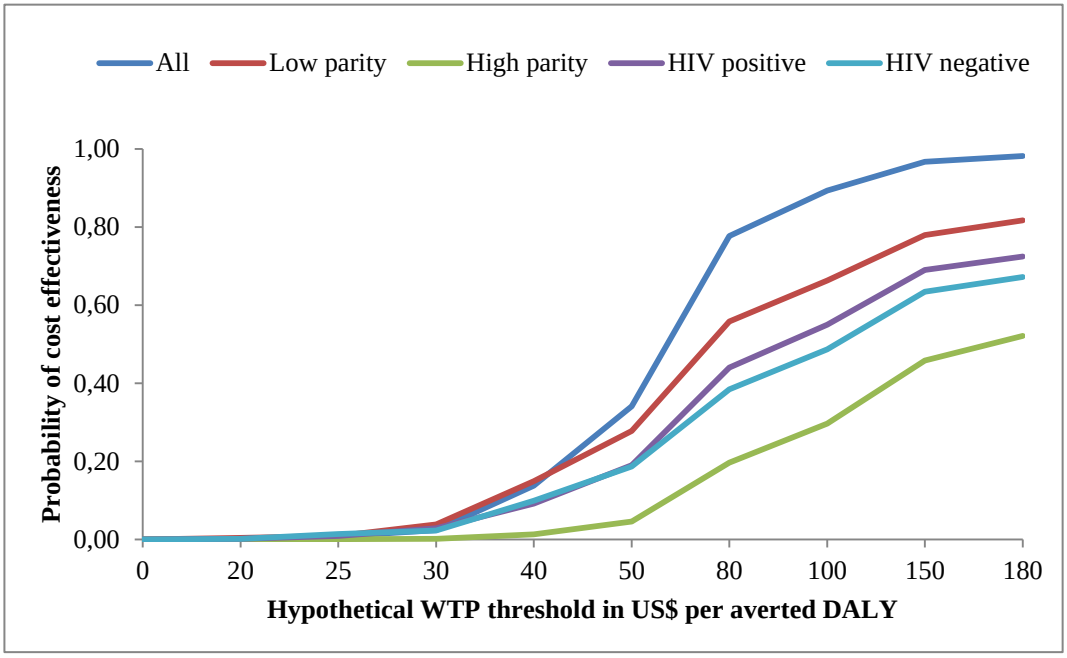
parity are targeted. Targeting HIV positive cohort will have an 89% probability of being effective while this will drop to 74% probability when HIV negative cohort is in focus. Probabilities of effectiveness will decline for all cohorts when the consequence costs are ignored (78% for low parity, 46% for high parity, 68% for HIV positive and 63% for HIV negative women).

Figure 13: Cost-effectiveness acceptability curves (cost of consequences included)



Source: Author's own figure

Figure 14: Cost effectiveness acceptability curves (cost of consequences excluded)



Source: Author's own figure

6.4 Discussion of the economic evaluation findings

With the advent of alternative service delivery innovations, scaling up IPTp-SP3 to remote at risk populations have the potential to further reduce the burden of malaria in pregnancy. Model-based analyses can assist decision-makers faced with choosing or adopting strategies used in delivering essential interventions that have the potential to be more beneficial than current strategies. Consistent with another analysis (Fernandes et al. 2016, Mbonye et al. 2008), we found that increasing coverage of IPTp-SP3 to pregnant women can be more cost-effective than waiting to treat the consequences of malaria, for all women regardless of their parity and HIV status.

To our knowledge, this is the first analysis to evaluate the cost-effectiveness of using MHC to provide maternal health interventions in Tanzania. We expand upon previous modelling studies, which look at cost-effectiveness of providing IPTp-SP3 in preventing malaria adverse effect via routine antenatal clinics(Fernandes et al. 2016) and community based platforms(Mbonye et al. 2008). Due to differences in the mode of delivery, our findings cannot be compared directly with findings from those studies which provided IPTp-SP3 via routine static facility portals; rather they attempt to report on a service delivery approach that aims at increasing coverage of IPTp-SP3 to women residing in remote areas that are not reached by static health services. There is growing evidence which suggests that the coverage of intermittent preventive treatment remains far below international targets(van Eijk et al. 2013), with many obstacles that hinders access to IPTp-SP including women lacking money

for transport to come to the clinic and long travel distances to the health facilities(Hill et al. 2013, Mbonye et al. 2007, Ndyomugyenyi et al. 1998).

In general, we expected our costs of delivering the full IPTp-SP3 to a woman and those of the consequences to differ from those estimated in previous studies (Fernandes et al. 2016, Mbonye et al. 2008). While our model predicted the average cost of provision of a full course of SP to be of US$12 per woman, Mbonye and Fernandez estimated the cost of delivery of a full course of IPTp-SP via community platforms to be US$2.5 and US$1.6 per woman via normal antenatal clinic, respectively. These differences are mainly due to differences in the type of costs included in which our study included a wide range of costs such as administrative costs, cost related to health education and the cost of running the mobile vans together with other overhead costs, unlike in those studies which included almost exclusively the cost of time of a nurse who administered the IPTp-SP3. Differences in the cost of the consequences were a result of the type of consequences included in the analysis in which our study considers only maternal adverse effect and ignores the effect that occurs in the neonate.

In the same note, DALYs lost predicted by our model among those women who received the intervention were also higher compared to those predicted in those previous studies despite the fact that those studies included DALYs attributed to low birth weight(LBW), which contributed to a large extent on the total number of DALYs. Nevertheless, ignoring the DALYs attributable to LBW in those studies, our estimations remained higher than in those studies. For instance, Mbonye(Mbonye et al. 2008) using a life time horizon, estimated DALYs lost due to malaria and anaemia were 0.8 and 0.9 per 1404 pregnant women in community platform arm, respectively, while 74 and 17 per 1000 women respectively were estimated by Fernandez(Fernandes et al. 2016) in IPTp-SP3 arm. These differences may be explained by the differences in the type of the model used in those studies. While those studies adopted a decision tree model, which ignores the recurring nature of the disease that the intervention was aiming to prevent, we adopted the Markov decision modelling which accounted for the recurring nature of the disease (Briggs et al. 2006, Gray et al. 2010).

Despite the aforementioned differences in estimates, our findings led us to similar suggestions as those reported by a previous study that compared provision of IPTp-SP3 with intermittent screening and treatment with AL(Fernandes et al. 2016), in which IPTp-SP3 remained to be more beneficial than waiting to treat the consequence regardless of the woman parity or HIV status. Furthermore, these findings correspond with what has been indicated by the recent mathematical models, which suggested that despite the ongoing debate of resistance of malaria parasites to IPTp-SP, the intervention still holds the potential of preventing the adverse effect of malaria(Walker et al. 2017). It is also encouraging that the estimated ICER

per DALY averted in our study had remained within the recommended ranges (Goodman et al. 2000, Goodman et al. 2001, Shillcutt et al. 2009). Of policy implication, these findings together with those from other studies elsewhere(Breman et al. 2006, Fernandes et al. 2016, Goodman et al. 2001) continue to support the WHO campaign on scaling up IPTp-SP3 to all eligible women regardless of their parity and HIV status in order to close the existing gap(WHO 2017).

We are convinced that the estimated incremental costs and ICER in this study were low because IPTp-SP3 provision was provided in an integrated manner. Economic theories indicate potential efficiency advantages that are associated with provision of health care interventions in an integrated approach(McPake et al. 2013). It is suggested that integration of services has the potential to improve both technical efficiency (providing services or producing output at lowest costs) and allocative efficiency (achieving health outcomes at the lowest cost)(Flessa 2009). Integration may have led to improved technical efficiency through economics of scope and scale. The cost of provision of IPTp-SP3 may have been low as a result of combining services through shared use of common infrastructure, overheads and certain invisible operational resources, hence achieving the economics of scope. Additionally, the reduction in IPTp-SP3 cost of provision associated with increased scale of service provision because MHC enabled expansion of service coverage to clients who have not previously accessed them, hence achieving the economics of scale. Just as it was observed in the sensitivity analysis in our model, evidence elsewhere in other health interventions indicates that the costs of integrated HIV counselling and testing, for instance, is likely to be lower than that of a stand-alone counselling and testing provision(Sweeney et al. 2011).

The results indicate increasing benefits when MHC is used to scale up IPTp-SP3 to specific populations. Low parity pregnant women (those on their first or second pregnancy) and those who are HIV positive had lower ICERs as compared to high parity and HIV negative population. This was expected since the evidence on the effectiveness of IPTp-SP3 had long suggested the intervention to be beneficial to low parity women as compared to high parity women(Radeva-Petrova et al. 2014). Evidence is also clear in terms of the increased risk to malaria among women who are HIV positive(Ayisi et al. 2003), which may mean that the intervention will be beneficial when targeting this group. However, it remains unclear in which direction the cost-effectiveness ratio goes when it comes to women who are both high parity and HIV positive. Understanding that the estimated ICERs varied according to differences in groups characteristics, having wide range of information on women baseline characteristic is crucial in order to provide decision makers with the full understanding of health gains according to subgroups. Models can never replace true-life evaluation; therefore,

when services provided at the MHC are well documented and all useful data are collected; our model can be refined and revised.

No study is immune to limitations and our study was limited by several factors. One limitation of the proposed strategy, which requires continuous operation of the mobile vans, consists in uncertainties of sustainability. Operations of mobile health vans and other outreach services in Tanzania have been challenged by budget constraints which threaten their existence(Evjen-Olsen et al. 2009). If the importance of continuing to support these services is not emphasized and prioritized, the estimated benefits in terms of cost saving due to the consequences and averted DALY will be missed.

Our model is based on the assumption that at least 78% of the women who attended the MHC were provided with at least 3 doses of IPTp-SP as indicated in registry data presented in Chapter four, which is also in line with the estimation of the effectiveness that comes from studies in which complete data were available for at least 70% of the participants. That means that our estimations both in costs and effect may not be generalizable in settings with IPTp-SP3 coverage different from ours. Lastly, we assumed that women when sick, they will seek and be treated at the public health facilities. However, this is not always the case since an extensive literature on treatment seeking for malaria and fever in SSA demonstrates that medicine sellers are a widely used source of drugs for fever and malaria (Biritwum et al. 2000, Goodman 2005, Hamel et al. 2001, Tsuyuoka et al. 2001). Therefore, the estimates on outcomes of treatment, which were based on treatment of malaria with ALU, severe malaria with Quinine and severe anaemia with Fefol may be not the representative of what is actually happening.

7.1 Introduction of sub-study V

To this point, it is already known that IPT-SP3 is more cost-effective for women of low parity as compared to their counterpart. That is suggested to be a result of differences in risks between the two groups, with low parity women having a higher risk of the disease compared to multiparous women. The differences in risk may make some pregnant women experience repeated episodes while others, despite exposure, experience only occasional episodes or escape disease altogether. Heterogeneity in the risk of malaria in pregnancy may also be attributed to the presence of a subgroup within the population that has weak immune system due to other chronic infections like HIV and AIDS (Ayisi et al., 2003; Steketee et al., 2001; Van Eijk et al., 2003).

Since heterogeneity is part of clinical care (Briggs et al., 2006), it is essential to consider it in the economic evaluation of healthcare interventions. Because economic evaluations are aimed at informing decision making like reimbursement and specifically for low-income countries, decisions to expand coverage of the interventions, knowledge on these variations may be useful. Additionally, relying on the mean cost-effectiveness of the intervention compared to its relevant comparator is weak in reflecting the actual effects that are primarily brought by patients' heterogeneity(Sculpher, 2008) and can lead to either overestimation or underestimation of ICER depending on the intervention(Coyle et al. 2003). Therefore, reporting on significant gains associated with heterogeneity in the decision making process has the potential to significantly increase the population health gains by allocating the interventions to the subpopulation whom the effect of interventions yield more significant health and monetary gains(Basu and Meltzer 2007, Coyle et al. 2003, Grutters et al. 2013, Sculpher 2008).

This chapter is not set to undermine decision making using mean cost-effectiveness results; instead, it aims at providing information beyond ICER. A recent review had argued that since the primary concern of economic evaluations is on absolute benefits(Grutters et al. 2013); hence it makes sense to acknowledge the heterogeneity that is around those benefits. In their study, Goldman et al. had recommended that further research on the economics of malaria should provide information on the benefit of the intervention while disaggregating the benefits by population groups (Goodman et al., 2000). Nevertheless, many policy decisions are not universal for all patients –for instance, decisions to fund interventions publicly in many countries consider patients' characteristics like age groups, sex or disease severity, to name few (Briggs et al., 2006; Sculpher, 2008). In this subgroup analysis, we used the net benefit framework to estimate the differences in incremental net health benefits gained when using MHC to scale up IPTp-SP3 compared to waiting to treat the consequences (WTCn).

7.2 Methodology adopted for sub-study V

Study design

This particular study adopted the net health benefits framework proposed by (Briggs et al. 2006, Gray et al. 2010) and demonstrated in several studies(Coyle et al. 2003). Extending from the previous section where data on costs and effect were presented, we conducted a subgroup analysis of the effect of the intervention according to parity and HIV status. These two groups appear ideal because current evidence reports significant differences in risk to malaria and severe anaemia according to parity(Brabin 1991, Brabin 1983, Brabin et al. 2001, Desai et al. 2007) and HIV infection(Ayisi et al. 2003, Flateau et al. 2011). Stratification allows application of the overall relative treatment effect to different groups stratified by parity and HIV status to derive estimations of absolute effect(Stevens and Normand 2004).

For this analysis, several assumptions were made. The total number of clients was set to 100 to calculate the population net benefits; we assumed that the strata or subgroup that will be optimal to receive the treatment is the one that will display the maximum NHB within the given threshold. The WTP threshold was set to include levels that are below and twice as much above the recommended WTP per DALY averted for developing countries(Shillcutt et al. 2009). For each of these groups, we assumed that using MHC to scale up provision IPT-SP3 is more beneficial to one, and not to the other.

The cost-effectiveness of IPT-SP3 that is provided via MHC was expressed by calculating the mean NHB by assigning the hypothetical willingness to pay thresholds (λ). We calculated NHB for each cohort *c* by:

$$INHB_c = \Delta DALY_c - \frac{\Delta Cost_c}{\lambda}$$

Whereby

λ = maximum monetary value of the unit of the effect (DALY).

$INHB_c$=Incremental health benefit for a woman in the particular cohort

$\Delta DALY_c$=incremental effects for a particular cohort

$\Delta Cost_c$=incremental cost for a woman in a particular cohort

The total gain in net health benefit (TNHB) was calculated by

$$TNHB_c = n_c \times INHB_c$$

Whereby

n_c=number of patients in the cohort

The total net benefit was calculated by taking the sum of each of the incremental net benefits in the specified cohort. We used the NHB instead of the ICERs because the former allows the calculation of values of gains and losses at each threshold(Briggs et al. 2006).

Selection of Optimal cohort

We used two frameworks to select the optimal cohorts. First, we used the efficiency-based criteria, in which the cohort producing the positive NHB was selected. Second, we adopted the equity trade-off framework, in which we considered selecting the cohort based on either parity alone or HIV status alone and compared that with no stratification.

Based on efficiency, selection of the optimal cohorts at each WTP threshold was based on selecting the cohort that produced the positive NHB. In case the NHB at a given WTP threshold are all negative, then no cohort would be selected as optimal; hence the TNB for that particular WTP threshold will be zero. In the case at the given WTP threshold, some or one of the cohorts produced the negative NHB while other cohorts produced a positive NHB, the selected cohort will be the one that produced the positive NHB. However, the gains in the total net benefit from adopting the stratification method will be the population sum of all cohorts that produced the negative NHB.

Using the trade-off framework we explored further the loss incurred for not choosing one stratification base over the other (Briggs et al. 2006, Glick et al. 2014). Here we compared the gains produced when using HIV status only or using parity only. In this case selection of the optimal cohort considered only one stratification base, either HIV or parity and not both. For instance, for HIV stratification base, the cohort that produced the positive NHB was selected and, as explained earlier if at a particular WTP, one of the two cohorts produced a negative NHB, the selected cohort will be the one that produced the positive NHB, but the recorded gains will be the one saved from the cohort that produced the negative NHB.

7.3 Results of the net health benefit analysis

Incremental cost-effectiveness ratio and incremental net health benefit

The mean ICER and INHB of scaling up the IPT-SP3 MHC for each cohort are presented in Table 15 based on the monetary WTP threshold of 5 to US$300 per DALY averted. The

incremental cost per DALYs averted for all women were US$40, which varied by parity and HIV status from –US$5 to US$133. The negative ICERs at the HIV positive cohort were observed due to cost saving. In general, when the WTP threshold increases, the proportion of women who become optimal for the therapy also increases. In this situation, the proportion of women who produced a positive net health benefit increases as the threshold increases. However, this is dependent on the location of the cohort on the cost-effectiveness plane. At the WTP threshold of less than 20, the strategy would not produce positive NHB to all women, but it will do so when targeting low parity and HIV positive women. Except for HIV positive cohort, all cohorts produced a less or equal to zero INHB at US$5 WTP threshold. As the WTP threshold increased to US$15 per averted DALY, only low parity and HIV positive cohorts had a positive INHB. While HIV negative cohort started to have a positive INHB at the WTP threshold of US$50 per averted DALY, high parity cohort continued to have a negative NHB up until when the WTP threshold was US$100 per averted DALY.

Incremental net health benefit gained with and without stratification

Table 16 presents the net health benefit of the strategy for each cohort of 100 women based on the WTP threshold of US$5 to US$300. The optimal cohort assuming the WTP threshold of US$5 is to target low parity and HIV positive women only. The gain in total net health benefits from adopting this limited use criteria will be 295 (the population-weighted sum of all cohorts that produced negative net benefits). The same was done for WTP threshold from US$15 to US$100 while from higher WTP than US$100, all cohorts produced the positive net health benefits hence the strategy targeted all women. Generally, the net health benefits gained increases as the WTP threshold increases regardless of stratification, and they stop to increase at WTP threshold of more than US$300 (not shown here). At very low threshold levels, gains, when stratification was adopted, were higher than those gained without considering stratification.

Table 15 Incremental costs, averted DALYs and net benefit for mIPTp-SP3 compared to WTC*n* per woman.

				Incremental net health benefit per woman per DALY averted								
Cohort	Incr. Costs	Averted DALYs	ICER	λ= 5	λ=15	λ=30	λ=50	λ=80	λ=100	λ=150	λ=200	λ=300
All women	8	0.20	40	-1.38	-0.33	-0.07	0.04	0.10	0.12	0.15	0.16	0.17
Low parity	1	0.17	5	0.00	0.11	0.14	0.15	0.16	0.16	0.16	0.16	0.17
High parity	10	0.08	133	-1.91	-0.59	-0.26	-0.12	-0.05	-0.02	0.01	0.03	0.04
HIV positive	-1	0.14	-5	0.27	0.18	0.16	0.15	0.14	0.14	0.14	0.14	0.14
HIV negative	6	0.12	48	-1.04	-0.27	-0.07	0.00	0.05	0.06	0.08	0.09	0.10

Source: Author's own

Note:

λ = Willingness to pay threshold in US$ per woman per DALY averted

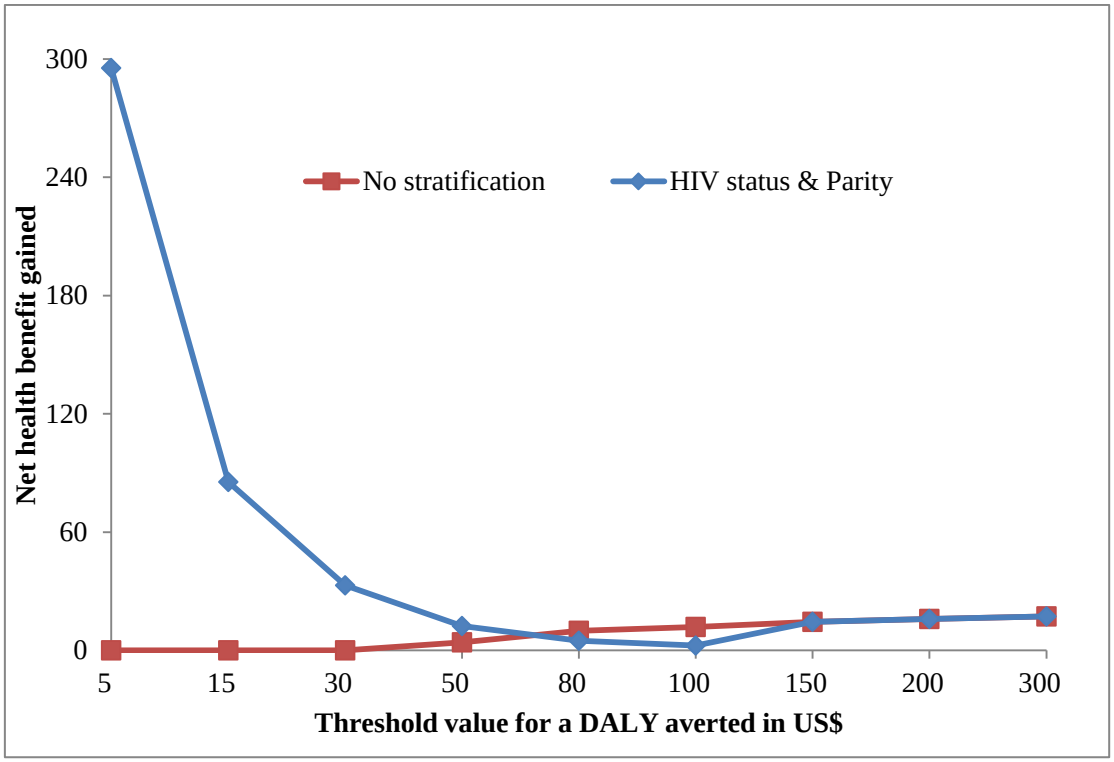
Table 16. Comparison of NHB gained with stratification and no stratification

No subgroup analysis (n^a=100)			With subgroup analysis (n^a=100)	
Threshold	Optimal Cohort	INHB gained	Optimal Cohort	INHB gained
5	All	0	Low parity and HIV positive	295
15	All	0	Low parity and HIV positive	85
30	All	0	Low parity and HIV positive	33
50	All	15	Low parity and HIV positive	12
80	All	19	Low parity, HIV positive and HIV negative	5
100	All	20	Low parity, HIV positive and HIV negative	2
150	All	22	All	22
200	All	22	All	22
300	All	23	All	23

Source: Author's own table; Note [a]Total number of women in the hypothetical cohort

In Figure 15 depicts the net health gains when providing the intervention based on the subgroup that had maximum INHB compared to providing the intervention to all women without considering the gains attributed to subgroup differences.

Figure 15: Gains in NHB with and without stratification



Source: Author's figure

Incremental net health benefit gained due to trade off

Table 17 presents the INHB gained according to each stratification basis (assuming that the strategy will target clients according to either their parity or HIV status and not all). Considering parity only as the stratification basis, at the WTP threshold of US$5 to US$100, the optimal cohort to be targeted by the intervention was low parity: The total net health gains attributable by adopting this limited use criteria at each of these thresholds were 191, 59, 26, 12, 5 and 2, respectively (the ones from the negative health benefits produced by the high parity cohort). Above the WTP threshold of US$100, both low parity and high parity produced positive net health benefit, and here all women were provided with the intervention. When HIV status was considered as the stratification basis, the gains at WTP threshold of 5, 15 and 30 were the values of the negative net health benefits produced from the HIV negative cohorts (104, 27 and 7, respectively). All cohorts produced the positive net health benefit from WTP threshold above US$30. In general, using parity as a stratification basis produced high net health gains at very low WTP threshold than using HIV status, while no differences were observed when the WTP threshold exceeded above US$100.

Table 17: INHB maximisation because of a trade-off

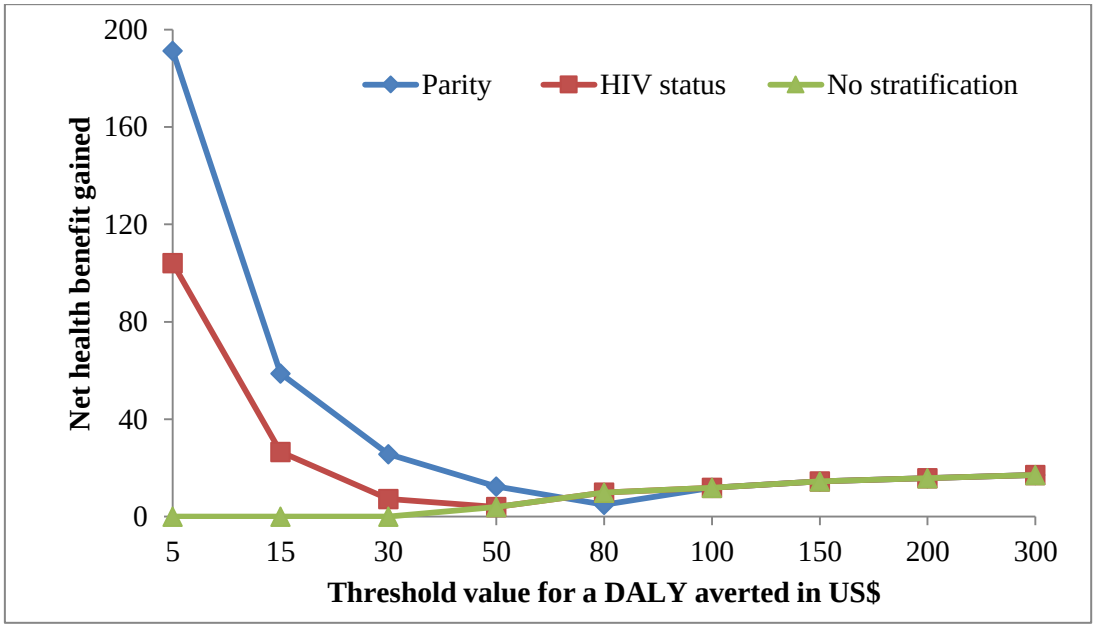
	HIV status stratification(n*=100)		Parity stratification(n*=100)	
Threshold**	Optimal cohort	INHB gained	Optimal cohort	INHB gained
5	Low parity	191	HIV positive	104
15	Low parity	59	HIV positive	27
30	Low parity	26	HIV positive	7
50	Low parity	12	All	15
80	Low parity	5	All	19
100	Low parity	2	All	20
150	All	22	All	22
200	All	22	All	22
300	All	23	All	23

Source: Author's own; Note:*Total number of women in the hypothetical cohort;

**Hypothetical willingness to pay threshold per DALYs averted in US$

In Figure 16, the gain in total net benefits according to hypothetical WTP thresholds is depicted. It shows the net health high gains when providing the intervention based on only one stratification basis. As indicated, when the WTP thresholds lower than US$30, high gains are observed when using parity as the stratification basis as compared to using HIV status. However no differences exist when the WTP increases.

Figure 16. Gains in NHB with and without stratification (based on trade-off)



Source: Author's figure

7.4 Discussion of the net health benefit results

In this paper, we compared the net benefits of scaling up SP provision via MHC resulting from considering the effect of heterogeneity in cost and effect. Adopting the NHB framework, we conducted the stratified analysis with the aim of exploring heterogeneity based on parity and HIV status using data from an economic evaluation reported in chapter six of this thesis. As far as we are aware, this is the first time that the economic evaluation of SP in pregnant women was done while considering relevant subgroups. Our findings suggest that stratification according to parity and HIV status result in a higher NHB as compared to no stratification. These results extend and stress on what has been previously indicated on the heterogeneous effect of SP in preventing maternal parasitaemia and severe anaemia.

Our findings indicated there are efficiency gains that are associated with stratification or providing the intervention to specific cohort according to baseline characteristics that are evidenced to affect the outcome of the intervention. It suggests that scaling up the intervention to women of low parity and those living with HIV and AIDS yield large total NHB— hence being much more beneficial than sending the intervention to all women. The main reason for this is the already known fact that risk of malaria is higher among low parity women and those with HIV infection (Ayisi et al. 2003, Brabin 1991, Steketee et al. 2001). Additionally, the evidence reported in systematic reviews that had explored the effect of the SP on malaria, and severe malaria had suggested that the intervention shows a sizeable protective effect among the aforementioned (Radeva-Petrova et al. 2014).

Because of unavailability of effectiveness data for high parity women stratified according to HIV status, the effectiveness data that was used to estimate the gains of the HIV positive subgroup come primarily from low parity women. Therefore, our findings point to the relevance of multiple risk factors of malaria—herein low parity and HIV infection and their implication on the net health benefits. That was expected due to the vast body of evidence that suggested an increased prevalence of severe anaemia and malaria among HIV infected women and more so among those of low parity (Ayisi et al. 2003, Van Eijk et al. 2003). While the current study highlighted the benefit of scaling up SP via mobile health clinic targeting subpopulations and ignoring others, it gives rise to some relevant questions in need of further investigation regarding the role of HIV interventions in malaria intervention and what benefits would be achieved when the two interventions are provided together. It also raises the question of whether the benefit observed to be gained when the intervention as provided to HIV positive women would be the same if the cohort had HIV positive women who are also multiparous. Studies indicate that all HIV women regardless of parity are at high risk of acquiring malaria(Van Eijk et al. 2003). However, it would be interesting to know to what extent the inclusion of high parity HIV positive women in the cohort will change the estimates.

Given that findings were based on a limited number of SP effectiveness studies, the results of such analyses should, therefore, be treated with considerable caution. For instance, the net health benefits estimated here did not take into account the role of SP resistance; hence they might only apply to the level of resistance that was present at the study areas where the effectiveness data used in this analysis were obtained. Moreover, the MHC is fixed to a certain degree (costs for the van, staff travel time to move from village to village). Therefore, providing SP3 to other strata has (theoretically) reduced incremental costs.

Nevertheless and regardless of whether scaling up SP for malaria prevention to a low parity and HIV positive women achieves maximum NHB, its practical application has raised debates on the equity and ethics of selecting one group over the other(Cookson et al. 2009, Grutters et al. 2013). Scholars have cautioned that decision-makers should be provided with the necessary available information and adopt the results according to their local policies (Briggs et al. 2006, Sculpher 2008). In general, the current Tanzania health policy guides the provision of essential interventions while prioritising most at risk population(MoHSW 2008). However, it does not recommend subdividing pregnant women further concerning their risks profiles and maternal services that are provided to all and not based on risks.

Our study has several limitations due to restricted data availability. First, because the data that we used for HIV positive women came primarily from a trial that had low parity women, meaning that the net health benefits explored represent those that will be achieved when the intervention will be provided to such a group and may not hold true when the intervention will be provided to high parity women living with HIV. Second, this analysis could not explore the extent to which the intervention would be beneficial among HIV positive women concerning their CD4 counts which would be more informative if there was a possibility of stratifying the HIV positive groups according to CD4 counts and viral load level.

Preamble

For more than forty years, MHC has been used to provide health care to increase coverage of essential health care interventions. The decade since the Alma Ata declaration(WHO 1978) and the Health for All Campaign, has witnessed some improvement in reduction of maternal mortality because of collective efforts including using all possible strategies to reach the unreachable. In some countries including Tanzania, MHC has proven beneficial in delivery of a number of health interventions in the areas of immunization, cancer and HIV (Babigumira et al. 2009, Bassett et al. 2014, Hanson 2017, Mudur 2010, O'Connor et al. 1998, O'Connell et al. 2010), and researchers are working to identify more and more information that can help improve the implementation of this service delivery portal. Despite these advances, a general sense of dissatisfaction on the progress of coverage of essential maternal health interventions remains(WHO 2017). So far, utilisation of antenatal interventions is below the required level, delivery by skilled personnel remains just a dream for many, and family planning missed opportunity is on the rise (Ensor and Cooper 2004, Jacobs et al. 2012, O'Donnell 2007). Besides the scientific and operational challenge associated with the implementation of those strategies, the impact of those programs has raised economic questions for payers, the healthcare system, and development partners. In the current chapter, the main findings from the four sub-studies are presented and discussed. Furthermore, recommendations for practice and future research will be provided.

8.1 Discussion of the main findings of this thesis

8.1.1 *On the methodologies adopted*

During our research for this thesis, it became evident that for consistency in performing an economic evaluation of MHC there is a need to use mixed methodologies to gather information that will inform the economic evaluation study. The in-depth interview conducted with policymakers laid the foundation for understanding the resource available for MHC, the policy directions and the challenges facing the program. Although this method has strength in its ability to acquire detailed information related to knowledge, perceptions and practice(Baxter and Jack 2008), it is prone to both recall bias (Tversky and Marsh 2000) and interpretation bias during data analysis(Baxter and Jack 2008). However, the analysis was done using a standardised protocol that ensures all aspect of the studies have been reported and cross-checked (Tong et al. 2007).

An activity-based costing approach was used which improves the reliability and validity of the cost estimates, especially in hospitals where costs are not adequately documented(Drury 2013, Waters and Hussey 2004, Wordsworth et al. 2005); however, this method is prone to bias and inaccuracies in case of missing or poor quality data sources(Mogyorosy and Smith 2005). Hence, efforts were made to minimise such biases by inspecting and comparing different hospital sources that report on the same output. Yet, the likelihood of our estimates to be incorrect is there because records'

keeping in most of the health facilities in low-income countries is reported to be low(Barnum and Kutzin 1993). We used a direct allocation approach to distribute overhead costs across the departments. However, this method tends to ignore the interaction between departments (Drummond et al. 2015). Using a direct allocation approach was associated with a challenge in the allocation of shared resources (Mogyorosy and Smith 2005), however using this method could not be avoided due to the lack of documents showing how overhead costs related to the administration or how utilities were shared between department. In theory, it is recommended for the cost valuation to reflect the actual utilisation (Drury 2013). However, this is reported to be not the case in practice and, as seen in this work, the final judgement was made based mainly on interviewing relevant informants(Conteh and Walker 2004).

The adoption of the Markov decision analytic model was based on the recommendation from existing guidelines(Drummond et al. 2015, Gray et al. 2010) and used the CHEERs guidelines to create consistency in reporting of our findings. Its ability to capture recurring event(Husereau et al. 2013), however, limitation due to the model structure used in this thesis have introduced bias in our estimates. For instance, we assumed that distance was the only barrier to access to care, hence 100% of women had access to the MHC, and this may not be true in practice given evidence on factors that affect maternal health care utilization in low and middle-income countries (Hill et al. 2013, Jacobs et al. 2012, O'Donnell 2007). However, this was motivated by the policy question guiding this thesis which was to investigate whether the MHC managed to break the barrier of distance to health care access. Nevertheless, our effectiveness data came from trials, and we assumed all women receive the needed intervention uninterrupted which may not be the case in practice. Studies show that out of stock situations are among the barriers of increasing coverage of SP in Tanzania(Marchant et al. 2008). Avoiding this problem may involve increasing real-life data generation, perhaps via prospective cohort studies. Accounting for compliance and adherence will provide insight into the variability of findings and should be incorporated into sensitivity analyses.

Nevertheless, effectiveness data which is the primary driver of the estimated ICER since it is the denominator in ICER calculation(Drummond et al. 2015) that was synthesised through the systematic review and meta-analysis the findings of which are reported in chapter five. We used the random effect model to generate the precise estimates of between studies heterogeneity which might have provided precision in the treatment effect estimates(Brockwell and Gordon 2001). However, only two out of the three included trials were conducted against placebo, and the quality of evidence ranges from moderate to low as reported in chapter five. This may require additional analyses, especially when addressing heterogeneity that exists within the targeted population. These findings highlight areas of future work in this field. It may be desirable to reach a consensus on observational research methods to generate effectiveness evidence for MHC, with the aim to improve the quality of economic evaluations and avoid relying on literature for effectiveness data.

8.1.2 Policymaker perspective on the feasibility of MHC

Sub-study I of this thesis considers the policymakers' perspective on the feasibility and practicability of using MHC to provide maternal health interventions. In this case, policymakers are of the opinion that MHC will function at its best when the overall system is strengthened. The perspective on the cost of running MHC was generally similar, with the agreement that MHC is costly but needed, and it agrees with the ongoing discussions across the globe(Roodenbeke et al. 2011). It became evident that improving the infrastructure in which these MHC operate and utilising community resources like CHW is critical for these services to run at low cost and achieve maximum benefits. In this context, research in chapter six highlights the key economic drivers and conditions that will affect service costs and justify the investment in MHC as a strategic option. An integrated approach can reduce the cost of service and reach pregnant women with more than one intervention achieving the economies of scale. This shows that the success of implementing MHC will depend much on using integration approach and proper utilisation of task shifting policies which will reduce the costs of using nurses for every service. A further result of this analysis indicates that sending the MHC when the population in need is small is not going to be economically viable. Hence, having a good data monitoring system that include population survey will facilitate these clinics to work efficiently and allow increasing market share gains within the targeted populations.

8.1.3 Users costs of accessing services at the MHC

Although MHC had significantly reduced the time costs of service utilisation to women, and these costs were primarily driven by consultation time and waiting time. These findings resonate similarly to those reported by previous cost studies in antenatal care(Kowalewski et al. 2002, Sauerborn et al. 1995). Those similarities were expected because both of these studies were done in areas where human resources are limited and, specifically for the current study, the MHC had only two nurses responsible for providing not only ANC but also the full range of maternal and child health interventions. It can be argued that the time cost will be reduced if some of the tasks done by nurses will be delegated to CHW who at the moment are only tasked with offering health education and promotion and supporting growth monitoring activities. Reductions in waiting times have been reported in studies which investigated the impact of task shifting in HIV care (Braitstein et al. 2012, McGuire et al. 2008, Torpey et al. 2008, Udegboka and Moses 2009)

Apart from time costs, direct costs related to unavailability of essential medicine and reagents remain to be a challenge. Reduction in cost of access regarding the reduction of time spent travelling to seek care were expected. However, the costs related to unavailability of medicine were surprising. This is in contrast to the expectations that since maternal health is among the target priorities of the national health expenditure as indicated by the recent health accounts report(MoHSW 2015), women seeking maternal health will not incur direct costs. This indicates

that funding is not the only culprit of unavailability of essential medicine and supplies; instead, other health systems factors play a huge role. It has been long ago argued that poor and inadequate health information system impede planning and budgeting, hence may lead to districts ordering fewer supplies than the ones needed. That also arose among the challenges facing the MHC during the key informant interviews with policymakers. These direct costs have a potential of demoralising women from utilising service. A discrete choice experiment done on women in Tanzania indicated that women valued most facility attributes related to having a respectful provider attitude and availability of drugs and medical equipment(Kruk et al. 2009). That study also predicted that if those attributes were improved at existing facilities, the proportion of women preferring facility delivery would rise from 43% to 88%.

8.1.4 Economic evaluation of delivering IPTp-SP3 through MHC

The second part of this thesis consists of one case study in which the potential added value of using MHC was examined using IPTp-SP3 as an example. That entailed first to conduct a systematic review of the effect of three doses of SP on malaria and severe anaemia, followed by an economic evaluation and a stratified analysis.

Cost of providing IPTp-SP3

The estimated cost of providing at least three doses of SP at the MHC was US$12.12 per woman per pregnancy. Our literature review did not find similar studies that could be compared with ours; however, costing studies conducted at the static health facilities in Uganda, Ghana and Malawi reported lower costs of providing IPTp-SP (Fernandes et al. 2016, Mbonye et al. 2008). We expected the differences in cost estimates between our study and others because of the differences in the type of service delivery and the costs that are attributed to the mobile vans. Nevertheless, these differences can also be explained by varying clinical practices among the countries in which these costs are estimated. We presented the estimates that were costed based on the current Tanzanian practice in which all cost drivers were identified according to how they are implemented. In that way, our estimates are subject to the costing inefficiencies that are embedded in these practices. For instances, in this current study nurses used a significant amount of time travelling, which means not all of their time was productive. That is also reported in another case study done in Tanzania which indicated that only 57% of health workers' time in Tanzania is used in productive activities(Kurowski et al. 2004).

Another avenue to explore in this case would be to see if task shifting policies can be adopted in antenatal care provision. To our knowledge, the current Tanzania health policies promote task shifting and strategies to reduce the workload for health professionals are underway. That includes the introduction and formalisation of the CHW carders who live within the community and are tasked with activities that are simple(MoHSW 2008,2015). Task shifting has been implemented in

SSA in HIV care and prevention, to name a few, and its impact on the reduction of the resource is encouraging. A recent review quantified time saved by implementing task shifting on the assumption that delegating tasks gives senior clinical staff more time to deal with complicated patients(Callaghan et al. 2010). Authors of an extensive study in Rwanda assessed time savings from nurse-initiated and monitored antiretroviral therapy (ART), and concluded that such task shifting at the national level would result in a 183% increase in doctor capacity for non-HIV related tasks(Shumbusho et al. 2009). In our cost estimates, nurses' salaries are higher than those of the CHW, and nurses are doing a wide range of tasks at the MHC compared to CHW and that of a mobile van driver. Other tasks such as data recording can be delegated to the mobile van driver and dispensing simple interventions like SP can be allocated to CHW. Reducing dependence on nurses for ANC and especially for simple interventions like SP could reduce clinic operating costs or increase patient load for the same cost. A study comparing total average annual clinic-level costs per ART patient in Uganda and South Africa found that mean costs were almost a third less in the former ($US331 vs $US892) and concluded that task-shifting might have helped to reduce clinic costs and improve overall efficiency(Stearns et al. 2008).

Providing IPTp-SP3 through MHC is worth the costs

The economic evaluation in this thesis is an analysis that used a Markov Decision modelling technique. In sub-study IV a malaria model was constructed using analytical decision techniques to perform a cost-effectiveness analysis for a cohort of pregnant women who receive IPTp-SP3 at the MHC in the Tanzania healthcare setting. The findings indicated that using MHC to scale up IPTp-SP to clients living in remote populations potentially reduce the cost of consequences and reduce the number of DALYs. Assuming that the WTP threshold applied in this analysis represents the actual cost per health gain of a least efficient intervention provided by the Tanzanian health system, and then the opportunity cost in terms of health forgone from the activities to be displaced will be lower than expected health gains(Drummond et al. 2015, Gray et al. 2010). In sub-study V we conducted a subgroup analysis that used the net benefit framework to allow assessment of incremental cost per averted DALY and net health benefits according to women parity and HIV status. This analysis was based on the existing evidence that IPTp-SP is more efficacious to low parity women(Radeva-Petrova et al. 2014), and, the growing evidence that implies co-infection undermines the effectiveness of interventions(Ayisi et al. 2003, Flateau et al. 2011).

Appropriateness of the decision rule adopted

In our analysis, we used ICER and the net monetary benefit framework as a decision rule while applying a recommended WTP threshold of US$150 per averted DALY. Net benefit method allows identification of the cost-effectiveness option to be conceptually more straightforward than under ICER method where a decision maker must identify the greatest ICER with a value below their

WTP threshold. This type of value measure is also beneficial if decision-makers are trying to determine the best way to allocate healthcare funds between alternative uses(Drummond et al. 2015, Gray et al. 2010). Thus, if they have a fixed healthcare budget and want to get the best value from that budget, they should allocate the funds to the uses that give the most return for each dollar spent. That is, they should allocate funds first to the uses with the lowest cost-effectiveness ratios. Yet the validity of our estimates can be questioned in practice because recent academic debates have criticised the use of any decision rule that lacks information on the budget impact as a practice that leads to increased expenditure(Sullivan et al. 2014). They argued that decision-makers in a constrained budget need to know by how much their annual budget is likely to increase or decrease in year 1, 2, and so on, after its introduction, if the strategy is added to the health plans. They indicate that decision-makers need to know what annual health benefits are likely to be associated with this budget increase or decrease (Mauskopf et al. 2005). However and as it was seen in our case, conducting a budget impact analysis requires the availability of population data on malaria and severe anaemia cases from the study area where MHC are being implemented to validate the predicted number of cases.

An assumption that the program is cost-effective if it's ICER is not more than the recommended WTP threshold has recently received scrutiny. It is criticised because it is not based on assessing the health benefits that will be lost because resources required will not be available to implement other programs that will help other patients with the same or different disease. We tried in our analysis to bypass that problem by adding on the net benefit framework to provide the probabilities while using different WTP threshold but affirming the probability of cost-effectiveness using the US$150 WTP threshold recommended for low and middle-income countries(Shillcutt et al. 2009). We are aware that the appropriateness of the multiplier of 1 to 3 times the GDP used in deriving this threshold has recently been kept under scrutiny and argued that it lacks empirical basis(Robinson et al. 2016). However, with the current Tanzania GNP per capita of US$867, the scaling up of IPTp-SP via the MHC program remains to be cost-effective even with the proposed range of the multiplier of 1 to 9 times per GDP per capita.

On the type of the intervention to be scaled up

Although MHC can deliver care to remote populations, not all interventions can be delivered through this mode. Evidence from the literature review (Hanson 2017, Hill et al. 2014, Kerber et al. 2007) and the views of the policymakers' gathered in chapter three interview indicated that only some and not all health interventions are suitable for delivery via MHC. The limitation of MHC is largely based on the capacity both regarding human resources(Roodenbeke et al. 2011) and medical equipment that is needed for wide range of curative services(Hanson 2017, Hill et al. 2014). Nevertheless, the argument of the suitability of MHC to deliver health interventions does not end

with the type of the interventions that should be delivered; rather, it extends to include the effectiveness of the intervention that should be delivered(Kerber et al. 2007). Therefore, assuming that the SP still offers protection against maternal malaria and severe anaemia as estimated in chapter five and as predicted in other evaluations(ter Kuile et al. 2007, Walker et al. 2017), our model results would still recommend to scale up SP to the isolated population via MHC. However if the protective effect of SP against malaria and severe anaemia is hampered due to any reasons, be it resistance or non-adherences(Roper et al. 2003, ter Kuile et al. 2007), then our model recommendations for scaling up this particular intervention will be greatly affected because it will be ineffective, and the "wait to treat option" will be a better option.

8.2 Towards ´smart´ implementation of MHC

The appropriate tailoring of most at risk client subgroups may be beneficial. An integrated approach that allows delivery of more than one intervention need to be strengthened to allow efficiency in resource use. Entirely a significant amount of money is spent in improving maternal health in Tanzania, and the increase in developing support in the area has triggered an increasing number of proactive outreach approaches, which are currently under development. However, it is essential to recognise that without ensuring these outreach approaches are well equipped to reach the needy and improve coverage there is no economic rationale to pursue a stratified approach. The findings in chapter three suggest ensuring generation of data at the MHC program to understand the impact of the program regarding a number of those served the characteristics of the population and common conditions reported at the MHC, and other resource use information. This may help the country get enough information to plan and make an informed budget and reduce the challenge of unavailable medicines and supplies.

The sensitivity analysis performed during the CEA analysis in chapter six evaluated the impact of different parameters on the predicted ICER, and it became clear that integration and an understanding of the number of women who need services drive cost and hence a good data management plan of routine data is essential. While the information on the impact of integration on the efficiency of service delivery in Tanzania and other countries is widely reported (Evjen-Olsen et al. 2009, Sweeney et al. 2011), lacking is the information on the impact of not having reliable data for planning and budgeting purposes. However, having reliable data to inform budgeting for the needed material may reduce the problem of out of stock situations, and may make services more preferable to the women. Findings from the demographic survey indicated that, compared to other eastern and southern African countries, Tanzania has better geographic coverage of health services, yet we see high maternal mortality compared to countries where the distance to health care is a challenge(UNFPA 2017). This implies the need to ensure that all health services outlets

including MHC offer maximum maternal health services and uninterrupted availability of essential medicine and supplies.

With the prospect of a wave of promoting CHW carders, it is very likely that more benefits regarding cost reduction for service delivery will be introduced in Tanzania. While HIV programs were able to realize substantial reductions of program costs as well as clients' time costs(Callaghan et al. 2010, Chung et al. 2008, McGuire et al. 2008, Shumbusho et al. 2009), their adoption in other health interventions in Tanzania like maternal health may be practiced(Munga et al. 2012) but is not well documented. Identifying aspects of intervention within the maternal health services that can be provided by CHW or other personnel whose time is cheaper than those of nurses can lead to "win-win" scenarios for MHC clients, health care providers and the overall healthcare system. However, researchers in the country have pointed out the need to have a regulatory framework that will guide task shifting practices to avoid jeopardising the quality of care(Munga et al. 2012).

The conceptual attractiveness of targeting may also reduce costs of the intervention in case of reduced or no protective effect of SP among subpopulations like seen in the case study in chapter seven, especially of low parity and those with HIV infection. Hence, adopting that route on the long term, a higher percentage of MHC programs in countries like ours may enhance overall coverage of essential interventions with better benefit-risk profiles, leading to a reduction of costs of the consequences and improved health outcomes. Regardless of the net health benefits that are anticipated in targeting subpopulations with interventions, the moral and ethical aspect of this continues to be under debate, and the implementation of this suggestion may not be feasible(Cookson et al. 2009).

8.3 Recommendations

Policy recommendations

The recommendations stemming from this thesis are highly relevant to the current health situation in Tanzania. Despite the ongoing debates on the effectiveness of SP, recommending scaling up this intervention to where there are no health facilities cannot be overemphasised. This work offers and contributes to valuable information on the implementation of MHC in resource-poor countries and their associated cost and effectiveness. Policy makers may consider revisiting the way MHC are run by ensuring implementation of policies that will generate efficiency gain in the current practice, such as implementing task shifting policies as seen in this case. Although we could not conduct evaluations of each intervention delivered at the MHC, and hence we cannot provide an overall answer to the cost-effectiveness of this program, findings from this work can be considered a step towards evaluating other interventions delivered in this mode like family planning, immunisation,

growth monitoring and health education. Such information will be crucial to value the significance of MHC regarding their costs and effects.

Research recommendations

MHC is implemented all over the country. However, this study only assessed the effect of these services on one district in the Eastern part of the country that was selected purposively. A substantial cost analysis may be ideal to predict the cost implication in different regions and districts better. That is because the good or bad impact of MHC depends on factors that will be different from one district to the other. This ranges from infrastructure, climate situations like heavy rainfalls, the population of the people living in remote areas. A large costing study that will select these districts randomly will allow a better understanding of the cost of MHC and provide the insight on which districts will benefit most from this program and which will not. Nevertheless, this study only looked at the use of MHC to deliver maternal health intervention while focusing on delivery of SP for prevention of malaria; therefore, more research is needed to understand the role of MHC in other preventive interventions like HIV, diabetes, hypertension, and other chronic illness that need routine health care. As noted in the discussion, more research is also needed in Tanzania to understand the extent to which MHC have impacted on the overall budget and what aspect of this delivery platform need modifications to improve efficiency. Additionally, economic evidence despite its significance may not provide a better understanding of the government's ability to continue implementing these programs

Introduction: Geographical access to antenatal intervention is a growing problem in sub-Saharan Africa (SSA). Countries in the regions have for more than 40 years deployed mobile health clinics (MHC) to address that problem, yet, their feasibility, costs, and effectiveness of are poorly known.

Methods: A qualitative case study in chapter three using key informant interviews to explore the feasibility of using MHC to deliver maternal health care was conducted. Thematic analysis was done using NVivo software for Mac version 10.5.8. In chapter four exit interviews were conducted to estimate client time and direct costs incurred by clients when they use services. Data were entered in EpiData software version 3.1 and analysed in STATA version 12. In chapter five, a systematic review and meta-analysis of randomised control trial were conducted to synthesis effectiveness data used in the cost-effectiveness analysis (CEA). In chapter six a CEA was conducted from the provider perspective. DALYs lost due to malaria, and severe anaemia was calculated based on recommended guidelines. Cost data were collected from the public district hospital that oversees the MHC. The activity-based costing methodology was adopted to identify measure and value resource used. The Markov decision model was used to compare the cost-effectiveness of using MHC to scale up the provision of IPTp-SP3 and a "wait to treat" strategy. The model was built in Microsoft Excel version 15.37. Probabilistic sensitivity analyses with 10,000 simulations were used to test the robustness of model results. In chapter seven-a, stratified analysis and a net health benefits analysis was conducted to explore the impact of heterogeneity on the estimates when considering parity and HIV status as focus subgroups.

Results: Policymakers perceive MHC as an important mode of service delivery to scale up essential interventions in areas that lack static health facilities. Yet, this approach is challenged by scarce resource, poor road infrastructure, and a weak health information system. MHC indicates to have reduced client travel time; however, women incur direct costs due to out of pocket payments driven by out of stock of medicine. The cost of IPTp-SP3 per pregnancy was estimated to be US$ 12.87. The model predicted the total cost to roll out the intervention to 1,000 women to be US$ 20,185 compared to US$ 12,283 if the "wait to treat" strategy is adopted. The strategy was predicted to be more cost-effective than waiting to treat, with an incremental cost-effectiveness ratio (ICER) of US$ 40 per DALY averted. The strategy was also associated with lower costs of the consequences as compared to wait to treat strategy (US$6 086 versus US$12 365). Additionally, more net health benefits (NHB) were predicted when the intervention was provided to low parity and HIV positive women alone.

Conclusions: Using MHC to scale up IPTp-SP3 in Tanzania is worth the cost with more NHB predicted for low parity and HIV positive women. Although the presented evidence may help guide decision in scaling up essential health intervention, yet more evidence is needed on the impact of this mode of service delivery on a budget of the ministry of health and social welfare.

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Appendix 1: List of Figures and Tables

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List of Abbreviations

AIDS	Acquired Immunodeficiency syndrome
ALU	Arthemether and Lumefantrine
ANC	Antenatal care
ICER	Incremental Cost Effectiveness Ration
NMB	Net Monetary Benefit
NHB	Net Health Benefit
CBA	Cost Benefit Analysis
CCA	Cost consequence analysis
CEA	Cost effectiveness Analysis
CEAC	Cost-effectiveness acceptability curve
CMA	Cost Minimization Analysis
CUA	Cost utility Analysis
DALYs	Disability adjusted life years
DSA	Deterministic sensitivity analysis
Fefol	Iron sulphate and Folic acid tablets
GDP	Gross domestic product
Hb	Haemoglobin
HIV	Human immunodeficiency syndrome
HMIS	Health management information system
IEC	Information, education and communication
IPTp	Intermittent Preventive Treatment for malaria in pregnancy
IPTp-SP	Intermittent Preventive Treatment for Malaria in Pregnancy with sulfadoxine-pyrimethamine

IPTp-SP3	Intermittent Preventive Treatment for Malaria in Pregnancy with three or more doses of sulfadoxine-pyrimethamine
MHC	Mobile Health Clinic
MCH	Maternal and Child health services
MRDT	Malaria rapid diagnostic test
MSD	Medical Store Department
NBS	National Bureau of Statistic
NIMR	National Institute for Medical Research
OPD	Outpatient department
QALY	Quality Adjusted Life Years
PSA	Probabilistic sensitivity analysis
RCT	Randomized controlled trial
SSA	Sub Saharan Africa
SP	Sulfadoxine-pyrimethamine
TZS	Tanzanian Shillings
US$	United States dollars
WTP	Willingness to pay
YLDs	Years lived with Disability
YLLs	Years of life lost due to the disability
URT	United Republic of Tanzania
UNAIDS	Joint United Nations Program on HIV and AIDS
UNICEF	United Nations Children's Fund
UNFPA	United Nations Population Fund
WHO	The World Health Organization

Ethical Approval from National Institute for Medical Research Tanzania

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CLEARANCE CERTIFICATE FOR CONDUCTING MEDICAL RESEARCH IN TANZANIA

This is to certify that the research entitled: Feasibility, practicability and cost-effectiveness of using mobile van to provide maternal health services in Kisarawe District, Pwani region, (Neke N M *et al*), has been granted ethical clearance to be conducted in Tanzania.

The Principal Investigator of the study must ensure that the following conditions are fulfilled:

1. Progress report is submitted to the Ministry of Health and the National Institute for Medical Research, Regional and District Medical Officers after every six months.
2. Permission to publish the results is obtained from National Institute for Medical Research.
3. Copies of final publications are made available to the Ministry of Health & Social Welfare and the National Institute for Medical Research.
4. Any researcher, who contravenes or fails to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine. NIMR Act No. 23 of 1979, PART III Section 10(2).
5. Sites: Dar es Salaam region, and Kisarawe district, Pwani Region.

Approval is for one year: 12th November 2015 to 11th November 2016.

Name: Dr Mwelecele Malecela

Signature
CHAIRPERSON
MEDICAL RESEARCH
COORDINATING COMMITTEE

Name: Prof. Muhammad Bakari Kambi

Signature
CHIEF MEDICAL OFFICER
MINISTRY OF HEALTH, SOCIAL WELFARE

CC: **RMO**
DED
DMO

Ethical Approval from the University of Duisburg Essen

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Essen, den 20. August 15 / SB

✉ Herrn Prof. Dr. Jürgen Wasem, Lehrstuhl für Medizinmanagement, Universität Duisburg-Essen

Studientitel: **Feasibility, practicability and cost-effectiveness of Mobile Health Clinic in providing Maternal Health Services in Eastern Tanzania**
Antragsteller: **Dr. Neke, Prof. Dr. Wasem, Lehrstuhl für Medizinmanagement**
Unser Zeichen: **15-6512-BO**

Sehr geehrte Frau Dr. Neke,

als Vorsitzender habe ich im Auftrag der Mitglieder der Ethik-Kommission der Medizinischen Fakultät der Universität Duisburg-Essen Ihren o. g. Antrag geprüft.

Auf der Grundlage der übersandten Unterlagen vom 14.08.2015 und dem derzeitigen Informationsstand besteht kein Anlass, ethische oder rechtliche Einwände gegen diese Studie zu erheben.

Die Verantwortung für die Studie und ihre Durchführung verbleibt uneingeschränkt bei den Projektleitern und wird nicht von der Ethik-Kommission übernommen.

Die Kommission erwartet, dass sie über alle für die Teilnehmer relevanten Änderungen des Prüfplans informiert wird. Nach Abschluss der Studie erbittet die Kommission einen kurzen Bericht über den Ausgang der Studie.

Es wird Befreiung von den Gebühren der Ethik-Kommission gewährt.

Die Kommission wünscht Ihnen viel Erfolg.

Mit freundlichen Grüßen

Prof. Dr. W. Havers

Universitätsklinikum Essen

Key Informants information and consent form (English version)

Background information

An increasing number of women lack access to cost effective maternal health interventions in Tanzania. This is hindering the effort towards reducing maternal mortality in the country. MHC can be used as a platform to reach the women who would otherwise not access services with maternal health services. Recent studies suggest that MHC can provide an alternative portal into the health care systems for the medical disenfranchised that is providing people who are otherwise outside the reach and mainstream of health care due to simple issues like location and remoteness. In response to this the Tanzanian government through development partners is currently implementing delivery of maternal health services through this portal. This study aims to explore the feasibility and practicability of providing maternal health services through mobile clinics. Ideally, the mobile health vans which are equipped with all necessary equipment's and manpower needed to offer all maternal health services goes through the remote villages and put a station and offer services. In some cases, they also offer delivery services when it happens that there is a need. Acknowledging that providing maternal health services out of the health facility setting is not the same as providing them in the usual health facility settings, understanding practicalities of implementation of this portal of service delivery is necessary. Furthermore, is important to understand that not many mobile health services in the country have been used to provide other reproductive health interventions like family planning, immunization, and screening for STDs among other health interventions, however, their application in maternal health services may be different from those. This study is part of the requirement for the fulfillment of the PhD studies of Dr. Nyasule Neke, who is currently enrolled at the Duisburg-Essen University, and, she is also working with the National Institute for Medical Research in Mwanza Centre. We have requested permission to conduct this study by the Medical Research Coordinating Committee of the Tanzanian government and the Duisburg-Essen University of the Germany.

Procedures

To know your views regarding the practicability and feasibility of using this portal to deliver maternal health services we will ask you to participate in an interview with one of our research team. This interview should take no longer than I hour and will be conducted in a private place. You can ask any questions regarding the study, and after you have had all your questions answered and you are satisfied with the response and you understand what you will have to do, we will request you to sign, or put your thumbprint on this consent form. The researcher will ask for your permission to record the interview. The interview will take a style of one on one discussion, and it will be casual, and you will be encouraged to talk freely about anything you feel that is related to the questions about the provision of maternal health services through MHC.

Study Duration

We are planning to conduct the interview over a period of one month; however, you will only be interviewed once.

Risks, Stress, or Discomfort

There are no risks associated with your participation to this study. However, when it happen that you feel that you have suffered any harm as a result of your participation in this study kindly feel free to contact the person whose name is written below the end of this form.

Benefits

It is hoped that the information gained from the study will be useful in improving delivery of maternal health services through the MHC in Tanzania.

Participation

We hope that you will be available and willing to participate in this research. However, feel free not to participate in case you do not wish to participate in the interview. Additionally, you can withdraw from this research project at any time.

Confidentiality

Kindly lest assured that your contact details will be confidential and will only be shared within the staff involved in the study.

If you have any questions

If you have any questions about what we are doing or about the study in general, please contact Dr Nyasule Neke (Tel +255 717 816673). The project office is in the NIMR Mwanza Centre in Isamilo, Mwanza. The postal address and telephone number of NIMR is given at the top of this form.

What you are required to do

If you are willing and agree to participate in this research, please sign below.

Subjects Statement and Signature

The study described above has been explained to me and I have been given a chance to ask questions. Moreover, I have received information and answers that made me understood the overall and specific aims of this study. I am hereby consenting to participate in this study by providing the answers to the questions according to my knowledge and ability. I am also aware that there is a

possibility of asking further questions in the future regarding the study, and, I have been explained how that can be done together with the availability of the contacts details of the study corresponding personnel in this form. I will also remain with the signed version of this form.

Participant's Signature/ thumbprint

Signature or Thumbprint		Date	
Name in Capital Letters			

Witness's signature (if participant is illiterate)

Signature		Signature date	
Name in Capital Letters			

Put a mark inside the box if participant is illiterate and does not want a witness ☐

Signature of researcher obtaining consent

Signature		Signature date	
Name in Capital Letters			

Research Team Addresses

1. Universität of Duisburg-Essen, Fachbereich Wirtschaftswissenschaften, Thea-Leymann-Str. 9, D-45127 Essen, Germany. Tel.: +49 (201) 183-4075, Fax: +49 (201) 183-4073
2. National Institute for Medical Research (NIMR) P.O. Box 11936, Isamilo Street Mwanza, Tanzania. Tel: +255-28-2500019, Fax: +255-28-2542162.

Patient Questionnaire

Study of the Costs of Maternal Health Services at the Mobile Health Clinic

Information Sheet and Informed Consent

I …….. am here on behalf of Institute for Health Management and Research of the University of Duisburg-Essen (Germany) research team. As part of our project, we are working on a research study of the patient costs of accessing maternal health interventions at the mobile vans run by Plan International in Kisarawe District.

Purpose of the study: The survey aims to estimate provider and patient's costs of various maternal health interventions that are provided by the vans like antenatal care and postnatal care so that it could be compared to effectiveness of using this mode of service delivery for maternal health service.

Participation and what it involves: The mobile clinic that provides you with maternal health service is the primary focus of this study. We will collect information so that we can calculate what it costs to provide maternal health services at this mobile van. We also want to calculate the costs that patients pay in order to receive these interventions at the mobile health vans. To do this, we will ask you questions about how much time and money you spend getting services that you need at this particular mobile health van. We will also ask you questions about how far away you live and how you live.

Confidentiality: The study is anonymous and we will not record your name or any other personal information. Unauthorized persons will have no access to the data collected.

Risks and Benefits: We do not expect any harm to happen to you because of participating in this study. There are no direct benefits to you from taking this survey. Your participation will help with planning for the future of maternal health services delivery strategies in this country. This may help design better way to reach women with maternal health interventions.

Voluntary participation: Your participation is **voluntary** and you can withdraw from the survey after having agreed to participate. You are free to refuse to answer any question that is asked in the questionnaire. There is no penalty if you do not wish to participate or wish to stop.

Contact Information: If you have any questions regarding this survey or the study, please feel free to ask the interviewers on site. You may keep a copy of this information sheet for your records. If you have any later questions you can contact the principal investigator Nyasule Neke of the National Institute for Medical research, Isamilo Street, P.O.Box 1462, Tel No 07596638845 Mwanza, Tanzania.

RESPONDENT COPY

Study of the Costs of maternal Health services at the mobile health clinic

Information Sheet and Informed Consent

I …….. am here on behalf of Institute for Health Management and Research of the University of Duisburg-Essen (Germany) research team. As part of our project, we are working on a research study of the patient costs of accessing maternal health interventions at the mobile vans run by Plan International in Kisarawe District.

Purpose of the study: The survey aims to estimate provider and patient's costs of various maternal health interventions that are provided by the vans like antenatal care and postnatal care so that it could be compared to effectiveness of using this mode of service delivery for maternal health service.

Participation and what it involves: The mobile clinic that provides you with maternal health service is the primary focus of this study. We will collect information so that we can calculate what it costs to provide maternal health services at this mobile van. We also want to calculate the costs that patients pay in order to receive these interventions at the mobile health vans. To do this, we will ask you questions about how much time and money you spend getting services that you need at this particular mobile health van. We will also ask you questions about how far away you live and how you live.

Confidentiality: We will not record your name or any other personal information only the study identification numbers will be used. Unauthorized persons will have no access to the data collected.

Risks and Benefits: We do not expect any harm to happen to you because of participating in this study. There are no direct benefits to you from taking this survey. Your participation will help with planning for the future of maternal health services delivery strategies in this country. This may help design better way to reach women with maternal health interventions.

Voluntary participation: Your participation is **voluntary** and you can withdraw from the survey after having agreed to participate. You are free to refuse to answer any question that is asked in the questionnaire. There is no penalty if you do not wish to participate or wish to stop.

Contact Information: If you have any questions regarding this survey or the study, please feel free to ask the interviewers on site. You may keep a copy of this information sheet for your records. If you have any later questions you can contact the principal investigator Nyasule Neke of the National Institute for Medical research, Isamilo Street, P.O.Box 1462, Tel No 07596638845, Mwanza, Tanzania.

Consent to participate: Signing this consent indicates that you understand what will be expected of you and are willing to participate in this survey.

Participant agrees…….. Participant refuses…….

I…… have read the contents of this form. My questions have been answered. I agree to participate in this study

Signature of participant……..

Signature of the research assistant……..

Date of signed consent…….....

Patient Questionnaire

Study of the Costs of Maternal Health Services at the Mobile health Clinic

Name of the village	Village code:
Name of the nearest Health facility	
Parity	
Interviewer Name	
Date (mm/dd/yyyy)	_____/ _____/ _____. **Start time:**

Basic Information/Demographic			
NO.	QUESTIONS AND FILTERS	RESPONSES	SKIPS
1	Enter respondent's marital status:	Married .....0 Single…….1 Cohabiting …2	
2	What is your age?	……Years old	
3	During the last 12 months, what was your main activity?	Farming or livestock keeping.....0 Fishing.....1 Paid Employee (Government).....2 Paid Employee (Private).....3	

Basic Information/Demographic			
NO.	QUESTIONS AND FILTERS	RESPONSES	SKIPS
		Self-employed (with employees)..... 4 Self-employed (without employees)..... 5 Unpaid helper in family business..... 6 Not working (available for work)..... 7 Not working (not available for work)..... 8 Homemaker/Housewife/ House chores 9 Student..... 10 Unable to work (old/retired/sick)..... 11 Other (describe)..... 12 If Other describe→ _____	
4	Is this your first time to receive care from this mobile van?	Yes……0 No……..1	5
5	How many visits have you made to this mobile van in the past six months?	1 visit..... 0 2 visits..... 1 3 visits..... 2 4 or more visits..... 3	
6	For which specific maternal health services are you here for today? (mark all that apply)	Antenatal care..... 0 Childbirth..... 1 Postnatal care..... 2 Others..... 3 If other describe→ _____ If O indicate the number of the visit →_	

Time and Travel Costs			
NO.	QUESTIONS AND FILTERS	RESPONSES	SKIPS
7	How did you get here today? (mark all that apply)	No / Yes Walk ..... 0 1 Bicycle ..... 0 1 Bus or other public transport ..... 0 1 Private car or motorbike ..... 0 1 Other (describe) ..... 0 1 If other specify→ _____	
8	How much does it normally cost for transport to this place (one way), for yourself and anybody who normally comes with you?	☐☐☐☐☐☐ Shillings	
9	Do you come to this place and return home on the same day? If you stay overnight near the point where the mobile health van park, how much does it cost you for accommodation? [only record accommodation required for attending clinic]	Return home on same day ..... 0 Stay overnight ..... 1 If 1 → ☐☐☐☐☐☐ Shillings	
10	How long does it normally take you to get to where the mobile van park to deliver services (one way)?	☐☐ Hours ☐☐ Mins	
11	How long do you normally have to wait at the waiting area before your appointment?	Routine appt…… ☐☐ Hrs ☐☐ Mins ☐☐ ☐☐	

Time and Travel Costs			
NO.	QUESTIONS AND FILTERS	RESPONSES	SKIPS
		Emergency appt…... Hrs Mins Drug refill appt……. ☐☐ Hrs ☐☐ Mins	
12	How long does your appointment normally take? [Including all parts of clinic visit, e.g. doctor visit, counseling session, laboratory investigation sessions, pharmacy visit, if applicable]	Routine appt……..… ☐☐ Hrs ☐☐ Mins Emergency appt…... ☐☐ Hrs ☐☐ Mins Drug refill appt……. ☐☐ Hrs ☐☐ Mins	

Costs of Clinic Treatment			
NO.	QUESTIONS AND FILTERS	RESPONSES	SKIPS
13	Have you had to pay for any of the following services at this clinic (include any in-kind payments)?	<u>No</u> <u>Yes</u> Initial registration appt..... 0 1 Routine appt..... 0 1 Emergency appt..... 0 1 Laboratory tests..... 0 1 X-rays..... 0 1	

Costs of Clinic Treatment			
NO.	QUESTIONS AND FILTERS	RESPONSES	SKIPS
		Ultrasound……. 0 1	
14	[If 'Yes' to any of Q13] How much did you pay for each service, and how many times did you pay for this service in the past 2 months?	Initial registration apt ☐☐☐☐☐☐ Shillings, ☐☐ Times Routine appt ☐☐☐☐☐☐ Shillings, ☐☐ Times Emergency appt ☐☐☐☐☐☐ Shillings, ☐☐ Times Blood tests ☐☐☐☐☐☐ Shillings, ☐☐ Times X-rays/Ultrasound ☐☐☐☐☐☐ Shillings, ☐☐ Times	
15	Were there any other services you have had to pay for at this mobile van? [If YES] Please describe these services, how much you paid for each service, and how many times you paid for this service in the past 6 months.	Other 1:_____ ☐☐☐☐☐☐ Shillings, ☐☐ Times Other 2:_____	

Costs of Clinic Treatment			
NO.	QUESTIONS AND FILTERS	RESPONSES	SKIPS
		☐☐☐☐☐☐ Shillings, ☐☐ Times Other 3: _____ _____ ☐☐☐☐☐☐ Shillings, ☐☐ Times	
16	Have you had to pay for any drugs or other health supplies that were needed for your maternal care, or have you ever been given a prescription to go buy the drugs or other health supplies? [If YES] How much have you spent on these drugs or health supplies in the last 6 months?	No ..... 0 Yes ..... 1 If 1 → ☐☐☐☐☐☐ Shillings	
17	Have you made any informal payments to staff at this health van in order to receive treatment? [If YES] How much have you paid in the last 6 months (include value of in-kind payments)?	No ..... 0 Yes ..... 1 If 1 → ☐☐☐☐☐☐ Shillings Shillings	

Costs of Clinic Treatment			
NO.	QUESTIONS AND FILTERS	RESPONSES	SKIPS
18	Apart from the things we have discussed, are there any other costs you have had to pay in order to get services at this mobile van? (for example childcare, lost wages) [If YES] Please describe what the costs were for, how much you paid, and how many times you had to pay this in the last 6 months.	No ..... 0 Yes ..... 1 Other 1: _____ _____ ☐☐☐☐☐☐ Shillings, ☐☐ Times Other 2: _____ _____ ☐☐☐☐☐☐ Shillings, ☐☐ Times Other 3: _____ _____ ☐☐☐☐☐☐ Shillings, ☐☐ Times	

Costs as a Barrier to Care			
NO.	QUESTIONS AND FILTERS	RESPONSES	SKIPS
19	Have you ever missed a scheduled clinic appointment because you could not afford to pay for transport, childcare, or other costs?	No ..... 0 Yes 1	

Costs as a Barrier to Care			
NO.	QUESTIONS AND FILTERS	RESPONSES	SKIPS
20	If YES how often?	Very often ..... 0 Often ..... 1 Occasionally 2	
21	Have you ever wanted to come to the clinic for an unscheduled visit but could not come because of the cost?	No ..... 0 Yes 1	
22	If YES how often?	Very often ..... 0 Often ..... 1 Occasionally 2	

Time as a Barrier to Care			
NO.	QUESTIONS AND FILTERS	RESPONSES	SKIPS
23	Have you ever missed a scheduled clinic appointment because you did not have time?	No ..... 0 Yes 1	
24	If YES how many times in the past three visits?	More than twice ..... 0 Twice ..... 1 Once 2	
25	Have you ever wanted to come to the clinic for an unscheduled visit but could not come because of lack of time?	No ..... 0 Yes 1	
26	If YES how many times in the last three visits?	More than twice 0 Twice 1 Once 2	

***Cost to the Caregivers**			
NO.	QUESTIONS AND FILTERS	RESPONSES	SKIPS
27	Does anyone take care of you because of your **current condition**? If so who does that	Immediate f\member ..... 0 Distant relative..... 1 Maid\paid worker..... 2 Friend.....3 Neighbor…….. .. 4	
28	How long do they normally use taking care of you in a normal day?	Hours …… ☐☐	
29	Have you make any payments to these caregivers? [If YES] How much have you paid in the last 6 months (include value of in-kind payments)?	No..... 0 Yes..... 1 If 1 → ☐☐☐☐☐☐ Shillings	
30	Any suggestions about the cost of maternal health services?		
		End Time:	

Interviewer Comments:

"Thank you for taking part in this study."

Acknowledgement

Although it is just my name on the cover of this thesis, many amazing people have contributed to it in their own special way. I would like them to know that because of their support, encouragement and prayers I managed to reach where I am today. Till hell freezes over, I will hold dear my PhD experience and I will forever be indebted to all the wonderful people who made it possible.

My greatest gratitude goes to my supervisor, Univ. Prof. Dr.rer. pol. Jürgen Wasem; you created the invaluable space for me to do this research and developed myself as a researcher in the best possible way. I greatly appreciate the freedom you have given to me to find my own path and the guidance and the support you offered when needed. Alongside Jürgen, I received enormous technical supervision from Barbara, Anja and Antonius, whom over time I have come to regard them as my co supervisors. Your mix of straightforward criticism combined with heart-warming support has given me great confidence as a researcher. *Danke schön ihr Lieben!*

My studies were made possible by the generous financial support from the Katholischer Akademischer Ausländer-Dienst (KAAD). Your contribution made my vision a reality by offsetting the cost of studying for more than three years in a competent academic environment as this. The support I received from Dr Marko Kuhn, Frau Simone Saure and Frau Gisela Sahler will remain in my heart. Although I cannot thank them personally for privacy reasons, but for my research I am greatly indebted to all my study participants. Without your effort and willingness to take your time and respond to my questions I would have been nowhere. *Asanteni sana*!

Of course, I want to thank my mother, whose prayers and support never ceased, come rain come sun. *Wakondya muno!* To my sisters, Nyang'ubha, Bigeyo and Bhalende, to my brothers Mafuru, Wanjara, Mnubhi and Muyenjwa, the way you believed in me, made a huge difference. You continued to demonstrate to me that we will always be together through thick and thin. *I continue to ask you to please hold my hand forever*!

My life as a student in a foreign country was made easy by the enormous support and encouragement from my partner, Martin. You took the task of editing work, from the beginning to the end. I am truly indebted. Besides you were your parents, Manfred and Wera, who happily took the responsibility of becoming my German parents. *Ich sage Tausend Dank*!

And then, of course, big thanks to Neema, Theodora and Frida, my friends all the way back from the Medical School, and ever greater ones since. The way you encouraged me during each step of this journey will never be forgotten. I am also indebted for the continuous support I received from Mr John Changalucha, of the National Institute for Medical Research in Mwanza; my gratitude goes also to Susan and Dunstan, my dear friends for their encouragement and prayers. Above all, I thank my God, the author of my life, whose mighty hand made me complete this journey.

CURRICULUM VITAE

The biography is not included in the online version for reasons of data protection.