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SAWUBONA MAMA: USING MHEALTH TO IMPROVE MATERNAL, NEONATAL AND CHILD HEALTH OUTCOMES IN SOUTH AFRICA

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THESIS FOR DOCTORAL DEGREE (Ph.D.)

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ABSTRACT

BACKGROUND: At the end of the first decade of the 2000's, South Africa had poor, and worsening, maternal and neonatal health outcomes. In parallel, the use of mobile phone technology to support health care (mHealth) increased dramatically. Maternal mHealth has potential to support maternal care; studies of its effects have been limited, but the results have been encouraging. The Mobile Alliance for Maternal Action (MAMA) project launched a maternal mHealth project in South Africa aiming to improve maternal, neonatal, and child health outcomes using informational SMS/text messages.

AIM: To assess the informative maternal health SMS intervention, MAMA SMS, in Johannesburg, South Africa by comparing maternal and infant health outcomes of users with non-users, conducting a cost-effective analysis on the intervention, reporting on feedback given during focus group discussions attended by users, and conducting a comparison study on users of MomConnect, the maternal mHealth programme that replaced MAMA SMS.

METHODS: **Sub-study I** was cluster observational study of mother-infant-pairs who were followed from pregnancy to one year postnatal to monitor maternal health outcomes. The intervention arm which received the SMS intervention included 87 pairs while the control arm included 90 pairs. **Sub-study II** was a cohort study of HIV-positive women and their infants who were followed from pregnancy until one year postnatal, to monitor maternal health and HIV-related outcomes. The intervention arm, which received the SMS intervention included 235 mother-infant-pairs, while the control arm included 586 pairs. **Sub-study III** was a cost-effectiveness analysis study measuring costs at the societal level, along with measured changes in health care utilisation and health outcomes measured in sub-study I. Data were entered into the Lives Saved Tool and used to forecast lives saved and DALYs averted of gradually scaling up program activities to reach 60% of pregnant women across Gauteng province within 5 years. **Sub-study IV** was a qualitative study based on data from four FGDs with MAMA SMS participants who had been receiving messages for at least four months. 15 females and three males participated with ages ranging from 20 to 36 years. **Sub-study V** used the same methods as sub-study I to investigate the MomConnect maternal mHealth intervention implemented by the National Department of Health and based on MAMA SMS. The intervention arm included 115 participants while the control arm had 37 participants.

RESULTS: Intervention participants were more likely to attend all recommended antenatal and postnatal visits including all recommended first year vaccinations (RR: 1.71, 95% CI: 1.30-2.23) and were more likely to attend at least the recommended four antenatal visits (RR: 1.59, 95% CI: 1.23-2.04) (**sub-study I**). HIV-positive intervention participants also attended more ANC visits (5.16 vs. 3.95, $p < 0.01$) and were more likely to attend at least the recommended four ANC visits (relative risk (RR): 1.41, 95% confidence interval (CI): 1.15–1.72). Birth outcomes of intervention participants improved as they had an increased chance of a normal vaginal delivery (RR: 1.10, 95% CI: 1.02–1.19) and a lower risk of delivering a low-birth weight infant (<2500 g) (RR: 0.14, 95% CI: 0.02–1.07). In the intervention group, there was a trend towards higher attendance to infant polymerase chain reaction (PCR) testing within six weeks after birth (81.3% vs. 75.4%, $p = 0.06$) (**sub-study II**). Incremental costs per DALY averted from a societal perspective ranged from $1,985 USD in the first year of implementation to $200 USD in the 5th year. At a willingness to pay threshold of $2,000 USD, the intervention had a 40% probability of being cost effective in year 1 versus 100% in years 2 through 5 (**sub-study III**). Focus group participant feedback regarding the health system was mixed, with some participants having positive experiences, and a number of participants sharing negative experiences such as long waiting times, understaffed clinics and poor service. They reported that the messages were timely, written clearly and seemed

supportive. Most participants reported regularly sharing the messages with both friends and family (**sub-study IV**). MomConnect recipients showed no differences in health outcomes measured, including complete maternal health coverage, number of ANC visits attended, likelihood of low-birthweight infants, or EPI coverage compared to the control arm. The control arm had higher than expected baseline coverage for all outcomes measured (**sub-study V**).

CONCLUSIONS: The results from the clinical studies show an improvement in achieving complete maternal-infant continuum of care, provide evidence of a positive impact of informative maternal mHealth messaging sent to pregnant women and new mothers, particularly if the baseline or starting health outcomes are sub-optimal (**sub-studies I, II and V**). The cost effectiveness evaluation findings suggest that SMS-based maternal health information messages delivered to pregnant women may be a cost-effective strategy for bolstering ANC and childhood immunizations, even at very small margins of coverage increases. Primary data obtained prospectively as part of more rigorous study designs are needed to validate modelled results (**sub-study III**). By providing timely and relevant information to pregnant women and new parents, contextually relevant maternal mHealth interventions could play a cost-effective part in improving maternal and child health outcomes and quality of care across the globe (**sub-study IV**).

POPULAR SCIENCE SUMMARY

This research was conducted to measure any benefit or drawback of a maternal SMS project which sent pregnancy and child support information to pregnant women and new mothers in Johannesburg, South Africa. The maternal health information was sent to mobile phones twice a week, starting during pregnancy, and continued after delivery until the child was one year of age.

Five studies were conducted, three compared changes in pregnancy and child health issues among SMS recipients which was compared to women and children who did not receive the messages. One of the studies compared the costs of the project with the health improvements that were observed to estimate cost-effectiveness. The last study was based on feedback from recipients, both men and women, who participated in focus group discussions consisting of three to six individuals each.

The results from the comparison studies showed when average health outcomes are less than ideal (i.e.: too few maternal health visits during pregnancy), individuals who received the messages showed increased levels of attendance to maternal and infant health care visits and improvements in some health issues. However, when average health outcomes are already within recommended levels, there is no difference between the two groups. The cost-effectiveness study showed that if the SMS project was continued and expanded throughout the province at the same rate over five years it would be cost-effective after only two years. Lastly, feedback from the users showed that they found the messages trustworthy, timely, useful, and some women reported regularly following advice that was given in the messages more than that of their own mothers. Together, the results from this study provide evidence that maternal mHealth messages improve maternal health outcomes and can be cost effective to run when used where there is a strong need for better outcomes.

SCIENTIFIC PAPERS INCLUDED IN THE THESIS

The papers will be referred to in the text as sub-study I-V.

I. **Improving Maternal and Infant Health Using mHealth Text Messages in a Low-Resource Urban Setting in South Africa.**
Coleman J, Lau Chan V, Black V, Thorson A, Eriksen J. *Manuscript.*

II. **Effectiveness of an SMS-based Maternal mHealth Intervention to Improve Clinical Outcomes of HIV-Positive Pregnant Women.**
Coleman, J, Bohlin, K C, Thorson, A, Black, V, Mechael, P, Mangxaba, J, Eriksen, J.
AIDS Care 2017, Jul;29(7):890-897

III. **Forecasting the Value for Money of Mobile Maternal Health Information Messages on Improving Utilization of Maternal and Child Health Services in Gauteng**
LeFevre A, Cabrera-Escobar MA, Mohan D, Eriksen J, Rogers D, Neo Parsons A, Barre I, Jo Y, Labrique A, Coleman J.
JMIR Mhealth Uhealth 2018; 6(7):e153

IV. **A Qualitative User Study of a Maternal Text Message-based mHealth Intervention: MAMA South Africa SMS**
Coleman, J, Eriksen J, Black V, Thorson A, Hatcher A. *Manuscript.*

V. **Effectiveness of a Maternal Health Text Message Intervention Aiming to Improve Maternal, Neonatal and Child Healthcare Service Utilisation**
Coleman J, Black V, Eriksen J. *Manuscript.*

SCIENTIFIC PAPER NOT INCLUDED IN THE THESIS

- **The Clinic-Level Perspective on mHealth Implementation: a South African Case Study.**
Wolff-Piggott B, Coleman J, Rivett U.
Information Technology for Development, 2017. Jan 7:1-22

CONTENTS

LIST OF ABBREVIATIONS

ANC   Antenatal Care

ART   Antiretroviral Treatment

AZT   Zidovudine (HIV medicine)

CEA   Cost Effectiveness Analysis

DALY   Disability Adjusted Life Year

EPI   Expanded Programme on Immunisation

FGD   Focus Group Discussion

HIV   Human Immunodeficiency Virus

ICER   Incremental Cost Effectiveness Ratio

MAMA   Mobile Alliance for Maternal Action

mHealth   Mobile phone-based health care support

MNCH   Maternal, Neonatal and Child Health

NDoH   (South African) National Department of Health

NVD   Normal Vaginal Delivery

NVP   Nevirapine (HIV medicine)

PCR   Polymerase Chain Reaction

PDA   Personal Digital Assistant

PNC   Postnatal Care

QALY   Quality Adjusted Life Year

RCT   Randomised Control Trial

SMS   Short Messaging System (Also known as 'text messages')

SSA   Sub-Saharan Africa

RTH   Road to Health (South Africa NDoH child health booklet)

TAC   Treatment Action Campaign

USAID   United States Agency for International Development

WHO   World Health Organisation

OPPERATIONAL DEFINITIONS

Complete coverage — Attendance to all (South African) government-recommended maternal and infant health visits from conception to one year postnatal. Specifically, complete coverage entails at least 4 ANC visits and all 16 infant immunizations.

eHealth — The use of electronic devices to support or augment health care provision. Often used as a short-hand for electronic medical record databases, but also used to entail any electronic device or system.

Healthcare worker — A medically trained staff member employed at a healthcare facility.

Health facility — A physical structure where health services are offered. In South Africa this means primary clinics, community care centres and hospitals.

Health outcomes — A measurable result related to a specific aspect of health care. For example: a change in infant weight over time.

MAMA — The Mobile Alliance for Maternal Action, a consortium founded by the mHealth Alliance, USAID, United Nations Foundation, Johnson & Johnson and BabyCentre.

MAMA Global — The headquarters for the MAMA consortium, based in Washington, DC.

MAMA SMS — A free twice-weekly SMS/text message-based maternal health service offered by MAMA South Africa.

MAMA South Africa — The South African-based consortium implementing MAMA in South Africa. Organisationally, MAMA SA consisted of Praekelt Foundation (management and technology implementation), Cell-Life (content) and Wits RHI (clinical implementation, monitoring and evaluation).

mHealth — A subset of eHealth, often defined as the use of a mobile technology device (e.g.: cell phone, pager, etc.) to support or augment health care services.

Mother-infant-pair — The combination of a mother and her infant. Usually used when monitoring postnatal care visits.

Participant — An individual who has agreed to be part of the MAMA SMS research projects.

PNC/EPI visit — A postnatal visit with a health care worker at a healthcare facility to check on a mother-infant-pair and provide vaccinations.

Service uptake — The use of a health care service as intended.

User (of MAMA SMS) — An individual who has registered to receive the MAMA SMS maternal health messages.

1 INTRODUCTION

1.1 MHEALTH

1.1.1 History of mHealth

mHealth, or the use of mobile devices to augment health care services (1) is a growing area of interest in the medical field. mHealth is a subset of eHealth (2). Starting in the 1980s, the first electronic devices that could be thought to be mHealth devices were small 'vest pocket computers' used by physicians as reference tools (3). Later, in the 1990s, pagers and personal digital assistants (PDAs) became popular and were used by physicians (4). mHealth has become more pervasive since the price of mobile phones (cell phones) has fallen and affordable to the general population.

1.1.2 SMS as mHealth

Short message system (SMS) or phone-based text messages were first offered to the public in 1993. SMS-based patient communication was available to confirm appointments for patients of some Singaporean doctors' offices and was reported as early as the year 2000 (5). By 2003, scientific articles reporting on pilot studies on the use of SMS-based communication for patient support were being reported in medical journals covering eating disorders (6) and diabetes (7). In the same year a physician-written opinion piece in the British Medical Journal was recommending patient communication using SMS for sharing test results and follow-up advice, to receive feedback about a patient's treatment intervention, upcoming tests to be done, or to book appointments (8). However, this view was not without its detractors as communication with patients using new mediums of communication technology brings with it medicolegal issues (9).

SMS remained the primary focus of mHealth throughout the first decade of the 2000s). Of this research, many early in the decade were pilots or feasibility studies (10–14). As the decade wore on, results from a variety of randomised control trials (RCTs) were reported in scientific journals (15–20), some of which showed no significant effect on the primary outcome. Systematic reviews of mHealth interventions also started being published around this time (21 and section 1.1.5, below). Of note, most mHealth research done in the mid-to-late noughties was completed in high-resource settings, albeit with a few exceptions (10,22,23).

1.1.3 mHealth for HIV in Africa

In the early 2010s a pair of seminal studies were published reporting RCTs using mHealth interventions in Africa. Lester et al. (24) published an RCT in the Lancet looking at HIV-positive patients starting antiretroviral treatment (ART) in Nairobi, Kenya. The results showed that one SMS a week containing a one word question, and expecting a reply every week for a year was sufficient to significantly increase medicine adherence and suppress viral loads compared to those receiving no weekly message (the standard of care). Pop-Eleches et al. (25) provided additional evidence for mHealth interventions for HIV-positive patients from their

mHealth RCT, also in Kenya. In this study, patients in four intervention arms received a variety of message length (short and long) or frequency (daily and weekly), and compared to a control arm which received the standard of care with no messages. The results showed that participants who received a weekly short SMS had a statistically significant increase in the primary outcome, 90% adherence to ART. Together, these two studies provided strong support to the idea that weekly SMSs could improve health outcomes of HIV-positive patients on ART.

1.1.4 History of maternal mHealth research

1.1.4.1 Wired mothers and antenatal care

One of, if not the first, maternal mHealth research studies was a cluster-randomised controlled conducted in Zanzibar, starting in 2009 (26,27) using SMSs and mobile phone airtime credit, to support pregnant women and new mothers. The study included 2550 women at 24 facilities on the island and the first study results showed that urban intervention participants were more likely to deliver with a skilled birth attendant (Odds Ratio, 5.73; 95% CI: 1.51–21.81) (26). The second article to come from the study showed an increase in the portion of women who attended at least four ANC visits in the intervention group (adjusted OR: 2.39; 95% CI: 1.03–5.55) (27). This increase in achieving four or more ANC visits was also found in other maternal mHealth studies, in Thailand (28) and India (29), however these were not RCTs. These similar outcomes are of interest as multiple other non-mHealth intervention research has shown difficulty achieving a statistically significant increase in at least four ANC visits (30,31).

1.1.4.2 Text4Baby

Arguably, the first large-scale maternal mHealth intervention was Text4Baby, launched in the USA in February, 2010 (32). Text4Baby offered free bi-weekly SMSs to pregnant women throughout the United States and expected to reach over one million pregnant women per year (32). While Text4Baby reached hundreds of thousands of individuals and seemed to have the desired impact (33,34), it no longer is promoted to the same extent, likely due to the proliferation of other, often web-based, sources of maternal health information available in the USA.

1.1.4.3 MAMA & MomConnect

The Mobile Alliance for Maternal Action (MAMA) Global partnership was launched in late 2011 by then Secretary of State, Hillary Clinton, as a public-private partnership between USAID, Johnson & Johnson, the UN Foundation and BabyCentre and was created to promote the use of mHealth to improve maternal health outcomes in Bangladesh (where the service was called Aponjon), India and South Africa (35,36). Academic research output on the global MAMA projects has been limited. One example is from Ahsan and Raihan (37) who wrote about a self-reported increase in attendance to at least four or more ANC visits. In South Africa, the MAMA SMS project was handed over to the National Department of Health (NDoH) in 2014 and relaunched nationally as MomConnect, with mother 'help desk'. MomConnect had reached half a million users by early 2016 (38).

1.1.4.4 Maternal mHealth supporting postnatal care

Studies looking at improving attendance to clinical visits during postnatal period are limited in number. One of the first, an observational study in Nigeria showed that SMS reminder messages reduced the number of women who failed to attend scheduled appointments by half compared to a historical control (39). Another, larger study in Bangladesh used a pre-post intervention methodology to study the mTika project (40). This program sent SMS reminders for EPI (Expanded Program on Immunization) visits to new mothers and showed an increase in the difference in difference of rural and urban groups by 29.5% (p<0.001) and 27.1 (p<0.05) respectively (40). No published results from RCTs looking at the effect of mHealth on postnatal care only have been identified.

1.1.5 Systematic reviews of maternal mHealth interventions

A handful of systematic reviews addressing maternal mHealth in low-resource settings were recently published (41–44). Each of the reviews highlight evidence of improvements in maternal and neonatal health outcomes as evidence in RCTs and non-RCTs and there is agreement that further and higher quality research is needed. Watterson et al. suggest "...further rigorous evaluation of mHealth programmes is needed in a broader variety of settings" (43) while Lee et al. state "...overall the available evidence is weak and the results, in most cases, are too inconsistent to enable robust conclusions to be drawn about impacts on patient health outcomes" (42). Additionally, a lack of registered RCTs was identified as a concern by Sondaal (41). A gap that has been identified is the exclusive focus on a single component of the maternal and child health continuum of care instead of providing "...an integrated system that follows women and children through the maternal, neonatal, and child health continuum" (43).

Another common use for maternal mHealth interventions are those targeting health care workers. A recent systematic review included ten intervention and nine descriptive studies conducted in low and middle income countries (45). The intervention studies were broken down into two types of mHealth use; data collection and SMS communication/education; both of which were reported to be effective tools for communication, education and data collection (45). Technology issues were found to be a challenge for multiple mHealth projects. The review did not discuss interventions that communicated directly with patients, but more effective maternal health care workers could translate into healthier, better informed patients.

1.1.6 Economic evaluation of mHealth interventions

Economic evaluations in healthcare, in the form of cost effectiveness analyses (CEAs) have been part of public health since at least the late 1970s (46). CEAs are still part of most economic evaluation (47,48) however they are not without critique, including the theoretical basis of some analysis tools used and type of efficiency (allocative vs technical) used (49). Economic evaluations of mHealth interventions have been recommended by health researchers since at least 2012 (50) as they provide a more holistic approach to understanding the viability of an intervention. A number of mHealth-based projects and interventions have conducted economic evaluations, 39 of which were highlighted in a recent systematic review which concluded that

a large portion of the articles reviewed showed cost effectiveness (51). The review also cautioned that not all articles reported sufficient detail according to the CHEERS checklist (52), an economic evaluation reporting standard, which made them difficult to compare and interpret.

1.1.6.1 Economic evaluation of maternal mHealth interventions

To date there have been few economic evaluations of maternal mHealth interventions (42). One that has been published looked the results from an RCT which aimed to increase physical activity in new mothers with children under one year using a holistic multimethod intervention which included SMS (53). The study showed the intervention to be cost effective, but seems to have ignored the study outcome showing there was no effect six months after the intervention. A review of the literature shows that at least one additional economic evaluation on maternal mHealth is planned for in the near future; the Weltel PMTCT study is planning to conduct a cost effectiveness analysis and a cost utility analysis on the intervention (54), but further evidence is needed.

1.1.7 Acceptability of mHealth

User acceptability testing which reviews the method of communication and the information communicated to the users is an important, but often neglected aspect of any mHealth intervention (55). In 2012, Coomes et al. provided an overview of the various elements that must be decided on for any mHealth intervention, including functionality, number of components, interactivity, frequency, timing and tailoring (56). While the articles' focus is on HIV care specifically, the elements discussed are arguably important for all mHealth interventions. When dealing with health issues that potentially have stigma, such as HIV, issues around confidentiality will undoubtedly arise (57). Conducting investigations into acceptability and feasibility to advise the intervention (55,58–61) is encouraged.

Research highlighting routine assessments of ongoing mHealth interventions are published much less frequently. One example of this was in rural Ghana where researchers investigated the impact of a smartphone app used by community health nurses (62). The study showed that while the app improved productivity, was easily integrated into care and accepted by its users, there were issues relating to usability and feasibility due to patient volumes, staffing issues and technology issues (62). Being able to become aware of these challenges is the first step towards remedying them and thus highlights the importance of ongoing acceptability assessments.

1.1.8 Gaps in current maternal mHealth research

Despite increasing and more rigorous research being conducted, there are many gaps in the maternal mHealth literature. These include; limited cost-effectiveness evaluation (42) and ongoing user acceptability testing, few studies that follow the continuum of care from confirmation of pregnancy through to at least one year of age (41,43,63), and a lack of a deep understanding on how mHealth can support provision of ART to pregnant women and new mothers (64). This thesis aims to provide additional scientific evidence around these topics.

1.2 THE HIV/AIDS EPIDEMIC

1.2.1 Global burden of HIV

The human immunodeficiency virus (HIV), which causes acquired immunodeficiency syndrome (AIDS), has been a major global public health issue for the past few decades (65). In 2015, 36.7 million individuals were living with HIV globally and 1.1 million died from AIDS-related illnesses in that year (65).

Since the mid-1990s, combination ART for HIV-positive individuals was first identified as a viable treatment (66). Since then, combination ART has drastically improved the quality of life and delayed the onset of AIDS-related illnesses (67). Since September 2015, the WHO has recommended ART for all HIV-positive individuals (68) and in June 2016, it was estimated that roughly 18.2 million people were accessing ART (69). With increased access to ART over the past decade, the number of HIV-related deaths and number of babies born HIV-positive has decreased, but continues to be much too high (69).

1.2.2 HIV burden in Sub-Saharan Africa

Sub-Saharan Africa (SSA), has the largest burden of HIV globally with almost 1 out of 25 adults (4.4%) living with HIV, which makes up almost 70% of the people living with HIV worldwide in 2015 (65). In 2016 there was an estimated 6000 people newly infected with HIV per year, with two-thirds of these new infections occurring in SSA (70). In 2014, 41% of all HIV-positive individuals in the WHO African region were able to access ART (71). Additionally, over 70% of global AIDS-related deaths in 2013 occurred in SSA (72). To grapple with this huge disease burden, many high-income countries are supporting countries in SSA with HIV testing, care, research and treatment projects (73). In South Africa, it is estimated that just over 7 million people are living with HIV while national HIV prevalence rates stand at 12.7% of the general population, 18.9% of adults 15-49 years old, and 22.3% of adult women; the national incidence rates among adults was 1.27% in 2016 (74). As of March 2016, over 3.4 million South Africans were on ART (75), which is only half of the WHO goal of providing ART to all people living with HIV.

1.2.3 Mother-to-child-transmission of HIV

Vertical HIV transmission, or mother to child transmission (MTCT) is the most common route through which children are infected by HIV. There is minor disagreement regarding the exact rate of vertical HIV transmission among untreated women; Navér et al (76) suggest it sits at 18-25% while Stek (77) suggests the rate is between 14% and 40%. Nonetheless, research into medicines that support prevention of mother to child transmission (PMTCT) has been ongoing since 1994 when the first available antiretroviral (zidovudine or AZT) for reducing MTCT was reported in the ACTG 076 study (78) and more effective regimens have been identified since. Using the 2016 WHO Consolidated Guidelines on the Use of the Antiretroviral Drugs for Treating and Preventing HIV Infections (79), and with appropriate retention and adherence, it is possible to cut the risk of mother-to-child transmission to less than 5% for breastfeeding

women and to zero amongst women who do not breastfeed (80). Globally, national prevention of mother to child transmission of HIV (PMTCT) programmes have been launched and been quite successful (81–85).

1.2.4 HIV & reproductive health

1.2.4.1 HIV in pregnancy

Due to high rates of vertical transmission without treatment, the WHO has been recommending pregnancy HIV testing on an opt-out (i.e.: done by default) basis (86) and since 2012, lifelong ARV treatment for all HIV-positive pregnant women, also called Option B+ (87). There is evidence to suggest that increased usage of ART during pregnancy by HIV-positive women decreases maternal mortality (88).

1.2.4.2 HIV transmission in new-borns

Birth and breastfeeding are high-risk activities for vertical HIV-transmission (89). Previous research has shown that exclusive breastfeeding or exclusive bottle feeding have a lower risk of HIV transmission than mixed feeding, (90,91). For this reason, the current recommendation for resource-limited settings is for postnatal Nevirapine (NVP) syrup to be provided to all HIV-exposed new-borns, ART to the mother, and exclusive breastfeeding for the first six months to minimise the chance of transmission (92). Regular HIV testing of exposed infants is also recommended (92), however the testing timeline protocol varies over time and by country.

1.2.5 Treatment of HIV

The impact of suppressive ART on sexual infection risk has been comprehensively demonstrated; ART should be started early as this has been shown to decrease morbidity and mortality in the infected individual (93,94). Additionally, there is strong evidence that shows effective ART suppresses the HIV virus and almost completely eliminated the risk of transmission (95). Together, the evidence from the last few years has demonstrated clinical benefit starting modern ART immediately, irrespective of immunological status, leading to a widespread recommendation for a "test and treat" approach (68,96). Test and treat has further enjoyed support from mathematical models and observational studies, demonstrating public health benefit in that increasing ART coverage may substantially impact on new infections (97,98).

UNAIDS and WHO have driven the "90-90-90" initiative since 2015, as a strategy aiming to maximise the expansion of ART coverage for both individual health as well as decreasing new infections. The initiative calls for 90% of people living with HIV to know their status, 90% of those to be initiated on ART and 90% of those on ART maintaining viral suppression (68,99). 90-90-90 relies on effective case finding and successful referral for ART initiation, as well as retention, a problem across the world documented widely in the so-called "care cascade'' (100,101). To date, at least seven countries have achieved the 90-90-90 targets, including Botswana, Cambodia, Denmark, Iceland, Singapore, Sweden and the United Kingdom of Great Britain and Northern Ireland (102).

1.3 SOUTH AFRICA

1.3.1 History of HIV/AIDS care and treatment in South Africa

South Africa has a history of delayed reaction to the HIV epidemic. The first confirmed AIDS-related deaths in South Africa were in December 1981 (103). By 1987 the South African government acknowledged AIDS as a public health issue when it was added to the official list of communicable diseases (104). In 1988 the Department of Health created a structure for promoting awareness about HIV/AIDS, and by 1990 there were an estimated 74,000 to 120,000 South Africans living with HIV (104). Following that, and with the starting of a new, inclusive democracy in the early and mid-1990s, HIV/AIDS was not the main focus of the day (105).

In 1998 the then Minister of Health, Dr. Nkosazana Zuma, stopped a research project that was to test AZT, one of the early ARVs, to HIV-positive pregnant women (106). In early 2000 a new Minister of Health created SANAC, the South African National AIDS Council which provided support services around HIV and AIDS, but notably was silent about ARV treatment (104). Access to NVP as an early antenatal PMTCT drug was mandated to be provided by the public health system through the South African High Court in 2002, an order that was generally ignored which resulted in the launching of the civil society group, Treatment Action Campaign (TAC) (104). Through TAC's coordinated lobbying efforts, the government approved a plan for ART coverage, including PMTCT, in 2003. It was launched in 2004 with the support of a number international partners, and in 2005 achieved its target of having at least one care and treatment centre on every one of South Africa's 53 health districts (105), despite the number of individuals on treatment being significantly below targets (104).

1.3.2 Public health care in South Africa

South Africa has a two-tier health system, public and private, with approximately 85% of the population using some of the largely free government-run public system, which is funded from the country's tax base (107). There are over 4300 public health care facilities across the country, which provide comprehensive health services from primary to tertiary level, with the majority providing HIV care (108). Provision of health services is the responsibility of provincial and local governments. The NDoH provides policy on minimum standards and standardised protocols, and assists the Department of Treasury in setting budgets, but implementation of these are left to the provincial and local governments. Since 2003, the American PEPFAR (President's Emergency Plan for AIDS Relief) programme had been a significant funder of HIV/AIDS projects in the country (109).

Given national HIV prevalence rates in South Africa, a large portion of government health care funding goes to supporting HIV-positive patients. ART has been offered to HIV-positive patients since 2004 if they meet a certain CD4 cell count threshold; this threshold was originally set at 200 cells/mm3 in 2004, raised to 350 cells/mm3 in 2010, 500 cells/mm3 in 2013, and with the introduction of test and treat, the threshold was removed completely in 2016 (110). The HIV programme, largely due to accurate costing forecasts leading to decreased costs of medicines, has received South African government Treasury support as it has expanded over

the last 12 years (108). An example of this success can be seen in the national adult (ages 15-49) HIV incidence rate which has steadily fallen from its peak of 1.83% (adults aged 15-49 years infected by HIV per year) in 2006 to 1.27% in 2016 (74).

South African HIV testing rates are relatively high, with over 65% of adults knowing their status (111). However, immediate linkage to the next levels of care of newly diagnosed HIV-positive individuals has historically been low (100) as in the past it has required those individuals to await laboratory results prior to starting treatment. Prior to the 2015 WHO ART initiation guidelines (68), improved access to point-of-care CD4 diagnosis was widely anticipated to improve linkage to care due to the possibility of initiating newly identified HIV-positive patients on ART immediately. Unfortunately, the point-of-care CD4 diagnosis implementation yielded disappointingly limited success, suggesting other interventions were required (112–114). Supporting patients within the cascade of care may require multiple disparate but complementary interventions (114). HIV diagnosis is usually performed by lay counsellors, sometimes outside of clinical flow of patient care within facilities or away from conventional clinical environments.

1.3.3 Mobile phone ownership in South Africa

South Africa has had a regular increase in mobile phone ownership for many years and recently almost 90% of all South Africans reported ownership of a mobile phone (115). Another measure of mobile phone access shows that in 2015 there were 164 subscriptions per 100 inhabitants, with a total of almost 88 million active mobile phone accounts in a country with 54.5 million (116). SMS is a common method of communication in South Africa with high mobile phone ownership combined with high literacy rates (117). Therefore, SMS is an essential tool when it comes to South African mHealth interventions, at least until smartphones become as common as non-smartphones.

1.4 MATERNAL AND NEWBORN HEALTH

1.4.1 Antenatal care

Attendance to professional maternal and infant health services during pregnancy (ANC) and postnatal follow-up (PNC), including maternal and infant vaccinations, are key factors contributing to a healthy pregnancy, delivery and child (118,119). Together, ANC, PNC and infant vaccinations constitute the core of the maternal, neonatal, and infant health continuum of care (120), along with delivery with a skilled birth attendant (121). ANC visits allow medical professionals to identify health problems related to the pregnancy (122). Lassie et al. (123) note that "groups [that] have more antenatal-care visits have lower maternal, foetal, and neonatal morbidity and mortality than those who have fewer antenatal-care visits" (p. 8). The WHO currently recommends a minimum of four visits for all pregnancies (124).

1.4.2 Postnatal care

Visits to health care professionals during the postnatal period allows health care workers to provide both preventative and curative care such as detecting and identifying potential health

challenges, while offering prophylactic vaccines on a regular schedule and extra support, such as HIV testing for HIV-exposed infants, when necessary (120).

Starting with the introduction of the smallpox vaccine in 1796, vaccines have revolutionised global public health. The 2016 WHO Expanded Programme on Immunization (EPI) guidelines recommend infant immunization start within 24 hours of birth and continue along a planned schedule until all recommended doses are received (125). Globally, EPI programmes have been successful and immunization rates in the first year of life are high; rates for DTP (diphtheria, tetanus and pertussis) and polio immunization stood at 86% in 2014, with measles and Hepatitis B coverage at 85% and 83% respectively (126). In South Africa, although official (NDoH) rates are generally quite high, WHO estimates are generally lower; the official DTP1 coverage rate is 85% and estimated to be 74% by the WHO, the official measles (MCV1) coverage rate of 81% is estimated to be 60%, and the official Hepatitis B (HepB3) coverage rate of 84%, is estimated to be 66% (127).

1.4.2.1   Postnatal PMTCT

Early identification of HIV in infants is a key aspect of PMTCT as early diagnosis and access to ART significantly reduces infant HIV-related morbidity and mortality (128–130). Approximately 30-40% of MTCT HIV infections occur during the breastfeeding period and therefore ART adherence and exclusive breastfeeding are important (131,132). Infant ARV prophylaxis has also been found to decrease the vertical transmission rate (133). Early infant diagnosis through regular HIV testing to detect and treat HIV-positive infants is also strongly encouraged (68).

1.4.3   Maternal and infant health in South Africa

South Africa did not meet the key child and maternal mortality UN Millennium Development Goals four and five, largely due to the burden of HIV (134). However, infant health figures have been improving since the mid-noughties; after peaking at 61.8 deaths per 1000 live births in 2005 (135), the infant mortality rate has almost halved to 32 per 1000 in 2016 (136). Childhood mortality improved too; between 2004 and 2015, overall under-five mortality decreased from 80 to 41 deaths per 1000 (137). Despite those improvements HIV-related illness was responsible for approximately 42% of South African maternal deaths in 2013 (138).

WHO immunization data on South Africa (126) combined with previous research on EPI coverage in South Africa (139), reported measles outbreaks (140), and articles highlighting poor treatment of maternal health patients (141) highlight that ANC and PNC is not being utilised optimally in South Africa.

1.4.3.1   PMTCT in South Africa

PMTCT protocols in South Africa have changed a number of times since 2003 when treatment was first offered to HIV-infected pregnant women and their infants (142) due to advances in medication regimens. By 2008 the vertical transmission rate was approximately 12% and in that year AZT and NVP were provided from the 28th week of pregnancy with NVP given

during labour, NVP syrup for the infant within 72 hours after birth and lifelong ART provided to women with a CD4 count of 200 cells/mm3 or lower and or WHO clinical stage 4 disease (142). In 2010, coverage of AZT for pregnant mothers in South Africa was estimated to be over 95% (104) and the PMTCT protocol evolved to WHO PMTCT Option A; AZT from 14 weeks of pregnancy for women with CD4 counts higher than 350 cells/mm3 with NVP and ART in labour, combination treatment for women with CD4 counts of 350 cells/mm3 or lower (143). WHO PMTCT Option B was introduced in 2012, followed by B+ in 2015, and in 2016 vertical HIV transmission was estimated to be 4% (144).

While ART access has contributed to decreasing vertical HIV transmission from mother to child to 2.8% in 2011 (145) and to 1.6% in 2014 (134), there are still many service gaps and missed opportunities throughout the country (146,147). These unresolved issues, combined with the maternal healthcare issues described above shows there is room for improvement along the maternal and infant health continuum in South Africa's public healthcare system.

1.5 RESEARCH OVERVIEW

1.5.1 MAMA SMS 'Pilot'

The implementation of MAMA SMS was planned prior to the current study. Funding for the project was secured in 2011 from the United National Foundation, BabyCentre, Johnson & Johnson, and the mHealth Alliance. Planning was done in early 2012, which included an FGD with potential MAMA SMS users to investigate acceptance of the name, the use of PMTCT messaging, and content writing level.

MAMA SMS was first offered in one health facility in early July 2012 as a pilot. Between 2012 and 2013 early recruitment challenges were identified and remedied and additional facilities were added while a detailed RCT-based research plan to evaluate the effectiveness of MAMA SMS was developed. Throughout this period the implementation/study team conducted operations research procedures as part of routine project monitoring and evaluation. As rollout began, the MAMA SMS team was in regular communication with the NDoH as part of regular participating in the Department's National Maternal and Child mHealth Task Team meetings discussing potential transfer of this program to the national government.

The RCT research plan was accepted by the University of Witwatersrand Human Research Ethics Committee in January 2014 and this author joined the Karolinska Institutet's PhD programme in March. In April 2014, the South African NDoH publicly announced MomConnect, based on MAMA SMS, would be launched country-wide in August 2014, replacing MAMA SMS. This timeline resulted in the need to significantly modify the planned evaluation study of MAMA SMS given the fact that that even if the RCT started recruiting immediately, there would be insufficient time to recruit the required number of participants identified in the sample size calculations. In addition, changing the target participant base to MomConnect enroulees was not possible due to a request by the NDoH that all health facilities offering ANC services across the country start to offer MomConnect concurrently, eliminating the possibility of an RCT-based study with a control arm.

1.5.2 Changes to research plan

The study team re-evaluated the situation and analysed the options available to move forward with research while simultaneously ensuring that high quality and relevant outcomes resulted. Based on this goal, the study team modified the study plan to instead use the 'pilot' MAMA SMS users as intervention participants, and retrospectively identify other mother-infant-pairs who received ANC & PNC care at the same time at other healthcare facilities to act as controls (sub-studies I & II). During the research plan re-evaluation, funding was identified to add a health economist to support an economic evaluation of the MAMA SMS data (sub-study III). Furthermore, focus group discussion (FGD) transcripts from FGDs conducted as part of the pilot were available to add to the quantitative sub-studies (sub-study IV). The last piece of the research plan was added in 2015, after early results from sub-study I & II were shared with the NDoH. Upon review of the results, the NDoH formally requested a study of MomConnect users using the same methods and outcome measures as sub-study I, resulting in sub-study V.

1.6 AIM OF THESIS

1.6.1 General aim

To evaluate the effectiveness of the MAMA SMS intervention from health care utilisation, cost effectiveness and user perspectives, in order to add to the scientific body of evidence of maternal mHealth.

1.6.2 Specific aims of each sub-study

1. To determine the effectiveness of a mobile phone-based maternal health SMS-based intervention, MAMA SMS versus a control arm, in increasing attendance to maternal, neonatal and child health (MNCH) services by women (HIV-infected and who are non-HIV infected) and their infants (Sub-study I).
2. To determine the effectiveness of MAMA SMS versus a control arm in improving infant and maternal health indicators in HIV-positive women (Sub-study II).
3. To conduct a cost effectiveness analysis of implementing and scaling up an SMS-based mobile phone intervention of maternal and new-born health messages to inform sustainability discussions for the South African NDoH and other maternal mHealth project implementers (Sub-study III).
4. To investigate experiences of male and female MAMA SMS participants through focus group discussions in order to identify and understand factors that can lead to its impact (Sub-study IV).
5. To determine the effectiveness of the newer MomConnect SMS-based mobile phone intervention of maternal and new-born health messages versus a control arm (Sub-study V).

2   METHODS

2.1   STUDY SETTING

2.1.1   Socio-economic setting

Gauteng province is located in the north-centre of the country, is the smallest of South Africa's nine provinces at just over 18,000 km^2 and has the largest population with approximately 14 million inhabitants (149). Gauteng contributes one third of South Africa's GDP, with a GDP per capita of R80,486 in 2014 ($7541 in 2014 USD); almost 50% more than the national per capita GDP (150).

Figure 1: Location of the city of Johannesburg (red) in relation to Gauteng province (light yellow) and South Africa (tan). (Image Source: Wikipedia Commons)

The research for was conducted in public sector hospitals and clinics in Hillbrow, part of the inner-city of Johannesburg within Gauteng province, South Africa. Hillbrow is a densely populated inner-city urban area with high levels of immigration, poverty, under- and unemployment, alcohol abuse, gender violence and sex work (113,148).

Despite Gauteng province having the largest GDP per capita, income is not evenly distributed while the average annual income per household was R57,500 in 2011 ($8,550 in 2011 USD) (151). A more precise review of the data shows that 54% of households have a total annual income of under R40,000 ($5,947 in 2011 USD).
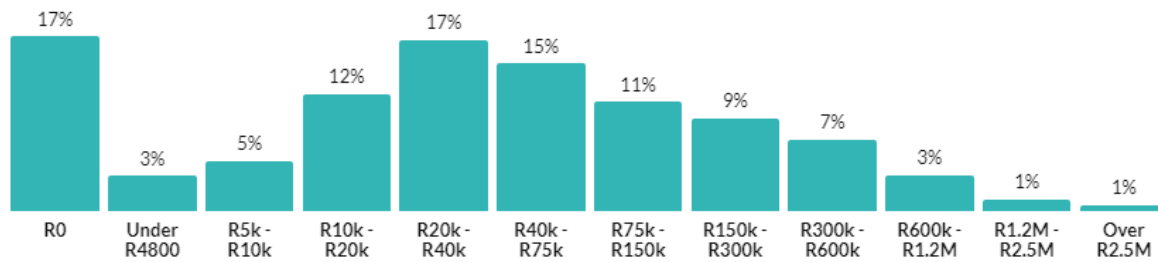
Annual household income

Figure 2: Categorised average annual household income (2011 data)
(Source: South African Census 2011. Image credit: WaziMaps.co.za)

2.1.1.1 Immigration

As an economic powerhouse within the Southern Africa region, South Africa has seen a number of immigrants from neighbouring countries. The 2011 census showed that 4.2% of the population, or 2.2 million individuals were born outside of South Africa, with over 70% of those born in other African countries (151). In 2008 there were a number of xenophobic attacks on migrants, highlighting the relative deprivation felt by many South Africans and a sense of nationalism and blaming others for their circumstances (152). Violence against African immigrants occurred again in 2013 and 2015 (153). Gauteng province has the largest percentage of population born outside of South Africa which was 6% in 2016 (154).

2.1.1.2 Phone ownership & internet access

In 2016, 98.4% of households in Gauteng owned a mobile phone while less than 15% of households had internet access at home (155).

2.1.2 Inner-city Johannesburg

2.1.2.1 Health care system overview

In Johannesburg's Health Region F public health care system there are 16 primary health care facilities (clinics) run by the city, a community health centre and a specialised maternity centre both also run by the city, and a tertiary hospital, run by the province of Gauteng. One of the largest ART treatment sites in South Africa is based in Hillbrow (148). Public sector health resources in the area are chronically under-resourced and in high demand.

2.1.2.2 HIV rates, risk factors & care

HIV prevalence in the City of Johannesburg was estimated to be 11% in 2012 (111), with antenatal HIV prevalence estimated to be 29.6% (156). HIV-related risk factors include the aforementioned high levels of alcohol abuse, violence, sex work, migration in an overcrowded urban environment with significant poverty (148,157). Together, the high HIV rates and multitude of risk factors result in a complex situation given the ongoing stigma associated with HIV which has resulted in unique methods to respond to the ongoing challenges of providing care to underserved populations, such as immigrants (158).

2.1.2.3   Reproductive health

All public sector health clinics in the region offer ANC and PNC services, most provide family planning services, and there are two delivery sites; the specialised maternity centre (Shandukani Maternity Centre) and the tertiary hospital (Charlotte Maxeke General Hospital). Reproductive health services are offered as a first-come-first-serve basis and are often in high demand and chronically understaffed, resulting in significant wait times for patients. Antenatal care is generally quite high, at approximately 90%, which is lower than the national average which is 95% (156). The lower than national rate could be partly due to ANC first visits (new pregnancy confirmation) are usually limited in number per day, meaning women can, and are, regularly turned away if they do not arrive to the health care facility sufficiently early, often hours before operating hours (141).

2.2   MAMA OPERATIONS RESEARCH

MAMA SMS was in operation from 2 July 2012 until 21 August 2014, when MomConnect was launched. It was initially offered in one health care facility with ANC and PNC/EPI services, and was scaled up to six facilities over its lifespan. While the MAMA program was active, there was a large focus on operations research which included detailed face-to-face interviews which collected sociodemographic information, costing data, quality of health data and permission to access health records of MAMA users. This data was used to both improve the MAMA project and prepare for the RCT that was planned at the time.

2.3   SUB-STUDIES OVERVIEW

Table 1: Overview of sub-studies.

Sub-study	Design & population	Research question(s)	Timeline of Data Collection	Methods
I	Cluster observational study Intervention (n=87) vs control (n=90)	Is the MAMA SMS intervention an effective strategy to increase rates of ANC attendance, EPI coverage, and comprehensive maternal, neonatal and infant care, among mother-infant pairs?	June 2012 - May 2015	Study participants recruited at healthcare facilities during ANC visit; half of facilities offered SMS intervention to participants. All participants invited to in-person interviews one year postnatal. Clinical data recorded from ANC card and infant Road-to-Health booklet.
II	Retrospective cohort study Intervention (n=235) vs	Is the MAMA SMS intervention an effective strategy for improving retention-in-ANC, increasing postnatal infant HIV	April 2013 - April 2015	Study participants recruited at healthcare facilities during ANC visit; all HIV positive; intervention participants received SMS intervention. Demographic data collected

	control (n=586)	testing and improving birth outcomes for HIV-positive women, and their infants?		during in-person interview and from clinical database. Clinical data recorded from clinical database.
III	Economic Evaluation modelling incremental cost effectiveness based on results of sub-study I and projecting forward using a five year analytic time horizon.	Based on the MAMA SMS implementation, would it be cost effective to expand this programme throughout Gauteng Province?	June 2011 - August 2014	Using outcomes from sub-study I and MAMA SMS, data was modelled outwards on a five-year time horizon. Programmatic, health facility and user costing data was collected from programme partners, health facilities and users, and compared between intervention and control cohorts. Incremental changes in service utilisation were entered into the Lives Saved Tool to forecast lives saved and DALYs averted by scaling intervention across the province over 5 years.
IV	Focus Group Discussions 3 Female groups (n=15) 1 male group (n=3)	What are the factors that led to the impact of the MAMA project? What feedback do female and male MAMA users participants have about the programme?	October 2013 - October 2014	Four focus group discussions sixty to ninety minutes in length were held with MAMA SMS recipients in English using a guide. FGDs were transcribed and entered into Dedoose qualitative data analysis software, themes were identified and coded for analysis.
V	Cohort study Intervention (n=115) vs control (n=37)	Is MomConnect an effective strategy to increase utilisation of maternal health care services, among mother-infant pairs?	September 2014 - December 2016	Intervention participants received SMS intervention. Study participants identified through intervention recipient database and ANC delivery cards at delivery facility. All participants invited to in-person interviews one year postnatal. Clinical data recorded from ANC card and infant Road-to-Health booklet.

2.4 SUB-STUDY METHODOLOGY
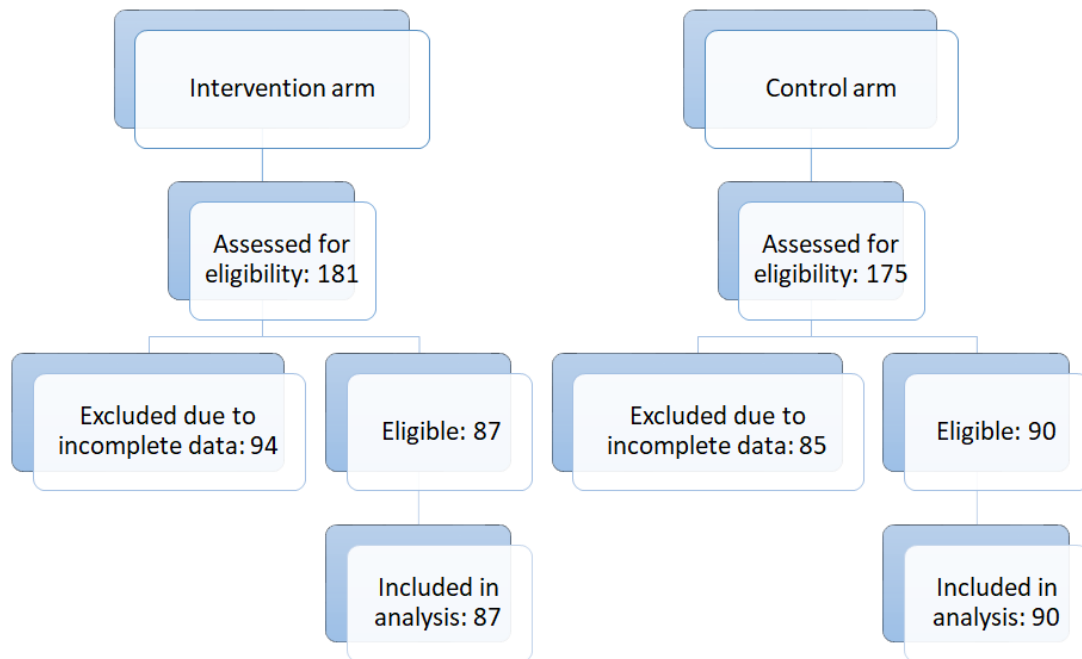
2.4.1 Sub-study I

Figure 3: Sub-study I participant flow chart

Sub-study 1 was a cluster observational trial of mother and infant pairs attending public health care services in inner-city Johannesburg, South Africa. Intervention participants were identified from a list of women who joined MAMA SMS during their pregnancy while control participants were recruited while receiving PNC at participating health facilities. Individuals were eligible if they were over the age of 18, received ANC and PNC care at participating facilities between June 2012 and June 2014, delivered at one of two participating delivery sites, had regular access to a mobile phone and would attend an in-person study interview. The primary outcome was receiving 'comprehensive care' by completing the maternal-and-infant continuum of care. Comprehensive care was defined as attending all NDoH recommended MNCH care from pregnancy until the infant was one year of age which was a binary variable including attending four or more ANC visits and receiving all infant vaccinations. Secondary outcomes included proportion of participants who attended at least two, three, four and five ANC visits, mean number of ANC visits attended, and mean vaccination coverage.

Standard of care: The standard of care offered for maternal and infant care in the provincially-run ANC/PNC sites included testing and retesting for HIV, diabetes and anaemia as per national protocol, provision of vitamin and mineral supplements, recommendations to attend at least four ANC visits before delivery, encouragement to deliver at a health facility, and attend all five PNC/EPI visits. An ANC card was provided to patients who were responsible for bringing it to each ANC visit and delivery. A Road to Health (RTH) booklet was provided to them at the delivery site which they were instructed to bring to each PNC/EPI visit.

Intervention: Intervention participants received the standard of care, plus the intervention which consisted of free twice-weekly one-way maternal health SMSs sent throughout pregnancy and for one year postnatal. The SMSs contained supportive and informative information timed to the stage of pregnancy and age of the child. Content for the message was created as part of the MAMA South Africa project (159) by a team of local maternal and infant health professionals. A range of maternal and infant health topics were included, such as healthy eating, psycho-social support, reminders of ANC/EPI/PNC appointments, HIV-related information and delivery planning.

Sub-study procedures: All participants attended an in-person interview where socio-demographic data were collected and they provided their infants Road to Health (RTH) booklets containing ANC history. ANC attendance data were collected from clinical ANC records and EPI coverage data were collected from infant RTH booklets. All study data were digitised and stored using Research Electronic Data Capture (REDCap), hosted at the University of Witwatersrand. REDCap is a secure, web-based application designed to support data capture for research studies (160). Data analysis was conducted using STATA version 14.0 (161) using an export from the REDCap database.

Sample Size: No reliable local baseline data for complete EPI coverage at one year of age could be identified to calculate sample size. Study team therefore used 2013 WHO data on South Africa's measles vaccination coverage rate at one year of age, which was 66%, as a proxy baseline (162). To identify an increase in coverage from 66% to 86%, the minimum required for herd immunity from most childhood vaccines (163), at 80% power and 95% confidence, a sample size of 71 individuals per arm was identified.

2.4.2 Sub-study II

Sub-study II was a retrospective cohort study of HIV-positive women receiving maternal health care in inner-city Johannesburg, South Africa. Individuals were eligible to participate if they were over the age of 18, attended their first ANC visit between 1 April 2013 and 18 August 2014, received ANC and PNC care at participating ANC/PNC facilities, delivered at a local health facility site, had regular access to a mobile phone and their ANC card and delivery records could be identified at the delivery site. The study population consisted of a sample of individuals included in sub-study I, plus additional individuals identified by the study team. The primary outcome was uptake of HIV PCR testing within six weeks postpartum. Secondary outcomes included the total number of ANC visits attended; the likelihood of attending, at least, four ANC visits; the proportion of normal vaginal deliveries and proportion of new-borns with low birth weight.

Standard of care: The standard of care was similar to sub-study I, with the addition of PMTCT support from healthcare workers and a recommendation to attend infant PCR testing at 6-weeks postnatal
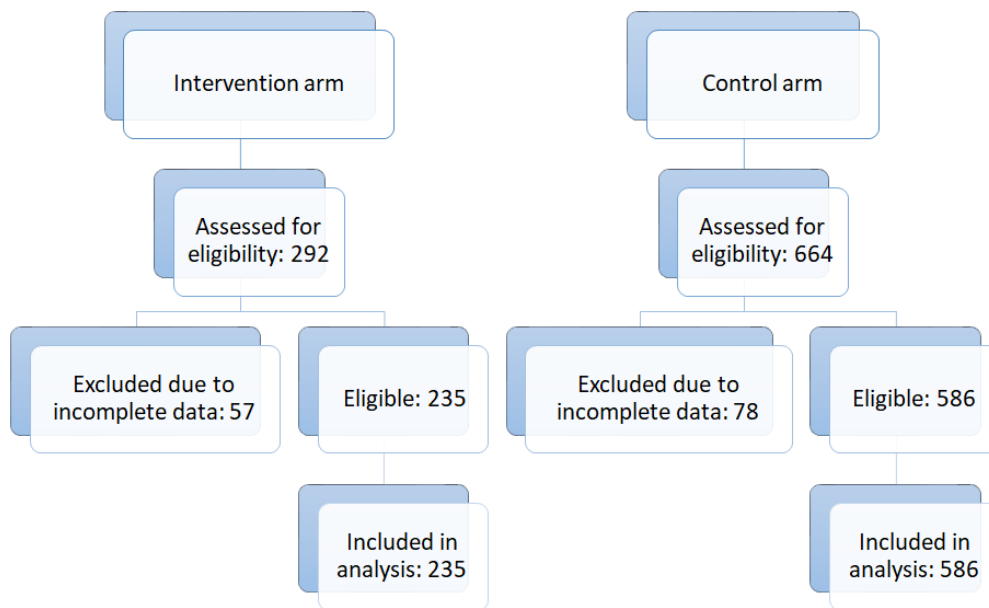
Figure 4: Sub-study II participant flow diagram

Intervention: The intervention was the same as sub-study I with additional PMTCT-related messages for individuals that requested them. The PMTCT SMSs replaced approximately 20 general support SMSs but were not mandatory due to HIV-related stigma and disclosure issues.

Sub-study procedures: HIV positive individuals were identified through a record review at the delivery sites by the study team. These individuals were contacted by telephone to invite them to participate in the study and upon their acceptance, participant data was recorded from the ANC cards and delivery reports. 6-week PCR testing data was collected from the delivery site PCR testing database. All data was entered into REDCap for centralisation (as described in section 2.4.1) and exported to SPSS version 22 (164) for analysis.

Sample size: To see an increase attendance to the 6-week PCR testing from the baseline of 67% to the facility's target of 75%, with 90% power and 95% confidence, sample size calculations indicated that a sample size of 504 individuals per study group was required.

2.4.3 Sub-study III

Sub-study III was an economic evaluation of MAMA SMS using data from the first two years of MAMA SMS implementation, the outcomes from sub-study I, and modelling that data outwards on a five-year time horizon. Modelling was based on the average rate of expansion during the MAMA SMS pilot project, found to be approximately 7% per month.

Perspective: Sub-study III used a societal perspective which included MAMA SMS user time and costs, health care system time and costs, plus programme implementation costs.
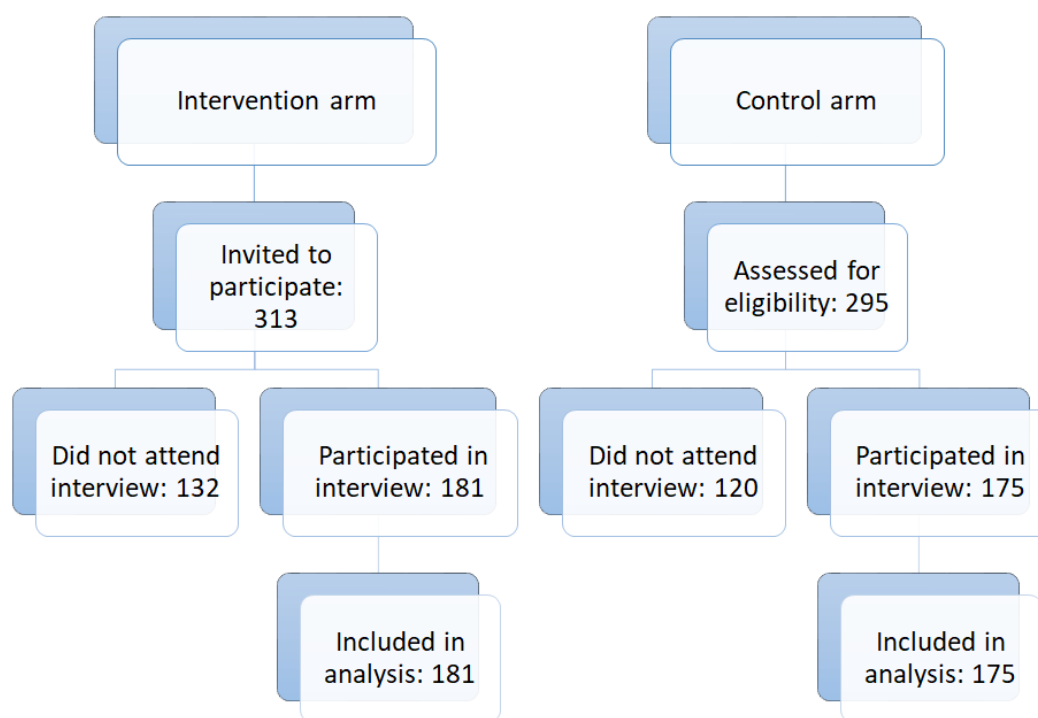
Figure 5: Sub-study III participant costing data flow chart

Data sources: The study team created three data collection tools, based on previous economic evaluation studies. These tools consisted of 1. a MAMA SMS user costs incurred survey which covered costs associated to owning a mobile phone, amount of time and money spent travelling to and from each clinic visit, amount of time spent at the clinic per visit, cost of wages lost to attend clinic visits, amount of money spent on child care per clinic visit, and number of unplanned health care visits attended for maternal or child health care. 2. Health care system costs, including amount and cost of each consumable used at each planned ANC and PNC/EPI visit, and amount and cost of health care worker time spent per planned health care visit. 3. Programmatic costs for the three MAMA SMS implementing partners, including planning, initiation and rollout costs for each organisation including human resources, facilities and technology (SMS sending) costs. Additionally, the WHO Quality of Life-BREF (165), a standardised quality of life survey tool was used to measure health-related quality of life of participants.

Sub-study procedures: A sample of MAMA SMS users were interviewed and completed the user costing tool, health care workers providing ANC and PNC services completed the health care systems costs tool, health care staff costs were collected from an online database of South African health care worker wages. Incremental changes in utilization from sub-study I were inputted into the Lives Saved Tool (LiST), a tool used to model the impact of scaling-up health-related interventions used to reduce maternal, neonatal and child mortality, (166) to forecast lives saved and DALYs averted of gradually scaling up program activities to reach 60% of pregnant women across Gauteng province within 5 years. Uncertainty was characterized using one way and probabilistic uncertainty analyses.

2.4.4 Sub-study IV

Table 2: Focus group discussion participant overview

FGD	Gender of participants	Number of participants	Age Range
1	Female	5	20-36
2	Female	4	28-35
3	Female	6	21-36
4	Male	3	22-32

Sub-study IV consisted of focus group discussions (FGDs) with users of the MAMA SMS service with the aim of identifying factors that led to the impact of the MAMA project and elicit feedback from female and male MAMA users about the service. A purposive sampling method was used to identify participants. Recruitment of females was done at the ANC and PNC clinics on the day of the FGD by identifying women in line if they were MAMA users for at least two months and their child was under one year of age to determine eligibility. Upon confirmation of eligibility they were informed about the FGD and participation fee. Women who expressed interest were then invited to participate that day. Four FGDs were held between October 2013 and October 2014 in Johannesburg's inner-city. Three FGDs were comprised of both pregnant and postnatal females while one included males with children.

Male FGD recruitment was done via telephone a week before the FGD was held. All individuals who had identified as male during the MAMA signup process were contacted and invited to participate in the FGD on the following Saturday. Saturday was selected as it was thought it would increase the chances of employed participants attending. During the telephone call, eligibility was confirmed and the potential participants were informed of the FGD and of the participant reimbursement.

Focus group tools: The FGD guide was created by the study team and used to guide the discussion over a set of topics relevant for the study team. These topics included participant previous experiences of receiving healthcare services in the public and private sectors, their experiences of the MAMA SMS service including signup, message content and frequency, trust in and sharing of messages, acceptability and a discussion of changes in behaviour that might be due to the messages.

Analysis: The FGDs transcripts were analysed and coded using the Framework Method based on codes and categories. Thematic analysis was used identify the overarching themes from the FGDs. The study team then categorised transcript excerpts to identify quotes pertaining to identified topics, themes and sub-themes.
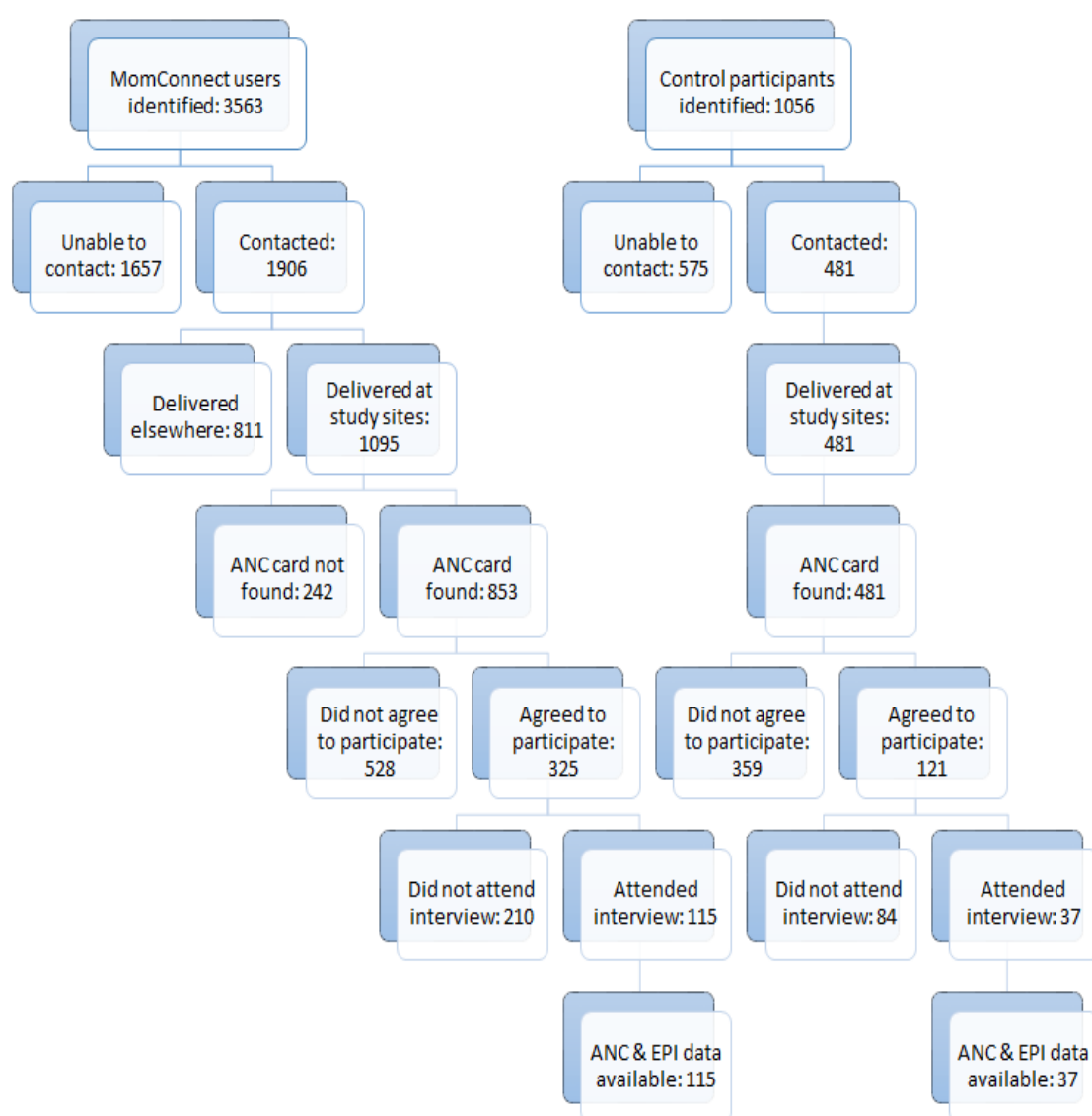
2.4.5 Sub-study V

Figure 6: Sub-study V study recruitment flow chart

Sub-study V was a follow-up to sub-study I, including women who had received MomConnect messages rather than MAMA SMS messages. At the time sub-study V was conducted, MAMA SMS had ended and MomConnect was part of the maternal health standard of care across public sector ANC sites throughout South Africa. Due to the national roll-out of MomConnect, and specifically having no ANC sites not offering MomConnect to act as controls, a number of minor changes to study methodology from sub-study I, were required:

Sub-study V was a retrospective cohort study of mother-infant-pairs who received maternal health care in inner-city Johannesburg. Individuals were eligible to participate if they were over the age of 18 at study recruitment, attended ANC services at one of the public ANC sites in Johannesburg's Health Region F between 1 September 2014 and 1 July 2015, delivered at one of the two delivery sites in the same area, their ANC card could be identified at the delivery site and they agreed to participate in the study.

To identify eligible intervention participants the NDoH provided a list of 3563 MomConnect users who were thought to be pre-eligible based on dates and location of signup. The order of the list was randomised and individuals were contacted one-by-one to identify where they delivered and inform them of the study. Of the MomConnect users identified, 1100 were reached and gave birth in the participating study sites; each of these were invited to participate. When a participant agreed, the ANC card was searched for at the delivery sites and if found, it was entered into the study REDCap database. The participant was called back and invited to attend an in-person interview, similar to the interview that was part of sub-study I.

In aiming to increase comparability between study cohorts, potential control participants were identified during the identification process of intervention ANC cards. The identification of control participants was done based on finding ANC cards of women who were not part of MomConnect. Upon finding the intervention participants ANC card, additional ANC cards were found from women who delivered within five days, did not subscribe to MomConnect (cross checked on the MomConnect database), and attended ANC at the same facility as the intervention participant. These potential control participants were then called and invited to participate in the study and scheduled an in-person interview.

Outcomes: The primary and secondary outcomes were the same as sub-study I.

Standard of care: The standard of care was the same as sub-study I.

Intervention: Intervention participants received the standard of care, plus twice-weekly stage-based MomConnect SMSs throughout their pregnancy and until their child was one year of age. The MomConnect SMSs were based on the MAMA SMSs described above, however there was no set of special HIV-related messages; all women received the same messages (timed to the stage of their pregnancy), some of which were HIV-related messages.

Sub-study procedures: The procedures for this study were the same as sub-study I the only difference being a sample of participants did not provide their RTH booklets, so only their ANC data was included for analysis.

Sample size: Comprehensive coverage in sub-study I control participants was used as a baseline to calculate sample size. To identify the same 56% increase, from 46% to 72% at 90% power and 95% confidence, a sample size of 74 participants were required.

2.5 ETHICS

2.5.1 Ethics training, ethical practice and ethics approval

As Principal Investigator for the study and being affiliated with both Karolinska Institutet and the University of Witwatersrand, completed a Good Clinical Practice (GCP) training programme based on the most recent version of the Declaration of Helsinki (167). Attending GCP training and receiving GCP certification is a requirement of the University of Witwatersrand ethical review board approval process for all study team members. For this reason, all research team members were trained and certified in GCP as well as provided with

additional training and support around completing participant informed consent, ensuring participant privacy and confidentiality, best practice around patient data storage and data quality issues which were important for both the study, but also participants who participated in the sub-studies. These practices ensured that even though ethical permission from the University of Witwatersrand was given and participants provided informed consent, the entire research process was conducted in an ethical manner.

At the time of the study, there was significant stigma around HIV, which remains to this day. To ensure participant privacy and minimise the likelihood of accidental disclosure of HIV status, the study team established a plan. It included analysing the touch-points with study participants and implementing strategies to minimise accidental disclosure during participant recruitment, during the study, and during follow-up. For recruitment, study staff were provided detailed training around patient privacy, recruitment was completed in private, and participants were informed about the message content prior to agreeing to participate. During the study accidental disclosure was minimised by offering two streams of messages, allowing participants to choose how explicit the SMS information would be around HIV-related issues (see section 4.10.1 below for more detail). And during follow-up all study participants who attended FGDs or surveys were informed at multiple points that they were not required to disclose their HIV status to anyone, at any time. There were no known cases of accidental disclosure at any point of the research project.

All sub-studies were approved under University of Witwatersrand Human Research Ethics Committee (Sub-studies I, II, III, & V under clearance certificate: M140984; sub-study IV under clearance certificate: M120649). All participants provided informed consent prior to participation and their identity remains confidential. Study transcripts had personal details of participants removed and confidentiality was maintained during all steps of the research process. Copies of study data has been held on password protected access-limited databases.

3 RESULTS

3.1 MAMA SMS OPERATIONS RESEARCH

MAMA operations research provided information for two groups of users; select basic information from all MAMA SMS recipients, and a more complete demographic profile of a selection of MAMA SMS study participants.

A total of 12,681 individuals signed up to MAMA SMS. Of that, 4,215 individuals or 33.2% were recruited at facility 1, 4,024 individuals, or 31.7% were recruited at facility 2, 1676 or 13.2% at facility 3, 268 or 2.1% at facility 4, 1,133 or 8.9% at facility 5, and 1,365 individuals or 10.8% at facility 6.
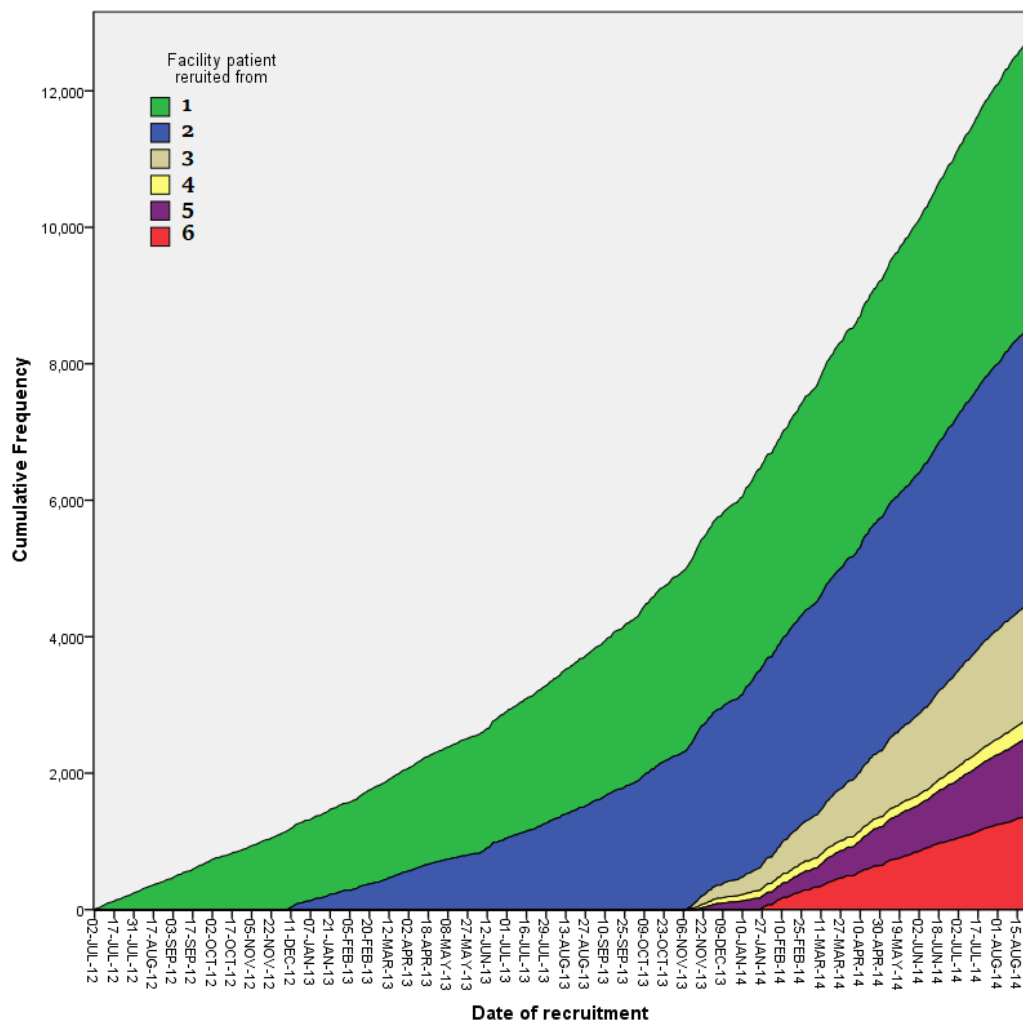

Figure 7: Cumulative recruitment to MAMA SMS by facility from July 2012 through August 2014.

The age range at recruitment was 18 to 52, with an average age of 26.92 years (SD: 5.47 years). There were 68 (0.5%) individuals did not want to share their age.

8,837 (69.7%) individuals provided their average monthly household income at signup. The most common response was under R1000 per month (42.5%, N=3,756) followed by R3000-

R4000 per month (26.2%, N=2,314) and R2000-R3000 per month (10.5%, N=927). The remaining income groups included fewer than 10% of participants.
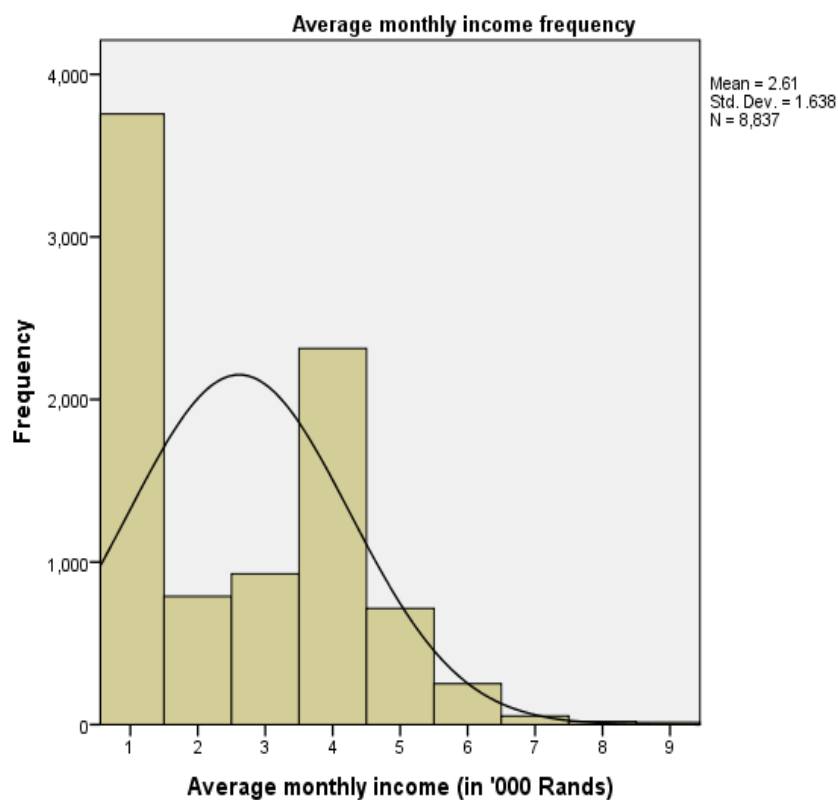

Figure 8: Histogram showing MAMA SMS participant average monthly income.

The number of previous live births was reported by 12,666 (99.9%) of participants with an average of 0.94 (SD=0.922) and a range from 0 to 6.
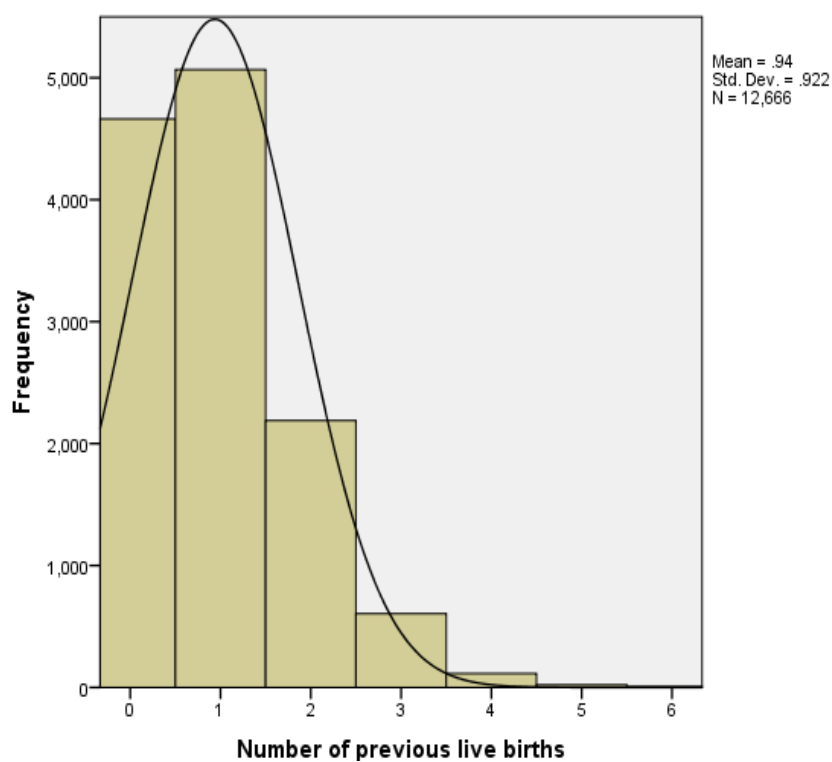

Figure 9: Histogram showing number of previous live births of MAMA SMS participants.

Starting August 2012, participants were asked if they have access to the internet either on their phone or at home/work. Of the 9295 individuals asked, most answered that they did not have access to the internet (60.9%, N=5,660), while 39.1% said they did (N=3,635).
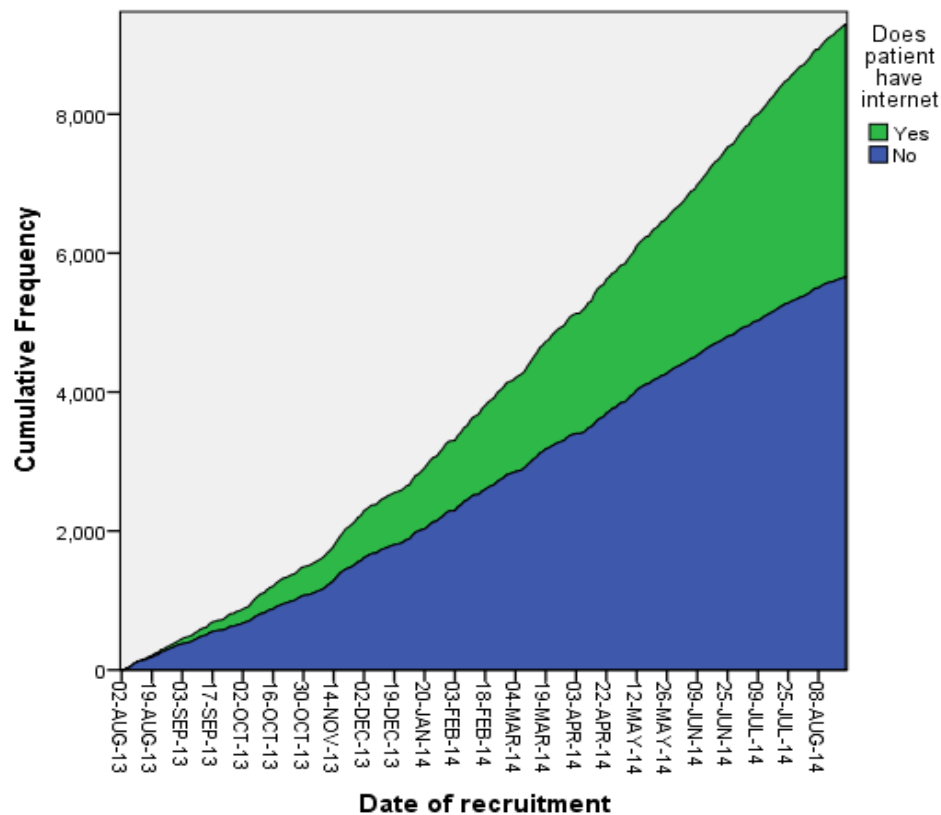

Figure 10: Cumulative frequency by date of response to question "Do you have access to the internet?" by MAMA SMS participants at signup.

As the internet became more ubiquitous and a part of everyday life, internet usage increased. A large change can be seen when comparing the number of people who said "Yes" to having internet during the first three months of the question being asked (27.8%) with the last three months of the project (49.8%).

Participants were not asked their HIV status. They were asked if they would like to receive HIV-related messages. Almost half (44%, N=5,579) of all MAMA SMS participants requested the HIV-related messages at sign up, despite there being an approximate HIV-positivity rate of 30% among pregnant women in the region.

Results from the MAMA face-to-face interviews showed that most were born outside of South Africa (247/431, 57.3%), a majority had completed secondary school (296/432, 68.5%); most were living with a partner (290/425, 68.2%), a majority were employed (237/432, 54.9%), either full time (23.6%), part time (23.8%), or self-employed (7.4%); more than half of women came from households where the average monthly income was under R4,001 per month (233/409, 53.9%).

3.2 PARTICIPANT OVERVIEW

Table 3: Number of intervention and control participant per sub-study.

Sub-study	Number of intervention participants	Number of control participants
I	87	90
II	235	586
III	18	N/A
IV	N/A	N/A
IV	115	121

For the comparative sub-studies (I, II & V) participant demographics were compared across arms to test for homogeneity. Demographic results in sub-study I showed that both arms were homogeneous with the exception of country of birth, with the intervention group having more South African-born participants (intervention: 45% vs control: 29%, p=0.04). In sub-study II control participants were found to have had a higher mean parity (1.16 intervention vs 1.58 control, p<0.001) and more intervention participants attended their first ANC visit prior to 20 weeks gestation (intervention: 36.2% vs control: 19.4%, p<0.001). In sub-study V, the demographic results of both study arms were found to be homogeneous. Demographic heterogeneity, where found in sub-studies I and II, was controlled for during data analysis (see manuscript I and II for details).

3.3 MEDICAL OUTCOMES

Three of the sub-studies (I, II & V) were comparative and investigated at medical outcomes related to mother-infant-pairs.

Table 4: MNCH topics and outcomes included in sub-studies I, II & V.

Topic	Outcome of interest	Sub-study I	Sub-study II	Sub-study V
ANC	Average visits	X	X	X
	Four of more visits	X	X	X
	Five or more visits	X		X
Delivery	Delivery method		X	
	Mean birth weight		X	X
	Low birth weight		X	X
PNC/EPI	Infant age at first HIV test		X	

	EPI coverage at 1 year of age	X		X
"Complete ANC & PNC/EPI coverage"		X		X

3.3.1 ANC

3.3.1.1 Mean ANC visits

Intervention participants in sub-study I were found to average 4.4 ANC visits (95% Confidence Interval: 4.0-4.7), those in sub-study II averaged 5.16 visits (95% CI: 4.71-5.61) and 4.24 visits (95% CI: 4.02-4.63) in sub-study V. This compares to an average of 3.2 visits (95% CI: 2.9-3.5) for control participants in sub-study I, 3.95 visits (95% CI: 3.55-4.35) in sub-study II and 4.32 visits (95% CI: 3.93-4.55) on average in sub-study V. Comparing the results from each study individually showed that the differences in mean ANC visits was statistically significant in sub-study I for the unadjusted data (p<0.001) and adjusted data (p<0.001), and in sub-study II (P<0.001), but not sub-study V (p=0.709).

3.3.1.2 Four or more ANC visits

In sub-study I, 72.4% (63/87 of intervention participants attended at least four ANC visits versus 45.6% (41/90 of control participants (p<0.001). Sub-study II showed 82.2% (60/73) of intervention participants attend at least four ANC visits compared to 58.5% (55/94) of control participants (p<0.001) with a relative risk of 1.4 (95% CI: 1.15-1.72). Outcomes from sub-study V showed intervention and control participants attendance to four or more ANC visits at 67% and 67.7% respectively (77/115 and 82/121, p=0.894).

3.3.1.3 Five or more ANC visits

In sub-study I, 41.4% of intervention participants attended five or more ANC visits compared to 17.8% of control participants (p=0.001). Whereas, in sub-study V, 42.6% of intervention participants attended five or more ANC visits versus 41.3% of control (p=0.841).

3.3.2 Delivery

3.3.2.1 Delivery method

Investigating the method of delivery analysed in sub-study II showed that intervention participants had a statistically significant higher likelihood of a normal vaginal birth (84.2% vs 76.5%, p=0.03) and a lower likelihood of a caesarean section (15.8% vs 22.9%, p=0.039). The relative risk of a vaginal birth by a control participant was 1.10 (95% CI: 1.02-1.19) and of a caesarean section 0.21 (95% CI: 0.15-0.28). A breech birth occurred in 0.7% (3/467) of control participants and no intervention participants (p=0.558).

3.3.2.2 Mean birth weight

Both arms of sub-study's II and V has similar mean birthweights. Intervention participants in sub-study II had a mean of 3.1 kg (Standard deviation (SD): 0.32 kg) while intervention participants had a mean birth weight of 3 kg (SD: 0.47 kg) which was not statistically significant (p=0.188). Both arms of sub-study V had a mean birth weight of 3.07 kg (SD: intervention: 0.47 kg and control: 0.51 kg, p=0.948).

3.3.2.3 Low birth weight

There was a trend of control participants having a higher likelihood of giving birth to a low birth weight infant (<2.5 kg) than intervention participants (1.4% vs 9.9%), but this was not statistically significant (p=0.054). The opposite trend was found in sub-study V with control participants being less likely to give birth to a low birth weight infant than intervention participants (8.3% vs 9.7%) which was also non-significant (p=0.813).

3.3.3 PNC/EPI

3.3.3.1 6 week PCR attendance & mean age of infant at 6-week PCR

Data from sub-study V showed that 81.3% of intervention participants attended their infants 6-week PCR visit on time, compared to 75.4% of control participants who did (p=0.064). Further, there was a trend towards a lower average age of infant at their first PCR test for intervention participants (9.5 weeks, SD: 10.6 weeks) compared to control participants (11.1 weeks, SD: 13.6 weeks) which was not statistically significant (p=0.138).

3.3.3.2 Full EPI coverage

EPI coverage for participants in both arms of sub-study's I and V was similar with intervention arms in both having slightly results. In sub-study I, 95% of intervention participants had complete coverage (95 CI: 91%-100%) compared to 89% of control participants (95% CI: 82%-96%, p=0.110). The results from sub-study V showed that 93.9% of intervention participants had complete EPI coverage compared to 91.7% of control participants (p=0.636).

3.3.4 'Comprehensive care'

The likelihood of receiving comprehensive care in sub-study I was 71% higher among intervention participants compared to control participants (Relative Risk (RR): 1.71, 95% CI: 1.29-2.26). Adjusting for participant country of birth, the relationship continued to be significant (OR = 3.2, 95% CI: 1.63-6.31). No such difference was found in sub-study V; intervention participants were as likely to receive comprehensive care as control participants (RR: 0.87, 95% CI: 0.68-1.11).

3.4 ECONOMIC EVALUATION

Based on actual MAMA SMS expansion, found to be 10% per month, the number of individuals enrolled during years 3, 4 and 5 being 18,419, 57,214, and 179,562 respectively. During year 5, approximately 60% of all pregnant women in Gauteng would be enrolled.

Program cost per user and per case of comprehensive care decreased as the number of individuals enrolled per year increased. In year 1, the cost was approximately $56.65 per user and $84.55 per case of comprehensive care (all costs in USD). By the end of year 5, the cost per user would been $2.27 and $3.39 per case of comprehensive care (see figure 11).
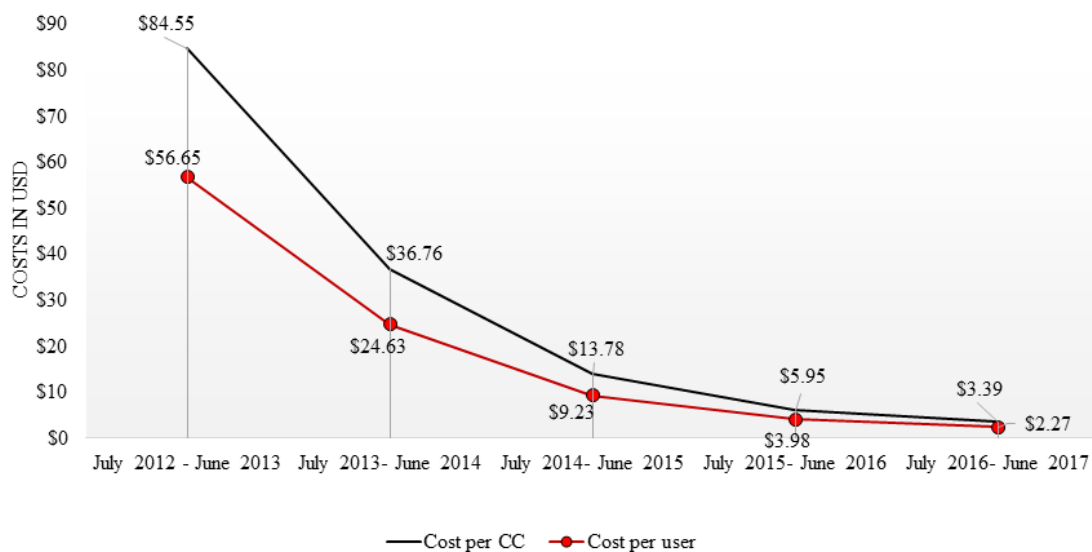

Figure 11: 5-year trends in the total program cost per registered user and per case of comprehensive care (CC) received among MAMA users over 60 months.

Inputting the individual coverage data from sub-study I into LiST, it was estimated that 182 (range of 109 to 199) lives would be saved in year five, in addition to the DALYs averted through expansion of the program.

The implementation cost per user and case of comprehensive care was combined with the forecast lives saved and DALYs averted during project scale up and 1000 bootstrap with replacement were run resulting in the following cost effectiveness plane.
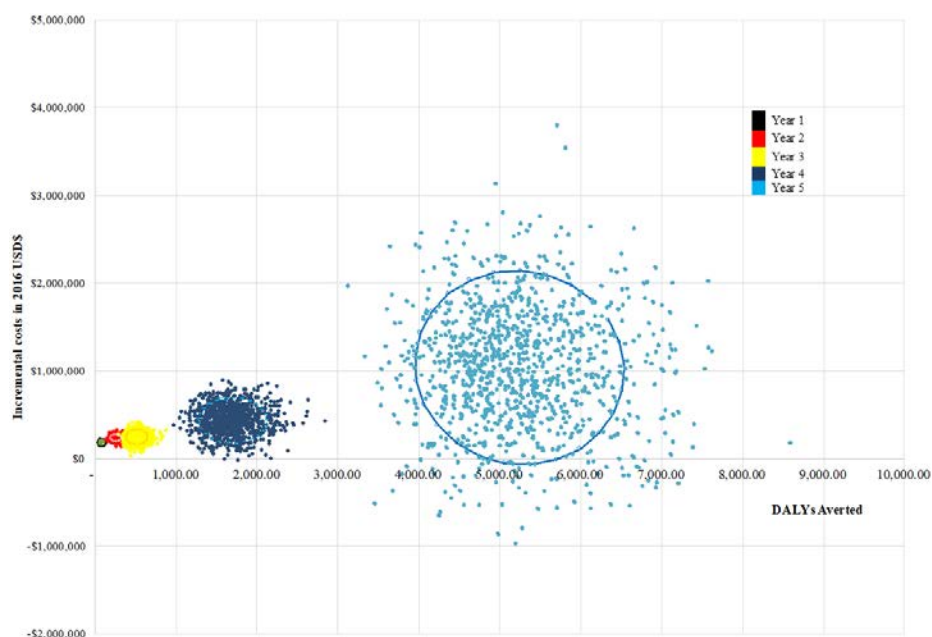

Figure 12: Cost effectiveness plane of years 1-5 of MAMA implementation vs. status quo in Gauteng, South Africa. Individual dots represent the incremental costs and incremental DALYs averted for each of 1,000 simulations conducted by year of implementation.

Figure 12 (previous page) shows that incremental cost per DALY averted from a societal perspective fell from $1985 in year one to $200 in year 5.

Figure 13, below, shows that assuming a willingness to pay threshold of $2000 in year 1, there would be a 40% probability of the intervention being cost effective in year 1. Using the same willingness to pay threshold, years 2 to 5 have a 100% probability of being cost effective. Using a lower willingness to pay threshold, the probability of being cost effective ranges from 0% in year 1 to approximately 64% in year 5.
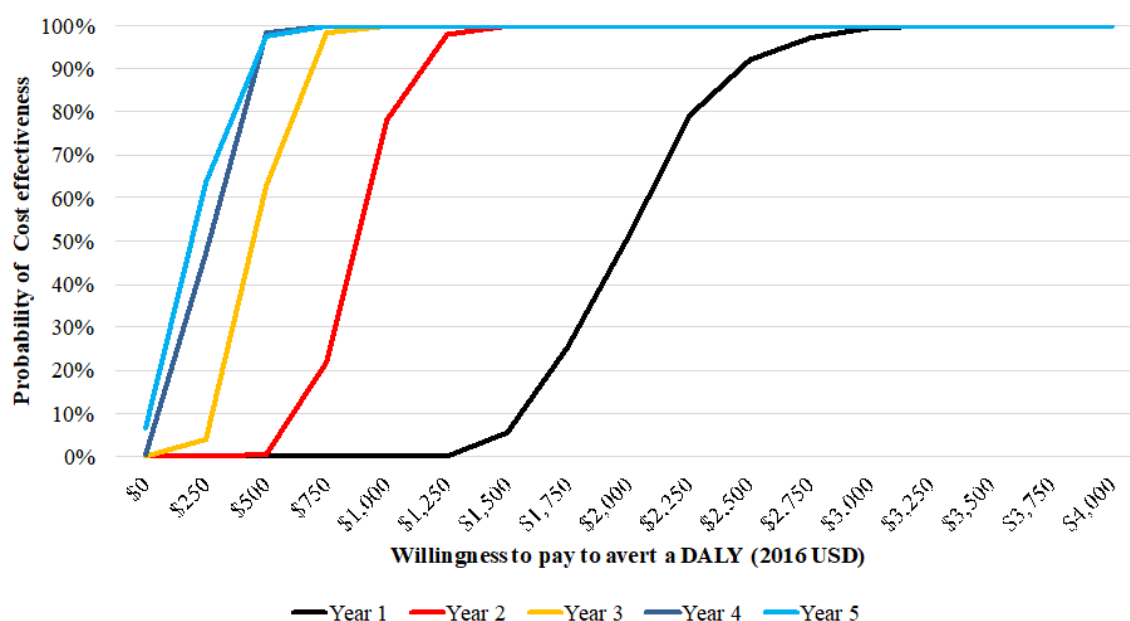

*Figure 13: **Incremental cost effectiveness acceptability curve of years 1-5 of MAMA implementation vs. Status quo in Gauteng, South Africa.** Using the South Africa's GNI per capita for 2015 of US$6,080 as the threshold, program activities have a 100% probability of being cost effective. At lower willingness pay thresholds, the probability of MAMA being cost effective increases over time as the number of users' increases along with anticipated health effects.*

An analysis of participant responses to the WHO Quality of Life-BREF tool showed no statistical difference between intervention and control participant responses among four of the five domains included (Table 5). The exception was the physical domain, where intervention participants had higher ratings than their control peers (intervention: 3.37 vs control: 3.29, p=0.009). No difference was found in the psychological, social relationships, environment or self-evaluation domains.

Table 5: MAMA SMS participant responses to the WHO Quality Of Life-BREF survey tool.

	Arm	Mean response (out of 5)	Std. Dev.	95% CI	p
Physical Domain					
	Intervention (n=433)	3.37	0.381	3.34-3.41	0.009
	Control (n=174)	3.29	0.322	3.24-3.33	

Psychological Domain					
	Intervention	3.71	0.433	3.67-3.75	0.157
	Control	3.66	0.386	3.60-3.71	
Social relationships Domain					
	Intervention	3.92	0.708	3.86-3.99	0.070
	Control	3.81	0.662	3.71-3.91	
Environment Domain					
	Intervention	3.3	0.476	3.25-3.34	0.233
	Control	3.35	0.439	3.28-3.41	
Self-Evaluation Domain					
	Intervention	3.93	0.624	3.87-3.99	0.077
	Control	3.82	0.669	3.73-3.93	

3.5 QUALITATIVE

Four focus groups, segregated by gender, were held. The three women-only FGDs included a total of 15 participants while there was three participants in the male FGD. Many of the same themes and feedback came through at each of the FGD's. Three overarching themes were identified; project context, factors possibly contributing to project success, and feedback on the project.

Contextually, participants mentioned money-related issues regularly, sub-optimal social support, and a variety of experiences of the public health care system. Money issues included having to share their accommodation with other families, not being able to afford the 'perfect' doctors in the private health care system, and how a lack of money can cause marital strife. Thus, the lack of cost associated to registering to MAMA was seen as a strong positive as it did not add to their cost of living. Social support, while often offered, was not always appreciated or was in contradiction to the MAMA messages. However, the male FGD participants mentioned the pride they felt in being able to support their partners. It was discussions about the public health system that provided the strongest reactions at all FGD's. While there were a handful of positive stories (usually around HIV testing and support), the majority were negative. Together, the negative experiences highlighted how the existing health system was not supporting the needs of the patients.

Given the contextual factors, some factors that could have contributed to the health outcomes observed in sub-study's I & II relate to appropriateness of implementation methods. For

example, the registration process was assisted by MAMA staff whose only job was to help with registration. This allowed recruiters to put all their effort in ensuring the registration experience was fruitful and appropriate. An example of the appropriateness was shown by one participants who mentioned they were provided sufficient empathy and privacy with their HIV-positive status. Additionally, the use of SMS was seen as the best communications choice available, and the messages arrived on a reliable schedule. Lastly, the messages were seen as accessible and no participants mentioned having difficulty with understanding them. Asked if they would have preferred another language, all participants agreed that English was best.

Feedback from the project covered three broad categories; relevance of the SMS content, a trust in the content and acceptability of the messages by participants. Participants repeatedly mentioned that messages arrived containing information just was they needed it; for example, explaining how to identify teething and how to deal with it just as a child started teething. Furthermore, participants would mention that their mothers often tried to offer advice on baby care, but rather than follow their advice on the 'old way' of doing things, they would prefer to follow the advice given in the MAMA SMSs. Asked if they appreciated the messages, all participants said they did. Additionally, many participants requested additional messages past their child's first birthday, while some participants appreciated the messages to such an extent that they claimed to be willing to pay for them.

4 DISCUSSION

The research described in this thesis investigated the impact of an SMS-based maternal mHealth intervention in inner-city Johannesburg, South Africa. It explored health outcomes of intervention participants compared to control participants, analysed the results of focus group discussions with users, and conducted a cost-effectiveness analysis modelling a provincial-wide expansion of the intervention over a five-year time horizon using actual data from years one and two.

Results from the research suggest that the MAMA SMS maternal mHealth intervention increased maternal and infant health care uptake, improved some delivery outcomes and showed a trend towards improving others. An assessment of MAMA SMS user focus group discussion feedback identified that individuals were able to differentiate the highly reliable and acceptable MAMA SMS service as being different and separate from the health care system, which was generally seen as providing poor, unfriendly service. Economies of scale allowed by mHealth, meant that the improvements in health outcomes seen by MAMA SMS users would be cost-effective upon scale-up. A follow-up study of users from the government implemented MomConnect program showed that those receiving similar maternal health SMSs had no difference in health outcomes or service uptake compared to non-recipients.

4.1 ANTENATAL OUTCOMES

The observed increase in mean ANC visits, attendance to four or more and five or more ANC visits, among the intervention arms in sub-studies I and II is supported by a number of other maternal mHealth studies conducted in low-resource settings (27,28). In each of these studies, the baseline ANC attendance rate was suboptimal and attendance by intervention participants was increased by a statistically significant amount.

On the contrary, sub-study V showed essentially no difference between study arms when looking at mean ANC visits or four or more ANC visits. Over two-thirds of participants in both arms attended at least four ANC visits and the average number of ANC visits was above four for both arms. Ideally 100% of SMS-recipients would attend four or more ANC visits, but this did not occur. This is similar to some maternal mHealth studies (30,31) that showed no statistically significant increase in attendance to four or more ANC visits however both of the other studies had lower rates in both intervention and control arms, when compared to sub-study V. It is hypothesized that there were health care system improvements at the health care facilities which resulted in an improvement in baseline ANC visits. This is likely the reason that there was a marked improvement in average number of ANC visits among control participants in sub-study V compared to control participants in sub-studies I and II.

4.1.1 Delivery outcomes

Infant birth weight has not been reported in previous mHealth studies. It was included in the current study for two reasons; firstly, due to the specific messaging related to having a healthy and diverse diet during pregnancy, based on feedback from early MAMA participants who

reported that the recommendation to eat a variety of foods and food groups during pregnancy was not previously suggested, and secondly, the study team hypothesised that the pregnancy diet messaging could result in healthier babies at birth, as measured by birth weight, due to the potential preference of inexpensive less nutritious foods of this population.

Results from sub-studies II and V, the two with birth weight data, showed no difference in average birth weight when comparing intervention and control arms. A trend towards fewer low-birthweight infants (<2.5 kg) born to intervention participants was noted in sub-study II (intervention: 1.4% vs control: 9.9%) which was non-significant (p=0.054). In sub-study V, which saw better health outcomes among the control arm for all health outcomes compared to sub-study I, there was no difference in low birthweight infants between study arms.

It appears that the healthy and diverse diet messaging in the MAMA SMSs had an effect in maternal diet. This comes from both the strong trend found in the data, combined with the feedback from MAMA SMS users who stated that the recommendation to have a diverse diet during pregnancy was new information. Much of the feedback received was that women thought that only increases in the quantity of food during pregnancy was important (resulting in increases in consumption of 'pap', an inexpensive and filling coarse maize meal staple) and did not understand the importance of variety and quality.

The trend towards fewer low-birthweight infants is interesting and should be explored in further detail. It is unfortunate that birth weight was only included in sub-studies II and V and not in I as a there is an established link between ANC attendance and low birth weight (168). Furthermore, there is evidence that low birth weight contributes to both infant mortality and childhood morbidity (169). For these reasons, it's recommended that future maternal mHealth research that include interventions around diet should include infant birth weight as an outcome. The original Text4Baby maternal mHealth project that MAMA SMS was based on had planned to evaluate birthweight as an outcome indicator (170), however no published work on birthweight of Text4Baby users is available. In Thailand, an RCT with 68 maternal health participants did not identify differences in birth weight between intervention and control arms, however it was not powered to identify a difference in birth weight (171).

4.2 POSTNATAL OUTCOMES

4.2.1 PCR testing

Data from sub-study II showed a non-significant trend towards intervention participants being more likely to have a PCR test within 6 weeks of birth (intervention: 81.3% vs control: 75.4%, p=0.064). This trend is similar to another South African study (172) which found that an mHealth SMS & voice call service increased infant 10-week PCR increase from 63.3% to 90% (p=<0.001). These studies had two major differences. One, the other study used a combination of SMS and voice contact, compared to the MAMA SMS project which was SMS only. Secondly, the end-points were different, 6 weeks postnatal vs 10 weeks postnatal. This is due to the study sites in the non-MAMA study already having implemented WHO PMTCT Option B+, which recommends 10-week postnatal PCR testing, while the MAMA SMS study site was

still using the previous 6-week postnatal PCR testing recommendation that was adherent to NDoH guidelines at the time, which has since changed to birth and 10-week testing (173).

A MAMA SMS message was sent to women receiving the PMTCT messaging to attend their ANC visits at 6-weeks post-natal. However, in sub-study II, the average age at first PCR testing, in weeks, was much higher for both groups than the government-recommended 6-weeks and statistically similar (intervention: 9.5 weeks vs control: 11.14 weeks, p=0.138). It is notable that the mean age of testing is so close to the current government recommendation of 10-week PCR testing. It is possible that women attending the clinics might have been told by staff to attend PCR testing at 10 weeks post-natal, as per the guidelines that were upcoming but not officially implemented at the time. This could account for the average attendance of PCR visits being so close to 10 weeks postnatal, with the MAMA SMS messaging accounting for the small, non-significant trend towards earlier testing due to the 6-week PCR message that was sent.

4.2.2 PNC/EPI attendance

No significant difference in EPI attendance (defined as attendance to and receiving of a vaccination) was found in either sub-studies I or V. In sub-study I, a trend was noted, but there were too few participants to achieve statistical significance (intervention: 95% vs control: 89%, p=0.110). In sub-study V, the control arm had higher than expected baseline EPI attendance date, resulting in the two study arms having similar outcomes (intervention: 93.9% vs control: 91.7%, p=0.636). Domek (174) also found a non-statistically significant trend towards higher EPI coverage among participants in a mHealth pilot intervention. This contrasts with a similar study in Bangladesh; Uddin (40) found a strong increase in completed EPI coverage in that intervention group. However, the Bangladesh study started with a lower baseline of EPI coverage of under 66% at one year postnatal.

A baseline population level EPI coverage rate of over 90% is usually the goal for most public health programmes as it will result in the necessary herd immunity required for the entire population (163). Therefore in this population, vaccination outcomes are not as significant as the other health outcomes, if the baseline coverage at population level is already above 90%. Given the relatively small study size and high baselines rates of EPI attendance, it is not surprising that the current studies were unable to identify a difference between the study arms in either sub-study.

4.2.3 Complete coverage

Sub-studies I and V both looked at 'complete coverage' of attendance to all government recommended ANC and PNC visits, spanning from conception through to one year postnatal which has not been reported on previously. The results from sub-study I showed statistically significant difference between the two study arms. Data from sub-study V was inconclusive due to the high baseline ANC and EPI attendance rates for control arm participants and missing participant data; no trend was seen based on the data that was available.

Despite there being no previous studies investigating maternal mHealth outcomes from conception until one year post-natal, this will change soon. There is currently an ongoing study in China (175) which is including the same 'complete coverage' outcomes as the current study, which will be a welcome addition to body of evidence.

In situations with relatively high baseline (maternal health) outcomes, it can be difficult to identify slight improvements in individual health indicators due to an intervention. Inclusion of maternal health outcomes over a longer time period and including more individual data points in a composite indicator such as 'complete coverage' for maternal (or other health) mHealth interventions should become more common and be more useful.

4.3 ECONOMIC EVALUATION

Sub-study III showed that based on continued expansion of MAMA SMS and the same health outcomes that were identified in sub-study I, MAMA SMS would be a cost effective intervention as modelled. This is an interesting finding, and surprisingly difficult to compare with other published research. To my knowledge, no other maternal mHealth cost effectiveness research has been published previously, despite calls highlighting its importance (42,176).

A cost-utility analysis looking at mHealth-based tuberculosis infection control in Thailand is likely the closest costing study to sub-study III. In that study (177), patients were sent daily SMSs from community health workers, reminding them to take their medicine. Results from the study showed that the incremental cost-effectiveness ratio (ICER) was US $4270 per disability adjusted life year (DALY) averted. However, the uncertainty ranges were wide, crossed zero, and were no different than the comparator. This contrasts with sub-study III which showed the societal costs per DALY averted was approximately US $1985 in year 1, decreasing to US $200 per DALY averted by year 5 and had much less uncertainty.

Results from analysing the WHO Quality of Life-BREF tool showed that the population generally had the same quality of life score at the end of the study, with the exception of the physical domain, with intervention participants indicating they had less pain, along with more energy and sleep. While it is not possible to know for sure, one hypothesis for this difference is that the intervention participants had healthier children due to the intervention which translated to less psychological stress more and better sleep. On the other hand, the difference could be representative of a statistical anomaly.

Cost-effective analysis are complex and include assumptions. Sub-study III was based on research data from sub-study I which was a retrospective, non-randomised study. At the same time, sub-study III utilised a societal perspective when looking at costs, so all possible costs were included, and the model still showed that the intervention would be cost effective.

4.4 QUALITATIVE OUTCOMES

Feedback from users during the focus group discussions (FGDs) discussed in sub-study IV was generally negative with regards to the health care system, while essentially exclusively positive

in relation to the MAMA SMS intervention. Previous qualitative maternal mHealth studies have also reported that users of mHealth interventions often have preconceived positive notions of the intervention even before they use or interact with it (178,179). Additionally, participants in another maternal mHealth FGD, this time in rural northern Canada, reported that the intervention was both relevant and highly acceptable (180). This 'technology halo' effect can positively influence the impact or effect of a technology-based intervention. For this reason, long term studies of technology-based interventions are essential. Sub-study IV included FGD transcripts from users who had been using the MAMA SMS intervention for at least four months and a maximum of 11 months; possibly not sufficient time for the halo to have worn off.

The trust in the content of the messages by the MAMA SMS participants was the most unexpected aspect of the FGDs. Having many participants report following recommendations and advice in the messages despite receiving contradicting advice from friends, family members, and even their mothers, was a testament to the trust in the intervention. The first time a participant mentioned they followed message advice over family and friends, the study team chalked it up to participants providing a socially desirable response (181). Once multiple participants reported similar stories across focus groups, it gave evidence to the fact that what was being reported was a factual representation of reality. It is hypothesized that the trust in the messages was in part due to the intervention being offered out of a healthcare facility. It is possible that if the intervention had been offered from a random street corner or a for-profit media company it would have been less trusted by the participants (182).

Including men in the FGDs for a maternal mHealth intervention was important in that it has, surprisingly, been described very infrequently (183). This is despite a call for men to be more involved in maternal health generally (184–186). While there was little difference in the responses between the male and female participants, including both is an important aspect of research. Hopefully future maternal mHealth research will include male partners and/or caregivers more frequently.

4.5 CHANGE IN INTERNET ACCESS

MAMA SMS was conducted at an interesting point in time: there was an inflection point of internet adoption in South Africa. When MAMA SMS started, internet usage was limited to early adopters, usually those with the means to pay for internet access at an internet cafe, buy an early smartphone, use an internet enabled device through work, or buy a computer for their home. While less than 30% of respondents claimed to have internet access at the in late 2013, this number increased to just under 50% by mid-2014. It's likely that internet access among the population was lower when MAMA SMS launched in 2012. This increase in internet usage is important to the study. At the start of the study and during the FGDs, SMS was identified as the preferred method of communication because there was no other inexpensive method of personalised information. Increasing internet access, especially by smartphone, results in additional methods of communicating personalised maternal health information and allows for relatively inexpensive two-way communication between patient and health care system.

4.6 MATERNAL HEALTH SMSS AS PART OF BEHAVIOUR CHANGE COMMUNICATION

Behaviour change communication (BCC), using various strategies to change attitudes and in-turn behaviour, is a broad topic that has been a target of public health and other research for decades (187,188). Much has been written about the use of mHealth interventions as BCC throughout the world (21,51,176,189). This section is not meant to be a deep dive into the topic, but rather a note regarding how BCC links to the current research and included sub-studies and show the linkages.

Clinical maternal and child health visits are short and full of new information, especially for individuals pregnant for the first time. When provided an overload of information during a short clinical visit, some of it will be forgotten. Maternal health SMSs, by virtue of being small pieces of relevant information that advises on behaviour that are sent regularly by a trusted source and can be reviewed at any time, can be an important source of knowledge. These short pieces of text corroborate and augment the information provided during clinical visits or other sources. Together, these aspects could change attitudes, leading to positive health outcomes.

4.7 MAMA SMS INCREASED MNCH SERVICE UPTAKE WHEN BASELINE IS LOW

Sub-studies I and II showed that when baseline health outcomes data is sub-optimal, maternal mHealth messages like MAMA can nudge population-level data upwards. In contrast, when baseline health outcomes are within an optimal range it is more difficult to see any kind of change/improvement, as per sub-study V. A maternal mHealth intervention like MAMA SMS or MomConnect is therefore likely to be more cost effective when implemented where there are poorer baseline health outcomes.

What does this mean for national-level maternal mHealth implementations if there are pockets of poor health outcomes amid mostly optimal health outcomes? How about the opposite; pockets of optimal health outcomes amid mostly poor health outcomes? Or, what happens when there are high average levels of MNCH outcomes, but a sizeable population with poor outcomes evenly interspersed throughout the country? These are issues that policy makers must decide; should a maternal mHealth service be only focussed on individuals with poor health outcomes? Is the cost of offering the maternal mHealth service to everyone in the region/province/country justified by the improvements throughout the population even if 80% or 90% (or 95%) of the population is already achieving the optimal levels of MNCH service and outcomes? Some of these issues are discussed below.

4.8 ARE PSYCHO-SOCIAL AND DIFFICULT-TO-MEASURE BENEFITS OF MESSAGES WORTH THE COST?

Qualitative data from the FGDs from sub-study IV show that users had a strong positive psychological connection to message content of the maternal mHealth intervention messages. The messages were able to provide information and psycho-social support to recipients when the health system is overstretched and under resourced. Assuming the same connection to the

messages was also felt by intervention participants in sub-study V, which showed no health outcome improvements in the intervention arm, how does one measure or value the positive connection that participants felt and the unmeasured maternal health knowledge improvement?

One method to investigate further would be to find ways to measure the impact that was not able to be measured in the current research project. Future research could include factors such as health facility visits that were avoided due to the messages. MAMA users had casually reported to the study team multiple times that they did not need to bring their child in to a facility due to the information contained in an SMS that was specifically relevant to an immediate or ongoing child health issue.

4.9 METHODOLOGICAL CONSIDERATIONS

It was a disappointment that the originally planned RCT could not be conducted. However, the subsequent methodological re-evaluation of the study was a tremendous learning experience. While the resulting sub-studies might not have the same rigour, validity and reliability as an RCT, they do benefit from the use of 'real world' data (and all the benefits and drawbacks that entails) (190). The study team did our utmost to ensure the highest levels of rigour, validity and reliability possible. Below is an overview of how this was done.

4.9.1 Quantitative methodological considerations

4.9.1.1 External validity

The populations included are from Hillbrow in inner-city Johannesburg. This population is both relatively heterogeneous and unrepresentative of the South African population in general. The study population was more urban than most of South Africa and had a higher proportion of immigrants. However, the study sample was relatively representative of the general population of South Africa along socio-demographic characteristics, including education, employment, income levels, HIV rates and usage of the public health care system. It was also representative of the Hillbrow population.

In addition, all control and intervention participants were invited to participate in the study after their children were over one year of age. No data, demographic or otherwise, was collected on non-participants. This is unfortunate since the study team has no information about how the individuals who agreed to participate are similar (or different) than those who did not agree to participate. It is of particular interest for sub-studies I, II and V as a large number of invited individuals did not agree to participate, and even a large number of individuals who initially agreed to participate did not attend the in-person interview.

The exact number of individuals offered MAMA SMS but declined was not methodologically recorded, but reports from recruiters suggested approximately 95% (or higher) uptake. The two common reasons for declining MAMA SMSs included not having a phone and already having (a number of) children (with the implicit assumption that having children makes one a maternal and child health expert).

The three sub-studies which used health outcome data (sub-studies I, II & V) included retrospective data of non-randomised participants. Ideally, each of these studies would be conducted prospectively, but this was not possible due to the issues described above (see section 1.5.2) resulting in the need to utilise data that was collected as part of routine data collection procedures within the health care system in the current research project. The resulting lack of prospective, RCT-based study methodology brings with it questions of internal validity. To counter these issues, two methods were used. In sub-study I, there was a randomisation of the intervention at the clinic-level, which goes some way towards improving the methodological issues. In sub-studies I and IV participants were matched by ANC clinic, birth month delivery site. For sub-study V control participants were matched by ANC clinic attended and delivery site.

Conversely, the data were collected in 'real world' situations (190), without the 'aura' or involved preparation processes that prospective studies entail, potentially contaminating results by informing participants of participation in a trial and therefore potentially changing their behaviour even before the intervention is introduced. This does not negate the limitations that comes with the methodology, but provides a benefit that is missing in RCTs (190 Ch. 6).

The study methodologies left a potential for bias in the data for sub-studies I, II and V. To attempt to counter some of the bias, the intervention and control arms were tested for homogeneity. Difference in the population were found in sub-studies I and II which was adjusted for using ANCOVA, with adjusted and unadjusted results reported on. In sub-study V no difference was found between the study arms, which could be due to the small control population size which provided demographic data. Thus, bias could be present in sub-study V, which was noted in the study limitations.

Utilization of data from routinely collected 'real word' retrospective health care records meant that the study team regularly encountered incomplete data. When missing non-clinical data was encountered, it was defined as missing and not included in the data analysis. To ensure that the clinical outcomes were not over-reported, missing clinical data, such as ANC & EPI attendance, was marked as not completed or not done and included in the data analysis. This resulted in a possible under-reporting of actual outcomes, but there was no reason to believe that there was a difference in missing data or under-reporting between study arms.

Since the WHO Quality of Life-BREF tool was administered at only one time point, the end of the study, it is not possible to measure changes in quality of life among participants. Having two time-points, at the start and end of the study, would have allowed the team to add a quality of life outcome, specifically, QALY (quality adjusted life years), to the economic evaluation, adding to its methodological rigour (191,192).

Because the MomConnect intervention was (theoretically) offered to all ANC patients during sub-study V, being able to identify such a large number of non-recipients (n=1056) of the intervention (193) was surprising. The reasons could have been that the intervention was not

offered to everyone at the same time or because of a more problematic reason in that some individuals did not want to receive the intervention, introducing confounding (194). Was there a specific reason why members of the control population chose not to receive the intervention that was not measured and/or identified by the research team?

A further issue with retrospective data collection is the uncontrolled environment of the sub-studies. In sub-studies I, II and V, MAMA SMS and MomConnect users were contacted to participate in the study more than a year after their babies were born. Control participants were also were invited to participate one year after their babies were born and informed the study was relating to maternal health, thus unaware of the MAMA SMS or MomConnect interventions.

4.9.2 Qualitative methodological considerations

Sub-study IV suffered from sample size limitations. Over-all the sample size was on the small side, with 18 total participants; according to Guest et al (195), optimally, there should have been an overall sample size of 25 or more across three FGD's with each subpopulation (male and female). The small population size in the current research meant that the opinions of users was likely not exhaustive. Additionally, with only three men included, the male user perspective is therefore limited. While there were only nine male users in the whole population at the time the focus group was held, it is possible that had more men been included, additional perspectives would have been shared. However, analysis of the male FGD transcripts showed that the three participants had similar views, giving evidence that they reached a saturation point (196) and including additional participants might not have provided additional insight.

Additionally, two of the focus groups (the male FGD and one of the female FGDs) included only three participants, which is small for an FGD. A FGD with fewer than five individuals can result in few people speaking or providing input and/or can 'take over' the FGD resulting in the rest not providing their opinion (197). While the moderator(s) strived to ensure everyone was provided an opportunity to share their opinion (198), there is still a strong potential for bias when the FGD is so small (199). Conversely, small FGD sizes do allow those who are present, especially individuals who might be sky, to provide more input and feedback than they might have in a larger group (200).

4.10 STUDY-RELATED ETHICAL CONSIDERATIONS

4.10.1 Ensuring acceptance by end users

The message content within MAMA SMS was based on a set of SMSs provided by BabyCentre, which is based in the UK (201). The original messages did not include any references to HIV or PMTCT. With high rates of HIV among pregnant women, the MAMA implementation and study teams realised it was morally imperative to include general HIV & PMTCT-specific content in the SMSs (142,202). This was a unique situation as the first set of messages had been provided by BabyCentre, which is based in the UK and did not include any references to HIV or PMTCT. A team of maternal paediatric health clinicians and PMTCT

specialists were selected to create the HIV/PMTCT messaging. Finding a balance of HIV/PMTCT and general (non-HIV) maternal health content was a challenge. To answer the 'how' to support these women, focus group discussions (FGDs) with potential users were held (203). During these FGDs participants requested a stream of HIV content that was different than the general content, while others mentioned they wanted some HIV content in the general messages in case they find out they are HIV positive while receiving the messages. After discussing these ideas further, it became clear that a number of HIV-positive women had not disclosed their status to their partner for fear of violence or having their partner leave them and thus did not want accidental disclosure of their HIV status due to the messages (204–206). This feedback resulted in the project offering two sets of messages; one set containing a significant portion of PMTCT content, geared for HIV-positive women, and another general set of messages that included only a handful of generic PMTCT messages.

4.10.2 Inclusion of males

The messages were created and customised for pregnant women. This made sense at the time they were created since historical patriarchy in South African society meant practically no men attended antenatal care (ANC) or postnatal care (PNC) visits. However, during MAMA's second year, it became clear that a number of men were bringing their infants to postnatal check-ups and showed interest in the MAMA SMS messages. This was a positive surprise for the project team but there was unfortunately no funding at the time to create a new set of messages for men. Not wanting to exclude fathers or limit who received the messages, the MAMA SMS project team decided that any father or other interested person supporting the mother or infant and attending ANC or PNC should be encouraged to sign up to the messages. Additionally, anyone who was not the mother was to be informed that while the messages were made for the mom, they also included useful information for those who were supporting the mother or infant as well.

4.10.3 'Big picture' issues

mHealth in general has another ethical issue; its own success. Should comprehensive maternal mHealth interventions have the desired impact and improve outcomes for women and their children, governments will want to offer them nationally. Due to the relatively low cost (i.e.: under US $4 per person per pregnancy for MAMA SMS) and ease of use and scalability, resources will be put towards these mHealth interventions which are made to supplement existing care. The ethical issue, and my concern, is that once the maternal (or any) mHealth intervention is implemented and improvements are realised, future austerity could result in other, crucial but 'un-sexy', aspects of the healthcare system being cut, leaving the cheaper mHealth intervention. This is a problem as I feel that mHealth should only be meant to be an add-on to health systems that are already in place. This is since very little is known about the continued medium-to-long term impact of mHealth in the face of budgetary cuts in other areas. Unfortunately, this research project is beyond the scope of answering these difficult and complex questions.

5 CONCLUSIONS

The results from this thesis adds to the body of knowledge of maternal mHealth interventions in low-resource settings.

- Maternal mHealth messaging can improve MNCH service uptake both pre- and postnatally when starting from a suboptimal baseline (Sub-studies I & II).
- Maternal mHealth interventions can be cost effective when implemented where MNCH service uptake is suboptimal (Sub-study III).
- Regular SMS-based maternal and infant health information was welcomed and highly valued by MAMA SMS recipients (Sub-study IV).
- There was no evidence that maternal mHealth messaging improves clinical outcomes at a population level when baseline outcomes are already within optimal levels (Sub-study V).

Altogether, this thesis provides evidence that implementing maternal mHealth projects like MAMA SMS and MomConnect can be successful when there is established need and are introduced with local customisation, ongoing evaluation and detailed operations research to measure impact.

6 RECOMMENDATIONS

Insights from this thesis for policy makers at local, national and global levels, researchers, funders, programme developers and implementers are as follows:

1. Costs of implementing maternal mHealth interventions are 'front heavy'; there can be significant up-front costs, but the cost per user decreases significantly as user numbers increase. For this reason, a larger implementation is more likely to achieve cost-effectiveness than a small offering.

2. SMS-based mHealth services can be used to support pregnant women diagnosed or at high risk of hypertension, gestational diabetes, HIV, anaemia, asthma, or other complications to provide customised risk- or diagnosis-specific information regarding minimising risk or identifying danger signs and advise on steps to take if danger signs are found.

3. As internet enabled smartphones increase in ubiquity, additional messaging services become available. WhatsApp or Facebook messenger maternal health message systems are already being created and should be monitored as they have a zero cost-per-message price tag (assuming the end user has access to data on their phone).

Further research is needed to determine if maternal mHealth interventions have similar outcomes in other settings. Specifically, cost effectiveness research of large-scale maternal mHealth interventions is strongly recommended, as are stakeholder research (one-on-one interviews, FGDs, surveys) and regular project/implementation evaluation.

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8 REFERENCES

1. Kay M, Santos J, Takane M. mHealth: New horizons for health through mobile technologies. World Health Organization [Internet]. 2011;3:66–71. Available from: http://www.who.int/entity/ehealth/mhealth_summit.pdf

2. Lewis T, Synowiec C, Lagomarsino G, Schweitzer J. E-health in low- and middle-income countries: findings from the Center for Health Market Innovations. Bull World Health Organ [Internet]. 2012 May 1;90(5):332–40. Available from: http://dx.doi.org/10.2471/BLT.11.099820

3. Grams R. Medical application of vest pocket computers. J Med Syst [Internet]. 1990 Jun;14(3):129–44. Available from: https://www.ncbi.nlm.nih.gov/pubmed/2266328

4. Milch RA, Ziv L, Evans V, Hillebrand M. The effect of an alphanumeric paging system on patient compliance with medicinal regimens. Am J Hosp Palliat Care [Internet]. 1996 May;13(3):46–8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/8716377

5. Chin R. The Internet: another facet to the paradigm shift in healthcare. Singapore Med J [Internet]. 2000 Sep;41(9):426–9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11193114

6. Bauer S, Percevic R, Okon E, Meermann R, Kordy H. Use of text messaging in the aftercare of patients with bulimia nervosa. Eur Eat Disord Rev [Internet]. 2003 May 1;11(3):279–90. Available from: http://dx.doi.org/10.1002/erv.521

7. Franklin V, Waller A, Pagliari C, Greene S. ' Sweet Talk': text messaging support for intensive insulin therapy for young people with diabetes. Diabetes Technol Ther [Internet]. 2003;5(6):991–6. Available from: http://online.liebertpub.com/doi/abs/10.1089/152091503322641042

8. Pal B. Personal views: The doctor will text you now: is there a role for the mobile telephone in health care? BMJ : British Medical Journal [Internet]. 2003 Mar 15 [cited 2017 Feb 11];326(7389):607. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1125508/

9. Norwell N. Text messaging raises medicolegal issues. BMJ: British Medical Journal [Internet]. 2003; Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC514072/

10. Anhøj J, Møldrup C. Feasibility of collecting diary data from asthma patients through mobile phones and SMS (short message service): response rate analysis and focus group evaluation from a pilot study. J Med Internet Res [Internet]. 2004 Dec 2;6(4):e42. Available from: http://dx.doi.org/10.2196/jmir.6.4.e42

11. Bielli E, Carminati F, La Capra S, Lina M, Brunelli C, Tamburini M. A Wireless Health Outcomes Monitoring System (WHOMS): development and field testing with cancer patients using mobile phones. BMC Med Inform Decis Mak [Internet]. 2004 Jun 15;4:7. Available from: http://dx.doi.org/10.1186/1472-6947-4-7

12. Dunbar PJ, Madigan D, Grohskopf LA, Revere D, Woodward J, Minstrell J, et al. A two-way messaging system to enhance antiretroviral adherence. J Am Med Inform Assoc [Internet]. 2003 Jan;10(1):11–5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/12509353

13. Kubota A, Fujita M, Hatano Y. Development and effects of a health promotion program utilizing the mail function of mobile phones. Nihon Koshu Eisei Zasshi [Internet]. 2004;51(10):862–73. Available from: http://europepmc.org/abstract/med/15565995

14. Salvador CH, Pascual Carrasco M, Gonzalez de Mingo MA, Muñoz Carrero A, Márquez Montes J, Sosa Martín L, et al. Airmed-cardio: a GSM and Internet services-based system for out-of-hospital follow-up of cardiac patients. IEEE Trans Inf Technol Biomed [Internet]. 2005 Mar;9(1):73–85. Available from: https://www.ncbi.nlm.nih.gov/pubmed/15787010

15. Ostojic V, Cvoriscec B, Ostojic SB, Reznikoff D, Stipic-Markovic A, Tudjman Z. Improving asthma control through telemedicine: a study of short-message service. Telemed J E Health [Internet]. 2005 Feb;11(1):28–35. Available from: http://dx.doi.org/10.1089/tmj.2005.11.28

16. Márquez CE, de la Figuera von WM, Gil GV, Ylla-Catala A, Figueras M, Balana M, et al. Effectiveness of an intervention to provide information to patients with hypertension as short text messages and reminders sent to their mobile phone (HTA-Alert). Atencion primaria/Sociedad Española de Medicina de Familia y Comunitaria [Internet]. 2004;34(8):399–405. Available from: http://europepmc.org/abstract/med/15546536

17. Downer SR, Meara JG, Da Costa AC. Use of SMS text messaging to improve outpatient attendance. Med J Aust [Internet]. 2005 Oct 3;183(7):366–8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16201955

18. Rodgers A, Corbett T, Bramley D, Riddell T, Wills M, Lin R-B, et al. Do u smoke after txt? Results of a randomised trial of smoking cessation using mobile phone text messaging. Tob Control [Internet]. 2005 Aug;14(4):255–61. Available from: http://dx.doi.org/10.1136/tc.2005.011577

19. Hurling R, Catt M, Boni MD, Fairley BW, Hurst T, Murray P, et al. Using internet and mobile phone technology to deliver an automated physical activity program: randomized controlled trial. J Med Internet Res [Internet]. 2007 Apr 27;9(2):e7. Available from: http://dx.doi.org/10.2196/jmir.9.2.e7

20. Kim H-S. A randomized controlled trial of a nurse short-message service by cellular phone for people with diabetes. Int J Nurs Stud [Internet]. 2007 Jul;44(5):687–92. Available from: http://dx.doi.org/10.1016/j.ijnurstu.2006.01.011

21. Fjeldsoe BS, Marshall AL, Miller YD. Behavior Change Interventions Delivered by Mobile Telephone Short-Message Service. Am J Prev Med [Internet]. 2009 Feb 1;36(2):165–73. Available from: http://dx.doi.org/10.1016/j.amepre.2008.09.040

22. Tomlinson M, Solomon W, Singh Y, Doherty T, Chopra M, Ijumba P, et al. The use of mobile phones as a data collection tool: a report from a household survey in South Africa. BMC Med Inform Decis Mak [Internet]. 2009 Dec 23;9:51. Available from: http://dx.doi.org/10.1186/1472-6947-9-51

23. Chang LW, Kagaayi J, Nakigozi G, Packer AH, Serwadda D, Quinn TC, et al. Responding to the human resource crisis: peer health workers, mobile phones, and HIV care in Rakai, Uganda. AIDS Patient Care STDS [Internet]. 2008 Mar;22(3):173–4. Available from: http://dx.doi.org/10.1089/apc.2007.0234

24. Lester RT, Ritvo P, Mills EJ, Kariri A, Karanja S, Chung MH, et al. Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. Lancet [Internet]. 2010 Nov 27;376(9755):1838–45. Available from: http://dx.doi.org/10.1016/S0140-6736(10)61997-6

25. Pop-Eleches C, Thirumurthy H, Habyarimana JP, Zivin JG, Goldstein MP, de Walque D, et al. Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders. AIDS [Internet]. 2011 Mar 27;25(6):825–34. Available from: http://dx.doi.org/10.1097/QAD.0b013e32834380c1

26. Lund S, Hemed M, Nielsen BB, Said A, Said K, Makungu MH, et al. Mobile phones as a health communication tool to improve skilled attendance at delivery in Zanzibar: a cluster-randomised controlled trial. BJOG [Internet]. 2012 Sep;119(10):1256–64. Available from: http://dx.doi.org/10.1111/j.1471-0528.2012.03413.x

27. Lund S, Nielsen BB, Hemed M, Boas IM, Said A, Said K, et al. Mobile phones improve antenatal care attendance in Zanzibar: a cluster randomized controlled trial. BMC Pregnancy Childbirth [Internet]. 2014 Jan 17;14:29. Available from: http://dx.doi.org/10.1186/1471-2393-14-29

28. Kaewkungwal J, Singhasivanon P, Khamsiriwatchara A, Sawang S, Meankaew P, Wechsart A. Application of smart phone in 'Better Border Healthcare Program': a module for mother and child care. BMC Med Inform Decis Mak [Internet]. 2010 Nov 3;10:69. Available from: http://dx.doi.org/10.1186/1472-6947-10-69

29. Balakrishnan R, Gopichandran V, Chaturvedi S, Chatterjee R, Mahapatra T, Chaudhuri I. Continuum of Care Services for Maternal and Child Health using mobile technology - a health system strengthening strategy in low and middle income countries. BMC Med Inform Decis Mak [Internet]. 2016 Jul 7;16:84. Available from: http://dx.doi.org/10.1186/s12911-016-0326-z

30. Ediau M, Wanyenze RK, Machingaidze S, Otim G, Olwedo A, Iriso R, et al. Trends in antenatal care attendance and health facility delivery following community and health facility systems strengthening interventions in Northern Uganda. BMC Pregnancy Childbirth [Internet]. 2013 Oct 18;13:189. Available from: http://dx.doi.org/10.1186/1471-2393-13-189

31. Mushi D, Mpembeni R, Jahn A. Effectiveness of community based Safe Motherhood promoters in improving the utilization of obstetric care. The case of Mtwara Rural District in Tanzania. BMC Pregnancy Childbirth [Internet]. 2010 Apr 1;10:14. Available from: http://dx.doi.org/10.1186/1471-2393-10-14

32. Whittaker R, Matoff-Stepp S, Meehan J, Kendrick J, Jordan E, Stange P, et al. Text4baby: development and implementation of a national text messaging health information service. Am J Public Health [Internet]. 2012 Dec;102(12):2207–13. Available from: http://dx.doi.org/10.2105/AJPH.2012.300736

33. Evans WD, Wallace Bihm J, Szekely D, Nielsen P, Murray E, Abroms L, et al. Initial outcomes from a 4-week follow-up study of the Text4baby program in the military women's population: randomized controlled trial. J Med Internet Res [Internet]. 2014 May 20;16(5):e131. Available from: http://dx.doi.org/10.2196/jmir.3297

34. Gazmararian JA, Elon L, Yang B, Graham M, Parker R. Text4baby program: an opportunity to reach underserved pregnant and postpartum women? Matern Child Health J [Internet]. 2014 Jan;18(1):223–32. Available from: http://dx.doi.org/10.1007/s10995-013-1258-1

35. Gagnaire K. Goodbye from MAMA [Internet]. [cited 2017 Mar 12]. Available from: http://unfoundationblog.org/goodbye-from-mama/

36. USAID. TRAction Project Final Report. 2016;24. Available from: http://pdf.usaid.gov/pdf_docs/PA00N8D9.pdf

37. Ahsan A, Raihan A. Understanding mHealth impact among Aponjon (MAMA Bangladesh) subscribers through a phone survey in Bangladesh. In: Proceedings of the Sixth International Conference on Information and Communications Technologies and Development: Notes - Volume 2 [Internet]. ACM; 2013 [cited 2017 Mar 12]. p. 1–4. Available from: http://dl.acm.org/citation.cfm?doid=2517899.2517920

38. Barron P, Pillay Y, Fernandes A, Sebidi J, Allen R. The MomConnect mHealth initiative in South Africa: Early impact on the supply side of MCH services. J Public Health Policy [Internet]. 2016 Nov 1 [cited 2017 Feb 13];37(2):201–12. Available from: http://link.springer.com/article/10.1057/s41271-016-0015-2

39. Adanikin AI, Awoleke JO, Adeyiolu A. Role of reminder by text message in enhancing postnatal clinic attendance. Int J Gynaecol Obstet [Internet]. 2014 Aug;126(2):179–80. Available from: http://dx.doi.org/10.1016/j.ijgo.2014.02.009

40. Uddin MJ, Shamsuzzaman M, Horng L, Labrique A, Vasudevan L, Zeller K, et al. Use of mobile phones for improving vaccination coverage among children living in rural hard-to-reach areas and urban streets of Bangladesh. Vaccine [Internet]. 2016 Jan 4;34(2):276–83. Available from: http://dx.doi.org/10.1016/j.vaccine.2015.11.024

41. Sondaal SFV, Browne JL, Amoakoh-Coleman M, Borgstein A, Miltenburg AS, Verwijs M, et al. Assessing the Effect of mHealth Interventions in Improving Maternal and Neonatal Care in Low- and Middle-Income Countries: A Systematic Review. PLoS One [Internet]. 2016 May 4;11(5):e0154664. Available from: http://dx.doi.org/10.1371/journal.pone.0154664

42. Lee SH, Nurmatov UB, Nwaru BI, Mukherjee M, Grant L, Pagliari C. Effectiveness of mHealth interventions for maternal, newborn and child health in low- and middle-income countries: Systematic review and meta-analysis. J Glob Health [Internet]. 2016 Jun;6(1):010401. Available from: http://dx.doi.org/10.7189/jogh.06.010401

43. Watterson JL, Walsh J, Madeka I. Using mHealth to Improve Usage of Antenatal Care, Postnatal Care, and Immunization: A Systematic Review of the Literature. Biomed Res Int [Internet]. 2015 Aug 25;2015:153402. Available from: http://dx.doi.org/10.1155/2015/153402

44. Poorman E, Gazmararian J, Parker RM, Yang B, Elon L. Use of text messaging for maternal and infant health: a systematic review of the literature. Matern Child Health J [Internet]. 2015 May;19(5):969–89. Available from: http://dx.doi.org/10.1007/s10995-014-1595-8

45. Amoakoh-Coleman M, Borgstein AB-J, Sondaal SF, Grobbee DE, Miltenburg AS, Verwijs M, et al. Effectiveness of mHealth Interventions Targeting Health Care Workers to Improve Pregnancy Outcomes in Low- and Middle-Income Countries: A Systematic Review. J Med Internet Res [Internet]. 2016 Aug 19;18(8):e226. Available from: http://dx.doi.org/10.2196/jmir.5533

46. Weinstein MC, Stason WB. Foundations of cost-effectiveness analysis for health and medical practices. N Engl J Med [Internet]. 1977 Mar 31;296(13):716–21. Available from: http://dx.doi.org/10.1056/NEJM197703312961304

47. Muennig P, Bounthavong M. Cost-Effectiveness Analysis in Health: A Practical Approach [Internet]. John Wiley & Sons; 2016. 480 p. Available from: https://market.android.com/details?id=book-P14BCgAAQBAJ

48. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the Economic Evaluation of Health Care Programmes [Internet]. Oxford University Press; 2015. 445 p. Available from: https://market.android.com/details?id=book-lvWACgAAQBAJ

49. Donaldson C, Currie G, Mitton C. Cost effectiveness analysis in health care: contraindications. BMJ [Internet]. 2002 Oct 19;325(7369):891–4. Available from: https://www.ncbi.nlm.nih.gov/pubmed/12386045

50. Schweitzer J, Synowiec C. The economics of eHealth and mHealth. J Health Commun [Internet]. 2012;17 Suppl 1:73–81. Available from: http://dx.doi.org/10.1080/10810730.2011.649158

51. Iribarren SJ, Cato K, Falzon L, Stone PW. What is the economic evidence for mHealth? A systematic review of economic evaluations of mHealth solutions. PLoS One [Internet]. 2017 Feb 2;12(2):e0170581. Available from: http://dx.doi.org/10.1371/journal.pone.0170581

52. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated health economic evaluation reporting standards (CHEERS)—explanation and elaboration: a report of the ISPOR health economic evaluation publication guidelines good reporting practices task force. Value Health [Internet]. 2013;16(2):231–50. Available from: http://www.sciencedirect.com/science/article/pii/S1098301513000223

53. Burn E, Marshall AL, Miller YD, Barnett AG, Fjeldsoe BS, Graves N. The cost-effectiveness of the MobileMums intervention to increase physical activity among mothers with young children: a Markov model informed by a randomised controlled trial. BMJ Open [Internet]. 2015 Apr 29;5(4):e007226. Available from: http://dx.doi.org/10.1136/bmjopen-2014-007226

54. Awiti PO, Grotta A, van der Kop M, Dusabe J, Thorson A, Mwangi J, et al. The effect of an interactive weekly mobile phone messaging on retention in prevention of mother to child transmission (PMTCT) of HIV program: study protocol for a randomized controlled trial (WELTEL PMTCT). BMC Med Inform Decis Mak [Internet]. 2016 Jul 11;16:86. Available from: http://dx.doi.org/10.1186/s12911-016-0321-4

55. Vélez O, Okyere PB, Kanter AS, Bakken S. A usability study of a mobile health application for rural Ghanaian midwives. J Midwifery Womens Health [Internet]. 2014 Mar;59(2):184–91. Available from: http://dx.doi.org/10.1111/jmwh.12071

56. Coomes CM, Lewis MA, Uhrig JD, Furberg RD, Harris JL, Bann CM. Beyond reminders: a conceptual framework for using short message service to promote prevention and improve healthcare quality and clinical outcomes for people living with HIV. AIDS Care [Internet]. 2012;24(3):348–57. Available from: http://dx.doi.org/10.1080/09540121.2011.608421

57. Rodrigues R, Poongulali S, Balaji K, Atkins S, Ashorn P, De Costa A. 'The phone reminder is important, but will others get to know about my illness?' Patient perceptions of an mHealth antiretroviral treatment support intervention in the HIVIND trial in South India. BMJ Open [Internet]. 2015 Nov 2;5(11):e007574. Available from: http://dx.doi.org/10.1136/bmjopen-2015-007574

58. Nachega JB, Skinner D, Jennings L, Magidson JF, Altice FL, Burke JG, et al. Acceptability and feasibility of mHealth and community-based directly observed antiretroviral therapy to prevent mother-to-child HIV transmission in South African pregnant women under Option B+: an exploratory study. Patient Prefer Adherence [Internet]. 2016 Apr 28;10:683–90. Available from: http://dx.doi.org/10.2147/PPA.S100002

59. Jennings L, Ong'ech J, Simiyu R, Sirengo M, Kassaye S. Exploring the use of mobile phone technology for the enhancement of the prevention of mother-to-child transmission of HIV program in Nyanza, Kenya: a qualitative study. BMC Public Health [Internet]. 2013 Dec 5;13:1131. Available from: http://dx.doi.org/10.1186/1471-2458-13-1131

60. Odeny TA, Newman M, Bukusi EA, McClelland RS, Cohen CR, Camlin CS. Developing content for a mHealth intervention to promote postpartum retention in prevention of mother-to-child HIV transmission programs and early infant diagnosis of HIV: a qualitative study. PLoS One [Internet]. 2014 Sep 2;9(9):e106383. Available from: http://dx.doi.org/10.1371/journal.pone.0106383

61. Shet A, Arumugam K, Rodrigues R, Rajagopalan N, Shubha K, Raj T, et al. Designing a mobile phone-based intervention to promote adherence to antiretroviral therapy in South India. AIDS Behav [Internet]. 2010 Jun;14(3):716–20. Available from: http://dx.doi.org/10.1007/s10461-009-9658-3

62. Rothstein JD, Jennings L, Moorthy A, Yang F, Gee L, Romano K, et al. Qualitative Assessment of the Feasibility, Usability, and Acceptability of a Mobile Client Data App for Community-Based Maternal, Neonatal, and Child Care in Rural Ghana. Int J Telemed Appl [Internet]. 2016 Dec 14;2016:2515420. Available from: http://dx.doi.org/10.1155/2016/2515420

63. Tamrat T, Kachnowski S. Special delivery: an analysis of mHealth in maternal and newborn health programs and their outcomes around the world. Matern Child Health J [Internet]. 2012 Jul;16(5):1092–101. Available from: http://dx.doi.org/10.1007/s10995-011-0836-3

64. Geldsetzer P, Yapa HMN, Vaikath M, Ogbuoji O, Fox MP, Essajee SM, et al. A systematic review of interventions to improve postpartum retention of women in PMTCT and ART care. J Int AIDS Soc [Internet]. 2016 Apr 25;19(1):20679. Available from: http://dx.doi.org/10.7448/IAS.19.1.20679

65. World Health Organisation. WHO [Internet]. HIV/AIDS Factsheet. 2016 [cited 2017 Mar 12]. Available from: http://www.who.int/mediacentre/factsheets/fs360/en/

66. Collier AC, Coombs RW, Schoenfeld DA, Bassett RL, Timpone J, Baruch A, et al. Treatment of human immunodeficiency virus infection with saquinavir, zidovudine, and zalcitabine. AIDS Clinical Trials Group. N Engl J Med [Internet]. 1996 Apr 18;334(16):1011–7. Available from: http://dx.doi.org/10.1056/NEJM199604183341602

67. Arts EJ, Hazuda DJ. HIV-1 antiretroviral drug therapy. Cold Spring Harb Perspect Med [Internet]. 2012 Apr;2(4):a007161. Available from: http://dx.doi.org/10.1101/cshperspect.a007161

68. World Health Organization. Guideline on When to Start Antiretroviral Therapy and on Pre-Exposure Prophylaxis for HIV [Internet]. Geneva: World Health Organization; 2015. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26598776

69. UNAIDS. Fact sheet November 2016 [Internet]. 2016 [cited 2017 Feb 7]. Available from: http://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf

70. Kharsany ABM, Karim QA. HIV Infection and AIDS in Sub-Saharan Africa: Current Status, Challenges and Opportunities. Open AIDS J [Internet]. 2016 Apr 8;10:34–48. Available from: http://dx.doi.org/10.2174/1874613601610010034

71. World Health Organisation. Antiretroviral therapy (ART) coverage among all age groups. World Health Organization website http://www who int/gho/hiv/epidemic_response/ART_text/en/(accessed 17 February 2014) [Internet]. 2016; Available from: http://www.who.int/gho/hiv/epidemic_response/ART_text/en/

72. UNAIDS. 2014 Gap Report. http://emtct-iatt. org/2014/07/unaids-2014-gap-report. 2014.

73. Global HIV/AIDS Organizations [Internet]. AIDS.gov. 2012 [cited 2017 Mar 12]. Available from: https://www.aids.gov/federal-resources/around-the-world/global-hiv-aids-organizations/

74. Statistics South Africa. Mid-year population estimates - 2016 [Internet]. 2016. Available from: http://www.statssa.gov.za/publications/P0302/P03022016.pdf

75. South African Department of Health. 2015/2016 Annual Report. 2016 Nov.

76. Navér L, Lindgren S, Belfrage E, Gyllensten K, Lidman K, Gisslén M, et al. Children born to HIV-1-infected women in Sweden in 1982-2003: trends in epidemiology and vertical transmission. J Acquir Immune Defic Syndr [Internet]. 2006 Aug 1;42(4):484–9. Available from: http://dx.doi.org/10.1097/01.qai.0000224571.30119.3d

77. Stek AM. HIV in Pregnancy. In: Management of Common Problems in Obstetrics and Gynecology [Internet]. Wiley-Blackwell; 2010. p. 150–5. Available from: http://dx.doi.org/10.1002/9781444323030.ch33

78. Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, O'Sullivan MJ, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. N Engl J Med [Internet]. 1994 Nov 3;331(18):1173–80. Available from: http://dx.doi.org/10.1056/NEJM199411033311801

79. World Health Organization. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach: Second Edition [Internet]. Geneva: {World Health Organization}; 2016. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27466667

80. UNAIDS. 2015 Progress Report on the Global Plan [Internet]. 2015. Available from: http://www.unaids.org/sites/default/files/media_asset/JC2774_2015ProgressReport_GlobalPlan_en.pdf

81. Mugwaneza P, Umutoni NWS, Ruton H, Rukundo A, Lyambabaje A, Bizimana J de D, et al. Under-two child mortality according to maternal HIV status in Rwanda: assessing outcomes within the National PMTCT Program. Pan Afr Med J [Internet]. 2011 Aug 3;9:37. Available from: https://www.ncbi.nlm.nih.gov/pubmed/22145068

82. Wang A-L, Qiao Y-P, Wang L-H, Fang L-W, Wang F, Jin X, et al. Integrated prevention of mother-to-child transmission for human immunodeficiency virus, syphilis and hepatitis B virus in China. Bull World Health Organ [Internet]. 2015 Jan 1;93(1):52–6. Available from: http://dx.doi.org/10.2471/BLT.14.139626

83. Mirkuzie AH, Hinderaker SG, Mørkve O. Promising outcomes of a national programme for the prevention of Mother-to-Child HIV transmission in Addis Ababa: a retrospective study. BMC Health Serv Res [Internet]. 2010 Sep 9;10:267. Available from: http://dx.doi.org/10.1186/1472-6963-10-267

84. Plipat T, Naiwatanakul T, Rattanasuporn N, Sangwanloy O, Amornwichet P, Teeraratkul A, et al. Reduction in mother-to-child transmission of HIV in Thailand, 2001-2003: Results from population-based surveillance in six provinces. AIDS [Internet]. 2007 Jan 11;21(2):145–51. Available from: http://dx.doi.org/10.1097/QAD.0b013e328010e02d

85. Jackson DJ, Chopra M, Doherty TM, Colvin MS, Levin JB, Willumsen JF, et al. Operational effectiveness and 36 week HIV-free survival in the South African programme to prevent mother-to-child transmission of HIV-1. AIDS [Internet]. 2007 Feb 19;21(4):509–16. Available from: http://dx.doi.org/10.1097/QAD.0b013e32801424d2

86. UNAIDS Global Reference Group on HIV/AIDS and Human Rights. UNAIDS/WHO policy statement on HIV testing [Internet]. 2004. Available from: http://www.who.int/pub/vct/en/hivtestingpolicty04.pdf

87. World Health Organisation. Use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants [Internet]. 2012. Available from: http://www.who.int/entity/hiv/pub/pmtct_update.pdf

88. Black V, Black AD, Rees HV, Guidozzi F, Scorgie F, Chersich MF. Increased Access to Antiretroviral Therapy Is Associated with Reduced Maternal Mortality in Johannesburg, South Africa: An Audit from 2003-2012. PLoS One [Internet]. 2016 Dec 29;11(12):e0168199. Available from: http://dx.doi.org/10.1371/journal.pone.0168199

89. McIntyre J. HIV in pregnancy: a review. 1999; Available from: http://www.popline.org/node/523858

90. Coovadia HM, Rollins NC, Bland RM, Little K, Coutsoudis A, Bennish ML, et al. Mother-to-child transmission of HIV-1 infection during exclusive breastfeeding in the first 6 months of life: an intervention cohort study. Lancet [Internet]. 2007 Mar 31;369(9567):1107–16. Available from: http://dx.doi.org/10.1016/S0140-6736(07)60283-9

91. Iliff PJ, Piwoz EG, Tavengwa NV, Zunguza CD, Marinda ET, Nathoo KJ, et al. Early exclusive breastfeeding reduces the risk of postnatal HIV-1 transmission and increases HIV-free survival. AIDS [Internet]. 2005 Apr 29;19(7):699–708. Available from: https://www.ncbi.nlm.nih.gov/pubmed/15821396

92. World Health Organisation. Guideline: Updates on HIV and Infant Feeding: The Duration of Breastfeeding, and Support from Health Services to Improve Feeding Practices Among Mothers Living with HIV [Internet]. Geneva: World Health Organization; 2016. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27583316

93. The INSIGHT START Study Group. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. N Engl J Med [Internet]. 2015 Aug 27;373(9):795–807. Available from: http://www.nejm.org/doi/abs/10.1056/NEJMoa1506816

94. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Antiretroviral Therapy for the Prevention of HIV-1 Transmission. N Engl J Med [Internet]. 2016 Sep 1;375(9):830–9. Available from: http://dx.doi.org/10.1056/NEJMoa1600693

95. Rodger AJ, Cambiano V, Bruun T, Vernazza P, Collins S, van Lunzen J, et al. Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy. JAMA [Internet]. 2016 Jul 12;316(2):171–81. Available from: http://dx.doi.org/10.1001/jama.2016.5148

96. TEMPRANO ANRS 12136 Study Group, Danel C, Moh R, Gabillard D, Badje A, Le Carrou J, et al. A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa. N Engl J Med [Internet]. 2015 Aug 27;373(9):808–22. Available from: http://dx.doi.org/10.1056/NEJMoa1507198

97. Granich RM, Gilks CF, Dye C, De Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. Lancet [Internet]. 2009 Jan 3;373(9657):48–57. Available from: http://dx.doi.org/10.1016/S0140-6736(08)61697-9

98. Tanser F, Bärnighausen T, Grapsa E, Zaidi J, Newell M-L. High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa. Science [Internet]. 2013 Feb 22;339(6122):966–71. Available from: http://dx.doi.org/10.1126/science.1228160

99. UNAIDS. Global AIDS update 2016 [Internet]. Geneva, Switzerland; 2016. Available from: http://www.unaids.org/sites/default/files/media_asset/global-AIDS-update-2016_en.pdf

100. Rosen S, Fox MP. Retention in HIV Care between Testing and Treatment in Sub-Saharan Africa: A Systematic Review. PLoS Med [Internet]. 2011 [cited 2016 Nov 20];8(7):e1001056. Available from: http://journals.plos.org/plosmedicine/article/file?id=10.1371/journal.pmed.1001056&type=printable

101. Hill A. Generics: The Facts [Internet]. 21st Annual Conference of the British HIV Association (BHIVA); 2015 Apr; The Brighton Centre, Brighton, UK. Available from: http://www.bhiva.org/documents/Conferences/2015Brighton/Presentations/150422/AndrewHill.pdf

102. UNAIDS. Ending AIDS: progress towards the 90–90–90 targets [Internet]. 2017 Jul [cited 2018 Jun 26]. Available from: http://www.unaids.org/sites/default/files/media_asset/Global_AIDS_update_2017_en.pdf

103. Ras GJ, Simson IW, Anderson R, Prozesky OW, Hamersma T. Acquired immunodeficiency syndrome. A report of 2 South African cases. S Afr Med J [Internet]. 1983 Jul 23;64(4):140–2. Available from: https://www.ncbi.nlm.nih.gov/pubmed/6306851

104. McNeil J. A History of Official Government HIV/AIDS Policy in South Africa [Internet]. South African History Archives. [cited 2017 Feb 7]. Available from: http://www.sahistory.org.za/topic/history-official-government-hivaids-policy-south-africa

105. Simelela NP, Venter WDF. A brief history of South Africa's response to AIDS. S Afr Med J [Internet]. 2014 Mar;104(3 Suppl 1):249–51. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24893502

106. Newsline People AIDS Coalition New York. Despite epidemic, South Africa cuts AZT project [Internet]. Newsline People AIDS Coalit. N. Y. 1999. p. 16. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11367177

107. Coovadia H, Jewkes R, Barron P, Sanders D, McIntyre D. The health and health system of South Africa: historical roots of current public health challenges. Lancet [Internet]. 2009 Sep 5;374(9692):817–34. Available from: http://dx.doi.org/10.1016/S0140-6736(09)60951-X

108. Mayosi BM, Lawn JE, van Niekerk A, Bradshaw D, Abdool Karim SS, Coovadia HM. Health in South Africa: changes and challenges since 2009. Lancet [Internet]. 2012;380(9858):2029–43. Available from: http://www.sciencedirect.com/science/article/pii/S0140673612618145

109. Katz IT, Bassett IV, Wright AA. PEPFAR in Transition — Implications for HIV Care in South Africa. N Engl J Med [Internet]. 2013;369(15):1385–7. Available from: http://dx.doi.org/10.1056/NEJMp1310982

110. National Department of Health. Implementation of the Universal Test And Treat Strategy For HIV Positive Patients and Differentiated Care for Stable Patients [Internet]. 2016. Available from: http://www.sahivsoc.org/Files/22%208%2016%20Circular%20UTT%20%20%20Decongestion%20CMT%20Directorate.pdf

111. Shisana O, Labadarios D, Simbayi LC, Onoya D. South African national HIV prevalence, incidence and behaviour survey, 2012 [Internet]. ecommons.hsrc.ac.za; 2015. Available from: http://ecommons.hsrc.ac.za/handle/123456789/2490

112. Larson BA, Schnippel K, Brennan A, Long L, Xulu T, Maotoe T, et al. Same-Day CD4 Testing to Improve Uptake of HIV Care and Treatment in South Africa: Point-of-Care Is Not Enough. AIDS Res Treat [Internet]. 2013 Jul 16;2013:941493. Available from: http://dx.doi.org/10.1155/2013/941493

113. Faal M, Naidoo N, Glencross DK, Venter WDF, Osih R. Providing Immediate CD4 Count Results at HIV Testing Improves ART Initiation. JAIDS Journal of Acquired Immune Deficiency Syndromes [Internet]. 2011 Nov;58(3):e54–9. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00126334-201111010-00019

114. Fox MP. Are we shifting attrition downstream in the HIV cascade? Lancet HIV [Internet]. 2016 Dec;3(12):e554–5. Available from: http://dx.doi.org/10.1016/S2352-3018(16)30149-7

115. South African Audience Research Foundation. AMPS Jul - Dec15 6 months report [Internet]. 3 May, 2016. Available from: http://www.saarf.co.za/amps-presentations/2015/SAARF%20AMPS%20Jul%20-%20Dec%2015.pdf

116. International Telecommunication Union. Mobile_cellular_2000-2015.xls [Internet]. 2015 [cited 14 February, 2016]. Available from: https://www.itu.int/en/ITU-D/Statistics/Documents/statistics/2016/Mobile_cellular_2000-2015.xls

117. Statistics South Africa. Statistical release [Internet]. Available from: https://www.statssa.gov.za/publications/P0302/P03022015.pdf

118. Spietz A, Kelly J. The importance of maternal mental health during pregnancy: theory, practice, and intervention. Public Health Nurs [Internet]. 2002 May;19(3):153–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11967099

119. Byrom S, Edwards G, Bick D. Essential Midwifery Practice: Postnatal Care. Wiley; 2009. 282 p.

120. Kerber KJ, de Graft-Johnson JE, Bhutta ZA, Okong P, Starrs A, Lawn JE. Continuum of care for maternal, newborn, and child health: from slogan to service delivery. Lancet [Internet]. 2007 Oct 13;370(9595):1358–69. Available from: http://dx.doi.org/10.1016/S0140-6736(07)61578-5

121. Graham WJ, Bell JS, Bullough CHW. Can skilled attendance at delivery reduce maternal mortality in developing countries. In: Van Lerberghe VDBAW, editor. Safe Motherhood Strategies : a Review of the Evidence. ITG Press, Antwerp; 2001. p. 97–130. (Studies in Health Services Organisation & Policy; vol. 17).

122. EBCOG Scientific Committee. The public health importance of antenatal care. Facts Views Vis Obgyn [Internet]. 2015;7(1):5–6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25897366

123. Lassi ZS, Mansoor T, Salam RA, Das JK, Bhutta ZA. Essential pre-pregnancy and pregnancy interventions for improved maternal, newborn and child health. Reprod Health [Internet]. 2014 Aug 21;11 Suppl 1:S2. Available from: http://dx.doi.org/10.1186/1742-4755-11-S1-S2

124. World Health Organization. Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice. 2009. 2009.

125. World Health Organization. Summary of WHO Position Papers—Recommended Routine Immunizations for Children [Internet]. 2016. Available from: http://www.who.int/immunization/policy/Immunization_routine_table2.pdf

126. World Health Organization. Global Immunization Data [Internet]. 2017 [cited 2017 Jun 1]. Available from: http://www.who.int/mediacentre/factsheets/fs378/en/

127. WHO, UNICEF. South Africa: WHO and UNICEF estimates of immunization coverage: 2017 revision [Internet]. 2018 Jul. Available from: http://www.who.int/immunization/monitoring_surveillance/data/zaf.pdf

128. Violari A, Cotton MF, Gibb DM, Babiker AG, Steyn J, Madhi SA, et al. Early antiretroviral therapy and mortality among HIV-infected infants. N Engl J Med [Internet]. 2008 Nov 20;359(21):2233–44. Available from: http://dx.doi.org/10.1056/NEJMoa0800971

129. Woldesenbet S, Jackson D, Lombard C, Dinh T-H, Puren A, Sherman G, et al. Missed Opportunities along the Prevention of Mother-to-Child Transmission Services Cascade in South Africa: Uptake, Determinants, and Attributable Risk (the SAPMTCTE). PLoS One [Internet]. 2015 Jul 6;10(7):e0132425. Available from: http://dx.doi.org/10.1371/journal.pone.0132425

130. Schnippel K, Mongwenyana C, Long LC, Larson BA. Delays, interruptions, and losses from prevention of mother-to-child transmission of HIV services during antenatal care in Johannesburg, South Africa: a cohort analysis. BMC Infect Dis [Internet]. 2015 Feb 6;15:46. Available from: http://dx.doi.org/10.1186/s12879-015-0778-2

131. Kourtis AP, de Vincenzi I, Jamieson DJ, Bulterys M. Antiretroviral drugs during breastfeeding for the prevention of postnatal transmission of HIV-1. Adv Exp Med Biol [Internet]. 2012;743:173–83. Available from: http://dx.doi.org/10.1007/978-1-4614-2251-8_12

132. Taha TE, Kumwenda J, Cole SR, Hoover DR, Kafulafula G, Fowler MG, et al. Postnatal HIV-1 transmission after cessation of infant extended antiretroviral prophylaxis and effect of maternal highly active antiretroviral therapy. J Infect Dis [Internet]. 2009 Nov 15;200(10):1490–7. Available from: http://dx.doi.org/10.1086/644598

133. Chasela CS, Hudgens MG, Jamieson DJ, Kayira D, Hosseinipour MC, Kourtis AP, et al. Maternal or infant antiretroviral drugs to reduce HIV-1 transmission. N Engl J Med [Internet]. 2010 Jun 17;362(24):2271–81. Available from: http://dx.doi.org/10.1056/NEJMoa0911486

134. Statistics South Africa. Millennium Development Goals: Country Report 2015 [Internet]. Statistics South Africa; 2015 [cited 2015 Nov 26]. Available from: http://www.statssa.gov.za/MDG/MDG_Country%20Report_Final30Sep2015.pdf

135. Central Intelligence Agency. The CIA World Factbook 2006. Washington DC: Central Intelligence Agency; 2006.

136. Central Intelligence Agency. The CIA World Factbook 2017 [Internet]. Washington, DC: Skyhorse Publishing, Inc.; 2016. 976 p. Available from: https://market.android.com/details?id=book-qf6LDAAAQBAJ

137. UNICEF. Countdown To 2015: A Decade of Tracking Progress for Maternal, Newborn and Child Survival [Internet]. UNICEF; 2015. 100 p. Available from: http://books.google.co.za/books/about/Countdown_To_2015.html?hl=&id=vsL7sgEACAAJ

138. Pattinson R, editor. Saving Mothers 2011-2013: Sixth report on the Confidential Enquiries into Maternal Deaths in South Africa [Internet]. National Committee for Confidential Enquiry into Maternal Deaths; [cited 2015 Dec 27]. Available from: http://www.kznhealth.gov.za/mcwh/Maternal/Saving-Mothers-2011-2013-short-report.pdf

139. Wiysonge CS, Ngcobo NJ, Jeena PM, Madhi SA, Schoub BD, Hawkridge A, et al. Advances in childhood immunisation in South Africa: where to now? Programme managers' views and evidence from systematic reviews. BMC Public Health [Internet]. 2012 Jul 31;12:578. Available from: http://dx.doi.org/10.1186/1471-2458-12-578

140. Siegfried N, Wiysonge CS, Pienaar D. Too little, too late: measles epidemic in South Africa. Lancet [Internet]. 2010 Jul 17;376(9736):160. Available from: http://dx.doi.org/10.1016/S0140-6736(10)61100-2

141. Solarin I, Black V. 'They told me to come back': women's antenatal care booking experience in inner-city Johannesburg. Matern Child Health J [Internet]. 2013 Feb;17(2):359–67. Available from: http://dx.doi.org/10.1007/s10995-012-1019-6

142. Barron P, Pillay Y, Doherty T, Sherman G, Jackson D, Bhardwaj S, et al. Eliminating mother-to-child HIV transmission in South Africa. Bull World Health Organ [Internet]. 2013 Jan 1;91(1):70–4. Available from: http://dx.doi.org/10.2471/BLT.12.106807

143. Goga A, Dinh T, Jackson D, Group SS, Others. Population-level impact of the national PMTCT programme: 2010 and 2011. In: Johannesburg: PMTCT Symposium. 2012. p. 23–4.

144. Leach-Lemens C. South Africa has driven mother-to-child HIV transmission down to 4% [Internet]. AIDS Map. 2016 [cited 2017 Mar 12]. Available from: http://www.aidsmap.com/South-Africa-has-driven-mother-to-child-HIV-transmission-down-to-4/page/3073056/

145. Barron P, Pillay Y, Doherty T, Sherman G, Jackson D, Bhardwaj S, et al. Eliminating mother-to-child HIV transmission in South Africa. Bull World Health Organ [Internet]. 2013 Jan 1;91(1):70–4. Available from: http://dx.doi.org/10.2471/BLT.12.106807

146. Schnippel K, Mongwenyana C, Long LC, Larson BA. Delays, interruptions, and losses from prevention of mother-to-child transmission of HIV services during antenatal care in Johannesburg, South Africa: a cohort analysis. BMC Infect Dis [Internet]. 2015 Feb 6;15:46. Available from: http://dx.doi.org/10.1186/s12879-015-0778-2

147. Woldesenbet S, Jackson D, Lombard C, Dinh T-H, Puren A, Sherman G, et al. Missed Opportunities along the Prevention of Mother-to-Child Transmission Services Cascade in South Africa: Uptake, Determinants, and Attributable Risk (the SAPMTCTE). PLoS One [Internet]. 2015 Jul 6;10(7):e0132425. Available from: http://dx.doi.org/10.1371/journal.pone.0132425

148. Rees H, Delany-Moretlwe S, Scorgie F, Luchters S, Chersich MF. At the Heart of the Problem: Health in Johannesburg's Inner-City. BMC Public Health [Internet]. 2017 Jul 4;17(Suppl 3):554. Available from: http://dx.doi.org/10.1186/s12889-017-4344-2

149. Statistics South Africa. Mid-year population estimates 2017 [Internet]. 2017 Jul. Available from: http://www.statssa.gov.za/publications/P0302/P03022017.pdf

150. Gauteng Provincial Government. Socio-Economic Review and Outlook 2016 [Internet]. 2016. Available from:

http://www.treasury.gov.za/documents/provincial%20budget/2016/3.%20Provincial%20Appropriatio
n%20Acts/5.%20Guide%20to%20the%20Budget/GT/Gauteng%20-%20Social-
Economic%20Review%20and%20Outlook.pdf

151. Statistics South Africa. Census 2011 [Internet]. 2011. Available from:
http://www.treasury.gov.za/documents/national%20budget/2002/ene/vote_13.pdf

152. Human Sciences Research Council. Violence and Xenophobia in South Africa: Developing
Consensus, Moving to Action [Internet]. Hadland A, editor. 2008. Available from:
http://www.hsrc.ac.za/en/research-data/ktree-doc/6450

153. Dixon R. Attacks on foreigners spread in South Africa; weekend violence feared. Los Angeles Times
[Internet]. 2015 Apr 17 [cited 2018 Feb 26]; Available from: http://www.latimes.com/world/africa/la-
fg-south-africa-foreigners-20150417-story.html

154. Statistics South Africa. Community Survey 2016 in Brief [Internet]. 2016. Available from:
http://www.statssa.gov.za/publications/03-01-06/03-01-062016.pdf

155. Statistics South Africa. General Household Survey 2016 [Internet]. 2017 May. Available from:
https://www.statssa.gov.za/publications/P0318/P03182016.pdf

156. Gumede S, Black V, Naidoo N, Chersich MF. Attendance at antenatal clinics in inner-city
Johannesburg, South Africa and its associations with birth outcomes: analysis of data from birth
registers at three facilities. BMC Public Health [Internet]. 2017 Jul 4;17(Suppl 3):443. Available from:
http://dx.doi.org/10.1186/s12889-017-4347-z

157. Bello B, Moultrie H, Somji A, Chersich MF, Watts C, Delany-Moretlwe S. Alcohol use and sexual
risk behaviour among men and women in inner-city Johannesburg, South Africa. BMC Public Health
[Internet]. 2017 Jul 4;17(Suppl 3):548. Available from: http://dx.doi.org/10.1186/s12889-017-4350-4

158. Scorgie F, Vearey J, Oliff M, Stadler J, Venables E, Chersich MF, et al. 'Leaving no one behind':
reflections on the design of community-based HIV prevention for migrants in Johannesburg's inner-
city hostels and informal settlements. BMC Public Health [Internet]. 2017 May 20;17(1):482.
Available from: http://dx.doi.org/10.1186/s12889-017-4351-3

159. Den Hartigh W. Mama puts power in mom's hands [Internet]. Brand South Africa. 2013 [cited 2017
Jun 5]. Available from: http://www.mediaclubsouthafrica.com/tech/3343-mama-puts-power-in-mom-
s-hands

160. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture
(REDCap)--a metadata-driven methodology and workflow process for providing translational research
informatics support. J Biomed Inform [Internet]. 2009 Apr;42(2):377–81. Available from:
http://dx.doi.org/10.1016/j.jbi.2008.08.010

161. StataCorp. Stata Statistical Software: Release 14. College Station, TX; 2015.

162. World Health Organisation. Global Health Observatory data repository - Measles (MCV) -
Immunization coverage estimates by country [Internet]. World Health Organisation. {World Health
Organisation}; 2016 [cited 2017 Jan 2]. Available from: http://apps.who.int/gho/data/node.main.A826

163. Fine PE. Herd Immunity: History, Theory, Practice. Epidemiol Rev [Internet]. 1993;15(2):265–302.
Available from: https://www.ncbi.nlm.nih.gov/pubmed/8174658

164. IBM Corp. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY; 2013.

165. World Health Organization. WHOQOL-BREF: introduction, administration, scoring and generic
version of the assessment: field trial version [Internet]. 1996 Dec. Available from:
http://apps.who.int/iris/bitstream/handle/10665/63529/WHOQOL-BREF.pdf

166. LiST: The Lives Saved Tool [Internet]. [cited 2018 Mar 1]. Available from:
http://www.livessavedtool.org/

167. World Medical Association. Declaration of Helsinki Ethical Principles for Medical Research
Involving Human Subjects [Internet]. 2016 Oct. Available from: https://www.wma.net/wp-
content/uploads/2016/11/DoH-Oct2013-JAMA.pdf

168. Coria-soto IL, Bobadilla JL, Notzon F. The effectiveness of antenatal care in preventing intrauterine
growth retardation and low birth weight due to preterm delivery. Int J Qual Health Care [Internet].
1996 Feb;8(1):13–20. Available from: https://www.ncbi.nlm.nih.gov/pubmed/8680812

169. McCormick MC. The contribution of low birth weight to infant mortality and childhood morbidity. N
Engl J Med [Internet]. 1985 Jan 10;312(2):82–90. Available from:
http://dx.doi.org/10.1056/NEJM198501103120204

170. Parker RM, Dmitrieva E, Frolov S, Gazmararian JA. Text4baby in the United States and Russia: an opportunity for understanding how mHealth affects maternal and child health. J Health Commun [Internet]. 2012;17 Suppl 1:30–6. Available from: http://dx.doi.org/10.1080/10810730.2011.649162

171. Jareethum R, Titapant V, Chantra T, Sommai V, Chuenwattana P, Jirawan C. Satisfaction of healthy pregnant women receiving short message service via mobile phone for prenatal support: A randomized controlled trial. J Med Assoc Thai [Internet]. 2008 Apr;91(4):458–63. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18556852

172. Schwartz SR, Clouse K, Yende N, Van Rie A, Bassett J, Ratshefola M, et al. Acceptability and Feasibility of a Mobile Phone-Based Case Management Intervention to Retain Mothers and Infants from an Option B+ Program in Postpartum HIV Care. Matern Child Health J [Internet]. 2015 Sep;19(9):2029–37. Available from: http://dx.doi.org/10.1007/s10995-015-1715-0

173. National Department of Health. National Consolidated Guidelines for the Prevention of Mother-to-Child Transmission of HIV (PMTCT) and the Management of HIV in Children, Adolescents and Adults [Internet]. 2015 Apr. Available from: http://www.sahivsoc.org/Files/ART%20Guidelines%2015052015.pdf

174. Domek GJ, Contreras-Roldan IL, O'Leary ST, Bull S, Furniss A, Kempe A, et al. SMS text message reminders to improve infant vaccination coverage in Guatemala: A pilot randomized controlled trial. Vaccine [Internet]. 2016 May 5;34(21):2437–43. Available from: http://dx.doi.org/10.1016/j.vaccine.2016.03.065

175. Su Y, Yuan C, Zhou Z, Heitner J, Campbell B. Impact of an SMS advice programme on maternal and newborn health in rural China: study protocol for a quasi-randomised controlled trial. BMJ Open [Internet]. 2016 Aug 10;6(8):e011016. Available from: http://dx.doi.org/10.1136/bmjopen-2015-011016

176. Gurman TA, Rubin SE, Roess AA. Effectiveness of mHealth behavior change communication interventions in developing countries: a systematic review of the literature. J Health Commun [Internet]. 2012;17 Suppl 1:82–104. Available from: http://dx.doi.org/10.1080/10810730.2011.649160

177. Hunchangsith P, Barendregt JJ, Vos T, Bertram M. Cost-effectiveness of various tuberculosis control strategies in Thailand. Value Health [Internet]. 2012 Jan;15(1 Suppl):S50–5. Available from: http://dx.doi.org/10.1016/j.jval.2011.11.006

178. Cormick G, Kim NA, Rodgers A, Gibbons L, Buekens PM, Belizán JM, et al. Interest of pregnant women in the use of SMS (short message service) text messages for the improvement of perinatal and postnatal care. Reprod Health [Internet]. 2012 Aug 6;9:9. Available from: http://dx.doi.org/10.1186/1742-4755-9-9

179. Hmone MP, Dibley MJ, Li M, Alam A. A formative study to inform mHealth based randomized controlled trial intervention to promote exclusive breastfeeding practices in Myanmar: incorporating qualitative study findings. BMC Med Inform Decis Mak [Internet]. 2016 Jun 4;16:60. Available from: http://dx.doi.org/10.1186/s12911-016-0301-8

180. Munro S, Hui A, Salmons V, Solomon C, Gemmell E, Torabi N, et al. SmartMom Text Messaging for Prenatal Education: A Qualitative Focus Group Study to Explore Canadian Women's Perceptions. JMIR Public Health Surveill [Internet]. 2017 Feb 7;3(1):e7. Available from: http://dx.doi.org/10.2196/publichealth.6949

181. Breen RL. A Practical Guide to Focus-Group Research. Journal of Geography in Higher Education [Internet]. 2006 Nov 1;30(3):463–75. Available from: https://doi.org/10.1080/03098260600927575

182. Edelman. 2018 Edelman Trust Barometer Global Report [Internet]. 2018 Feb [cited 2018 Jul 11]. Available from: http://cms.edelman.com/sites/default/files/2018-02/2018_Edelman_Trust_Barometer_Global_Report_FEB.pdf

183. Fairbanks J, Beima-Sofie K, Akinyi P, Matemo D, Unger JA, Kinuthia J, et al. You Will Know That Despite Being HIV Positive You Are Not Alone: Qualitative Study to Inform Content of a Text Messaging Intervention to Improve Prevention of Mother-to-Child HIV Transmission. JMIR mHealth and uHealth [Internet]. 2018 [cited 2018 Jul 20];6(7):e10671. Available from: http://mhealth.jmir.org/2018/7/e10671/

184. Atuahene MD, Arde-Acquah S, Atuahene NF, Adjuik M, Ganle JK. Inclusion of men in maternal and safe motherhood services in inner-city communities in Ghana: evidence from a descriptive cross-sectional survey. BMC Pregnancy Childbirth [Internet]. 2017 Dec 14;17(1):419. Available from: http://dx.doi.org/10.1186/s12884-017-1590-3

185. Comrie-Thomson L, Tokhi M, Ampt F, Portela A, Chersich M, Khanna R, et al. Challenging gender inequity through male involvement in maternal and newborn health: critical assessment of an emerging evidence base. Cult Health Sex [Internet]. 2015 Jul 10;17 Suppl 2:S177–89. Available from: http://dx.doi.org/10.1080/13691058.2015.1053412

186. Yargawa J, Leonardi-Bee J. Male involvement and maternal health outcomes: systematic review and meta-analysis. J Epidemiol Community Health [Internet]. 2015 Jun;69(6):604–12. Available from: http://dx.doi.org/10.1136/jech-2014-204784

187. Fishbein M, Triandis HC, Kanfer FH, Becker M, Middlestadt SE. Factors influencing behavior and behavior change. 2000; Available from: https://www.popline.org/node/275460

188. de Mooij M. Behavior Change Communication. In: de Mooij M, editor. Human and Mediated Communication around the World: A Comprehensive Review and Analysis [Internet]. Cham: Springer International Publishing; 2014. p. 395–415. Available from: https://doi.org/10.1007/978-3-319-01249-0_12

189. Levine R, Corbacio A, Konopka S, Saya U, Gilmartin C, Paradis J, et al. mHealth Compendium. Volume Five. 2015; Available from: http://www.popline.org/node/639414

190. Robson C, McCartan K. Real World Research [Internet]. John Wiley & Sons; 2016. 560 p. Available from: https://market.android.com/details?id=book-AdGOCQAAQBAJ

191. Brazier J, Ratcliffe J, Saloman J, Tsuchiya A. Measuring and Valuing Health Benefits for Economic Evaluation [Internet]. Oxford University Press; 2017. 348 p. Available from: https://market.android.com/details?id=book-r3R4DQAAQBAJ

192. Harris J. QALYfying the value of life. J Med Ethics [Internet]. 1987 Sep 1 [cited 2018 Jul 10];13(3):117–23. Available from: http://jme.bmj.com/content/13/3/117.short

193. Coleman J, Xiong K. Gauging the Impact of MomConnect on Maternal Health Service Utilisation by Women and Their Infants in Johannesburg, South Africa [Internet]. MEASURE Evaluation; 2017 Sep [cited 2018 Jun 22]. Available from: https://www.measureevaluation.org/resources/publications/tr-17-210

194. Wunsch G. Confounding and control. Demogr Res [Internet]. 2007;16:97–120. Available from: http://www.jstor.org/stable/26347930

195. Guest G, Namey E, McKenna K. How Many Focus Groups Are Enough? Building an Evidence Base for Nonprobability Sample Sizes. Field methods [Internet]. 2016 Apr 28;29(1):3–22. Available from: https://doi.org/10.1177/1525822X16639015

196. Carlsen B, Glenton C. What about N? A methodological study of sample-size reporting in focus group studies. BMC Med Res Methodol [Internet]. 2011 Mar 11;11:26. Available from: http://dx.doi.org/10.1186/1471-2288-11-26

197. Lederman LC. High communication apprehensives talk about communication apprehension and its effects on their behavior. Commun Q [Internet]. 1983 Jun 1;31(3):233–7. Available from: https://doi.org/10.1080/01463378309369509

198. McLafferty I. Focus group interviews as a data collecting strategy. J Adv Nurs [Internet]. 2004 Oct;48(2):187–94. Available from: http://dx.doi.org/10.1111/j.1365-2648.2004.03186.x

199. Kitzinger J. Qualitative research. Introducing focus groups. BMJ [Internet]. 1995 Jul 29;311(7000):299–302. Available from: https://www.ncbi.nlm.nih.gov/pubmed/7633241

200. Fern EF. The Use of Focus Groups for Idea Generation: The Effects of Group Size, Acquaintanceship, and Moderator on Response Quantity and Quality. J Mark Res [Internet]. 1982;19(1):1–13. Available from: http://www.jstor.org/stable/3151525

201. Murray LJ, editor. Babycentre Pregnancy - From Preconception to Birth. Dorling Kindersley Ltd; 2010. 320 p.

202. Sprague C, Chersich MF, Black V. Health system weaknesses constrain access to PMTCT and maternal HIV services in South Africa: a qualitative enquiry. AIDS Res Ther [Internet]. 2011 Mar 3;8:10. Available from: http://dx.doi.org/10.1186/1742-6405-8-10

203. Anderson C. Presenting and evaluating qualitative research. Am J Pharm Educ [Internet]. 2010 Oct 11;74(8):141. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21179252

204. Horwood C, Haskins L, Vermaak K, Phakathi S, Subbaye R, Doherty T. Prevention of mother to child transmission of HIV (PMTCT) programme in KwaZulu-Natal, South Africa: an evaluation of PMTCT implementation and integration into routine maternal, child and women's health services: PMTCT in

Kwa-Zulu. Trop Med Int Health [Internet]. 2010 Jun 17;374:no – no. Available from: http://doi.wiley.com/10.1111/j.1365-3156.2010.02576.x

205. Mepham S, Zondi Z, Mbuyazi A, Mkhwanazi N, Newell ML. Challenges in PMTCT antiretroviral adherence in northern KwaZulu-Natal, South Africa. AIDS Care [Internet]. 2011 Jun;23(6):741–7. Available from: http://dx.doi.org/10.1080/09540121.2010.516341

206. Peltzer K, Mlambo G. HIV Disclosure Among HIV Positive New Mothers in South Africa. Journal of Psychology in Africa [Internet]. 2013 Jan 1;23(2):327–33. Available from: https://doi.org/10.1080/14330237.2013.10820631