INTEGRATING POINT-OF-CARE TESTING (POCT) FOR HIV, SYPHILIS, MALARIA AND ANAEMIA INTO ANTENATAL CARE SERVICES AT DISPENSARIES IN WESTERN KENYA

Thesis submitted in accordance with the requirements of the Liverpool School of Tropical Medicine for the degree of Doctor in Philosophy

by Nicole Young

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Declaration

I hereby declare that this PhD thesis is a presentation of my original research work. Material contained herein has not been previously published, accepted or presented for the award of any University degree. Wherever contributions of others are involved, every effort has been made to indicate this clearly, with due acknowledgement to the relevant sections made in the thesis

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"Although we set out primarily to study reality, it does not follow that we do not wish to improve it; we should judge our researches to have no worth at all if they were to have only speculative interest. If we separate carefully the theoretical from the practical problems, it is not to neglect the latter, but on the contrary, to be in a better position to solve them"

- Emile Durkheim, The Division of Labour in Society

Abstract

HIV, syphilis, malaria, and anaemia are major causes of adverse pregnancy outcomes in sub-Saharan Africa (SSA). Despite global and national policies advocating for screening of these conditions, only HIV testing has achieved good coverage, precluding early detection and appropriate management in pregnancy. Rapid point-of-care tests (POCTs) provide an opportunity to integrate diagnosis and provide timely treatment of these conditions in rural antenatal care (ANC) settings.

After an introductory chapter, a review of the literature on these four conditions in pregnancy is presented with a focus on SSA. The thesis then shifts attention to Kenya, a country that embodies many of the disease challenges and health system characteristics of the region. Kenyan ANC policy recommends testing for HIV, syphilis and anaemia and preventive strategies for malaria. The following chapters are comprised of three linked studies conducted in western Kenya, that use different methods to progressively investigate the implementation success of integrated point-of-care testing (POCT) for HIV, syphilis, malaria and anaemia at seven peripheral dispensaries.

Baseline data confirmed that testing requirements for syphilis, malaria and anaemia are not currently met at dispensary level. We implemented an intervention where test kits were supplied and training plus supervision were provided to enable healthcare workers to conduct integrated POCT for pregnant women. Adoption and fidelity were measured quantitatively using exit interviews, antenatal registers and proficiency scores (Study 1: Integrating point-of-care testing (POCT) for HIV, syphilis, malaria and anaemia in antenatal care at dispensary level in western Kenya: an implementation study) while acceptability, appropriateness and feasibility were assessed qualitatively (Study 2: Exploring healthcare workers and pregnant women's perspectives on appropriateness, acceptability and feasibility of integrating point-of-care testing: A qualitative study). Our findings show that the innovation was highly adopted, meaning almost all pregnant women received the essential tests. This was supported by the qualitative findings where healthcare workers and pregnant women found the innovation acceptable and appropriate. However, fidelity to

clinical management guidelines can still be improved. Our qualitative findings provide some explanation for these gaps. One common sentiment among interviews with healthcare workers was that workload was perceived to be a barrier to providing quality care. We explored this further with discrete-event simulation modelling (Study 3: Investigating the operational impact of integrating HIV, syphilis, malaria and anaemia point-of-care testing in antenatal care clinics in western Kenya: a discrete event simulation model) and found the healthcare workers were actually under-utilized. This suggests that nurses should, in theory, have sufficient time to deliver essential ANC services. While integrating POCT addresses one gap, additional interventions to support and supervise healthcare workers are needed to ensure appropriate and high quality of care. An integrated approach to strengthening health system infrastructure and more investment in implementation and translation research using multi-methods are needed.

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List of acronyms

ACT	Artemisinin-based combination therapies
AL	artemether/lumefantrine
ANC	Antenatal care
ART	Antiretroviral therapy
ARV	Antiretroviral
CDC	Centers for Disease control
CFIR	Consolidated Framework for Implementation Research
CITC	Client Initiated Testing and Counselling
CO	Clinical officer
CSO	civil society organizations
CTX	cotrimoxazole
DES	Discrete event simulation
DHS	Demographic Health Survey
DOT	Directly observed treatment
DP	Dihydroartemisinin-piperaquine
FANC	Focused antenatal care
FBOs	Faith based organizations
FGDs	Focus group discussions
GDP	Gross Domestic Product
GHE	Government health expenditure
HAART	Highly active antiretroviral therapy
Hb	Haemoglobin
HDSS	Health and Demographic Surveillance System
HIV	Human Immunodeficiency virus
HRD	Human Resource Development
HRM	Human Resource Management
HTC	HIV testing counsellor
HTS	HIV Testing Services
ICAP	International Center for AIDS Care and Treatment Programs
ICC	Inter-agency coordinating committees
ICT	Information Communication Technology
IPTp	Intermittent preventive therapy in pregnancy
IQR	Interquartile range
ITN	Insecticide-treated nets
KEMRI	Kenya Medical Research Institute
KP	Known positives (for HIV)
LLIN	Long lasting insectide treated nets
LMP	Last menstrual period

LOS	Length-of-stay
M&E:	Monitoring and evaluation
MCH	Maternal and child health
MDGs	Millennium Development Goals
MU	Million units
NASCOP	National AIDS and STIs Control Programme
NMCP	National Malaria Control Programme
OECD	Organisation for Economic Co-operation and Development
OOP	Out-of-pocket
OP	Out-patient
OPD	Out-patient department
PEPFAR	President's Emergency Plan for AIDS Relief
PITC	Provider-initiated testing and counselling
PMTCT	Prevent mother-to-child transmission
POCT	Point-of-care testing
POCTs	Point-of-care tests
PRO	Public record office Resource Management
QA	Quality assessments
RDT	Rapid diagnostic test
RPR	Rapid plasma reagin test
SAGAS	Semi-autonomous government agencies
SCMD	Supply chain management division
SDG	Sustainable Development Goals
SP	Sulfadoxine-pyrimethamine
SSA	Sub-Saharan Africa
SSI	Semi-structured interviews
STI	Sexually transmitted infections
TB	Tuberculosis
THE	Total health expenditure
TWGs	Technical working groups
UNAIDS	The Joint United Nations Programme on HIV and AIDS
UNICEF	United Nations Children's Fund
USAID	US agency for international development
USD	US dollar
VDRL	Venereal Disease Research Laboratory
VIF	Variance inflation factor
WHO	World Health Organization

1 Chapter 1 Introduction to the Thesis

This chapter provides a brief background and justification of the thesis research, the research aims and objectives, my role and contribution, and lays out the contents of the thesis.

1.1 Background

1.2 Major diseases in pregnancy in sub-Saharan Africa (SSA)

In sub-Saharan Africa (SSA), HIV, syphilis, malaria and anaemia are leading causes of maternal mortality and adverse pregnancy outcomes:

1. Maternal HIV prevalence in SSA is estimated to be 5.3% (95% CI 4.2-6.6%), composing 92% of the world's HIV positive pregnant women [1, 2]. Roughly 24% of deaths in women during pregnancy or post-partum are attributable to untreated HIV [3]. Without antiretroviral therapy, risk of mother-to-child transmission cumulates over the gestation period which makes early detection and viral suppression critical [4].
2. The Africa region contains 63% of global syphilis infections in pregnancy, representing an estimated 1.68% maternal syphilis prevalence [5]. Syphilis is associated with spontaneous miscarriage, stillbirth, preterm birth, low birthweight, neonatal death, and congenital infection in infants [6]. The duration of exposure in utero is a major determinant of foetal transmission and late treatment may be too late to reverse damage to foetal development caused by the bacterium [7].
3. In malaria endemic regions, 45% of pregnancies that arise would experience malaria infection without preventive measures [8]. From early to late pregnancy, malaria infections are associated with anaemia, intrauterine growth restriction, preterm delivery, foetal loss, neonatal and infant mortality [9].

Africa has the world's highest prevalence of anaemia: among pregnant women, it is estimated that 46.3% (95% CI 40.6-51.0%) are anaemic and 1.5% (95% CI 1.0-2.3%) are severely anaemic in 2011 [10]. Anaemia during pregnancy causes fatigue and is

associated with increased risk of maternal mortality, low birth weight, and perinatal mortality [11]. There is also substantial evidence that maternal iron deficiency early in pregnancy (first and second trimester) contributes to higher risk of pre-term delivery and low-birth weight than if it occurred later [12].

4. These conditions do not exist in isolation [13-19]: malaria is more common in women with HIV [20]; risk of HIV transmission is increased through genital ulcer disease, including syphilis [21]; malaria is both associated with HIV [16, 20] and a major risk factor for anaemia [22, 23]. Approximately 26% of severe anaemia in pregnant women is attributable to malaria [24].

Because the risks of HIV, syphilis, malaria and anaemia cumulates with exposure over the gestation period and their propensities of co-occurring, addressing these conditions together, as early as possible during pregnancy is an essential goal of antenatal care (ANC) [25].

1.2.1 Antenatal care and integrated service delivery

World Health Organization (WHO) global antenatal guidelines require testing for HIV, syphilis, and anaemia at the first ANC contact which should occur early in the first trimester [26]. For malaria, in areas of stable transmission, intermittent preventive therapy with sulfadoxine-pyrimethamine (IPTp-SP) and the use of insecticide-treated bednets (ITNs) together with effective case management of clinical malaria is the current strategy [26]. There is currently no recommendation for screening the blood for parasites for women not presenting with symptoms. The exception is Tanzania, who recently introduced malaria testing as a strategy to manage anaemia at first visits into their antenatal guideline [27].

In practice, antenatal testing, treatment and preventive strategies to protect pregnant women against these conditions are poorly implemented and coverage rates are suboptimal despite approximately 70% of pregnancies in SSA having contact with the healthcare system through ANC [28].

1.2.2 Integrated point-of-care diagnostic testing

An integrated approach to ANC service delivery to address the multiple health needs and infections in pregnancy is recommended [29, 30]. The concept of 'integration' refers to "the organization and management of health services so that people get the care they need, when they need it, in ways that are user-friendly, achieve the desired results and provide value for money"[30]. One barrier to effective coverage of antenatal testing is the disintegration of care: women need to attend multiple clinics in different locations on separate occasions because many facilities lack testing equipment and women need to be referred to more distant facilities with laboratories for testing [31-33]. A potential solution to address this could be availing simple-to-use rapid diagnostic point-of-care tests (POCTs) at close-to-community facilities. They add minimal workload on the healthcare workforce, can simplify the diagnostic process, and can reduce the cost for pregnant women because they no longer need to wait long for test results or to be referred for testing elsewhere. Their simplicity and immediacy of results can greatly benefit resource-constrained settings by improving early diagnosis and allowing same-day management of conditions and their co-infections.

1.3 Rationale for the study

The promise of evidence-based practices may not always translate to implementation success [34]. Over the last 2 decades, researchers are increasingly recognizing the crucial role of implementation research "to promote the systematic uptake of research findings and other evidence-based practices, and hence, to improve the quality and effectiveness of health services and care" [35]. Rural facilities in low-resource settings are usually understaffed [36], and overstretched healthcare workers may not readily adopt or comply with an innovation when introduced. Data are required to understand whether an integrated testing strategy is an acceptable, appropriate, and a feasible service delivery approach to healthcare workers and pregnant women. This implementation research aims to addresses this gap in western Kenya.

Kenya is a country that embodies many of the disease challenges and health system characteristics of the SSA region and that is why this country was chosen to introduce and evaluate an integrated testing strategy for HIV, syphilis, malaria and anaemia.

1.4 Aims and Objectives

Aim: We aim to investigate the implementation outcomes and operational impact on service delivery of an integrated testing strategy for HIV, syphilis, malaria and anaemia for antenatal care in peripheral facilities in western Kenya.

Objectives:

1) To determine the proportion of pregnant women who receive all four tests at a single visit (adoption) and the proportion of pregnant women who receive treatment, advice or referral appropriate for the test result (fidelity).

2) To evaluate end-user (healthcare workers and pregnant women) perceptions of acceptability, appropriateness and feasibility of integrated POCT for HIV, syphilis, malaria and anaemia.

3) To explore the operational impact (patient wait times and nurse utilizations) of integrated POCT on service delivery in the facilities.

1.5 Description of the intervention

The research intervention was the provision all four tests together, by a single healthcare worker at one service delivery point, during a woman's first ANC visit (Figure 1.1). All the facilities' healthcare workers who see ANC women were trained either at a central location or on-site. All trainees received training manuals and visual aid testing placemats with step-by-step instructions (Appendix 1 Integration operating procedure placemat. Training included using one finger-prick blood draw to run all four tests concurrently per standard operating procedures, safety, and appropriate preventive care and clinical management of positive results following Kenyan guidelines. Study facilities used existing HIV drugs and HIV POCTs supplied by the Government of Kenya per its standard national algorithm at the time: HIV (1+2)

Antibody Colloidal Gold (KHB, Shanghai Kehua Bio-engineering Co Ltd, China) for screening, First Response HIV-1-2 kits (Premier Medical Corporation Ltd., Kachigam, India) for confirmation and Uni-Gold™ (Trinity Biotech, Ireland) for tie-breaking. Other drugs provided by the government for free antenatal care were iron, folic acid, SP and malaria treatment drugs. The research team supplied the facilities with sufficient stocks of rapid tests for syphilis (SD BIOLINE Syphilis 3.0 test for antibodies against Treponema pallidum, Standard Diagnostic Inc., Korea), malaria (CareStart™ Malaria HRP2 Pf, AccessBio, USA) and haemoglobin concentrations (HemoCue® Hb 201+, HemoCue AB, Sweden). Batteries were also supplied for HemoCue®. Lot validation was done at Kenya Medical Research Institute and Centers for Disease Control and Prevention's (KEMRI/CDC) reference laboratory in Kisumu by randomly selecting 1% of tests per lot and testing them against known positive and negative samples. HemoCue® machines were collected from the facilities and calibrated every three months at the same laboratory in Kisumu. The research team provided the facilities with digital Brannan™ triple timers, gloves, and benzathine penicillin for treating syphilis based on projected prevalence of syphilis in the area.

Figure 1.1: Healthcare workers using the integrated placemat to test pregnant women during antenatal care visits

1.6 Descriptions of research site

The intervention was implemented within the research collaboration site of Kenya Medical Research Institute (KEMRI) and United States' Centers for Disease Control and Prevention (CDC) in Siaya County, western Kenya **(Figure 1.2)**. This international

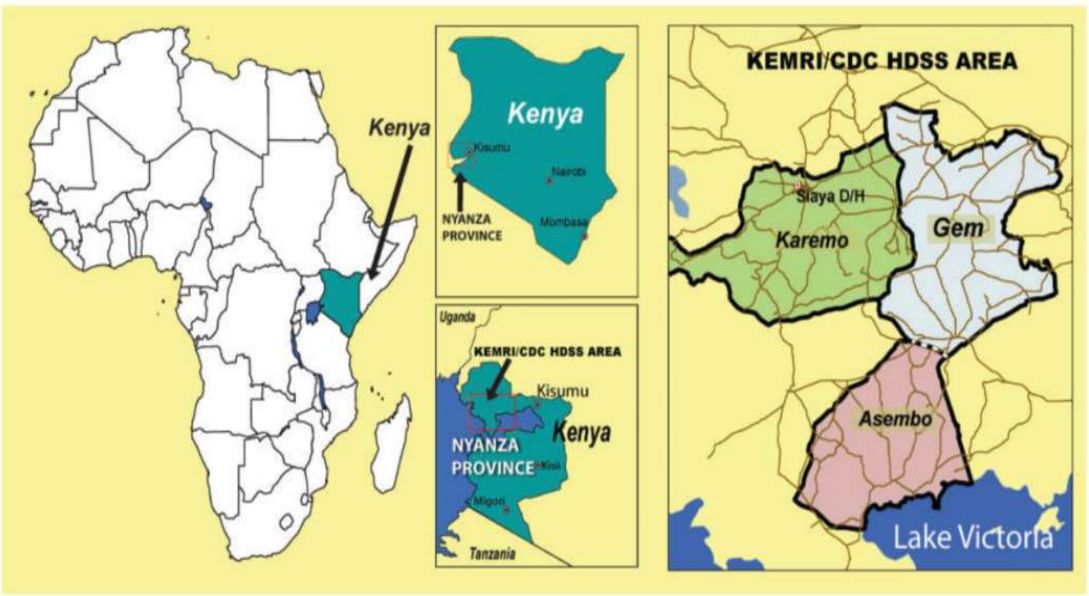
collaboration started in 1979 and in 1996, a Health and Demographic Surveillance System (HDSS) was created to collect longitudinal population-based demographic data on disease and health service access for on-going surveillance after a large insecticide treated bed-net trial for malaria. This infrastructure provided an important backdrop for many health interventions studies who can take advantage of its robust sampling frame, and comprehensive multi-level data. The study site is situated northeast of Lake Victoria and the population is 95% ethnically Luo, mostly lives in rural villages through subsistence farming, fishing and local trading. Villages are made of sparsely spaced compounds interspersed with farmlands and streams. The Luo are polygamous: each compound has an average of 4 houses consisting of one for the male head and others for his wives and children. Houses are simple, made of mud, brick or cement with iron sheet or papyrus grass roofs. Most of them do not have electricity or running water. Many of the men work outside the village grounds during the day and return in the evening or weekends. Women work in the fields growing food for subsistence around the home. Sources of income include farming, fishing and small business [37].

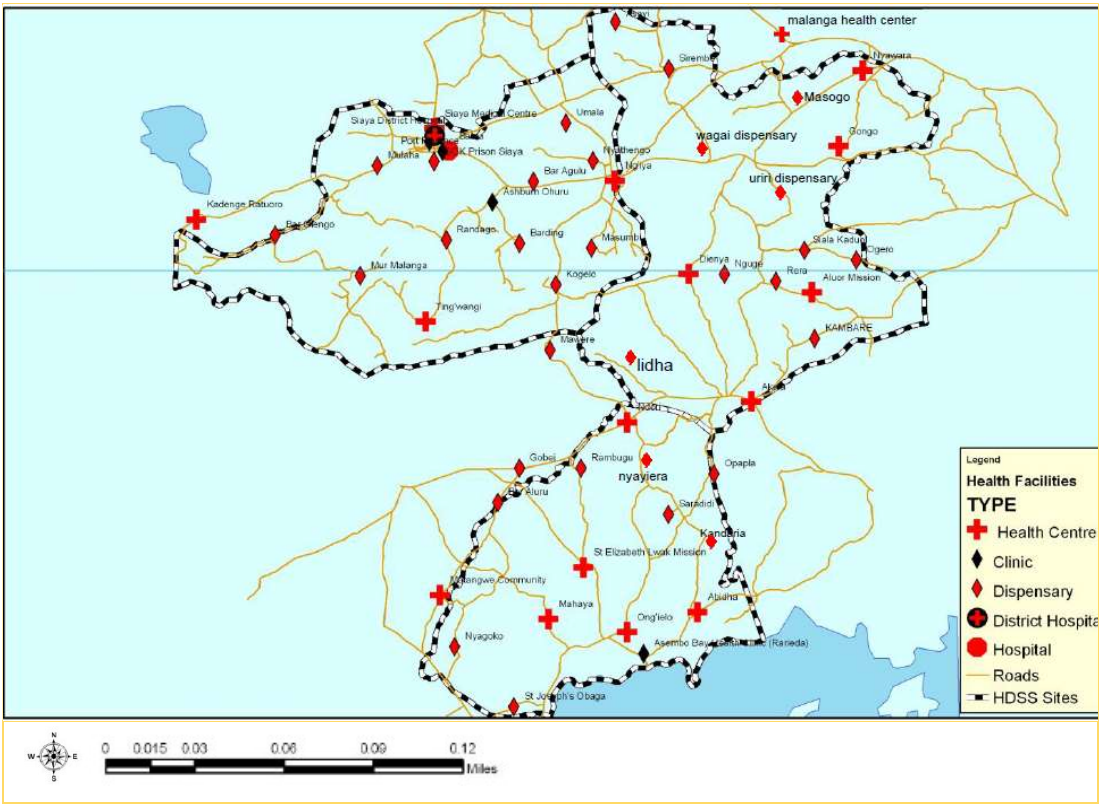
At the time of the study, there were 37 public facilities in the study area: one district hospital, nine health centres and 27 dispensaries. Dispensaries comprise the lowest level (tier-2) of the formal health system and offer basic maternal and child health services, rudimentary out-patient curative care and support care for HIV positive patients. They are usually staffed by two nurses who are trained to either certificate (30 months post-secondary training) or diploma (36 months post-secondary training) level, and a part-time clinical officer (36 months post-secondary training). On days when there are at least two nurses working, one nurse would attend to out-patients while the other attends to women and children who seek maternal and child health services. The clinical officer typically oversees HIV positive patients seeking antiretroviral therapy. Dispensaries are small so task shifting often happens among nurses and clinical offers and when any skilled healthcare workers are absent, the others would take on the patient load. There are also sub-ordinate staff who help with weighing, dispensing drugs, and registration. Some dispensaries also have HIV testing counsellors (HTC) who are trained specifically to do HIV testing and

counselling and link test positives to antiretroviral therapy (ART) and care. In Siaya county, within the Nyanza region, prevention of mother-to-child transmission (PMTCT) services are integrated within antenatal care. The implementation partner in this region during the time of this research was the International Center for AIDS Care and Treatment Programs (ICAP) at Columbia University's Mailman School of Public Health. They provide training, and supervision for PMTCT activities at health facilities in Nyanza. They also train and support the lay HTCs. ICAP began implementing Option B+ (providing lifelong comprehensive ART to HIV pregnant women regardless of CD4 count) in 2014 [38].

HIV and malaria programmes are supported by external funding sources and implementation partners so supplies and commodities for these programmes have their own procurement systems to reduce stock-outs. For other drugs and non-pharmaceuticals, dispensaries are given a budget and an item list with corresponding prices to order from by the county. Additionally, they are given a small budget for facility maintenance such as paying for electricity and subordinate staff.

Figure 1.2: KEMRI and CDC Health and Demographic Surveillance System (HDSS) in Siaya County, western Kenya [37]





1.7 Thesis outline

The thesis is presented in the format of three linked studies which are preluded by an introduction to the overall thesis, a literature review and concluded with a discussion that synthesized the overall findings.

Chapter 1 Introduction is a general introduction of the thesis which includes a brief background on major diseases in pregnancy and antenatal care, rationale for conducting the research, research aims and objectives, description of the intervention, information about the research site, and summary of the three studies.

Chapter 2 Literature review discusses the literature and outlines the burden of disease of HIV, syphilis, malaria and anaemia in pregnancy, importance of early testing and treatment and global antenatal strategies. It describes the gaps in coverage of interventions to protect pregnant women against these conditions and their corresponding barriers and enablers. Then it discusses the use of POCTs in resource-poor contexts as a suitable innovation to reduce the coverage gap and available evidence on combining multiple POCTs into ANC is also presented. Introducing new approaches within existing systems can be challenging and a review

of relevant conceptual frameworks that help frame implementation science and innovation diffusion from a health system perspective is also presented. The chapter then focuses on Kenya, a country that embodies many of the disease challenges and health system characteristics of the region. It describes Kenyan ANC policy, the Kenyan health system structure, and gaps in ANC policy implementation.

1.7.1 Three studies that investigate implementation using three different methods

Three studies were conducted to investigate implementation outcomes and service delivery impact of the intervention. Findings from one study were used to inform and build the next study.

Chapter 3 (study 1) Integrating point-of-care testing (POCT) for HIV, syphilis, malaria and anaemia in antenatal care at dispensary level in western Kenya: an implementation study. Introduction of new diagnostic approaches or technologies has the potential to improve uptake of testing and management of pregnant women visiting antenatal care but implementation success can vary. This study describes the intervention and evaluates the *adoption* (proportion of women receiving all four tests) and *fidelity* (proportion of women receiving appropriate advice and treatment for the four conditions based on test results) of the integrated strategy. Details of the intervention and measurements of implementation outcomes are described in the chapter's methods. The study found that integrating POCTs into ANC at dispensaries with established HIV testing programmes resulted in a significant increase in testing rates, without disturbing HIV testing rates. While more cases were detected and treated, treatment fidelity still requires strengthening and an integrated monitoring and evaluation system needs to be established.

Chapter 4 (study 2) Exploring healthcare workers and pregnant women's perspectives on appropriateness, acceptability and feasibility of integrating point-of-care testing: A qualitative study. Fundamental to the uptake of and adherence to new diagnostic approaches are healthcare workers' and pregnant women's buy-in and their willingness to adopt the tests into their everyday practice. The study 1 found high rates of adoption but sub-optimal fidelity. This study evaluates end-user perceptions

of acceptability, appropriateness and feasibility of the integrated testing strategy using qualitative methods that capture more textured layers of experiences in order to further understand the adoption and fidelity outcomes. Details of the qualitative approach used are given in the methods. The study found that healthcare workers and pregnant women thought the innovation was desirable and beneficial, but general health system weaknesses such as workload, stock-outs and poor working conditions challenged the delivery of quality ANC services and the effective management of the four conditions.

Chapter 5 (study 3) Investigating the operational impact of integrating HIV, syphilis, malaria and anaemia point-of-care testing in antenatal care clinics in western Kenya: a discrete-event simulation model. Availing POCTs at peripheral dispensaries has the potential to improve access to essential services but could over-stretch systems that are usually burdened with human resource shortages and long queues. Our qualitative findings show that workload was perceived to be one of the major barriers to providing quality health services. This study applied discrete-event simulation (DES) modelling using detailed time-motion data to explore the impacts of integrating POCTs on wait times and resource utilization in ANC clinics in western Kenya. The study found that delivering integrated POCTs had minimal impact on wait times for the majority of women, while ensuring they received essential diagnostics for timely treatment. We also found that nurses should have sufficient time to deliver WHO's required ANC activities. Resource neutral strategies should be explored to improve staff availability, for example through minimising off-site trainings. More frequent supervision and audit feedback could help with ensuring essential services are performed.

Chapter 6 Discussion summarises the main findings of all the chapters. It then draws important insights from these findings, and discusses their implications for health systems. It reflects on study strengths and limitations and gives recommendations for the future.

Chapter 7 Appendices: supporting materials are provided in the appendices:

Appendix 1	Testing placemat
Appendix 2	Proficiency observation checklist (chapter 3)
Appendix 3	Focus group discussion guide with pregnant women (chapter 4)
Appendix 4	Semi-structured interview guide with healthcare workers (chapter 4)
Appendix 5	Sample time-motion data collection form (chapter 5)
Appendix 6	Dispensary patient pathways for women seeking maternal and child health services (chapter 5)
Appendix 7	Screenshot of DES modelling in WITNESS© (chapter 5)

1.8 Role in research

The idea of using POCTs for an integrated testing approach for ANC at rural dispensaries in Kenya was conceived by Dr. Miriam Taegtmeyer. Dr. Taegtmeyer spent considerable time at health facilities in Kenya and observed that the coverages of testing for HIV, syphilis, malaria and anaemia were variable and sub-optimal. While the use of HIV POCTs has improved access and coverage of HIV testing, syphilis, malaria and anaemia testing still relied on laboratory-based methods. She observed that even at facilities with laboratories, women would receive testing at separate service locations and given multiple finger-pricks. Separate vertical disease control policies and implementation mechanisms were partly responsible for the disintegration of care and there were no national programmes that enforced testing and quality control for all four conditions. To address this vital gap in antenatal care, Dr. Taegtmeyer and colleagues wrote a proposal for the "*Scale up of integrated antenatal interventions in resource-limited settings using quality-assured point-of-care testing for the diagnosis of infections and anaemia*" in response to the FP 7-Health 2011 3.4-1 call from the European Commission for the "*Development and assessment of comprehensive and integrated interventions and programmes to improve reproductive health and health equity*". While the proposal was not funded by the European Commission, the project aim was deemed suitable for USAID's Global Health Initiative (GHI) objectives in Siaya Country, Kenya to "*Evaluate the impact of interventions to address determinants of maternal and child health*". The intervention was invited to be implemented in the HDSS area with KEMRI/CDC and

the Liverpool School of Tropical Medicine. This opportunity met well with my background and interests to strengthen health systems for women and vulnerable populations in low resource settings and so I was chosen to lead the study and adapt the intervention to the local settings. After conducting a baseline assessment in health facilities in the study area, I designed the three implementation studies to evaluate the impact of the integrated point-of-care testing strategy on health service delivery. As project lead, I oversaw all study activities: directing USAID/CDC funded budget of US $250,000, institutional review board (IRB) processes, liaising with Ministry of Health for effective community entry, organizing and designing the training of healthcare workers, creating the quality assurance tools, design of training and data collection tools, procuring study materials, training data collectors, managing database, cleaning the data, analysing the data and writing the first draft of manuscripts. A data manager helped with creating scannable data collection forms (Teleforms©), scanning them into the data base and exporting the data into excel. Garazi Zulaika, a co-author of the third study (chapter 5), helped with some of the cleaning of time-motion data.

I am the first and corresponding author for all three manuscripts and drove the process for co-authors, institutional (KEMRI and CDC) and peer reviews. At the time of this thesis submission, the first manuscript (chapter 3) has been published with Plos One. The second manuscript (chapter 4) has been recommended for acceptance after minor revisions with BMC Health Services Research. The third manuscript has been peer reviewed with CDC and KEMRI and approved for journal submission. Full author contributions are given in the beginning of each study (chapter 3-5).

1.8.1 Positionality statement

Reflexivity is particularly valuable to the research process, especially in qualitative research so as to acknowledge how the researchers' personal experiences and biases may influence the research process and interpretation of data.

I have always been curious about the natural world such as the nature of inequality, the processes that shape society and the interactions with the environment that

influence health and well-being. In my social epidemiology course with Harvard professor Ichiri Kwachi during my Masters in Public Health, I came upon French sociologist Emile Durkheim's The Division of Labour in Society in which he writes: "Although we set out primarily to study reality, it does not follow that we do not wish to improve it; we should judge our researches to have no worth at all if they were to have only speculative interest. If we separate carefully the theoretical from the practical problems, it is not to neglect the latter, but on the contrary, to be in a better position to solve them". This inspired my interest in implementation work and the translation of our research endeavours into practical solutions to better the human condition.

I grew up in a multi-cultural environment. My parents are from Hong Kong and we spoke Cantonese at home. We emigrated to Canada when I was five where I learned English and became acquainted with western culture. After five years, we moved back to Hong Kong where I lived until I attended university in the USA. Growing up, I had to navigate two diametrically different cultures that has forced me to be more reflective towards different archetypes and worldviews. After university, I spent two years in the Sahara Desert of Morocco as a Peace Corps volunteer where I learned Moroccan Arabic and the Berber language of Tamazight. I worked at the town birthing clinic with healthcare workers and lived with host-country nationals. I hope these experiences have given me closer insight to low-resource environments and helped shed biases and prior-assumptions during the research process.

As this was a small study, with limited budget, I was heavily involved with field work including introducing the study to the various county health management teams and health facilities, visiting and observing facility activities, building relationships with healthcare workers, and with training and supervision of the intervention. This gave me a dual role as implementor of the intervention and as researcher trying to understand its implementation feasibility. On one hand the role as implementor gave me great insight into the implementation environment and personalised healthcare workers' experiences. It also humanized the research process. This may have led me to sympathize with healthcare workers and adopt some of their frustrations with the

healthcare system. It helped to speak with others outside the research for a broader and more objective perspective. Other Kenyan colleagues were also involved with training and quality assurance procedures and group discussions with other implementors were helpful to gain different perspectives and avoid biases. As non-Kenyan and Chinese female visiting rural areas where there is very little cultural diversity, I am aware how I would be seen as an outsider which could influence behaviour and expectations. I tried to take a back-seat approach to so that participants (healthcare workers) can feel more autonomous. I also worked closely with Kenyan colleagues so participants can see the project as a collaboration. Qualitative interview guides were developed closely with Kenyan researchers from the Nyanza area to ensure they were locally adapted and appropriate. Interviews with healthcare workers and discussions with pregnant were also led by Kenyan researchers to maximize comfort and willingness to share personal experiences. Transcripts were also interpreted together with Kenyan researchers to reduce misunderstandings and biases.

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2 Chapter 2 Literature review

This chapter presents an overview of HIV, syphilis, malaria and anaemia in pregnancy with a focus on sub-Saharan Africa (SSA). It describes the current burden of disease, importance of early testing and treatment, and present-day global antenatal guidelines. It highlights the gaps in coverage and reviews the barriers and enablers to achieving high coverage of HIV, syphilis, malaria and anaemia interventions. Then it discusses the use of point-of-care tests (POCTs) in resource-poor contexts as a suitable innovation to close the coverage gap and available evidence on combining point-of-care tests into antenatal care is presented. Introducing new approaches within existing systems can be challenging and the chapter reviews several conceptual frameworks that help frame implementation and innovation adoption in health systems. The field research was conducted in Kenya and the final section details antenatal care in the Kenyan context.

Box 2.1. Search terms

Literature searches were conducted using Google, Google Scholar, PubMed and MEDLINE. Published papers from peer reviewed journals as well as grey literature including policy documents, reports by WHO and non-government organization (NGO) research groups, and national guidelines were identified. The bibliographies of relevant papers and reports found during the search were also reviewed. HIV was searched together with PMTCT [e.g. “HIV” OR “PMTCT”] and the syphilis was searched with congenital syphilis [e.g. “syphilis” OR “congenital syphilis”]. Search strings used for the various sections are as follows:

Section 2.2 Burden and aetiology of disease

Burden of disease in sub-Saharan Africa were mostly obtained from global reports. Databases were also searched with the conditions and the terms [“prevalence” OR “burden of disease” OR “epidemiology” OR “*etiology” OR “infection” OR “co-infection”] AND [“pregnan*” OR “antenatal”] AND “Africa”.

Section 2.3 Coverage of testing and treatment

Coverage rates of testing, treatment or prevention for HIV, syphilis, malaria and anaemia were mainly obtained from global reports. Databases were searched with the conditions and terms [“uptake” OR “coverage” OR “utilisation”] AND [“test*” OR “screen*” OR “treatment” OR “prevent*”] AND [“pregnan*” OR “antenatal”] AND “Africa”. Malaria was also further

searched with [“uptake” OR “coverage” OR “accept*” OR “utilisation”] AND [“pregnan*” OR “antenatal”] AND [“intermittent preventive treatment” OR “sulfadoxine pyrimethamine” OR “bednet”].

Section 2.4 Barriers and enablers to coverage of testing and treatment

[“Barriers” OR “challenges” OR “enablers” OR “facilitators” OR “factors”] AND [“antenatal attendance” OR “antenatal access” OR “test*” or “screen*” OR “treatment” OR “prevention”] AND [“pregnan*” OR “antenatal”] AND “Africa”. Malaria was further searched with [“Barriers” OR “challenges” OR “enablers” OR “facilitators” OR “factors”] AND [“pregnan*” OR “antenatal”] AND [“intermittent preventive treatment” OR “sulfadoxine pyrimethamine” OR “bednet”].

Section 2.5 Point-of-care tests

Each of the conditions were searched with [“diagnostic” OR “point-of-care test*” OR “RDT” OR “rapid test” OR “blood test*”] AND [“pregnan*” OR “antenatal” OR “antenatal care” OR “ANC” OR “integration”].

Section 2.6 Implementation science and operational research

For background and frameworks on implementation, databases were searched with [“implementation research” OR “implementation science” OR “implementation” OR “implementation outcome”] AND [“models” OR “theories” OR “conceptual framework” OR “framework” OR “methods”]. For background on operational research, databases were searched with “operation* research” AND [“methods” OR “application”] AND [“health* services” OR “health”].

Section 2.7 Kenya

Kenya national guidelines, national reports, government websites and reports from non-government organizations were consulted for background on health burden and health system in Kenya. Further searches were done in databases with search string used in section 2.2 and “Kenya”.

2.1 Maternal health a key development goal in sub-Sahara Africa (SSA)

Today, approximately 10% of the world live in extreme poverty with less than US $1.90 per day, improving drastically from 35% in 1990. However, much of this progress has been driven by recent economic developments in China and Indonesia, leaving half of the extreme poor in SSA [1]. The inequality gap is drastic: in 2014, Gross Domestic Product (GDP) and health spending per capita was US $36,741 and $4,739 per annum among OECD[1] countries compared to just $1,450 and $98 in SSA countries [2]. Economic deprivation translates to lower life-expectancy and quality of life.

In 2000, 191-member states of the United Nations met to establish global targets for improving the health and livelihood of those in the world's poorest countries. Eight Millennium Development Goals (MDGs) were established, of which two centred on maternal and child health and one on combating HIV, malaria and other diseases. By 2015, SSA achieved 52% reduction in child mortality, 49% reduction in maternal mortality, 51% reduction in new HIV infections, and 69% reduction in malaria mortality among under-5 age group [3]. However, many MDG targets were still underachieved and necessitated a new global effort to advance human development. A new set of 17 Sustainable Development Goals (SDGs) were created with health occupying a central focus [4]. The SDG effort emphasizes sustainability and recognizes that integrated and system wide collaborations are needed to avoid fragmentation and duplication of effort that was believed to have limited the MDG endeavour **(Table 2.1)** [4]. Women and children are key populations across multiple goals as they are especially vulnerable due to the sensitive course of pregnancy, dependency during the early years of an infant's life, and long term developmental consequences acquired during this period.

[1] OECD: The Organisation for Economic Co-operation and Development, an intergovernmental economic group of 35 high-income countries founded in 1961.

Table 2.1: Disease burden and maternal and child health indicators in sub-Saharan Africa: current indicators and 2030 goals		
MDG Indicator	2015 burden in SSA	SDG goals for 2030 [4]
Maternal mortality	546 per 100,000 live births [5]	Reduce global maternal mortality ratio to less than 70 per 100,000 live births
Neonatal mortality	29 per 1000 live births [6]	Reduce neonatal mortality to 12 per 1000 live births
Under-5 mortality	83 per 1000 live births [6]	Reduce under-5 mortality to 25 per 1000 live births
HIV, TB, malaria [4]	2.6 new HIV infections per 1000 uninfected* 281 new TB cases per 100,000 population* 246 new malaria cases per 1000 persons at risk	End the epidemics of AIDS, TB, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases
*2014 data for WHO Africa region		

2.2 Burden and aetiology of major diseases in pregnancy in sub-Saharan Africa

Fertility rate in SSA is high with about 4.8 births per woman, compared to 1.7 in high income countries (2016 data) [2]. This means women in SSA may spend several years in pregnancy, rendering them especially vulnerable to the risks of adverse pregnancy and child health outcomes. In fact, the region carries the world's greatest burden of maternal and child deaths [4] as well as the greatest disease burden of HIV, syphilis, malaria and anaemia [3]. They and their co-occurrences are some of the area's major contributors to poor maternal and child health [4, 7, 8]. The following sections describe the burden and aetiology of these diseases and conditions in pregnancy.

2.2.1 HIV in pregnancy

Sub-Saharan Africa is home to 92% of the world's HIV positive pregnant women and the maternal HIV prevalence is estimated to be 5.3% (95% CI 4.2-6.6%) [9, 10]. Women with untreated HIV infection are 8 times more likely to die during pregnancy or post-partum and roughly 24% of deaths in women during this period are attributable to untreated HIV [11].The risk of transmitting the virus to the baby varies over the gestation period

with the highest risk during delivery (10-20%) and breastfeeding (10-20%), followed by the intrauterine period (5-10%) [12]. Without antiretroviral therapy, the risk cumulates with length of exposure and reaches 25-45% over the whole intrauterine, intrapartum and breastfeeding periods [12]. In addition, high maternal plasma viral load is a key determinant for transmission [12]. This makes early detection and viral suppression a key strategy in reducing HIV exposure and vertical transmission. Testing is therefore recommended at the first contact with ANC in the first trimester (Figure 2.1).

2.2.2 Syphilis

Maternal syphilis prevalence in the African region is estimated to be 1.68%, representing 63.1% of global syphilis infections in pregnancy in 2012 [7]. Syphilis, caused by the bacteria *Treponema pallidum* is sexually transmitted disease that can also be passed vertically from mother-to-child. The disease has 4 stages (primary, secondary, latent and tertiary) with different symptoms and characteristics at each stage.[13]. Most syphilis infections are latent and asymptomatic but can still contribute to substantial adverse pregnancy outcomes [7]. A mother with untreated syphilis risks vertical transmission to the foetus which occurs through haematogenous spread: 70-100% for primary syphilis, 40% for early latent syphilis (latent syphilis occurring before 1 year of infection) and 10% for late latent syphilis (latent syphilis occurring after 1 year of infection) [13]. Thus, the newly infected are the most infectious and the longer the lag between initial infection and pregnancy, the less likely the foetus will be affected: most infants born to women with late latent syphilis are uninfected [13-15].

The stage of maternal syphilis and the duration of exposure in utero affect the probability of foetal transmission [15]. Early in pregnancy, the foetus is protected because syphilis spirochaetes cannot penetrate the placental barrier[15]. The foetus becomes vulnerable from 9-14 weeks onwards and accumulates infection risk over time with most infections occurring after the 6^{th} month [14, 16]. Thus, the earlier the treatment the more effective it is against congenital disease. Although later treatment will cure the infection, it may be too late to reverse damages of foetal development

caused by the disease. Therefore, it is important to test in the first trimester at the first contact with ANC (Figure 2.1).

Syphilis-associated adverse pregnancy outcomes include spontaneous miscarriage, stillbirth, preterm birth, low birthweight, neonatal death, and congenital infection in infants. Congenital syphilis has been estimated to occur in 15% of sero-reactive mothers [17].

2.2.3 Malaria

In malaria endemic regions, about 27.6 million pregnancies arise that result in live births annually and 45% of these pregnancies would experience malaria infection [18, 19]. Reviews of studies that have reported on the prevalence of peripheral and placental parasitaemia in Africa estimates that approximately 1 in 4 have evidence of infection at the time of delivery [19]. Malaria infection is defined by the presence of *Plasmodium falciparum* parasites in the blood and has a very unique epidemiological profile in pregnancy. First, pregnant women are more likely to be infected than non-pregnant women and men [19-21]. Second, the manifestation of infection differs geographically: in high transmission areas, where most adults have acquired immunity, infections are rarely symptomatic, thus eluding clinical detection and treatment [19]. Third, primigravidae and secundigravidae are more predisposed than multigravidae in high transmission areas whereas this relationship becomes more tenuous in unstable or epidemic areas [19-21]. Fourth, young maternal age is an independent risk factor for malaria in pregnancy and this may interact with gravidity to produce more severe infections [19]. Fifth, there is evidence that the prevalence of parasite changes during a woman's pregnancy with peak prevalence occurring at the second trimester and decrease with gestation [20]. Malaria parasitic infection during pregnancy is associated with severe anaemia, intrauterine growth restriction, preterm delivery, neonatal and infant mortality [18-22].

2.2.4 Anaemia

Africa region has the highest prevalence of anaemia [8] and among pregnant women it is estimated that 46.3% (95% CI 40.6-51.0%) are anaemic and 1.5% (95% CI 1.0-2.3%) are severely anaemic in 2011 [23]. It occurs when there are low concentrations of haemoglobin in the blood which can be caused by infectious diseases, nutrition and genetics [8]. The condition is also socially patterned and affects those with low socioeconomic status, poor education and rural residence more [8]. About 50% of anaemia cases are due to iron deficiency [23]. Haemoglobin concentrations drop naturally during pregnancy because of physiological changes and the large amounts of iron needed to support placenta and foetal growth. Haemoglobin concentrations drop 1-2 g/dL by late second trimester before re-stabilizing in the third trimester [24].

Anaemia during pregnancy causes fatigue and is associated with low-birth weight, pre-term birth and maternal mortality [8, 25]. There is substantial evidence that maternal iron deficiency early in pregnancy (first and second trimester) contributes to higher risk of pre-term delivery and low-birth weight than if iron deficiency occurred in the third trimester [26]. It is therefore important to ensure iron is supplemented early in pregnancy. Daily iron supplements during the antenatal period increases haemoglobin levels in maternal blood and reduces the likelihood of iron-deficiency anaemia at term [27]. It is estimated that about half of the anaemia found in pregnant women can be improved by iron supplementation; however, this may vary by location and lower in areas with higher proportions of malaria induced anaemia [23, 27].

2.2.5 Co-occurrence of illnesses

HIV, syphilis, malaria and anaemia do not exist in isolation and often overlap in pregnant women [28-34]; having one disease or condition may also be a risk factor for another. Malaria is more common in women with HIV [31]; one study estimated that in places with high *Plasmodium falciparum* parasite rates, the odds of acquiring HIV increase by 2.44 (95% CI 1.85–3.21) for women [35]. Risk of HIV transmission is increased through

genital ulcer disease and the odds of having HIV is 3.3-fold higher in women presenting with syphilis [36]. Malaria is a major risk factor for anaemia [37, 38]. It is estimated that 26% of severe anaemia in pregnant women is attributable to malaria and successful prevention of *Plasmodium falciparum* infection in pregnancy can reduce severe maternal anaemia by 38% [19]. Because of their individual and combined contribution to illness, interventions on their prevention and treatment in antenatal care would have great impact towards mortality and morbidity reduction in women and children. Moreover, optimal management relies on adapting treatment to account for co-occurrences and possible adverse reactions.

2.3 ANC guidelines for HIV, syphilis, malaria and anaemia

The ill consequences of HIV, syphilis, malaria and anaemia can be prevented through prophylaxis, early diagnosis and treatment. It is important to do this as early as possible because, in all four conditions, risk cumulates with exposure over the gestation period. WHO global antenatal guidelines recommend screening and management of HIV, syphilis, and anaemia at the first ANC visit, ideally in the first trimester [39]. For malaria, in areas of stable transmission, there is currently no global recommendation for screening the blood for parasites for nonclinical cases but the current strategy recommends intermittent preventive therapy with sulfadoxine-pyrimethamine (IPTp-SP) and the use of insecticide-treated bednets (ITNs) together with effective case management of clinical malaria. The exception is Tanzania who recently introduced malaria testing at first visits into their antenatal guideline [40]. Table 2.2 summarizes the latest WHO antenatal guidelines for the four conditions.

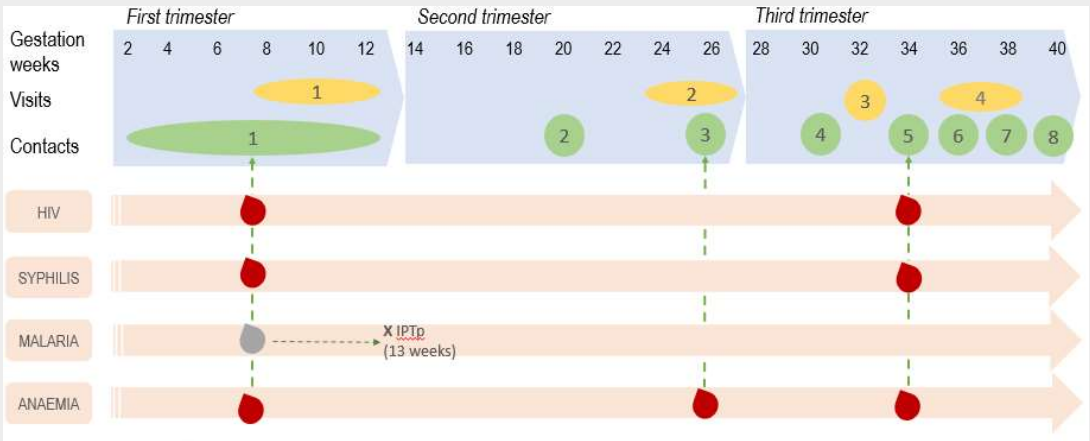
Table 2.2: Summary of WHO antenatal guidelines for testing, treatment and prevention of HIV, syphilis, malaria and anaemia: recommendations for sub-Saharan Africa	
HIV	
Testing	In high prevalence settings, provider-initiated testing and counselling (PITC) for HIV should be considered a routine component of the package of care for pregnant women in all antenatal care settings. Retest all HIV-negative pregnant women in the third trimester, during labour or postpartum because of the high risk of acquiring HIV infection during pregnancy. On testing strategies: In settings with greater than 5% HIV prevalence in the population being tested, a diagnosis of HIV-positive should be issued to people with two sequential reactive tests [39].
Treatment	ART, following national regimen for combination therapy, should be initiated in all pregnant women diagnosed with HIV at any CD4 count and continued lifelong. This recommendation is based on evidence that shows that providing ART to all pregnant and breastfeeding women living with HIV improves individual health outcomes, prevents mother-to-child transmission of HIV, and prevents horizontal transmission of HIV from the mother to an uninfected sexual partner [39].
Prevention	Oral pre-exposure prophylaxis (PREP) containing tenofovir disoproxil fumarate should be offered as an additional prevention choice for HIV negative pregnant women at substantial risk of HIV infection as part of combination prevention approaches [39].
Syphilis	
Testing	To prevent mother-to-child transmission of syphilis, all pregnant women should be screened for syphilis with on-site RPR or other available rapid test at the first ANC visit in the first trimester (ideally before 16 weeks gestation) to prevent congenital infection and again in the third trimester of pregnancy. Review syphilis test results at subsequent visits and at time of delivery. If the woman was not tested during pregnancy, syphilis screening should be offered after delivery [39, 41].
Treatment	Treat all sero-reactive women with benzathine benzylpenicillin at the recommended dosage of at least 2.4 million units (MU) intramuscularly as a single dose, after having excluded allergy to penicillin. In the case of penicillin allergy, the attendant should desensitize and treat with penicillin if trained to do so, or refer the patient to a higher level of care. Advise women who test positive that their partner(s) must also be treated with the same regimen, as well as the baby as soon as possible after birth [41]. When benzathine or procaine penicillin cannot be used (e.g. due to penicillin allergy where penicillin desensitization is not possible) or are not available (e.g. due to stock-outs), the WHO sexually transmitted infections (STI) guideline suggests using, with caution, erythromycin 500 mg orally four times daily for 14 days or ceftriaxone 1 g intramuscularly once daily for 10–14 days or azithromycin 2g once orally [42].
Malaria	
Testing	In malaria-endemic areas, malaria should be suspected in any patient presenting with a history of fever or temperature ≥37.5°C. In all settings, suspected malaria should be confirmed with a parasitological test. Malaria

	RDTs should be used if quality-assured malaria miscroscopy is not readily available. In settings where parasitological diagnosis is not possible, a decision to provide antimalarial treatment must be based on the probability that the illness is malaria [43].
Treatment	Treat pregnant women with uncomplicated *P. falciparum* malaria during the first trimester with 7 days quinine plus clindamycin. Treat uncomplicated *P. falciparum* malaria during the second and third trimesters with artemisinin-based combination therapies (ACT). Treat severe malaria with intravenous or intramuscular artesunate for at least 24 hrs. Once a patient has received at least 24 hrs of parenteral therapy and can tolerate oral therapy, complete treatment with 3 days of ACT [43].
Prevention	In moderate-to-high malaria transmission areas of Africa, WHO recommends a package of interventions for all pregnant women, which includes promotion and use of insecticide-treated nets (ITNs), as well as intermittent preventive treatment with sulfadoxine-pyrimethamine (IPTp-SP). IPTp-SP dosing should start in the second trimester, and doses should be given at least one month apart, with the objective of ensuring that at least three doses are received. To ensure that pregnant women in endemic areas start IPTp-SP as early as possible in the second trimester, policy-makers should ensure health system contact with women at 13 weeks of gestation. Policy-makers could also consider supplying women with their first SP dose at the first ANC visit with instructions about the date (corresponding to 13 weeks of gestation) on which the medicine should be taken. Women on cotrimoxazole should not be given IPTp-SP [39].
Anaemia	
Testing	Full blood count testing is the recommended method for diagnosing anaemia in pregnancy. In settings where full blood count testing is not available, on-site haemoglobin testing with a haemoglobinometer is recommended over the use of the haemoglobin colour scale as the method for diagnosing anaemia in pregnancy [39].
Treatment	If a woman is diagnosed with anaemia (Hb < 110 g/L) during ANC, she should be given 120 mg of elemental iron and 400 µg (0.4 mg) of folic acid daily until her Hb concentration rises to normal (Hb 110 g/L or higher). Thereafter, she can continue with the standard daily antenatal iron and folic acid dose (or the intermittent regimen if daily iron is not acceptable due to side-effects) to prevent recurrence of anaemia [39].
Prevention	Daily oral iron and folic acid supplementation with 30 mg to 60 mg of elemental iron and 400 µg (0.4 mg) of folic acid is recommended for pregnant women. In settings where anaemia in pregnant women is a severe public health problem (i.e. > 40% of pregnant women have a blood haemoglobin [Hb] concentration < 110 g/L), a daily dose of 60 mg of elemental iron is preferred over a lower dose. Intermittent oral iron and folic acid supplementation with 120 mg of elemental iron and 2800 µg (2.8 mg) of folic acid once weekly is recommended for pregnant women to improve maternal and neonatal outcomes if daily iron is not acceptable due to side-effects, and in populations with anaemia prevalence among pregnant women < 20% [39].
ART: antiretroviral therapy; RPR: rapid plasma reagin test; RDT: rapid diagnostic test	

2.3.1 Schedule of ANC contacts

In 2002, the WHO put forth a focused antenatal care (FANC) model that reduced the number of required visits from 12 to four, making visiting schedules more suitable to health systems in developing countries where facilities may be hard to reach and human resources strained [44]. Recently, evidence has suggested that risk of perinatal death is significantly higher in the four-visit model compared to models with eight or more visits. Therefore, in 2016, the WHO changed the recommendation to eight 'contacts', where contacts imply any exchange with a healthcare provider irrespective of the setting [39]. Figure 2.1 shows when strategies for HIV, syphilis, malaria and anaemia should to be delivered in the old four-visit and new eight-contact models.

Figure 2.1: Comparison of ANC schedules from 2002 FANC model with four visits and 2016 ANC model with eight contacts and timing of blood testing adapted from WHO antenatal guidelines [39]



ANC: antenatal care; FANC: focused antenatal care

2.3.2 Recommendation for integrated health services

An integrated disease approach to antenatal service delivery is recommended as the best strategy to address the various health needs and infections in pregnancy [45]. Integration can be thought of as a concept that means "the organization and

management of health services so that people get the care they need, when they need it, in ways that are user-friendly, achieve the desired results and provide value for money"[45]. This could refer to several things: 1) for users (e.g. pregnant women), integration could mean receiving all required services packaged together at a one-stop shop and avoiding referrals or separate visits [45]; 2) it could also mean specifically for the user to remain at one service delivery point during a visit and receives all the interventions from one healthcare provider in order to achieve more co-ordinated care [45]; 3) integration can also refer to continuum of individual care over time for chronic conditions like HIV or over life-cycles stages like antenatal, postnatal and child care in order to ensure linkages and reduce loss to follow-up [46]; 4) integration can also happen at the level of policy-making, financing and management so there is co-ordination across sectors for joint decision-making, monitoring and supervision. However integration occurs, the common idea is to improve user access to health services and to create synergies among the investments in health programmes [45]. Implementation experiences have shown that integrating services into a one-stop shop for maternal health allows women to receive comprehensive diagnostic and appropriate treatment in a single visit, avoiding the need to visit the facility at multiple occasions or at different locations which costs money and takes time away from parenting or work [47-50]. Integrating services has been shown to encourage more pregnant women to attend ANC, increase the number of women who receives test results, shorten time to receiving results, and increase the number of women who initiate and adhere to HIV treatment [48-54]. PMTCT programmes integrated into ANC also give better confidentiality and improve patient-provider relationships [52].

2.4 Coverage of ANC guidelines

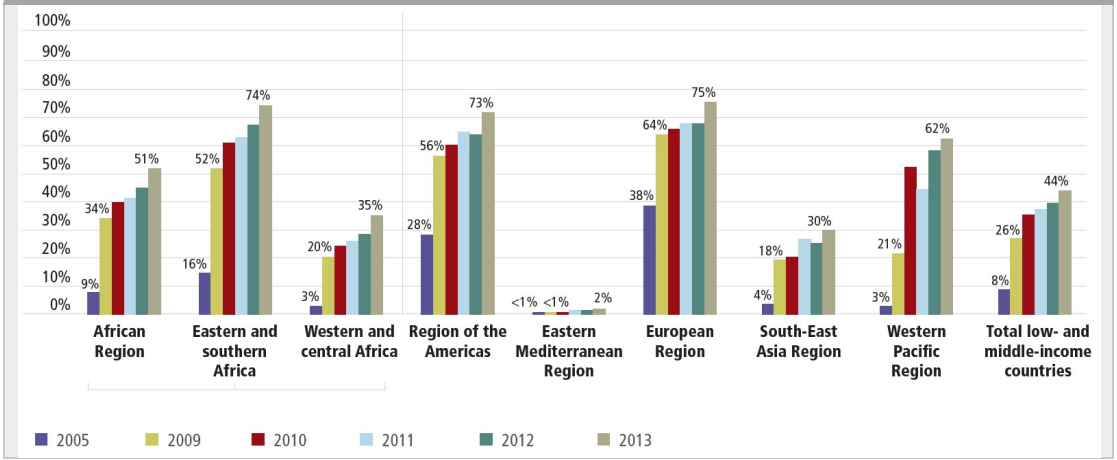
Populations in SSA have been widely reached through antenatal care channels, with approximately 90% of pregnancies having had contact with the healthcare system [55]. Despite this, not all those who have had contact receive the preventive and curative services necessary for preventing adverse pregnancy outcomes. Missed opportunities

for ANC to deliver comprehensive and integrated care to women are still widespread. The following section will describe the current state of coverage in ANC for HIV, syphilis, malaria and anaemia interventions.

2.4.1 Coverage of HIV testing and ARV treatment

Testing coverage for HIV among pregnant women in the African Region has been gradually expanding over the years, from 9% in 2005 to 51% in 2013, but still short of 95% universal testing target **(Figure 2.2)**. Not all regions have improved testing coverage at the same rate and regional differences exist: in the most severely prevalent areas of eastern and southern Africa, 74% of pregnant women were tested for HIV and know their results compared to only 35% in western and central Africa [56]. Antenatal care is a vital opportunity for HIV testing which is a critical entry point into PMTCT care, but not all women who attend ANC receive an HIV test, underachieving ANC's potential to reach HIV positive pregnant women [57]. Demographic Health Survey (DHS) data from 2011 to 2013 for four countries show that Ugandan women had 81.5% HIV testing rate at ANC, compared with 69.4% in Mozambique, 54.4% in Nigeria and 45.4% in Congo [57]. Kenya's HIV testing coverage at ANC is relatively high and has improved greatly over the years: 93.1% of women who attended ANC from 2008 to 2012 for their last live birth were tested compared to only 64.9% in 2002-2007 period [58].

Figure 2.2: Estimated HIV testing and counselling coverage among pregnant women, low- and middle-income countries overall and by WHO region, 2005 and 2009–2013 [56]



Sources: number of pregnant women tested reported by countries: Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS); estimated number of live births as a proxy for the number of pregnant women: Population Division, United Nations Department of Economic and Social Affairs.

Treatment coverage is also short of the global target of having 90% of pregnant women living with HIV to be on ART. Overall in the Africa Region, 68% (range 62-74%) of HIV positive pregnant women were receiving ARV medicines in 2013. This also varies considerably among different countries: coverage of pregnant women living with HIV receiving ARV medicines for PMTCT ranges from 27% in Nigeria to over 95% in Botswana and Swaziland. 58% in Burundi to 90% in South Africa [56].

2.4.2 Coverage of syphilis testing and treatment

Coverage of syphilis testing and treatment is suboptimal in countries within the WHO African region. Of those that reported data in 2013 for the Global AIDS Response Progress Report (WHO/UNICEF/ UNAIDS), 58% of women in antenatal care were tested for syphilis during their first visit and about 2.2% of these women tested positive. Of women tested positive, 96% reported receiving treatment [56]. Proportion of women tested for syphilis in ANC has not improved much from 59% in 2008 **(Table 2.3)**. These are higher than estimates from a 2001 survey of 22 countries in SSA which found 38% of pregnant women who received ANC were screened for syphilis [59].

Table 2.3: Proportions of pregnant women in antenatal care who were tested for syphilis, who tested positive and who received treatment, 2008/2010 and 2013 [56]

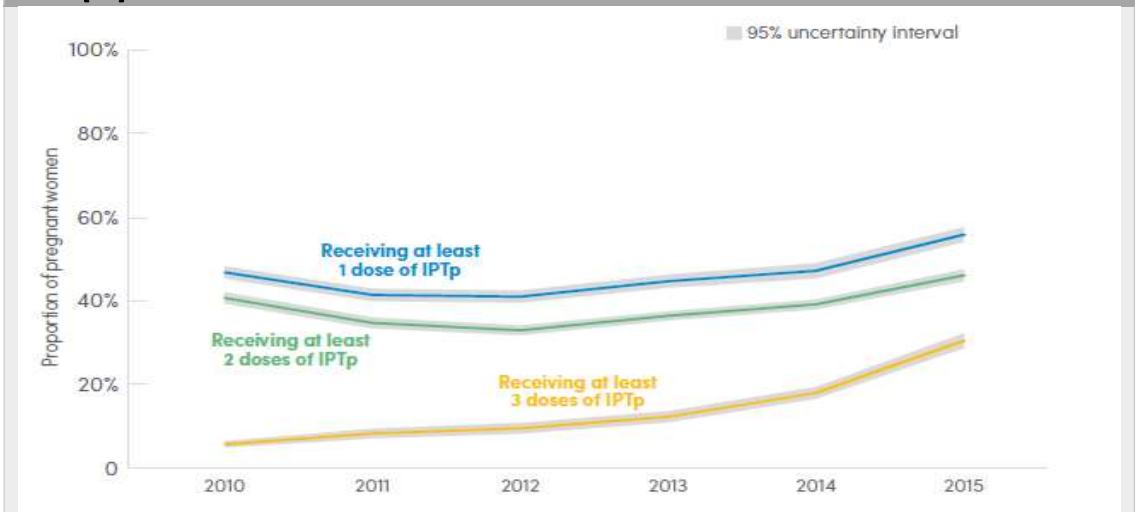
	Indicator 1: Percentage of antenatal care attendees tested for syphilis				Indicator 2: Percentage of antenatal care attendees tested who are positive for syphilis				Indicator 3: Percentage of antenatal care attendees who tested positive for syphilis and who received treatment			
	2008		2013		2008		2013		2010		2013	
	No. of reporting countries	Median value reported	No. of reporting countries	Median value reported	No. of reporting countries	Median value reported	No. of reporting countries	Median value reported	No. of reporting countries	Median value reported	No. of reporting countries	Median value reported
Africa region	18	59%	23	58%	30	2.3%	30	2.2%	15	100%	16	96%

Source: Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS)

2.4.3 Coverage of malaria prevention strategies

Malaria prevention strategies in pregnancy are mainly delivered through ANC clinics but they have not been very effective in providing IPTp and ITNs to pregnant women [60, 61]: among approximately 80% of those who attend ANC, 30% did not receive a single dose of IPTp in 2015 estimates [62]. It is also estimated that only 31% (UI: 29-32%) of eligible pregnant women received at least three doses of IPTp among the 36 African countries that reported data in 2015 (**Figure 2.3**) [62]. Some countries achieved better coverage than others: 24 reported that more than 50% of pregnant women received at least 1 dose, and 17 reported that more than 50% received at least 2 doses and 3 countries reported that more than 50% received at least 3 doses of IPTp [62]. Zambia has one of the highest IPTp coverages in Africa, with 72% of pregnant women who attend ANCs receiving a second dose of SP in 2012 [63]. For ITN strategy, the median use of an ITN the previous night among pregnant women was only 35.3% (range 5.2%–75.5%) among 37 reporting countries in the period between 2009-2011 [60, 61].

Figure 2.3: Proportion of pregnant women receiving IPTp, by dose in sub-Saharan Africa, 2010-2015 [62]



IPTp: intermittent preventive treatment in pregnancy; Source- National malaria control programme reports and United Nations population estimates

2.4.3.1 Alternative strategies for malaria in pregnancy

In addition to the inadequate coverage of IPTp-SP, resistance to SP has been increasing due to the accumulation of mutations in two genes in the *Plasmodium falciparum parasite [64-66]. In areas with high prevalence of parasites with the quintuple K540E mutation, more common in eastern and southern Africa, there is decreased ability of SP to clear infections and decreased duration of post-treatment prophylaxis with SP [67] but still some protection against low-birth weight from SP [67-70]. However, when an additional mutation at the allele A581G exists, creating a sextuple mutation, the protection of SP against low birth weight becomes increasing compromised with resistant prevalence [71, 72]. A study from Tanzania suggested the use of IPTp-SP may even competitively facilitate the growth of parasites with resistant mutations[73] but this effect was not supported by other studies [74]. In areas where malaria transmission is declining, there is interest to withdraw IPTp-SP. However, studies are a detecting protective effect of IPTp-SP against low-birth weight even in areas of very low endemicity [72, 75]. In addition to the possibility that SP offers continued protection against placental malaria, SP may offer additional protection against other causes of low-birth weight such as sexually transmitted infections from its antibacterial properties [76-79]. Nevertheless, SP's effectiveness is threatened with increasing* sextuple mutants and requires alternative or additional strategies to safeguard pregnancies. Unfortunately, possible alternative drugs such as mefloquine, azithromycin, and chloroquine have not been more effective and are poorly tolerated [67, 80]. Recently dihydroartemisinin-piperaquine (DP) has been shown to be a promising alternative to SP in reducing malaria infection at delivery in western Kenya and Uganda where transmission is high and the SP resistant quintuple mutations are near universal but with less than 6% sextuple mutation [81, 82].

An alternative strategy to chemoprophylaxis that is being considered is screening pregnant women with rapid malaria test and treating with an antimalaria. This has been tested in five clinical trials summarized below in Table 2.4.

Table 2.4: Trials of replacements for IPTp-SP and of ISTp						
Trial	**Location**	**Study population**	**Comparison groups**	**Primary outcomes**	**Malaria diagnosis using**	**Findings**
Tagbor et al 2010 [83]	Ghana -perennial moderate transmission with marked seasonality, -moderate SP resistance	HIV negative pregnant women of gravidae, first ANC visit of 16-24 weeks gestation, 71% LLIN usage	1) IPTp-SP x3 and LLIN 2) ISTp-SP x3 and LLIN 3) ISTp-modiaquine + artesunate (AQ+AS) x3 and LLIN	3rd trimester severe anaemia, Low birth weight	OptiMal dipstick	ISTp-SP and ISTp-AS+AQ non-inferior to IPTp-SP in preventing maternal anaemia and low birth weight
Tagbor et al 2015 [84]	The Gambia, Mali, Burkina Faso and Ghana - malaria transmission is moderately high or high and seasonal -low SP resistance	HIV negative paucigravidae between 16-30 weeks gestation, 59% LLIN usage	1) IPTp-SP x2/3 and LLIN 2) ISTp-AL x2/3 and LLIN	Low birth weight, 3rd trimester anaemia, placental malaria	First Response HRP2/pLDH *P.falciparum* test	ISTp-AL non-inferior to IPTp-SP in preventing low birth weight, anaemia and placental anaemia. More women in the ISTp-AL than in the IPTp-SP group presented with malaria parasitemia between routine antenatal clinics
Desai et al 2015 [81]	Western Kenya -perennial high transmission -high SP resistance	HIV negative pregnant women of all gravidae between 16-32 weeks gestation, 57% LLIN usage	1) IPTp-DP x3/4 and LLIN 2) ISTp-DP x3/4 and LLIN 3) IPTp-SP x3/4 and LLIN	Malaria infection (peripheral and placental) at delivery	First Response HRP2/pLDH *P.falciparum* test	Compared to IPTp-SP, prevalence of malaria infection at delivery lower in IPTp-DP group and higher in ISTp-DP group
Madanitsa et al 2016 [85]	Malawi -high transmission -high SP resistance	HIV negative pregnant women of all gravidae between 16-24 weeks gestation, 20% LLIN usage	1) IPTp-SP x3/4 and LLIN 2) ISTp-DP x3/4 and LLIN	Adverse live birth outcome (composite of small for gestational age, low birthweight [<2,500 g], or preterm birth [<37wk]) in paucigravidae and maternal or placental plasmodium	First Response Malaria pLDH/HRP2 combo test	Prevalence of adverse live outcome similar between the two groups in all gravidae Prevalence of malaria at delivery higher in ISTp-DP group in all gravidae.

				infection at delivery in multigravidae		
Esu 2018 [86]	Nigeria -perennial high transmission, peak in rainy season -moderate SP resistance	HIV negative pregnant women of all gravidae between 16-24 weeks gestation, 15% LLIN usage	1) ISTp-AL x4 and LLIN 2) IPTp-SP x4 and LLIN	3rd trimester anaemia and peripheral malaria, placental malaria, low birth weight	SD bioline HRP2/pLDH pan test	3rd trimester parasitaemia and low birth weight lower in ISTp-AL group. Prevalence of 3rd trimester anaemia similar between groups, however samples were underpowered for this outcome.

Meta-analysis of the Tagbor et al 2010, Tagbor et al 2015, Desai et al 2015 and Madanista et al 2016 trials favoured IPTp-SP over ISTp with antimalarial [74]. There is evidence to suggest that ISTp relative to IPTp-SP may increase the risk of malaria at delivery, and result in lower mean birthweight compared to IPTp-SP. This is likely due to the absence of prophylactic protection between antenatal visits and the low sensitivity of the current generation of malaria RDTs which are not picking up many of the low-density asymptomatic infections [81]. The inferiority of ISTp with antimalarial may change as *A581G mutation increases and more sensitive RDTs become available. Screening with an RDT may still be applicable for: 1) first trimester women when SP is contraindicated and parasitaemia is the highest (between 9 and 16 gestation weeks) [87] and RDTs are more likely to detect infection [88] 2) HIV positive women on cotrimoxazole which is contraindicated with SP. Also, in times of SP stock-out, screening with an RDT may be the best alternative, especially if testing synergies with syphilis, HIV and anaemia can be created.* A hybrid strategy that combines IPTp with ISTp early in pregnancy (first ANC visit) when prevalence of parasitaemia is highest and RDT performance good, may potentially increase coverage of protection for pregnant women.

2.4.4 Coverage of anaemia screening and haematinic supplementation

To our knowledge there is no global estimates of anaemia screening, but local studies in SSA have shown that screening for anaemia and haematinic supplementation has the poorest coverage among all the 4 conditions. A study in 16 rural coastal clinics in Rufiji district in Tanzania found only 2 out of 10 dispensaries had diagnostic instruments (e.g. the Tallqvist colour scale, HemoCue@ machines, etc) to assess anaemia. Of the 85 women surveyed from these facilities, 14.5% were assessed clinically and 6.4% were assessed using the Tallqvist method), despite a high prevalence of anaemia (66.5%) among women who attended these clinics [89]. Iron was available in 90% of the facilities [89] but frequent shortages have been reported in another longitudinal study in Tanzania [90, 91]. In Kenya, a community survey of women who had a recent birth in two sub-counties in western Kenya found only 35% of women were tested for haemoglobin concentration, 74% received iron and 57% received folic acid supplementation [92]. According to Ethiopia Demographic Health Survey (EDHS) 2011, only 17.3% of women took the iron supplement during their recent pregnancy in the preceding 5 years and less, 0.4%, were supplemented for 90 or more days [93].

2.5 Barriers and enablers to achieving high coverage for HIV, syphilis, malaria and anaemia in antenatal care

So far, this review has described the burden and aetiology of four of the most deleterious illnesses for pregnant women in SSA and emphasized the importance of delivering strategies to protect mother and child early. It has also outlined the gaps and missed opportunities of ANC for delivering preventative and screen-and-treat strategies for pregnant women. The following section looks at some of the reasons for sub-optimal coverage in SSA through an implementation pathway framework.

2.5.1 Conceptual framework for the analysis of coverage of antenatal health services

This section will look at the barriers and enablers of achieving effective coverage of antenatal strategies through an implementation pathway that was first described by

Tanahashi and further adapted by Baker et al. [94, 95]. The framework breaks down the pathway into three conditional stages where each stage has unique determinants, enabling a more practical guide to devising solutions. The first condition requires that the target population (e.g. pregnant women) can geographically, financially, and socio-culturally access the location where the interventions are delivered which are usually the antenatal care facilities (*access*). Once pregnant women arrive at the facilities, there must be adequate human resources, drugs, supplies and equipment to deliver the health interventions (*health facility readiness*). The third condition is that the intervention is delivered with sufficient skill, equity, knowledge and quality to generate the target health outcome (*clinical practice*) [94]. Additionally, we also look at some of the broader patient and community socio-cultural factors that may contribute to completing the implementation pathway. Attrition in coverage at any stage leads to compromises in desired health outcomes.

2.5.1.1 ANC attendance (Access)

As most of the interventions to prevent adverse pregnancy outcomes are delivered through ANC facilities, ANC attendance is the first step to ensuring women get what they need for healthy pregnancies. In SSA, approximately 70% of women aged 15-49 reported had at least one antenatal visit with a skilled attendant but less, approximately 54% had the recommended four visits [96]. Furthermore, women often attend ANC late. Only approximately 28% attend clinic in the first trimester, and 40% before the third trimester leaving a third of women receiving antenatal care in the third trimester, too late for effective diagnostic and preventive services [96].

Urban dwelling, education and household wealth are consistent predictors of antenatal care use [96, 97]. Women who are teenagers or older compared to those in their 30s, and women with higher parity tend to use antenatal care less [96, 98] as do women with unintended pregnancies and who are single [98]. Family members also affect ANC usage [99] and some studies have found that husband's refusal or mother-in-law's disapproval discourages women from using ANC [98]. Long distance, expensive and inconvenient

travel to health facilities are associated with starting ANC late and making less visits [98]. Poor quality of care, negative attitudes of health workers and punishments for late attendance have been found to stymie timely ANC utilization [98, 100]. Qualitative studies have suggested that some women do not start ANC early because they are unsure of the pregnancy status or they do not see the benefit of attending ANC unless there is a problem [98]. Late attendance compromises timely access to screening tests and treatment effectiveness. These socio-demographic determinants mean that rural, uneducated, and poor women are most disadvantaged when it comes to access coverage.

2.5.1.2 Availability of commodities (Health facility readiness)

Unavailability of diagnostic tools is a major barrier to achieving universal screening coverage for HIV, syphilis and anaemia. This was more pronounced for syphilis and haemoglobin testing than for HIV testing [28, 101-105]. Using household interviews and survey data from 122 health facilities between 2011 and 2014 in rural south-eastern Tanzania and eastern Uganda, ANC coverage was estimated to be near universal but test shortages at facilities caused 57% and 42% of those attending ANC to not receive testing for syphilis and haemoglobin respectively in Tanzania and 79% and 69% in Uganda [103]. Test shortages for HIV was less severe but was still responsible for 17% of women not being tested in Tanzania and 39% in Uganda [103]. A 12-month assessment of 8 antenatal clinics in Kenya found no syphilis tests available at low-level facilities and inconsistently available at higher-level facilities whereas HIV test kits were more consistently available but occasional stock-outs still occurred [104]. Lack of rapid plasma reagin (RPR) test kits and benzathine penicillin to treat syphilis was a major obstacle in survey of 9 Tanzanian health facilities around the country in 2000/2001 where only 3 out of 9 facilities had enough supplies to test and treat ANC women for syphilis for one week [106]. Stock-out of HIV testing commodities occurred 51.4% of the time during a study of integrated maternal health services in Mozambique [107].

In addition to the unavailability of test supplies, stock-outs of prevention and treatment commodities undermines fidelity to antenatal management guidelines. Directly observed treatment (DOT) of IPTp and distribution of ITNs are the current strategies to prevent malaria in pregnancy in most malaria endemic countries. While this removes the requirement for testing, periodic stock-outs of SP have undermined the delivery of chemoprophylaxis to pregnant women [100, 108-119]. A study in two rural districts in Tanzania reported that 9% of women miss IPTp because of drug shortages [100]. The situation is exacerbated by healthcare workers incorrectly using SP to treat malaria cases in the general population, leaving less for prevention in pregnant women [115, 120]. Consequently, women are not given the drug or are asked to buy it elsewhere and many do not have the funds to do so [109, 118]. Shortage of ITNs is a major reason women are not receiving the nets at ANC clinics [61, 115]. Iron and folic acid supplementation also suffers from frequent stock-outs: in 2010, only 40% of health facilities in Kenya had ferrous sulphate and 74% had folic acid [121].

Shortages are caused by insufficient funds, low government prioritizations, communication failures, poor stock quantification and management, and ineffective procurement systems that delay delivery of stocks [61, 113, 115, 120-123]. HIV programmes have received more support, and have suffered less from shortages after the Bush administration in the United States established the President's Emergency Plan for AIDS Relief (PEPFAR) programme in 2003, the largest donor to the global AIDS response [124]. Various other donor bodies joined the fight against HIV which led to substantial financial backing for vertical HIV programmes resulting in dramatic increases in testing and treatment coverage in the first decade of the 21st century [124]. These vertical programs have also been found to create parallel procurement and supervisory systems which lead to duplication and confusion in ordering stocks for other antenatal needs [59, 103, 106, 125]. Syphilis and haemoglobin screening, despite the strong evidence for their clinical effectiveness [17, 59, 126-128], lack donor advocacy and consequently achieve less coverage [59, 103, 129].

Integration of health programmes and improving stock-availability and has vast potential to close the coverage gap. In addition to shortages of tests and drugs, lack of potable water at some facilities have precluded women from taking the drug at the facilities [100, 130]. Not wanting to share cups has also been reported by urban women in Nigeria as reasons for not taking SP under DOT [130]. These environmental factors need attention when designing antenatal interventions.

2.5.1.3 Human resources (Health facility readiness)

Critical healthcare worker shortages, skill mix imbalance and maldistribution of the workforce are significant barriers for scaling interventions in SSA [131-136]. Reviews of integrated service delivery of HIV, syphilis, and malaria programmes have identified staff shortages, overburden and frequent turn-overs as major limitations to the success of adding on new tasks [47, 49, 101, 106, 107, 113, 116, 137-141]. Healthcare workers are often required to fill out various paper-based registers for specific services, generating large amounts of paperwork that burden staff workload [142]. Additionally, disease-specific short training, polio eradication campaigns, and leave pull staff away from already strained facilities [106, 131, 143, 144], leaving sites understaffed and compromising quality [117].

Despite healthcare worker shortages, the existing workforce is not always fully utilized [145-147] and the World Report 2010 estimates that 20-40% of health spending is wasted through inefficiency [148]. Time and motion studies in Tanzania revealed staff productivity of approximately 60% [147]. Reproductive health staff in one study in Cameroon were found to spend only 27% of their time on service provision [145]. Productivity gains from less time spent on prolonged breaks, waiting for patients, excessive socializing and unexplained absences have been estimated to be 26%, suggesting improvements in productivity through incentives to boost morale and better management could close the human resource requirements for universal coverage [147]. Low productivity has been attributed to demoralization from meagre and delayed salaries, lack of choice in placement, poor working conditions, job grade stagnation, and

feeling helpless due to stock-outs of commodities and drugs [100, 131, 134, 136]. These frustrations lead to poor quality of care and increased absenteeism, dual practices (having other income generating activities) and cultures of predatory provider-client relationships (abusive behaviour towards clients) [149-154]. Staff have asked women to pay for SP when they are supposed to be delivered freely, which deters women from accessing services [61]. Moreover, vertical well-funded HIV programmes attract staff with higher salaries, pulling human resources away from other reproductive health priorities, often creating two tiers of salaried health workers side by side which can affect the morale of the lower paid staff [131, 143, 155]. Better qualified staff migrate to urban areas or private practices, leaving rural public facilities with less skilled personnel, widening the equity gap [116, 136].

Improving healthcare work performance will require addressing the multiple determinants that affect performance [150, 156]. Integration of services has been shown to increase motivation and enthusiasm of healthcare workers. For example, integrating HIV programs with MCH have increased healthcare worker morale and satisfaction in Mozambique and Kenya by enabling providers to deliver more effective services to people [52, 107]. Integrating the use of simple syphilis POCTs with ANC have been shown to improve healthcare worker's job satisfaction by enabling them with tools to diagnose disease [50, 104, 157]. Evidence also suggests that supervision and audit with feedback, as well as packages of interventions that address multiple factors are more effective in improving performance than just disseminating guidelines or single interventions [150]. Human resource management (HRS) and quality improvement (QI) methods should be explored to understand how to better manage performance low-resource health systems [156, 158].

2.5.1.4 Training, knowledge and guidelines (Clinical practice)

Inconsistencies in training, knowledge and guideline adherence affect staff competence in delivering quality ANC services. Comprehensive training on all aspects of integrated maternal health services should be given to ANC providers. Some of the gaps found in

Malawi were that ANC providers were only trained in HIV counselling and referred women to other providers for HIV testing leading to inefficiencies and poor uptake [159]. In Mwanza, Tanzania, nurses and health aides who were trained to use RPR for diagnosing syphilis were not permitted to treat medical conditions and women were frequently told to return on another day for treatment [106]. Trade-offs between more training and pulling staff away from facilities in a resource-strained system needs to be carefully considered and pre-service or in-house training may be more beneficial.

National level policy guidelines are sometimes unclear, incomplete or inconsistent with WHO guidelines [61, 115, 160]. Case studies from Kenya found no specific guidelines on syphilis available at facilities and it is known by healthcare workers to be covered under genital ulcer diseases in the syndromic management of STI flowcharts which is inappropriate for the management of asymptomatic syphilis [101]. Cut-offs of haemoglobin for defining anaemia and severe anaemia are inconsistent in Kenyan guidelines where some guidelines use WHO haemoglobin cut-offs (non-anaemic Hb ≥11 g/dL, mild Hb 10-10.9 g/dL, moderate Hb 7-9.9 g/dL, severe Hb <7 g/dL) while others do not (Figure 2.4) [161, 162]. This may explain why iron dosing regimens given to pregnant women do not consistently adhere to prophylactic or treatment guidance based on anaemia status [163]. In Tanzania, two different guidelines with conflicting information on IPTp were found to be circulating at the same time [164].

Figure 2.4: Hand-written guideline on the diagnosis of anaemia based on haemoglobin concentrations at a dispensary in western Kenya, 2015

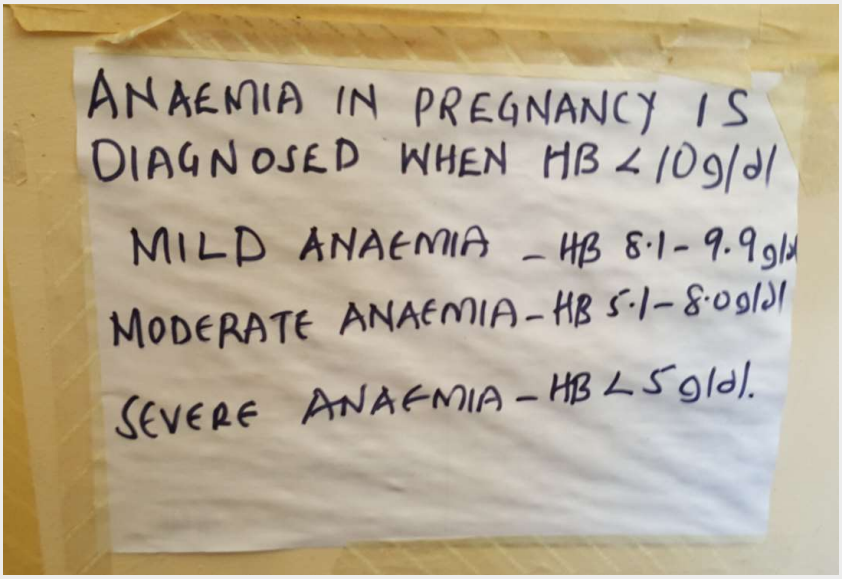


Photo taken by Nicole Yan

Inadequate training and inaccurate guidelines leads to poor healthcare worker knowledge and if healthcare workers are confused they may opt for doing nothing for fear of doing harm [165]. In Tanzania, a general lack of awareness of the implications of untreated maternal syphilis by healthcare workers led to low prioritization of testing [106]. Knowledge of how to conduct penicillin desensitization was found to be poor in South Africa [101]. In western Kenya, correct malaria case management knowledge and practice was observed in less than half (45%) of health facilities and SP was prescribed as treatment in 3% of health facilities [166]. Poor knowledge of IPTp use and giving SP for treating clinical malaria cases has been observed in other SSA countries as well [115, 116, 120]. In Kenya, distribution of a memo with clear and simple instructions for IPTp administration, together with explanation of the guidelines in follow-up supervisory visits, resulted in significant increases in uptake of IPTp in the districts that received the intervention [165]. However, longer lasting effects of the memo have not been assessed. Kenyan government surveys on iron and folic supplementation conducted in 2013 reported that providers' poor knowledge of dosing and duration, inadequate

knowledge given to pregnant women about anaemia, and side effects led to low adherence of haematinic supplements by pregnant women [121].

2.5.1.5 Supervision, monitoring and evaluation systems (Clinical practice)

Supportive supervision and audit feedback, even for uncomplicated innovations, are essential to ensuring quality of performance [150, 167]. Lack of supportive supervision have been found to undermine health facility readiness to deliver antenatal services [122, 123]. They have been found to be infrequent and have suboptimal quality where officials would focus mainly on crosschecking facility registers rather than evaluate processes and content of ANC services [116]. Most HIV testing programmes in developing countries have no quality assurance programmes to ensure that point-of-care tests are properly performed [168]. Managers may have competing duties with little time left for monitoring performance [169]. Good supervision with feedback is an important determinant of healthcare worker performance [150]. It also makes them feel valued, increase their motivation, improve their skills and help them gain new knowledge [107].

Clear supervisory roles are important for effective management but often in low-resource settings, different and uncoordinated programmes, each with their own agendas, are involved in the planning and monitoring of different maternal health interventions. In Kenya, integration of PMTCT services with ANC began in 2004 and was widely available in over 3000 facilities by 2007 but quality of the services was elusive and supervision was provided through distinct HIV teams [159]. A joint supervision tool was created to address disjointed supervisory roles between HIV and maternal health programmes and quality has improved as a result [159]. Supervision provided through vertical programmes was also seen in South Africa where TB and PMTCT services had each their own management guideline and the lack of co-ordinated leadership from implementing bodies undermined benefits of comprehensive integration [170, 171]. Horizons (an operational research programme tasked to identify best practices in HIV/AIDS [172]) identified separate bodies for providing HIV testing and counselling,

ARVs and infant formula, and iron supplementation in Zambia [169]. These parallel systems create duplications, increases programme costs and add extraneous workload [143].

2.5.1.6 Patient pathways (Clinical practice)

Integration on an operational level is also important to improve ease of receiving services by streamlining client flow and reducing wait times. Services that require referrals to separate rooms, laboratories, or facilities pose significant challenges to access and acceptability of HIV and syphilis services [47, 173-176]. HIV treatment provided in separate specialized ART centres increases the attrition rate between diagnosis and treatment [48, 177, 178]. Many countries have physically integrated PMTCT with ANC service delivery points and are moving away from separated horizontal programmes [179].

2.5.1.7 Patient and community centred influencers of ANC uptake

Perceived disease related stigmas and their social acceptability poses challenges to accepting maternal health services. In Tanzania, syphilis is stigmatized because it is associated with promiscuity and believed to cause infertility [50]. It is also believed to be a less harmful disease when compared with HIV and the lack of overt symptoms may lead women to underestimate its danger [50].

In cultures where women have low socio-economic statuses, partner support is influential to women's health seeking behaviour: women have been found to want permission from their husbands before taking SP [130] or delay attending ANC because their husbands have not given them money for transport [61]. Partner involvement is also necessary to end the cycle of re-infection of syphilis or to protect sero-discordant couples. However, men have been under-targeted [99] by health programmes and often refuse to be tested for HIV out of fear [50].

Lack of knowledge of the benefits of SP, why it needs to be given, the required doses and timing have been identified as barriers to the acceptability IPTp by pregnant women

[61]. Experience, fear of side-effects and misconceptions that SP may cause abortions have led to some women to reject the intervention [130, 180-182]. Since IPTp needs to be started early and doses given over several visits, the reasons outlined above (section 2.5.1.1) for women not starting ANC early and returning for revisits are barriers to full protection [183-185]. For ITNs, several studies have found that women feel uncomfortable and hot when sleeping under them or that they are inconvenient to put up at night [61]. Beliefs that chemicals on the nets are harmful or that they do not prevent malaria also have been raised [61].

2.6 Point-of-care tests (POCTs) to address the underachievement in antenatal care

The barriers to effective coverage of antenatal HIV, syphilis, and anaemia testing are multi-faceted and overcoming them will require various system-wide strengthening efforts. Unfortunately, there are no good alternatives to diagnostic testing: 1) most syphilis cases are asymptomatic and would require screening tests to detect [7], 2) clinical pallor examinations for anaemia have variable sensitivity, ranging from 53%-100% [186, 187] and 3) although the current malaria strategy in pregnancy consist of chemoprophylaxis and insecticide treated nets (ITNs) without the need to test for parasites in the blood, expanding malaria testing at the first ANC visit to all pregnant women, regardless of clinical symptoms may be an attractive strategy in the near future in parts of Africa where SP may no longer be effective, such as areas where high-grade SP resistance is increasing [67], or where SP may no longer be required due to markedly reduced malaria transmission. Furthermore, women who attend ANC in the first trimester or HIV positive women on cotrimoxazole are not eligible for SP. This is also the period where parasitaemia is highest and more likely detectable by rapid tests [87]. Addition of malaria testing at first visits can benefit from testing synergies with HIV, syphilis and anaemia and may address a gap not covered by current policies.

The availability of ASSURED[2] rapid point-of-care tests (POCTs) can fulfil antenatal testing requirements and address some of the barriers to coverage. They require no electricity and can be used in rudimentary facilities without sophisticated testing equipment [188]. Their simplicity means they require only basic training and add minimal workload on the healthcare workforce. POCTs can shorten the diagnostic process, allowing same-day management of conditions and their co-infections, potentially increasing client/clinician satisfaction [188] and subsequent adherence to the ANC testing schedules. Pregnant women no longer need to wait long for test results or to be referred to distant laboratories for testing, reducing time and financial costs.

POCTs have been instrumental in the scale-up of identifying HIV infection and initiation of ART in pregnant women to prevent vertical transmission in low and middle-income countries where laboratory-based diagnoses cannot be easily accessed [189]. Rapid HIV tests have high sensitivity and specificity and are generally well accepted by pregnant women and providers [190]. The skills healthcare workers have gained from HIV testing can be expanded to integrate the use of POCTs for syphilis, malaria and anaemia at dispensaries, so coverage of diagnosis and timely treatment can be improved. For these reasons, an integrated testing strategy would be an attractive intervention that would potentially improve maternal health outcomes. Moreover, availability of HIV/syphilis multiplex tests and their increasing popularity will likely lead to improved testing coverage of syphilis, and more cost-savings from efficiencies in procurement and service delivery [191]. For syphilis, replacing the more labour and equipment intensive RPR and VDRL screening methods with simpler POCTs have increased the number of women diagnosed and treated on the same day [50, 54, 102, 105, 129, 176]. POCTs are also more acceptable to women because less blood is needed to run the tests [50].

[2] **A**ffordable, **S**ensitive, **S**pecific, **U**ser-friendly (simple to perform in a few steps with minimal training), **R**obust and rapid (can be stored at room temperature and results available <30 mins), **E**quipment-free and **D**eliverable to those who need them

Healthcare workers have also appreciated their simplicity, ease-of-use [50]. Some barriers to the implementation of rapid tests include difficulty integrating the tests into clinical workflows, lack of quality assurance, time and complexity of performing the tests, distrust in test results, and staff reluctance to do testing [192]. Ensuring adequate training and understanding guidelines in conducting the tests, interpreting results, and stock management is challenging, especially when frequent staff turnovers occur [193, 194]. Pregnant women have also reported feeling they are not given enough information about the tests but were uncomfortable asking the nurses [104]. Studies that have evaluated the use of malaria rapid tests showed that providers were enthusiastic about rapid tests, believed they were relevant tools for diagnosing malaria in fever cases and felt increased confidence and respect from patients. However, providers would sometimes prescribe antimalarials based on their clinical judgement despite a negative test result [194-196]. While many studies have assessed the integration of point-of-care tests with health services delivery, no study has described or assessed the implementation process of an intervention that integrates HIV, syphilis, malaria and anaemia testing with antenatal care. Integrating multiple tests has the potential to improve overall health system performance if training, and quality assurance measures are in place [102]. Moreover, in addition to implementation studies on the processes of delivering integrated testing, impact studies of point-of-care testing on pregnancy outcomes and low-birth weight are needed.

2.6.1 Implementation science and operational research

Over the last 2 decades, researchers are increasingly recognizing the crucial role of implementation research in reducing the gap between the promise of evidence-based practices and their implementation success [197]. Implementation research is defined as the "scientific study of methods to promote the systematic uptake of research findings and other evidence-based practices into routine practice, and, hence, to improve the quality and effectiveness of health services and care" [198].

The literature is teeming with conceptual frameworks and theories to guide implementation questions and of relevance to this thesis are those on the assessment of innovation diffusion in healthcare. Much of this work is based on Roger's seminal Diffusion of Innovations theory, published in 1962 to explain how, why and at what rate new innovations (an intervention which can be ideas, technology or new ways of doing things) spread [199]. These concepts have been applied by many to understand service delivery of innovations in healthcare organizations. Glasgow et al.'s RE-AIM evaluation model from 1999 defined the impact of an intervention as a product of 5 functions: reach, efficacy, adoption, implementation and maintenance. In Greenhalgh et al.'s 2004 exhaustive systematic review of studies assessing innovations in health service organizations, concepts such as the attributes of the innovation, the social networks and system characteristics through which it operates, as well as the non-linear and interrupted nature of the implementation process, were drawn to create an inter-linking framework of determinants for implementation success [200]. In an attempt to consolidate the various models, theories, frameworks and terminologies in the published literature, a Consolidated Framework for Implementation Research (CFIR) was developed to facilitate convergence of construct ideas applied in implementation research [197]. The CFIR draws its foundation in Greenhalgh et al.'s work and builds upon it with other theories of dissemination, innovation, organizational change, knowledge translation and research uptake. The final structure overlaps with Greenhalgh's and comprises of 5 domains with multiple constructs under them: the intervention characteristics (e.g. relative advantage, adaptability, trialability, complexity), outer setting (patient needs and resources), inner setting (culture and leadership), individual characteristics (e.g. knowledge and beliefs about the intervention, self-efficacy) and the implementation process [197]. The existence of a multitude of frameworks speaks to the complexity of the field. Implementation science is an emerging field where consistency in nomenclature and conceptual distinctions are still evolving [201, 202].

Many of the discussed frameworks have used different definitions for the same construct while some constructs have similar definitions that could be conceptually sharpened [197, 203]. This lack of a common vocabulary makes it difficult to aggregate and cross-compare findings of different strategies [197]. Proctor et al. attempted to resolve this issue by combing through the literature to identify commonly used concepts and create a precise working taxonomy of implementation outcomes for researchers to measure implementation success [202, 203]. Table 2.5 provides summary definitions for the eight implementation outcomes with the most consistency and use in existing literature.

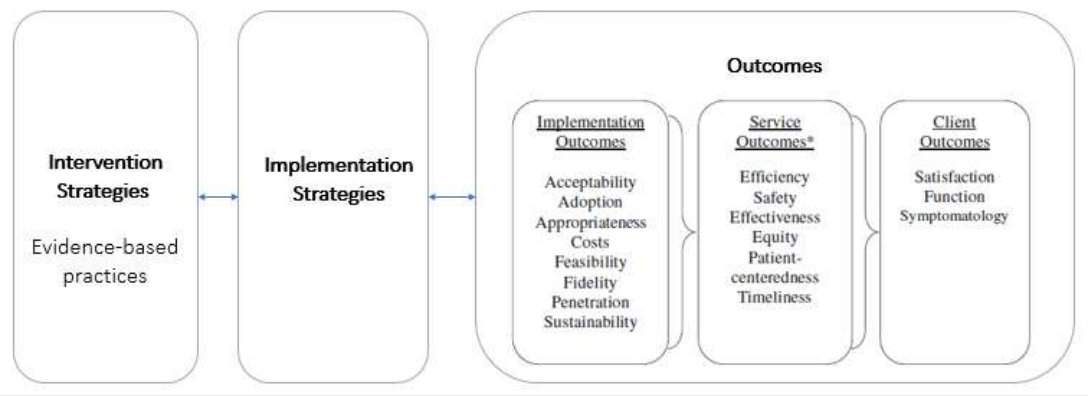
Table 2.5: Taxonomy of implementation outcomes synthesized from a narrative review approach of the literature

Outcome	Construct definition [202, 203]
Acceptability	Extent to which implementation stakeholders perceive that a given treatment, service, practice, or innovation is agreeable, palatable, or satisfactory.
Adoption	The intention, initial decision, or action to try or employ an innovation or evidence-based practice. Adoption also may be referred to as ‘‘uptake.’’
Appropriateness	The perceived fit, relevance, or compatibility of the innovation or evidence-based practice for a given practice setting, provider, or consumer; and/or perceived fit of the innovation to address a problem.
Cost	Financial impact of an implementation effort. May include costs of treatment delivery, cost of the implementation strategy, and cost of using the service setting.
Feasibility	The extent to which a new treatment, or an innovation, can be successfully used or carried out within a given agency or setting.
Fidelity	The degree to which an intervention was implemented as it was prescribed in the original protocol or as it was intended by the program developers.
Penetration	The integration of a practice within a service setting and its subsystems.
Sustainability	The extent to which a newly implemented treatment is maintained or institutionalized within a service setting’s ongoing, stable operations.

These implementation outcomes can be described as the immediate effects of deliberate actions of practice and serve as indicators of success of the implementation process. They exist within a greater framework as intermediaries for clinical

effectiveness and service outcomes, assuming that a well-executed intervention is the pre-condition for subsequent improvements in health and quality of care (Figure 2.5).

Figure 2.5: Conceptual Framework of implementation outcomes adapted from Proctor et al. [202, 203]



*Service outcomes are derived from six quality improvement aims: the extent to which services are safe, effective, patient-centered, timely, efficient, and equitable (Institute of Medicine Committee on Crossing the Quality Chasm 2006; Institute of Quality of Care in America 2001)

Health systems are complex and adaptive meaning they consist of networks of interacting and interdependent elements (e.g. patients, providers, government agencies, non-government organizations), that are "bound by a common purpose but each acting on their own knowledge" [204]. Complex adaptive systems are largely self-organizing and the actors within these networks are in constant feedback loops, adapting to the dynamic environment which in turn are influenced by the actors [205]. This makes traditional methods of identifying risk factors by determining single exposure effects on an outcome by controlling for confounders limiting because they assume linear, unidirectional causal pathways [206].

Operational research (OR) methods can be useful to aid decision making for implementation problems in complex systems [207]. OR is founded on the concept of systems thinking which is "concerned with the interrelationships between parts and their relationships to a functioning whole, often understood within the context of an even greater whole"[205]. It is an established discipline that originated in pre-World War II British military where advanced mathematical and modelling methods were used

to help make decisions for complex problems. It has been widely applied in the manufacturing sector to improve process performance and efficiency [208]. Since the 1950s, the healthcare sector has adopted OR methods to identify and improve effectiveness of programmes in real implementation settings [207]. Bottlenecks are identified during the implementation process and analytical techniques are applied to provide answers to these challenges with direct relevance to solving the intervention's healthcare delivery problems [209]. As such, its utility tends to be local and focused on specific aspects of service delivery [208-210]. Analytical techniques used in operational research include both qualitative (e.g. systems mapping) approaches in participatory group sessions and quantitative approaches (e.g. mathematical and simulation modelling) done by individual analysts using empirical data to represent system components [208]. Operational research methods are thus a very useful tool for implementation research [207].

2.7 Kenya

The above sections reviewed reasons screen-and-treat strategies for HIV, syphilis, and anaemia and preventive strategies for malaria are delivered inadequately through ANC and an integrated testing approach using POCTs was suggested as a potential innovation to close the coverage gap. The next section describes Kenya, where the study took place. It shows that Kenya embodies many of the disease challenges and health system characteristics of the region.

2.7.1 Health situation in Kenya

Kenya has a population of about 44 million. Most people in Kenya live in rural areas (67.7%) and a third of the population live on less than $2 a day [2]. Life expectancy dropped in the early 2000s to a low of 50 years, due to the impact of the HIV epidemic, but has since risen to 61 years in 2015 [2]. Maternal mortality is high with a 2015 estimate of 338 (95% CI: 261-429) deaths for 100,000 live births and stagnating annualised rate of change of -0.4% (95% CI: -1.6-0.8) from 1990-2015 [211]. The under-5

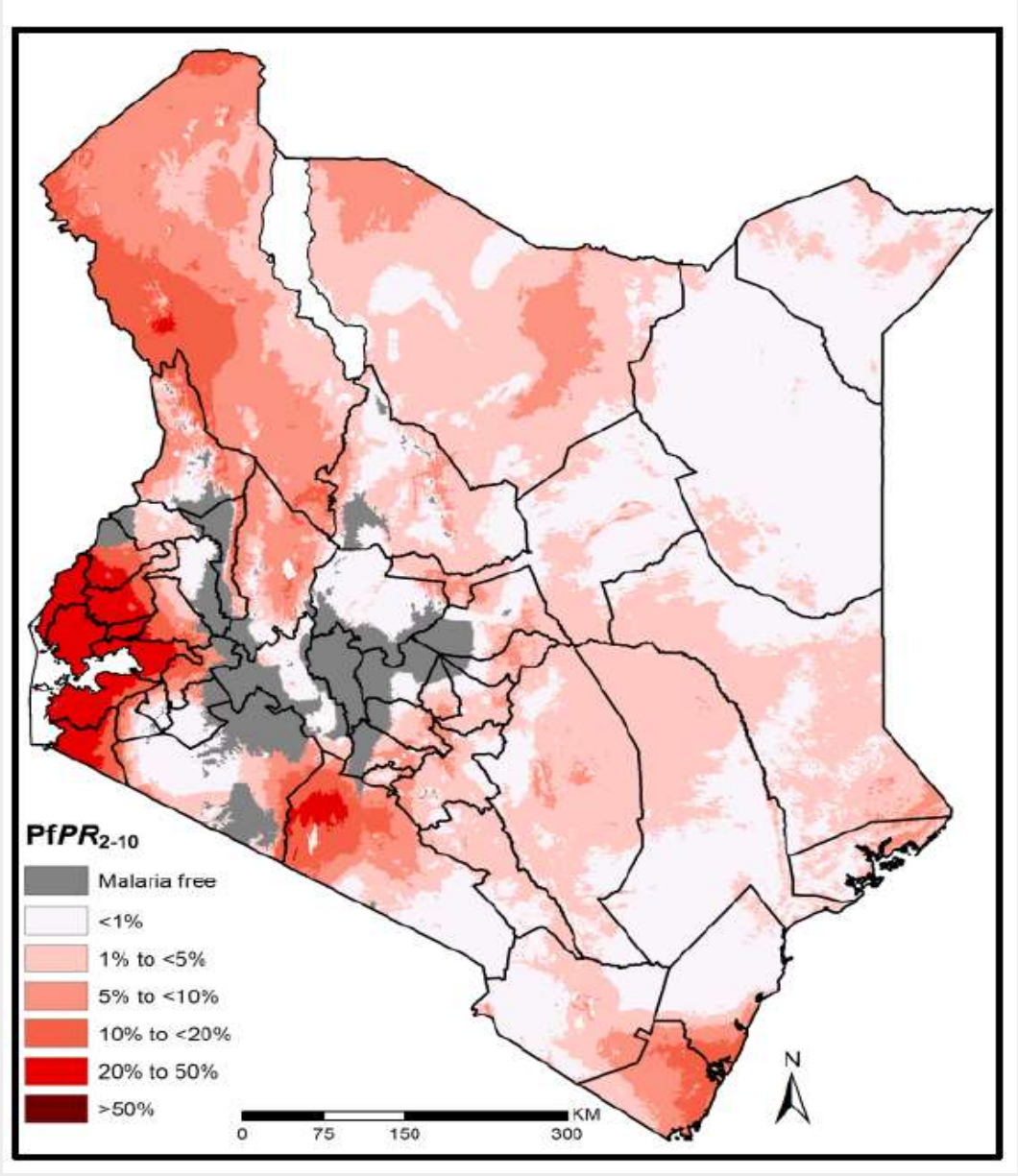
mortality was estimated to be 49 (90% CI: 38-64) per 1000 live births in 2015 and declining at 2.9% (90% CI: 1.8-4.0%) annually from 1990-2015 [6]. HIV/AIDS is by far the most fatal disease, accounting for a third of the country's deaths (29.3%), followed by conditions arising during the perinatal period which accounted for 9% [212]. Malaria is the 6th leading cause, contributing to 5.8% of deaths [212].

Within the country, vast disparities exist and reproductive health problems disproportionately affect areas in western Kenya in the Lake Victoria basin (Figure 2.6). In 2012, the country's HIV prevalence was 5.6% among those aged 15-64 but 15.1% in Nyanza, western Kenya [58]. Among women of reproductive age in Nyanza, HIV prevalence was 17.6% [58]. The last nationally representative data on syphilis was captured in the 2007 Kenya AIDS Indicator survey and estimated the prevalence among adults 15-64 years old to be 1.8% and among pregnant women to be 1.6% [213]. Nyanza has a higher prevalence of 2.3% among women 15-64 years old [213]. Even higher pockets of syphilis prevalence have been found in Asembo in Nyanza Province where one observational study found a prevalence of 11.5% (n=282) in pregnant women using different treponemal and non-treponemal tests [214].

Figure 2.6: Map of Kenya [215]

Malaria is endemic in western Kenya and transmission intense throughout the year with all-age prevalence ranging from 20-50% (Figure 2.7) [216]. Malaria parasites were found in a third of pregnant women attending health facilities in Siaya county [81]. Prevalence of anaemia (Hb <11 g/dl) among pregnant women is estimated to be 55.1% in the country [121] and a similar prevalence of 58-63% was found among pregnant women at rural health facilities in Siaya county [81].

Figure 2.7: Kenya 2015 Population-adjusted *P. falciparum* Prevalence by County Map [217]



2.7.2 Health system in Kenya

Kenya spends 5.7% of its GDP on health [2]. The total health expenditure per capita was $77 in 2014, compared to an average of $98 in sub-Saharan Africa and $4739 in OECD countries [2]. Kenya's healthcare is financed by a combination of government health

expenditure (GHE), development partners (through external aid and borrowing), out-of-pocket (OOP) contributions from households and individuals, and insurance or employer contributions (Table 2.6). Public sector financing has remained constant at approximately a third over the last decade whereas donors' contributions have more than doubled which helped drive down OOP expenditures significantly.

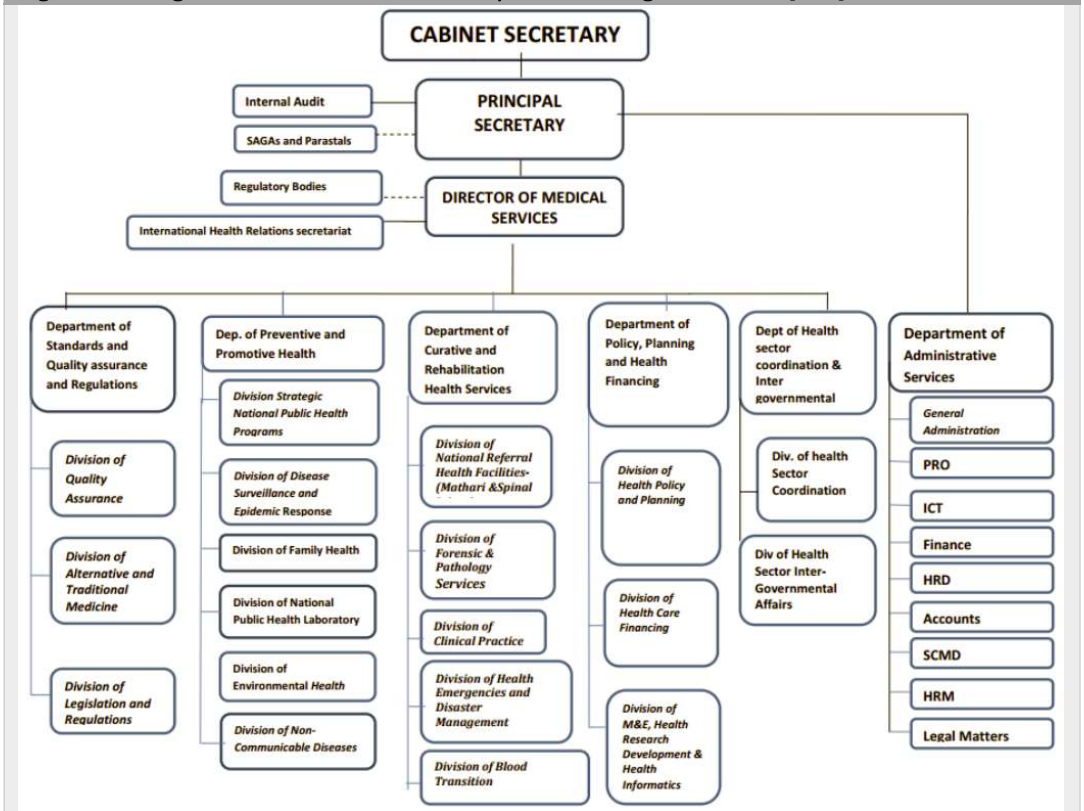
Table 2.6: Kenya's health financing 2014 [2]	
THE as % of GDP	5.7%
THE per capita (USD)	$77.7
GHE as % of THE	33.5%
External resources as % of THE	27.5%
OOP as % of THE	26.1%
Other private and insurance schemes as % of THE	12.6%
USD: US dollar; THE: total health expenditure; GDP: Gross domestic product; GHE: government health expenditure; OOP: out of pocket expenditure	

2.7.2.1 Devolution and new structure of government

Kenya renewed its constitution in 2010 which introduced the devolution of the government's administrative power to 47 counties under one national government [212]. The transfer of decision-making from central government to local bodies aimed to make healthcare services more tailored to the needs of local populations and increase access to medicines and treatment across the country through improved efficiency, responsiveness and accountability [218]. Under the devolved government, the national government holds responsibility for health policy formation, national referral health facilities and reference laboratories, disease surveillance, monitoring and evaluation, health commodity procurement, technical assistance, capacity building and co-ordinating partners and donors [212]. The national Ministry of Health is organized into five main directorates under the Director of Medical Services (Figure 2.8). Under one of these directorates, the Department of Preventive and Promotive Services, the National Malaria Control Programme (NMCP), the National AIDS and STIs Control Programme (NASCOP) and the Division of Family Health manage and create policies for malaria in

pregnancy, PMTCT and reproductive health programmes respectively [219, 220]. There are inter-agency coordination committees (ICCs) and technical working groups that meet quarterly or on an *ad hoc* basis to discuss issues and promote coordinated technical support and policy development across programmes. However, the 2013 Health Sector Strategic Plan found that there are too many ICCs, their programmes are not aligned to sector policies and their linkages are weak [221].

Figure 2.8: Organizational structure of Kenya's national government [222]



SAGAS: semi-autonomous government agencies; M&E: monitoring and evaluation; PRO: Public record office; ICT: Information Communication Technology; HRD: Human Resource Development; SCMD: supply chain management division; HRM: Human Resource Management

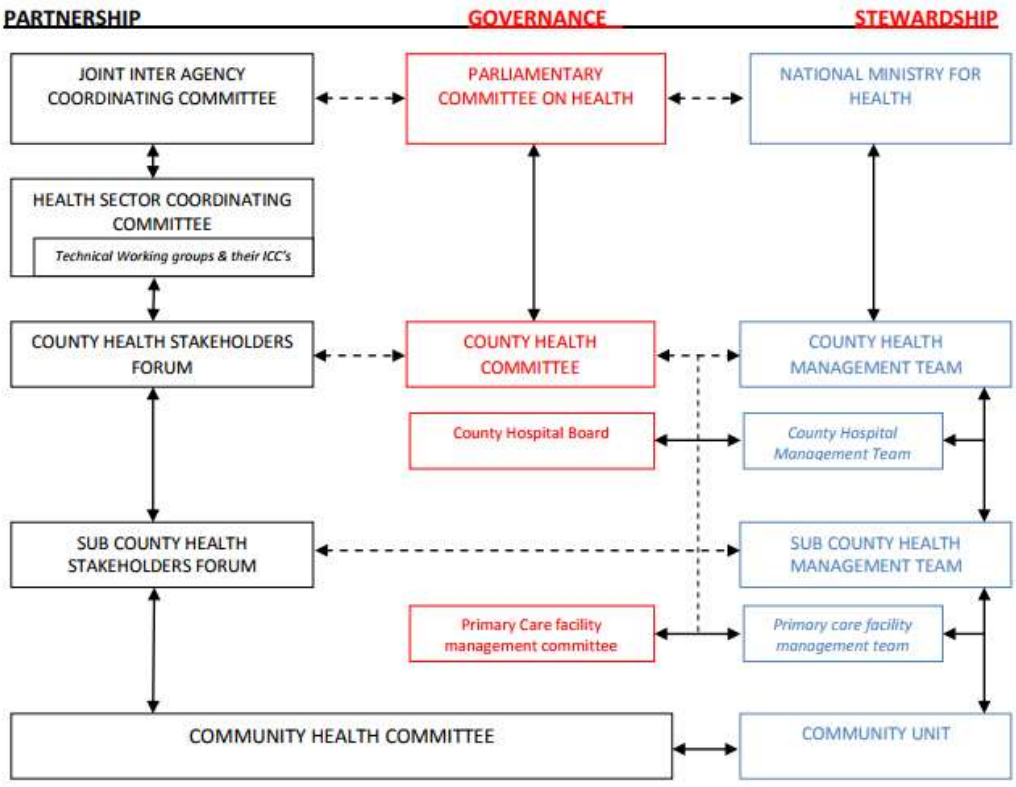
Service delivery and disease management and control are under the jurisdiction of the county governments. Counties have increased their budget for health from 13% in 2013/2014 to 21.5% in 2014/2015, suggesting increasing priority given to health despite competing demands from other sectors such as transportation, education and

agriculture [223]. Siaya in particular increased their health budget allocation from under 10% in 2013/2014 to 31% in 2014/2015 [223]. However, a large share of recurring county budget allocations in 2014/2015 (70%) went to employee compensation and only 8% went to medical drugs and supplies [223]. Improvement in allocative efficiencies is needed to better match the needs and demands for optimal service delivery. Counties oversee curative and rehabilitative services, health promotion and disease prevention, sector planning, and governance and administration. Each county has a health executive and director for health who oversees the county health management team. The county manages the first three hierarchal levels of service delivery [212]. It begins at the community (level 1) under a Comprehensive Community Strategy which focus on prevention and demand creation activities. This strategy is powered by community providers who are village members with linkages to health facilities within the area. These community providers identify and refer those who need services, such as pregnant women, to formal health infrastructures. They also give prevention and drug adherence advice, follow-up on ART adherence for HIV positive persons, as well as trace those who default on facility visits [212, 224] . Levels above the community are primary care units which consist of dispensaries (level 2) and health centres (level 3). Together they focus on preventive and promotive services such as basic maternal and child health services, including antenatal services, rudimentary out-patient curative care and support care for HIV positive patients. Dispensaries are smaller, more pervasive and peripheral while health centres are slightly larger, tend to be located in hubs, and usually have laboratory services capable of performing diagnostic tests. Non-state implementation partners also play a role in delivering primary care services and they include civil society organizations (CSOs), faith based organizations (FBOs), non-governmental organizations (NGOs) and private sector organizations and development partners. Most antenatal care services are preventive and are delivered by primary care providers [212].

The national government oversees levels 4-6 which consists of the primary, secondary and tertiary referral facilities respectively. They offers more complex and sophisticated services focusing on curative and rehabilitative care which are managed under the

national government [212]. To facilitate communication and co-ordination between national and county governments, a health sector inter-governmental forum meets quarterly to address health issues that span across county and national government concerns [212]. Figure 2.9 summarizes the different governance bodies and linkages within the health system.

Figure 2.9: Health sector leadership framework [221]



ICC: Inter-agency coordinating committees

2.7.2.2 Human resources

Kenya's workforce for health services delivery faces significant shortages and skewed distribution [221]. The number doctors, clinical officers and nurses average 20.7, 31.6, and 159.3 per 100,000 persons in 2013 respectively [212]. While the number of doctors per 100,000 persons almost meets WHO's recommended 21.7, the number of nurses fall below the recommendation of 228 per 100,000 [212]. To provide 80% of pregnant

women with skilled birth attendance [132], there should be a minimum of 23 doctors, nurses and midwives per 10,000 and Kenya falls short with only 13 doctors, nurses and midwives per 10,000 [225]. Moreover, the organization of personnel deployment is erratic, resulting in mal-distributions that favour high socioeconomic and urban regions despite 70% of the population live in the rural. This leaves marginalised and hard-to-reach areas with shortage of staff while better-off regions report surpluses in staff. In addition, healthcare workers, especially in rural areas, face remote and poor work environments, low remuneration, job grade stagnation, lack of essential medicines and supplies leading burn out, low morale and productivity [212]. Task shifting to lay workers for certain services such as HIV testing and counselling is now recommended to relieve some workload from nurses [39, 226].

2.7.2.3 Kenya Medical Supplies Authority (KEMSA)

KEMSA, a state-owned logistics company that was incepted in 2000, procures drugs and health commodities from manufacturers and contracts private transport companies for distribution. Development partners such as World Bank and USAID provide technical support. Before devolution, health facilities directly ordered commodities from KEMSA using a pull system, and this was paid for by the MOH. Since devolution, counties became responsible for ordering and paying for medical supplies, including fees for warehousing and distribution, for all the facilities in the counties. Drugs for HIV, malaria, TB and reproductive health are financed separately by donors and procured by their respective programmes [227].

2.7.2.4 Health information system (HIS)

In 2010, Kenya has implemented the District Health Information Software (DHIS2), an open source, cloud web-based data infrastructure for reporting routine health data for monitoring and evaluation [228]. Each month, health facilities tally register data into several monthly summary reporting forms which are sent to the sub-county government offices (by 5th of each month) for inputting into the DHIS2 (by 15th of each month) [228, 229]. Filling out these forms is a tedious process that takes a considerable amount of

time as facilities have multiple registers with duplicate information [229]. This usually interrupts normal service delivery as healthcare workers rush to meet reporting deadlines at the end of each month. More integration of tools and use of technology may alleviate the burden from data reporting.

2.7.3 Antenatal care in Kenya

In Kenya, the proportion of pregnant women aged 15-54 years who attend ANC at least once is over 95% country-wide [58]. However, only 10% of pregnant women attend ANC in the first trimester and less than 40% attend before the third trimester [58]. Reasons for not attending ANC visits include distance, cost, cultural restrictions, fear, lack of time, use of traditional birth attendants, and not feeling the need for ANC [58, 230]. Antenatal care services are mostly delivered by the primary care facilities. Within the Kenya national antenatal policy guidelines, addressing the conditions of HIV, syphilis, malaria and anaemia as early as possible during pregnancy is an essential component (Table 2.7) [161]. However, coverage of prevention, screening and treatment has yet to reach global targets. Dispensaries, where most women attend ANC, do not typically stock diagnostic tests for syphilis or anaemia and pregnant women are referred to distant facilities with laboratory capacity to complete their testing. Referrals further delay testing, narrowing the opportunity where treatment to prevent adverse outcomes are effective.

Table 2.7: Kenya's most current national antenatal guidelines.	
HIV	
Testing	Serial testing of HIV (see Figure 2.10) at first ANC visit and repeated every three months [231]
Treatment	Facilities with ability to initiate and monitor all HIV positive pregnant mothers on HAART should initiate triple ARVs (HAART) for life (uninterrupted) regardless of their WHO clinical stage or CD4 count in order to attain maximal viral load suppression WHO staging and CD4 testing is recommended at baseline to monitor progress [232, 233].
Syphilis	
Testing	Screening using non-treponemal serologic test, RPR or VDRL, at first ANC visit before 16 weeks gestation. Confirm reactive non-treponemal serologic tests treponemal-specific tests [161].
Treatment	Provide single dose of 2.4 MU benzathine penicillin or if penicillin allergic and unable to access penicillin desensitization give erythromycin 500 mg three times daily for 7 days and counselling on partner notification [161].
Malaria	
Prevention	In malaria endemic areas, give IPTp with SP to all pregnant women at every scheduled antenatal visit commencing at the start of the second trimester. Each SP dose should be given at least one month apart and ensuring women receive a minimum of 3 doses. IPTp should be given under DOT in the antenatal clinic and can be given on an empty stomach. Pregnant women who are HIV positive and are on daily cotrimoxazole chemoprophylaxis should not be given SP for IPTp. Each pregnant woman living in a malaria risk area should receive a LLIN at the first contact visit to the ANC [234].
Testing	In all pregnant women with fever or history of fever the use of parasitological diagnosis (microscopy or RDT) is recommended. At health facilities where malaria diagnostics are not available, patients suspected to have malaria should be treated for malaria [234].
Treatment	For uncomplicated *p. falciparum* malaria, treat pregnant women in the first trimester with seven days of quinine plus clindamycin (if unavailable use an ACT). For pregnant women in second or third trimester, treat with an artemisinin-based combination therapy (ACT). The current recommended first line ACT is artemether plus lumefantrine, (AL). The second line ACT is dihydroartemisinin plus piperaquine, (DHA/PPQ) [234]. Treat all adults including pregnant women in all trimesters and children with severe *p. falciparum* malaria with intravenous or intramuscular artesunate for a minimum of 3 doses/or 24hrs. At health care levels where treatment of severe malaria is not possible, but injections are available, give a single dose of intramuscular artesunate 2.4mg/kg for adults and 3.0mg/kg for children <20 kg and refer to an appropriate facility for further care. Use artemether 3.2 mg /kg or quinine 20 mg/kg if artesunate is not available [234].
Anaemia	
Prevention	Not anaemic (Hb ≥ 10 g /dL): give 60 mg elemental iron and 0.4 mg folic acid daily [161].
Testing	Hb blood test at first visit or referral if blood test not available. Repeat Hb test if Hb at previous visit was below 7.0 g/dl or signs of anaemia are detected on examination [161].
Treatment	Mild anaemia (Hb <10 g/dL): 120 mg elemental iron daily; Moderate anaemia (Hb 5-7.9 g/dL): same as for mild and provide additional iron dextran; Severe anaemia (Hb is <5 g/dL): admit to hospital. Treat any underlying cause of anaemia as appropriate [161].
ANC: antenatal care; ARV: antiretrovirals; ART: antiretroviral therapy; HAART: highly active antiretroviral therapy; IPTp: Intermittent Preventive Treatment; SP: sulfadoxine pyrimthamine; RPR: Rapid Plasma	

Reagin; VDRL: Venereal Disease Research Laboratory; DOT: directly observed treatment; LLIN: long lasting insectide treated nets; RDT: rapid diagnostic test; Hb: haemoglobin

2.7.3.1 HIV and PMTCT

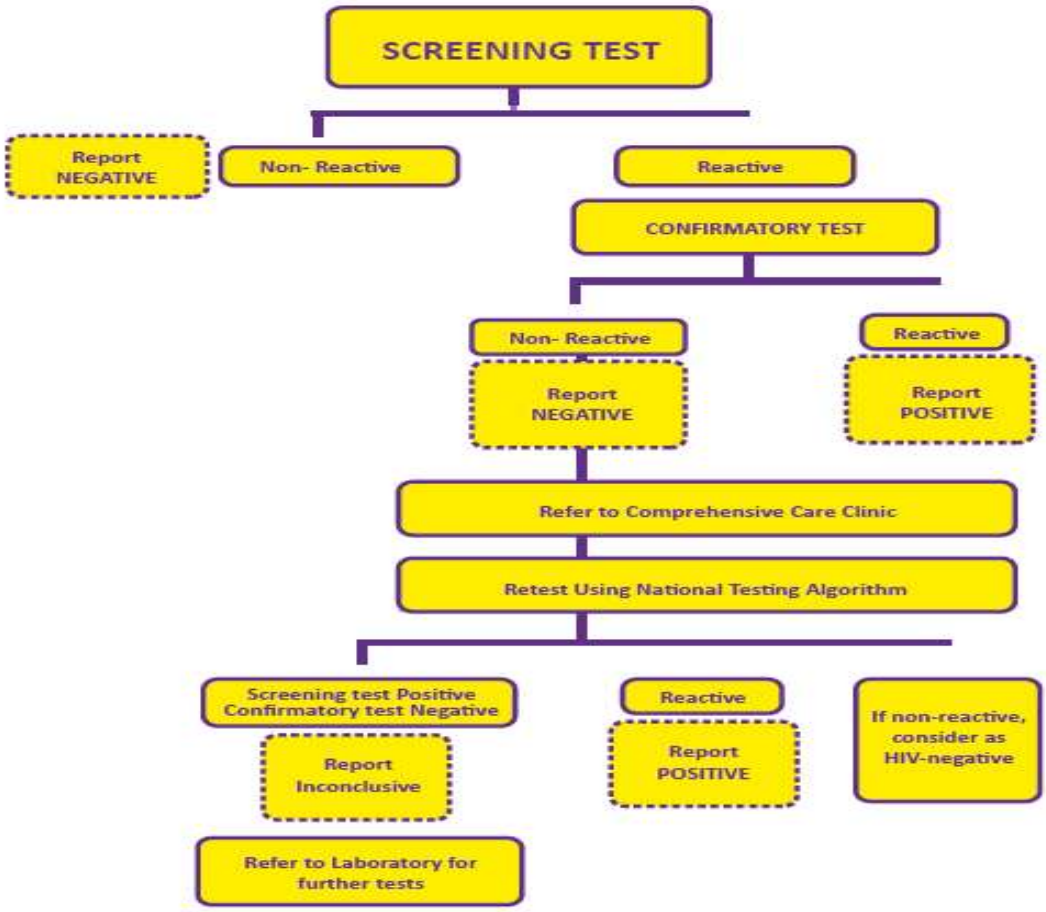
In Kenya, 96% of the HIV population reside in 34 of 47 counties, and 45% are concentrated in the 5 high burden counties of Nairobi, Homa Bay, Kisumu, Siaya and Migori [235]. PEPFAR, through implementation partners, provides technical and financial support to these 34 counties, which covers 78% of the national PMTCT needs [235]. In Kenya's eastern and Nyanza region, the International Center for AIDS Care and Treatment Programs (ICAP) at Columbia University's Mailman School of Public Health is the main implementation partner [236].

Overall HIV testing rates in Kenya vary among the regions. In women aged 15-49, an overall average of 53% were tested for HIV and received results in the preceding 12 months prior to the 2014 Health and Demographic survey. Among the same group, Nairobi had the highest HIV testing coverage at 90%, Nyanza region had 60%, and the North-eastern counties (Garissa, Wajir, Mandera) had the lowest coverage between 36-53% [237]. ANC is one of the main avenues for women to learn of their HIV statuses in Kenya; 92.5% of women who visited an ANC in their last pregnancy received an HIV test there [58].

HIV testing services in Kenya are delivered in both the community and at health facilities. Both facility and community based testing offer two approaches: provider Initiated Testing and Counselling (PITC) approach where the service provider offers HIV testing and the client can decline based on informed choice and the Client Initiated Testing and Counselling (CITC) where clients request testing services. All pregnant women visiting a health facility for antenatal care should be given PITC and repeat testing in the third trimester if the first test is done within the first trimester [231]. Rapid diagnostic tests have been used for point-of-care HIV testing in ANC since 2000 and have formed the cornerstone of rapid scale up since then. Since 2002 and prior to 2015, serial

testing with 3 rapid tests for screening, confirmation and tie-breaking was used but the rapid tests used for this algorithm was changed several times. In 2013, the national algorithm changed from Determine HIV 1-2 (Alere Scarborough, Inc., USA), Uni-Gold™ (Trinity Biotech, Ireland), and long Eliza to HIV 1-2 Antibody Colloidal Gold (KHB, Shanghai Kehua Bio-engineering Co Ltd, China), First Response HIV 1-2 kits (Premier Medical Corporation Ltd., Kachigam, India) and Uni-Gold [238]. In late 2015, the HIV testing algorithm was changed again to using only 2 serial rapid tests (Determine and First Response) and the tie-breaker test was no longer recommended (Figure 2.10) [231]. These frequent changes have implications for training, guidelines and quality of care.

Figure 2.10: Kenya's latest HIV testing algorithm [231]



Note: Use of tie breaker is no longer recommended as of 2015

Providing comprehensive ART to HIV pregnant women regardless of CD4 count (option B+) is the recommended treatment for HIV positive pregnant women in settings that have the capacity to initiate and monitor triple ARV therapy [233]. ICAP has taken the provision of option B+ in the Nyanza region to scale beginning in 2014 [236].

2.7.3.2 Syphilis and anaemia screening

Less than half of pregnant women attending ANC are tested for syphilis in Kenya, even though screening is a major country policy of antenatal care. In Nyanza, western Kenya, only about 8-22% of pregnant women are tested for syphilis at ANC [92, 104, 239]. At the time of this study the recommended screening strategy for syphilis was the use of non-treponemal tests, either the Rapid Plasma Reagin (RPR), or the Venereal Diseases Research Laboratory (VDRL) test [161]. Both these tests require electricity and equipment not readily available at most peripheral facilities most women in rural areas access ANC [105]. The RPR first requires a venous blood sample that needs to be centrifuged to obtain the plasma which is then mixed with the antigen (cardiolipin plus lecithin and cholesterol) on a rotator that will become agglutinated if an antibody/antigen complex is formed. The VDRL test uses the same antigen and the presence of antibody/antigen complex is observed under the microscope.

In western Kenya, only about 30-49% of pregnant women are tested for anaemia at ANC [92, 239]. Without blood tests, health workers need to rely on clinical examinations for pallor to detect severe anaemia, a method that has been shown to have variable sensitivity, ranging from 53%-100% [186, 187].

The difference in availability between tests for HIV and those for syphilis and anaemia may reflect the heavy reliance of healthcare expenditure on donor funding (almost a third) skewing priorities towards those of the international community [125]. The substantial donor support given to vertical HIV programmes often results in parallel

procurement and supervisory systems developed to ensure their accessibility and use [59, 122, 240].

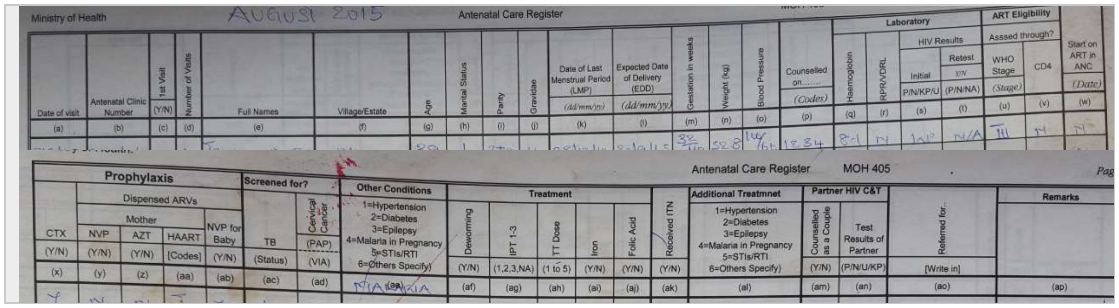
2.1.1.1 Malaria in Pregnancy

Kenya's 'Malaria in Pregnancy' policy does not require screening for blood parasites (although it is practiced by many facilities in western Kenya with microscopy capacity) but instead emphasizes prevention and treatment (Table 2.7). Country-wide, only 10% of pregnant women aged 15-49 with a live birth between 2012-2014 received the minimum three doses of SP as recommended by the national guidelines [215]. Regional differences exist with the coastal region achieving the highest coverage of 32.7%, followed by western region of 26.2% and Nyanza with 9.7% [241]. Compliance on bednet usage is also low, despite high ownership [242]. Findings from the 2014 Demographic and Health survey found that only 51% of pregnant women slept under an treated bednet the previous night [215]. Unclear guidance and stock-outs are some of the reasons for the policy's underachievement [61]. Parasitic screening of malaria with POCT at the first antenatal visit may be an attractive strategy due to missed opportunities of the current strategy.

2.7.3.3 Antenatal care registers

Data on ANC services delivered are routinely collected in hand-written ANC registers. These include information on HIV testing and retesting, syphilis testing and treatment, haemoglobin concentrations, iron folic acid supplementation, IPTp and bednets given. For malaria, there is a column under 'Other conditions screened for' to indicate malaria testing and a column under 'Additional treatments' to indicate if treatment was given for malaria (Figure 2.11). This is usually inconsistently filled out and does not give accurate data on the number of women receiving malaria tests or treatment.

Figure 2.11: Column headings for antenatal care registers in Kenya



2.8 Conclusion

Many of the strategies to lessen the burden of HIV, syphilis, malaria and anaemia in pregnancy in sub-Saharan Africa struggle at the implementation stage because of health system weaknesses and lack of a co-ordinated and integrated effort. For pregnant women who do have contact with ANC, comprehensive and quality care is still elusive. Stock-out of drugs and commodities inadequate training of healthcare workers, lack of clear guidelines, weak supervision and monitoring systems, convoluted patient pathways, and the socio-cultural beliefs from the community are some of the things that stymie effective coverage. Addressing these challenges would require concerted efforts from multiple parties on a grand scale.

A simple strategy of bringing point-of-care testing services to dispensaries, the lowest level of the health system, can improve accessibility coverage for the most hard-to-reach women living in the periphery, saving them the need to travel long distances, with time and cost implications, to laboratories. The intervention provided testing commodities and treatments to address the poor availability coverage identified from the baseline assessment. It also gave training, and supervision to healthcare workers to ensure good clinical practice and effective delivery of the intervention.

Integration of multiple POCTs in service delivery can reduce redundancies among programmes and maximize synergies by bundling together healthcare worker training and supervision. This strategy is also a step towards delivering holistic antenatal care but will need to be evaluated in the health system to ensure that it can be adopted,

accepted and that the intervention can be delivered as intended. It is also important to assess the implementation process to identify barriers and promoters to understand how the intervention can be best supported. Western Kenya is a suitable place to test this strategy as this is where an under-resourced health system meets high rates of disease. Therefore, three studies were designed to assess the implementation outcomes of integrated testing at peripheral health facilities in rural western Kenya. Chapter 3 assessed rates of adoption and fidelity to clinical management guidelines as well as healthcare worker performance of testing. Chapter 4 explored healthcare workers' and pregnant women's experiences of testing to give richer narratives of findings from Chapter 3. Chapter 5 explored the operational impact of introducing the strategy at a dispensary to elucidate effects on wait times and health resource utilization.

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3 Chapter 3: Study 1

Integrated point-of-care testing (POCT) of HIV, syphilis, malaria and anaemia in antenatal clinics in western Kenya: a longitudinal implementation study

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Box 3.1 Contributions

NY: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Visualization, Writing – original draft, Writing – review & editing.
MT: Conceptualization, Methodology, Supervision, Writing – review & editing
GA and GB: Project administration, Writing – review & editing
PPA: Conceptualization, Methodology, Supervision, Writing – review & editing
JH: Methodology, Writing – review & editing
KL: Funding Acquisition, Writing – review & editing
FTK and MD: Conceptualization, Methodology, Resources, Supervision, Writing – review & editing

3.1 Abstract

Background: In sub-Saharan Africa, HIV, syphilis, malaria and anaemia are leading preventable causes of adverse pregnancy outcomes. In Kenya, policy states women should be tested for all four conditions (malaria only if febrile) at first antenatal care (ANC) visit. In practice, while HIV screening is conducted, coverage of screening for the others is suboptimal and early pregnancy management of illnesses is compromised. This is particularly evident at rural dispensaries that lack laboratories and have parallel programmes for HIV, reproductive health and malaria, resulting in fractured and inadequate care for women.

Methods: A longitudinal eight-month implementation study integrating point-of-care diagnostic tests for the four conditions into routine ANC was conducted in seven purposively selected dispensaries in western Kenya. Testing proficiency of healthcare workers was observed at initial training and at three monthly intervals thereafter. Adoption of testing was compared using ANC register data 8.5 months before and eight months during the intervention. Fidelity to clinical management guidelines was determined by client exit interviews with success defined as $\geq$90% adherence.

Findings: For first ANC visits at baseline (n=529), testing rates were unavailable for malaria, low for syphilis (4.3%) and anaemia (27.8%), and near universal for HIV (99%). During intervention, over 95% of first attendees (n=586) completed four tests and of those tested positive, 70.6% received penicillin or erythromycin for syphilis, 65.5% and 48.3% received cotrimoxazole and antiretrovirals respectively for HIV, and 76.4% received artemether/lumefantrine, quinine or dihydroartemisinin–piperaquine correctly for malaria. Iron and folic supplements were given to nearly 90% of women but often at incorrect doses.

Conclusions: Integrating point-of-care testing into ANC at dispensaries with established HIV testing programmes resulted in a significant increase in testing rates, without disturbing HIV testing rates. While more cases were detected and treated, treatment fidelity still requires strengthening and an integrated monitoring and evaluation system needs to be established.

3.2 Background

In sub-Saharan Africa (SSA), the most preventable leading causes of maternal mortality and adverse pregnancy outcomes are maternal HIV, syphilis, malaria and anaemia [1-4], with co-infections common [5-9]. SSA has an estimated maternal HIV prevalence of 5.3%, representing 92% of the world's HIV positive pregnant women [10, 11]. Roughly 24% of deaths in women during pregnancy or post-partum are attributable to untreated HIV [1]. Maternal syphilis in the African region has a prevalence of 1.7%, which constitutes 63.1% of infections in pregnancy globally [2]. Syphilis is associated with spontaneous miscarriage, stillbirth, preterm birth, low birthweight, neonatal death, and congenital infection in infants [2]. The risk for both HIV and syphilis mother-to-child transmission cumulates with duration of exposure in utero [12, 13] and late treatments of syphilis may not avert damage to foetal development [14]. Where malaria is endemic, 45% of pregnancies would be infected [3, 15]. Starting from early gestation throughout, malaria parasitaemia is associated with anaemia, intrauterine growth restriction, preterm delivery, foetal loss, neonatal and infant mortality [3, 15-19]. Anaemia is also most prevalent in Africa: about 46% of pregnant women are anaemic and 1.5% are severely anaemic [20]. Anaemia during pregnancy is associated with increased risk of post-partum haemorrhage, maternal mortality, low birth weight, and perinatal mortality [4]. There is substantial evidence that iron deficiency early in pregnancy (first and second trimester) contributes to higher risk of pre-term delivery and lower birth weight than if it occurred later [21, 22]. Thus, early prevention, diagnosis and treatment is key to protect women and their pregnancies. Many of these conditions do not exist in isolation and having one disease or condition may also be a risk factor for another: malaria is more common in women with HIV [23-25]; risk of HIV transmission is increased through genital ulcer disease [5]; malaria is a major risk factor for anaemia [26]; approximately 26% of severe anaemia in pregnant women is attributable to malaria and can be reduced by 38% from preventing malaria infection in pregnancy [3]. Because of their individual and combined contribution to disease, addressing these conditions

together, as early as possible during pregnancy is an essential goal of antenatal care (ANC) [27].

Since 2001, Kenya has adopted the World Health Organization's (WHO) focused ANC guidelines which call for a minimum of four visits [28] (recently updated to eight 'contacts' by WHO [27]). For the first visit, Kenyan guidelines recommend screening for HIV, syphilis and anaemia, urinalysis, and blood typing (together known as the ANC profile). To prevent the consequences of malaria in pregnancy, the current strategy recommends parasitic diagnosis of malaria only if the patient is febrile, together with the use of insecticide-treated nets (ITNs) and ANC administered intermittent preventive therapy with sulfadoxine-pyrimethamine (IPTp-SP). Expanding malaria testing at the first ANC visit to all pregnant women, regardless of fever [29-31], may be an attractive strategy in parts of Africa for various reasons including concerns about the impact of high-grade SP resistance [32] or that some populations may no longer require IPTp because of marked reductions in malaria transmission. Furthermore, IPTp alone may be an inadequate intervention because women who attend ANC in the first trimester are not eligible for SP, and the uptake of IPTp has been low, with only half of pregnant women receiving at least one of three or more recommended doses of SP [19, 33, 34].

Rates of testing for syphilis and anaemia remain low among pregnant women in Kenya [35-37] even though 95% of pregnant women attend at least one ANC visit [35]. This is largely because most women attend ANC at dispensaries (tier-2 health facilities in the periphery) which do not typically stock diagnostic tests (except for HIV) and are referred, with additional costs and time implications, to distant facilities with laboratory capacity to complete their ANC profile [38, 39]. The difference in availability between tests for HIV and those for syphilis and anaemia reflects the high international priority and substantial financial support given to vertical HIV programmes resulting in parallel procurement and supervisory systems developed to ensure their accessibility and use [40, 41]. Syphilis and haemoglobin screening, despite the strong evidence for their

clinical effectiveness [42-44], lack such donor advocacy and prioritization and suffer inadequate coverage [40, 41].

Affordable and reliable rapid point-of-care tests (POCTs) that require minimal training and equipment are available to fulfil antenatal screening requirements [38]. Their simplicity and immediacy of results greatly benefit resource-constrained settings by allowing same-day initiation of management of conditions and their co-infections. POCTs use at dispensaries thus has potential to improve early diagnosis and treatment of conditions that cause adverse pregnancy outcomes. POCTs have been instrumental in the scale-up of prevention of mother-to-child-transmission (PMTCT) of HIV services, achieving over 90% of HIV testing coverage in women who attend ANC [35]. The skills healthcare workers have gained from HIV testing can be expanded to integrate the use of POCTs for syphilis, malaria and anaemia at dispensaries so coverage of diagnosis and timely treatment can be improved.

This longitudinal implementation study quantitatively evaluated the adoption and fidelity of a programme intervention integrating point-of-care testing (POCT) for HIV, syphilis, malaria and anaemia at ANCs in dispensaries in western Kenya. We evaluated whether integrated POCT can increase the proportion of pregnant women tested and treated correctly for each of the respective conditions at first ANC visit. Other implementation outcomes of appropriateness, acceptability and feasibility will be reported elsewhere.

3.3 Methods

3.3.1 Study setting

The study was conducted between December 2014 and August 2015 in the site of the KEMRI and CDC Health and Demographic Surveillance System (HDSS) in Siaya County, western Kenya. The population is 95% ethnically Luo, rural, and lives through subsistence farming and local trading [45]. At the time of the study, there were 37 public health facilities in the study area: one district hospital, nine health centres and 27

dispensaries. Dispensaries comprise the lowest level (tier-2) of the formal health system and offer basic maternal and child health services, rudimentary out-patient curative care and support care for HIV positive patients. Personnel typically include one to two nurses trained to certificate (at least 30 months training post-secondary) or diploma level (at least 36 months training post-secondary), a part-time clinical officer (36 months training post-secondary), an HIV testing counsellor and some support staff. The dispensaries receive approximately 40 antenatal visits per month.

3.3.2 Health facility evaluations pre-intervention

Initial facility assessments were conducted to assess capacity to offer POCTs in nine health centres and 24 dispensaries within the HDSS area (three dispensaries were not assessed). Facility evaluation covered information such as facility infrastructure, client load, number and type of antenatal health workers, testing services and client flow. The assessment used a survey and observation checklist adapted from the Demographic and Health Surveys (DHS) Program [46]. Instruments were pre-tested outside the catchment area and were carried out by trained data collectors.

Seven dispensaries were then purposively selected for inclusion in the study based on the following criteria: absence of other ongoing studies with pregnant women, geographic spread within the visual map area of HDSS, the number of monthly antenatal visits identified through retrospective register review, and willingness of the facility to participate. All seven facilities' ANC clinics routinely conducted HIV testing, two irregularly conducted anaemia testing, and three irregularly conducted malaria testing. Lack of test supplies was the main reason for not conducting ANC testing for syphilis and anaemia.

3.3.3 Implementation of programme

Integration here is defined as provision of all four tests concurrently, by a single healthcare worker, during a woman's first ANC visit. In facilities that have specialized HIV testing counsellors, the four tests may be done by the counsellor instead of the ANC

nurse. All the facilities' ANC healthcare workers were given a competency-based training either at a central location or on-site. All participants received training manuals and job aid testing placemats with step-by-step instructions (Appendix 1 Integration operating procedure placemat). Training included using one finger-prick blood draw to run all four tests per standard operating procedures, safety, and appropriate preventive care and clinical management of positive results following Kenyan guidelines as summarised in Table 3.1:

Table 3.1: Appropriate clinical management for positive test results and preventive care at first ANC visit [47]

Condition	For treatment	For prevention
HIV	Initiate PMTCT; counsel; give cotrimoxazole and start triple therapy with antiretrovirals	
Syphilis	Provide single dose of 2.4 MU benzathine penicillin or if penicillin allergic and unable to access penicillin desensitization, give erythromycin 500 mg three times daily for seven days and counsel on partner notification	
Malaria	Uncomplicated malaria: give quinine in first trimester; give artemether/lumefantrine (AL), quinine or dihydroartemisinin-piperaquine (DP) in second or third trimester; clinical severe malaria: refer to hospital	Give directly observed IPTp-SP for malaria for women in second or third trimester not on cotrimoxazole; give ITN and advise to sleep under it.
Anaemia	Mild anaemia (Hb <10 g/dL): give 120 mg daily elemental iron; moderate anaemia (Hb 5-7.9 g/dL): as above and provide additional iron dextran; severe anaemia (Hb is <5 g/dL): refer to hospital	Not anaemic (Hb >10 g/dL): give 65 mg daily elemental iron
Neural tube defects		Low dose (0.4 mg) folic acid daily; if low dose folic acid is not available, high dose (5 mg) tablets should not be administered with SP but can be taken 14 days following administration of IPTp-SP.

ANC: antenatal care; POCT; point-of-care testing; PMTCT: prevention of mother-to-child transmission; IPTp-SP: intermittent preventive therapy in pregnancy with sulfadoxine-pyrimethamine; ITN: insecticide-treated net

Study facilities used existing HIV drugs and HIV POCTs supplied by the Government of Kenya per its standard national algorithm at the time: HIV (1+2) Antibody Colloidal Gold

(KHB, Shanghai Kehua Bio-engineering Co Ltd, China) for screening, First Response HIV-1-2 kits (Premier Medical Corporation Ltd., Kachigam, India) for confirmation and Uni-Gold™ (Trinity Biotech, Ireland) for tie-breaking. Iron, folic acid, SP and malaria treatment drugs were also supplied free of charge by the government. The study supplied the facilities with POCTs for syphilis (SD BIOLINE Syphilis 3.0 test for antibodies against *Treponema pallidum*, Standard Diagnostic Inc., Korea), malaria (CareStart™ Malaria HRP2 Pf, AccessBio, USA) and haemoglobin concentrations (HemoCue® Hb 201+, HemoCue AB, Sweden) and ensured no stock-outs. For each lot number, 1% of the tests were selected at random and validated at KEMRI/CDC's HIV reference laboratory in Kisumu, western Kenya, using known positive and negative samples. HemoCue® machines were calibrated every three months. The study also provided Brannan™ triple timers, gloves, and benzathine penicillin for treating syphilis based on projected prevalence of syphilis in the area.

3.3.4 Data collection and outcome indicators

Photographs of routine ANC registers were taken for 8.5 months before and eight months during intervention and the data were double-entered into the study database. There was no distinct column for recording malaria results in the registers so no reliable data existed pre-intervention and a column was added to facilitate collection of malaria test results during the intervention. From the registers, testing uptake was assessed among women aged 15-49 years below 28 gestational weeks of pregnancy (<28gw) attending their first ANC visit. The gestational age was estimated using date of last menstrual period (LMP) or fundal height if LMP was unknown. The evaluation was done in this group of women because adverse pregnancy outcomes are most preventable with early treatment and so we concentrated on outcomes in this population.

During the intervention, these women were also asked to participate in exit interviews with trained research staff following their visits. Written informed consents were obtained. For illiterate women, the consent forms were read to the women in the presence of a literate witness and verbal consents with thumb prints and witness

signatures were obtained. Women who refused to participate or were unable to provide informed consent because of mental or physical disability were excluded. Those who consented were interviewed for 20-30 mins in a private area at the facility. Interviews asked whether women were given information about the blood tests, test results, any preventive care or treatments (including detailed information on type and dosage of drugs not captured by ANC registers) using picture cards or observed drugs by interviewers, counselling, and advice for partner notification.

Quality assessments (QA) through observed proficiency testing of healthcare workers to correctly perform rapid tests per manufacturers' instructions were done immediately after initial training and at three, six and nine months (shortly after eight months of the intervention) using a 57-step checklist (Appendix 2) by trained research staff. Those who performed ≥90% of the checklist correctly received reminders for any missed steps and proceeded to implement integrated POCT. Those who did not reach ≥90% were re-trained until proficient.

Endpoints for assessing programme adoption and implementation fidelity are summarised in Table 3.2. Adoption is defined as "the action to try or employ an innovation…also may be referred to as 'uptake'" and fidelity is defined as the "degree to which [the] intervention was implemented as intended by program developers and the quality of program delivery" [48]. Success was set at ≥90% in line with global testing and treatment targets for HIV and syphilis [49, 50]. Degrees of under-reaching the success target were categorised as follows: under-reached 60% to <90%, very under-reached 40% to <60% and severely under-reached <40%. Because introducing new services may affect existing services, synergy of integrating POCT with HIV testing was determined by change of HIV testing rates before and after the intervention.

Table 3.2: Indicators of adoption, fidelity, and proposed success endpoints [48]				
Indicators of adoption and fidelity		Indicator measure	Data source	Success endpoints
Adoption	Testing uptake and synergy into HIV programme	% of pregnant women tested for syphilis, malaria and anaemia by POCTs; unchanged or improved % of women tested for HIV	ANC register	≥ 90% tested; ≥0% change in HIV testing rates
Fidelity	Clinical management	% of pregnant women who receive appropriate: a) preventive care b) correct management for test positive cases	Exit interviews	≥90% received
	Information giving	% of pregnant women who were given: a) information about the four tests b) test results c) HIV counselling d) syphilis partner notification advice	Exit interviews	≥90% given/counselled/advised
	Health worker proficiency of POCT	Proficiency scores measuring the ability of the health care worker to correctly perform rapid diagnostic tests per manufacturer guidelines	Proficiency scores (%)	≥90% on check-list
POCTs: point-of-care tests; POCT: point-of-care testing; ANC: antenatal care				

3.3.5 Data analysis

Quantitative data were entered in Microsoft Excel 2016. Descriptive statistics and analyses were done in Stata 14. The command *metan* was used to graphically display before and during testing proportions. For categorical variables, proportions were calculated and Chi^2 was used to test for associations. For non-normal distributions of continuous data, medians and inter-quartile ranges (IQR) were calculated and Wilcoxon rank-sum tests were used to test for associations. Box and whisker plots of proficiency tests scores were created in Microsoft Excel 2016. Using individual and facility level variables collected from the study, we explored factors associated with women not having a complete testing profile. Relative risks of having an incomplete ANC profile were obtained for each variable by fitting a log-binomial generalized estimating equation model that took facility clustering into account. Variables that had a significance level of <0.20 in the univariate analysis were considered for inclusion. Multicollinearity of selected variables was tested by using the variance inflation factor

(VIF) command in Stata. Variables with a tolerance value (1/VIF) <0.1 were considered collinear with one of the other independent variables.

3.3.6 Ethical considerations

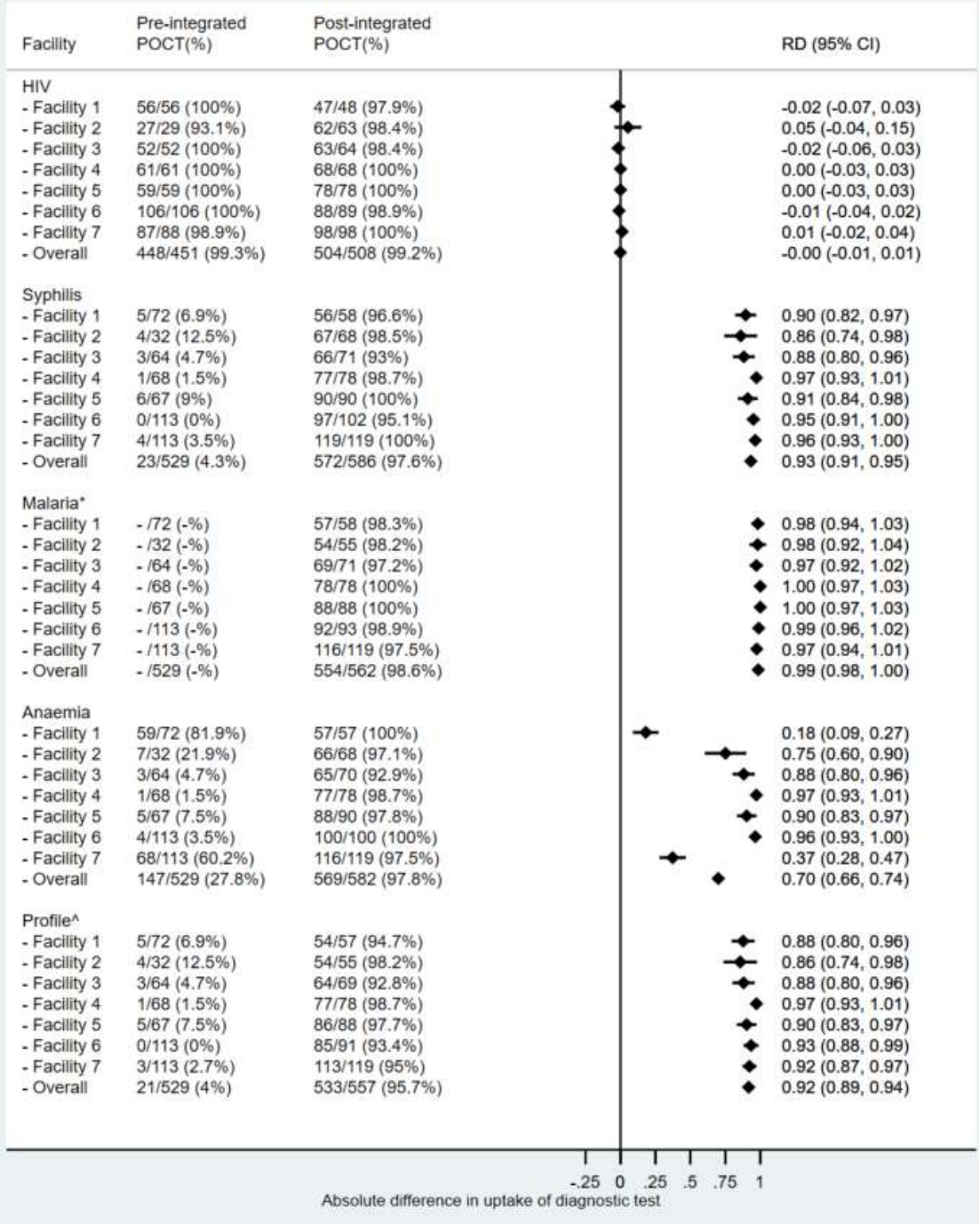
The protocol was reviewed and approved by the scientific and ethical steering committees of the Kenya Medical Research Institute (protocol 2271) and the Liverpool School of Tropical Medicine Ethics Committee (protocol 14.017). For U.S. CDC, while this activity was determined to be human subjects research, CDC staff involvement did not constitute engagement in human subjects' research, thus not requiring human subjects research review by the CDC institutional review board.

3.4 Results

3.4.1 Increase in testing uptake (ANC register data)

During 8.5 months before the integrated POCT programme, the seven facilities received 2279 ANC visits (median: 37, IQR: 28-37 visits per month) and 698 of them (median: 11, IQR: 8-11 visits per month) were first visits. Of the first visits, 529 (75.7%) women were <28gw and aged 15-49 years. During the eight months of integrated POCT programme, 2240 ANC visits were made at the seven facilities (median: 38, IQR: 32-38 visits per month). Of these, 728 were first ANC visits (median: 13, IQR: 10-13 visits per month), and 586 (80.5%) were by women <28gw aged 15-49. HIV testing rates remained over 90% in all facilities both before and during integrated POCT period. For syphilis and anaemia, overall testing proportions increased from 4.3% (mean: 5.4%, SD: 4.0%, range: 0-12.5%) and 27.8% (mean: 25.9%, SD: 29.8%, range: 1.5-81.9%) respectively to over 97%. The variations in syphilis and anaemia testing pre-intervention reflect the inconsistent availability of test supplies within and between facilities. Facility one and seven had noticeably higher testing rates for anaemia because they received test supplies from the district hospital and an external partner respectively. Malaria testing also reached over 97% in all facilities during the intervention (Figure 3.1).

Figure 3.1: Proportion tested for condition pre (n=529) and during (n=586) integrated POCT programme by facility



*No data on number of women tested for malaria were available from the antenatal care registers before the intervention and therefore pre- and post-proportions were not comparable; ^profile pre-integrated POCT includes HIV, syphilis and anaemia; profile during integrated POCT includes HIV, syphilis, malaria and anaemia; POCT: point-of-care testing; RD: risk difference, interpreted as the difference in testing proportions before and during integrated POCT

3.4.2 New infections and co-infections picked up by POCTs

Among the 529 pregnancies evaluated pre-intervention, 31 new HIV infections, no syphilis infections, and 58 anaemic women (Hb <10 g/dL) were detected. There were 78 women with known HIV positive statuses.

Among the 586 pregnancies during integrated POCT, 41 new HIV infections, 18 syphilis infections, 177 malaria infections, and 223 anaemic women were detected. There were 77 women with known HIV positive statuses (Table 3). Among 118 HIV positive women, co-infections with syphilis were found in five (4.2%) and with malaria in 30 (25.4%). Among 223 anaemic women, malaria was detected in 90 (40.4%). One woman tested positive for syphilis, malaria and anaemia while none tested positive for all four conditions. Among HIV known positives, one woman was tested syphilis positive and anaemic.

3.4.3 Mixed programme fidelity in management of conditions (self-reported from exit interviews)

Among 586 pregnancies eligible for exit interviews, 106 (18.1%) did not consent. Those interviewed were more likely to have had a previous miscarriage, or have been tested for malaria, and were less likely to be newly diagnosed HIV positive (Table 3.3).

Table 3.3: Test positivity rates and demographic characteristics of women aged between 15-49 years and <28 weeks pregnant, based on data from ANC registers 8.5 months before and 8 months during study

Conditions	Before integrated POCT (n=529)	During integrated POCT (n=586)			
	All	All	Not interviewed n=106	Interviewed n=480	P-value*
HIV	n=529	n=585	n=105	n=480	
known positive	78/529 (14.7%)	77/585 (13.2%)	16/105 (15.2%)	61/480 (12.7%)	0.487
tested for HIV	448/451 (99.3%)	504/508 (99.2%)	87/89 (97.8%)	417/419 (99.5)	0.087
tested positive	31/448 (6.9%)	41/504 (8.1%)	12/87 (13.8%)	29/417 (7.0%)	0.034
total HIV positive	109/526 (20.7%)	118/581 (20.3%)	28/103 (27.2%)	90/478 (18.8%)	
Syphilis	n=529	n= 586	n=106	n=480	
tested for syphilis	23/529 (4.3%)	572/586 (97.6%)	102/106 (96.2%)	470/480 (97.9%)	0.302
tested positive	0/23 (0%)	18/572 (3.1%)	2/102 (2%)	16/470 (3.4%)	0.449
Malaria		n=562	n=105	n=457	
tested for mal		554/562 (98.6%)	100/105 (95.2%)	454/457 (99.3%)	0.001
tested positive		177/554 (31.9%)	28/100 (28%)	149/454 (32.8%)	0.349
Anaemia (g/dL)	n=529	n=582	n=106	n=476	
tested for Hb conc.	147/529 (27.8%)	569/582 (97.8%)	101/106 (95.3%)	468/476 (98.3%)	0.056
Non-anaemic Hb ≥ 10 g/dL	89/147 (60.5%)	346/569 (60.8%)	60/101 (59.4%)	286/468 (61.1%)	
Mild Hb 8-9.9 g/dL	46/147 (31.3%)	166/569 (29.2%)	29/101 (28.7%)	137/468 (29.3%)	
Moderate Hb 5-7.9 g/dL	12/147 (8.2%)	56/569 (9.8%)	11/101 (10.9%)	45/468 (9.6%)	
Severe Hb <5 g/dL	0/147 (0%)	1/569 (0.2%)	1/101 (1%)	0/468 (0%)	0.185
WHO anaemic Hb <11 g/dL	91/147 (61.9%)	346/569 (60.8%)	65/101 (64.4%)	281/468 (60%)	
Demographic		During integrated POCT (n=586)			
		All	Not interviewed n=106	Interviewed n=480	P-value
Age		n=585	n=106	n=479	
<20		159 (27.2%)	30 (28.3%)	129 (26.9%)	
20 to <25		208 (35.6%)	40 (37.7%)	168 (35.1%)	
25 to <30		118 (20.2%)	18 (17%)	100 (20.9%)	
30 to <35		64 (10.9%)	12 (11.3%)	52 (10.9%)	
35+		36 (6.2%)	6 (5.7%)	30 (6.3%)	0.917*
Gestation in weeks		n=583	n=106	n=477	
median (IQR)		21.1 (16.9-24.1)	21.7 (17.6-24.4)	21.1 (16.9-24.1)	0.47†
Gravidity		n=586	n=106	n=480	
gravida 1		163 (27.9%)	38 (35.8%)	125 (26.1%)	
gravida 2		134 (22.9%)	24 (22.6%)	110 (23%)	
gravida 3		114 (19.5%)	14 (13.2%)	100 (20.9%)	
gravida 4		70 (12%)	12 (11.3%)	58 (12.1%)	
gravida 5+		105 (17.9%)	18 (17%)	87 (18.1%)	0.22*
Previous miscarriage		n=586	n=106	n=480	
Yes		21 (3.6%)	0 (0%)	21 (4.4%)	0.028*
Marital status		n=586	n=106	n=480	
married		466 (79.5%)	83 (78.3%)	383 (79.8%)	
widowed		9 (1.5%)	2 (1.9%)	7 (1.5%)	
single		93 (15.9%)	15 (14.2%)	78 (16.3%)	
divorced/separated		18 (17.2%)	6 (5.9%)	12 (12%)	0.363*

WHO Hb: World Health Organization standards for haemoglobin cut-offs for defining anaemia else Kenyan cut-offs; *p-value based on Chi^2 for the difference between those interviewed and not interviewed; †p-value based on Wilcoxon rank-sum for the difference in median between those interviewed and not interviewed; ANC: antenatal care; POCT: point-of-care testing; Hb: haemoglobin concentration

3.4.4 HIV

Of 29 women who were newly tested positive for HIV, treatment was commenced that same visit for less than the 90% target: 19 (65.5%) were given CTX, and 14 (48.3%) were given ARVs (Table 4). One woman was told to return the following day for treatment while seven (24.1%) women refused treatment citing reasons such as: they should consult their husbands; they will start therapy at other clinics; they need to confirm at other clinics; they did not like the nurse's attitude.

3.4.5 Syphilis

Among 441 women who self-reported receiving syphilis tests, 17 (3.9%) reported positive results of which 12 (70.6%) were given either penicillin (n=11) or erythromycin (n=1) the same day (Table 4). One woman was told to return the next day with her partner for couples' treatment and the remaining four were asked to buy penicillin or erythromycin at a pharmacy even though the study had supplied the facilities with sufficient penicillin based on projected prevalence. Thirteen women (76.5%) said they were advised by the nurse to inform their partners **(Table 3.5)**.

3.4.6 Treatment and IPTp-SP for malaria

Based on exit interviews, 469 women self-reported receiving malaria tests of which 161 (34.3%) were positive. Among those with positive malaria tests, eight were in their first trimester of whom two (25%) were given quinine and the rest were given or prescribed AL or DP. Of the 153 malaria positive pregnancies in their second trimester, 121 (79.1%) were given AL, DP, or quinine and the rest were given SP (n=2), prescribed quinine or AL (n=24) or not given or prescribed anything (n=6) **(Table 3.4).** Therefore 123/161 (76.4%) were given antimalarials in accordance with treatment guidelines.

SP was out of stock for most of the integrated POCT period and only 76 women reported receiving SP for IPTp. Of these, seven were given high dose (5 mg) folic acid

concurrently, which is not compliant with guidelines for women receiving IPTp-SP (Table 3.4). Of the women eligible for SP (in second trimester and not on cotrimoxazole), 19.2% (69/359) received IPTp-SP (Table 3.4).

3.4.7 Anaemia and haematinic supplementation

Among 480 women interviewed, 434 (90.4%) received iron supplementation. However, the reported dosing regimen did not adhere to prophylactic or treatment guidance based on Hb concentrations recorded in the ANC register (Table 3.4). None of the interviewed women had severe anaemia and six (13.3%) of 45 with moderate anaemia were asked to buy iron dextran. Folic acid was given to 421 (87.7%) women in either 0.4 mg folic-iron combination tablets or 5 mg tablets (Table 3.4).

Table 3.4: Self-reported treatments for test positives, IPTp for malaria, and haematinic supplementation given at first visit ANC among 480 interviewed women

	Proportion	Success threshold	Target reached for correct ANC strategies? *
HIV treatment			
Given CTX	19/29 (65.5%)	≥90%	Under-reached
Given ARVs	14/29 (48.3%)	≥90%	Very under-reached
Syphilis treatment			
Given 2.4 MU benzathine penicillin or erythromycin	12/17 (70.6%)	≥90%	Under-reached
Malaria intermittent preventive therapy and treatment			
Given SP for IPTp among women in 2nd trimester not on CTX†	69/359 (19.2%)	≥90%	Severely under-reached
Given SP for IPTp among women in 1st trimester not on CTX†	5/41 (12.2%)		
Given SP to women also on CTX‡	2/80 (2.5%)		
Given 5 mg folic acid with SP	7/76 (9.2%)		
Given AL, DP or quinine among malaria positives in 2nd trimester	121/153 (79.1%)	≥90%	Under-reached
Given quinine among malaria positives in 1st trimester	2/8 (25%)	≥90%	Severely under-reached
Haematinic supplementation for prophylaxis and treatment			
Given folic acid	421/480 (87.7%)	≥90%	Under-reached
- Told to take between 0.4-1.2 mg daily	378/421 (89.8%)		
- Told to take between 5-10 mg daily	43/421 (10%)		
Given iron	434/480 (90.4%)	≥90%	Reached
- Given iron and mentioned side effects	41/434 (9.4%)	≥90%	Severely under-reached
Iron dosing information given to women according to Hb level			
Normal Hb ≥10 g/dL	n=286		
- 60-65 mg elemental iron daily	193/286 (67.4%)	≥90%	Under-reached
- 120-130 mg elemental iron daily	4/286 (1.4%)		
- 180-195 mg elemental iron daily	49/286 (17.1%)		
- Not told dosing	12/286 (4.2%)		
- Not given any iron	28/286 (9.8%)		
Mild anaemia Hb 8-9.9 g/dL	n= 137		
- 60-65 mg elemental iron daily	86/137 (62.8%)		
- 120-130 mg elemental iron daily	4/137 (2.9%)	≥90%	Severely under-reached
- 180-195 mg elemental iron daily	32/137 (23.4%)		
- Not told dosing	3/137 (2.2%)		
- Not given any iron	12/137 (8.8%)		
Moderate anaemia Hb 5-7.9 g/dL	n=45		
- 60-65 mg elemental iron daily	20/45 (44.4%)		
- 120-130 mg elemental iron daily	9/45 (20%)	≥90%	Severely under-reached
- 180-195 mg elemental iron daily	9/45 (20%)		
- Not told dosing	2/45 (4.4%)		
- Not given any iron	5/45 (11.1%)		
No Hb recorded	n=12		
- 60-65 mg elemental iron daily	8/12 (66.7%)		
- 120-130 mg elemental iron daily	1/12 (8.3%)		
- Not told dosing	2/12 (16.7%)		
- Not given any iron	1/12 (8.3%)		

* ≥90% target reached; <90% to ≥60 - under-reached; <60% to ≥40 very under-reached; <40% severely under-reached; IPTp: intermittent preventive therapy in pregnancy; ANC: antenatal care; CTX: cotrimoxazole; ARV: antiretroviral; SP:sulfadoxine-pyrimethamine; AL: artemether/lumefantrine; DP: dihydroartemisinin-piperaquine (DP) ; Hb: haemoglobin concentration; †not on CTX includes women who were tested HIV negative, unknown status, and new positive but were not given CTX same day; ‡on CTX includes known HIV positives and new HIV positives who were given CTX same day

3.4.8 Information giving

General information and advice given to women about the four conditions is shown in Table 5. Over 90% reported they received the blood tests. Furthermore, over 90% reported test results for HIV, syphilis and malaria that were concordant with those from the ANC register, while only half of those tested for Hb reported anaemia statuses that agreed with those from the register (Table 3.5). Women who reported not being told results for HIV, syphilis, or malaria were all negative for those conditions based on the ANC register.

Table 3.5: Self-reported information given about the tests at first ANC visit among 480 interviewed women

	Proportion	Success threshold	Target reached for correct ANC strategies?*
Information about HIV			
Received HIV counselling	167/480 (34.8%)	≥90%	Severely under-reached
Reported receiving an HIV test among those who had an HIV	411/417 (98.6%)	≥90%	Reached
test result in ANC register			
Reported told HIV status that	399/411 (97%)	≥90%	Reached
agree with result in ANC register			
Reported told HIV status that did not	0/411 (0%)		
agree with result in ANC register			
Reported not told any results for HIV†	12/411 (2.9%)		
Information about syphilis			
Explained what syphilis is	83/475 (17.5%)	≥90%	Severely under-reached
Reported receiving a syphilis test among those who had a syphilis test result in ANC register	438/470 (93.2%)	≥90%	Reached
Reported told syphilis status that	417/438 (95.2%)	≥90%	Reached
agree with result in ANC register			
Reported told syphilis status that did not agree	2/438 (4.6%)		
with result in ANC register			
Reported not told any results for syphilis†	19/438 (4.3%)		
Advised to inform partners of syphilis positivity	13/17 (76.5%)	≥90%	Under-reached
Information about malaria			
Given advice to use mosquito net to prevent malaria	346/478 (72.4%)	≥90%	Under-reached
Given a mosquito net (n=349)	331/349 (94.8%)	≥90%	Reached
Reported receiving a malaria test among those who had a malaria result in ANC register	445/454 (98%)	≥90%	Reached
Reported told malaria status that	420/445 (94.4%)	≥90%	Reached
agree with result in ANC register			
Reported told malaria status that did not agree	11/445 (2.5%)		
with result in ANC register			
Reported not told any results for malaria†	14/445 (3.1%)		
Information about anaemia			
Given advice to eat food with iron	132/480 (27.5%)	≥90%	Severely under-reached
Explained what anaemia is	107/480 (22.3%)	≥90%	Severely under-reached
Reported receiving an anaemia test among those who had an Hb result in ANC register	448/468 (95.7%)	≥90%	Reached
Reported told an anaemia status that	235/448 (52.5%)	≥90%	Very under-reached
agree with Hb level in ANC register			
Reported told an anaemia status that	60/448 (13.4%)		
did not agree with Hb level in ANC register			
Reported not told any results for anaemia test	153/448 (34.2%)		

* ≥90% target reached; <90% to ≥60 under-reached; <60% to ≥40 very under-reached; <40% severely under-reached; ANC: antenatal care; Hb: haemoglobin concentration; KP: known HIV positives; †Women reported not told results for HIV, syphilis or malaria were all negative based on ANC registers

3.5 Healthcare worker training, turnover, and performance

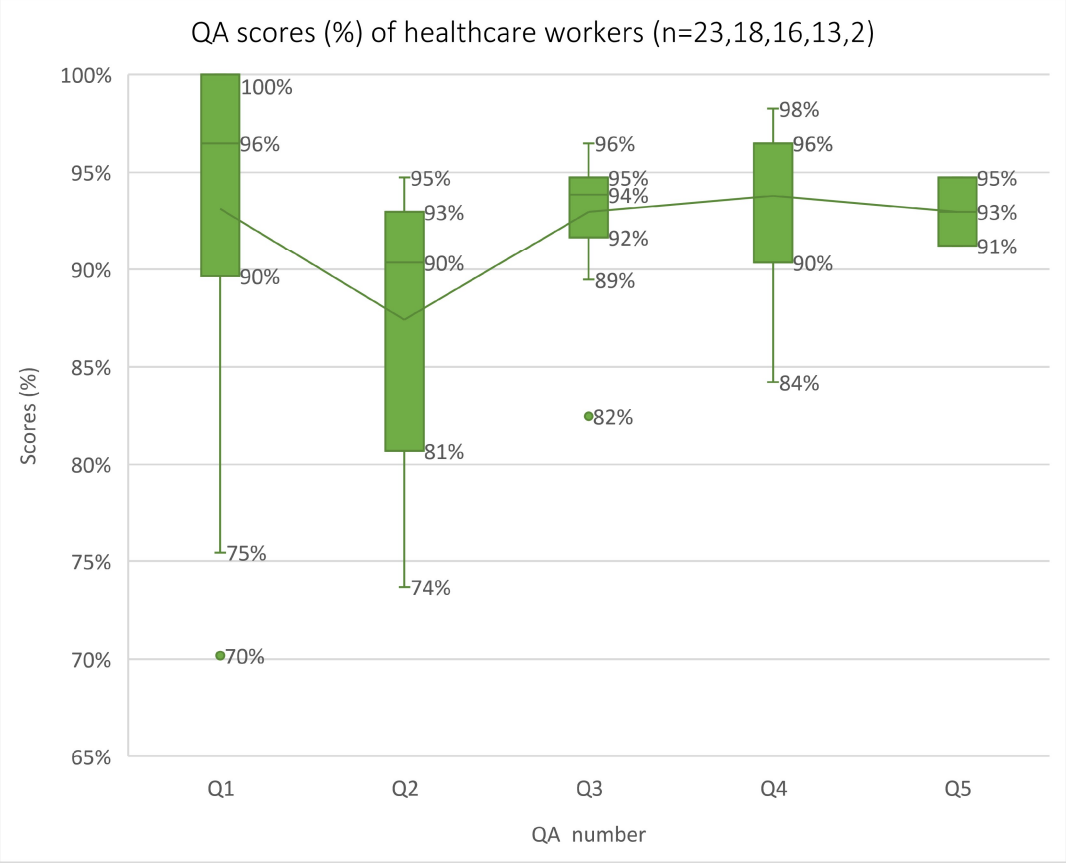
Overall 23 healthcare workers (14 nurses: eight females, six males; two clinical officers: two males; six HIV testing counsellors: one female, five males; and one laboratory technician: female) received training and underwent at least one testing QA. All nurses were trained to certificate or diploma level through the government system. Fourteen (60%) of the healthcare workers attended central trainings (eight were trained for five days in November and six for three days in February for those who were unable to make it in November), while nine (40%) received half-day on-site trainings. Turnover of staff was high: of the 16 original healthcare workers at the beginning of the study, only 10 remained by the end of the eight months. Seven new healthcare workers transferred to the facilities during the study and remained until the end. The predictor model suggested that high turnover (adjusted for age, marital status and electricity) was associated with a three-fold increased risk of antenatal women not having a full screening profile (Table 3.6).

Table 3.6: Predictors of pregnant women not having a full antenatal screening profile at first visits						
			Univariate analysis		Multivariate model	
Individual-level variables	n=728	Women without full profile in ANC register	RR (95% CI) of not having a full profile in ANC register	p-value*	RR**(95% CI) of not having a full profile in ANC register	p-value
Age in years				0.003		
≥30	143 (19.6%)	6 (4.2%)	Reference		Reference	
≤ 20 to <30	398 (54.7%)	46 (11.6%)	2.7 (1.5-4.8)		2.9 (1.7-4.9)	<0.0001
< 20	187 (25.7%)	18 (9.6%)	2.1 (1.2-3.7)		2.9 (1.6-5.1)	<0.0001
Marital status *(N=727)*				0.01		
single	116 (16.0%)	6 (5.2%)	Reference		Reference	
married	579 (79.6%)	59 (10.2%)	2.4 (1.2-5.0)		2.6 (1.5-4.7)	0.001
widowed/separated	32 (4.4%)	5 (15.6%)	3.7 (1.5-9.1)		4.1 (1.7 -9.6)	0.001
Gravidity				0.89		
1	194 (26.7%)	19 (9.8%)	Reference			
2	157 (21.6%)	17 (10.8%)	1.1 (0.5-2.4)			
3+	377 (51.8%)	34 (9.0%)	0.9 (0.7-1.3)			
Previous miscarriage				0.52		
no	701 (96.3%)	68 (9.7%)	Reference			
yes	27 (3.7%)	2 (7.4%)	0.6 (0.1-2.9)			
Trimester				0.35		
1st/2nd	587 (80.6%)	54 (9.2%)	Reference			
3rd	141 (19.4%)	16 (11.3%)	1.2 (0.8-1.9)			
Facility-level variables						
Staff turnover†				0.0006		
low	446 (61.3%)	27 (6.1%)	Reference		Reference	
medium	151 (20.7%)	20 (13.3%)	2.2 (0.8-6.1)		1.9 (0.6-5.6)	0.253
high	131 (18.0%)	23 (17.6%)	2.9 (1.7-5.0)		3.0 (1.8-5.1)	<0.0001
Facility volume‡				0.4		
low	151 (20.7%)	20 (13.2%)	Reference			
medium	297 (40.8%)	19 (6.4%)	0.5 (0.2-1.6)			
high	280 (38.5%)	31 (11.1%)	0.9 (0.3-2.9)			
Skilled staff¥				0.8		
2	206 (28.3%)	16 (7.8%)	Reference			
3	167 (22.9%)	19 (11.4%)	1.5 (0.4-5.5)			
4	355 (48.8%)	35 (9.9%)	1.2 (0.4-3.3)			
Electricity				<0.0001		
not present	91 (12.5%)	3 (3.3%)	Reference		Reference	
present	637 (87.5%)	67 (10.5%)	3.3 (2.0-5.5)		2.1 (1.2-3.7)	0.01

*Wald test; **n=727; † *Staff turnover* was categorized into low, medium and high defined as having 2, 1, and 0 skilled healthcare workers who received training at the start of the programme and remained for all 8 months of implementation respectively; ‡*Facility volume* was split into low, medium, and high for <30, 30-40, and 50-70 monthly ANC visits respectively; ¥ *Skilled staff* was defined as the total number of nurses, clinical officers, and HIV testing counsellors the facility had; ANC: antenatal care; RR: relative risk

Due to turnover and new staff joining, 18 received at least two QAs, 16 received three, 13 received four and two received five. Out of a total of 72 QA scores, 20 (28.6%), belonging to 15 healthcare workers, were below 90% and required more intensive re-training on the same day for steps such as obtaining enough blood from one finger-prick, correctly using the pipette and how to set the timer. Seven of the 15 were evaluated again within a month. Minimum scores improved over the proficiency tests from 70% to 91%. Distribution of scores from the QAs are shown as box and whisker plots in **(Figure 3.2)**. The results of the five QAs suggested that most healthcare workers could accurately conduct integrated POCT after training and remedial training.

Figure 3.2: Proficiency scores (%) of healthcare worker checklists in point-of-care testing



The boxes represent interquartile ranges (25% to 75% percentile); the solid line in the box is the median (50th percentile); The lower and upper whiskers represent the minimum and maximum values, excluding outlier; the dots represent outliers, defined as values less than 1.5 times the lower quartile.

3.6 Discussion

This is the first intervention study to evaluate the implementation success of integrating four POCTs into ANC in rural dispensaries in western Kenya. We showed a substantial increase in testing for syphilis, malaria and anaemia that provided an opportunity for the improved management of these conditions in a context of a well-established HIV rapid testing programme in pregnancy. Our results suggest that integrated POCT increases the number of cases detected and treated at the first antenatal visit in these small rural dispensaries without distortion of HIV testing which remained near universal throughout. Despite the management of conditions not reaching our target of 90% fidelity to guidelines, we suspect the treatment for syphilis, malaria and anaemia represented a laudable improvement from baseline. By bringing POCTs to peripheral dispensaries, accessibility and coverage of these tests for pregnant women residing in remote areas, who were otherwise not able to access testing at larger facilities farther away, was significantly improved.

We found prevalence rates of 20.3%, 3.1%, 31.9%, and 60.8% for HIV, syphilis, malaria, and anaemia (WHO cut-off Hb <11 g/dL, or 39.2% when using Kenyan guideline cut-offs of <10 g/dL) respectively, consistent with those reported in other studies [31, 35, 36, 51, 52]. Siaya is about 1,200 meters above sea level and the altitude adjusted prevalence of anaemia using the WHO cut-off was 70% [53].

The success of near universal HIV screening in ANC in Kenya, as reflected in our baseline and intervention data, is the result of concerted vertical program efforts and external partnerships [54-58]. Although WHO has endorsed an integrated disease approach to service delivery of antenatal care [59, 60], development assistance for HIV activities has risen disproportionately since 2000 compared to assistance for other sexual reproductive health activities [61], shifting agendas and priorities away from strengthening systems and building linkages between programmes [41, 56, 62-64]. Funds are often earmarked for specific purposes with deliverables defined by coverage and uptake, creating strong incentives for focused vertical programmes that result in

rapid outputs rather than overall health system improvement [56, 65, 66]. In Kenya less than half of the pregnant women attending ANC are tested for syphilis or haemoglobin concentrations [37, 67], even though antenatal screening is a major country policy and over 90% of pregnant women attend ANC. These gaps can likely be reduced by combining funding to support comprehensive ANC programmes and better coordination mechanisms at national and county levels among the National AIDS and STI Control Programme, the Department for Reproductive Health and the National Malaria Control Programme [39, 68]. For malaria, there is currently no national recommendation for screening at the first antenatal clinic visit, but this is commonly practiced in most of the larger facilities with laboratories in the highly malaria endemic areas in western Kenya. Furthermore, there is an increasing interest in this hybrid strategy that combines IPTp-SP with testing at the first visit because of concerns about missed opportunities with IPTp and increasing SP resistance.

A quarter of newly diagnosed HIV positive women declined immediate treatment. This low uptake of ARVs is consistent with the finding of a meta-analysis in 2012 that reported only 73.5% of pregnant women in low, middle and high-income countries achieved optimal adherence to ARV therapy during and after pregnancy [69]. Quality of HIV counselling, lack of emphasis of the importance of ARV adherence at post-test counselling, lack of male involvement, and lack of trust of ANC staff are reasons reported to be associated with low adherence [69]. In our study, we found low HIV counselling rates, which could explain why many women were unprepared for positive results [70]. Dosing of iron among healthcare workers at the seven dispensaries was not consistent and did not follow the national guidelines for iron supplementation. These inconsistencies have also been highlighted in government surveys conducted in 2013 which reported a lack of consistency in implementation of haematinic supplementation at health facilities, poor knowledge of dosing and duration, inadequate knowledge given to pregnant women about anaemia, low adherence and compliance, and limited understanding of side effects leading to discontinuation [67]. The uptake of IPTp-SP was very low or the intervention was incorrectly implemented, mostly because of stock-outs

and poor understanding of guidelines, falling well short of the target for 80% coverage by 2016 [71]. Poor IPTp-SP program implementation by health providers, stemming from unclear guidelines, stock-outs, poor facility organization, and low provider knowledge, had been reported elsewhere [34, 72]. Case-management of malaria test-positive cases was much better than IPTp-SP coverage, with almost 80% of women receiving treatment with an ACT or quinine. Consistent with a previous study in this area by Riley et al [73], adherence to the national case-management guidelines for women in the first trimester was inadequate and most women were prescribed ACTs instead of the first line treatment with quinine. Starting in 2013 and during the integrated POCT study period, Kenya was devolving the healthcare system and transferring authority for decision making, finance and management of health commodities to the county level. This resulted in a disruption of the malaria commodity supply chain during this transition period and corresponding stock-outs of SP and antimalarials, which may explain some of these findings.

Ensuring all healthcare workers were trained to standard and have quality maintained over time was challenging. High turnover of staff meant on-site training of new staff would pose challenges if the intervention were to scale in real-life conditions unless training for POCTs were incorporated into nursing school or was done on a country-level. Small, focused trainings with interactions are more effective than didactic ones and will require time and planning [74]. Since healthcare worker behaviours are complex with many contextual and environmental influencers, single, one-off interventions such as trainings or dissemination of guidelines are less effective than routine supervisions and feedback to maintain high-quality performance [74]. Quality improvement (QI) strategies that are step-wise, iterative, locally grown and adapted to existing systems may be more appropriate for long-term sustainability but context specific strategies need to be cultivated and effectiveness monitored in real-time [74-76].

There are several limitations to our study. We did not randomly sample the facilities and therefore they may not be representative of all tier-2 facilities in the region. The

evaluation excluded women who attended their first ANC visits in the third trimester, which was about 20% of first ANC attendees. While they also received the same services as first and second trimester women, their late attendance precludes early management of conditions and interventions would be needed to address this population. We used routinely collected ANC register data to calculate testing uptake but there were inconsistencies in how the registers were filled. For example, there were no columns for recording malaria test results in the existing ANC register and so we hand-drew a column during the study period. This was not always communicated to rotating ANC staff which resulted in 23 missing records for malaria testing. ANC registers do not record treatment and so we relied on interviews with women to obtain information on treatments and there were minor incongruences between self-reported and register recorded test results. More effort is needed to ensure accurate record keeping. Exit interviews were done with women at the facility immediately after an ANC visit; while this minimizes recall bias, women may be less inclined to report on negative experiences or give perceived acceptable responses without having understood the questions fully (courtesy bias). We did not assess the continuum of clinical management fidelity at revisits or at delivery. For example, new-borns of women given erythromycin for syphilis need to be treated immediately with a regimen of penicillin injections [77] but this was not measured. Effort would be needed to ensure healthcare worker's understanding and adherence to clinical management *throughout* the pregnancy and perinatal period. This study assessed clinical practice at the service delivery stage of the implementation pathway [40] where the conditions of having test supplies available, training and supervision were met through provision by the study. To effect positive health outcomes, wider health system concerns of supply chains, stock-outs and human resource management would need to be addressed.

3.7 Conclusion

This study showed near universal HIV testing in rural dispensaries that lack laboratory facilities and increased uptake of testing for syphilis, malaria and anaemia following

training and availability of POCTs. However, poor clinical management of conditions, frequent staff turnover and inadequate information given to pregnant women remain significant challenges that will require integrated funding channels and a robust quality assurance programme to ensure that standards are achieved and maintained in these peripheral facilities.

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4 Chapter 4: Study 2

Integrated point-of-care testing (POCT) for HIV, syphilis, malaria and anaemia at peripheral antenatal care facilities in western Kenya: a qualitative study exploring healthcare workers' and pregnant women's perspectives on appropriateness, acceptability and feasibility

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Box 4.1 Contributions

NY: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Visualization, Writing – original draft, Writing – review & editing
FA: Data collection, Methodology
MD: Conceptualization, Methodology, Resources, Supervision, Writing – review & editing
PPA: Conceptualization, Methodology, Supervision, Writing – review & editing
JH: Methodology, Writing – review & editing
GA and GB: Project administration, Writing – review & editing
KL: Funding Acquisition, Writing – review & editing
FTK: Supervision, Writing – review & editing
MT: Conceptualization, Methodology, Supervision, Writing – review & editing

4.1 Abstract

Background: HIV, syphilis, malaria and anaemia are leading preventable causes of adverse pregnancy outcomes in sub-Saharan Africa. Despite global and national policies advocating an integrated approach to antenatal care (ANC), testing coverage for conditions other than HIV is low. Availing point-of-care tests (POCTs) at ANC clinics in rural health facilities (dispensaries) has the potential to improve access and timely treatment. Fundamental to the adoption of and adherence to new diagnostic approaches are healthcare workers' and pregnant women's (the end-users) buy-in. A qualitative approach was used to capture end-users' experiences of using POCTs for HIV, syphilis, malaria and anaemia to assess the appropriateness, acceptability and feasibility of integrated testing at ANC. ~~We evaluated the acceptability, appropriateness and feasibility of integrating POCTs for HIV, syphilis, malaria and anaemia for ANC at seven purposively selected rural facilities (dispensaries) in western Kenya during an eight-month longitudinal implementation study.~~

Methods: Seven purposively selected dispensaries that have been conducting integrated point-of-care testing for 8 months in western Kenya participated in this study. Semi-structured interviews were conducted with 18 healthcare workers to explore acceptability and relevance of POCTs to ANC, challenges with testing, training and supervision, and patient experience. Twelve focus group discussions with 116 pregnant women were conducted to explore their knowledge of these conditions, experience of ANC point-of-care testing services, treatments received, relationships with healthcare workers, and experience of talking to partners about HIV and syphilis results.

Findings: Healthcare workers reported that they enjoyed gaining new skills, were enthusiastic about using POCTs, ~~and~~ found ~~tests~~ them easy to use and appropriate to their practice. Initial concerns that performing additional testing ~~integrating additional POCTs~~ would increase their workload in an already strained environment were resolved with experience and proficiency with the testing procedure. However, despite having the diagnostic tools, general health system weaknesses such as ~~workload~~ high patient to healthcare worker volume, stock-outs and poor working conditions challenged the delivery of quality ANC services, including inadequate counselling and the effective management of the four conditions. Pregnant women appreciated POCTs, but reported poor healthcare worker attitudes, drug stock-outs, and fear of HIV disclosure to their partners as shortcomings to their ANC experience in general.

Conclusion: The study provides insights on the acceptability, appropriateness, and feasibility of integrating POCTs into ANC services among end-users. While the innovation was desired and perceived as beneficial, future scale-up efforts would need to address health system weaknesses if integrated testing and subsequent effective management of the four conditions is to be achieved.

4.2 Background

HIV, syphilis, malaria, anaemia, and their co-occurrences are leading preventable causes of adverse pregnancy outcomes in sub-Saharan Africa (SSA) [1-9]. Global antenatal guidelines require integrated screening and management of these four conditions at first antenatal care (ANC) contact in the first trimester [10]. There has been success in increasing antenatal HIV testing coverage [11, 12], but rates of testing for the other conditions are still low and few examples of integrated disease approaches to antenatal care exist at the programme level [13-15].

Kenya's ANC guidelines, which follow WHO's recommendations, require testing for HIV, syphilis, febrile women for malaria, and anaemia at first ANC visits [16]. While over 95% of pregnant women attend ANC and over 90% of them receive HIV testing [17], less than 50% are tested for syphilis or anaemia [18-20]. While there is currently no national recommendation to screen pregnant women for malaria infection unless a woman has a recent history of fever, screening with microscopy is commonly practiced in facilities with laboratories. Recently, neighbouring Tanzania has introduced malaria testing at first visits to their antenatal policy as a strategy to manage anaemia [21]. There is also increasing interest internationally for a strategy that adds malaria testing to current recommendations of intermittent preventive therapy with sulfadoxine-pyrimethamine (IPTp-SP) and bednet use [22-28].

Affordable and reliable point-of-care tests (POCTs) that require minimal training and no durable equipment are available for HIV, syphilis, malaria and anaemia and have been used successfully at the point-of-care [29, 30]. Such POCTs have the potential to improve screening coverage at peripheral facilities by shifting antenatal testing from laboratory technicians, who are often based at distant centrally-located facilities, to nurses, midwives and lay healthcare workers at peripheral facilities [31, 32]. Task-shifting, combined with an opt-out approach, has transformed antenatal HIV testing in SSA over the last two decades [33], alleviating barriers of stigma, relieving human resource shortages, improving access and reducing the need for repeated visits for test results or to access laboratories [32]. This transformation has

required the buy-in and willingness of ANC staff to conduct HIV testing and on the acceptability of testing among pregnant women.

There are concerns that donor support to HIV programmes may have drawn attention away from non-HIV services [34, 35]. With the new Global Fund call for strengthening health systems through HIV funding, more synergies and integrated programmes can be achieved [35-37]. Studies that have assessed the integration of syphilis POCTs with ANC have shown increased job satisfaction among healthcare workers, ease-of-use of the tests and increased trust of diagnosis among pregnant women [20, 38, 39].

To examine the integration of syphilis, malaria, and anaemia point-of-care testing (POCT) with antenatal HIV testing, we conducted an eight-month longitudinal implementation study from December 2014 to August 2015 among seven purposively selected rural facilities (dispensaries) within the study area of the Kenya Medical Research Institute (KEMRI) and Centers for Disease control (CDC) Health and Demographic Surveillance System (HDSS) in Siaya County, western Kenya [40]. These seven were selected based on geographical spread within the HDSS area, no other ongoing antenatal studies, antenatal care visit volume, and willingness to participate. Competency-based training was given to 23 healthcare workers: 14 nurses, two clinical officers, seven HIV testing counsellors, and one laboratory technician. Training included how to run all four tests per standard operating procedures, safety and appropriate preventive and clinical management of positive results following Kenyan guidelines [16]. Quality assessments (QA) through observed proficiency testing of healthcare workers performing rapid tests compared to manufacturers' instructions was done immediately after initial training and at three, six and nine months. Implementation outcomes of adoption and fidelity, using definitions from a conceptual framework by Proctor et al [41], were measured quantitatively [40]. In summary, we found that adoption was good as over 95% of pregnant women received all four POCTs at first ANC visit over the study period but treatment fidelity did not reach targets defined by the study. Healthcare workers' minimum testing proficiency scores from quality assessments (QA) through performance observations

improved from 70% to 91% over the study period, suggesting that most healthcare workers could accurately use integrated POCTs after remedial trainings and practice.

As with the initial expansion of HIV testing, buy-in from healthcare workers and their ability to use four POCTs simultaneously during routine ANC visits are fundamental to sustained testing adoption and subsequent clinical management of test results. The intervention's success in improving pregnancy outcomes rests upon healthcare workers' willingness and ability to use four POCTs simultaneously during routine ANC visits, pregnant women's early ANC attendance and their openness to testing and treatment, and partner involvement in the management of sexually transmitted infections. Further investigation is therefore needed to understand healthcare workers' and pregnant women's perceptions of the intervention's appropriateness, acceptability and feasibility where appropriateness and acceptability are the perceived relevance and agreeableness of the intervention respectively while feasibility is the extent to which the innovation can be carried out in the implementation environment [41]. These constructs, rather than naturally occurring, are interpreted through human experience within the social milieu of the local context. Thus, a relativist social science perspective is needed to describe the depth and breadth of meaning end-users attach to their experiences of using the intervention[42]. A range of implementation environments is needed to include as many factors as possible that may influence the interventions perceived appropriateness, acceptability and feasibility. As such, purposive sampling to capture diversity is favoured over representativeness through random sampling [43]. A qualitative approach was used to capture healthcare workers' and pregnant women's perceptions of the integrated testing strategy at first ANC visits in dispensaries in western Kenya. ~~This paper presents healthcare workers' and pregnant women's experiences and perceptions of an integrated approach to point-of-care testing (POCT) at first ANC visits in dispensaries in western Kenya.~~

4.3 Methods

4.3.1 Data collection

One-on-one semi-structured interviews (SSI) were conducted with healthcare workers to capture individual experiences of providing integrated testing services. A structured topic guide with open questions related to the intervention's appropriateness, acceptability and feasibility was developed to explore areas such as relevance of integrating POCTs to dispensary ANC services, challenges with testing, experience with training and supervision, and experience with patients. Barriers to integration and health system constraints beyond participants' control were also explored. Interviews were designed to last 30-40 minutes. To ensure representativeness of ideas surrounding implementation, all healthcare workers who were trained, had experience doing integrated POCT, and were still working at the facilities 8-12 months after the intervention began were interviewed. Interviews were conducted in English at the facilities by trained members of the research team (NY and FA). FA is a social scientist from the study area and NY is a non-local researcher.

Focus group discussions (FGDs) were conducted with pregnant women to stimulate sharing of experiences of ANC and blood testing services. Group discussions allow participants to communicate more naturally which can give more insight into knowledge, attitudes and cultural norms. They can also generate more critical comments perhaps because the group setting is less intimidating [44]. A topic guide was developed to elicit pregnant women's feelings and perspectives of integrated POCT services received. The following domains were covered: knowledge of conditions, experience of ANC testing services and treatments received, relationships with healthcare workers, and experience of talking to partners. Discussions were designed to be one-hour long. Pregnant women attending ANC during the first two weeks of August 2015 and had ever attended a first ANC visit at the study facilities (147 women) during the intervention were recruited by data collectors to participate in the FGDs which were conducted at a location away from the facility on a later date within the same month. We recruited women from the last month of the study to

allow healthcare workers enough experience with delivering the intervention. A trained social scientist (FA) from the study area conducted the FGDs in the local language (Dholuo) and a trained moderator, also from the study area, took notes. FGDs were led by local researchers to mitigate power dynamics and cultural differences among researcher and participants. One or two FGDs were held at each facility depending on the total number of women recruited.

Non-English topic guides were translated and back-translated from English to Dholuo and piloted before use. All interviews and FGDs were digitally recorded with consent and transcribed verbatim. Non-English transcripts were first transcribed in Dholuo then translated to English by experienced translators and quality checks of the translation were done by FA. All transcripts were anonymized. Data collectors received training in data collection and ethical considerations.

We interviewed 18 healthcare workers: eight females, 10 males. The lengths of time the healthcare workers have spent at their facilities ranged from one month to seven years. Healthcare workers who have spent more time with the intervention were generally more verbose than those who were more recently transferred to the intervention facilities. Twelve FGDs were conducted with 116 women who attended first ANC visits at the study facilities between December 2014 and August 2015 (*Error! Reference source not found.*). Women who participated in the FGDs ranged from 15-46 years old, one-nine gravida and from three weeks pregnant to recently delivered. The level of interaction in the focus groups was generally well engaged and relaxed. However, there were a few groups that were quieter, and the moderator tried to stimulate more discussion among respondents using open-ended probes.

Table 4.1: Baseline testing services and number of semi-structured interviews (SSIs) with healthcare workers and focus group discussions (FGDs) with pregnant women by facility

Facility	Turnover *	Volume†	Testing at baseline‡				SSIs	FGDs
			HIV	Syphilis	Malaria	Hb¥		
1	Low	High	Yes	No	Yes	Yes	1 F nurse, 1 M nurse	group 1: n=5; group 2: n=12
2	Low	Medium	Yes	No	Yes	No	1 F nurse, 1 M nurse	group 1: n=9; group 2: n=9
3	Low	Medium	Yes	No	No	No	1 F nurse, 1 M nurse, 1 clinical officer	group 1: n=10
4	Medium	Low	Yes	No	No	No	2 M nurses	group 1: n=10
5	Medium	Low	Yes	No	Yes	No	1 F nurse, 1 M nurse, 1 M HTC	group 1: n=9; group 2: n=10
6	Low	Medium	Yes	No	No	No	1 F nurse, 1 M nurse	group 1: n=12; group 2: n=13
7	High	High	Yes	No	No	Yes	1 F nurse, 1 M nurse, 1 F HTC, 1 F lab tech	group 1: n=11; group 2: n=8

**Turnover of staff* categorized into low, medium, and high defined as having 2, 1, and 0 skilled healthcare workers who received training at the start of the programme and remained for all 8 months of implementation respectively
† *Facility volume* was categorized as low, medium, and high for <30, 30-40, and 50-70 monthly ANC visits respectively.
‡ All 7 facilities' routinely conducted HIV testing, 2 conducted anaemia testing irregularly, and 3 conducted malaria testing irregularly for ANC.
¥ Haemoglobin test for anaemia
M=male; F=female; HTC=HIV testing counsellor; lab tech: laboratory technician Hb=haemoglobin; ANC=antenatal care

4.3.2 Analysis

Regular meetings were held among the research team to review transcripts and notes from the interviews and update topic guides iteratively. Thematic analysis was used to identify emerging themes in end-user narratives to extract meaning in the experiences surrounding the use of POCTs. The process started with re-reading of transcripts to become familiar with the data. Segments of text that offered insight into user experiences were labeled and the interpretations of these labels were discussed among two researchers (NY and MT) and a set of codes each for healthcare workers and pregnant women interviews were agreed upon. These coding frameworks were then applied to the rest of the transcripts. Any new codes were further discussed and incorporated into the framework. The data were felt to be saturated after the first half of the data (9 SSIs, 6 FGDs) were analysed as no new codes emerged. Coded data were collated and sub-themes around appropriateness,

acceptability and feasibility of integrated POCT were formed, with triangulation across the participant types and sites. Viewpoints from healthcare workers and pregnant women were triangulated to create an overall narrative. The team then interrogated the findings against several existing conceptual frameworks describing the adoption of innovations into health systems [41, 45-48], and adapted them to best reflect the findings.

4.3.3 Ethics

For SSIs, written informed consents were obtained from all interviewed healthcare workers. For FGDs, consent forms were read together with the group. Written informed consents were obtained from literate women and verbal consents with thumb prints and witness signatures were obtained from illiterate women. The protocol was reviewed and approved by the scientific and ethical steering committees of the Kenya Medical Research Institute (protocol number 2271) and the Liverpool School of Tropical Medicine Ethics Committee (14.017). While this activity was determined to be human subjects research, CDC staff involvement did not constitute engagement in human subjects' research.

4.4 Findings

The findings were synthesized across the two participant types. Feasibility was inferred from participants' views on barriers and enablers to delivering integrated testing and ANC services. Three sub-themes emerged from participants' discussions: sub-themes related to community culture and concerns, local service delivery issues at the dispensaries, and wider health system organization (Table 4.2).

Table 4.2: Sub-themes of pregnant women and healthcare worker reflections on integrated point-of-care testing's appropriateness, acceptability and feasibility [48]			
	Service delivery at dispensaries	Community context of cultures and concerns	Wider health system: policy, programme and management
Appropriateness	Healthcare worker's job description and professional motivations Services pregnant women want at ANC	Time and costs of reaching facilities	National guideline requirements
Acceptability	Healthcare workers: Complexity of POCTs Proficiency of testing Observability† of test results Trialability‡ of POCTs Workload Attitude towards gaining knowledge and new skills Pregnant women: Trust and confidence in results	Community stigma, gender violence and partner involvement	County level decision makers would need to value and prioritize integrated antenatal testing and allocate funds to ensure its continuity
Feasibility	Motivation of healthcare workers Drugs and commodities for services Training and quality assurance of healthcare worker performance Pregnant women's degree of comfort in asking for services	Community culture and attitudes that influence timing of first ANC visit	Procurement and funding systems for commodities and drugs Sufficiency of human resources to meet demand Working conditions Quality and synergy of training
POCTs: point-of-care tests; †Observability: the degree to which the results of an innovation are visible; ‡Trialability: the degree to which an innovation can be experimented with on a limited basis so as personal meaning ca be ascribed			

4.4.1 Appropriateness of integrated POCT

4.4.1.1 Local service delivery and wider health system

Intervention meets healthcare worker's needs and policy expectations but misses some essential tests: All healthcare workers were excited about integrated POCT as it satisfied their professional goals by enabling them to meet pregnant women's ANC needs in accordance with national guidelines. Some healthcare workers suggested enhancements to the programme such as retesting women's haemoglobin (Hb) levels at revisits to monitor improvement if anaemia was detected at the first visit.

Many were concerned that the intervention still missed urinalysis, blood grouping and rhesus tests and women still needed to be referred for these.

Healthcare workers experienced the tangible benefits of testing, which allowed them to manage diseases like syphilis and malaria that they were not testing for before. They found anaemia testing to be of importance because they saw many women with low haemoglobin (Hb) readings:

> "Malaria, we were not also doing it but I think integration is better because ... and these days you will get to find that, I usually get so many positives for malaria and Hb, I've even got Hb of 4.9. Now I was imagining if we did not have this Hb machine, like if you just test the mother for HIV as usual and tell her to go. Maybe she does not even have money to go to the District hospital to go for other tests, what will happen to that mother? I think that is what brings these maternal deaths because we do not take the precaution during the antenatal period." -female nurse (facility 6)

Intervention meets pregnant women's intentions for going to ANC: Some healthcare workers said they noticed an increase in ANC attendees during the study suggesting that more pregnant women visited as the community became aware of POCT services. This was consistent with pregnant women's reasons for attending ANC visits as mentioned in the FGDs: they believe ANC services are beneficial and seek them for finding out the position of their babies, learning how to take care of themselves during pregnancy and diagnosing and treating harmful diseases.

4.4.1.2 Community context

Addresses community need for time and cost savings: Many healthcare workers cited the advantage of not having to refer pregnant women to laboratories for syphilis and anaemia testing as most do not go because of distance and transport costs, leaving vital conditions undiagnosed.

> "it was very challenging, you find the mother at the first visit, you tell them: go to diagnosis, go to district, go and test this and this. They don't go. They

don't always go and the next day when they come it is just blank" – clinical officer (facility 3)

4.4.2 Acceptability of integrated POCT

4.4.2.1 Local service delivery

Complexity of POCTs is acceptable and healthcare worker proficiency improved with experience: All healthcare workers found POCTs easy to use. Some healthcare workers felt like they had some initial difficulties, such as trouble obtaining enough blood for all four tests from a single finger prick (which was believed to be attributed to women having thick blood or low haemoglobin levels), remembering how to set the times on the triple timer, and controlling the pipettes. These issues were felt to be resolved with supervisory feedback and experience as they gained proficiency in the testing procedures.

Healthcare workers open to gaining knowledge and new skills: Healthcare workers saw the programme as an opportunity to learn new skills and were eager to receive support such as training and supervision. Proficiency observations and remedial training were especially appreciated as they served as corrective reminders for forgotten procedures, which supported POCTs' continued use. One healthcare workers mentioned that the attitude of the supervisors should be positive and constructive rather than fault-finding. Many healthcare workers were happy to learn how to use syphilis POCTs and the HemoCue@ machine, which they had not used before. One clinical officer requested more support as he felt on-site training was less sufficient than multi-day central training and found it difficult to perform with the same quality as those attended multi-day trainings. Because more conditions were tested for, some healthcare workers felt they needed more training on counselling.

Concerns over workload: Some healthcare workers were initially sceptical about the intervention and raised concerns about the extra workload in an already strained environment. The intervention's trialability (degree to which healthcare workers were able to experiment with the intervention) allowed healthcare workers to 'try-

out' the new testing procedures and adapt them to work under their own conditions which helped dispel initial uncertainty. The concerns over added workload were mostly appeased as testing adeptness improved. One healthcare worker re-organized her work to see first ANC women together for group counselling and group testing. She would perform the testing procedures for multiple women in an assembly line, starting the timer for the first woman and roughly estimating the extra waiting time for subsequent women. She requested that more timers should be given to accommodate testing multiple women together. Some healthcare workers still felt the 20-minute waiting time for results was too long and the need to counsel for more conditions was also felt to be time-consuming.

Observability of tests results improves trust in diagnosis: Healthcare workers liked the ease of observing test results as it helped them communicate the diagnoses directly:

> "but they will not take it very serious because they have seen you have not even tested but when I test them I always show them and tell them your Hb is this and you are supposed to have this. At least the mother can now understand because she has read it directly from [the machine] and I have explained they should be at what level, in fact they take it very serious." - male nurse (facility 2)

Pregnant women welcomed the POCT service. They were taught to observe their own results from the test cassettes which increased their trust of diagnoses. However, a few healthcare workers mentioned problems with the HIV tests, which sometimes gave faint positive lines, making women question the validity and deny the results.

> "we had some problem with it [HIV test] and actually…in interpreting the results, it used to give some faint line at the test site. It was causing a lot of problems with the clients. They are saying the line was faint." -male nurse (facility 2)

4.4.2.2 Community context

Stigma and difficulties of partner involvement: Some women mentioned there is still stigma around HIV testing while syphilis, malaria and anaemia testing were not perceived to be threatening. Women suggested that more information and counselling would help with acceptance and treatment compliance.

While all women believed that partners should be tested and treated, they stated that most of their male partners could not be convinced to be tested because they feared the health facilities. Some women recounted tricking their husbands into going for HIV testing. Other women said some partners would assume they shared the same test result as their wives and some even share the women's HIV drugs. Women also reported that they feared blame and violence from their husband if they disclosed their HIV positive status.

4.4.3 Feasibility of integrated POCTs

4.4.3.1 Local service delivery and wider health system

Healthcare workers and pregnant women talked about their direct experiences at facilities with implications for wider health system functioning concerns.

Working conditions compromise the quality of care for service users: Sentiments of frustration and impatience were pervasive among healthcare workers which they believed to be due to heavy workload and chronic staff shortages. This sentiment was expressed by many:

> "if you are stationed in MCH that is ok, but if you are taking care of PSC [patient support care for HIV positives], taking care of outpatient clients…you don't give quality, let me say this."-male nurse (facility 2)

In addition, healthcare workers complained of demotivation from lack choice in postings and transfers, often requiring them to be far away from their spouse and children. They noted that dispensaries are remote, the emotional and physical hardships were not compensated adequately, job grades had stagnated without

promotion, and salaries were often delayed for months. From the FGDs, many women expressed how healthcare worker's attitudes affected their experiences:

> *"*But you know when we come to the clinic we find different types of nurses sometimes you find her not in the moods and you get afraid of asking but if you find a happy one then you are also happy such that you share with her your problems*."*-pregnant woman (facility 6)

Delay of facility funds and stock-outs made it difficult to provide care: Healthcare workers do not have control over how or when funds are allocated. Delay in facility maintenance funds and reimbursement for maternity services left facilities strained as explained by one nurse:

> *"*But this was a promise by the national government...that all pregnant mothers will deliver free of charge, all health centers and dispensaries outpatient cases will be treated free of charge, ...and they were to reimburse but there was delay, there was delay… The whole of last year up to now as we speak I've not received any funds, imagine, and my casuals, we have not paid for the last six months, those who were helping me. I've not paid electricity for the last six months…You know...some are beyond me... That one needs managers of the county." -male nurse (facility 2)

Healthcare workers were frustrated about the devolution of government control and management to the counties and thought it to be the cause of stock-outs:

> "it has been worse…things have changed…when we were still under the national government, drugs used to come to facilities…and they were punctual…but nowadays, you can even stay for months without drugs and when they bring in drugs, they bring that which you are going to use for about two weeks." -female nurse (facility 6)

> "Actually… personally I believe that health should have been devolved much, much later but it was rushed and you can see, the management is poor. Just the other day, health workers within the county were threatening to go on

> strike. And part of the problem is just the management. I think some of these staff was devolved from the national government when the county government had not put in the structures to manage this work force from the national government and probably make some input. And again also the input of the county government in terms of even staff employment, supplying of drugs … all these like I told you earlier that we have experienced shortage of drugs for quite a long time." - Clinical officer (facility 4)

Drug shortages left pregnant women untreated because they could not afford to go to pharmacies to purchase drugs for themselves:

> "There is no right treatment given to us because you can be prescribed for drugs and you don't have money to go and buy them so there is no good treatment given."- pregnant women (facility 2)

Inadequate training and supervision: There were some healthcare workers who mentioned never having received training for HIV and malaria testing even though these are among the commonly used tests at dispensaries. One nurse said she was grateful for POCT training because before she would directly squeeze blood from the finger to the cassette for HIV testing as she did not know how to use the pipette. Another reported she had never used, or seen people use, timers for malaria POCTs and the training had enlightened her on the importance of timing so that she can now trust the results.

A small minority of respondents described that currently in western Kenya, HIV and PMTCT services are supported by international partner programmes and receive frequent on-site mentorship, while other maternity services, supervised by the Ministry of Health, rarely receive this level of support.

4.4.3.2 Community context

Delayed ANC attendance: Pregnant women's first ANC visit was often late in the pregnancy and the potential effectiveness of integrated POCT was thought by healthcare workers to be undermined by the delayed management of conditions. Women explained that late attendance was because they did not like to go to ANC

before their pregnancy was certain, which was around the fourth month. Additionally, they stated that long distances, the cost of transport, poor staff attitudes, and a wish to avoid multiple revisits delayed initiation of their first visit.

4.5 Discussion

This study presents healthcare workers' and pregnant women's narratives on using POCT to diagnose HIV, syphilis, malaria and anaemia at dispensaries in western Kenya. The POCT intervention was perceived to be highly acceptable and appropriate: healthcare workers felt positive about offering POCTs and pregnant women appreciated the extra services. Data from elsewhere suggest that innovations are more likely to be adopted and implemented if they are easy to use, appropriate to the practice setting and accompanied by training and feedback support [41, 46, 48]. Overall, healthcare workers found POCTs user-friendly, aside from a few technical challenges that were addressed through experience and remedial training, which led to greater confidence in using the tests. This highlights the importance of supervision and audit with feedback, even for uncomplicated innovations, for improving performance [49, 50]. Other studies on implementation of POCTs have shown that healthcare workers and pregnant women appreciate their simplicity, which reduces diagnosis time [38, 51, 52]. A common finding from these studies is that the greatest bottleneck to scale-up is not in the satisfaction with the tests, but rather weakness of the wider health system. Test stock-outs, inadequate training and supervision, human resource constraints, and vertical funding structures have undermined scale-up of rapid syphilis testing in ANC [53-58]. Similar challenges with implementing malaria POCTs have also been reported [59, 60]. Sustaining a skilled, motivated and well-supported workforce with adequate commodities to effectively deliver integrated services, beyond the end of the study intervention period, will require effort on several levels. An integrated supervision and monitoring solution to support holistic ANC would also be needed.

Despite the prominent health burden of syphilis, malaria and anaemia and the availability of simple cost-effective solutions, interventions to address these illnesses at ANC have been poorly delivered in Kenya and elsewhere in SSA [15, 27, 54, 61-65].

This could be due to a low prioritization of these conditions: 1) national targets and indicators for syphilis and anaemia are missing despite being an essential part of ANC policy [53, 54]; 2) national data on syphilis prevalence was captured in the 2007 Kenya AIDs Indicator Survey but was dropped in the 2012 survey [17, 66]. Several factors shape the disparate prioritizations of countries' health programmes [67]. International advocates play a significant role in norm promotion and shaping countries' policy preferences [67, 68]. These transnational players offer technical and financial support for priority interventions, often outcompeting resources for other health problems that are just as dire but receive less attention. For example, well-funded donor HIV programmes attract staff with higher salaries, pulling human resources away from the already strained public sector and creating two tiers of salaried healthcare workers side by side [65, 69]. There is also a lack of an integrated policy community [67] and the networks of donors, government bodies, and non-government organizations (NGOs) are siloed into domains of expertise with insufficient cross-communication [65]. As a result, there is no coalesced force to push for the integrated management of conditions. More transnational advocacy and co-ordination among influencers to shift the paradigm from single-focused programmes to comprehensive maternal health care is needed [65, 70, 71]. Moreover, proper governance with checks and balances is crucial to ensure limited funds are distributed to their target needs and not squandered or misappropriated [72-74].

During the time of this study, the Kenyan government was politically motivated to rapidly execute the decentralization process of transferring decision-making power from the central government to the 47 newly-formed counties after 2013 elections [75]. In the devolved system, health service delivery functions are placed under the jurisdiction of the county governments [76]. Unfortunately, poor organization and rapid execution of the decentralization process resulted in widespread confusion and unpreparedness for the structural changes in finance and administration [75]. The county governments had limited technical capacity to set priorities and allocate funds, which created challenges in the county's financial flows during the study (three years since devolution), causing stock-outs and funding delays [75]. For an

integrated testing strategy to be sustained beyond the end of the study, county authorities involved with selecting priorities will need to understand the importance of antenatal screening and be willing to allocate funds towards it. Healthcare decisions since devolution increasingly involves local politicians and technical actors; it is important to engage with them, as well as women within the community, to highlight the equity benefits associated with an integrated testing strategy at peripheral facilities that can extend diagnostic services to a much larger demographic of women.

Healthcare workers suffer low morale from meagre and delayed salaries, lack of choice in placement, job grade stagnation, and feeling helpless due to stock-outs of commodities and drugs [69, 71, 77], resulting in recurring healthcare worker strikes to demand for better wages and working conditions [78]. Poor healthcare worker management, and the resulting frustrations can lead to low productivity, poor quality of care and cultures of predatory provider-client relationships [49, 79, 80]. Low morale among healthcare workers and resulting poor attitude have previously been found to lead to pregnant women attriting from the HIV testing and treatment cascade, non-disclosure of status during delivery, and knowingly forfeiting nevirapine for new-borns [81]. All healthcare workers interviewed expressed concerns about workload. This is a common problem in SSA health systems in where critical workforce shortages, skill mix imbalance and mal-distribution have been described as a serious obstacle to scaling up priority interventions [69]. Additionally, disease-specific short training, polio eradication campaigns, and staff leave often pull already strained personnel away from facilities [65, 69, 82], leaving staff 'alone' to manage all the clients.

Late attendance to ANC precludes effective treatment to protect the foetus. Our research has revealed that poor relationships between pregnant women and health providers, pregnancy uncertainty and the number of revisits required for the full ANC schedule of visits were reasons given by pregnant women for delaying ANC initiation. Other factors such as age, parity, money for transport, ignorance of gestation age to start ANC, not having any perceived problems with the pregnancy, and social

pressures have previously been reported as reasons for delaying the start of ANC [83-86]. Effectiveness of testing for syphilis also requires partner treatment to prevent reinfection from occurring. Our findings suggest stigma, fear of spouse violence, and beliefs that men do not participate in reproductive health programmes impede male partner involvement in treatment of HIV and STIs. To ensure pregnant women are effectively covered by antenatal guidelines, gender dynamics and health-seeking behaviours in the community need be addressed.

There were several limitations in this study. Our interviews and discussions were limited to frontline users and did not include management and implementation partners at county and national levels who have ultimate policy setting and budgeting decisions. Stakeholder insights, priorities and engagement are necessary to assess sustainability, readiness and intention for scale-up. Their insights will form a critical area for future research. We also did not rank the interviewees' perceived significance of each barrier with participatory methods, which would have been useful to help future programmes prioritize resources. The SSIs and FGDs were also conducted towards the end of the implementation study and may not have captured early adoption experiences. Self-reported information is inclined to have desirability or courtesy bias, which we tried to minimise by emphasizing anonymity and conducting the focus groups away from the facility. Healthcare worker interviews elicited several critical comments which suggests that the courtesy bias is not limiting. Our study was small, only involving seven facilities in western Kenya. We purposively chose the facilities based on geographical spread, and client volume which may not have represented all the different implementation environments in the region. The facilities ranged from low to high client load and staff turnover rates. Some facilities charged for ANC booklet or testing services, and some facilities had partner NGOs that provided support. Despite these differences, the acceptability of POCT was positive across facilities among both healthcare workers and pregnant women. Several sentiments were consistent throughout including healthcare workers' perceived high workload, pregnant women's perceived lack of information and counselling given, and frustrations with stock-out of drugs and commodities. Finally, the study was conducted within the HDSS, a high research density area

where several research studies run simultaneously within a facility and this may distort the service delivery environments.

4.6 Conclusions and recommendations

The study provides insight on the acceptability, appropriateness, and feasibility as well as potential explanations of high adoption and low fidelity of the integrated POCT programme among end-users. Healthcare workers and pregnant women found the innovation acceptable and appropriate. Recommendations for scale-up efforts include the need to address vertical programming structures by engaging donors and programme managers to encourage horizontal thinking of disease management and to create synergies across programmes. Human resource constraints will need to be addressed and commodity supply chains strengthened to ensure no stock-outs. Community engagement to encourage early ANC attendance and involve male partners to decease stigma and threat of gender violence is important to generate demand and safeguard pregnant women. This will require a committed and united effort from county, national and international leaders.

4.7 Declarations

The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the U.S. Centers for Disease Control and Prevention.

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4.9 Data and materials

The transcripts from the interviews and focus groups are currently not publicly available due to confidentiality, but may be available upon reasonable request.

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5. Chapter 5: Study 3

Integrating HIV, syphilis, malaria and anaemia point-of-care testing (POCT) for antenatal care at dispensaries in western Kenya: discrete-event simulation modelling of operational impact

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Box 5.1 Contributions

NY: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Visualization, Writing – original draft, Writing – review & editing

MT: Supervision, Writing – review & editing

GZ: Data curation, Writing – review & editing

GA: Project administration

MD: Supervision, Writing – review & editing

FTK: Supervision, Writing – review & editing

IV: Conceptualization, Methodology, Formal analysis, Supervision, Writing – review & editing

5.1 Abstract

Objectives: Despite WHO advocating an integrated approach to antenatal care (ANC), testing coverage for conditions other than HIV remains low because of low test availability. Using point-of-care tests at peripheral dispensaries could improve access and timely treatment but implications for human resources and client wait times are unknown. We use discrete-event simulation modelling to understand the intervention's effect on service delivery and run 'what-if' scenarios.

Methods: We collected detailed time-motion data from one high volume dispensary which has been integrating point-of-care testing for HIV, syphilis, malaria and anaemia for 8 months (2014-2015) in western Kenya. We constructed the model using empirical arrival distributions, activity times and patient pathways. We found low staff utilization and short antenatal consultations. We modelled a scenario where consultations were increased to allow sufficient delivery of all WHO recommended services and compared outcome distributions of wait times.

Findings: The dispensary received 183 women for maternal and child health (MCH) services and 14 women received the intervention. With the intervention, wait times increased for 26(14%) women (median increase: 12 mins, IQR: 8-22 mins). Ensuring sufficient consult durations resulted in wait times increasing for 60(33%) women (median increase: 31 mins, IQR: 17-54 mins). The two nurses' daily utilization with sufficient consult durations was 72% and 75%.

Conclusion: Integrating point-of-care tests does not greatly impact women's wait times while ensuring they receive essential diagnostics. Nurses should have sufficient time to deliver WHO's required ANC activities, making integration a potential resource neutral strategy to improve quality of care.

5.2 Background

HIV, syphilis, malaria, and anaemia are leading preventable causes of adverse pregnancy outcomes in sub-Saharan Africa (SSA) and addressing them as early as possible during pregnancy is an essential goal of antenatal care (ANC) [1]. Kenyan guidelines require screening for HIV, syphilis, and anaemia at first ANC visit [2]. While over 95% of pregnant women have contact with ANC and over 90% are tested for HIV in Kenya [3], fewer than half are ever tested for syphilis or anaemia during their pregnancy [3-5]. This difference in coverage is partly due to low test availability at peripheral facilities (dispensaries) [6, 7]. Women who attend dispensaries for ANC are referred, with additional time and cost implications, to distant laboratories for testing. International advocacy for HIV has promoted near universal testing coverage [8, 9] and similar support is needed for syphilis and anaemia screening given the strong evidence of their clinical effectiveness in improving pregnancy outcomes [1, 10, 11]. For malaria endemic regions, Kenya currently does not require parasitological screening, but microscopy is commonly practiced in facilities with laboratories in western Kenya; its neighbour, Tanzania has already introduced malaria testing at first contact for managing anaemia [12]. Furthermore, there is heightened interest in malaria testing and treatment at first contact during pregnancy because of concerns with current preventive strategies including 1) poor coverage of intermittent preventive therapy with sulfadoxine-pyrimethamine and bednet use [13], 2) increasing drug resistance [14] and 3) contra-indications to the use of sulfadoxine-pyrimethamine in the first trimester of pregnancy and HIV positive women on cotrimoxazole [15].

An integrated approach where antenatal testing and appropriate treatment are delivered as a one-stop-shop at a single service delivery point are advocated to reduce missed opportunities and improve coverage of interventions [16]. No-equipment rapid diagnostic point-of-care tests (POCTs) are available to fulfil antenatal testing requirements in low-resource settings [17]. Studies that have assessed the use of syphilis or malaria POCTs have reported ease-of-use, increased healthcare workers' satisfaction and improved patients' trust in the diagnoses due to

the observability of results [4, 9, 18-21]. While dual HIV/syphilis tests are now available and countries are beginning to adopt them [22], no study to our knowledge has examined the integration of four essential POCTs for ANC at dispensaries.

At the lowest level, dispensaries offer basic maternal and child health services, rudimentary out-patient curative care and support care for HIV-positive patients and referrals. Staff at peripheral facilities tend to be overburdened [23] and adding new tasks may impose additional time and resource demands on service delivery which can lead to longer wait times, negatively affecting patient experiences and their health seeking behaviour [24, 25]. Despite this, the World Health Report 2010 estimates that 20-40% of health spending is wasted through inefficiency [26] and there is evidence that the existing workforce is not fully utilized [27-29]. Quantifying wait times and staff utilization is important to understand the likely impact of expanding POCT beyond HIV alone so strategies can be targeted to improve adoption and quality of care.

Health systems are complex and adaptive: they are the emergence of multi-layered, sometimes competing, inter-relationships of the systems' interdependent elements (e.g. patients, providers, government/non-government agencies) [30]. Complex systems are nonlinear and traditional analytic approaches, such as regression modelling, have limitations because they cannot account for nonlinear dynamics [31]. On the other hand, operational research (OR) methods, that make use of advanced mathematical and modelling techniques, can be more appropriate to aid complex decision-making [32]. Discrete-event simulation (DES) modelling is particularly useful for quantifying changes in wait times and resource utilization because it captures 'discrete' events such as patient pathways and can introduce decision logic at specific points to simulate competition for resources [33]. While DES has been used extensively in developed countries [34] few examples are available from SSA [35-37]. Using DES, we aim to explore the impact of the integrated testing strategy for ANC on patient wait times and resource utilization and test 'what-if' scenarios for optimization. The results of this study will also demonstrate the

applicability of the method for understanding intervention adoption in complex systems.

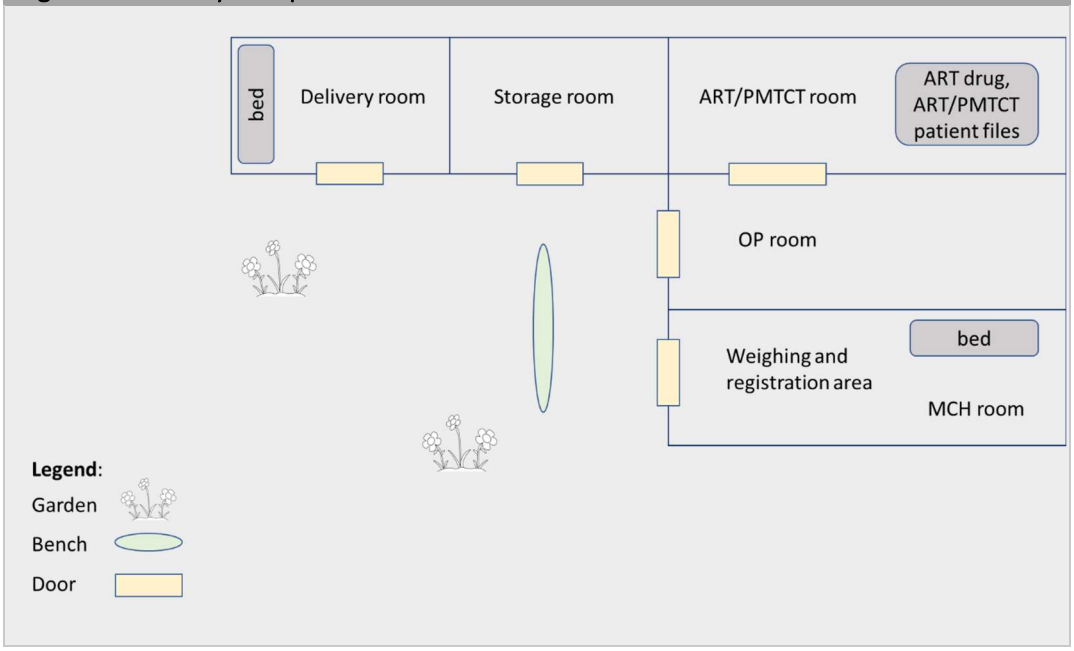
5.3 Methods

5.3.1 Study setting

Modelling was nested within an 8-month longitudinal study (December 2014 to August 2015) that implemented an integrated testing strategy for HIV, syphilis, malaria, and anaemia in seven dispensaries within the KEMRI/CDC Health and Demographic Surveillance System (HDSS) area in Siaya County, western Kenya [7]. Detailed population characteristics and setting descriptions are available [38]. The Government of Kenya routinely supplied HIV POCTs per its standard national algorithm at the time: HIV (1+2) Antibody Colloidal Gold (KHB, Shanghai Kehua Bio-engineering Co Ltd, China) for screening, First Response HIV-1-2 kits (Premier Medical Corporation Ltd., Kachigam, India) for confirmation and Uni-Gold™ (Trinity Biotech, Ireland) for tie-breaking. The study supplied POCTs for syphilis (SD BIOLINE Syphilis 3.0, Standard Diagnostic Inc., Korea), malaria (CareStart™ Malaria HRP2 Pf, AccessBio, USA) and haemoglobin concentrations (HemoCue® Hb 201+, HemoCue AB, Sweden). During implementation, the seven study dispensaries received a monthly median of 38 (IQR: 32-38) antenatal visits, of which a median of 13 (IQR: 10-13) were first visits. Implementation outcomes from the study showed high adoption of POCTs, resulting in increased case detection and 70% treatment fidelity for syphilis and malaria [7].

Of the seven dispensaries, we conducted our modelling study in one with high patient volume. The facility had the typical staff of a dispensary: two nurses, one focused on maternal and child health (MCH) and the other on out-patients (OP); a part-time CO who oversaw HIV-positive patients seeking anti-retroviral treatment (ART) or prevention of mother-to-child transmission (PMTCT) services; and two to three subordinate support staff who helped with registration, weighing, and dispensing drugs. The facility had three main rooms, one each for MCH, OP, and ART/PMTCT **(Figure 5.1)**. Staff rotated among these rooms for the respective services.

Figure 5.1: Facility floorplan



5.3.2 Time-motion study

We collected process times of all activities undergone by MCH/PMTCT women over four weeks in August 2015 during the intervention. Six data collectors were stationed across each facility service point: two by the entrance, two at MCH, one at OP, and one at ART/PMTCT. Any woman arriving at the facility for MCH/PMTCT purposes was greeted and introduced to the study. A short statement explained the study purpose (to measure activity and wait times), study procedures (wear a number badge and carry a time sheet throughout the visit), and confidentiality (no personal information such as name or test results would be collected). Women who disagreed would be free to continue their visits without timesheets and their badge numbers would be skipped. All facility patients' arrival times and visit purposes were recorded on a data form at the entrance to inform client mix and arrival time distributions. Data collectors were present at each service point to record process times, service locations, provider type, and any blood tests done on the MCH/PMTCT women's timesheets. The data were recorded with established reference codes and any unforeseen items were given new codes that were communicated to the team immediately. Watches were synchronized daily at the beginning and end. Healthcare

worker (nurses, and CO) activities were recorded on 15-minute intervals from the time of their arrival until departure. All timesheets were scanned by TeleForm® (Hewlett-Packard) and exported into an excel database.

5.3.3 Modelling

A DES model of the entire dispensary was built in the WITNESS© (Lanner Group Limited) simulation software. The core of the model is made of entities, attributes, resources, queues, and activities. Entities are people or items that enter the system (e.g. patients, paperwork) and require attention from resources (e.g. nurses, HTC, CO). The resources attend to entities in activities (e.g. consultation, registration). Attributes are intrinsic features of entities such as the patient types, pathways and the time spent on activities. Queues are generated in the DES model when entities compete for resources who are often needed in several activities simultaneously.

5.3.4 Development and validation of the base-model with integrated POCT

Model input parameters: 1) arrival times of patients; 2) sequences and durations of activities of women attending MCH services; 3) durations of OP and ART patient consultations 4) activity locations; and 5) activity resources. We made assumptions about OP and ART consultation times. We assumed every OP and ART patient arriving sees either a nurse or a CO and none of them were turned away except for those who came on the strike day. Their durations were estimated from those of MCH women who received OP or ART services with an average of 6.5 minutes for OP consult with nurses, 5 minutes for ART consult with nurses and 10 minutes ART consult with CO.

Shifts for the two nurses and CO were collected because these were the resources servicing MCH women and providing the intervention. Their shifts were estimated based on the time they arrived and left the facility. The total wait times and length-of-stay for MCH women were generated from the model and their distributions validated by comparing them with the empirical distributions using non-parametric Wilcoxon rank-sum tests.

5.3.5 Isolating the impact of integrated POCT

The intervention was defined as the additional syphilis, malaria and anaemia testing added onto routine antenatal HIV testing. To capture the impact of the intervention, we generated process durations without integrated POCT by reducing the estimated durations for testing from the collected process times. This additional time was estimated to be 8 minutes: 5 minutes to read the syphilis test results (HIV tests require 15 minutes for a negative reading while the syphilis test requires 20 minutes) and 3 additional minutes for preparing the syphilis, malaria and anaemia tests. Distributions of wait times and length-of-stay were compared to those of the base-model using the non-parametric Wilcoxon rank-sum test because of non-normality. Resource utilizations were also generated.

5.3.6 'What-if' scenario

We explored a 'what-if' scenario where each ANC consult was of sufficient duration to cover all recommended services, including integrated testing. Using simulated data from Tanzania [39], we estimated that a minimum of 58 minutes would be required to cover all services during first visits and 36 minutes for re-visits (**Table 5.1**).

Table 5.1: Estimated ideal times for antenatal first visit and antenatal revisit based on simulated consultations from Tanzania

ACTIVITY	FIRST VISIT	REVISIT
Welcoming the woman	00:01	00:01
Registration	00:05	00:00
History taking/updating	00:10	00:05
Physical exam	00:08	00:08
Drugs administration	00:03	00:03
Immunization	00:01	00:01

Pre-test counselling and set up	00:05	00:00
Health education and counselling while waiting for POCTs results	00:20	00:15
Post-test results counselling and treatment	00:02	00:00
Filling ANC book and register	00:03	00:03
TOTAL TIME	00:58	00:36
POCTs: point-of-care tests		

5.3.7 Ethics

The protocol was reviewed and approved by the scientific and ethical steering committees of the Kenya Medical Research Institute (protocol number 2271) and the Liverpool School of Tropical Medicine Ethics Committee (14.017). For U.S. CDC, while this activity was determined to be human subjects research, CDC staff involvement did not constitute engagement in human subjects' research.

5.4 Results

5.4.1 Facility characteristics

All women agreed to the time-motion study. There was a total of 838 patients over 20 days: 13% HIV-positive patients for ART, 65% general out-patients and 22% MCH/PMTCT women. MCH services include ANC first and re-visits, family planning and under-5 child welfare services for growth monitoring and immunizations. Figure 5.2: shows the distribution of daily arrivals and Figure 5.3 shows the client load per day.

Figure 5.2: Facility patient arrival times over 20 working days

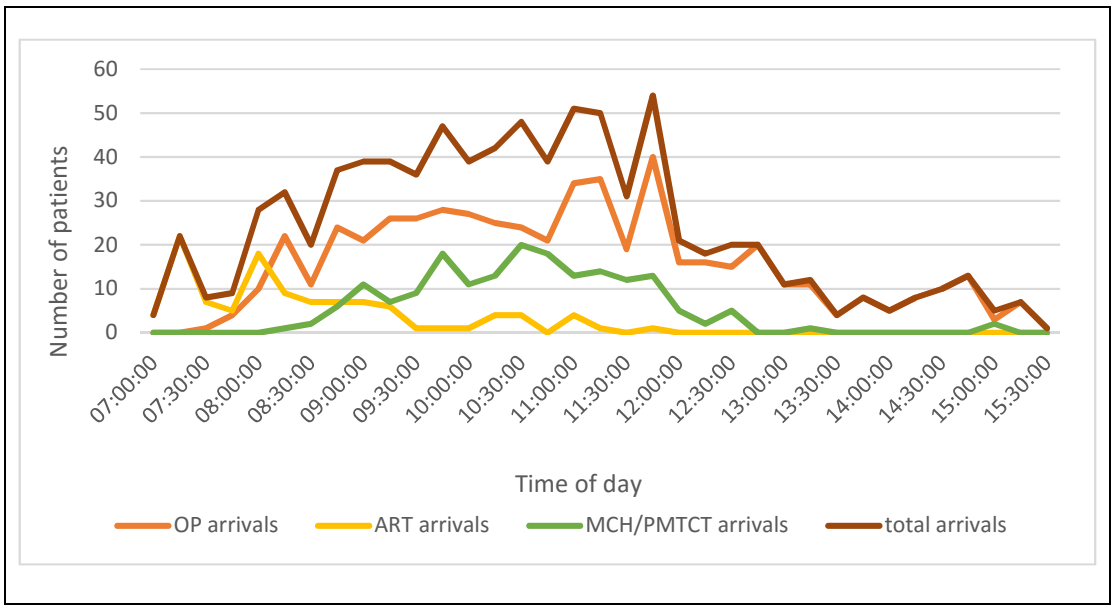
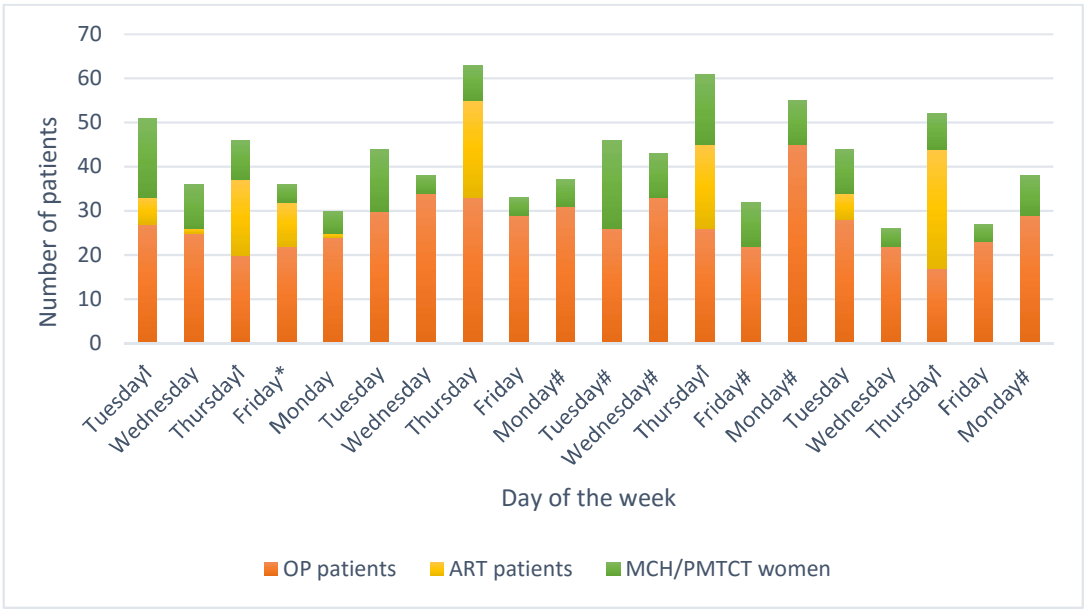

60
50
40
30
20
10
0
Number of patients
07:00:00
07:30:00
08:00:00
08:30:00
09:00:00
09:30:00
10:00:00
10:30:00
11:00:00
11:30:00
12:00:00
12:30:00
13:00:00
13:30:00
14:00:00
14:30:00
15:00:00
15:30:00
Time of day
OP arrivals
ART arrivals
MCH/PMTCT arrivals
total arrivals

Figure 5.3: Facility patient load by day of the week



* strike, no healthcare workers on duty and all patients turned away

† clinical officer on duty

two nurses on duty, else only one nurse on duty

Nurses typically arrive at 08:00 and finish their work by 16:00 contributing to an 8-hour (480 minutes) day. The CO was part-time and present on most Thursdays which is the facility's designated PMTCT/ART day. Healthcare workers were on strike on the first Friday and no patients were seen that day.

5.4.2 Model validation

Data exploration showed that the input distribution of OP and ART consult durations were best described using a negative exponential. Output distribution of wait times and LOS for MCH women were non-normal even after log and square transformations. Wilcoxon rank-sum tests show no statistically significant difference between empirical and model generated distributions **()**. We concluded that the base-model was representative of the operational environment of the facility.

Figure 5.4: Distribution of total wait times for MCH women (Wilcoxon rank-sum p=0.1234)

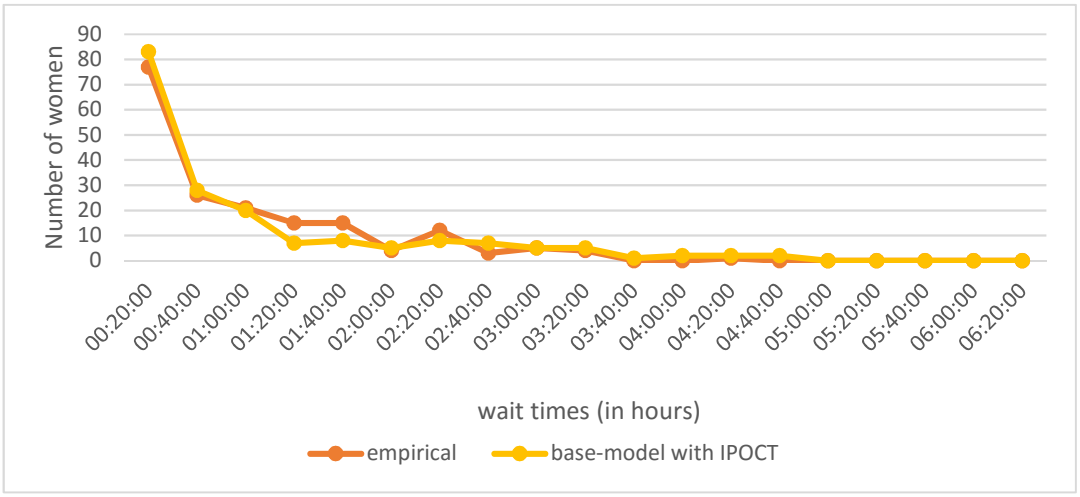
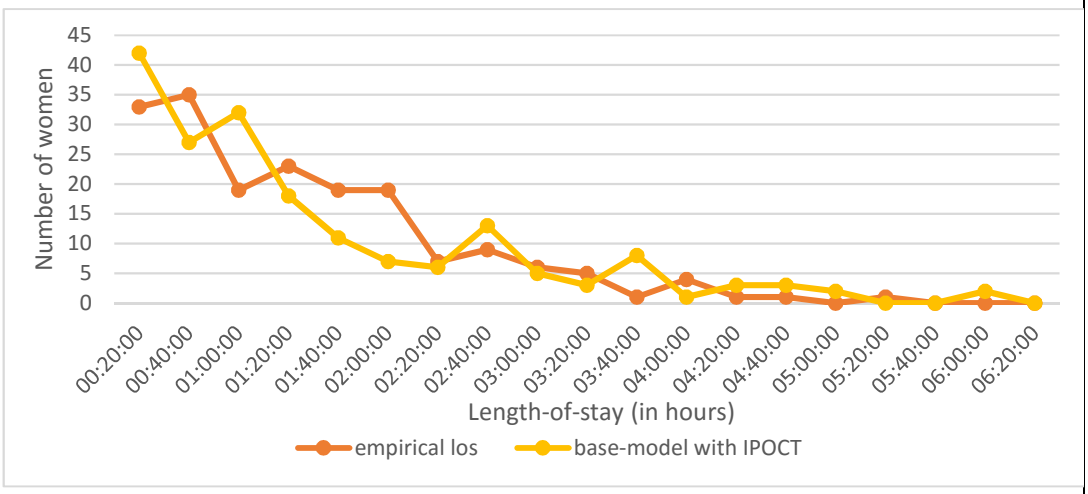


Figure 5.5: Distribution of total length-of-stay for MCH women visiting (Wilcoxon rank-sum p=0.4614)



5.4.3 Wait times and length-of-stay

The intervention was given to 14 ANC (11 first visits, 3 re-visits) women during their nurse consultations. For the scenario without integrated POCT testing, 11 of these women had their consultation times reduced by 8 minutes while 3 women did not have any time reduced because they were already less than 20 minutes, the

minimum time needed for negative results to be read (positive results can be read before 20 minutes). With the intervention, first visit consultations took a median time of 00:32 (n=11, range: 00:15-1:14, IQR: 00:23-00:36) and re-visits 00:13 (n=28, range: 00:05-00:55:00, IQR: 00:09-00:23). Ten out of 11 first visit consult times were increased to 00:58. For re-visits, 23 consultations were increased to 00:36. Wait times and length-of-stay under the three scenarios are shown in Table 5.2. While some women have increased wait times, most women's wait times remain unchanged: this seems reasonable as the intervention was only given to 14 women and due to gains from synergies with HIV testing. The model also showed that adding the intervention can result in shorter wait times for some women because of system dynamics.

Table 5.2: Changes in wait times and length-of-stay under the three different scenarios

Wait times	N	Median	Range	IQR	p-value
[0] Without integrated POCT	183	00:22	00:00-04:31	00:01-01:21	
[1] With integrated POCT	183	00:24	00:00-04:31	00:01-01:13	[1] vs [0] p=0.0012
Increase	26 (14%)	00:12	00:03-00:53	00:08-00:22	
Decrease	7 (4%)	00:29	00:03-00:42	00:21-00:34	
Unchanged	150 (82%)				
[2] With integrated POCT and adequate consult times	183	00:31	00:00-05:35	00:04-01:30	[2] vs [1] p<0.0001
Increase	60 (33%)	00:31	00:02-02:33	00:17-00:54	
Decrease	18 (10%)	00:34	00:26-3:18	00:05-01:34	
Unchanged	105 (57%)				
Length-of-stay	**N**	**Median**	**Range**	**IQR**	**p-value**
[0] Without integrated POCT	183	00:52	00:00 -05:54	00:23-01:55	

[1] With integrated POCT	183	00:55	00:02-05:53	00:23-01:59	[1] vs [0] p<0.0001
Increase	34 (19%)	00:11	00:05-01:18	00:08-00:20	
Decrease	5 (3%)	00:37	00:29-01:04	00:32-00:42	
Unchanged	144 (79%)				
[2] With integrated POCT and adequate consult times	183	01:08	00:02-07:03	00:31-02:13	[2] vs [1] p<0.0001
Increase	76 (42%)	00:33	00:02-02:33	00:23-00:59	
Decrease	17 (9%)	00:19	00:26-03:18	00:03-01:30	
Unchanged	90 (49%)				
IQR: inter-quartile range					

5.4.4 Nurse availability and utilizations

Nurse utilization is reported as a percentage of the time they were engaged in activities during their shifts. A Canadian study on cardiovascular nursing care in hospitals shows 85% (±5%) daily nurse utilization rate is ideal and sustained utilization above this range can lead to increase in costs, decrease in quality of care as well as poorer nurse and patient outcomes [40]. For a regular 480-minute day, 80% utilization would leave 20% (96 minutes) for breaks and shuffling among service points. Healthcare worker shift patterns were irregular and rarely did two nurses work simultaneously. Nurse availability and daily utilization rates, with those above 80% bolded, are shown in **Table 5.3**. Our data show that consultation times for first and re-visits were inadequate for completing all the recommended ANC activities and that nurses were under 80% utilized on most days, suggesting there is capacity to increase the time they spend with pregnant women. Increasing the minimal duration of first and revisit consultations led to higher nurse utilizations but remained under 80% on most days. For two days the OP nurse reached 100% utilization: one was because the nurse was alone and only present part-time (300

minutes) and the other was because the nurse was alone on a Thursday when PMTCT/ART patients were scheduled and the facility client load was highest, reaching 63. On days when a nurse is working alone without another nurse or clinical officer, he or she may manage if the client load is relatively low (under 40 clients per day). However, when a nurse works shorter days or is absent and this happens on a day with high client load, the remaining nurse's utilization can reach over 80%.

Table 5.3: Nurse utilization under 3 scenarios

Day of the week (total clients)	NURSE 1 (OP) utilization			NURSE 2 (MCH) utilization		
	Without integrated POCT [0]	With integrated POCT[1]	With integrated POCT & adequate consult times [2]	Without integrated POCT [0]	With integrated POCT [1]	With integrated POCT & adequate consult times [2]
Tuesday† (51)	-	-	-	323/480 (67%)	345/480 (72%)	**408/480 (85%)**
Wednesday (36)	-	-	-	232/480 (48.3%)	248/480 (52%)	326/480 (68%)
Thursday† (46)	-	-	-	186/480 (38.7%)	186/480 (39%)	227/480 (47%)
Friday (36)	-	-	-	-	-	-
Monday (30)	293/480 (61%)	301/480 (63%)	323/480 (67%)	-	-	-
Tuesday (44)	**246/300 (82%)**	**246/300 (82%)**	**305/300 (102%)ǂ**	-	-	-
Wednesday (38)	295/480 (61%)	295/480 (61%)	295/480 (61%)	-	-	-
Thursday (63)	**529/570 (93%)**	**529/570 (93%)**	**575/570 (101%)ǂ**	-	-	-
Friday (33)	378/480 (79%)	378/480 (79%)	378/480 (79%)	-	-	-
Monday (37)	302/480 (63%)	302/480 (63%)	332/480 (69%)	323/480 (67%)	323/480 (67%)	344/480 (72%)
Tuesday (46)	166/480 (35%)	166/480 (35%)	178/480 (37%)	230/360 (64%)	230/360 (64%)	**293/360 (81%)**

Wednesday (43)	**413/480 (86%)**	**413/480 (86%)**	**422/480 (88%)**	293/480 (61%)	293/480 (61%)	**385/480 (80%)**
Thursdayǂ (61)	0	0	0	303/480 (63%)	314/480 (65%)	377/480 (78%)
Friday (32)	62/120 (52%)	62/120 (52%)	62/120 (52%)	331/480 (69%)	331/480 (69%)	**424/480 (88%)**
Monday (55)	**431/480 (90%)**	**431/480 (90%)**	**431/480 (90%)**	**383/480 (80%)**	**383/480 (80%)**	**399/480 (83%)**
Tuesday (44)	-	-	-	369/480 (77%)	**383/480 (80%)**	**419/480 (87%)**
Wednesday (26)	-	-	-	141/480 (30%)	141/480 (30%)	141/480 (30%)
Thursdayǂ (52)	-	-	-	195/480 (41%)	195/480 (41%)	211/480 (44%)
Friday (27)	-	-	-	301/480 (61%)	301/480 (63%)	301/480 (63%)
Monday (38)	216/360 (60%)	216/360 (60%)	216/360 (60%)	275/360 (77%)	283/360 (79%)	**300/360 (83%)**
OVERALL (838)	3330/4710 (71%)	3338/4710 (71%)	3517/4710 (75%)	3887/6480 (60%)	3958/6480 (61%)	4556/6480 (70%)
p-value ¥		[1] vs [0] p=0.3173	[2] vs [1] p=0.0148		[1] vs [0] p=0.0258	[2] vs [1] p=0.0008

Nurse 1 spent approximately 870 minutes (18.5%) and Nurse 2 spent approximately 1410 minutes (21.8%) of their utilization time on paperwork.; Clinical officer on duty- out of 390-minute shifts, the clinical officer had less than 50% utilization each day. For scenario 3, the CO was modelled to help with child immunization when he was available.

ǂNurse utilizations can be over 100% because the resource is given an allowance to carry on processing any on-going activity after the shift has finished; ¥ Wilcoxon sign-rank test

5.5 Discussion

We used DES to quantify wait times, length-of-stay and nurse utilization after adopting an integrated testing strategy to fulfil antenatal testing guidelines at first ANC visits in a rural dispensary in western Kenya. We found considerable variation in resource availability, consult durations and patient pathways. Using time-motion data, we captured the varied nature of these factors allowing high level of detail in our representation of the local environment not afforded by other methods to study time allocation [28]. This study demonstrates the applicability of simulation modelling to help understand the operational consequences of implementing priority interventions in low-resource settings to inform decision-making.

While there are concerns about inadequate healthcare worker numbers to implement the workload needed to scale priority interventions in healthcare systems in SSA [23], our study shows an under-utilization of skilled healthcare workers, suggesting that current staffing numbers in small dispensaries should have sufficient time to deliver full ANC services, including integrated point-of-care testing. This suggests that improving performance of the existing workforce can have substantial gains in quality of care. Case studies from Tanzania and Chad found that only 55-60% of staff time was spent on productive activities [29]. Worse has been reported in Cameroon where reproductive health staff spend only 27% on service provision [27]. Motivation and performance have several determinants and explanatory frameworks but in general, salaries, prestige, work conditions, frequent high-quality supervision with audit feedback and multifaceted interventions have strong evidence to support their contribution to achieve better healthcare worker performance [41].

We also observed high absences which creates excess workload for the healthcare worker on shift and this is likely to undermine the quality of care delivered [42, 43]. Absenteeism, whether planned or unplanned, is characteristic of facilities in low-resource settings [42]. Staff are often pulled out of facilities to attend disease-specific trainings, or participate in outreach campaigns [23]. Reducing parallel programmes, integrating training, building on synergies between disease programmes, ensuring appropriate skills are covered in pre-service curricula, and

conducting on-site trainings when possible can reduce disruptions [44]. On the other hand, healthcare workers may feel poorly motivated to show up because of low morale from meagre and delayed salaries, lack of choice in placement, workload, poor working conditions, job grade stagnation, and feeling helpless due to stock-outs of commodities and drugs [41, 42]. Frustration with the system have resulted in recurring healthcare worker strikes to demand for better wages and working conditions in Kenya [45]. Resource neutral strategies, which are more likely to be acceptable to service providers and adopted as national policy, need to be explored to address performance and absenteeism [46].

The domain of this study was operational and its aim was to develop insight to the local implementation conditions of integrated POCT and thus may not be readily generalizable to other settings [47]. The study may also be weakened by the Hawthorne effect: having data collectors present at the facilities may alter healthcare worker's behaviour. Healthcare workers may have been more inclined to treat clients better and not turn them away or provide more complete services. They may also be inclined to take less breaks if they know their activity times were being recorded. The number of women who receive integrated testing over a month is low at dispensary level because there are very few first ANC visits. We also only collected data for one month and this may not be entirely representative of the operational environment over time. Therefore, the results may not be readily generalisable to other settings with different client loads and healthcare worker mix. We focused only on women who visited the facility for MCH/PMTCT purposes and did not quantify wait times for OP or ART patients. While we have collected detailed data for MCH and PMTCT activities, we made assumptions for the model regarding OP and ART activities. We used an average OP consult time of 6.5 minutes which was similar to 7 minutes found in Nigeria [48] and slightly longer than 5.3 minutes found in Mozambique [49]. Another study found ART patients spend an average of 21.8 minutes on services which included time spent in registration, with CO and in pharmacy [35]. Thus, our estimate for consult time of 10 minutes with the CO seems reasonable. These findings need to be reviewed with frontline healthcare workers and stakeholders to better interpret and understand their implications so that

suitable strategies can be devised to adequately address these operational challenges.

5.6 Conclusion

Using discrete-event simulation modelling with detailed facility-level data, we quantified operational outcomes of wait times, length-of-stay and nurse utilization after integrating syphilis, malaria and anaemia point-of-care testing with HIV testing during ANC consultations. We showed that nurses were under-utilized on most days and that sufficient time for ANC first and re-visits could be achieved within the current number of healthcare staff. While this would increase wait times and length-of-stay for a portion of women, it would significantly improve the quality of care through ensuring pregnant women receive essential antenatal services and counselling. Resource neutral strategies to reduce healthcare worker absenteeism and improve their motivation and performance should be explored to ensure limited resources are used efficiently without over-stretching the system.

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5.8 Competing interests

Competing interests: None declared.

5.9 Disclaimer

The findings and conclusions in this manuscript are those of the authors and do not necessarily represent the official position of the United States Centers for Disease Control and Prevention or the Department of Health and Human Services.

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6 Chapter 6 Discussion

This chapter presents a summary of the main findings and how the three studies informed implementation of integrated point-of-care testing strategy. It then draws important insights from these findings and reflects on their implications for health systems. It discusses on study strengths and limitations and gives recommendations for the future.

6.1 Summary of main findings

The intervention of providing integrated point-of-care testing for four important conditions in dispensary level antenatal care (ANC) services addressed a gap in implementation of antenatal guidelines in Kenya. Baseline testing coverages (chapter 3) in dispensary level was high for HIV but low for syphilis and anaemia because of low test availability. The number of women tested for malaria at baseline could not be assessed because no data were captured in ANC registers. In practice, women are referred to facilities with laboratories for malaria microscopy screening together with their syphilis and anaemia screening requirements. However, data on referral uptake were not available. These baseline findings were not surprising given that previous studies from the literature review had identified low test availability for syphilis and anaemia as a common barrier to testing coverage among health systems in sub-Saharan Africa (SSA) [1, 2]. The literature review also found that preventive strategies for malaria using intermittent preventive therapy (IPTp) with sulfadoxine pyrimethamine (SP) and bednets were poorly covered. The reasons for inadequate coverage of services for these antenatal conditions are summarised in Table 6.1 using Tanahashi's 3-stage conditional implementation pathway [3, 4]. The intervention provided some of the critical early components on the implementation pathway by bringing testing services closer to the community at dispensaries (improving access coverage), availing testing supplies (improving availability coverage), training and supervision (improving clinical practice). Three studies then assessed the intervention's implementation success using Proctor et al.'s taxonomy of implementation outcomes. Because there was a lack of consistency in the use of implementation constructs among researchers, the authors synthesised these

outcomes from the literature to provide common working definitions. We assessed five of the eight outcomes which were adoption, fidelity, acceptability, appropriateness, and feasibility.

Adoption was high during the intervention period: the number of tests done and the number of cases of syphilis, anaemia and malaria that were detected in these small rural dispensaries increased significantly among first antenatal visits, without affecting the already high rates of HIV testing in pregnant women. Adoption was slightly diminished in facilities that had more frequent turnover of healthcare workers perhaps because new staff had to be re-trained and oriented with the intervention which led to slower uptake. When interviewed healthcare workers and pregnant women were highly enthusiastic about testing and found the innovation acceptable and appropriate. While more women received tests and correct treatment because of the intervention, fidelity to clinical management guidelines can still be improved. Our qualitative findings provide some explanations for the gaps in fidelity: poor working conditions, stock-outs, inadequate training, high workload and stress, delayed salaries, and devolution were common sentiments perceived to be barriers to providing quality care found among interviews with healthcare workers.

During interviews with healthcare workers (Chapter 4: Study 2), concerns of high workload affecting the ability to give quality care frequently appeared. Human resource shortages have been a major concern for scaling of the interventions needed to achieve the health outcomes of the Sustainable Development Goals (SDGs) in SSA health systems. However, there is also evidence to suggest that the existing workforce is not operating optimally [5-7]. When we modelled data on client flow and staffing resources (Chapter 5: Study 3) we found healthcare workers were often under-utilized. We tested a 'what-if' scenario where consultation times were increased to sufficient durations for delivering ANC's essential services recommended by WHO. Our model suggested that nurses should, in theory, have sufficient time to deliver ANC services fully in dispensaries. However, because dispensaries are small, they may be more sensitive to staff absences. Usually with only two nurses and one part-time clinical officer, absence of any skilled healthcare

worker shifts workload to those remaining, creating spikes in patient volume to healthcare worker ratio. This happened often, ~~However, healthcare workers were often absent and when this happened, the~~ straining the remaining healthcare workers.~~would be strained.~~

These studies demonstrate that integrated POCT is an appropriate and acceptable strategy, but additional health systems solutions are needed to ensure test availability, healthcare worker availability and retention, and quality of care.

Table 6.1: Synthesis of findings on coverage of antenatal testing for HIV, syphilis, malaria & anaemia

Chapter 2: Literature review (what we know)			Intervention (what we did)
Coverage level	Determinants of coverage	Assessment indicators of coverage determinants	Integrated POCT intervention
Access coverage	• Transport costs • Geographical distance • Socio-cultural factors • Provider attitudes	• All mothers during pregnancy attend ANC • Early ANC attendance • Sufficient number of ANC contacts • Partners are involved with treatment of syphilis and HIV	By availing and integrating POCTs at peripheral facilities, the strategy brings coverage closer to the community
Availability coverage	• Poor stock-management systems • Funding and international donor priorities and lack of co-ordination • Human resource planning • Political economy • Transnational influence • Policy environment • Vertical systems inter-sectoral response and activism	• Tests, drugs, and commodities are available • Sufficient and rightly skilled human resources at the facilities that corresponds to the facilities' workloads	Baseline revealed that low availability of tests was the main reason for poor testing coverage. The study supplied tests for syphilis, malaria, anaemia and penicillin drugs for syphilis treatment.
Clinical practice	• Funding and international donor priorities • Socio-political economy vertical systems	• Competence: healthcare workers have sufficient knowledge, right skills mix, training and supervision to deliver quality services • Motivation: healthcare workers are motivated to give sufficient and quality services	The study provided training for testing and treatment of syphilis, anaemia and malaria, and supervision for testing quality
	What we found		
	Chapter 3	**Chapter 4**	**Chapter 5**
Access coverage	• 20% of women attended ANC visits in their 3rd trimesters	• Pregnant women found POCTs acceptable and appropriate as testing for conditions satisfied their reasons for going for ANC visits. • Some facilities noticed an increase in pregnant women • Socio-cultural factors delayed ANC attendance	

		• Stigma and gender disparities impeded partner involvement • Poor healthcare worker attitudes decrease health seeking behaviour	
Availability coverage	• High testing adoption • Inadequate fidelity to management of conditions • High healthcare worker turnover had implications for training and supervision	Factors that threaten feasibility: • stock-outs, funds and salary delays threaten healthcare workers' ability to offer antenatal services • government devolution interrupted financial and stock flows	• Suggests that human resource numbers may be sufficient in some small facilities to manage the client load • Healthcare workers are absent often which disrupts the resource needs of the facilities for those days and over-burden the staff who remain
Clinical practice	Healthcare workers could perform testing with training and supervision	• Healthcare workers found testing to be appropriate as it satisfied their work requirements • Healthcare workers found testing to be acceptable as POCTS were easy to use • Training and supervision were welcomed if constructive, non-critical feedback was given. Factors that threaten feasibility: • staff are demotivated from workload, job grade stagnation, delayed salaries, poor working conditions and stock-outs • adequate training and supervision are lacking • unhappy healthcare workers have trickle-down effect on women: poor healthcare worker attitudes make pregnant women demotivated to seek health services	
POCT: point-of-care testing; POCTs: point-of-care tests			

6.2 The limits of ANC for controlling diseases in pregnancy

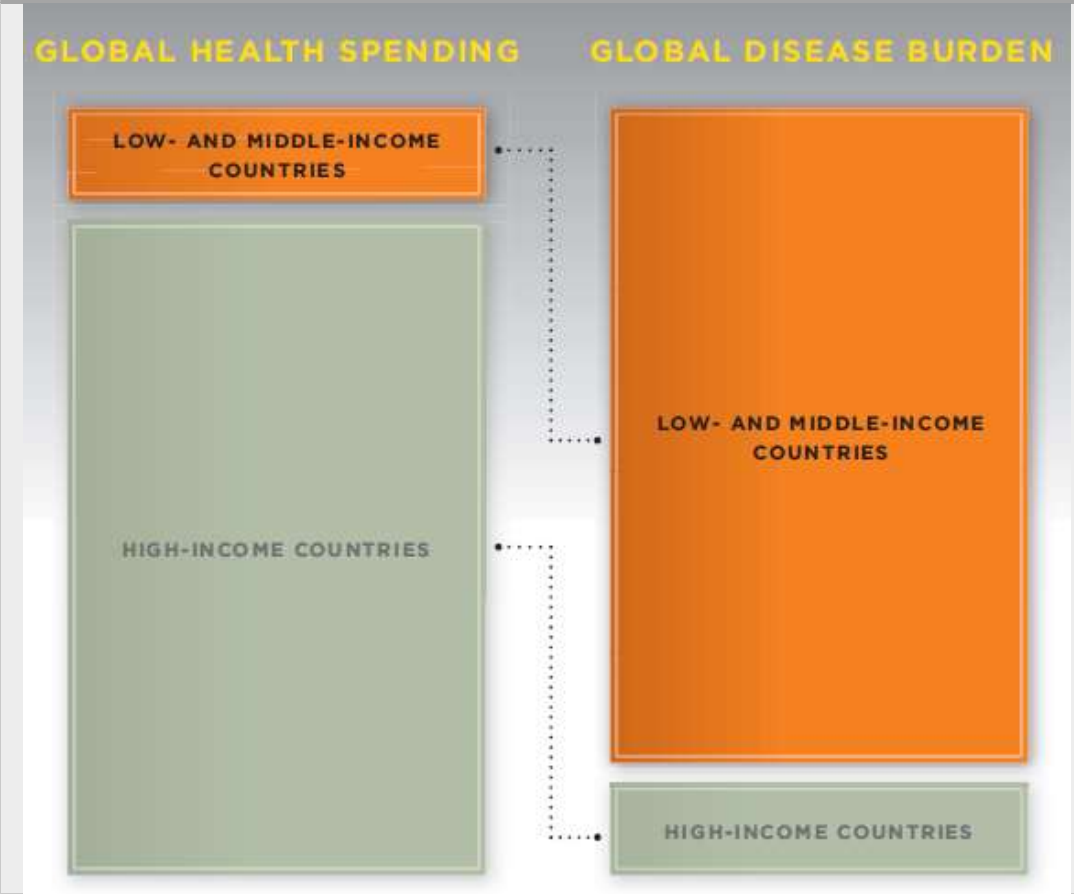
This integrated POCT strategy addressed a facility-level accessibility coverage gap by bringing essential testing services to peripheral facilities, circumventing the need for women to be referred to distant facilities for testing. However, it still rests upon the condition that women attend ANC at these facilities in the first place, attend early enough, have sufficient number of contacts, and involve partners in the treatment of HIV and syphilis. Although ANC attendance in Kenya is high (>90%), a third of those who did not use ANC at last pregnancy cited distance as the main reason in the 2012 Kenya AIDS Indicator Survey (KAIS) [8]. Moreover, a quarter of pregnant women seek

ANC after the first trimester (our study found 20% of women visited ANC in their 3rd trimester, chapter 3) and fewer yet return for re-visits [9], precluding full protection against illnesses that require early interventions or several interventions over time. Moreover, sexually transmitted infections such as HIV and syphilis require involvement from male partners which ANC has not been good at capturing [10]. Narratives from pregnant women describe the difficulties of disclosing HIV status to their husbands (Chapter 4). To address these gaps in accessibility coverage and improve partner involvement, a community based healthcare strategy may help [11, 12]. Kenya launched a community health strategy in 2006 [11] which has demonstrated success for some health indicators such as health facility delivery, antenatal care usage, water treatment, latrine and insecticide treated nets use [13]. However, challenges with high community healthcare worker attrition and quality of care still need to be resolved [14].

6.3 The need for overall health system strengthening

Developing nations make up 80% of the global population, contains 90% of the world's disease burden but accounts for only 12% of global health expenditure (Figure 6.1Error! Reference source not found.) [15].

Figure 6.1: Mismatch between global health spending and global disease burden [15]



The conditions of the poor and the disparity in wealth distribution has spurred a united global pledge (Millennium Development Goals, MDGs) to improve the health and livelihood of those in low and middle-income countries [16]. However, instead of abiding to the Alma Ata of 1978 which committed to health improvement by building strong health systems through comprehensive primary care, short-cut focuses on instituting selective programmes to tackle the most severe diseases were adopted based on the argument that comprehensive care would be too costly [17]. It was believed that disease-specific efforts would lead indirectly strengthen the system as a whole. Major global health initiatives were created around priority areas to tackle the major diseases including Global Fund to Fight AIDS, TB and Malaria, The Presidential Emergency Plan for AIDS Relief (PEPFAR), Stop TB, Roll Back Malaria, and the Global Alliance for Vaccines and Immunization. While achievements were made in the health focused MDGs, targets were still under-reached. Reflecting from the

experience, there is growing recognition that fragile systems cannot be bypassed and their inherent shortfall in key areas renders them incapable to thrive and sustain on the opportunities that global interventions bring [18]. In the age of the Sustainable Development Goals (SDGs), integration and system-wide collaborations are now emphasized to overcome the limitations that plagued the MDGs [19].

Not only are there endemic constraints related to the healthcare workforce, commodity supply chains, health financing, and information infrastructure, but also the existence of disease specific focuses additionally crowd-out resources for other equally important areas [18]. Analysis of health system barriers to improving coverage and service delivery of different health inducing interventions or programmes have yielded similar results which our study attests to [18]. The disparate coverage among HIV, syphilis, malaria and anaemia services found in our baseline analysis (Chapter 3) are the results of PMTCT programmes being financed and carried out by PEPFAR and external partners which has led to wide coverage of HIV care [20]. While this is laudable, conditions such as syphilis and anaemia that have not received strong international advocacy remain poorly managed. Having supplies available improves healthcare worker motivation and pregnant women's desire to seek services. Findings from Chapter 4 and elsewhere [21-25] show that healthcare workers are enthusiastic about providing testing services to pregnant women as it allowed them to perform their jobs and increased their satisfaction. Indeed, the lack of supplies was one of the reasons for healthcare worker strikes in Kenya (chapter 4) [26]. A well-resourced facility will improve working conditions and healthcare worker motivation [27].

The existence of parallel systems likely result in distortions [18] where separate cadres of staff with higher salaries paid for by specific programmes are created, draining human resources away from other core tasks or demotivating those not in higher salaried positions [18, 28, 29]. We saw this during our study when HIV care providers (supported by PEPFAR) did not participate in country-wide healthcare worker strikes demanding on-time and better pay which may lead to further demotivation of core staff who were striking.

Parallel programmes also cause disruptions [18] where many uncoordinated programmes pull staff away from the facilities for trainings, workshops, and outreach [28]. A study of polio eradication in Tanzania, Nepal and Lao found that healthcare staff had their regular work disrupted around immunisation campaigns which happens several times a year [30]. While a few training workshops or outreach a year may be manageable, the combined number of in-service training to deliver various disease programmes means healthcare workers are absent frequently making this strategy more and more unsustainable. These extra-curricular trainings are often supplemented with per diems and generous transport reimbursements, providing extra incentives to be away. A disturbing finding from Chapter 5 was how often nurses were absent from the facility and that rarely do two nurses work simultaneously together, causing excessive workload to be shifted onto one nurse. This also came up in the narratives (Chapter 4) where healthcare workers complained of being 'alone' and unable to give quality when they were over-stretched.

International players influence norms and shape countries' policy preferences [31, 32]. Overseas development assistance (ODA) funds are usually provided on short-term cyclical basis and drive health ministries to create disease specific silos to expedite the scale-up of priority services with short term targets [33]. Also, there are often weak synergies among programmes which lead to inefficiencies and duplications [18]. In Kenya, the National Malaria Control Program (NMCP), the National AIDS and STIs Control Programme (NASCOP) and the Division of Family Health manage and create policies for malaria, HIV and reproductive health programmes respectively [34, 35]. While there are inter-agency coordination committees (ICCs) and technical working groups (TWGs) that meet to co-ordinate across programmes, the 2013 Health Sector Strategic Plan found too many ICCs, poor programme alignments and weak linages (chapter 2) [36]. This type of environment does not nurture the development of long term strategies to enhance strengthening health infrastructure which would require strategic long term planning with less tangible short term benefits [37].

This disintegration is also commonplace in the organization of research monies and institutes which are divided into disease specific departments. For example, there was no obvious place to lead this integrated testing study from within the host institution of KEMRI/CDC because the study's focus did not fit strictly within the branch concentrations of either malaria, HIV, TB or emerging infectious diseases. It is important to be cautionary against continued investments in disease specific interventions without concurrently building knowledge on how to improve basic health system infrastructure as almost all studies identified shared health system related barriers to the successful implementation of their disease specific programmes (chapter 2). Changing this trend would require funding bodies and champions to influence agendas from the top down.

Broader approaches to tackling system failures will take long-term planning, political will and an understanding that several root causes may need to be addressed simultaneously and that benefits may not be evident for a long time [18]. Committing to achieving long haul gains is advantageous as health-system barriers cut across disease profiles: procurement and distribution systems, healthcare workforce, training and supervision are shared resources. A shift from disease-specific responses to system-wide responses will create efficiencies and raise the common good. While we may still need a deeper understanding of how and what broader system strategies can and to what extent contribute to overall health system strengthening, it is important to be guided by this collective vision so we can start shifting our intentions toward long-term goals [18]. The simple fable of the three little pigs can remind us that foundations built from brick are sturdier and better prepared for catastrophic forces than those built from sticks and hay.

6.4 Addressing the political economy

While the above section discussed how vertical structures within global health initiatives and the international donor agendas may contribute to an inadequate system strengthening response to population health needs, this section will discuss some endemic health system weaknesses rooted in the institutional environment.

These constraints may not have simple stand-alone technical solutions but would require institutional reform.

Political changes and upheavals affect the functioning country's health systems. During the time of this study, politics motivated the Kenyan government to rapidly execute the decentralization process of transferring decision-making power to the counties. The county governments were unprepared for the transition and their limited technical capacity created disruptions in the county's financial flows causing stock-outs, salary delays and insufficient funding (Chapter 4) [38, 39]. After devolution is complete, healthcare decisions would involve local politicians and technical actors. To sustain antenatal testing, county authorities involved with selecting priorities will need to see the importance of antenatal screening and allocate resources towards it. This would require civil society pressure and policy champions to push antenatal care priority amongst several competing social demands from agriculture, transport, education et cetera [37].

A country needs good checks and balances to make effective use of foreign investments and ODA [40]. Within a good policy environment with robust economic management, a 1% of GDP in assistance translates to 1% reduction in poverty and infant mortality [40]. Many SSA countries have poor governance and corrupt politicians who squander or misappropriate development assistance funds, usually through fake contracts [41, 42]. It is estimated that stolen money from seven Kenyan government officials exposed in 2005 could have paid for the entire countries' antiretroviral drugs needs for a decade [43]. Development assistance should strengthen institutions so that important services can be absorbed and the performance of these institutions are the key to poverty reduction [40]. Solutions to address institutional and environmental constraints are beyond the realm of health alone and might require a disruption in innovation or the political economy to change the status quo [37].

6.5 Systems thinking and the need to go beyond trial designs

Increasingly, policymakers and implementers are looking beyond trial outcomes of efficacy to consider the operational feasibility of interventions within the local

environment [44]. While controlled trials are robust in estimating the *efficacy* of treatment effects, they are more limited in their evaluation of *effectiveness* of population health interventions [45]. Public health is the emergent product of behaviours, policy environments and disease contexts evolve and interact in complex ways that can affect the sustainability of the intervention. This creates an adaptive complexity that is best understood through systems thinking and applying multi-disciplinary enquiry [46]. The reductionist approaches of experimental methodology where linear causal patterns are to be predicted through regression in controlled comparisons are limiting and we need to shift beyond randomized control trials as the gold standard for capturing valuable information [45]. Rather, the goal of implementation research is to understand how an intervention functions within its contextual environment and the range of factors that mediate its impact [47]. As such generalizability cannot always be produced because the environment in which the interventions are implemented highly determines the outcomes [18, 47].

This study demonstrated the application of multi-methods to progressively investigate a health service gap. Implementation outcomes of adoption and fidelity were measured quantitatively using exit interviews, antenatal registers and proficiency scores. Acceptability, appropriateness and feasibility were assessed qualitatively through social science perspectives which captured the textured layers of experiences and behaviour [48]. An operational simulation method [49] that introduced competition at discrete events was applied to describe the service delivery environment and emergent consequences of the intervention introduction and virtually experiment 'what-if' scenarios without the cost of real-life experimentation. They each contribute essential information towards answering questions around the implementation of strategies in complex systems.

Methodological challenges of health systems research need to be addressed and developed more thoroughly to incorporate a wide range of quantitative, qualitative and multi-disciplinary approaches. Effectiveness-implementation hybrid designs that blend testing clinical effectiveness and measurements of implementation outcomes can help close the translational gaps between research and practice early in the

research process [50]. Combining multi-disciplinary perspectives and methods would require expanding paradigms and acknowledging that no one method is sufficient in itself to understand complex systems [46, 48].

6.6 Limitations of point-of-care tests (POCTs)

Point-of-care tests (POCTs) should be ASSURED: affordable, sensitive, specific, user-friendly, robust and rapid, equipment-free and deliverable to those who need them [51]. The HIV and malaria POCTs used in this study followed national guidelines and the tests for syphilis and haemoglobin concentrations have been evaluated and recommended by WHO according to the ASSURED criteria [52, 53]. POCTs are not gold standards and their sensitivities and specificities are not 100% meaning there will always be false positives and negatives when testing at the population scale. This may be mitigated by establishing testing algorithms which requires either parallel or serial testing to guard against false positives, especially in populations that are tested often [54]. Those who test negative often do not require re-testing but it is important to make an accurate risk assessment to identify populations who may have exposure or on-going risks [54].

The rapid test for syphilis detects antibodies against Treponema which remains positive even after successful treatment which may lead to overtreatment. In places with the capacity (electricity for refrigeration of reagents, rotator and blood centrifugation) to perform a Rapid Plasma Reagin (RPR), a testing algorithm beginning with a treponemal rapid diagnostic screening test followed by an RPR confirmatory test can be considered [55]. However, in most peripheral facilities, the use of RPR is not possible or practical and over-treatment is more beneficial than the risk of congenital syphilis.

The use of POCTs will still require some central laboratory support for quality control because new batches of tests need to be validated with positive and negative controls per standard operating procedures. HemoCue© machines also need to be calibrated once every 3 months using standard known haemoglobin concentrations. These supportive networks would need to be organized to ensure quality should programmes be scaled nationally. Tests should also be stored under 30^{o}C and there

may be days well over this temperature at the facilities. Although we did not monitor the average temperatures where the tests were stored, temperature control would be important to ensure tests are not damaged and retain their quality.

The currently used standard malaria rapid diagnostic tests have limited sensitivity and were designed to diagnose malaria in clinical patients and not to detect low-density or subclinical parasitaemia in asymptomatic women, which would be the main target population in antenatal screening strategies. The limitations of the current generation of malaria rapid diagnostic tests (RDT) when used to screen asymptomatic pregnant women were recently shown in four trials of intermittent screen and treat strategies in pregnancy (ISTp), which suggested that regular screening with malaria RDTs is inferior to the existing preventive strategy of intermittent preventive strategy (IPTp) with sulfadoxine pyrimethamine (SP) [56]. This is likely explained by the high number of low-density infections missed by malaria RDTs and the absence of prophylactic protection from SP for test-negative women [57, 58]. However, these studies also showed that the performance of malaria RDT relative to PCR is best at the antenatal first visits when the prevalence of RDT detectable parasitaemia and parasite densities were highest. New ultra-sensitive diagnostic tests such as the Alere Malaria Ag P.f RDT ULTRA SENSITIVE (SD/Alere, Yongin-si, Republic of Korea) that are reportedly 10 times more sensitive may change the efficacy of ISTp and they are currently under-going performance evaluations in the field [59]. These ultra-sensitive tests would be increasingly important as we move towards elimination and eradication goals when all parasite reservoirs need to be destroyed.

6.7 Limitations of the study and gaps

6.7.1 Study site and study design

The study was conducted in the HDSS area of KEMRI/CDC and the area's high burden of disease has drawn an increasing number of foreign research groups since the 1980s. The community has frequent contact with researchers due to active demographic surveillance. Health facilities often have several research studies on-going within them from various research groups. Often, research studies hire study

nurses to recruit patients and collect data, but they also work side by side with the routine ministry of health staff and taking on their workload. This may distort the local implementation environment and may not reflect the true staffing capacity of the facilities. While we tried to minimize the staffing distortion by selecting facilities with no other on-going MCH studies, this may not have entirely avoided the issue. Healthcare workers may also be more inclined to accept the intervention because of facility data collectors who may serve as additional subordinate staff to help with facility errands. Women's receptivity of the intervention may also be higher than other less research heavy areas because of exposure to researchers and interventions. These factors should be considered and rates of adoption may be different in other settings.

We used a quasi-experimental before-and-after design with no concurrent controls to measure adoption of testing. These designs are considered weak because without concurrent controls they cannot account for secular trends; any improvements seen cannot be categorically attributed to the intervention. However, this weakness may not be applicable to this study. Our baseline measure revealed that testing was low because of no test availability and so our objectives were formed around understanding the implementation process if tests were made available. Since the intervention was the availability of tests, it was pointless to compare adoption with control facilities where tests were not available because by definition it meant testing could not be done.

When Chapter 3: Study 1 went out to peer review with Plos Med, the reviewers questioned why random sampling was not applied as purposive sampling reduces external validity. However, our goal was to capture a range of different environments where testing is done to understand the range of factors that could influence implementation success. There were only 24 dispensaries in the KEMRI HDSS area with some receiving less than 10 antenatal clients per month and some with other antenatal studies ongoing. A random sample may not have given us enough variations in implementation environments. Therefore, after conducting a baseline

assessment of all facilities in the KEMRI HDSS area, we selected facilities with the greatest geographical spread, and medium to high patient volume.

The study is likely to have over-estimated the adoption of the integrated testing strategy because of the study (Hawthorne) effect on primary and other outcomes. During the time of the study, data collectors were present to interview ANC women and their presence may have influenced healthcare worker behaviour. Moreover, data collectors inadvertently end up helping with menial tasks around the facility which distorts the real-life working conditions.

Our qualitative findings (Chapter 4: Study 2) were context specific and may not generalize to other settings. Kenya was experiencing government devolution and many of the grievances healthcare workers expressed may have been related to devolution challenges. Staff turnover was high and some healthcare workers who were involved with the intervention in the beginning and later transferred were not interviewed which may have missed some information. The findings from the healthcare worker interviews and focus group discussions were not surprising and are mostly supported by the literature. As an early qualitative researcher, I may not have had the experience and skills to obtain as rich of data as more experienced researchers.

Finally, we did not assess pregnancy outcomes which is the ultimate goal of testing and treating women. The assumption is that availing point-of-care tests at dispensaries with good implementation would result in pregnant women receiving early testing, diagnosis and appropriate treatment and this would result in less adverse outcomes compared to those not tested. Originally, we had planned to link test and treatment results to women's pregnancy outcomes to test this assumption using the HDSS surveillance data but institutional financial mismanagement during the study period precluded this from happening. This research may serve as proof-of-concept for integrated testing at dispensary level in preparation of a larger and more costly study to evaluate the impact of testing on pregnancy and birth outcomes.

6.7.2 Stakeholder engagement

The idea for introducing an integrated testing strategy was also not locally conceived, and our study lacked sufficient engagement with stakeholders and policy makers at the design stage. Understanding decision-makers' priorities and advocating the importance of integrated testing would ensure relevant research outputs and higher policy impact. Early engagement with HIV, malaria and reproductive programmes and their implementation partners would be essential to ensure uptake and policy change. Since the country was undergoing devolution during the time of the research, working closely with the county management team would have been ideal to understand the county priorities and assess intentions to improve antenatal care.

During the research period, three of the facilities added new laboratory technicians and research staff had to encourage facilities to continue implementing testing within the ANC with the ANC nurse or HTC counsellor and not refer the women to the laboratories. These conflicts in practice of where integrated ANC testing would take place and who should be responsible for testing would need to be clearly delineated by management and communicated to front-line workers so healthcare workers would not feel they are being asked to perform outside their duties.

The original study budget was reduced significantly after some institutional financial challenges at KEMRI and we did not have the budget to sufficiently disseminate the research finding to obtain feedback from the healthcare workers and the county health management teams. Modelling of operational impact of integrated testing (Chapter 5: Study 3) should have been visually presented to healthcare workers to assess the accuracy of the model. Policy makers and frontline healthcare workers should have been consulted to understand their concerns on service delivery, identify bottlenecks, and devise potential resource neutral solutions that could be viable and acceptable. These strategies should then be tested and assessed for improvement. These steps are vital to translating research to practice.

6.7.3 Costing

The study did not do a costing analysis of the integrated testing strategy. While a costing exercise may be informative, multiple studies have already established that syphilis testing is one of the most cost-effective interventions in pregnancy, even in low prevalence settings [54, 60]. Moreover, maternal syphilis is a co-factor for mother-to-child transmission of HIV and the importance of its integration with HIV management is well established and uncontended. HIV/syphilis multiplex tests are now available in the market and their use will likely lead to more cost-savings because of efficiencies in procurement and service delivery [54]. Cost-effectiveness studies of intermittent screening and treatment of malaria in pregnancy (ISTp) currently show that the strategy is not superior to chemoprophylaxis with sulfadoxine pyrimethamine (SP) and bednet use but modelling work suggests that as SP resistance increases, ISTp can potentially be a beneficial and suitable option [61]. Successful management of malaria will also help reduce cases of anaemia and these benefits need to be accounted for as well. HemoCue© has been shown to be the most accurate and appropriate method for haemoglobin measurements compared to others such as pallor and colour scales [62-64] but also the most expensive at approximately US$0.75/test [53, 62]. Haemoglobin testing with haemoglobinometer is the recommended method for diagnosing anaemia in pregnancy [65] despite the lack of studies weighing accuracy and cost-benefit considerations of different anaemia detection strategies in different prevalence environments.

6.8 Conclusion and recommendations for future work

This thesis demonstrates that an integrated testing strategy for HIV, syphilis, malaria and anaemia was well received by healthcare workers and pregnant women and may fill an important gap in antenatal testing requirements. The high adoption, increased number of cases detected, and good performance of healthcare workers are testaments to the potential that can be achieved when test supplies, training and supervision are available. It also highlights some of the healthcare system deficiencies that exist and the need for concurrent strengthening of these service delivery channels in order for coverage to be effective, that is, to achieve desired

health outcomes. Table 6.2 suggests some health system level responses to overcome some of the identified constraints to antenatal testing coverage.

Table 6.2: Potential health system responses to overcome constraints to antenatal testing coverage	
Barrier	Strategy
Pregnant women accessibility of antenatal testing including early attendance and multiple contacts	-Development of community-based care to orient women on how to take care of their pregnancy such as the importance of antenatal care and diagnosis of HIV, syphilis, malaria and anaemia early -Availing POCTs at peripheral facilities -Addressing social-cultural barriers to encourage women to attend ANC early in first trimester so interventions can be given early enough to safeguard pregnancy.
Lack of male partner involvement	-Understanding male barriers to reproductive health involvement and targeting men to participate in antenatal care through community based and gender-integrated interventions [10, 66] Encourage men to test for sexually transmitted infections such as HIV and syphilis.
Vertical funding structures	-Global health community, researchers, implementers and development assistance funding bodies must work together to address overall health system strengthening and refrain from favouring disease specific programmes that only address the major diseases of HIV, and malaria [18, 67].
Inadequate financing for reproductive health	-County governments to commit more of their budgets to health and antenatal care ensure that test kits and drugs are available. This would require policy champions and advocacy to raise reproductive health agenda in face of competing social demands.
Lack of inter-departmental partnerships and communication	-Improving communication across departments and strengthening the inter-agency coordination committees (ICCs) and technical working groups (TWGs) so HIV, malaria and reproductive health programmes can benefit from synergies. -Strive towards integration of of HIV, malaria, STI and reproductive health programmes and guidelines to avoid duplications and ensure co-infections are addressed and managed properly.
Ineffective procurement and commodity distribution systems	-Improve and integrate procurement and transport of commodities such as test supplies and medicines so ordering channels are streamlined and benefit from economies of scale.
Poorly motivated healthcare workers	-Review of salaries, job grades and promotions, improve working condition, invest in training and supervision, ensure no stock-outs of test kits and treatments and invest in non-financial incentives to improve healthcare worker performance and retention [68]. This will ensure trained healthcare workers do not leave with their testing skillsets and avoid having to retrain new healthcare workers. Healthcare workers should be adequately motivated to provide counselling and information to pregnant women about the four conditions, especially syphilis, during antenatal care.
Staff shortages and workload	-Integration of healthcare worker training and supervision so healthcare workers are not pulled out of duty for programme specific trainings. -Ensure basic comprehensive antenatal care services including how to conduct point-of-care testing should be part of nurse training curricula to decreases the length and frequency of long in-service training. -Reducing healthcare worker shortages and absences through long-term investment in human resource development and retention [37].
Neglect of health systems and policy research	-Diversify research funding sources to encourage more multi-disciplinary systems research such as incorporating qualitative and operations research[18]. -Stipulate studies to incorporate implementation and translational component into their design and budget so implementation processes are studied and the constraints to scale-up are acknowledged and addressed adequately

	-Encourage the use of multi-methods such as social science and operational research methods to answer a range of implementation questions [48]. -High impact journals should call for and publish more implementation research studies [44].

It is important to recognize that no one single strategy is sufficient but that each may be a necessary contribution. Long term strategic planning and political will is needed. A systems' thinking perspective should be adopted and interdisciplinary creativity encouraged to guide future implementation work. There is also a need for consistency and conceptual distinction of implementation outcomes so the field can be more robust and findings more comparable. Finally, we must keep in mind that great achievements take time and sustained effort. Researchers should remember that our work is not just speculative in nature, but rather to place us in better position to improve the human condition through successful implementation.

6.9 References

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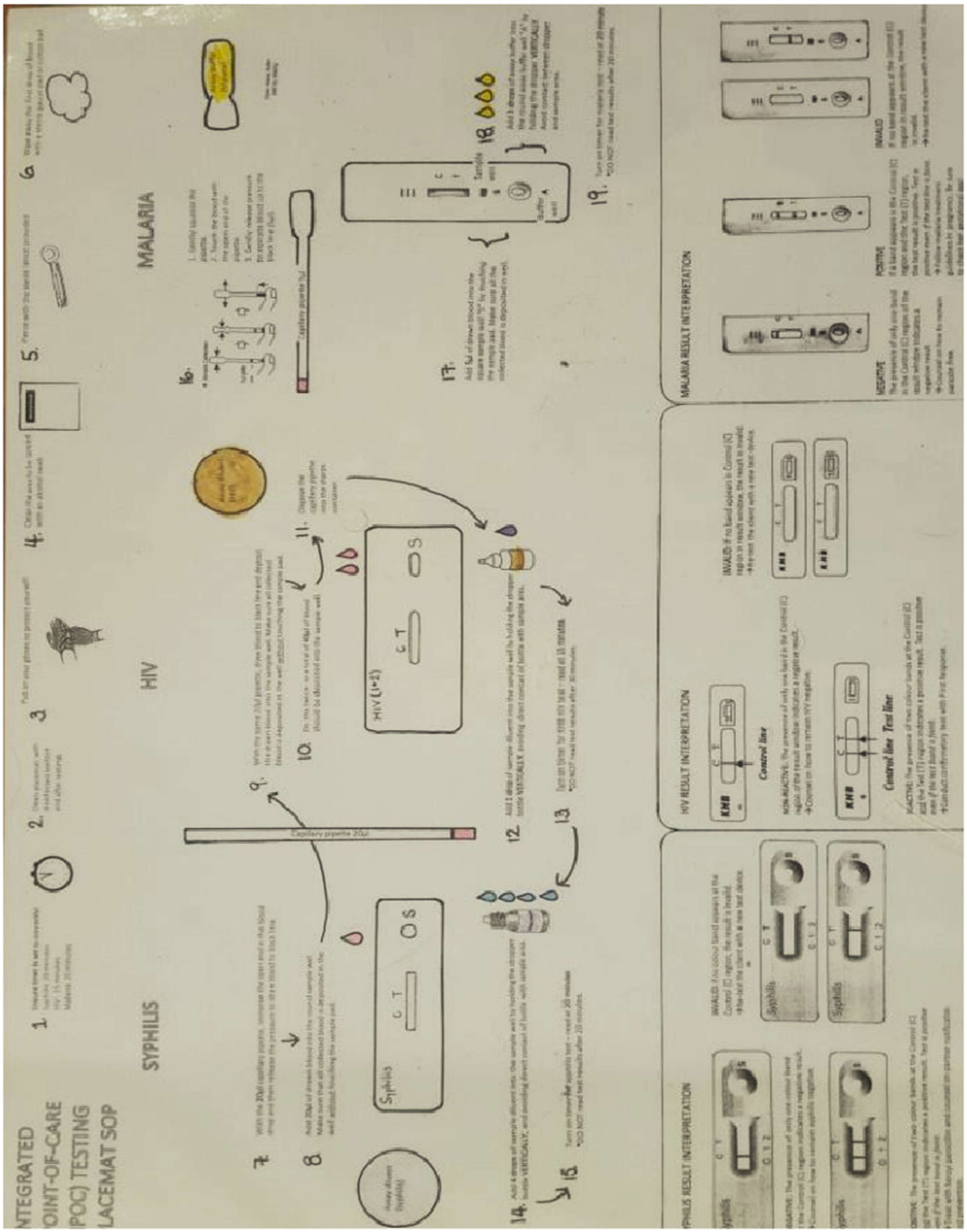
7 Appendices

7.1 Appendix 1 Integration operating procedure placemat



7.2 Appendix 2 Text proficiency testing monitoring checklist

IPOCT EXTERNAL MONITORING CHECKLIST

Name of facility:

Name of staff:

Date:

		Y	N		Y	N
Safety:	Sharps container	☐	☐	Gloves	☐	☐
	Biohazard waste bin/bag	☐	☐			

PERFORMANCE OF PROCEDURES

		Y	N		Y	N
Preparation	Label initials onto cassette	☐	☐	Check lot number	☐	☐
	Correct use of timer	☐	☐	Check expiration date	☐	☐
Finger prick	Sterile lancet	☐	☐	Correct position of prick	☐	☐
	Correct massage	☐	☐	Dispose lancet in sharps	☐	☐
	Correct disinfection	☐	☐	Correct wiping of first drop	☐	☐
				Sufficient volume of blood for IPOCT using 1 prick (4 tests)	☐	☐

		Y	N		Y	N
Syphilis Testing:	Syphilis pipette	☐	☐	Deposit all blood onto sample well *without* touching sample pad	☐	☐
	Syphilis buffer	☐	☐	Dispose pipette in sharps	☐	☐
	Syphilis cassette	☐	☐	Correct number of buffer drops into sample well	☐	☐
	Correct pipetting	☐	☐	Starting timer immed'ly after buffer	☐	☐
	Sufficient volume drawn to line (20µl)	☐	☐	Waiting full time to read -ve result	☐	☐
				Correctly interpret result	☐	☐

		Y	N		Y	N
HIV Testing:	HIV pipette	☐	☐	Deposit all blood onto sample well *without* touching sample pad	☐	☐
	HIV buffer	☐	☐	Dispose pipette in sharps	☐	☐

	HIV cassette	☐	☐	Correct number of buffer drops into sample well	☐	☐
	Correct pipetting	☐	☐	Starting timer immed'ly after buffer	☐	☐
	Sufficient volume drawn to line (40µl)	☐	☐	Waiting full time to read -ve result	☐	☐
				Correctly interpret result	☐	☐
		Y	**N**		**Y**	**N**
Malaria Testing:	Malaria pipette	☐	☐	Deposit all blood onto sample well *touching* **sample pad**	☐	☐
	Malaria buffer	☐	☐	Dispose pipette in sharps	☐	☐
	Malaria cassette	☐	☐	Correct number of buffer drops into **buffer well**	☐	☐
	Correct pipetting	☐	☐	Starting timer immed'ly after buffer	☐	☐
	Sufficient volume drawn to line (5µl)			Waiting full time to read -ve result	☐	☐
				Correctly interpret result	☐	☐
		Y	**N**		**Y**	**N**
HB testing:	Hemocuvettes	☐	☐	Correct wiping of cuvette on both sides	☐	☐
	Hemocue machine	☐	☐	*Gently* closing machine	☐	☐
	Kimwipe	☐	☐	Correctly reading result	☐	☐
	Correctly turn on hemocue machine	☐	☐	Taking cuvette out of machine	☐	☐
	Correct drawing of blood into cuvette	☐	☐	Dispose cuvette in sharps	☐	☐

7.3 Appendix 3 Focus group discussion guide with pregnant women

Focus group discussion guide for pregnant women who completed first ANC visits in participating antenatal clinics (ENG)

FGD ID No [___]___]___] Moderator Initials [___]___]___] Note-taker Initials [___]___]___]
Recorder Number: _____ Folder/File Name (location on recorder): _____
Date [___]___]/[___]___]/[___]___] Interview location _____
Time: Start _____ Time: Stop_____
No. Participants at start of FGD: _____ No. Participants at the end of FGD: _____
Introduction
I am _____from _____(moderator)
I am _____from_____(note-taker)

- ✓ General purpose of the study
  - We are trying to find out what health checks and blood tests are done in the antenatal clinic, what you understand and are told about these checks in the clinics and what care you get if the tests show you need treatment. We would like to know about the care you and other pregnant women have experienced and in particular what difficulties you experience when you try to get the care you need. This information will help us understand what issues are important to you and other pregnant women, and if there are any problems.
- ✓ Aims of the interview and expected duration
  - Perceptions of ANC service and health workers
  - Perceptions of HIV, syphilis, malaria and anaemia in pregnancy
  - Perceptions of blood tests and treatment
  - Identify best way to provide diagnosis and treatment at a single ANC visit.
  - We will have a discussion that will from 1-2 hours
- ✓ Who is involved in the process (other participants)
  - We will hold discussions with women early in their pregnancies who have visited one of the antenatal clinics for their 1st ANC visit.
- ✓ Why the participant's cooperation is important
  - We are asking you to help us better understand what health checks and blood tests are now done in pregnancy, and if pregnant women receive the treatment that they need. We want to learn about what more you think is needed for antenatal care and what you do when you get ill. We will also talk about care that is needed for pregnant women with health needs such as infections with HIV and syphilis. We also want to know about the experiences of you and other pregnant women with local health staff or other providers of health care or medicines, such as traditional healers or shop keepers. This knowledge will help us understand how to improve the care available in your community.
- ✓ What will happen with the collected information and how the participant/target group will benefit
- ✓ Ground rules:

- Only one person talks at a time.
- It is important for us to hear everyone's ideas and opinions. There are no right or wrong answers to questions – just ideas, experiences and opinions, which are all valuable.
- You do not need to share experiences that make you feel uncomfortable. You can leave at any time.
- It is important for us to hear all sides of an issue – the positive and the negative.
- Confidentiality is assured. "What is shared in the room stays in the room."
- Turn off mobile phones

✓ Any questions?

✓ Consent to record
We would like to use a tape recorder so that information is collected correctly – please let us know if this is acceptable

Please note the questions here:

Demographic information for every FGD participant *[to be completed on a one-to-one basis, immediately after consent is obtained]*

Participant no.	Age	Date of 1st ANC	Gravidity	Gestation age	Marital status	Education	Ethnic group

MODERATOR: *Allow group to decide; assign fake names or use participant numbers. Make sure to use these fake names or participant numbers in note-taking and transcription. Make name tags using the fake names or participant numbers.*

* REMEMBER – you MUST ask same questions for all groups or you are biasing results

COMMENTS – reasons for withdrawal, refusal, ambience of FG, level of interest, disagreements, etc

Warm up

Can we go around the room and say which village you are from and whether this is this your first pregnancy?

Now I am going to introduce some topics I hope you can discuss together, about your experiences during pregnancy.

Theme	Opening questions and Probes

Services received at ANC	You all recently attended ANC at ____. Why do pregnant women choose to attend ANC at _____? Are you aware of what should be given to pregnant women at their first ANC visit? Can you tell us? Did you receive these services? Do pregnant women feel comfortable in asking for services they know they should have but did not receive from the healthcare worker? Do you know the blood tests that should be done for pregnant women at their first ANC visit? Can you mention them? What kind of blood tests were pregnant women given at the ANC at _____? What was your experience about counselling offered at the ANC? Probe: HIV counselling, blood test counselling, birth plan counselling, nutrition counselling
Knowledge of HIV, syphilis, malaria and anaemia and the blood tests	What do you know about HIV and how it affects the unborn child? Probe: risk of infection during pregnancy, risk of infection during childbirth, risk of infection during breast feeding? Syphilis? Probe: risk of infection during first/second trimester? Risk of infection during 3rd trimester? Assess knowledge of syphilis (A bacterial infection usually spread by sexual contact/blood transfusion/congenital,that starts as a painless sore on genitals, mouth or rectum. If transmitted to the baby during pregnancy, can cause malformations) Malaria? Anaemia? Probe: knowledge of different levels of anaemia: >8-10g/dl: Mild anaemia, 6-8g/dl: Moderate anaemia, <6g/dl: Severe anaemia What was pregnant women's experience of the blood tests they do at the ANC? Probe: How do you feel about the amount of explanation received about blood tests given by healthcare worker? How many times were the fingers pricked? Is that acceptable? How do pregnant women feel about the amount of explanation received about a positive result from the blood tests if done? Probe: How do the healthcare workers communicate the results? Do women understand what the results mean for them and their baby? Do pregnant women accept the results?

	If a blood test result is positive, what should be done for pregnant women? For HIV? Are pregnant women given the treatment they need? Probe: Do healthcare workers give enough counselling to pregnant women so they can accept their results? When are pregnant women given care for HIV? Syphilis? Are pregnant women given the treatment they need? Probe: Do pregnant women know the right treatment for syphilis? Do healthcare workers give adequate explanation for the treatment? Malaria? Are pregnant women given the treatment they need? Probe: Availability of quinine, co-artem in facilities? Availability of SP? Given bednets? Advised to sleep under bednet? Anaemia? Are pregnant women given the treatment they need? Probe: Do the healthcare workers tell pregnant women their blood level and give advice/treatment? Availability of iron/folic acid? Do pregnant women know the different levels of Hb and how much iron pills to take depending on blood level? Do pregnant women experience side effects of the iron pill? Are pregnant women referred for blood transfusion if blood level is very low? If positive for HIV or syphilis, it is important to treat the spouse as well. What is pregnant women's experience of talking to their spouse about testing and treatment at the health facility?
Quality of services received at ANC	What are pregnant women's experiences of the ANC at _____? Probe: How did you feel about the waiting time? Did you receive everything you expected? Do they prefer male or female health workers? How do the healthcare workers at ____ treat pregnant women? Probe: What advice do they give pregnant women? How is the attitude of the healthcare workers? Do you spend enough time with the healthcare workers? How do healthcare worker attitude influence where pregnant women seek advice? Were pregnant women asked to pay anything? Do pregnant women feel they can discuss their pregnancy with the healthcare worker?
Closing We are now approaching the end of our discussion. Is there anything else anyone would like to add about the blood tests that you get from ANC or health facilities that we have not talked about? ✓ Summarise	

- ✓ Thank participants
- ✓ Provide extra information and contacts to participants

7.4 Appendix 4 Semi-structured interviews with healthcare workers

Integrated point of care testing for HIV, syphilis, malaria and anaemia in dispenaries in western Kenya

Interview Guide

Objectives: To explore health workers' perceptions and experiences of the implementation integrated point of care testing services for HIV, syphilis, malaria and anaemia

A. Introduce the purpose of the study – its aims and scope
- Assure participant of confidentiality and how it will be maintained
- As for their consent to participate

B. Note details of participant.

1. Interviewee ID
2. Date of Interview
3. Name of RHs or HCs
4. Province
5. Title interviewee
6. Gender Male Female
7. Age
8. # of children
9. Family members
10. Education

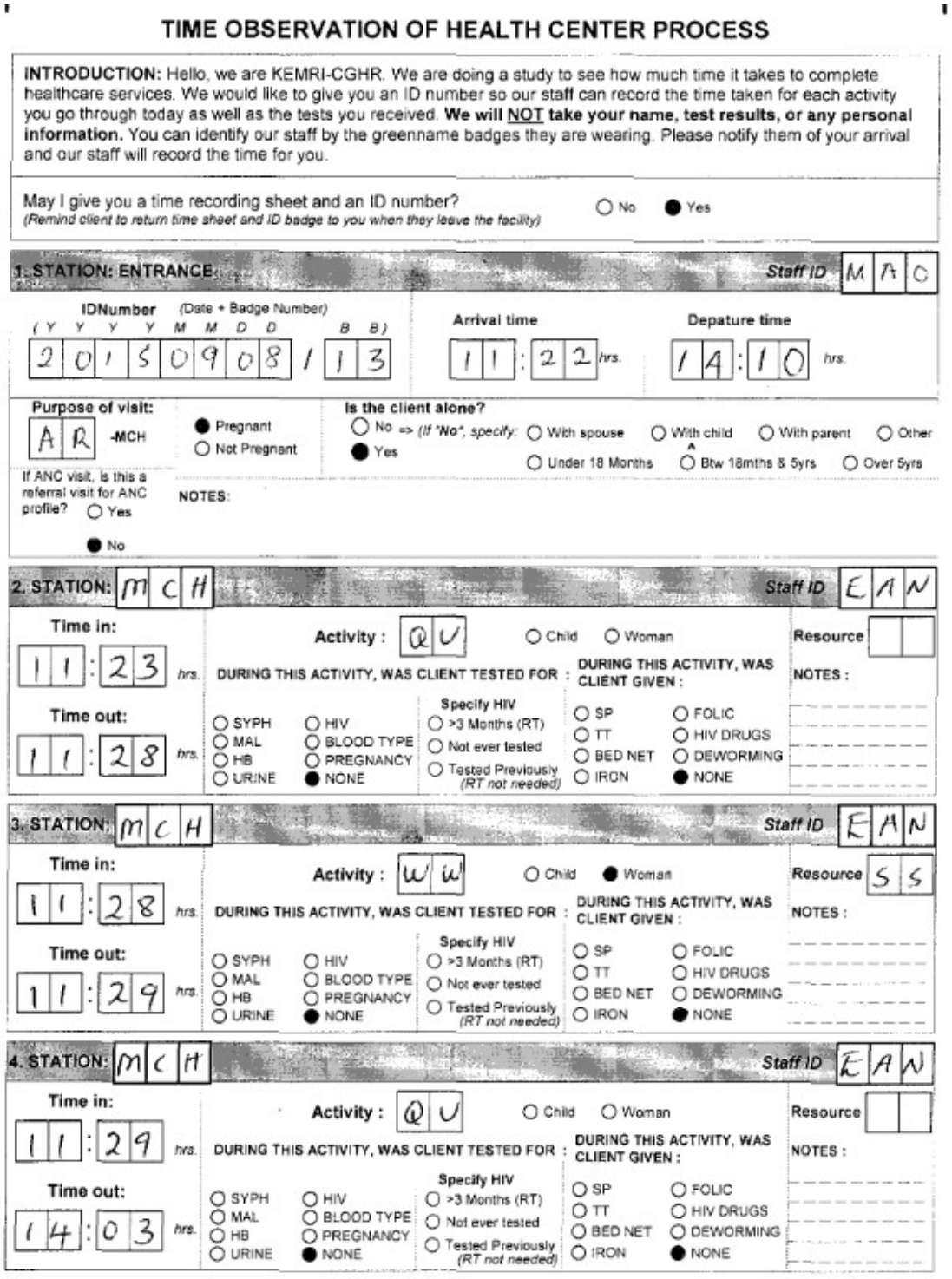
Questions

Probes:
- *When was that?*
- *Why did you do that?*
- *What did you enjoy about that?*
- *How did you manage in that situation?*
- *Where did you go next?*

1. Tell me a bit about yourself? How did you come to work in the health field?
2. How did you get this job?
3. Describe what you do now
4. How long have you been working here?
5. How do you feel about your current job?
6. *What do you like and dislike about it?*
7. Are you planning to stay? What are your plans for your future career?
8. Do you do other jobs as well, or other activities to make money? Tell me about them
9. Tell me about the different kinds of pay which you receive (probe: salary; allowances; user fees;
1. payments from patients; incentives for deliveries; private business etc.).
    a. Which ones are most valuable for you?
    b. Why?
    c. How do they change the way you work?
10. What are the main challenges you face in your professional life?
    a. How do you cope with them?
11. What sort of changes have you seen over your period of working?
12. Do you know about any policies to encourage health workers to stay in rural areas? Tell me

2. about them
    a. Have they worked?
    b. What do you think about them?
13. What do you think is the most important thing for the government to do to get health workers
3. to work and stay in rural areas?
4. Before Ipoc what kind of testing was done at this facility? Who does it?
5. Do you receive training for that test? By whom? How often do you have retraining?
6. When a new healthcare worker comes who trains them in doing the testing? Are they expected to know?
7. Do you feel comfortable in training new healthcare workers?
8. Which Ipoc process most challenging?
9. How did they view ipoc initially?
10. How do they view ipoc now?
11. What are the challenges?
12. Which part do you find most challenging
13. Blood prick/timer using/pipette/waiting for the full time?
14. How do you usually treat syphilis
15. How do you treat anaemia/do you have time to tell the client their anaemia status/syphilis status?
16. Do you have time to counsel the women?
17. Many women do not know what syphilis is around this area…Do you have time to tell them about syphilis?

7.5 **Appendix 5** Sample data collection for time-motion data



TIME OBSERVATION OF HEALTH CENTER PROCESS

INTRODUCTION: Hello, we are KEMRI-CGHR. We are doing a study to see how much time it takes to complete healthcare services. We would like to give you an ID number so our staff can record the time taken for each activity you go through today as well as the tests you received. **We will NOT take your name, test results, or any personal information.** You can identify our staff by the greenname badges they are wearing. Please notify them of your arrival and our staff will record the time for you.

May I give you a time recording sheet and an ID number? ○ No ● Yes
(Remind client to return time sheet and ID badge to you when they leave the facility)

1. STATION: ENTRANCE Staff ID: MAO

IDNumber (Date + Badge Number) (Y Y Y Y M M D D / B B): 2015090813

Arrival time: 11:22 hrs. Depature time: 14:10 hrs.

Purpose of visit: AR -MCH ● Pregnant ○ Not Pregnant

Is the client alone? ○ No => (If "No", specify: ○ With spouse ○ With child ○ With parent ○ Other ○ Under 18 Months ○ Btw 18mths & 5yrs ○ Over 5yrs) ● Yes

If ANC visit, is this a referral visit for ANC profile? ○ Yes ● No

NOTES:

2. STATION: MCH Staff ID: EAN

Time in: 11:23 hrs. Time out: 11:28 hrs.

Activity: QV ○ Child ○ Woman Resource:

DURING THIS ACTIVITY, WAS CLIENT TESTED FOR: ○ SYPH ○ MAL ○ HB ○ URINE ○ HIV ○ BLOOD TYPE ○ PREGNANCY ● NONE

Specify HIV: ○ >3 Months (RT) ○ Not ever tested ○ Tested Previously (RT not needed)

DURING THIS ACTIVITY, WAS CLIENT GIVEN: ○ SP ○ TT ○ BED NET ○ IRON ○ FOLIC ○ HIV DRUGS ○ DEWORMING ● NONE

NOTES:

3. STATION: MCH Staff ID: EAN

Time in: 11:28 hrs. Time out: 11:29 hrs.

Activity: WW ○ Child ● Woman Resource: SS

DURING THIS ACTIVITY, WAS CLIENT TESTED FOR: ○ SYPH ○ MAL ○ HB ○ URINE ○ HIV ○ BLOOD TYPE ○ PREGNANCY ● NONE

Specify HIV: ○ >3 Months (RT) ○ Not ever tested ○ Tested Previously (RT not needed)

DURING THIS ACTIVITY, WAS CLIENT GIVEN: ○ SP ○ TT ○ BED NET ○ IRON ○ FOLIC ○ HIV DRUGS ○ DEWORMING ● NONE

NOTES:

4. STATION: MCH Staff ID: EAN

Time in: 11:29 hrs. Time out: 14:03 hrs.

Activity: QV ○ Child ○ Woman Resource:

DURING THIS ACTIVITY, WAS CLIENT TESTED FOR: ○ SYPH ○ MAL ○ HB ○ URINE ○ HIV ○ BLOOD TYPE ○ PREGNANCY ● NONE

Specify HIV: ○ >3 Months (RT) ○ Not ever tested ○ Tested Previously (RT not needed)

DURING THIS ACTIVITY, WAS CLIENT GIVEN: ○ SP ○ TT ○ BED NET ○ IRON ○ FOLIC ○ HIV DRUGS ○ DEWORMING ● NONE

NOTES:

7.6 **Appendix 6** Dispensary patient pathways for MCH women

Visit purpose	Id yyyymmdd## N=183	Activity sequence											activity	location	resource
AN	2015090801	2	2	11	4	8	50					1	RGW	MCH	N1/N2
U5	2015090802	2	6	11	4	5	50					2	RGW	MCH	SS
U5	2015090803	11	4	2	5	6	50					3	BL	MCH	
U5	2015090804	11	4	1	9	50						4	TR	MCH	
U5	2015090805	11	4	2	5	6	50					5	IM	MCH	
PM/U5	2015090806	11	4	5	2	17	50					6	VA	MCH	
U5	2015090807	2	2	5	50							7	FP	MCH	
U5	2015090808	2	5	50								8	CN	MCH	
AR	2015090809	2	8	50								9	CSL	MCH	
AR	2015090810	2	8	50								10	LB	MCH	
AR	2015090811	2	8	8	50							11	HT	MCH	N2
U5	2015090812	2	50									12	RGW	OP	
AR	2015090813	2	8	50								13	BL	OP	
U5	2015090814	2	5	50								14	CN	OP	
U5	2015090815	2	5	50								15	FP	OP	
U5	2015090816	2	5	6	50							16	DR	OP	
U5	2015090817	2	50									17	RGW	PSC	
U5	2015090818	2	50									18	VL	PSC	
AN	2015090901	2	2	8	50							19	CN	PSC	N1/N2
AN	2015090902	2	2	8	50							20	CSL	PSC	
FP/OPD	2015090903	12	13	14	50							21	CN	PSC	CO
U5	2015090904	2	50									50	exit		
U5/OPD	2015090905	2	12	13	14	50									
AR	2015090906	2	8	50											
SP	2015090907	2	8	50											
U5/OPD	2015090908	2	12	13	14	50									
LB	2015090909	10	50												
FP	2015090910	7	50												
PM/AR	2015091001	17	19	8	50										
U5	2015091002	2	2	50											
PM/U5	2015091003	17	2	20	21	50									
PM	2015091004	20	17	20	21	50									
U5	2015091005	2	50												
PM/U5	2015091006	17	2	21	50										
PM/U5	2015091007	2	5	3	8	50									
PM/U5/OPD	2015091008	2	17	3	21	14	16	50							
AR	2015091009	1	8	50											
U5	2015091101	2	50												
U5	2015091102	2	50												
U5	2015091103	2	50												
U5	2015091104	2	50												
U5	2015091401	2	50												
AN	2015091402	2	8	50											
U5	2015091403	2	5	50											
U5	2015091404	2	50												
AN/NP	2015091405	8	4	8	50										
U5	2015091501	2	5	50											
U5	2015091502	2	5	50											
U5	2015091503	2	6	50											
AR	2015091504	2	8	50											
AR	2015091505	2	8	50											
U5	2015091506	2	5	50											
U5	2015091507	2	5	50											
U5	2015091508	2	50												
U5	2015091509	2	5	50											
U5/FP	2015091510	2	2	7	50										
U5	2015091511	2	50												
U5	2015091512	2	5	50											

Legend:

RGW: registration
BL: blood test
TR: waiting for test results
IM: immunization
VA: receiving vitamin
FP: family planning
CN: consultation
CSL: counselling
LB: labour
HT: health talk
DR: waiting for drugs
VL: viral load

OPD: out-patient room
MCH: maternal and child health room
PSC: patient support care room

N1: OPD nurse
N2: MCH nurse
CO: clinical officer
SS: support staff

U5	2015091513	2	9	50											
U5	2015091514	2	5	50											
U5	2015091601	2	50												
U5	2015091602	2	5	50											
U5/FP	2015091603	12	15	50											
U5/FP	2015091604	2	7	50											
PM/AN	2015091701	17	19	8	50										
U5	2015091702	2	5	50											
U5	2015091703	2	5	50											
FP	2015091704	2	7	50											
U5/OPD	2015091705	2	6	12	14	50									
U5	2015091706	2	5	50											
FP	2015091707	2	7	50											
FP	2015091708	2	7	50											
U5	2015091801	2	50												
U5/OPD	2015091802	2	13	14	50										
U5	2015091803	2	6	50											
U5/OPD	2015091804	2	2	14	50										
AR	2015092101	2	8	50											
U5/OPD	2015092102	1	5	12	13	14	50								
AN	2015092103	8	4	8	2	8	50								
FP	2015092104	7	50												
AR/OPD	2015092105	2	8	13	14	50									
U5	2015092106	1	5	50											
U5	2015092201	2	50												
U5	2015092202	2	11	4	5	50									
U5	2015092203	2	11	4	5	50									
U5	2015092204	2	6	11	4	5	50								
U5/OPD	2015092205	2	11	4	5	8	50								
U5	2015092206	2	6	50											
U5	2015092207	11	4	2	2	5	9	50							
U5	2015092208	11	4	2	9	50									
U5	2015092209	11	4	2	5	50									
U5	2015092210	2	5	50											
U5	2015092211	2	5	50											
U5	2015092212	2	50												
U5	2015092213	2	5	5	50										
U5	2015092214	2	5	50											
U5	2015092215	2	5	50											
AR	2015092216	1	8	50											
AR	2015092217	1	8	50											
AR	2015092218	1	8	50											
U5	2015092219	2	5	50											
FP	2015092220	7	50												
AR	2015092301	2	8	50											
AR	2015092302	2	8	50											
AR	2015092303	2	8	50											
AN	2015092304	2	2	8	50										
AR	2015092305	2	8	50											
U5	2015092306	2	50												
FP	2015092307	3	7	50											
U5	2015092308	2	5	50											
U5	2015092309	2	50												
U5/OPD	2015092310	2	5	8	50										
PM/U5	2015092401	2	18	5	3	21	50								
PM/U5	2015092402	2	21	50											
PM/U5/OPD	2015092403	2	2	12	21	50									
PM/U5	2015092404	2	2	21	5	3	20	50							
PM/U5	2015092405	2	2	21	50										
PM/U5	2015092406	2	21	50											
PM/U5	2015092407	2	5	3	20	21	3	4	8	50					
PM/U5	2015092408	2	21	50											
PM/U5	2015092409	2	21	50											
PM/U5/FP	2015092410	2	5	2	15	21	50								
PM	2015092411	17	21	50											
AR	2015092412	2	8	4	50										
AN	2015092413	2	2	8	4	50									

PM/U5	2015092414	17	2	5	3	20	21	50							
PM/U5	2015092415	2	17	21	50										
AN	2015092416	2	2	8	50										
U5	2015092501	1	50												
U5	2015092502	1	50												
U5	2015092503	2	50												
AR	2015092504	2	8	11	4	50									
AR	2015092505	2	8	4	11	4	50								
U5	2015092506	2	50												
AR	2015092507	2	8	4	8	11	4	50							
AR	2015092508	2	8	11	4	50									
U5	2015092509	11	4	2	5	50									
U5	2015092510	2	50												
AR	2015092801	2	8	50											
FP/OPD	2015092802	2	7	14	50										
U5	2015092803	1	5	9	50										
U5	2015092804	1	6	50											
U5	2015092805	1	8	50											
U5	2015092806	1	6	50											
FP	2015092807	2	7	50											
U5	2015092808	1	6	50											
U5	2015092809	2	1	5	50										
FP	2015092810	2	7	50											
AN	2015092901	2	8	50											
U5	2015092902	2	5	50											
U5	2015092903	2	5	6	50										
U5	2015092904	2	5	50											
U5	2015092905	2	5	50											
U5	2015092906	2	5	50											
U5	2015092907	2	5	8	50										
U5	2015092908	2	5	50											
AN	2015092909	2	8	50											
U5/OPD	2015092910	2	6	12	13	14	5	50							
U5	2015093001	2	50												
PM/U5	2015093002	2	19	50											
AR	2015093003	2	50												
U5	2015093004	2	50												
PM	2015100101	17	21	50											
U5	2015100102	2	50												
AR	2015100103	2	8	50											
FP	2015100104	2	3	7	50										
FP	2015100105	1	7	50											
U5	2015100106	2	5	50											
AR	2015100107	2	8	50											
PM/U5	2015100108	2	2	21	50										
U5	2015100201	2	50												
U5	2015100202	2	50												
U5	2015100203	2	50												
U5	2015100204	2	5	50											
U5	2015100501	2	50												
U5	2015100502	2	2	50											
U5	2015100503	2	5	50											
AR	2015100504	2	8	50											
U5	2015100505	1	5	50											
AR/U5	2015100506	2	2	8	50										
AN	2015100507	2	2	8	50										
U5	2015100508	2	50												
U5	2015100509	2	50												

7.7 Appendix 7 Screen shot of DES modelling in WITNESS©