Université de Montréal

Exploring health systems integration in urban South Africa: from integrating prevention of mother-to-child transmission of HIV to prevention of type 2 diabetes after gestational diabetes

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RÉSUMÉ

L'intégration du traitement et de la prévention des maladies chroniques non transmissibles (MNT) au sein des soins de santé primaires représente le principal défi à venir pour la santé publique et les systèmes de santé dans les pays à faible et moyen revenu comme l'Afrique du Sud. Il constitue le principal objectif de cette thèse. L'expérience de l'intégration de la prévention de la transmission du VIH de la mère à l'enfant (PTME) dans les soins de santé primaires (SSP) peut apporter des leçons importantes pour l'intégration de la prévention du diabète chez les femmes souffrant de diabète gestationnel récent (DSG) dans les SSP. Il a été estimé que le DSG touche plus de 9,1 % des grossesses en 2018 en Afrique du Sud. Le DSG augmente le risque de développer ultérieurement du diabète de type 2 (DT2). Le DSG multiplie par plus de 7 le risque de développer un DT2 ainsi que les risques de troubles métaboliques pour les bébés des femmes qui en sont atteintes. Cette thèse explore comment appliquer les leçons tirées de l'intégration de la PTME pour intégrer le dépistage du DSG et les initiatives de prévention du DT2 dans les soins de santé primaires de routine en Afrique du Sud. Le cadre conceptuel adapté pour cette thèse permet ainsi de comprendre les aspects de l'intégration au niveau du patient et du système de santé, englobant les contextes, les mécanismes et la mise en œuvre de l'intégration d'interventions préventives dans les services existants. L'étude s'inscrit dans le cadre du projet IINDIAGO, « Intervention intégrée du système de santé visant à réduire les risques de diabète de type 2 chez les femmes défavorisées après un diabète gestationnel en Afrique du Sud ».

La thèse présente d'abord une revue narrative de l'impact de la PTME sur les services et les systèmes de soins de santé en Afrique subsaharienne (Article 1). Les résultats de cette revue montrent que la PTME a eu l'impact positif et négatif sur d'autres services de soins de santé et que son intégration dans les systèmes de santé est de plus en plus privilégiée. L'article 2 est une étude

qualitative analysant l'histoire et l'expérience locales de l'intégration de la PTME dans les SSP de routine en Afrique du Sud de différents points de vue. Bien qu'elle ait constaté un fort soutien en faveur de l'intégration parmi tous les répondants, cette étude a fait état de multiples obstacles à la pleine intégration de la PTME dans les SSP, le post-partum en particulier. Les articles 3 et 4 ont utilisé les méthodes mixtes et révélé que l'intégration des services dans les SSP de routine, à base communautaire, pour dépister universellement le DSG et pour prévenir ou retarder le DT2 après le DSG, était perçue comme faisable, acceptable et nécessaire de toute urgence en Afrique du Sud. L'article 6 (dont le protocole est l'article 5) présentait une revue systématique et une méta-analyse sur la prise en charge intégrée du DSG et du DT2 dans le contexte de la multimorbidité en Afrique. Les 13 études incluses dans cette étude ont montré que la gestion intégrée du DSG et du DT2 dans le cadre de la multimorbidité était mise en œuvre avec succès, mais qu'elle nécessitait une formation et une supervision adéquates des infirmières, et la fourniture d'équipements et de médicaments additionnels au sein des systèmes de santé nationaux en Afrique.

Les conclusions de cette thèse suggèrent que, bien qu'elle n'ait pas toujours été retenue, en raison de défis structurels et opérationnels, l'intégration complète plutôt que partielle des services de santé est considérée comme souhaitable et réalisable par les femmes, les travailleurs de la santé, les gestionnaires et les experts. L'intégration complète pourrait être idéale pour dépister, diagnostiquer et soigner les maladies chroniques, y compris le DSG et le DT2, au sein des SSP de routine et selon l'approche de la PTME dont les leçons d'intégration n'ont pas été adaptées à ce prochain défi de santé publique.

Mots-clés : Intégration, systèmes de santé, santé mondiale, soins de santé primaires, prévention de la transmission mère-enfant du VIH, PTME, TME, diabète sucré gestationnel, diabète de type 2, Afrique du Sud.

ABSTRACT

Integrating chronic, non-communicable diseases (NCDs) and their prevention into primary health care is the next major challenge for public health and health systems in low and middle-income countries like South Africa and is the primary focus of this thesis. The experience of integration of Prevention of Mother-to-Child Transmission (PMTCT) of HIV into primary health care (PHC) may have important lessons for integrating prevention of diabetes among women with recent gestational diabetes (GDM) into PHC.

GDM was estimated to affect more than 9.1% of pregnancies in 2018 in South Africa. GDM increases the risk of developing subsequent type 2 diabetes (T2DM) more than 7-fold as well as increasing the risks of metabolic disorders for the babies of women who had GDM. This thesis conducted a systematised narrative synthesis, a systematic review and a convergent mixed methods study using primarily qualitative methods in South Africa (focus on Cape Town, Western Cape) to explore how to apply lessons from PMTCT integration in order to integrate GDM screening and T2DM prevention initiatives into routine PHC in South Africa. The adapted conceptual framework for this thesis enables to understand both patient-level and health system-level aspects of integration and encompassing the contexts, mechanisms and implementation for integrating preventive interventions in the existing services. The study was nested in the IINDIAGO project, "Integrated health system intervention aimed at reducing type 2 diabetes risks in disadvantaged women after gestational diabetes in South Africa".

The thesis first presents a narrative review of the impact of PMTCT on health care services and systems in sub-Saharan Africa (Paper 1). This review findings show that PMTCT has had positive and negative impacts on other health care services and that its integration into health systems is increasingly favored. Paper 2 qualitatively documented the local history and experience of PMTCT

integration into routine PHC in South Africa from different perspectives. Though it found strong support for integration among all respondents (N=20), this study reported multiple barriers for the full integration of PMTCT into PHC, especially in postpartum. Papers 3 and 4 used mixed methods and highlighted that integrating services within routine, community-based PHC to universally screen GDM and to prevent or delay of T2DM after GDM, was perceived as feasible, acceptable and urgently needed in South Africa – but that it is not currently occurring at a satisfactory level, despite international and national guidelines.

The fifth article is a published protocol for Paper 6, a systematic review and meta-analysis on the integrated management of GDM and T2DM in the context of multimorbidity in Africa. This was a study in which all 13 included studies showed that integrated management of GDM and T2DM within multimorbidity was successfully implemented but it required adequate training and supervision of nurses, provision of additional equipment and drugs to the existing resources within national health systems in Africa.

This thesis concludes that although not always opted for, due to structural and operational challenges, the full instead of partial integration of health services to screen, diagnose and care for chronic diseases including GDM and T2DM into routine PHC, following the PMTCT approach, was seen as both desirable and feasible by women, health workers, managers, and experts. However, the lessons learned through the history of PMTCT and its integration have not been adapted to this next public health challenge.

Keywords: Integration, health systems, global health, primary health care, Prevention of Mother-to-Child Transmission of HIV, PMTCT, MTCT, gestational diabetes mellitus, type 2 diabetes, South Africa.

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LIST OF ABBREVIATIONS

ADA	American Diabetes Association
AIDS	Acquired Immunodeficiency Syndrome
ANC	Antenatal care
ART	Anti-Retroviral Therapy
ARVs	Antiretrovirals
AZT	Azidothymidine or Zidovudine
BANC	Basic ANtenatal Care
BCW	Behaviour Change Wheel
CCRBT	Cochrane Collaboration Risk of Bias Tool
CDC	Centers for Disease Control
CHWs	Community Health Workers
CI	Confidence Interval
CNCICDs	Comorbid Non-Communicable and Infectious Chronic Diseases
COREQ	COnsolidated criteria for REporting Qualitative research
GDM	Gestational Diabetes Mellitus
DM	Diabetes Mellitus
DoH	Department of Health
DPSG	Diabetes Pregnancy Study Group

EASD	European Association for the Study of Diabetes
EPHPP	Effective Public Health Practice Project
FHCWs	Frontline Health Care Workers
FP	Family planning
GDM	Gestational Diabetes Mellitus
GFATM	Global Fund to fight against AIDS, TB and Malaria
GSH	Groote Schuur Hospital
HAART	Highly Active Anti-Retroviral Therapy
HCT	HIV Counselling and Testing
HCPs	Health Care Providers
HINARI	Health InterNetwork Access to Research Initiative
HIV	Human Immunodeficiency Virus
IADPSG	International Association of Diabetes and Pregnancy Study Groups
ICCC	Innovative Care for Chronic Conditions
IGT	Impaired Glucose Tolerance
IINDIAGO	Integrated INtervention for DIAbetes rIsk after GestatiOnal diabetes
IQR	InterQuartile Range
KIs	Key Informants
LMICs	Low- and Middle-Income Countries

MCH	Maternal and Child Health
MeSH	Medical subject heading
MMAT	Mixed Methods Appraisal Tool
MOU	Midwife and Obstetrics Unit
MSF	Médecins Sans Frontières
MTCT	Mother-To-Child Transmission
M2M	Mother-to-mother
NCDs	Non-communicable diseases
NDDG	National Diabetes Data Group
NGOs	Non-Governmental Organisations
NIMART	Nurse Initiated and Managed Anti-Retroviral Therapy
OGTT	Oral Glucose Tolerance Test
PACTR	Pan African Clinical Trials Registry
PCR	Protein-Chain Reaction
PEPFAR	President's Emergency Plan for AIDS Relief
PHC	Primary Health Care
PICO	Population, Intervention, Comparator and Outcome
PICT	Provider-initiated counselling and testing
PLHIV	People Living with HIV

PMTCT	Prevention of Mother-To-Child Transmission
PNC	Postnatal care
PRISMA	Preferred Reporting Items for Systematic review and Meta-Analysis
QCTs	Quasi-randomised Controlled Trials
RCTs	Randomised Controlled Trial
REML	Restricted maximum likelihood
ROBINS-I:	Risk Of Bias In Non-randomized Studies - of Interventions
RSA	Republic of South Africa
SA	South Africa
SRH	Sexual and reproductive health
SD	Standard Deviation
SE	Standard Error
SSA	Sub-Saharan Africa
STI	Sexually Transmitted Infection
TAC	Treatment Action Campaign
T2DM	Type 2 Diabetes Mellitus
TB	Tuberculosis
UNAIDS	The United Nations Programme on HIV and AIDS
UNFPA	The United Nations Population Fund

UNGASS	The United Nations General Assembly Special Session
UNICEF	The United Nations Children's Fund
USAID	United States Agency for International Development
WC	Western Cape
WHO	World Health Organisation

This work is dedicated to:

Sophie and our beloved children Joëlle and Caleb, my family for unceasing encouragement, my grandparents Mzee Samuel and Mukecuru Thérèse for raising me to love others and teaching me to work hard, and all my childhood friends whose lives were cut short; regardless of any political labelling.

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Studying during a difficult period following the Rwandan genocide and regional turmoil taught us to team-up and encourage each other in order to succeed and with my childhood friend Munezero Jean Victor and his family, Ntibilingirwa Alphonse and others we met at university, like Karugwiza Odette and her husband Anselme, Karangwa Dieudonné, Umutoni Grâce Carmen and others. We progressed together in our tertiary education. When the idea of completing my studies with a PhD crossed my mind as a lecturer at the University of Namibia (UNAM) and the then polytechnic of Namibia, now Namibia University of Science and Technology (NUST), no one else could have advised, encouraged and supported me as well at every step of my admission and immigration process as my dear friend and brother to whom I owe this humble thanksgiving, MUGABO Valens. My good friends in Namibia, Dr Muhoza Jean Claude, Nangigaye Aloys, Uzabakiriho Jean Damascène, Ntirampeba Dismas, Munezero Clémence, Prof. Peter Nyarang'o and their respective families deserve my appreciation for their inputs to my plans to pursue doctoral studies.

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When I arrived in Montreal, I had lost the contacts of Charles Kimenyi and he was the only person I knew to live in Montreal and without having any way to reach out to him, a longtime friend put me in contact with Agnès Nyirahabimana who came to pick me from the airport looking at my photo sent to her one day before my flight! From that afternoon on, she did more than hosting and showing me around for the first months in the city, I was well received by her extended family for lifelong friendship. After a short period of time, I got the contact and called Kimenyi who

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PART ONE: INTRODUCTION, AIMS, OBJECTIVES, CONCEPTUAL FRAMEWORK AND METHODS

CHAPTER 1: INTRODUCTION

1.1 Gestational diabetes, HIV and integration of care in health systems

Non-communicable diseases (NCDs) have become the first cause of deaths worldwide and their burden is now the leading cause of mortality in Sub-Saharan Africa (SSA) (Bigna & Noubiap, 2019; Gouda et al., 2019). Four major NCDs – cardiovascular diseases, cancers, respiratory diseases and diabetes – cause 80% of all NCD-related deaths and their management has emerged as a significant and challenging priority for health systems, especially for primary care in Africa (Bigna & Noubiap, 2019; Maher et al., 2010). Integrating chronic NCDs and their prevention into primary health care (PHC) is the next major challenge for public health and health systems in low and middle-income countries (LMICs) like South Africa (Bousquet et al., 2011; Gouda et al., 2019; Haque et al., 2020) and is the primary focus of this thesis.

In recent years, NCDs including DM have gained ground among global health priorities and were added in the Sustainable Development Goals (SGD), the agenda that replaced MDG (Kumar et al., 2016; Sachs, 2012), as well as in the 2018 Astana Declaration that reaffirmed the principles of Alma-Ata Declaration (Walraven, 2019). However, implementation and integration of diabetes mellitus (DM) and NCD-focused initiatives into PHC in LMICs like South Africa have not yet followed suit.

Though there has been progress on implementing comprehensive PHC since the 1978 Alma-Ata Declaration on "Health for All by 2000" (Bitton et al., 2017; Mahler, 2008; WHO, 1978), only a limited number of studies and interventions on DM at primary care level for the study population of this thesis (women and their babies), in Africa and South Africa have emerged (Adam & Rheeder, 2017b; Muche et al., 2019; Muhwava et al., 2018). Despite the efforts to improve maternal health following the Millennium Development Goals (MDG) agenda by 2015 (Kumar et al., 2016) and the

ongoing discussions on the broad landscape of NCDs, especially after the WHO Global Action Plan for the Prevention and Control of NCDs 2013-2020 (WHO, 2013b) was put forward, Africa has far to go in the implementation of strategies to curb them or their rising risk factors (Nyaaba et al., 2017).

Diabetes Mellitus (DM), simply known as diabetes, describes a group of metabolic disorders identified by a chronically elevated blood sugar or glucose due to insulin deficit; either in its secretion, its action or both (Dean & McEntyre, 2004; WHO, 1999). Based on the underlying causes, there are at least five DM sub-groups (American Diabetes Association, 2018; Kuzuya et al., 2002; WHO, 2018) and these are:

1. Type 2 diabetes mellitus (T2DM) (described further below);
2. Gestational diabetes mellitus (GDM) (described further below);
3. Type 1 diabetes mellitus, also formerly called insulin-dependent diabetes, juvenile or childhood-onset; due to deficient insulin production, unpreventable with the current knowledge and requires daily insulin administration;
4. Impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG) that are transition conditions between normality and diabetes with high but preventable risk of progressing to type 2 diabetes; and,
5. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation) (American Diabetes Association, 2018; Kuzuya et al., 2002; WHO, 2018).

T2DM, formerly known as non-insulin-dependent diabetes mellitus, is a chronic metabolic disease with very severe health complications. It occurs from interaction between genetic,

environmental, socio-economic and behavioral risk factors (Chen et al., 2011; Maitra & Abbas, 2005; Olokoba et al., 2012; The National Institutes of Health (NIH), U.S. Department of Health and Human Services, 2011; UK Prospective Diabetes Study (UKPDS) Group, 1998b, 1998a). T2DM is the most common of all types of diabetes, estimated at 90-95% of all types of diabetes, and it is identified primarily among adults and characterized by decreased insulin secretion, insulin sensitivity or insulin resistance (Kuzuya et al., 2002; Ramachandran et al., 2014). It has been increasing worldwide, affecting people from all geographic regions and ethnic backgrounds with an estimated 422 million patients by 2014 and 106 million direct deaths by 2016 (Alberti & Zimmet, 1998; Ramachandran, 2014; WHO, 2018). T2DM has thus become a major public health challenge and roughly 439 million people are globally projected to suffer from it by 2030 (Chamnan et al., 2011). In Africa, despite a large number of people who are unaware of having diabetes, recent surveys show that 15% of Africans between 15-64 years suffer from diabetes, with a regional prevalence estimated at 23.9 million patients by 2030 (WHO, 2017). Between 70-90% of DM cases in Africa are T2DM and are attributed to the high rates of obesity, physical inactivity and urbanisation (Azevedo & Alla, 2008; Osei et al., 2003; Levitt, 2008). Increasing prevalence of obesity among women of childbearing age has led to more cases of T2DM, even though many women remain undiagnosed (Lawrence et al., 2008) till they are pregnant and get screened for GDM at antenatal clinics.

GDM has been defined by the World Health Organisation as "any degree of glucose intolerance with onset or first recognition during pregnancy" (American Diabetes Association, 2004; Metzger, 1998). Pregnant women without either preexisting type 1 or type 2 diabetes are first screened and potentially diagnosed with GDM during second or third trimester of pregnancy. This diagnosis helps to mitigate GDM consequences to both women and their babies during and after delivery (American Diabetes Association, 2018; Kim et al., 2002; Noctor et al., 2016).

The prevalence of GDM in South Africa was estimated at 9.1 % among Black women in a recent study (Macaulay et al., 2018) including in the poor urban settings of Cape Town, and at greater than 15% in other studies (Macaulay et al., 2014; Peer et al., 2012). However, no consensus has been reached regarding the actual prevalence of GDM as its screening and diagnosis in South Africa are "chaotic" (Adam & Rheeder, 2017b). Women who are screened and diagnosed with GDM are referred from local clinics to receive their antenatal care (ANC) and delivery at their nearest tertiary facility and, in contrast to their intensive ANC, they receive little or no attention postpartum (Muhwava et al., 2018). Women with GDM face important risks to their own health and to the health of their infants (American Diabetes Association, 2018; Kim et al., 2011; Xiong et al., 2001). These women are also a high risk group for type 2 diabetes mellitus (T2DM) (Bellamy et al., 2009), a major and growing public and global health problem (Al-Lawati, 2017; Hu, 2011; Unnikrishnan et al., 2017).

Better follow up of women with GDM in order to reduce the risks of developing T2DM requires better coordination between antenatal and postnatal care (Nielsen et al., 2014; Warren et al., 2006), and ideally integration of services which tackle specific diseases and populations. Reports indicate that a small proportion of women with recent GDM (Levitt et al., 2015; Muhwava et al., 2018) return for the recommended postpartum oral glucose tolerance test (OGTT) or other diabetes-related intervention but little is known about the barriers to postpartum care after GDM in LMICs: the few available studies of these barriers have been conducted in contexts outside of Africa (Kugishima et al., 2015; Liu et al., 2019; Sterne et al., 2011). A contributing factor to poor postpartum care in South Africa is thought to be that women must navigate a fragmented health system for their care and the care of their babies; this has stimulated calls for integrated health systems and services that are easy for patients to navigate (Linenkugel, 2000).

In contrast to the scant literature on preventing and managing diabetes including GDM within PHC, the human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) has been extensively studied and addressed in South Africa. HIV/AIDS overwhelmed the South Africa health system before the health system was reorganised to cope with the pandemic and eventually come to offer the largest antiretroviral therapy (ART) programme in the world, including the Prevention of Mother-to-Child Transmission of HIV (PMTCT) within primary health care (PHC) (Cooper et al., 2015; Meyer-Rath et al., 2017). Beyond positioning PMTCT in maternal and child health (MCH) after the AIDS denialism era of 1999 to 2008 – during which any ART was resisted by the national government, as HIV was considered to be irrelevant to the pathology or treatment of AIDS (Barron et al., 2013c; Nattrass, 2008)- the Department of Health in South Africa worked with partners towards its integration into PHC. PMTCT has since been integrated and proven successful (R. Hoffman et al., 2010; Dinh et al., 2012; Barron et al., 2013a; Oelke et al., 2015; Goga et al., 2012), but this has involved a cascade of activities which require that pregnant and postpartum women and their infants be closely followed-up (Chi et al, 2013). It has also led to changes in routine practice in three levels of care which are usually not connected in South Africa: directly pregnancy-related care (antenatal care, delivery, post-natal care), adult women's care (for HIV), and infant care (with the addition of a 6 week test for HIV and further follow up of the infant) (Maphumulo & Bhengu, 2019; Myer et al., 2018). PMTCT integration brought all these services together and served both women and their babies, preventing them from having to navigate different health facilities and sub-systems for their separate services.

Some of these HIV-positive women are also diagnosed with GDM. The way GDM is managed among them in the course of their PMTCT follow up in Africa including South Africa, has not been widely researched on and reported in the literature. Studying integration of PMTCT into existing health care services on the one hand and examining current practice in screening and management of

GDM as a contribution to the efforts to reduce T2DM on the other hand, may offer lessons on how change towards integration of specific services happens in health services and systems. In addition, in light of the history of high prevalence of both HIV and GDM among pregnant women in South Africa (Barron et al., 2013a; Macaulay et al., 2014; Peer et al., 2012), there may be practical lessons learned about integration of care for multiple conditions, including diabetes, into existing health services and systems. Therefore, the experience of integration of PMTCT into PHC may have important lessons for integrating prevention of diabetes among women with recent GDM into PHC as both cover the same population (women and their babies), and in both cases vertical, disease-based programmes interact with broader health systems.

This thesis examines the processes and outcomes of integration of PMTCT, GDM care and prevention of Type 2 Diabetes among women with a history of GDM into routine public PHC in Africa, with a focus on South Africa and the Cape Town metropole. It begins with a systematised narrative review (Mutabazi et al., 2017) examining the integration of PMTCT into public health systems in sub-Saharan Africa (Paper One). It also includes a closer look at how PMTCT was integrated into PHC in South Africa (Mutabazi et al., 2020) (Paper Two). It then examines whether and how GDM screening and care are integrated for women who are already in PMTCT in Cape Town, South Africa, to prevent vertical transmission of HIV (Mutabazi et al., 2020 b) (Paper Three), and then it explores whether and how GDM care – especially postpartum – is integrated in routine PHC beyond PMTCT in this urban setting (Mutabazi et al., 2020 c) (Paper Four). Finally, the thesis returns to the broader context of Africa, concluding with a systematic review and meta-analysis examining the integration of diabetes screening, prevention and care within multimorbidity in public health systems in Africa (Mutabazi et al., 2019), Mutabazi et al., 2020 c) (Papers Five and Six).

The remainder of this chapter outlines relevant literature and background on HIV (especially pediatric HIV and PMTCT) and health systems integration, introduces the study context including a

larger intervention study to which this research contributed, presents the study objectives and hypotheses and the researcher background and outlines the structure and flow of the thesis.

1.2 Global burden of HIV and strategy for its control

HIV remains one of the greatest global public health challenges. Despite tremendous efforts to fight against HIV/AIDS with 21.7 million people on ART, 36.9 million people worldwide were living with HIV at the time of this study in 2017, including 1.8 million people newly infected in that year (Bain et al., 2017; UNAIDS, 2019) and 940,000 HIV-related deaths. Prevention and control of HIV has, for many years, relied on the successful implementation of approaches to prevent new HIV infections and to adequately initiate ART to already infected patients (Medley et al., 2004). Gaps in HIV testing and treatment resulted in 22 million people living with HIV without access to ART, including low coverage among children (UNAIDS, 2015). This situation was the context for launching the United Nations Programme on HIV and AIDS (UNAIDS) 2016–2021 Strategy, a policy and advocacy tool to reach the 90-90-90 target (UNAIDS, 2015). This strategy called for over 90% of all HIV positive persons to be diagnosed, 90% provision of ART for those diagnosed and 90% viral suppression for those treated by 2020 (Bain et al., 2017). This strategy, with an extension to 95–95–95 and the scale-up of other prevention measures by 2030, has so far shown unequal progress (Marsh et al., 2019). Success would require improvements in transparency, accountability and efficiency, as well as monitoring and evaluation systems and good data, including in low and middle income countries (LMICs) like those in sub-Saharan Africa where the HIV/AIDS burden is the highest in the world and in the context of limited resources (Granich et al., 2017).

1.3 HIV and mother-to-child transmission of HIV in Sub-Saharan Africa

Though HIV prevalence and geographical variations differ across and within countries in sub-Saharan Africa, HIV has shaped public health and clinical practice across the continent (Dwyer-Lindgren et al., 2019; LeVasseur et al., 2014). In 2018, there were respectively 20.7 million and 4.9 million people living with HIV in Eastern and Southern Africa (57% of global HIV prevalence) and Western and Central Africa (13% of global HIV prevalence) in 2019 (The U.S. Department of Health and Human Services (HHS), 2020; UNAIDS, 2019). Sub-Saharan Africa contributes more than two thirds of the burden of the global HIV epidemic. Its high prevalence includes a larger number of women of childbearing age than any other population groups (Kharsany & Karim, 2016). HIV positive women can pass the virus to their fetus or newborn during pregnancy, childbirth or breastfeeding, a phenomenon called "mother to child transmission of HIV (MTCT)" or "vertical transmission", which is the main cause of paediatric HIV (Taha, 2011; Yah & Tambo, 2019). Early mathematical models estimated the risk of MTCT of HIV at 7.7% during pregnancy (in-utero), 17.6% for intrauterine and intrapartum combined and 4.9% in late postpartum (John & Kreiss, 1996). Without any ART interventions and taking into consideration the key risk factors (maternal plasma and breast milk viral load and immunological and clinical stage), the models have showed that the risk of MTCT range between 15-45% (Flynn et al., 2016; John & Kreiss, 1996).

1.4 Paediatric HIV and PMTCT integration in South Africa

HIV prevalence was estimated at more than 20% among pregnant women seeking ANC in Botswana, Lesotho, South Africa and Swaziland clinics in 2007 (Taha, 2011). Efforts towards controlling HIV among women of childbearing age and reducing maternal to child transmission of HIV have yielded tangible results, even though HIV among women and children continues to be a serious public health problem (John-Stewart et al., 2017; Mutabazi et al., 2017). In 2008, UNAIDS estimated that 330,000 new paediatric HIV infections occurred worldwide, of which 90% were in Sub-Saharan Africa (Gourlay et al., 2013; UNAIDS, 2019). Since then, a clear trend of reduction has

been observed each year (reduction of 41% between 2010 and 2018) resulting in a decrease of new HIV infections among children to 150,000 in 2019 (Gourlay et al., 2013; UNAIDS, 2019).

The efforts to reduce vertical transmission converged into a consensus approach comprising a series of components and actions to be undertaken before and during pregnancy, at delivery, and after delivery. This set of interventions is known as PMTCT – Prevention of Mother-to-Child Transmission (Avert, 2015; Barron et al., 2013a; Dionne-Odom et al., 2016b; Fokam et al., 2017). The specific components and the guidelines for implementing and monitoring PMTCT evolved over time (Car et al., 2012; John-Stewart et al., 2017), but they have consistently included HIV counselling and testing (HCT), ART initiation and follow-up, HIV testing for babies after delivery, and advice about infant feeding among other services (Aizire et al., 2013; Akinleye et al., 2017; Both & van Roosmalen, 2010; Dionne-Odom et al., 2016b; Hamilton et al., 2017; PEPFAR, 2011). The PMTCT cascade is described in more detail in Paper 1 (Mutabazi et al., 2017).

While early and partial interventions to prevent vertical transmission were tested in South Africa (notably, early trials of single dose nevirapine during delivery (Barron et al., 2013a; Goga et al., 2018), the full multi-component PMTCT cascade that eventually became the preferred approach was considered by the South African National Department of Health (DoH) to be too complex to be successfully and immediately implemented at large scale (Department of Health, Republic of South Africa, 2010). Therefore, PMTCT roll-out to all South African local health facilities took place progressively and its results were encouraging from the very first attempts (Coetzee et al., 2005; Jackson et al., 2007). Health systems that were already overburdened (Doherty et al., 2009) had to adapt and overcome the initial ignorance, confusion and fear persisting from the era of AIDS denialism (D. Fassin, 2003). In the context of a country with a known history of high ANC attendance (90%) and professionally assisted delivery at 84% (Day & Gray, 2008), PMTCT integration was

poised to fit well within maternal and child health (MCH) programmes and services. This would seem to be a good example of health system integration.

1.5 Health systems, integration and integrated care

WHO defined health systems as "the combination of resources, organization, financing and management that culminate in the delivery of health services to the population" (WHO, 2000). They were also redefined as "all activities whose primary purpose is to promote, restore, and maintain health" and more recently broadened to include the prevention of household poverty due to illness (WHO, 2000). Health systems are open to different influences by people and organizations and continuously innovate, learn and adapt through changes and reorganisation that occur in both formal and informal ways (Atun, 2012; WHO, 2000). This is why health systems are referred to by many researchers as complex adaptive systems (Plsek & Greenhalgh, 2001). This complexity is seen through many approaches that have been adopted to roll-out different interventions throughout health systems around the world.

Health system programmes or interventions are considered "horizontal" when services are delivered within general health care and "vertical" when structures, budgets and organization of services focuses on specific health conditions or populations, such as malaria, HIV, or MCH (Elzinga, 2005; Kickbusch & Buckett, 2010; Mills, 1983; Oliveira-Cruz et al., 2003). The terminology of "diagonal" is used when a specific intervention is used with the accompanying aim of strengthening the overall health system (Frenk, 2010; Ooms et al., 2008). Since health systems face a longstanding history of failures and shortcomings in terms of clinical effectiveness while implementing various interventions using one or another of these approaches (Ahmad et al., 2014; Conrad & Shortell, 1996; Kickbusch & Buckett, 2010), another option was needed: integrated care.

The shift away from a vertical and siloed approach to health care and the advantages of integrated care have been increasingly argued (Baxter et al., 2018; Goodwin & Smith, 2011).

Integrated care is promoted as the most appropriate model of health services delivery to address increasing health problems among different population groups and improve patient experience, care outcomes and organisational efficiency in complicated cases of co-morbidity and fragmented health systems (Goodwin & Smith, 2011; Ham & Walsh, 2013). South Africa's quadruple burden of disease (infectious diseases such as HIV/AIDS and tuberculosis; NCDs such as hypertension, cardiovascular diseases, diabetes, cancer, mental illnesses and chronic lung diseases; maternal and child morbidity and mortality; as well as injury and trauma) fits very well in this description (Chopra et al., 2009; Wyk et al., 2016). However, integrated care is also complex and difficult to achieve as the necessary whole-system engagement and wide range of contributions from various stakeholders - both organisations and individuals - that are critical to overcoming fragmentation in health systems are not easily achieved (Ham & Walsh, 2013; Shaw et al., 2011). Effective coordination and strong leadership coupled with practical and technical support are needed to successfully implement truly integrated care at all levels (Goodwin et al., 2012; Lewis et al., 2010; Shaw et al., 2011).

1.6 Approaches to the integration of health care and health systems.

From the Latin verb "integer", which means ***to complete***, integration implies bringing together or merging elements or components that were formerly separate (Kodner & Spreeuwenberg, 2002). In health care, the term "integrated care" is used alternatively with other terms such as "coordinated care", "collaborative care", "patient-centred care", "continuity of care", "transmural care", "seamless care", among others (Atun et al., 2008; Kodner, 2009; Nolte & McKee, 2008). The term used in this thesis is "integrated care" or "integration".

The lack of an internationally accepted definition of integrated care and the use of "integrated service delivery" as well as "integration" as a keyword has enriched debate among health system experts (Atun et al., 2010b; PEPFAR, 2011; Tudor Car et al., 2011). Atun et al. define integration as

"the extent, pattern, and rate of adoption and eventual assimilation of health interventions into each of the critical functions of a health system" (Atun et al., 2010b). The United Nations Population Fund (UNFPA), WHO and International Planned Parenthood Federation (IPPF) defined integration in the following way: "integration can be understood as joining operational programmes to ensure effective outcomes through many modalities; multi-tasked providers, referral, 'one-stop shop', services under one roof" (UNFPA, WHO & IPPF, 2017). Integration is also defined as a process that "occurs at different levels of the health system (regional, district, health facility) and in relation to key health system functions namely governance, financing, planning, service delivery, monitoring and evaluation, demand generation" (Atun et al., 2010a; PEPFAR, 2011). Integration therefore appears to be an important tool for increasing "coordination, cooperation, continuity, collaboration and networking across different components of health service delivery" (Nolte & McKee, 2008). Integration may include but is not synonymous with:

1. Co-location, which means bringing together two services that were previously offered in a separate way in the same place, or
2. Decentralisation - allowing the local health authorities to decide or deliver services, or
3. Mainstreaming, that is making specific services, e.g., mental health, maternal health, indigenous health, part of a comprehensive and seamless health care package at local facilities (Levaggi & Smith, 2003; Odeny et al., 2013; Singer & Adams, 2014).

Integrated care has been defined as "*a concept bringing together inputs, delivery, management and organization of services related to diagnosis, treatment, care, rehabilitation and health promotion. Integration is a means to improve the services in relation to access, quality, user satisfaction and efficiency*" (Gröne & Garcia-Barbero, 2001; WHO European Office for Integrated Health Care Services., 2001). Integrated care also describes a range of organizational arrangements

with variable nature and intensity and refers to two main concepts: a) an organizational structure focused on economic benefits, notably efficiency gains, or b) a way of organizing service delivery: from no integration, to partial integration or full integration (Car et al., 2012; Shigayeva et al., 2010a). "Integrated care" combines processes and mechanisms in its development. "Integrative processes" establish links between the concept of integrated care (intent to deliver services with less duplication and disruption, high quality outcomes and patient experience) and the concept of integration (in terms of methods and approaches for aligning objectives of various professional groups, teams and organisations) (Shaw et al., 2011).

A range of integrative strategies with either a systems or structures emphasis, exists. This thesis considered four:

Firstly, through **the lens of health care system** (Delnoij et al., 2002; Nolte & McKee, 2008; Shaw et al., 2011; Shortell et al., 1996; Scott & Simoens, 1999), integration of care can be categorised as follows:

1. ***Functional integration*** at macro level that includes mainstreaming of the managerial functions (non-clinical and back-office) such as financial, human resources among others, social and regulatory services of cure, care and prevention;
2. ***Organisational integration*** at meso level, in the form of institutional health care networks, mergers, contractors or of strategic partnerships;
3. ***Professional integration***, also at meso level, in the form of professional mergers such as joint or practice groups), contracting or strategic institutional or organisational alliances in health care; and,
4. ***Clinical integration*** at micro level, representing continuity, co-operation and coherence in the service delivery to individuals and families. This clinical integration is achieved through coordinated patient care among various personnel and units mostly at PHC.

Second, considering **the breadth of integration** or the range of provided services in health care, there is:

1. ***Horizontal integration*** that happens between organizations or departments that are at the same level or with the same status on health care delivery; and,
2. ***Vertical integration*** that brings together organizations or units at different levels of hierarchy (Axelsson & Axelsson, 2006; Conrad & Shortell, 1996; Simoens & Scott, 1999).

Thirdly, various **levels of interaction** to improve health care exist between clinical services and people and their institutions (Guidotti, 1976). When the **levels/degree of integration is assessed through the lens of interaction**, it ranges from:

1. ***No integration***, when there are no interactions between health care programs or units;
2. ***Partial integration*** that includes (1) **linkage** or unstructured interactions, and (2) **coordination** with a committee to oversee their goal-oriented works but keeping the separate structures; to,
3. ***Full integration*** in which two programmes are merged in their structures (funds, human resources, informational system) and functional elements (strategic planning, resources allocation, intervention delivery) (Leutz, 1999; Shigayeva et al., 2010a).

Fourthly, based on **the process of integration**, the following types are distinguished:

1. ***Structural integration,*** concerning the alignment of tasks, functions and activities of organizations and healthcare professionals;
2. ***Cultural integration*** including the convergence of values, norms, working methods, approaches and symbols adopted by the various actors;
3. ***Social integration***, with the intensification of social relationships between all the concerned actors; and,
4. ***Integration of objectives, interests, power and resources*** of the involved actors (Fabbricotti, 2007).

Finally, 10 principles have been identified throughout all important integration types and were summarized by Suter et al. (Suter et al., 2007). These principles characterise successfully integrated health systems. These are:

1. Comprehensive service offered across the continuum of care;
2. Patient focus;
3. Geographic coverage and rostering;
4. Standardized care delivery through interprofessional teams;
5. Performance management;
6. Appropriate information technology and communication mechanisms;
7. Organizational culture with strong leadership and shared vision;
8. Physician integration;
9. Strong governance structure; and,
10. Sound financial management.

Based on preliminary formative research in South Africa and the consensus among key informants that PMTCT has been successfully integrated into PHC and that integration of NCDs and specifically diabetes prevention and care was desirable and should at least be attempted, the "no integration" approach was not explored in this thesis. All other types and degrees of integration were considered. In light of multiple challenges within and beyond health care organisations and programmes, full integration might be difficult to reach but all initiatives towards it need to be identified and evaluated. Most integrated health services and systems opt for partial integration with unstructured interactions or other types of collaborations and this study therefore concentrated on this middle option.

1.7 Limits to the current knowledge

Research studies on integrated programs and interventions have been focusing on structural transformation or regulation of existing health systems and universal access but less on learning from the successfully (or unsuccessfully) integrated programs or on the experience of providers, managers and patients (Armitage et al., 2009; Evans et al., 2014; Gillies et al., 1993; WHO, 2014a). Both positive and negative effects of specific interventions in health systems and services have been recognised (Atun et al., 2008; Keugoung et al., 2011; Msuya, 2004; WHO & WHO Study Group on the Integration of Mass Campaigns against Specific Diseases into General Health, 1965) in contrast to very limited studies on the processes and outcomes of integrated programmes (Hartgerink et al., 2013; Shigayeva et al., 2010b; Suter et al., 2009b). Major gaps in the literature are: 1) the lack of information on what successful integration looks like and how to measure achievement towards an integrated system (Armitage et al., 2009; Gillies et al., 1993; Oelke et al., 2015); and, 2) the limited analysis of processes and dynamics of integration and impacts or relationships with overall health systems (as opposed to closely related services). Integration of non-reproductive health activities with PMTCT has received little attention. We have not yet found any studies examining the combination of PMTCT, gestational diabetes, and T2DM prevention.

1.8 Researcher background

Before my journey to this PhD, I was a lecturer at both Namibia University of Science and Technology (then Polytechnic of Namibia) and University of Namibia. I taught health care management, health economics, epidemiology and environmental and occupational health. At the School of Medicine of University of Namibia, I was one of the staff responsible for community-based education and services (COBES), a practical training in the clinics and district hospitals in Namibia. This experience opened my eyes regarding many issues affecting health care delivery at primary and

secondary care levels in low income settings. With Master's degrees including Hospital Administration, Medical Sociology, Labour Management and MPhil in Health Care Management, I had theoretical knowledge but needed more exposure to the true contexts and real life for those working in health systems with limited resources. Previous to my postgraduate training, I had experience while being trained and working in health care in Rwanda, when I saw how health systems in LMICs face different resource shortages and lack of adequate training especially while dealing with outbreaks and chronic and infectious diseases like HIV and NCDs. I started this PhD with a clear objective of learning how more health services could be integrated and help to improve outcomes in health systems. The idea of learning from a programme that has been integrated into PHC like PMTCT in order to integrate screening and care of other health problems starting from those affecting the same population like GDM and T2DM became clear in me and I embarked in designing this study.

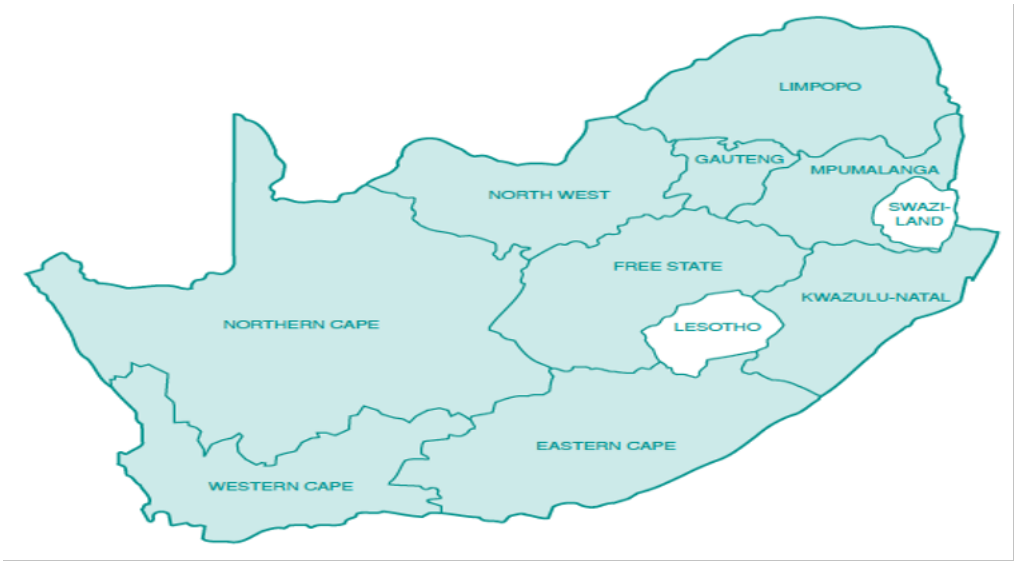
As a male researcher from a different background and without fluency in any local language or understanding of local contexts, carrying out research in Cape Town was not that simple. I am Rwandan and the socio-cultural and health systems contexts I was exposed to in Namibia and India were similar to but not the same as what I experienced in South Africa, where people are open to express their opinions in different ways, an attitude that facilitated my interactions during data collection and fieldwork. Conducting interviews and FGDs with women who were diagnosed with GDM while under PMTCT programmes and with health care providers including community health workers (CHWs) in local health facilities who were almost 100% women, exposed me to the risk of various biases or failure if fieldwork was not well planned. Fortunately, my supervisor who previously was active in public health and HIV research in Cape Town and throughout Western Cape and South Africa as professor at the University of the Western Cape, helped me to organise my research tools, advised me regarding social desirability bias and other contextual barriers. She as well as the South African principal investigators and researchers with the ongoing IINDIAGO (Integrated

INtervention for DIAbetes rIsk after GestatiOnal diabetes) project in which this study was nested (see section 1.8.3) suggested the best ways to minimise fieldwork biases. As they are known to the local health system and researchers, they introduced me to initial key informants who in turn helped me to identify and contact others. Working with the IINDIAGO team facilitated local ethics approvals and arrangements for meetings and to reach out to the local clinics for interviews and FGDs. Senior IINDIAGO researchers, Professor Naomi Levitt and Katherine Murphy were always available for feed-backs, to ensure that data collection was done appropriately and I did not lack necessary support during my entire fieldwork. My research assistant was a female IINDIAGO team member, who was fluent in both local languages, isiXhosa and Afrikaans, and her involvement, especially in FGDs was highly appreciated as she facilitated interactions explaining the research objectives and questions to the participants in their local language.

1.9 Study context

1.9.1: South Africa and its health systems

The Republic of South Africa is located in Southern Africa, covers 1,221,037 square kilometers, with a mid-year population estimated at 59,62 million in 2020 and life expectancy at birth estimated at 62,5 years for males and 68,5 years for females (Statistics South Africa, 2020). It has three capital cities: Pretoria, Cape Town and Bloemfontein, each representing a separate branch of Government; administrative, legislative and judicial respectively. It has 9 provinces and three distinctive, interdependent and interrelated levels of government: national, provincial and local governments with legislative and executive authority for each level (**Figure 1**, from Health Systems Trust review 2018) (Day et al., 2018).

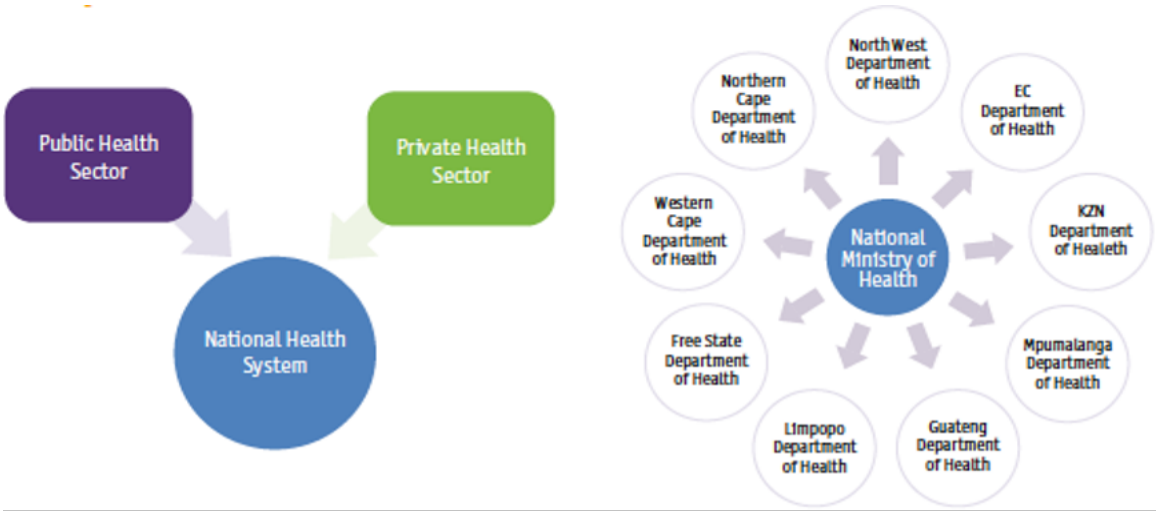


Map of South Africa by province

(Source: Health Systems Trust 2018, used with permission)

Apart from governance, all these government levels play roles in different life sectors of South Africans and foreign residents including immigrants and asylum seekers, including the health sector. This decentralised, multi-level approach has affected the way health care is provided to the population (Koelble & Siddle, 2014). South Africa is consistently ranked as one of the world's most unequal countries (Hundenborn et al., 2019). Its well-documented health inequalities have continued and have even expanded after the end of apartheid and need to be addressed by means of intersectoral approaches, including those starting from the health system (Ataguba & Alaba, 2012; Baker, 2010).

South Africa's health system is organised into public and private health sectors. The majority (84%) of South African residents access health services guaranteed to them by the Constitution (section 27 of the Bill of Rights), through the public health sector (**Figure 2,** from the report of the African Institute for Health and Leadership Development and WHO) (Mahlathi & Dlamini, 2015). In contrast, the private sector offers care to the minority (16%) (Naidoo, 2012), covered either through private insurance or paying out-of-pocket (Delobelle, 2013).



Organisation of South African public health system

(Figure from the report of the African Institute for Health and Leadership Development and WHO, used with permission)

The public health system is structured in different layers including: 1) Clinics (including Community Day Centres), mostly managed by nurses and midwives and offering PHC for basic health needs and referring patients if they require further treatment; 2) Community health centres that are larger clinics with nurses and doctors; and, 3) Hospitals that are grouped into five categories: (a) district hospital; (b) regional hospital; (c) tertiary hospital; (d) central hospital; and (e) specialized hospital. The health services by category throughout South Africa were initially specified in South Africa's National Health Act (61 of 2003) (Republic of South Africa, 2005) but their number increased over time.

1.9.2: Health System in Western Cape and Cape Town

Based on a framework of ensuring the right of every South African who does not hold private medical insurance or who cannot afford to pay out-of-pocket to be eligible for free PHC services, Western Cape Province has a publicly funded, publicly managed, not-for-profit PHC system

(Delobelle, 2013; Republic of South Africa, 2005). With two central, tertiary university teaching hospitals and one specialized pediatric hospital (Tygerberg Hospital, Groote Schuur Hospital and Red Cross War Memorial Children's Hospital) in the province for specialist services, Western Cape serves its population primarily through a network of clinics providing PHC services and standing as the entry point into the health care system (Western Cape Government, Department of Health, 2020). PHC services in the Western Cape province are managed by two separate health authorities, municipal City Health (in the Cape Metro Health District) and provincial Department of Health (DoH). Most district facilities are managed by the provincial DoH. The exception is Cape Metro Health District, which is managed by both City Health and provincial DoH. The Western Cape Province has 479 public PHC centres and these include clinics, of which some mobile and satellite clinics are under the authority of City Health. The provincial DoH manages Community Day Centres and Community Health Centres. All these clinics refer patients to the district provincially aided, regional, specialist and tertiary hospitals available in different parts of the province (Western Cape Government, Department of Health, 2020).

These clinics provide very important PHC preventive, curative and rehabilitative services to the disadvantaged populations, especially those in townships, also known as "locations", which are underdeveloped settlements in urban areas, housing low income racialized populations which still largely live in the racially segregated and economically disadvantaged patterns imposed under apartheid. Black African, "coloured" (mixed-race – in Western Cape representing nearly half of the population (Adhikari, 1991; Greenstein, 2016), and ethnically South Asian populations experience a very heavy burden of disease due to unhealthy environments and life conditions (Moyo, 2015; Smit et al., 2016). The Western Cape has one of the largest townships in the country and in the world, Khayelitsha, which is served by many clinics, a district hospital (Khayelitsha hospital) and neighbouring regional and specialist hospitals; many health research projects with positive impacts

have been conducted in that township (Barron et al., 2013b; Luque-Fernandez et al., 2013; Stinson et al., 2014). Data collection for this thesis was conducted in some of the above discussed facilities across all levels of the health system in Cape Town, the Western Cape, South Africa.

1.9.3: Study nested within complex intervention implementation research

This study was nested within the ongoing "Integrated health system intervention aimed at reducing type 2 diabetes risks in disadvantaged women after gestational diabetes in South Africa" project, known under its acronym IINDIAGO (Integrated INtervention for DIAbetes rIsk after GestatiOnal diabetes), Trial ID: PACTR201805003336174. The overall aim of the IINDIAGO project is to develop and evaluate a novel health system intervention to reduce the subsequent risk of developing T2DM among women with recent GDM, and to identify opportunities and barriers to subsequent scale-up and sustainability within routine, community-based PHC services (Levitt et al., 2015). The intervention comprises (i) shifting post-GDM care and prevention interventions that are currently referred to the day hospital for OGTT, from a hospital to a well-baby clinic setting where women bring their infants for care; (ii) integrating a six week post-partum oral glucose tolerance test into well-baby clinic practice; (iii) providing a brief behaviour change counselling intervention for post-GDM women; (iv) implementing a community-based intervention through the community health workers and outreach teams associated with well-baby clinics, to support women and communities to adopt and maintain healthier lifestyles in a difficult social and economic context. The intervention was developed and is being evaluated through formative research, a pilot randomized control trial (RCT) and mixed-methods process evaluation in two study sites in South Africa: the clinics linked to Chris Hani Baragwanath Hospital in Soweto, Gauteng Province and clinics linked to the University of Cape Town/Groote Schuur Hospital (UCT/GSH) service platforms in Cape Town, Western Cape Province (Levitt et al., 2015).

In relation to IINDIAGO, the study reported in this thesis focused on how vertical programmes and interventions could be integrated in South African health services and systems at the clinic and district levels. Lessons drawn from the PMTCT programme experience in this study informed the IINDIAGO intervention that seeks to integrate activities to prevent T2DM among women who have had GDM into routine PHC at facility and community levels. The doctoral project reported here analysed the perceptions of decision makers, health care providers and women on PMTCT integration, the management of GDM within PMTCT, the desirability and feasibility of integration of T2DM prevention interventions into routine PHC, and assessed how the PMTCT experience might inform more effective integration.

1.10 Relevance of the study

As PMTCT has been lauded as a vertical programme which is being increasingly and successfully integrated into public health care in South Africa, I decided to draw lessons from this apparent success story to explore integration of health systems. Integrating chronic non-communicable diseases and their prevention into PHC is the next major challenge for health systems in LMICs and is the primary focus of this study. This study also considered the ongoing change in South Africa's national health system that aims to develop an integrated district and PHC approach, including community health outreach, in order to integrate health promotion and prevention with disease-based programmes, continuum of care and comprehensive primary care. With this policy development and given the limits of current knowledge about the processes and outcomes of integration of health systems, there is an opportunity to enhance learning and integration across major health issues: HIV, obstetric care, and diabetes. This study has directly informed the final design and process evaluation of the IINDIAGO trial and generated new practical knowledge on how to integrate vertical programs in PHC with a special focus on interventions targeting GDM and T2DM. The findings also highlighted the opportunities and challenges of integration among services targeting key

health problems (postnatal care, GDM, T2DM prevention, and HIV) for the research population: disadvantaged HIV positive and HIV-negative women with recent GDM, and both frontline and management actors in health systems.

1.11 Study aim, objectives, questions and conceptual framework

1.11.1: Study aim

The aim of this thesis was to explore the integration of GDM management and prevention of T2D post-GDM within routine, community-based PHC services in urban South Africa, with a particular interest in whether the experience of PMTCT integration of HIV-positive women and of HCPs may offer insights into how T2DM prevention can be integrated into post-natal primary care. It sought to inform the final design, implementation and process evaluation of the IINDIAGO intervention.

1.11.2: Study objectives

The study aim was achieved through the following specific research objectives:

1. Document the history and experience of PMTCT integration into routine primary health care, particularly in South Africa.
2. Analyse how GDM and T2DM are currently managed and integrated within South African PMTCT programmes, and investigate the advantages and disadvantages of integration of PMTCT as perceived by the various stakeholders in the study site.
3. Explore stakeholders' perceptions (community health workers (CHWs), managers, policy makers, and women) regarding the current and optimal level of integration of GDM and T2DM with antenatal and postnatal PHC.

4. Assess the contextual facilitators and barriers to scale-up and sustainability of an integrated T2DM prevention intervention into routine, community-based PHC services in South Africa and evaluate the process of the initial part of the ongoing implementation of IINDIAGO prevention intervention.

1.11.3: Research questions

The overall question of this study is: How acceptable and feasible is the integration of GDM management and T2DM prevention interventions within community based PHC services, drawing on the lessons learned from PMTCT programmes?

Question 1:

a) Did integrating PMTCT programmes into PHC clinics help to substantially reduce pædiatric HIV and result in advantages for patients?

b) How did integration affect workloads and training needs for health care providers (HCPs) in PHC clinics?

Question 2:

a) What views do experts and HCPs in the local facilities hold regarding integration of GDM screening and prevention of T2DM post-GDM within community-based PHC services?

b) How do both of these stakeholder groups view training and resource issues?

Question 3: How supportive are all stakeholders (policy makers, managers, CHWs and women) of the integration of services through an intervention like IINDIAGO?

Question 4:

a) What are stakeholder perceptions about the desirability, feasibility and sustainability of fully rather than partially integrated interventions and the proposed IINDIAGO prevention intervention into PHC?

b) What are the stakeholder perspectives on the barriers that need to be addressed in order to achieve integration?

1.12 Conceptual framework

Theory based interventions tend to be more effective and successful than those that are not (Noar & Zimmerman, 2005) but unfortunately, there is no unique or common conceptual model for planning and researching health systems integration (Suter et al., 2009a).

Drawing on the discussion of integration and given the lack of a single model that could cover all objectives, this study focused on "levels of integration" and also included elements of three other conceptual frameworks to build the adapted conceptual framework for this thesis. These are: Complex adaptive systems and the WHO health system building blocks, in the light of the UK Medical Research Council guidance on complex interventions and process evaluation; and, the Behaviour Change Wheel.

1.12.1: Levels of integration

First, a description is necessary regarding to what extent and in what ways programmes are integrated. For this, the framework of "levels of integration examined through a lens of interaction" was used. It is based on work by Atun et al. (Atun et al., 2010c) and Shigayeva et al. (Shigayeva et al., 2010b) in which possible interactions between health care programs are specified. These functional relations range from "no formal interactions" when there is no integration, to linkage or coordination as partial integration, to full integration (Shigayeva et al., 2010b).

1.12.2: Complex adaptive systems (CAS) and the WHO health system building blocks in the light of Medical Research Council (MRC)

Next, knowing that many factors influence the degree and dynamics of integration and acknowledging the complexity of integrated preventive interventions, three models were used: the Complex Adaptive Systems framework and the WHO health system building blocks in the light of Medical Research Council guidance for complex health interventions (Begun et al., 2003a; Craig et al., 2008; WHO, 2015) and Behaviour Change Wheel (Cane et al., 2012). Various scholars have proposed complex-adaptive systems (CAS) theory or complexity sciences as a useful theory to understand and work towards integrated health care (Edgren, 2008; Lars Edgren & Keith Barnard, 2012; Nugus et al., 2010). CAS theory and the WHO health system building blocks were applied in the iterative approach to data collection and in seeking to combine predefined exploration of elements and determinants of integration. The CAS openness to emergent and unexpected themes was also applied to describing and analysing behaviour change (among health workers and managers) together with the "levels of integration through a lens of interaction" and Behaviour Change Wheel frameworks.

With respect to our research objectives and study design, the UK Medical Research Council (MRC) framework for the evaluation of complex interventions (Craig et al., 2008; Medical Research Council (MRC), 2000; Skivington et al., 2018) offers practical guidance for applying CAS theory to developing and implementing public health interventions , such as IINDIAGO, that cross-cut various health system building blocks. Complex interventions are defined in the MRC framework as *"built up from a number of components, which may act both independently and inter-dependently"* (M. Campbell et al., 2000). An early research phase is suggested as necessary to define the "active ingredients" of complex health interventions (M. Campbell et al., 2000; Craig et al., 2013). According to the new MRC guidance and considerations for its update (Craig et al., 2008; Skivington et al.,

2018), the development and evaluation of complex interventions go through different nonlinear stages and it is important to contextualize and adapt the programs and interventions to the local realities instead of standardizing them so that they can widely be implementable and replicable.

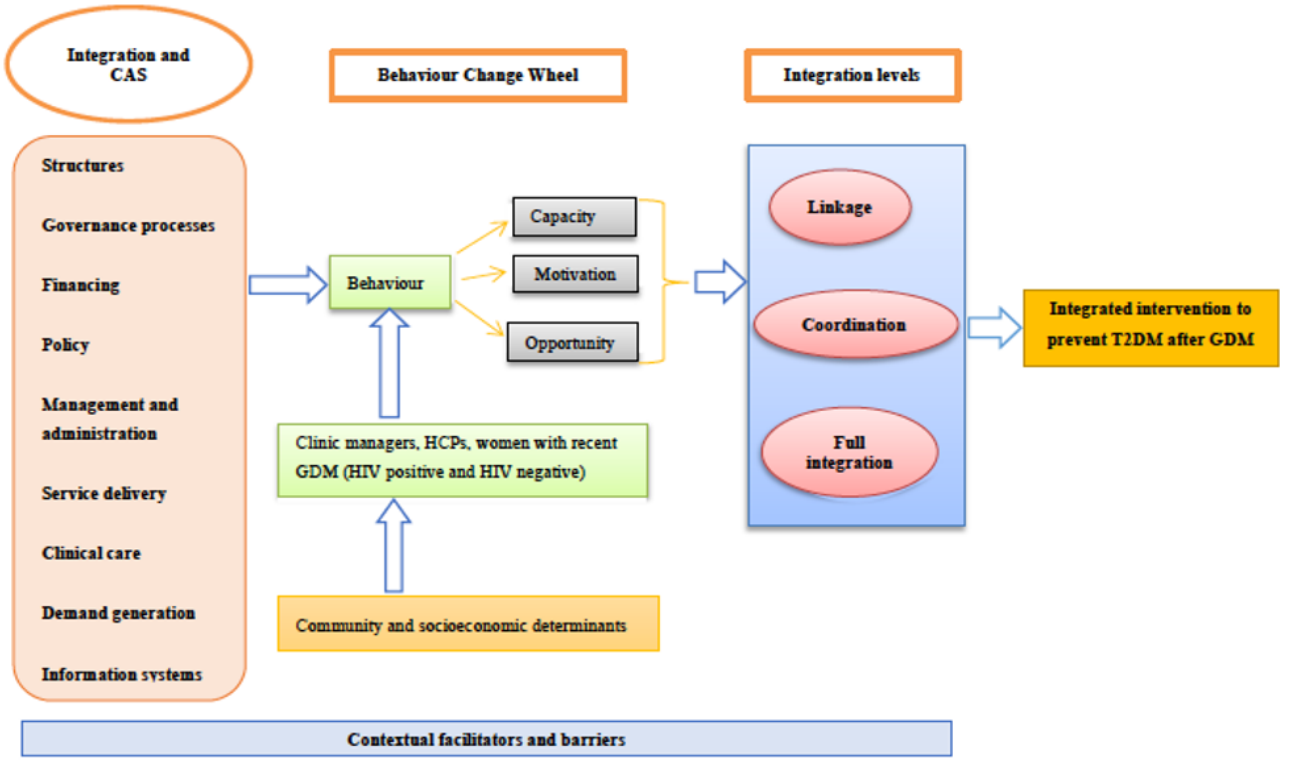
1.12.3: Behaviour Change Wheel (BCW) model

The Behaviour Change Wheel (BCW) model has been documented to be effective for planning and evaluating interventions targeting individuals, groups, programmes and behaviours including both patient and professional behaviours (Michie et al., 2015). Susan Michie's Behaviour Change Wheel underlines nine 'intervention functions' and seven 'policy categories' used to support the selected interventions (Michie et al., 2011). Motivation, capability and opportunity are the key categories of enablers for behaviour change (Moore et al., 2015a), and change (behaviour and systems) should be carried out at both collective and individual levels. In this research project, the behaviour change wheel was used to understand and influence the behaviours of health workers and managers – who as noted above must go beyond their usual practices and interests if integration is to succeed. Apart from approaches to design and evaluate research and interventions, the relations between implementation, mechanisms and contexts (Michie et al., 2015) demonstrate the increasing need and importance of models that can guide both behaviour change interventions and policies (Michie et al., 2011).

1.12.4: The adapted theoretical framework

Based on the above discussed concepts (Begun et al., 2003b; Demaio et al., 2014; Frenk, 1994; Michie et al., 2011; Shigayeva et al., 2010a; WHO, 1996, 2007, 2015) and the study objectives, our conceptual framework considers the core components of integrating preventive interventions in the existing services. It covers interactions between health systems or services, clinic managers and health care providers (HCPs,) women (HIV positive and HIV negative) and their communities within

contextual facilitators and barriers (Figure 3- (Shigayeva et al., 2010a; Michie et al., 2011; Begun et al., 2003b; WHO, 1996, 2007, 2015; Demaio et al., 2014; Frenk, 1994)).



Adapted study framework for integrated intervention to prevent T2DM after GDM

As the objectives included a detailed analysis of several discrete though eventually and potentially intersecting levels and activities, I could not use the entire adapted framework in every paper but rather developed a sub-model specific to the needs of each analysis, based on the particularly relevant components of the overall adapted conceptual framework. CAS components of this adapted framework were used in Paper 2, which explored the perspectives of experts and of frontline health workers on the history of integrating PMTCT into PHC in the context of post-AIDS denialism. Components of the WHO building blocks and of integration levels helped to analyse the lessons from PMTCT integration and assess whether or not this experience could be used to screen GDM and prevent T2DM for these women post-partum, in Paper 3. Paper 4 used the Behavior Change

Wheel framework to evaluate how GDM screening and subsequent T2DM prevention initiatives are and could be integrated into community based PHC services.

As seen in Figure 3, to reach the integrated intervention to prevent T2DM for women with previous GDM, all components need to be considered in the final design and implementation of such an intervention. Documenting the contextual facilitators and barriers based on the results from the already rolled-out and evaluated programmes, PMTCT in this case, enables to examine the adequacy of the existing structures and available resources within the health systems and services to initiate and integrate the desired intervention.

1.13 Structure of this dissertation

This thesis is organised in three parts and seven chapters that are summarised as follows:

Part One introduces the topic, context, conceptual framework and methods.

Chapter 1, Introduction, provides a general background of the study, limits to the current knowledge, study context, relevance of the research, study aim, objectives, questions and conceptual framework.

Chapter 2, Methods, introduces the overall research methods that were used. Detailed methods for each publication are reported in each of the 6 articles included in this thesis.

Part Two presents the results in the form of six articles in three chapters.

Chapter 3 introduces the results from the six articles with an overview.

Chapter 4 reviews the literature on the impact of PMTCT on other health care services and describes the integration of PMTCT and its extent within broader programs and health systems first in Sub-Saharan Africa. This narrative review (Paper One) was published in BMC Public Health Reviews (December, 2017) (Mutabazi et al., 2017).

Chapter 5 presents the main empirical results of this thesis in the form of three articles. The first article, Paper Two, is a qualitative study that documents the history of PMTCT integration and assesses the perspectives of experts and frontline health workers along with persistent barriers to PMTCT integration in South Africa. It was published in BMC Health Services Research (June 2020) (Mutabazi et al., 2020). The second (Paper Three) is a mixed methods study that examines indicators of PMTCT integration in the Western Cape and of GDM integration within PMTCTC. It draws lessons from PMTCT for integrating GDM and T2DM into PHC. It was accepted for publication by the PLoS One journal in December 2020. The third (Paper Four), a mixed methods study that assesses HCPs and women's perspectives and experiences regarding GDM screening and care and the integration of T2DM prevention after GDM into community-based PHC services in South Africa, was submitted to the International Journal of Integrated Care (IJIC) (August 2020).

Chapter 6 wraps up the results section and echoes the narrative review on integration of PMTCT in public health systems by describing the current practices and lessons learned from integrated management of GDM and T2DM within multi-morbidity in Africa through a protocol (Paper Five) that was published in BMJ Open (March 2019) (Mutabazi et al., 2019) and a systematic review and meta-analysis submitted to the International Journal of Integrated Care (IJIC) (August 2020) (Paper Six).

Part Three integrates and discusses all of the papers and key findings in one chapter.

Chapter 7 is the concluding chapter of the thesis. It synthesises the findings and the thesis and discusses areas for future research and global health action on PMTCT as well as GDM, T2DM and other NCDs in South Africa, Africa and other LMICs. It includes also the strengths and limitations of this study as well as the public health impact of this work.

CHAPTER 2: OVERVIEW OF RESEARCH METHODS

Chapter 1 introduced the thesis topic and structure and the notions of vertical, horizontal, diagonal and integrated health services and systems. It also introduced the objectives as well as the conceptual framework, which guided this thesis. This chapter summarizes the research methods of the study as a whole.

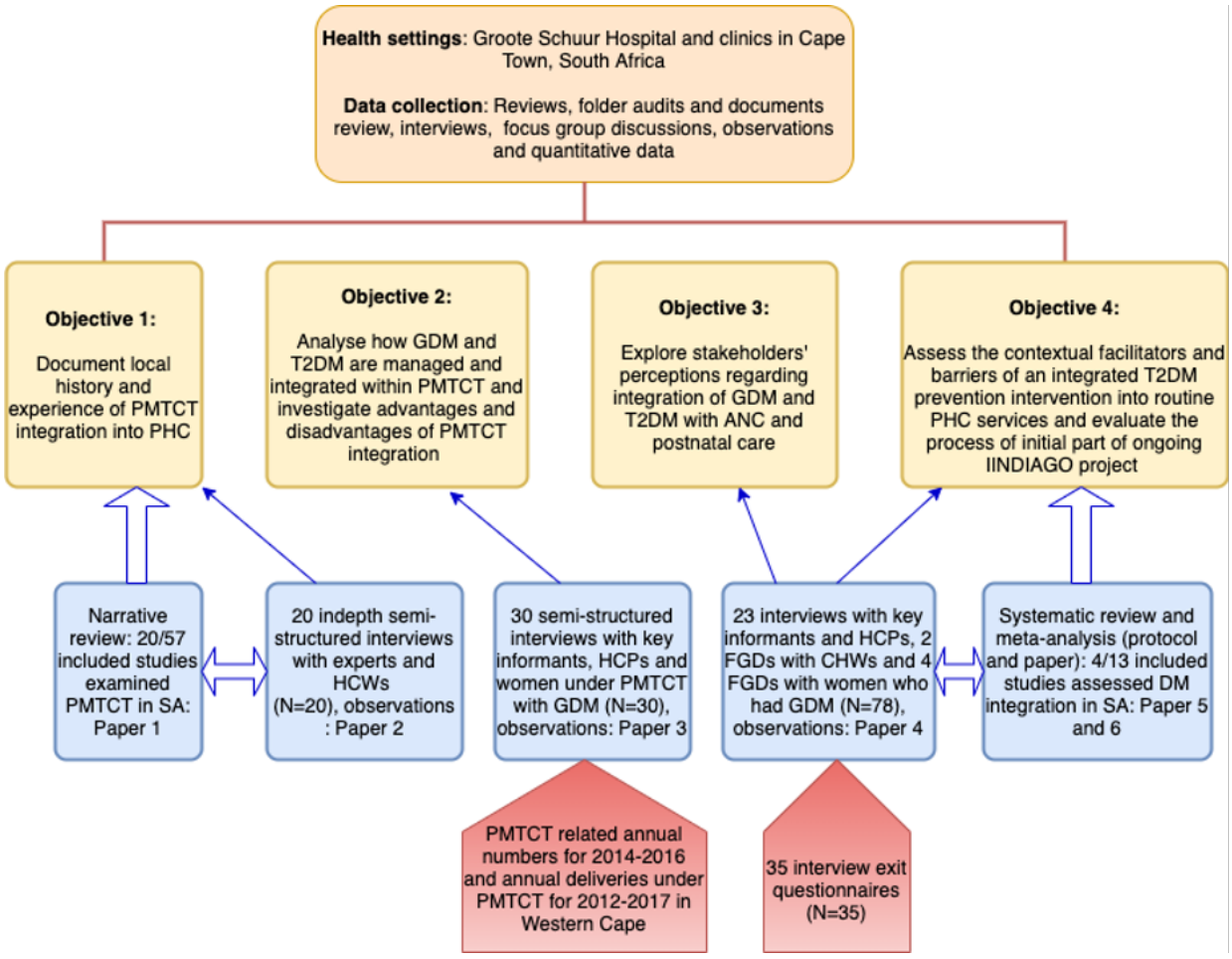
2.1: Overview of research methods

Each article in Chapter 3 (Literature review of PMTCT integration and health systems), 4 (Empirical Results) and 5 (systematic review and meta-analysis) explains the detailed research methods used for the component of the study reported in the article. The following summary outlines the overall methodology for this study.

2.1.1: Study design

This was a convergent mixed methods study, using primarily qualitative methods (Creswell, 2013). Qualitative and quantitative datasets were created through reviewing research papers, policies and guidelines; analysing routine data from hospital and health centre registers; individual interviews with key informants including experts in health systems, HIV/PMTCT, policy makers and specialists in HIV and NCDs like GDM; health care providers (HCPs) including clinic managers, nurses or midwives, community health workers (CHWs); and women in PMTCT and GDM care; focus groups with CHWs and women, and observations of clinic activities.

The overall data sources, study objectives and publications for this thesis are depicted in **Figure 4.**



Data sources, study objectives and publications

2.1.2: Data collection, processing and analysis for the reviews

For the reviews included in this thesis (Papers 1 and 6), published articles were searched using controlled terms (MeSH: Medical subject heading) and free texts. The following databases were searched: Cochrane Library, MEDLINE, PubMed, Embase, SCOPUS, AIDS journal and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). Additionally, manual searches were conducted in Google scholar, ClinicalTrials.gov (ClinicalTrials.gov*) and relevant journals for more studies.*

For the first review (Paper 1), I looked for the papers that examined PMTCT's positive and negative effects on other health care services or vice versa, and integration of PMTCT programs with

other health care services in the paper's title, results and discussion. The abstracts of pertinent papers were then retrieved following these inclusion criteria before selecting the full articles: (i) *Papers* - Research articles published in peer-reviewed scientific journals, grey literature and commentaries dealing with PMTCT in pregnant women in SSA were accepted for inclusion. (ii) *Participants* - Women at risk of transmitting HIV infection to their children. This could include pregnant women or those at risk of pregnancy and their children, regardless of HIV status. (iii) *Interventions* - All interventions to prevent or reduce HIV MTCT, including but not limited to strategies for antiretroviral therapy and replacement feeding.

The following study characteristics and data were extracted from included papers: authors, year of publication and country of study, study types or designs, paper's focus interface with PMTCT, brief topic of investigation and main results. The findings were organized according to the objectives and referred to as 'themes' pertaining to each of two review objectives. Throughout the whole selection process, the impact of PMTCT programmes on other health care services or vice versa was reported in order to describe to how and to which extent it occurred. Integration of PMTCT programs with other health care services at different levels was also described across all included papers.

For the second review (systematic review and meta-analysis protocol (Paper 5) and Systematic Review (Paper 6)), eligible studies were published and unpublished studies on integrated interventions for management of T2DM and GDM in the context of multimorbidity in Africa, without language restrictions. For the meta-analysis, only studies that reported number of patients screened, managed or early cases detected of T2DM and GDM in the context of multimorbidity were included. The following information was extracted for each included study: the baseline characteristics of the eligible research reports (author (s), year of publication, country of study, and study setting); study methodology (study design, target population, sampling strategy, total number of participants, and response rate); intervention and facility (diagnosis, other co-morbidities, service providers (Doctor,

Nurse, Both)), and point of entry/type of facility); study outcomes: (integrated screening outcome; integrated care outcome (preventive, treatment and referral services), cost-effectiveness outcome, and early detection of disease outcome); and approach and level of integration (integration through co-location of services (same room or same clinic), integration of two services OR integration into PHC-mainstreaming, partial integration (linkages, coordination), and full integration.

I performed a narrative synthesis of findings from included studies to facilitate its comparison. For each outcome, prevalence was pooled using the *metaprop* package in the software STATA/SE 14.2. A random effects framework was applied as the data from different studies were expected to be highly heterogenous. In the metaprop package, the prevalence estimates are modelled using the binomial distribution and a Freeman-Turkey double arcsine variance stabilizing transformation is used to normalize the estimates prior to pooling them and then back transformed. For each outcome, computation of the pooled estimates and their confidence intervals was done using the procedure described by DerSimonian and Kacker (Kalra et al., 2011). The Cochrane's Q statistic and I2 statistic were also computed the metaprop package in Stata. Heterogeneity was considered to be present if I^2 test statistics results were $> 50\%$ and Q test and its respective P-value were < 0.05. Forest plots were used to present the prevalence of each outcomes and their 95% confidence intervals (95% CI). Assessment of publication and other systematic biases was done using funnel plots and Egger's statistic (Egger & Smith, 1997).

2.1.3: Data collection, processing and analysis for empirical study (Papers 2,3,4)

South African policy (provincial, national) guidelines were accessed and analysed to document changes in policy guidelines over the period of integration post-2010.

Quantitative data were obtained from the Western Cape Department of Health (annual number of women tested for HIV and the proportion of HIV+ among women screened for the period 2014-2016

and the annual number of deliveries registered within the framework of the PMTCT program for the period 2012-2017) and analysed.

For qualitative data, interviews and FGDs were conducted using interview guides. The study population included PMTCT and health systems experts at provincial and national levels, clinic managers and HCPs who were involved in routine activities within facilities or with policies related to antenatal and postnatal care including PMTCT, GDM, and well-baby care in the public sector in Cape Town, and women who have had gestational diabetes with or without HIV in our study site (Cape Town). I used purposive sampling to ensure a representation of different views and inputs from the key informants including PMTCT and health systems' experts, clinic managers, HCPs and CHWs. Women who were diagnosed with GDM over past two years from the data collection period were identified through hospital databases/registries and invited to participate in this study. Most interviews and FGDs were conducted in English but the research assistant from IINDIAGO who was fluent in local languages (i.e. isiXhosa, isiZulu, Afrikaans) and in English helped to address the questions or clarifications of participants in their local languages to ensure they fully understood the interview questions and probes during the whole process of qualitative and quantitative data collection. A total of 128 different individuals participated in the study, for a total of 73 individual interviews and 6 FGDs (each including 6-10 individuals), as specified in the methods sections of each paper. In addition, descriptive field notes were taken and non-participant observations of clinic practices were conducted using observation guides at every facility visit. Both interview and observation guides are provided in each article appendix. All these datasets were collected and triangulated based on specific study objective as described with full details in every article included in this thesis.

Data from interviews and FGDs were recorded, transcribed verbatim and some responses that were in local languages were then translated in English. Data from clinic observations and field notes

were used to interpret some transcriptions from interviews and FGDs. All transcriptions of qualitative data were anonymised and all identifiable names were removed and replaced with codes before proceeding to their analysis. Policy documents were coded and thematically analysed (Nowell et al., 2017; Vaismoradi et al., 2013). Content analysis (Vaismoradi et al., 2013) was also used to quantify specific codes that were seen as particularly important to the study outcome. The interviews and FGDs were transcribed and all transcriptions were anonymised. All identifiable names were removed and replaced with codes before proceeding to their analysis using an inductive/deductive approach.

The data collected from experts or key informants, clinic managers, HCPs including CHWs and women were linked to information relating to clinic factors as documented in administrative reports and reported by participants as well as descriptions of how the various aspects of the intervention function, in order to explain outcomes. I used the study framework and interview or FGD guides to deductively develop initial codes before qualitative analysis started. With transcripts for analysis, more emerging codes were inductively added and all codes were continuously compared to either assign new or delete duplicated codes. Thematic analysis (Nowell et al., 2017; Vaismoradi et al., 2013) as well as content analysis (Vaismoradi et al., 2013) to quantify specific codes were used based on objectives and design throughout studies with a qualitative arm. The study framework was also used to analyse and interpret the different result components as discussed in the respective articles. ATLAS.ti was used for the overall management and analysis of qualitative data.

All quantitative data were cleaned and statistical analyses were carried out with the software STATA/SE 14.2. To analyse the trend over time for panel data (for women tested for HIV, the proportion of HIV+ among women screened and deliveries registered under the PMTCT program) and spatial data, obtained from GADM (https://gadm.org/data.html), a multilevel modeling approach was used. For each panel, a two-level linear hierarchical model with random intercept and slope (Commenges & Jacqmin-Gadda, 2015; Steele, 2014) was estimated. Categorical variables were

summarised using absolute frequencies and relative frequencies, while continuous variables were synthesized using central trend statistics (mean, median) and dispersion statistics (standard deviation (SD), interquartile range (IQR). To measure the correlation between qualitative variables, we used Cramér's V coefficient which is interpreted as follows : from 0.0 to <0.1 negligible association, from ≥0.1 to <0.3 weak association, from ≥0.3 to <0.5 moderate association and ≥0.5 strong association (Cohen, 2013).

Integration of qualitative and quantitative datasets in the mixed methods studies depended on each study's design. For Paper 3, data were concurrently collected, independently analysed but interpreted together as convergent design was applied (Creswell, 2013; Creswell & Clark, 2017). For Paper 4, exploratory sequential design (Creswell, 2013; Creswell & Clark, 2017) was used, which means that qualitative data were collected before moving to quantitative data collected through exit interviews and analysis was separately done but findings were interpreted together.

For the process evaluation section of the first part of IINDIAGO project that was at the recruitment stage during data collection for this thesis, observations and field notes were used to describe and interpret what was being done in health care facilities and in the study team and what was raised in discussion among IINDIAGO team members. These data were fed back to the team. I also specifically explored stakeholders' perceptions on the desirability, feasibility, and conditions needed for implementation and scaleup of an intervention such as IINDIAGO. These questions were integration into interviews and FGDs and the findings are integrated into Papers Three and Four. I wrote a reflexive synthesis of the process evaluation dimension in the discussion section of this dissertation.

2.1.4: Data collection and reporting

All datasets collected were reported using different evidence-based guidelines based on type of datasets. The Preferred Reporting Items for Systematic Review and Meta-analysis protocol (PRISMA-P) and PRISMA (Moher et al., 2009; Shamseer et al., 2015) flow charts were produced to facilitate transparency of the process for review protocol and reviews respectively. The domains of the Consolidated Criteria for Reporting Qualitative Research (COREQ) (Tong et al., 2007) guided the development of research and reporting of qualitative findings. The methodological quality criteria of the Mixed Methods Appraisal Tool (MMAT), version 2018 (Hong et al., 2018) were used for the design and reporting of results in mixed methods articles. All these appraisal tools are provided in each article appendix. Reflexivity was ensured through field diaries and regular consultation with supervisors, IINDIAGO principal investigators and IINDIAGO staff.

2.2: Ethics approval and consent to participate in the study

Ethics approval was obtained from the Human Research Ethics Committee, Faculty of Health Sciences, University of Cape Town (HREC REF: 946/2014), SA; and Comité d'éthique de la recherche (an accredited Research Ethics Board) du Centre Hospitalier de l'Université de Montréal (CHUM) (2018-6690, 17.044 - ID), Canada. Additional ethics approval was issued by Comité d'éthique de la recherche en sciences et en santé (an accredited Research Ethics Board of sciences and health) (CERSES) de l'Université de Montréal (CERSES-19-059-D), Canada. All certificates of ethics approval, participant information sheet and informed consent form are provided in appendix 6.

Data collection involved participants who voluntarily took part in discussions through interviews and FGDs with the researchers. No physical risks were expected to participants but they were advised to refuse to share some personal information if they did not wish or refuse to answer

questions they were not comfortable with. They were also informed that they had right to stop participating in the study at any point without giving reasons.

Other ethical considerations included written informed consent that was obtained from each participant prior to the interviews and FGDs and signed consent forms were filed for safekeeping for up to 10 years period before being destroyed. The anonymity of all study participants has also been maintained, using only codes assigned to them throughout this research process. A clear and simple language was used during interviews and FGDs and participants were allowed to ask questions and clarify any doubt or any other thing they wanted to know regarding the research and their participation. Participants information sheets containing contact information for a local researcher with IINDIAGO were also handed over to them in case they should need to contact them for further clarifications or counselling.

PART TWO: RESULTS

CHAPTER 3: OVERVIEW OF PART TWO - RESULTS

Chapters 1 and 2 introduced relevant literature on GDM, HIV and PMTCT in general in sub-Saharan Africa, on integrated health services and systems, on the objectives as well as the conceptual framework which guided this thesis.

Chapter 4 begins to address the first objective of the thesis, an analysis of the integration of PMTCT into health systems in sub-Saharan Africa, in the form of a systematised narrative review (Grant & Booth, 2009) which comprises Paper One of this thesis. This review examines the impact of PMTCT on health care services and systems in sub-Saharan Africa, the region with the highest prevalence of HIV in the world. It describes (1) the impact of PMTCT on health care services and assess whether the PMTCT has strengthened or weakened health systems in sub-Saharan Africa, (2) the integration of PMTCT and its extent within broader programmes and health systems in sub-Saharan Africa. We reviewed 225 and included 57 articles, of which 32 recorded the positive and negative impacts of PMTCT on other health care services as their main focus while 25 examined PMTCT and its integration in health systems in sub-Saharan Africa as a main focus. Of these 57 included papers, 23 were classified as multinational as they covered two or more SSA countries, 20 examined the research questions in South Africa, three in Kenya, two for Malawi, two for Tanzania and one for each of the following countries: Democratic Republic of Congo, Lesotho, Rwanda, Senegal, Swaziland, Uganda and Zambia. This systematised narrative review was published in BMC Public Health Reviews (December, 2017) (Mutabazi et al., 2017). It highlighted how PMTCT programmes were integrated into different health systems in SSA and the positive or negative impact this had on other health services. This review informed the final design of the empirical study and the papers, including the decision to focus on implementation in specific contexts but within a larger overall framework that includes complex adaptive systems, health systems and their “building

blocks", and the behaviour of both patients and health care providers in the context of micro, meso and macro systems.

In Chapter 6, we come back to the literature through a systematic review describing the current practices and lessons learned from integrated management of GDM and T2DM within multi-morbidity in Africa. This chapter continues the analysis of integration of vertical programmes into health systems and social systems, this time focusing on GDM, T2DM and multimorbidity to complement the earlier focus on PMTCT of HIV.

Chapter 5 includes three published or submitted papers exploring integration of vertical programmes into PHC in South Africa, seeking to understand the PMTCT experience in order to inform potential integration of GDM and T2DM prevention and management into PHC. While PMTCT is now considered a success story of integration, the history of its integration was complex and may inform integration of other programmes, such as those related to GDM. I used a convergent mixed methods design with primarily qualitative methods (Creswell, 2013) to conduct this empirical study exploring health systems integration in urban South Africa: from integrating prevention of mother-to-child transmission of HIV to prevention of type 2 diabetes after gestational diabetes. Paper 1 (Chapter 3) laid the foundations for a historical perspective on the integration of PMTCT into public health systems in the region and particularly in South Africa. Informed by this "big picture" review, I collected qualitative data to document the local history of the integration of PMTCT into PHC in South Africa during and after the end of AIDS denialism in the country. Paper 2 explores the perspectives of experts and of frontline health workers on the history of integrating PMTCT into PHC in the context of post-AIDS denialism. This second article adds a local perspective to the narrative review (Paper 1), complementing it to cover the first objective of this study. It was published in BMC Health Services Research in June 2020.

The findings from studies on PMTCT integration in South Africa provide a background for analysing whether the experience of integrating PMTCT into PHC has been extended to integrating the care for other problems faced by women with HIV into PMTCT and into PHC more broadly. Paper 3 explores whether one integrated programme – PMTCT – has achieved the goals of the vertical PMTCT programme, and whether it has extended the experience of integration to other conditions, specifically, GDM. It explores how the progress and lessons from PMTCT integration could be used to screen GDM among women under PMTCT and whether this approach could be used to prevent T2DM for these women post-partum. This article focussed on the second objective of this thesis. It was submitted to the PLoS One journal in June 2020 and minor revisions responding to reviewers were submitted in December 2020.

In the fourth article (Paper 4), I moved outside of PMTCT and assessed how GDM screening and subsequent T2DM prevention initiatives are and could be integrated into community based PHC services. This mixed method study documented the experience and knowledge of women who had GDM and navigated health systems for their integrated care and delivery at tertiary hospital but did not have any intervention postnatally planned for them and their babies. It also explored the perspectives of health workers, including community health workers (CHWs), as well as expert key informants, on integration of GDM screening and T2DM prevention into PHC, and asked health workers, women with GDM, and expert key informants their views on an intervention such as the one being tested through the IINDIAGO project. Paper 4 focussed on the third objective and partially addressed the fourth objective. It was submitted to the International Journal of Integrated Care in August 2020.

Building on the literature review examining the impact of PMTCT on health care services and health systems and the empirical exploration of the integration of PMTCT, GDM screening and care,

and T2DM prevention in Chapter 5, Chapter 6 concludes the Results section of this thesis with a systematic review and meta-analysis (Paper 6, and the published protocol, Paper 5) which aimed at identifying and analysing published interventions that integrated GDM and T2DM screening and care in the context of multimorbidity in Africa. The results from the first four articles have shown gaps and many challenges in integrating existing PHC services and interventions to deal with NCDs that are rising in LMICs including South Africa. This chapter moves back to the larger context of Africa and addresses a major challenge facing health systems: integrating programmes for specific conditions, such as diabetes, in a context of multimorbidity and resource constraints.

CHAPTER 4: LITERATURE REVIEW OF THE IMPACT OF PMTCT PROGRAMMES ON HEALTH SYSTEMS

Paper 1 – The impact of programmes for prevention of mother-to-child transmission of HIV on health care services and systems in sub-Saharan Africa - A review

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Status: This systematised narrative review was published in BMC Public Health Reviews (December, 2017) (Mutabazi et al., 2017).
https://doi.org/10.1186/s40985-017-0072-5

Abstract

Background: The global scale-up of Prevention of mother-to-child transmission (PMTCT) services is credited for a 52% worldwide decline in new HIV infections among children between 2001 and 2012. However, the epidemic continues to challenge maternal and paediatric HIV control efforts in Sub Saharan Africa (SSA), with repercussions on other health services beyond those directly addressing HIV and AIDS. This systematised narrative review describes the effects of PMTCT programmes on other health care services and the implications for improving health systems in SSA as reported in the existing articles and scientific literature. The following objectives framed our review:

1. To describe the impact of PMTCT on health care services and assess whether the PMTCT has strengthened or weakened health systems in SSA
2. To describe the integration of PMTCT and its extent within broader programs and health systems in SSA.

Methods: Articles published in English and French over the period 1st January 2007 (the year of publication of WHO/UNICEF guidelines on global scale-up of the PMTCT) to 31 November 2016 on PMTCT programs in SSA were sought through searches of electronic databases (Medline and Google Scholar). Articles describing the impact (positive and negative effects) of PMTCT on other health care services and those describing its integration in health systems in SSA were eligible for inclusion. We assessed 6,223 potential papers from Medline and 21 from Google scholar, reviewed 225, and included 57.

Results: The majority of selected articles offered arguments for increased health services utilisation, notably of ante-natal care, and some evidence of beneficial synergies between PMTCT programs and other health services especially maternal health care, STI prevention and early childhood immunization. Positive and negative impact of PMTCT on other health care services and health

systems are suggested in thirty-two studies while twenty-five papers recommend more integration and synergies. However, the empirical evidence of impact of PMTCT integration on broader health systems is scarce. Underlying health system challenges such as weak physical and human resource infrastructure and poor working conditions, as well as social and economic barriers to accessing health services, affect both PMTCT and the health services with which PMTCT interacts.

Conclusions: PMTCT services increase to some extent the availability, accessibility and utilization of antenatal care (ANC) and services beyond HIV care. Vertical PMTCT programs work, when well-funded and well-managed, despite poorly functioning health systems. The beneficial synergies between PMTCT and other services are widely suggested, but there is a lack of large-scale evidence of this.

Keywords: Maternal and child health, PMTCT, health systems integration, Sub Saharan Africa, narrative review.

Introduction

The global scale-up of Prevention of Mother-To-Child Transmission (PMTCT) services is credited for a 52% worldwide decline in new Human Immunodeficiency Virus (HIV) infections among children between 2001 and 2012 (UNAIDS, 2013). With adequate efforts, more funding and closely monitored progress, the United Nations Programme on HIV and AIDS (UNAIDS) still reported 160,000 new paediatric HIV infections in 2016 (UNAIDS, 2016b). Despite significant progress, the epidemic continues to challenge maternal and paediatric services in Sub-Saharan Africa (SSA), with repercussions on other health services beyond those directly addressing HIV and Acquired Immunodeficiency Syndrome (AIDS) (Mahy et al., 2010).

This systematised narrative review describes the impact and integration of PMTCT programs on other health care services. We begin with an overview of prevention of mother-to-child transmission of HIV in the context of global AIDS control efforts, as well as an introduction to the concepts of integration of "vertical" or disease-based programs into broader health systems. We then present and discuss the findings of our review after having presented the methodology.

Overview: HIV, PMTCT, and health system integration

Preventing – and eliminating – mother-to-child transmission of HIV

The highest prevalence of HIV infection is in sub-Saharan Africa, where rates of both prevalent and new infections are consistently higher among women than men and most women are now diagnosed during pregnancy or at delivery through antenatal and perinatal care (Psaros et al., 2015). The Mother-To-Child Transmission (MTCT) of HIV refers to the spread of HIV from an HIV positive woman to her child either during pregnancy, childbirth (labour, delivery) or breastfeeding. MTCT is the most common mode of transmission of HIV to children. Over 90% of children are infected with HIV through MTCT (Avert, 2015). The interventions aiming to prevent paediatric

HIV/AIDS and for better health of both mothers and their children are known as “prevention of mother to child transmission of HIV” or PMTCT (WHO, 2010a).

Since MTCT can be prevented through antiretroviral therapy (ART), a global campaign for its virtual elimination was launched on 21 May 2009 as one of the top priorities for the World Health Organisation (WHO), the Joint United Nations Programme on HIV and AIDS (UNAIDS), the United Nations Children's Fund (UNICEF) and the United Nations Population Fund (UNFPA) (UNAIDS, 2009). The policy of eliminating new paediatric HIV infections depends on countries reaching not only high rates of initiating ART among pregnant HIV-infected women but also maintaining and supporting them to adhere to treatment (Rollins et al., 2014).

PMTCT interventions

PMTCT, also called “prevention of vertical transmission”, (WHO, 2016a) has been widely implemented in hospital and clinic services particularly in those dealing with antenatal, perinatal and postpartum care. In 2007, WHO and UNICEF developed a guideline document to scale up PMTCT, focusing on resource-constrained settings and efforts towards universal access for women, infants and young children in order to eliminate HIV and AIDS among children (WHO & UNICEF, 2007). The intervention elements to prevent MTCT are known as the PMTCT cascade (WHO, 2010a; WHO & UNICEF, 2007), outlined in summary form (**Table 1**).

Table 1: PMTCT cascade

PMTCT CASCADE (based on our review objectives)		
Component	**Linked to**	
1. Utilisation of ANC	ANC services	**All pregnant women**
2. Receiving HIV pretest counselling	ANC unit or voluntary counselling and testing (VCT) services	
3. Acceptance of HIV test	ANC/VCT services	
4. Receiving HIV test results & post-test counselling	ANC/VCT services	
5. Get CD4 assessment	ANC/VCT services	**HIV-positive Pregnant women**
6. Use of ARV prophylaxis for mom and/or baby (for seropositive moms)	ANC services/ARV programs	
7. Adherence to ARVs during pregnancy	ANC unit/ARV programs	
8. Deliver with skilled attendant & Take ARVs	Obstetric services	
9. Follow safe infant feeding practices	Child health services	
10. Bring infant for HIV testing	Child health or VCT services	
11. Adhere to maternal/infant ARVs after birth	Child health, obstetric or VCT services	
12. Use postpartum family planning	Obstetric services	

This PMTCT cascade reduces the chances for HIV to pass from an HIV-positive mother to her baby during pregnancy, labor, or delivery, or through breastfeeding (Avert, 2015; Brou et al., 2007; WHO, 2010a). Four components of the comprehensive PMTCT programme are articulated by WHO and UNICEF, namely: (1) primary prevention of HIV infection among women of childbearing age; (2) preventing unintended pregnancies among women living with HIV; (3) preventing HIV transmission from a woman living with HIV to her infant; and (4) providing appropriate treatment, care and support to mothers living with HIV and their children and families (WHO, 2010a; WHO & UNICEF, 2007). The PMTCT cascade is partly or fully implemented by many actors from public and private for-profit and not-for-profit health care sectors (Non-Governmental Organisations (NGOs),

religious and community groups) operating locally but managed and funded at local, national and international levels (Both & Roosmalen, 2010; Schechter et al., 2014; WHO & UNICEF, 2012).

These multiple actors with their diverse agendas and policies initially delivered PMTCT services as a stand-alone and externally funded programme. The programmes progressively won the interest of governments and are now increasingly supported through public funding in many countries, while still requiring substantial donor support (Ooms et al., 2008). With time, the strong links this cascade has with maternal and child health services required closer collaboration with and increasing integration into broader services towards sustainable outcomes (Both & Roosmalen, 2010; Nutman et al., 2013).

The worldwide expanded access to PMTCT services prevented more than 670 000 children from acquiring HIV from 2009 to 2012 (UNAIDS, 2013). In 2012, over 900,000 pregnant women living with HIV globally accessed PMTCT services - a coverage of 62% - and only 160,000 new paediatric HIV infections were reported in 2016, compared to 300,000 in 2010 (UNAIDS, 2016a). Four African countries (Botswana, Ghana, Namibia and Zambia) had achieved 90% PMTCT coverage (UNAIDS, 2013) while the PMTCT coverage was over 90% and over 80% in Rwanda and South Africa respectively by 2014 (WHO, 2014c, 2014b).

Based on these promising PMTCT figures in SSA, it is possible to envisage achieving virtual elimination of MTCT. In addition, one could expect to see effects of PMTCT programs on other health care services because PMTCT is now largely implemented through existing maternal health programs and services. However, effects on health services and systems are likely to be uneven and complex.

PMTCT is a complex intervention with many involved actors and policies, flows of knowledge, materials, technologies and funds, interacting at global, national and local levels (Nguyen, 2005; Campbell et al., 2012b). Beyond the operational challenges of actually delivering the cascade on the

ground, this complexity and the history of HIV control programs globally raise systemic and political issues related to the involvement of external funders, experts and manufacturers – sometimes called the global AIDS industry - in funding and implementing HIV services in low and middle-income countries (Nguyen et al., 2007). In addition, PMTCT programs, especially those which aim to be integrated in and help to strengthen health services and systems, seek to address three health goals, each of which is itself a major effort involving different actors, structures and health strategies. These three goals are: combatting HIV/AIDS, reducing child mortality and improving maternal health (Theuring et al., 2009; WHO, 2012). Since health services in many countries are organized, funded and managed to deal with distinct diseases and populations but are seen as parts of an overall health system, these multiple interfaces raise questions of whether PMTCT programs have an overall weakening or strengthening impact on national health systems, or no impact at all beyond PMTCT services. For example, Rwanda's success in scaling up paediatric HIV services through effective utilisation of health resources may offer lessons for other developing countries with high prevalence of maternal and paediatric HIV. This successful integration of PMTCT in Rwanda may be attributed to its health system organisation, despite the weakness of the system (Binagwaho et al., 2013). Even so, in contrast to these reported good PMTCT outcomes in countries with a history of stagnating health systems like Rwanda (and most other SSA countries), there is little evidence-informed meaningful discussion about possible PMTCT effects on other maternal and child health services and on overall health systems. This review examines some of these questions.

PMTCT integration

If we conceptualise PMTCT as a service within a "continuum of care" approach addressing different periods of women's and children's life course, PMTCT programs could be seen to have potential beneficial synergies with other reproductive, maternal and child health interventions such

as Sexually Transmitted Infection (STI) control, early childhood immunization, antenatal and delivery care, family planning, nutrition supplementation (Nutman et al., 2013). For example, maternal deaths have been declining at 2.3% worldwide but this reduction is at only 1.7% in SSA where 9% of all maternal deaths were estimated to be due to HIV/AIDS. The slower rate of decline in maternal deaths in SSA has stimulated interest in a range of recent strategies to increase the coverage of good health care, notably free or very low-cost obstetrical care (Wilmoth et al., 2010). The improvement in HIV-related care of pregnant women should help to increase the impact of these other strategies, and thus contribute to accelerated decreases in maternal mortality in high-HIV burden countries.

The potential impact of PMTCT on health services may go beyond maternal and child health specialities and may involve other health care services indirectly, with potential opportunities to enhance overall quality of care but also posing threats such as brain drain and redirection of resources from programs not related to HIV in contexts where there is already weak infrastructure. This raises questions regarding the appropriate approaches to address the challenges regarding the accessibility, equity, and quality of healthcare in the efforts to facilitate service delivery and strengthen health systems (Uwimana et al., 2012a).

The global monitoring framework and strategy put in place toward elimination of new HIV infections in children (WHO & UNICEF, 2012), reflects this wider perspective of integration across programs and services and calls for comprehensiveness through seven priority areas. These priorities are: (i) Ensure leadership and country ownership; (ii) Improve coverage, access and utilization of services; (iii) Strengthen quality of Maternal, New born and Child Health services to deliver effective PMTCT of HIV and syphilis interventions; (iv) Enhance provision of linked services; (v) Strengthen human resource capacity, supply chain management and information systems; (vi) Improve measurement of performance and impact; and, (vi) Develop and engage community systems (WHO

& UNICEF, 2012). This framework does not take PMTCT as a self-sufficient entity but instead calls for seeing PMTCT as integrated within a health system. It thus echoes the WHO-recommended integration of PMTCT programs with other healthcare services to achieve the more accessibility and improvement of health interventions (Tudor Car et al., 2011). But what does integration entail, analytically and in practice?

Health system integration: Vertical, horizontal and diagonal approaches

The 2003 work of Oliveira-Cruz, Kurowski and Mills on the synergies between vertical and horizontal health interventions (Oliveira-Cruz et al., 2003), remains relevant today. They define vertical programs as free-standing programs delivering health care services, put in place to deal with a particular disease or condition with predetermined goals and designed for a known time frame and calculated financial means. Horizontal programs refer to service delivery through the infrastructure of the regular healthcare system (Oliveira-Cruz et al., 2003). While exploring the impact of vertical programs on health systems and experiences of integrating these programs, these authors encouraged the concerted use of both modes of delivery, according to the capacity of a health system as it changes over time (Frenk, 2010). The combination of both delivery models suggests what Julio Frenk and others refer to as a "diagonal approach" (Ooms et al., 2008). The "diagonal approach" has been referred to as using a disease-specific intervention (e.g. HIV/PMTCT) to strengthen a general health system (Ooms et al., 2008). Working together across initiatives can bring more benefits; for example, the major investments in vertical programs addressing specific diseases or conditions such as HIV can through diagonal financing cross-subsidize other programs and also the overall functioning of the health system because "horizontal" services like labs and human resources are essential to implement the AIDS, TB and malaria programs (Ooms et al., 2008).

There is no internationally recognised definition of integrated care and to further complicate analysis, some researchers who address what could be considered as integrated service delivery do

not use “integration” as a keyword (Tudor Car et al., 2011). Integrated care describes a range of organizational arrangements with variable nature and intensity and comprises two main concepts: a) an organizational structure focused on economic benefits, notably efficiency gains, or b) a way of organizing service delivery: from no integration, to partial integration or full integration (Car et al., 2012; Shigayeva et al., 2010a). For both of these approaches, integration is a process that “occurs at different levels of the health system (regional, district, health facility) and in relation to key health system functions namely governance, financing, planning, service delivery, monitoring and evaluation, demand generation” (Atun et al., 2010a; Tudor Car et al., 2011). Analysis of integrated health care requires a good understanding of health care services and health systems components and functions, and integration must be viewed as a process that accommodates complex agendas and issues as was concluded in a study of postnatal care integration into PMTCT in Swaziland (Car et al., 2012; Mazia et al., 2009).

In terms of implementation practices, PMTCT interventions may be carried out in one or more of the following health services: (1) antenatal clinic; (2) delivery/obstetric/labour ward care; (3) postnatal care; (4) neonatal/new born care; (5) paediatric/infant care; (6) nutritional programs; (7) HIV testing and support centres; (8) HIV treatment centres; (9) reproductive/gynaecological services; (10) sexually transmitted infection clinics; (11) family planning; (12) primary health care which in many settings may be largely focused on conditions such as malaria, acute respiratory infection, diarrhoea and malnutrition; (13) Emergency care; (14) Tuberculosis clinics; (15) Malaria clinics (in areas with high burdens of malaria and HIV); (16) Immunization; (17) or other service (Tudor Car et al., 2011). It is worth underlining the close ties between HIV including PMTCT and tuberculosis or/and malaria in terms of coinfection, prevalence, targeted groups and global funding initiatives (Maher et al., 2005; Ter Kuile et al., 2004; van Eijk et al., 2002). This variety of potential entry points in the context of the discussion of potential synergies suggests how, and how much, the integration

or non-integration of PMTCT could contribute to overall strengthening and integration or weakening and fragmentation of services and systems. In any case, the outcomes depend on how actors collaborate between themselves at health system level, and with the community or individuals seeking health care. A constructive cooperation is encouraged (Oliveira & Russo, 2015; Shigayeva et al., 2010a) to make integration work and minimise its potential negative effects.

One example that demonstrates the need for cooperative efforts to avoid negative effects of a vertical program on health systems and communities relates to the universal child immunization goals. A study in six countries in Africa and Asia documented how a top-down model in immunization interventions ended up creating conflicts between local demand and targets of immunization policy, leading the authors to argue for more intersectoral collaboration if a specific programme is delivered and managed in a vertical way (Oliveira-Cruz et al., 2003). This example is one among many that supports calls for shifting from a vertical view of PMTCT programs of HIV prevention and treatment towards a horizontal focus on maternal health care and other health care services (Both & Roosmalen, 2010; Taylor & Waldman, 1998). Unfortunately, the lessons that might be learned from immunization programs and applied to thinking about PMTCT and health systems have not yet been taken fully into account.

Methods

Objectives

Building on the above overview of PMTCT and health system integration, this systematically conducted narrative review (Grant & Booth, 2009) was based on the following two objectives:

1. To describe the impact of PMTCT on health care services and assess whether the PMTCT has strengthened or weakened health systems in SSA

2. To describe the integration of PMTCT and its extent within broader programs and health systems in SSA.

Search strategy

We searched Medline and Google Scholar databases for papers published in English or French between 1st January 2007 (the year of publication of guidelines on global scale-up of the PMTCT of HIV by WHO, UNICEF in partnership with other institutions) and October 2016. We complemented the Medline search with the Google scholar database, looking for any extra articles or grey literature such as policies and programme evaluations important to our review objectives. The following combined search terms were used:

Search 1: (prevention of mother to child transmission or MTCT or PMTCT or (Transmission* or spread*)) adj3 (Mother* adj3 child*)) or HIV or AIDS or acquired immune deficiency syndrome).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier].

Search 2: (Healthcare or Health care or Primary care or Health systems or Health services or community health systems or Primary health care or Maternal health services or Delivery of care or Health facility).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier].

Search 3: (sub-Saharan Africa or Africa or Africa south of the Sahara or western africa or eastern africa or central africa or southern africa).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier].

The identified papers through these three combined searches were all exported to Endnote bibliographic software (Reuters, 2009).

The search strategy did not explicitly require the terms "impact" and "integration" because we felt that some studies might address ''impact'' and "integration" indirectly, through services description. We defined impact based on the existence of one or more areas of public health action framework as demonstrated through the five aspects of Frieden's 2010 pyramid that underlies intervention with potential health impact (Frieden, 2010). These five aspects are: 1) socioeconomic factors; 2) changing the context to make individual's default decision healthy; 3) long lasting protective interventions; 4) clinical care; and, 5) counselling and education (Frieden, 2010). Integration was defined based on the concept of integrated care as it was above explained.

Inclusion and exclusion

We designed the review inclusion and exclusion criteria for the purpose of retaining all studies pertaining to comprehensive PMTCT components throughout health systems in SSA as discussed in the WHO PMTCT strategy (WHO, 2010a). We looked for the papers that examined this strategy in terms of PMTCT's positive and negative effects on other health care services or vice versa, and integration of PMTCT programs with other health care services in the paper's title, results and discussion.

The abstracts of pertinent papers were then retrieved following these inclusion criteria before selecting the full articles: (i) *Papers* - Research articles published in peer-reviewed scientific journals, grey literature and commentaries dealing with PMTCT in pregnant women in SSA were accepted for inclusion. (ii) *Participants* - Women at risk of transmitting HIV infection to their children. This could include pregnant women or those at risk of pregnancy and their children, regardless of HIV status. (iii) *Interventions* - All interventions to prevent or reduce HIV MTCT, including but not limited to strategies for antiretroviral therapy and replacement feeding. PMTCT collaboration with other health

care services especially maternal and child health (MCH) were included. The following types of articles were excluded: (i) Studies focusing on countries other than SSA countries; (ii) Studies focusing on general HIV/AIDS prevention or other health care services without reference to PMTCT; and, (iii) Editorials or commentaries generally describing the PMTCT programs on one or more pre-specified healthcare services without studying its effects or integration.

Data extraction and analysis

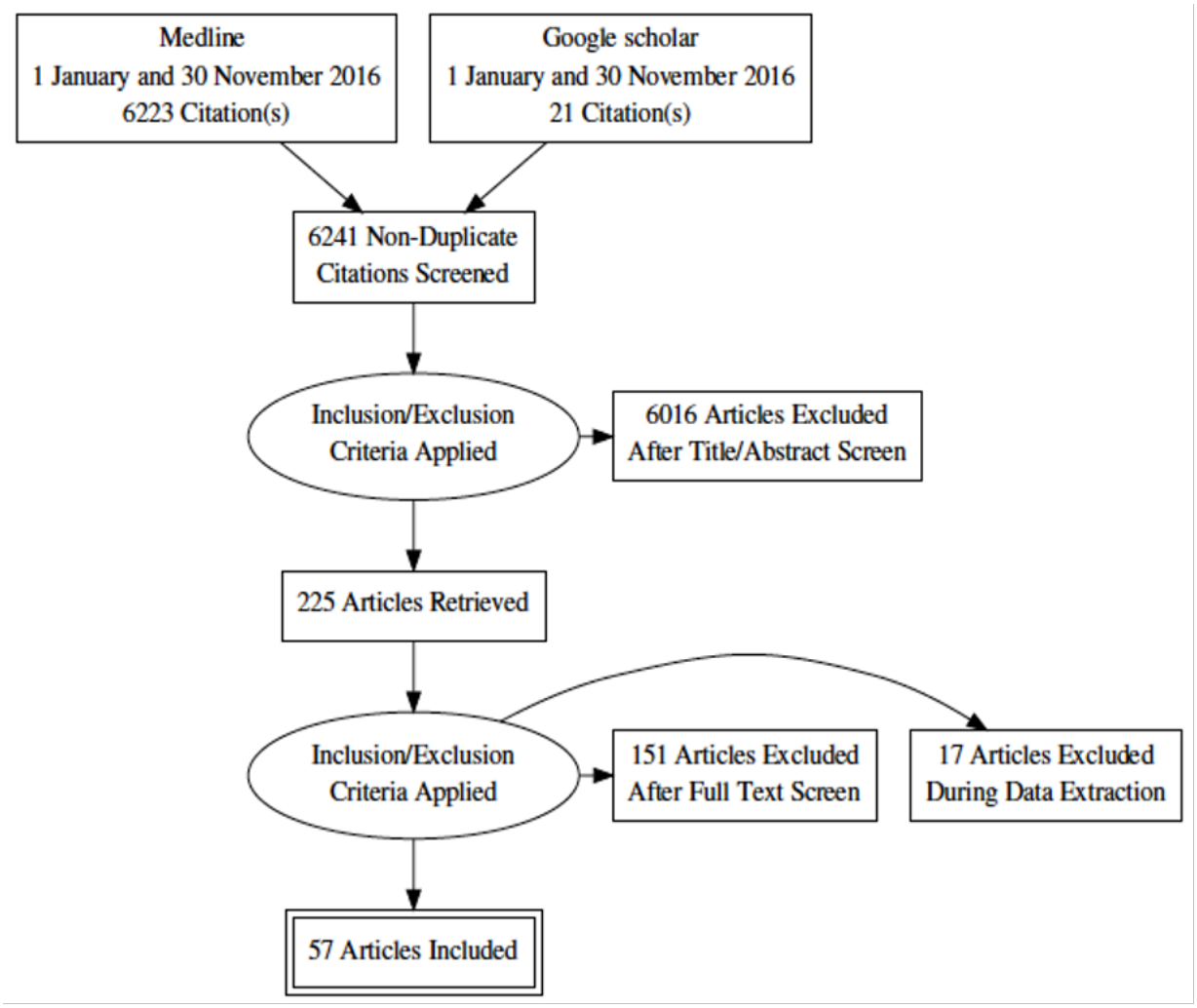
All three reviewers agreed on search strategy and inclusion and exclusion criteria. The initial database was created from the compiled electronic searches by one reviewer. All citations were firstly screened by title and abstract and duplicate citations were eliminated. The full texts of potentially eligible papers were then independently obtained for further screening. After resolving differences in data extraction or interpretation through consensual discussions based on the above stated inclusion and exclusion criteria, the final retrieval of papers was conducted. The following study characteristics and data were extracted from included papers: authors, year of publication and country of study, study types or designs, paper's focus interface with PMTCT, brief topic of investigation and main results. The findings were organized according to the objectives and referred to as 'themes' pertaining to each of two review objectives.

Throughout the whole selection process, the impact of PMTCT programs on other health care services or vice versa was reported in order to describe to how and to which extent it occurred. Integration of PMTCT programs with other health care services at different levels was also described across all included papers. Two guidelines on global scale-up of the PMTCT were also retrieved. The findings were organized or categorized according to the review objectives.

Results

We identified 6,223 citations from Medline and 21 from Google scholar and ultimately retained 57 articles, in addition to the above mentioned PMTCT guidelines also retrieved from google scholar as grey literature. These two guidelines are: 1) The global plan for elimination of new HIV infections among children by 2015 and keeping their mothers alive; and, 2) The PMTCT strategic vision 2010–2015: preventing mother-to-child transmission of HIV to reach the United Nations General Assembly Special Session (UNGASS) and Millennium Development Goals (Nakakeeto & Kumaranayake, 2009; PEPFAR, 2011; WHO, 2010a). The study selection process is presented in the form of an adapted PRISMA flow-diagram (Figure 5) and the retained articles are summarized in **Table 2**.

Table 2 describes the included studies in which different types of research designs and data collection methods were used. Two papers were categorised as policy-evaluative (one that evaluates PMTCT policies and one that assesses various national strategic plans in 20 countries in Eastern and Southern Africa). One descriptive study presented a health program. Eighteen reviews, nine qualitative studies, thirteen quantitative studies, and eight mixed methods studies were selected along with six controlled trials and one quasi-experimental study. In most of the studies, hospital and clinical records were reviewed and individual or group interviews with women and staff members involved in health care and PMTCT services were conducted by the researchers among the selected areas/sites and participants.



Adapted PRISMA flow-diagram

Table 2: Characteristics of included articles

No. Autors, year and country of study	Study types or designs	Focus interface with PMTCT	Brief topic of investigation	Main results
1. Bancheno WM et al. 2010/ Swaziland (Bancheno et al., 2010)	Mixed	Maternal and child health (MCH)	Reporting the outcomes and challenges of a comprehensive service to PMTCT	Provision of a complete package of PMTCT services in resource limited setting is possible but challenged by staff shortage, socio-economic and service-related factors

2. Barker PM et al. 2011/ RSA (Barker et al., 2011)	Quantitative	Health systems	The impact of health systems' performance on MTCT	It's necessary to support PMTCT interventions at scale to achieve gains in maternal and child survival
3. Barker PM; Mate K. 2012/ Multicountry (Barker & Mate, 2012)	Quantitative	MCH	Eliminating mother-to-child HIV transmission will require major improvements in maternal and child health services	Access to maternal and child health services along with prevention measures and HIV treatment before pregnancy need to dramatically be improved
4. Barry OM et al. 2012/ RSA (Barry et al., 2012)	Quantitative	ANC	The patient-provider relationship (PPR) in ANC and its importance in PMTCT	PPR scale is useful and context-appropriate instrument that could have an important role in future research focusing on improved PMTCT and decreasing the risk of pediatric HIV
5. Behets F et al. 2009/ RDC (Behets et al., 2009)	Quantitative	ANC, maternal health	Reducing vertical HIV transmission	Initiating vertical HIV transmission prevention embedded in improved antenatal services in a fragile, fragmented, severely resource-deprived health care system was possible and improved over time
6. Both JMC et al. 2010/ Multicountry (Both & Roosmalen, 2010)	Systematic review	Maternal health	The impact of Prevention of PMTCT programs on maternal health care (MHC)	Integrated PMTCT programs can lead to more positive effects despite its current positive and negative impact on MHC
7. Chi BH et al. 2013/ Multicountry (Chi et al., 2013)	Review	Health facilities, health policy	Antiretroviral drug regimens to prevent mother-to-child transmission of HIV	Global campaigns to "virtually eliminate" pediatric HIV and dramatically reduce HIV-related maternal mortality have mobilized new resources and renewed political will
8. Cotton MF et al. 2008/ RSA (Cotton et al., 2008)	Quantitative	Tuberculosis (TB)	Tuberculosis exposure in HIV-exposed infants in	Programs to prevent MTCT offer an important opportunity to screen for TB. In-depth assessment

			a high-prevalence setting	is required for evaluating TB exposure.
9. DeGennaro V; Zeitz P. 2009/ Multicountry (DeGennaro & Zeitz, 2009)	Review	Family, pediatric AIDS	Family-centred response to the HIV/AIDS epidemic for the elimination of pediatric AIDS	Governments must embrace family-centred and implement pediatric-friendly infrastructure, and train healthcare workers to treat children care in order to eliminate pediatric HIV/AIDS
10. Desclaux A et al. 2012/ Senegal (Desclaux et al., 2012)	Qualitative	Social issues	Social stakes to eliminate MTCT by 2015	Integration of HIV testing and treatment in RH services is not fully established and health services organization hinders family approach of prevention
11. Druce N; Nolan A. 2007/ Multicountry (Druce & Nolan, 2007)	Review	Maternal health	linking HIV and maternity care services	Experience in some countries has shown that progress can be made whenever nationals are committed to resources increase to meet HIV maternal and newborn needs
12. Du Plessis E et al. 2014/ Kenya (du Plessis et al., 2014)	Quantitative	ANC	Challenges to PMTCT implementation	Guideline implementation in low resource settings continues to be confronted with challenges related to late presentation, less than four ANC visits, low screening rates for opportunistic infections and limited contraception counselling
13. Ekouevi DK et al. 2012/ Multicountry (Ekouevi et al., 2012)	Mixed	Health facilities	Health facility characteristics associated with effective PMTCT	There is a positive relationship between an antenatal quality score and PMTCT coverage but variables to predict PMTCT coverage were not identified
14. Evjen-Olsen B et al. 2009/ Tanzania	Descriptive*	MCH	Integrating PMTCT on healthcare services	Horizontal and comprehensive services should be strengthened and supported at all

(Evjen-Olsen et al., 2009)				levels towards a sustainable MCH impact
15. Ferguson L et al. 2012/ Multicountry (Ferguson et al., 2012)	Systematic review	Maternal health, ANC and post-natal care (PNC)	Linking women who test HIV-positive in pregnancy-related services to long-term HIV care and treatment services	Providing 'family-focused care', integrating CD4 testing and providing HAART into PMTCT services are promising for increasing women's uptake of HIV related services
16. Gibbs A et al. 2012/ Multicountry (Gibbs et al., 2012)	Analytical **	MCH	Inclusion of women, girls and gender equality in National Strategic Plans for HIV and AIDS	There is poor inclusion, except the accessible post-exposure prophylaxis in the case of sexual violence and vertical transmission services
17. Govender T; Coovadia H. 2014/ Multicountry (Govender & Coovadia, 2014)	Review	ANC, MCH	Eliminating mother to child transmission of HIV-1 and keeping mothers alive	Family planning messages and provision of contraception methods to avoid unplanned pregnancies are more effective than HIV counselling and testing, and single dose Nevirapine in averting transmission of perinatal HIV infection.
18. Gunn JK et al. 2016/ Multicountry (Gunn et al., 2016)	Quantitative	ANC	Relationship between ANC and PMTCT in SSA. Analysis of data from four countries.	Integration of HIV testing into routine ANC service is needed to increase opportunities for PMTCT programs to reach HIV-positive pregnant women.
19. Harrington EK et al. 2012/ Kenya (Harrington et al., 2012)	Quantitative	Family planning (FP)	Fertility intentions and interest in integrated FP services among women living with HIV	Integration of FP and HIV services is acceptable and should be supported for preventing the unintended pregnancies through increased access to contraceptive methods and confidential services that take into account women's varied reproductive intentions

20. Hatcher AM et al. 2014/ RSA (Hatcher et al., 2014)	Qualitative	Partners of PMTCT women	Links between HIV and intimate partner violence in pregnancy	HIV diagnosis during pregnancy and subsequent partner disclosure are common trigger of IPV
21. Hoke T et al. 2014/ RSA (Hoke et al., 2014)	Mixed	FP	Contraceptive options for PMTCT clients	Consistent access to high quality FP services that are effectively linked to HIV services, attention must also be focused on resolving underlying health system constraints weakening health service delivery more generally.
22. Horwood C et al. 2010/ RSA (Horwood et al., 2010)	Mixed	MCH	Evaluating PMTCT implementation and integration into routine maternal, child and women's health services	Poor integration of PMTCT services into routine care, lack of clarity about health worker roles and poor record keeping constitute barriers to services accessibility in post-partum
23. Jashi M. et al. 2013/ Multicountry (Jashi et al., 2013)	Review	Pediatric HIV care	PMTCT - paediatric HIV joint technical missions	Joint technical missions bring together stakeholders for common action towards informed PMTCT and paediatric HIV policies
24. Kaida A et al. 2010/ RSA (Kaida et al., 2010)	Quantitative	Contraceptives	Investigating the contraceptive use and method preferences by HIV status and receipt of HAART among women	Integrated HIV and sexual and reproductive health services have potential to positively impact maternal, partner, and child health.
25. Karl Peltzer et al. 2009/ Multicountry (Peltzer et al., 2009)	Randomized control trial (RCT)	FP	Family Planning - effects of PMTCT	HIV prevention and FP should consider the reproductive desires of HIV positive women and men
26. Kerber KJ et al. 2013/ RSA (Kerber et al., 2013)	Systematic review	Child deaths	Meeting Millennium Development Goal 4 through HIV services	Failing to address other aspects of care like the integration of high-quality maternal and neonatal care leads to

				low decline in child mortality
27. Kerouedan D. 2010/ Multicountry (Kerouedan, 2010)	Evaluative ***	Global Fund-health policy and systems	Evaluating policy issues	Health systems' weaknesses at district level, such as human resources, laboratory commodities, and medicine shortages are major constraints to further expansion of services and impact of funds
28. Ladur AN et al. 2015/ RSA (Ladur et al., 2015)	Qualitative	Male involvement	Perceptions on Male Involvement in PMTCT	HIV testing, disclosure and direct health worker engagement with men increases male involvement in PMTCT.
29. Lassi ZS et al. 2014/Multicountry (Lassi et al., 2014)	Review	Neonatal health	Essential pre-pregnancy and pregnancy interventions	Proper implementation of a set of essential interventions leads to both improved and sustained maternal, neonatal and child health outcomes
30. Levy JM. 2009/ Malawi (Levy, 2009)	Qualitative	ANC, MCH	Examining women's decisions about HIV testing and their experience of PMTCT and HIV-related care	Women's own health was particularly marginalised within the PMTCT programs but good models exist for comprehensive care for women, infants and their families
31. Lyons C et al. 2012/ Multicountry (Lyons et al., 2012)	Commentary& supplement article	MCH	Ending pediatric AIDS and achieving a generation born HIV-free	Scale-up of PMTCT has provided a foundation for HIV prevention and care and treatment programs that are integrated within maternal and child health services
32. Nassali M et al. 2009/ Uganda (Nassali et al., 2009)	Qualitative	MCH, PNC	Adherence to the postnatal PMTCT program	Strategies to increase mothers' adherence to PN-PMTCT interventions leads to increased HIV/AIDS care access for mothers and children in SSA are recommended

33. Nutman S et al. 2013/ Multicountry (Nutman et al., 2013)	Systematic review	STIs and child immunization	Assessment of PMTCT impact in all low- and middle-income countries	There are beneficial synergies between PMTCT programs and both STI prevention and early childhood immunization.
34. O'Reilly KR et al. 2013/ Multicountry (O'Reilly et al., 2013)	Systematic review	FP and counselling	FP counseling for women living with HIV	There is a need for strengthened efforts to integrate family planning counseling and access to services into HIV prevention, and for greater consistency of effort over time.
35. Peltzer K et al. 2010/ RSA (Peltzer et al., 2010)	Mixed	Health systems	Assessment of the PMTCT implementation across health facilities	A well-functioning health system empowers PMTCT clients through strong leadership, coordination and collaboration between partners.
36. Pirkle CM et al. 2014/ Multicountry (Pirkle et al., 2014)	Quantitative	Nutrition	Training and nutritional components of PMTCT programs	Health professionals' training in maternal healthcare and PMTCT could be combined to improve the quality of obstetric care in the region.
37. Potter D. et al. 2008/ Zambia (Potter et al., 2008)	Quasi-experimental	MCH, Primary health care	Improve overall care for pregnant women	Broader primary care impact and full PMTCT integration should be targeted.
38. Rollins N et al. 2007/ RSA (Rollins et al., 2007)	Quantitative	Immunization	Surveillance of MTCT prevention programs at immunization clinics	Anonymous HIV prevalence screening of all infants at immunization clinics is feasible and could help to monitor the impact of PMTCT programs in peripartum infection, in identifying the infected children early for referral into care and treatment
39. Roxby AC et al. 2014/ Multicountry	Review	MCH	A lifecycle approach to HIV prevention in	The potential for synergistic and additive benefits of lifecycle interventions should be

(Roxby et al., 2014)			African women and children	considered when scaling up HIV prevention efforts in SSA
40. Ruton H. et al. 2012/ Rwanda (Ruton et al., 2012)	Mixed	Child health, community	PMTCT - community-based household survey	National PMTCT programs in SSA should assess the effectiveness of their interventions to achieve the MTCT elimination goals
41. Rutta E. et al. 2008/ Tanzania (Rutta et al., 2008)	RCT	MCH	PMTCT in a refugee camp setting in Tanzania	Integrated PMTCT (into existing ANC) is more successful and acceptable
42. Sarnquist CC et al. 2013/ Multicountry (Sarnquist et al., 2013)	Review	SRH and FP	Sexual and reproductive health and family planning needs among HIV-infected women in Sub-Saharan Africa	Integrated services that help prevent unintended pregnancy and optimize maternal and infant health before, during and after pregnancy are also useful for both resources maximization and improvement of reproductive outcomes
43. Shetty AK. 2013/ Multicountry (Shetty, 2013)	Review	MCH, PNC	Epidemiology of HIV infection in women and children: a global perspective	Rapidly implemented combination of HIV prevention packages provides quality PMTC services and improves maternal and infant survival.
44. Spangler SA et al. 2014/ Kenya (Spangler et al., 2014)	Quantitative	Maternal care	HIV-positive status disclosure as factor for the use of PMTCT and maternal care	Interventions to promote HIV disclosure must recognize the impact of HIV-related stigma on disclosure decisions and protect women's rights, autonomy, and safety.
45. Sprague C et al. 2011/ RSA (Sprague et al., 2011)	Qualitative	MCH	Women's experiences on continuum of maternal and child care	There are missed opportunities for HIV testing in ANC due to huge operational weaknesses in HIV services.
46. Sinunu MA et al. 2014/ Malawi	Quantitative	Immunization	Immunization clinic-based surveillance of	Successfully implemented PMTCT program averts HIV

(Sinunu et al., 2014)			PMTCT and evaluation of PMTCT impact	transmission and can be evaluated over time for impact through immunization settings.
47. Tomlinson M et al. 2014/ RSA (Tomlinson et al., 2014)	RCT	Health systems, community and MCH	Evaluate an integrated, scalable package of pregnancy and post-natal home visits	Implementation of a pro-poor integrated PMTCT and maternal, neonatal and child health home visiting model is feasible and effective.
48. Towle M; Lende DH. 2008/ Lesotho (Towle & Lende, 2008)	Qualitative	Community	Social groups and contextual determinants impacting PMTCT	Biomedical system, women, children and the community have to be considered as valuable partners in achieving positive health outcomes.
49. Uwimana J et al. 2012/ RSA (Uwimana et al., 2012a)	Mixed	NGOs, Community care Workers (CCWs) and TB/HIV	Engagement of NGOs and community care workers in collaborative TB/HIV activities including PMTCT	Efforts to engage the NGO/CCWs for implementing collaborative TB/HIV/PMTCT activities are beneficial but sub-optimal in practice.
50. Uwimana J et al. 2012/ RSA (Uwimana et al., 2012b)	Qualitative	TB/HIV	Health system barriers to implementation of collaborative TB and HIV activities including PMTCT	Accelerated implementation of collaborative TB/HIV activities including PMTCT requires political will and leadership to address these health systems barriers.
51. Uwimana J et al. 2012/ RSA (Uwimana et al., 2012c)	RCT	TB/HIV	Training community care workers to provide comprehensive TB/HIV/PMTCT integrated care	Up-skilling CCWs could be one avenue to enhance TB/HIV case finding, TB contact tracing and linkages to care.
52. Uwimana J; Jackson D. 2013/ RSA (Uwimana & Jackson, 2013)	Qualitative	TB	Assessing the integration of TB services into the PMTCT	The adequate integration of TB prevention and care into the PMTCT programme will require a strong leadership that addresses training and supervision barriers.

53. Uwimana J et al.2013/ RSA (Uwimana et al., 2013)	RCT	TB-HIV	Impact assessment of an intervention to enhance the provision of community-based integrated services for TB, HIV and PMTCT	The effective intervention in enhancing the provision of community-based TB-HIV and PMTCT services requires more attention to other primary health care services to ensure that all key services are provided.
54. Vermund SH; Hayes RJ. 2013/ Multicountry (Vermund & Hayes, 2013)	Review	MCH, PNC	Combination prevention to stop HIV	Combination approaches are complex and costly. They require substantial global commitments.
55. Wettstein C et al. 2012/ RSA (Wettstein et al., 2012)	Systematic review	MCH	Determining the magnitude and reasons of loss to program and poor antiretroviral prophylaxis coverage in PMTCT	Uptake of PMTCT interventions and early infant diagnosis is unsatisfactory. An integrated family-centered approach seems to improve retention.
56. Wiysonge CS et al. 2011/ Multicountry (Wiysonge et al., 2011)	Review	ANC, PNC, Vitamin A	Vitamin A supplementation for reducing the risk of MTCT	vitamin A supplementation probably has little or no effect on MTCT in ANC or in postpartum.
57. Woldesenbet S et al. 2015/ RSA (Woldesenbet et al., 2015)	Mixed	MCH, Communities and health facilities	Risk factors for low PMTCT service uptake	Strengthened linkages of referral-system and between communities and health facilities can address factors to low PMTCT service uptake.

***** The paper described a health program in presentation form
** National strategic plans in 20 countries were assessed in this study
*** The paper evaluated policy issues and commented on them

Key informants such as policy makers, district health workers, academicians, implementing partners and persons living with HIV were also contacted in the research process in most of selected articles. Many programs and services were classified as fully vertical while a few others were

perceived as either semi or fully integrated based on the extent of verticality or horizontality of PMTCT programs (Both & Roosmalen, 2010; Druce & Nolan, 2007).

Thirty-two articles recorded the positive and negative impact of PMTCT on other health care services as the main findings in the article's title and/or discussion, out of fifty-seven (Bancheno et al., 2010; Barker et al., 2011; Barker & Mate, 2012; Barry et al., 2012; Behets et al., 2009; Both & Roosmalen, 2010; Chi et al., 2013; Chi et al, 2013; Cotton et al., 2008; DeGennaro & Zeitz, 2009; du Plessis et al., 2014; Ekouevi et al., 2012; Gibbs et al., 2012; Govender & Coovadia, 2014; Hatcher et al., 2014; Kerouedan, 2010; Ladur et al., 2015; Lassi et al., 2014; Levy, 2009; Nassali et al., 2009; Nutman et al., 2013; Peltzer et al., 2009; Pirkle et al., 2014; Potter et al., 2008; Roxby et al., 2014; Ruton et al., 2012; Shetty, 2013; Sinunu et al., 2014; Spangler et al., 2014; Sprague et al., 2011; Towle & Lende, 2008; Wiysonge et al., 2011). Twenty-five articles examined PMTCT and its integration in health systems in SSA as the main findings (Desclaux et al., 2012; Druce & Nolan, 2007; Evjen-Olsen et al., 2009; Ferguson et al., 2012; Harrington et al., 2012; Hoke et al., 2014; Horwood et al., 2010; Jashi et al., 2013; Kaida et al., 2010; Kerber et al., 2013; Lyons et al., 2012; O'Reilly et al., 2013; Peltzer et al., 2010; Rollins et al., 2007; Rutta et al., 2008; Sarnquist et al., 2013; Tomlinson et al., 2014; Uwimana et al., 2012a, 2012b, 2012c, 2013; Uwimana & Jackson, 2013). Twenty-two papers out of 57 were classified as multinational as they covered two or more SSA countries , twenty examined our research questions in the Republic of South Africa (RSA) (Barker et al., 2011; Barry et al., 2012; Cotton et al., 2008; Hatcher et al., 2014; Hoke et al., 2014; Horwood et al., 2010; Kaida et al., 2010; Kerber et al., 2013; Ladur et al., 2015; Peltzer et al., 2010; Rollins et al., 2007; Sprague et al., 2011; Tomlinson et al., 2014; Uwimana et al., 2012a, 2012b, 2012c, 2013; Uwimana & Jackson, 2013; Wettstein et al., 2012; Woldesenbet et al., 2015), three in Kenya (du Plessis et al., 2014; Harrington et al., 2012; Spangler et al., 2014), two each for Malawi (Levy, 2009; Sinunu et al., 2014) and Tanzania (Evjen-Olsen et al., 2009; Rutta et al., 2008) and one for each of Democratic Republic

of Congo (Behets et al., 2009), Lesotho (Towle & Lende, 2008), Rwanda (Ruton et al., 2012), Senegal (Desclaux et al., 2012), Swaziland (Bancheno et al., 2010), Uganda (Nassali et al., 2009) and Zambia (Potter et al., 2008).

Integration as a theme was found in twelve papers on PMTCT integration in ANC, postnatal care (PNC) and child care (Druce & Nolan, 2007; Evjen-Olsen et al., 2009; Ferguson et al., 2012; Gunn et al., 2016; Horwood et al., 2010; Kerber et al., 2013; Peltzer et al., 2010; Rutta et al., 2008; Tomlinson et al., 2014; Vermund & Hayes, 2013; Wettstein et al., 2012; Woldesenbet et al., 2015), five papers examining PMTCT and HIV services integration with tuberculosis screening and treatment (Uwimana et al., 2012a, 2012b, 2012c, 2013; Uwimana & Jackson, 2013), six articles on integrating sexual and reproductive health (SRH) and family planning (FP) services to prevent unintended pregnancy and optimize maternal and infant health in ANC and PNC (Sarnquist et al., 2013; Desclaux et al., 2012; Harrington et al., 2012; Hoke et al., 2014; Kaida et al., 2010; O'Reilly et al., 2013), one article on linking immunization to HIV screening among children (Rollins et al., 2007) and one on paediatric HIV (Lyons et al., 2012). We found literature examining both impact and integration of PMTCT programs as part of maternal and child health (MCH) services. MCH in this review covers antenatal, delivery and post-partum or post-natal care for both the mother and child. Other elements related to direct MCH services were included, notably social factors such as women's perceptions, community and male involvements in mother and child services, intimate partner violence and gender equality. The above-mentioned MCH components appeared in a total of twenty-one articles (Bancheno et al., 2010; Barker & Mate, 2012; Barry et al., 2012; Behets et al., 2009; Both & Roosmalen, 2010; Chi et al, 2013; du Plessis et al., 2014; Ekouevi et al., 2012; Gibbs et al., 2012; Hatcher et al., 2014; Kerouedan, 2010; Ladur et al., 2015; Levy, 2009; Nassali et al., 2009; Potter et al., 2008; Roxby et al., 2014; Ruton et al., 2012; Shetty, 2013; Spangler et al., 2014; Sprague et al., 2011; Towle & Lende, 2008).

Impact of PMTCT on other health care services

PMTCT has been promoted by WHO as a reliable solution to paediatric HIV. As a comprehensive approach developed based on the four components, the scaling up of PMTCT became a cornerstone of countries' HIV prevention, care and treatment programs (PEPFAR, 2011). As mentioned above, 32 of the 57 retained articles addressed the impact of PMTCT on other health care services. The major findings are the potential improvement of existing MCH services and to some extent increasing the availability, accessibility and utilisation of other PMTCT-related services such as prevention of unintended pregnancies, control of STI, immunization, nutrition and vitamins supplementation (Druce & Nolan, 2007; Evjen-Olsen et al., 2009; Harrington et al., 2012; Nutman et al., 2013; Rollins et al., 2007; Sarnquist et al., 2013; Wiysonge et al., 2011). PMTCT services also offer, to some extent, opportunities for screening tuberculosis among exposed infants (Cotton et al., 2008) and may generally enhance diagnosis and treatment through collaboration efforts at both health care settings and community (Uwimana et al., 2012a, 2012b, 2012c, 2013; Uwimana & Jackson, 2013).

Several issues surrounding the PMTCT roll-out are reported to adversely impact PMTCT outcomes (Both & Roosmalen, 2010) and these include its process, services delivery, quality of supplies and tools, hiring and training of adequate staff, among others. However, conclusions regarding the impact of PMTCT must be cautious due to lack of detailed studies analysing such effects. In their attempt to quantify the impact of PMTCT programs on overall health systems in SSA, Sarah Nutman, Douglas McKee and Kaveh Khoshnood (Nutman et al., 2013) specifically assessed the existing knowledge and evaluated the PMTCT services impact beyond HIV transmission prevention. They also looked at how these programs contribute to the broader health outcomes. In the end, their systematic review of literature published up to 2011 found evidence of numerous beneficial

synergies with specific health services but that there was insufficient evidence to draw any firm conclusions about the broader impacts of PMTCT on health outcomes or health systems. They report serious gaps regarding appropriate recording, data availability and information flow, and argue that these gaps might mislead decision-making, funding allocation and implementation of initiatives.

Health system strengthening or weakening

Health systems link people with promotive, preventive, curative, rehabilitative or palliative health services to address health problems. The effectiveness of this linkage depends on many factors, including those outside the health sector as well as within the various components of a health system (Gochman, 2013; Nelson et al., 2008). We identified six articles explicitly or indirectly addressing the broader health system (Barker et al., 2011; Druce & Nolan, 2007; Kerouedan, 2010; Peltzer et al., 2010; Tomlinson et al., 2014; Uwimana et al., 2012b) while the remaining fifty-one focused internally, on one or more components of the building blocks and functioning of health systems and services.

Health care providers and funders across SSA have shown interest and engagement to make PMTCT services more and easily accessible to women and children (Baek et al., 2007; Barker & Mate, 2012; Lyons et al., 2012; Nutman et al., 2013) but their efforts have not eliminated many challenges underlying SSA health systems. Added to social problems, these health system issues create a situation in which it is difficult for women to actually utilize services during pregnancy and postpartum, even when these are offered free of charge (Auvinen et al., 2013; Bhardwaj et al., 2014; Evjen-Olsen et al., 2009). Looking within the health systems themselves, PMTCT services have positively impacted MCH and adequately reduced the spread of HIV infection (Nutman et al., 2013), but optimal outcomes occur where the health services are delivered in conducive working conditions, with adequately equipped facilities and committed management (Mkoka et al., 2015). Such conditions are rare in SSA where the vertical transmission of HIV is the highest in the world. PMTCT and other

HIV services in SSA depend on foreign funds estimated at billions of dollars but unfortunately the overall system and population-level results of such efforts and investments are seen as mixed (Campbell et al., 2012).

Studies in this review pointed to these shortcomings and deficiencies in service delivery, especially for the components regarding the uptake of PMTCT programs such as antenatal HIV testing and receipt of test results, ARV prophylaxis and postnatal mother-infant follow up (Doherty et al., 2009; Kasenga et al., 2009). Campbell et al. (Campbell et al., 2012) therefore argue for a strategy for (i) 'translating' intervention approaches into locally and culturally appropriate discourses and practices; (ii) building local capacity to sustain interventions once their funded period is over; and (iii) strengthening health systems in affected settings.

Analysing the impact of PMTCT on other health care services is often framed in terms of a debate over whether the roll-out of HIV/AIDS services including PTMTC did or did not strengthen the existing health systems and services. Studies in our review demonstrated the advantages of scaling up HIV services in terms of saving many lives, training health providers, and funding some key services like MCH, but the same findings highlighted the various shortcomings of HIV/AIDS interventions in health systems of low and middle-income countries and particularly in SSA (Bhardwaj et al., 2014; Both & Roosmalen, 2010; Druce & Nolan, 2007; Kasenga et al., 2009; Potter et al., 2008; Tudor Car et al., 2011). Some encouraging results suggest positive impact of PMTCT programs on health systems (Druce & Nolan, 2007), but also highlight the challenges that PMTCT and health systems did not meet; these unmet challenges are seen as negative effects mostly caused by poorly resourced settings facing a high disease burden (Both & Roosmalen, 2010). These challenges include among others: continued high rates of home deliveries, shortages of personnel, inadequate supplies of test kits, varying distribution and availability of PMTCT service delivery points, lack of supplementary feeds for women who may opt for non-breast feeding for their infants,

and logistical and social implications after testing HIV positive, such as a lack of spousal support and sometimes violence (Auvinen et al., 2013; Both & Roosmalen, 2010; Byamugisha et al., 2010; Kasenga et al., 2009). None of the retained papers showed or argued that PMTCT programs directly weaken health systems. In order to strengthen health systems, the implementation of PMTCT and disease-specific interventions needs more collaborative efforts to address structural, organizational, managerial and finance barriers.

Integration of PMTCT within broader programs and health systems

Even though some programs remain disease-specific, our review found that PMTCT programs and other health services mutually interact. PMTCT integration within general health care services in low- and middle-income countries has also been recommended to boost the utilisation of these interventions (Tudor Car et al., 2011). Some studies noted that under a PMTCT umbrella, the quality of other services in integration is also being closely monitored and improved (Bhardwaj et al., 2014; Doherty et al., 2009).

PMTCT integration has for example, positively influenced maternal and child care services regarding service availability, accessibility and utilisation (Druce & Nolan, 2007). Evjen-Olsen et al. (Evjen-Olsen et al., 2009) suggested that maternal and neonatal health can be improved by integrating health care services, supporting integration of health systems rather than separately organising and managing different vertical and horizontal programs especially in developing countries (WHO, 2005). The articles reviewed here also identified potential synergies between the integration or combination of PMTCT with specific health care activities outside of direct obstetrical and child care or MCH services, including sexually transmitted infection (STI) control and immunization (Nutman et al., 2013; Sinunu et al., 2014), sexual and reproductive health and family planning (Govender & Coovadia, 2014; Lassi et al., 2014; Peltzer et al., 2009), nutrition (Pirkle et al., 2014), tuberculosis (Cotton et al., 2008) and vitamin A supplementation (Wiysonge et al., 2011). The synergies are

variously achieved in different contexts through progressive efforts, such as staff training and motivation, planning and evaluation of services, restructured management and financing among others. In terms of integration itself as a theme, the following synergies were examined by retained studies, apart from MCH: HIV/PMTCT services integration with tuberculosis screening and treatment (Uwimana et al., 2012a, 2012b, 2012c, 2013; Uwimana & Jackson, 2013), with SRH, STIs and FP services (Sarnquist et al., 2013; Desclaux et al., 2012; Harrington et al., 2012; Hoke et al., 2014; Kaida et al., 2010; Nutman et al., 2013; O'Reilly et al., 2013) and with immunization and HIV screening among children (Rollins et al., 2007). These linkages helped to increase and improve training of care providers, to review and enhance funding and implementation policies, to increase access and adherence to services, to reduce drug stock outs and improve basic infrastructures.

While identifying and describing the effects of PMTCT on other health services and health systems or the integration of PMTCT and its extent within broader programs and health systems, collaborations and involvements at different levels emerged to be crucial. Since health services are not only provided by the public sector, our search included other organisations offering PMTCT services and other actors involved in offering such services outside of the public sector. We identified examples of service delivery provided by NGOs (Uwimana et al., 2012a), or delivered in refugee camps (Rutta et al., 2008) while one paper focused on male partner involvement (Ladur et al., 2015). While studies examining public health services tended to focus on activities within clinics and services, these additional papers reveal that PMTCT activities shape interactions between the community members, social organisations and clinics offering the PMTCT services. The collaborations reported in some articles were directed to implementation or evaluation of initiatives against stigma, for the "normalisation" of HIV as just another other disease and to increase the accessibility of other social and support services to women living with HIV (WHO, 2010a). Selected articles stressed collaboration initiatives so that the PMTCT programs could become a model in

"networking, nurturing relationships and bringing all available resources and agents to the table to find solutions and forge partnerships in order to procure all elements essential to a high quality, comprehensive, integrated program" (PEPFAR, 2011).

Discussion

The review aimed to document the possible impact of PMTCT on health care services and systems and the integration of PMTCT within broader programs and health systems in the available literature in SSA. The analysis of available evidence regarding the two main objectives of this review, namely PMTCT impact and integration, supports a generally positive evaluation of positive synergies with MCH as well as other health services, suggests increasing partial integration of PMTCT within health systems, and offers inconclusive arguments on whether and to what extent health systems as a whole have been strengthened or weakened by the PMTCT programs in countries of SSA. The discussion below addresses three issues that must be further studied and analysed in order to increase the likelihood that health systems will be demonstrably strengthened: the availability and quality of information, impacts and synergies within and beyond the health sector and the need to engage programmes and services beyond MCH, sexual and reproductive health, and TB.

Beyond the structural limitations on the positive impact that PMTCT programs might have on health systems in SSA, there is also a crucial continuing problem of accurate and timely information as highlighted by Theuring et al. (Theuring et al., 2009), and a lack of rigorous research regarding the impact of PMTCT programs on health care systems or vice versa. While all included papers contributed to one or another dimension of the research questions, only two among 32 retained articles that recorded the impact of PMTCT, explicitly and directly focused on or addressed the impact of PMTCT on other health services and on health systems (Both & Roosmalen, 2010; Nutman et al., 2013). This is a very unusual scenario, considering the large body of available literature on HIV/AIDS interventions in SSA. It is worth repeating that Sarah Nutman, Douglas McKee and Kaveh

Khoshnood (Nutman et al., 2013) specifically aimed to evaluate the impact of PMTCT services beyond transmission prevention and assessed the existing knowledge about such programs and how they contribute to broader health outcomes. Unfortunately, these research efforts were stymied by the weakness of health information systems, unreliable administrative and research data, and important evidence gaps. This research gap, coupled with under- or improper reporting practices, poses serious challenges to informed decision making, proper funding allocation and effective implementation.

Likewise, in their 2011 Cochrane review, Lorainne Tudor Car and colleagues did not find any study that evaluated the PMTCT interventions integration with other health care services to improve health outcomes (Tudor Car et al., 2011). In another study conducted in Swaziland, a country with a background of high, but stable HIV prevalence, an intervention with triangulated data of HIV testing and counselling, ART, PMTCT, and TB screening programs improved coverage and documented promising health outcomes. Even though the scale-up of this intervention was successful, the lack of data remained a non-negligible challenge throughout the study (van Schalkwyk et al., 2013). A situation like this is not an exception in SSA where health records are often incomplete or poorly managed. Without data storage and sharing, the combination of health interventions becomes more complicated and even impossible. This tendency can only be changed at national and regional levels through viable, coordinated investment and practice to monitor and to improve effects of major programs like PMTCT on other services and health systems or vice versa.

Synergies, collaborations and impacts on health systems: Positive contributions to a problem beyond the scope of PMTCT and the health sector

The included papers provided moderate evidence of mutual benefits between the PMTCT services and the existing health care services and they recommended a close relationship and more integration in order to maximise the advantages of working together and to mitigate some of the challenges of controlling HIV, a lifelong condition, in the conditions facing SSA (Both & Roosmalen,

2010; Rollins et al., 2014; Tudor Car et al., 2011). The available scientific studies and reports suggest the existence of both positive and negative effects generated by PMTCT on the maternal health services where they are mostly based and on child health services. The PMTCT services increase not only the accessibility but also the utilization of antenatal and other MCH services (Price et al., 2009). In addition, the increased access to HIV testing and treatment are transforming HIV into a chronic illness. However, the lifelong management of HIV requires continued commitment and engagement of different actors such as the funders, the health care system, the patients, their families and as well as the community (Psaros et al., 2015). The efforts to manage the HIV pandemic as a chronic disease and treat the opportunistic infections or any other HIV associated conditions overwhelm SSA's struggling health care systems. The systems that depend on conditional foreign aid do not enjoy managerial autonomy and cannot consistently plan for their future interventions. PMTCT services within such systems cannot, on their own, strengthen health systems.

As seen in the results section, the failure of PMTCT to demonstrably strengthen health systems is associated and sustained by the underfunded and poorly managed health care settings (Both & Roosmalen, 2010). HIV counseling and testing is not yet universal and many pregnant women come late to seek prenatal care and they then access all the services at the same time instead of progressing through the whole cascade. Lack of adequate resources and facilities (infrastructure, materials, and human resources among others) are major barriers to successful interventions in SSA where the operational and implementation problems arise from local contextual issues as well as the underlying poverty reflecting global economic forces.

The reality of plural health systems and multiple actors must also be addressed in research, policy, and practice. In SSA, the private for-profit sector and charitable and faith-based health care providers including mission hospitals and NGOs play an important role (Uwimana et al., 2012b, 2012a) and should be included in research and policy dialogue. This entails the widely advocated but

in practice difficult coordination between well-funded international organisations, struggling national public health systems, NGOs and people living with HIV in search of treatment (Denis, 2013).

Beyond general statements of goals of collaboration and consideration of intervention context, there should be a clear strategy to strengthen local responses to HIV which are often ignored by the top–down style adopted in order to comply with requirements of "the global funding architecture" (Kelly & Birdsall, 2010). This responsiveness to local conditions and actors takes time and requires flexibility. In contrast, the "emergency" nature of much HIV intervention combined with accountability requirements to funders tend to align with a more directive and hence less responsive and collaborative approach. Constructive collaboration is not only advised but critically needed in order to achieve both PMTCT and health services goals. This concerns all models of health care delivery, whether vertical, horizontal or diagonal.

Beyond MCH, sexual and reproductive health and TB

Malaria, severe anaemia, diarrheal diseases and acute respiratory diseases are some of the leading causes of death among women and children in many of SSA countries (Both & Roosmalen, 2010; Rao et al., 2006) including RSA, the source of most studies identified for this review. These are rarely, if at all addressed in PMTCT programs and their impacts on PMTCT or vice versa are not discussed in any study included in this review. This is possibly due to HIV interventions and research continuing to be seen as a separate issue from health conditions other than those directly related to sexual and reproductive health and TB.

In the cited systematic review of Lorainne Tudor Car et al. (Tudor Car et al., 2011) on integrating PMTCT programmes with other health services for preventing HIV infection and improving HIV outcomes in developing countries, the authors decided not to make any recommendation about the implementation of integrated PMTCT programmes based on the fact that only one study met their selection criteria. It is logical to conceive and integrate the PMTCT programs

within MCH services given the correlation of both services delivery but other services such as SRH or immunisation clinics as the point of entry to PMTCT programs need to be explored. In addition to publications for this review that recommend more research on the impact of PMTCT programs on health care services, the WHO, UNAIDS, UNICEF, UNFPA and PEPFAR calls to integrate the PMTCT and other disease stand-alone programs with other health care services (PEPFAR, 2011; WHO, 2010a; WHO & UNICEF, 2007, 2012) remain relevant.

Limitations

This is a comprehensive and complex review that included a range of issues related to PMTCT impact and its integration on other health services and systems. Even though it was rigorously conducted, not all PMTCT implementation details could be reviewed in this single paper.

The regional HIV prevalence and other crucial factors, such as relationships with donors and international researchers as well as publication outputs, are highly variable across countries and regions in SSA. Most of the identified studies covered eastern and southern Africa. Central and western parts of Africa are less covered in publications, a situation that makes it difficult to generalise this review's findings to those regions. Studies reporting good service delivery and adherence may also not reflect the full impact of PMTCT when implemented at scale at a national level. Some areas within countries may also have been left out in the retrieved studies.

As this review sought articles specifically addressing PMTCT and health services and systems, it may have missed publications reflecting recent increased attention and funding for health system strengthening through HIV programmes, which did not specifically address PMTCT. These papers may yield insights into broader health system challenges and promising approaches to integration of other HIV programmes, potentially including PMTCT

Conclusion

PMTCT improves maternal and child health through preventing the spread of HIV infection in SSA countries. There is evidence of a positive impact of PMTCT on primary care for mothers and children, beyond HIV. The provision of PMTCT services increases the availability, the accessibility and the utilization of ANC and other health care services, especially when the intervention is linked to PMTCT programs as part of mainstream MCH services. However, this review also documented a large number of challenges involved both in implementing and in understanding the effects of PMTCT integration. Without robust information systems and rigorous and systematic research on the health system as a whole as well as on its various services and activities, evidence will continue to be fragmented and firm conclusions will continue to be impossible to draw.

While some vertical programs persist, PMTCT services are increasingly being integrated at different levels within routine health services and the health systems. Our study documented the challenges and weaknesses that face health care services and health systems in connection with PMTCT services. These range from structural, governance and resourcing challenges within and between countries, to weak information reporting systems and require more and better coordination and collaboration within and beyond HIV programs, directly related health services, communities, the plural health sector, and other sectors at national and global levels. These broad health system and social challenges cannot be solved by PMTCT interventions alone and there is a need of working together or collaborating with other sectors out of health system.

Abbreviations

PMTCT: Prevention of mother-to-child transmission of HIV

MTCT: The Mother-To-Child Transmission of HIV

HIV: Human Immunodeficiency Virus

AIDS: Acquired Immune Deficiency Syndrome

UNAIDS: The United Nations Programme on HIV and AIDS

SSA: Sub-Saharan Africa

WHO: World Health Organisation

UNICEF: The United Nations Children's Fund

UNFPA: The United Nations Population Fund

UNGASS: The United Nations General Assembly Special Session

ART: Antiretroviral therapy

ARV: Antiretrovirals

NGOs: Non-Governmental Organisations

STI: Sexually Transmitted Infection

ANC: Antenatal care

MCH: Maternal and child health

PNC: Postnatal care

SRH: Sexual and reproductive health

FP: Family planning

CCWs: Community care workers

TB: Tuberculosis

RSA: The Republic of South Africa

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Authors' contributions

MJC, CZ, and HT designed the study. MJC wrote the first manuscript of the review. CZ and HT critically revised the review. All authors read and approved the final manuscript.

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MJC is a MHA, MSc, MA, MPhil and PhD candidate in Global Health. CZ is a MD, MPH and PhD in Medical Anthropology. HT is a M.Sc and PhD in Epidemiology.

Competing interests

MJC, CZ and HT declare no competing interests.

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CHAPTER 5: EMPIRICAL RESULTS

Paper 2 – Integrating the prevention of mother-to-child transmission of HIV into primary healthcare services after AIDS denialism in South Africa: Perspectives of experts and health care workers - A qualitative study

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Abstract

Background: Integrating Prevention of Mother-to-Child Transmission (PMTCT) programmes into routine health services under complex socio-political and health system conditions is a priority and a challenge. The successful rollout of PMTCT in sub-Saharan Africa has decreased Human Immunodeficiency Virus (HIV), reduced child mortality and improved maternal health. In South Africa, PMTCT is now integrated into existing primary health care (PHC) services and this experience could serve as a relevant example for integrating other programmes into comprehensive primary care. This study explored the perspectives of both experts or key informants and frontline health workers (FHCWs) in South Africa on PMTCT integration into PHC in the context of post-AIDS denialism using a Complex Adaptive Systems framework.

Methods: A total of 20 in-depth semi-structured interviews were conducted; 10 with experts including national and international health systems and HIV/PMTCT policy makers and researchers, and 10 FHCWs including clinic managers, nurses and midwives. All interviews were conducted in person, audio-recorded and transcribed. Three investigators collaborated in coding transcripts and used an iterative approach for thematic analysis.

Results: Experts and FHCWs agreed on the importance of integrated PMTCT services. Experts reported a slow and partial integration of PMTCT programmes into PHC following its initial rollout as a stand-alone programme in the aftermath of the AIDS denialism period. Experts and FHCWs diverged on the challenges associated with integration of PMTCT. Experts highlighted bureaucracy, HIV stigma and discrimination and a shortage of training for staff as major barriers to PMTCT integration. In comparison, FHCWs emphasized high workloads, staff turnover and infrastructural issues (e.g., lack of rooms, small spaces) as their main challenges to integration. Both experts and FHCWs suggested that working with community health workers, particularly in the post-partum

period, helped to address cases of loss to follow-up of women and their babies and to improve linkages to polymerase-chain reaction (PCR) testing and immunisation.

Conclusions: Despite organised efforts in South Africa, experts and FHCWs reported multiple barriers for the full integration of PMTCT in PHC, especially postpartum. The results suggest opportunities to address operational challenges towards more integrated PMTCT and other health services in order to improve maternal and child health.

Key words: integration, health systems, primary health care, Prevention of Mother-to-Child Transmission of HIV, PMTCT programme, PMTCT service, HIV prevention, South Africa.

Background

Health systems operate in conditions of increasing complexity, in which health care providers interact with patients and their families in the context of multiple diseases or health problems (Cohn, 2014; Greenhalgh & Papoutsi, 2018; Sturmberg & Martin, 2013) as well as with managers and political decision makers concerned with successful implementation and scale-up (Borgermans et al., 2017; Hawe et al., 2009). Integrating stand-alone interventions into comprehensive services at local facilities requires facing the challenges of limited health service accessibility, critical socio-economic conditions and the double burden of communicable and non-communicable diseases (Amon, 2002; Ekman et al., 2008; Temu et al., 2014). Integration of the prevention of mother-to-child transmission (PMTCT) of human immunodeficiency virus (HIV) programme in South Africa can serve as a case study of this adaptation under complex conditions – including the particularly challenging socio-political context of "AIDS denialism" in which PMTCT and other HIV-related interventions were developed and implemented in South Africa (Buckler, 2008; Wang, 2008; Fassin & Schneider, 2003). Efforts to integrate new interventions into routine primary care may be informed by reflecting on the technical and health system challenges of implementing the PMTCT cascade. In addition, the history of AIDS denialism and the challenges of initially launching PMTCT programmes in South Africa may shed light on adapting complex, costly and contested interventions into public health systems.

The transmission of HIV from mother to child can be reduced by more than 95% with effective interventions during pregnancy, labor, delivery and breastfeeding, known collectively as the PMTCT cascade (Avert, 2015; WHO, 2010b). The PMTCT cascade encompasses services aiming to virtually eliminate mother-to-child transmission (eMTCT) of HIV, reduce child mortality and improve maternal health (Dionne-Odom et al., 2016a; USAID, 2017). Since first reported in the 1980s, the proportion of infections by MTCT has decreased from an estimated 10% of new HIV cases to less than 2% (Cock et al., 2000; Paintsil & Andiman, 2009). The rollout of PMTCT has been particularly

successful where the burden is greatest in low and middle income countries (LMICs) including in sub-Saharan Africa (SSA) and in South Africa (Cock et al., 2000; Paintsil & Andiman, 2009). The acknowledgement of the impact of perinatal HIV on maternal and child health (MCH) (Cock et al., 2000; Kuhn et al., 2009) saw PMTCT services receive significant attention from various actors at local, national and international levels. These stakeholders included organisations such as the United States President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund to fight against AIDS, tuberculosis (TB) and Malaria (GFATM), United States Agency for International Development (USAID), Centers for Disease Control (CDC) and international non-governmental organisations (NGOs), different governmental initiatives and local health systems (Idele et al., 2017). This support allowed for the integration of PMTCT into existing health care services (Wiegert et al., 2014), with the ambition of achieving eMTCT (Bhardwaj et al., 2015; Gourlay et al., 2013).

PMTCT has been integrated into existing services within PHC or community outreach programmes to prevent other diseases such as tuberculosis, diarrhea, depression and others (Grimwood et al., 2012; Tolle, 2009). The impact of PMTCT on the improvement of MCH in SSA has been well documented, especially in improving service availability, accessibility and utilization (Fokam et al., 2017; Mutabazi et al., 2017). Unlike the situation for other health problems, this integration of PMTCT in PHC has provided the opportunity to improve preventive services and manage other common health issues within countries (Tolle, 2009), rather than shifting scarce resources to vertical programmes (Pfeiffer et al., 2010). Well-resourced PMTCT programmes have contributed to improving the quality and ensuring the sustainability of other services offered in the same clinics (Chi et al, 2013). However, sustaining such results through national rather than donor funding and management, has increased pressure on some facilities that face shortages in terms of human resources and medical supplies, or that lack required knowledge and training to deliver full service packages (Sprague et al., 2011).

These challenges of allocating scarce resources are political as well as technical. The South African experience highlights the interactions among politics, health care, and public health. Despite now having the world's largest antiretroviral therapy (ART) programmes and well-established PMTCT rollout (Burton et al., 2015), South Africa's initial response to HIV was stalled due to political interference in health policy during the time of Thabo Mbeki's presidency from 1999-2008. Mbeki subscribed to the AIDS denialist view that retroviruses are harmless and that other influences, such as drug abuse, poverty, and antiretroviral medications cause AIDS (Kalichman et al., 2010). Under his presidency, the government instituted policies denying antiretroviral drugs to AIDS patients and withdrew support from clinics that had started using azidothymidine (AZT) also known as zidovudine, to prevent mother-to-child transmission of HIV. In 1998, the Treatment Action Campaign (TAC) was founded, campaigning for measures to reduce new HIV infections. In 2001, TAC initiated legal proceedings against the government's policy of limiting treatment for the purpose of PMTCT. The use of ARV/AZT only resumed in 2002 when the constitutional court ruled that the denial of treatment was an infringement of the fundamental right to healthcare (Section 27 & 28) (Cullinan & Thom, 2009). In this time period an estimated 100,000 infants were believed to be infected (Burton et al., 2015; Heywood, 2003).

However, it was not until 2008 that the rapid implementation of PMTCT and ART services was prioritised (Barron et al., 2013b). In the period between the first Nevirapine regimen in 2002 and the national PMTCT plan in 2008 at least 330,000 preventable deaths were estimated to have occurred, with 35,000 babies born with HIV. The delay in the rollout of PMTCT caused inestimable financial and social loss, with HIV infection rates well above other SSA countries that had initiated PMTCT in the early 2000s (Chigwedere et al., 2008; Nattrass, 2008).

Since then, substantial achievements in PMTCT have been seen in South Africa. HIV testing coverage of pregnant women is now close to 100% and PMTCT services were provided in almost

98% of all health facilities by 2015 (National Department of Health, 2015). In 2011, MTCT decreased to 2.7%, with ART coverage reaching 87% in 2012 (Barron et al., 2013b; National Department of Health, 2015). These significant results were achieved following changes in National PMTCT guidelines to initiate treatment for all women living with HIV regardless of CD4 count. A timeline of South Africa's PMTCT Guidelines is summarized in the adapted table below (**Table 3**) (Burton et al., 2015).

***Table 3*: Adapted timeline of national PMTCT guidelines, South Africa**

(Burton et al., 2015)

PMTCT Guidelines	**Year**
National PMTCT programme begins after Constitutional Court judgement against the Government: • Single dose nevirapine to the mother in labour, and to the infant within 72 hours of birth.	2002
• AZT to mother from 28 weeks gestation; single dose nevirapine to mother in labour and to infant within 72 hours of birth and HAART for pregnant women.	2004
• AZT from 14 weeks gestation: single dose nevirapine plus tenofovir/3TC in labour; infant prophylaxis with nevirapine for 6 weeks if mother on HAART or formula feeding, or until the end of all breastfeeding if mother not eligible for HAART.	2010
• All pregnant women eligible for HAART, irrespective of CD4 count. Infant prophylaxis with nevirapine for 6 weeks. Women initiating HAART with CD4< 350 and no other indication for HAART, to stop treatment after all breastfeeding has ceased.	2013
• All pregnant and breastfeeding women eligible for lifelong HAART.	2015

AZT: zidovudine; HAART: highly active antiretroviral therapy

There are, however, few reports of research findings regarding the process, successes and failures of PMTCT implementation (Aizire et al., 2013; Bhardwaj et al., 2015; Okoli & Lansdown, 2014). Understanding the perspectives, experiences or practices of different health system and

PMTCT specialists, alongside frontline health workers who have been involved in daily PMTCT activities at PHC level, could facilitate the further integration of PMTCT services and inform efforts to integrate other vertical programmes into PHC. The objective of this study was to explore these perspectives in the context of post-AIDS denialism in South Africa and document important considerations for the integration of other comprehensive services in maternal and child health care.

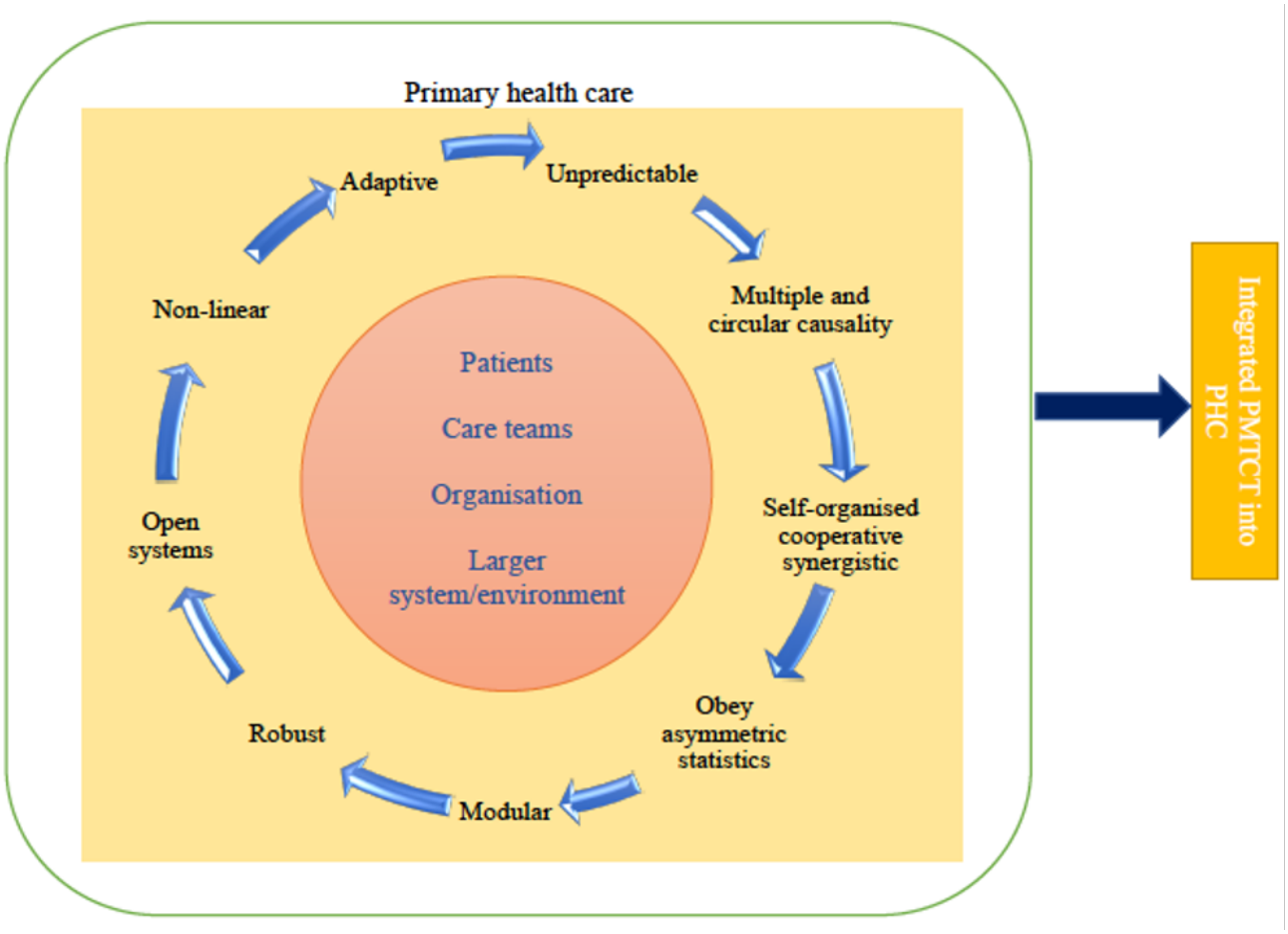
Methods

Study framework

For this study, an adapted Complex Adaptive Systems (CAS) framework to describe features explaining key components of integration of PMTCT (Martínez-García & Hernández-Lemus, 2013), was used. There are four nested levels that can be considered for health care system changes and improvement (Ferlie & Shortell, 2001; Reid et al., 2005). These include: individual patients; care teams (e.g., family members, nurses, doctors, pharmacists); organisation (e.g., clinics, hospitals, infrastructure, quality assurance); and, the larger system or environment (e.g., public and private regulators, insurance companies, research funders, legislative and policy frameworks) (Ferlie & Shortell, 2001; Reid et al., 2005). Many local, national and international actors, including individual or country initiatives and bilateral or multilateral organisations, also exist in PMTCT programmes.

CAS has been proposed as a theory to both understand, and work towards, integrated health care (Begun et al., 2003b; Edgren, 2008; Edgren & Barnard, 2012; Martínez-García & Hernández-Lemus, 2013; Nugus et al., 2010). Health systems are perceived as “complex” because they imply a wide variety of components, “adaptive” due to the ability to adjust or change over time and “system” because of its group of connections or interdependence (Begun et al., 2003b). Though there is no true consensus on the set of characteristics that define CAS (McDaniel et al., 2009), Cilliers, P. (Cilliers, 2002) proposed a list of important CAS characteristics, later summarised by Maguire, S. et al.

(Maguire et al., 2006). These characteristics can be applied to the South African health system and to PMTCT intervention and include: unpredictable, multiple with circular causality, self-organised cooperative synergistic, obey asymmetric statistics, modular, robust, open systems, non-linear and adaptive (these framework features are described in the supplemental material 1). Considering the complexity of the process and environmental/contextual elements, the following framework to understand the integration of PMTCT into PHC was proposed for this study (**Figure 6**).



Adapted study framework towards integrated PMTCT into PHC
(Begun et al., 2003b; Edgren, 2008; Lars Edgren & Keith Barnard, 2012; Martínez-García & Hernández-Lemus, 2013; Nugus et al., 2010).

Study design and sample

A descriptive qualitative study, using a narrative approach (Creswell & Poth, 2016) to explore different perspectives and experiences regarding PMTCT integration in the context of AIDS denialism was conducted. Two groups of informants were interviewed. The first were experts or key informants including health systems and HIV/PMTCT policy makers, researchers and activists at international, national and provincial levels in South Africa. The second were FHCWs and these were drawn from PHC facilities in Cape Town, Western Cape Province, in order to inform an ongoing intervention study in that province on the feasibility of integrating post-partum care and diabetes prevention activities for women with gestational diabetes mellitus into routine practice in public sector well-baby clinics. The domains of the consolidated criteria for reporting qualitative research (COREQ) (Tong et al., 2007) guided the development of this research and reporting of the findings (Additional file 1).

Experts were purposively selected and their recruitment occurred between June 2016 and October 2017. Eligibility criteria included experience in design or implementation of PMTCT in South Africa and other regional countries or at international level, and fluency in English. Those who did not meet these criteria were excluded. Twelve experts were contacted by email and introduced to the study, its objectives and the involved researchers. Those who responded were recruited for this study, but two respondents were unable to attend the interview due to their busy schedule, leaving a final sample of 10.

FHCWs included clinic managers, PMTCT nurses and midwives in clinics randomly selected from the clinics under the Public Health Department of Cape Town or Western Cape province, South Africa. Their recruitment occurred alongside the recruitment of experts. Eligibility included the following: managers of the local facilities offering PMTCT services, nurses or midwives delivering PMTCT services or dealing with PMTCT related problems in the clinics. Those without experience

in organising PMTCT services or who did not get involved in its delivery were excluded. A total of 15 FHCWs were contacted by introductory email for the study with a follow-up telephone. Only 10 were available and recruited for this study. Five who chose not to participate cited different reasons including conflicting agenda and urgent matters to attend to in their facilities.

Data collection

Participants completed the face-to-face interview at their workplace or any other suggested quiet setting. A self-administered questionnaire was used to collect sociodemographic information including age, sex, years of experience and institution or centre of affiliation before the interview. Interviews were conducted by a trained male researcher (JCM) under the supervision of a female experienced qualitative researcher (KM). The researcher (JCM) introducing himself as a doctoral student and briefly interacted with the participants about the study before commencing the interviews. Each interview lasted between 30 and 60 minutes, a timeframe in which the data saturation was reached. A semi-structured interview guide (Additional file 2) was developed by JCM and revised by CZ, and was used for both groups of respondents, experts and FHWCs. The development of the interview guide included a review of various PMTCT policies and implementation guidelines from both the World Health Organisation (WHO) and the South African Government, and questions were generated from these guidelines. Open-ended questions were used to explore participants experience of PMTCT service integration into PHC. The interview guide was modified over the course of the study, using an iterative process informed by the content of previous interviews. For example, questions regarding health information systems and PMTCT data and related statistics were added to understand how information and datasets are shared among various health professionals and institutions, and how monitoring and evaluation of PMTCT services were carried out. The interviewer used reflective probes to encourage respondents to clarify and expand on their statements. Interviews were ongoing until no new information was obtained and thematic saturation was achieved – no

additional themes could emerge from data) (Green & Thorogood, 2004) by the end of all scheduled interviews for both groups of study participants, experts and FHCWs. All participants were offered no compensation.

Data analysis

All interviews were audiorecorded and field notes were taken by JCM, and a verbatim transcription was conducted by a hired and trained assistant. Using an iterative approach to thematic analysis (Nowell et al., 2017; Srivastava & Hopwood, 2009), two investigators (JCM and CZ) independently read de-identified transcripts, identifying meaningful segments within the responses. All interviews were coded by JCM in collaboration with CG and CZ, and all discrepancies in the coding process were negotiated between these three investigators. The CAS framework was first applied in the process of identifying relevant categories and later in the interpretation of the themes that emerged from the transcripts. General themes and subthemes summarizing perspectives of the two groups of participants (experts and FHCWs) were discussed among members of the research team, and the representative quotes presented in this article were collectively selected. Atlas.ti software was used to assist data analysis and management. Characteristics of participants were analyzed by JCM using SPSS version 24.0.

Ethics approval

The study was approved by the Human Research Ethics Committee at the Faculty of Health Sciences, University of Cape Town (HREC REF: 946/2014) and the Centre de Recherche du Centre Hospitalier de l'Université de Montréal (2018-6690, 17.044 - ID). Written informed consent was obtained from all participants and the anonymity of participants was maintained throughout the research process.

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Results

Participant characteristics

Twenty participants were interviewed; 10 experts and 10 FHCWs. FHCWs included three PHC clinic managers and seven PHC clinic nurses. All recruited FHCWs were working in public local health facilities located in the disadvantaged communities of Cape Town suburbs including informal settlements. They normally serve a population overburdened by infectious like TB, HIV and others, but also chronic diseases including hypertension and diabetes. These FHCWs deal with enormous work pressure to offer comprehensive and quality care in these communities. The majority of interviewees in both groups were female (80%), with an age range of 29-61 years (mean age 45 years) (**Table 4**).

***Table 4*: Study participant characteristics**

Participant characteristics	N (%)
Participant category	
Experts	10 (50)
FHCWs:	
Clinic managers	3 (15)
Nurses and midwives	7 (35)
Sex	
Female	16 (80)
Male	4 (20)
Age mean and SD:	
- Experts	49.8
- FHCWs	40.1
- Overall mean (SD)	44.9 (8.2)

SD: Standard Deviation

Themes and categories

The key themes that emerged from all interviews were grouped into seven categories. These categories were then mapped onto three components of the adapted CAS framework, organised by the occurrence of events throughout PMTCT rollout during and after AIDS denialism. They were

classified as: "system" (experiences in trials and PMTCT adoption during AIDS denialism era); "adaptive" (gradual move towards PMTCT acceptance and integration, increased awareness and community participation, commitment to PMTCT services integration, community health workers' involvement, clinical training and retraining for nurses) and "complex" (persistent barriers to PMTCT integration). This classification with illustrative quotes is depicted in **Table 5**.

Table 5: **Key findings based on proposed CAS components**

CAS component and key findings	Illustrative quotes
System **1.** Experiences in PMTCT trials during after AIDS denialism era	*"We had to get special permission to roll out the programme, and… when there was a court instruction to roll it out; but then they were still controlling the roll-out and we were all, like, pilot projects"* – Expert 2. *"I think over the years what has happened is the pressure on the ground that has resulted in people changing their perspective and focus around PMTCT"* – Expert 1. *"I'm just thinking back now, in general and for Cape Town in particular,…So basically, we received global funding, and in 2006, we appointed quite a number of PMTCT coordinators, as well as PMTCT registered professional nurses within the PHC setting…"* – Expert 4. *"It was only AZT and Nevirapine that was given at that time. Then as time goes by then we changed"* – FHCW 1. *".....she started to run the PMTCT programme about 15 years ago, lots of patients were lost before that and statistics*

	were quite high when it came to PCRs. They weren't followed up appropriately. So, I think after the PMTCT programme started, there was somebody actually taking charge, invested in the patient's wellbeing, and they were being followed up, and if any other issues arose besides PMTCT, it could also be managed more appropriately and be referred" – FHCW 2. *"I believe there was a problem with a theft on medication. As a result now, the nurses that are doing ANC, they don't dispense medication"* – FHCW 3.
Adaptive **2.** Commitment to PMTCT integration	*"And in some settings, actually referring the patient involved having them moving from the facility to another to obtain the care for other conditions; and you've got to think of integration in terms of, at least, the making available within the same facility of other services"* – Expert 6. *"…transferring clients to specialists may cause gaps and some women become missing, even for a short distance…, they disappear within 50 meters to where you send them. They fall in hole in that walk and with this we can't defragment the system"* – Expert 10. *"It's a logical move for midwives and other health workers who are working in maternity, antenatal, and postnatal and delivery services to treat mothers who are infected with HIV in a holistic way"* – Expert 3. *"It's quite good, because we try to integrate services…..So we do the PCRs when the mothers are here for immunisation, I mean, it can be sooner done at once"* – FHCW 3.

3. Gradual move towards PMTCT acceptance and integration in the clinics	*"You want your baby to be immunised here; then we don't want you to go up and down, you must also be here and your baby, so that we can see both of you ....But the mother and the baby must be on the same facility"* FHCW 4. *"…because they see mother and child, then they also check which medication did the child get, or is the child a high risk infant or not? Does the mother still remain in care? All those check ups, PAP smears, they also check immunisations, deworming, nutrition,…everything possible"* – FHCW 5. *"…PMTCT figures almost synonymous with antenatal care, because the chances of being HIV infected are so high, relatively, that you almost don't see one without the other"* – Expert 8. *"So most of our nurses, our midwives are now trained, so which means they're offering integrated antenatal and antiretroviral treatment (PMTCT) and they're also doing TB screening"* – Expert 4. *"Western Cape was the only province to start integration of PMTCT and other ANC services and others did the same later. Different stakeholders used to meet once per week to discuss the progress and issues and everyone came together to assess how it was managed"* – Expert 9. *"The community is more open-minded now of what is expected of them once they are pregnant…So, it was an eye-opener, also for the nurses, because and the community as well; because now they know, once they are pregnant, they are eager to know their status"* – FHCW 6.

4. Increased awareness and community participation	*"…within the facility, it's now good that we realised that there is a need for that continuity of care…..when we started this project of Child Health"* – FHCW 1. *"I can say one in five years, we have only one child, one in five years that is positive. She didn't come to the clinic when she was pregnant, and yet she was positive. You see, it can take one in five years for one child due to PMTCT; and we are not happy with that"* – FHCW 4. *"It has so many adverse consequences affecting key public health indicators, such as maternal and under five and infant mortality, that it became a priority health problem for the health services to solve"* – Expert 3. *"…bringing HIV care back to the community, now increasingly having what they call community-based club, and you are going to see for instance more room for those people, to deal with more urgent issues, because they are overcrowded"* – Expert 6. *"….community support also plays a key role in supporting moms throughout this whole cascade. Peer support is important"* – Expert 10. *"We have got programmes like MomConnect where they are enrolled and they get all the support, like where they are sent sms's and stuff"* – FHCW 6. *"Mothers to Mothers services which is well supporting the mothers who are pregnant and those after delivery, so they work hand in hand with antenatal labour ward as well as Child Health for continuity of care"* FHCW 1. *"So, when we talk to them we get the social worker involved as well, then we will try*

5. Community health workers' involvement	*and make a plan to see if there are not other family members because, I mean, any support, it doesn't just have to be the partner, support in general is good"* – FHCW 2. *"CHWs are part of health care system to link clinics to the communities and enforce adherence among their other roles. They need to be trained"* – Expert 9. *"…if they were in place, in many communities, it would be relatively easy to send a message to those community health workers and teams"* – Expert 3. *"They (CHWs) can go to the houses and they can reinforce adherence…and the idea is that they go into that household and look at all the problems. They look at the teenagers, they counsel them about contraception, and look at the mother that's struggling with breastfeeding and at the father that's smoking"* – Expert 5. *"I will say they are helpful, because we use them as the bridge just to get to the communities, because they go the extra mile in this way that they go inside those houses; then they will go there and give talk…So we work hand in hand with them"* – FHCW 7. *"…but mostly our community health workers are working with TB and HIV,… Only if, for example, we need to recall our babies for immunisation…. then they will recall those mothers for us.* W*hen we are doing some bloods screening and there is an abnormality, they can't get that person from the phone, and then somebody has to go and do a home visit "* – FHCW 3. *"After delivery, CHWs maybe they visit them (women) at home"* – FHCW 8.
6. Clinical training and retraining for nurses	

	"We trained nurses and they are delivering ART and none believed that in those days, training changes everything…." – Expert 10. *"…When everyone diagnosed with HIV was to be initiated to treatment and nurses had to be train on ART initiation. NIMART was created and trained them"* – Expert 9. *"We said that the NIMART nurse who's got a dispensing licence can also dispense the medication in the MOU, to make sure that the mom gets more of an integrated service…"* – Expert 4. *"In South Africa, for special training, they have to do the NIMART training, and then they can dispense the drugs and look after the patients and the counselling…"* – Expert 5. *"We wanted all the midwives to be NIMART trained, so they would be able to initiate, so they don't send the patients from pillar to post. Then they get tired and don't start their medication because they must wait in other queues"* – FHCW 1. *"….just to send the staff to the trainings on PMTCT, on BANC….yes, I see who is running short, so that I send them for training through NIMART training programme"* – FHCW 4. *"I do BANC and most of the time… I don't have the HIV course, so I must run around and asking those sisters there for my patients all the time; and if they would send me for HIV training that would be resolved"* – FHCW 8. *"…because, the staff have to be trained, and especially on the PMTCT guidelines when they change again, so, they change a*

	lot and there should be uniformity" – FHCW 3.
Complex **7.** Persistent barriers to PMTCT integration	*"If we have an electronic system that talks to each other and the patient has got a single number, we can track her…it's not installed in all the computers and not everyone is trained how to use it...Other health problems like Hypertension is not integrated into the PMTCT services"* – Expert 5. *"I think that there was resistance to change. I remember there was a time, just before we introduced the same day initiation. When we spoke to nurses about it, they said it's impossible, we can't do it; and so there are attitudinal issues and they needed support and training and encouragement. So people don't really want to change necessarily, but when it's policy, you say, well we don't have a choice"* – Expert 7. *"Some mothers book late, and so don't benefit from the services available. Other mothers convert after they've been initially tested and they're especially at high risk, so identifying and getting the mothers onto treatment is one of the big challenges; and then keeping mothers adherent is another challenge"* – Expert 3. *"We wanted all the midwives to be NIMART trained, so they would be able to initiate, so they don't send the patients from pillar to post. Then they get tired and don't start their medication because they must wait in other queues"* – FHCW 1. *"…for stigma purpose, because they know in our communities if you breastfeed then you are regarded as negative….So we have that challenge, breastfeeding for two weeks then stop, swap to formula feeding"* – FHCW 7.

	"I believe there was a problem with a theft on medication. As a result now, the nurses that are doing ANC, they don't dispense medication. So now those mothers, they queue twice" – FHCW 3. *"Our waiting area is very congested. We don't even separate them, you know, like kids as such and mothers…, and also there's poor ventilation in there,… and then they come here and actually, those kids may leave this place more sicker"* – FHCW 3.

The following section discusses the results and demonstrates the sequence and complexity of integrating PMTCT services within PHC in South Africa.

1. Experiences in PMTCT trials and its adoption during AIDS denialism era

From the perspectives of HIV experts who were involved in the initial PMTCT trials, during the era of AIDs denialism, doctors and the other health care professionals, community groups and activists representing people living with HIV were the first to push for access to HIV treatment. These early actors in the campaign for treatment for mothers and children had tremendous and diverse experiences of how PMTCT was rolled-out during and after AIDS denialism. Several experts interviewed had participated in the design and implementation of PMTCT in local pilot sites and at national level. FHCWs interviewed had not been involved in the early stage of PMTCT rollout.

Experts, who to some extent played a key role in advocacy for HIV treatment or against AIDS denialism, recalled the introduction of PMTCT. The majority discussed how unsupportive the Department of Health (DoH) was, and the difficulty in obtaining approvals at local clinics. Six experts who were involved in the initial PMTCT trials in South Africa described how the PMTCT

intervention was vertically rolled-out in selected pilot sites prior to and following the constitutional court ruling in August 2002.

> *"In South Africa, when we started the PMTCT Programme, it was really a programme implemented in 18 pilot sites, and then based on a court order, we had to scale it up nationally, and at that time, it was very much a vertical programme*" – Expert 1.

Though campaigns to prevent MTCT had legal support, it took time for the DoH and all health care providers to fully cooperate with the teams that were delivering HIV interventions. Researchers and activists who were involved in the scaling-up of PMTCT interventions recounted how they personally sought support from health care providers, clinic committees and from pregnant women involved. Bringing together these different groups of stakeholders was essential in gaining support for implementing complex interventions such as PMTCT.

> *"We would first meet with the clinic… Every clinic had a clinic board made up of lay people and community leaders in that district; and so, the first strategy was you get those people to be on your side"* – Expert 2.

In contrast, the majority of the FHCWs knew very little about how PMTCT services were first implemented into PHC in South Africa. Through training and positive outcomes that followed PMTCT rollout in their facilities, FHCWs have learnt the importance of PMTCT within PHC package but most (n=7) were not able to comment on the history of its integration. One clinic manager assumed that PMTCT had been integrated from the beginning.

> *"It's always been integrated, so I don't want to say something that I don't have experience of. I don't want to talk based on assumptions"* – FHCW 1.

Another clinic manager who worked at the pilot site was unable to recall what happened when

PMTCT services were offered for the first time in her facility. Like others with the same experience, stories were short, imprecise and with few details on how PMTCT services were initiated and later integrated into PHC.

> *"We started by piloting it in 1999. We were the pilot site. I must try to think now where I was working in that time of the PMTCT; because I remember these babies, they were HIV affected. You know, it was that way..... We didn't even have registers, at that time, because we didn't even know how big the problem was at the time"* – FHCW 2.

2. Gradual move towards PMTCT acceptance and integration in the clinics

Most experts involved in this study reported that they were among the teams of researchers and activists that were pioneering this intervention and worked to mobilise buy-in and support for PMTCT at an individual and organisational levels. They opposed the government's stand, and worked with clinic boards and community leaders in every district for the acceptance and initiation of PMTCT, as illustrated in the following quote:

> *"It was in the beginning of AIDS denialism, and so the way we entered into the clinic, was we would first meet with the clinic board, and if the clinic board says, we sanction this, it's very hard for the clinic staff not to allow you into the hospital"* – Expert 2.

According to the experts who witnessed the whole evolution of PMTCT scale-up in South Africa, despite the Constitutional Court ruling in favour of PMTCT rollout, research teams, activists and NGOs continued to face challenges in efforts to implement the intervention in most of the provinces. Those championing the rollout encountered resistance from FHCWs who worried about HIV transmission to themselves and that the intervention would add to already heavy workloads. Meanwhile, HIV-related health care needs were increasing in the country, especially among pregnant women attending clinics for antenatal care, which put healthcare workers under increasing pressure

to respond. Health care research teams were also inspired by the civic-minded attitude of those women who willingly participated in early PMTCT trials to support efforts to rollout services to more women. These women were hailed as champions.

> *"… When there was a court instruction to roll it [PMTCT] out; we were all, like, pilot projects. We were doing rollouts, but it was always very controlled…. it was a placebo-controlled study, and the women said to us, "we don't mind being on placebo, as long as you promise us that if this drug works, you will roll it out, and you will give it to all other [women]… So, we will sacrifice ourselves for the future women". So we promised the women that if it worked, we would do whatever it took to make sure that other women in their situation [received the intervention]…"* – Expert 2.

All FHCWs interviewed spoke unreservedly about the benefits of the PMTCT programme, reporting that they had progressively embraced new initiatives and expressed their full support for PMTCT integration into PHC services. They saw how PMTCT integration at a facility level helped to deliver services to community, and how this had become crucial for the successful delivery of other services for maternal and child health. A researcher who participated in PMTCT rollout from the very beginning and a manager working at the PHC level discussed how integration of PMTCT services in local health facilities benefited other services.

> *"..Mother to child transmission is such a big problem. It has so many adverse consequences affecting key public health indicators, such as maternal and under five and infant mortality, that it became a priority health problem for the health services to solve. So the natural home for PMTCT is within the main stream services"* – Expert 6.

> *"With the integration, it's the best thing that ever happened, and also where we are now, compared to ten years ago, it's like a big improvement; from the infection perspective-wise, of cross-infection and stuff, from mother to child"* – FHCW 1.

Despite strong support from women and FHCWs, the rollout faced a number of challenges. Addressing HIV related stigma and increasing programme acceptance required support from community-based NGOs. NGOs included those with a special focus on treatment like Médecins Sans Frontières (MSF) and those with activism and advocacy aims like TAC. Experts and FHCWs who worked with NGOs on a daily basis in their local facilities praised them as key players in PMTCT intervention acceptability, in retaining women, or in boosting support from families of women attending PMTCT with their babies after delivery. Four FHCWs and three experts discussed how NGOs have helped from the very beginning - from awareness campaigns, assisting in the training of lay health workers and equipping clinics, as well as providing support and follow-up with women in their communities. NGOs using community health workers (CHWs) and lay counselors continue to play a vital role in working with national health department to reinforce governmental initiatives dealing with MTCT and increasing women retention.

"…So it has improved a lot based on other NPOs [*non-profit organisational staff*] *that assist us if we have a problem when we can't find, a patient, then mothers trace them, or the NPOs trace them*" – FHCW 3.

3. Commitment to PMTCT services integration

All participants discussed knowledge of health care services integration and their experience in the process of integrating PMTCT cascades in PHC. Experts considered PMTCT integration as the 'right process' to bring together clinical activities. All experts believed that PMTCT fitted well within other maternal and child health (MCH) services and felt that it had been smoothly integrated into other available services in the clinics such as tuberculosis treatment, sexually transmitted infections and mental health services.

"It's linking better with the MCH programmes… On the ground, I think, at facility level, there

always is integration" – Expert 1.

FHCWs who had been involved in service delivery at the clinics understood how challenging it had been to integrate various services in their facilities. However, they recognised the importance of PMTCT integration in daily service provision at the clinics. In striving to deliver a package of comprehensive services, PMTCT became the core component among the services offered at their local facilities. For example, one of the FHCWs shared how she worked to ensure all services were integrated for the convenience of women.

"So, what I did, I tried to integrate everything, and to make sure that whoever is working here is going to give a one-stop-shop… They [the woman] are going to get all the services they are supposed to get, instead of going there and there and there" – FHCW 1.

4. Increased awareness and community participation

In addition to combined efforts from both national and provincial health systems, local authorities and NGOs to increase PMTCT awareness, community involvement was also essential to increasing uptake and sustainability of the programme. PMTCT mobilisation and integration campaigns have therefore included community-members to share first-hand messages and experiences to peers, relatives and neighbours and ensure the intervention is widely known and accepted. The following two groups were, based on our interviews, identified to have carried out important advocacy and treatment messages about PMTCT and boosted its successful implementation: mothers-to-mothers, and male partners of women who accessed PMTCT.

Mother-to-mother services

Barriers to accessing services, treatment initiation and adherence to it, were acknowledged by both experts and FHCWs. Mother-to-mother (M2M) was perceived as the core peer-support

organisation to offer services that helped to address these challenges. First initiated and registered as an NGO partnering with other governmental, multilateral and individual organisations, M2M started in South Africa employing trained mothers living with HIV to provide psychosocial support to pregnant women and mothers of babies diagnosed with HIV, to promote retention and to encourage disclosure (Shroufi et al., 2013). Strong support for mother-to-mother' initiatives was expressed by both experts and FHCWs:

> *"Mother-to-mother initiatives have been fantastic for making sure moms come back and take the medication…community support also plays a key role in supporting moms throughout this whole cascade. Peer support is important"* – Expert 3.

> *"Mothers to Mothers services which are supporting the HIV mothers who are pregnant and those after delivery, work hand in hand with antenatal labour ward as well as Child Health for continuity of care"* – FHCW 3.

Both groups of participants also discussed how the M2M peer support group meetings were forums in which women discussed appropriate solutions in responding to HIV infection in their communities, as well as issues they experience, such as difficulties with treatment adherence, social support and poverty. M2M also provides an opportunity for health education and counseling to address any concerns and increase understanding of HIV transmission, MTCT and basic health preventive health practices.

Male involvement in PMTCT

Active involvement of males in supporting pregnant women living with HIV was regarded as important by both experts and FHCW. However, experts described how antenatal and postnatal health services in the country are 'womanised' - a situation that did not foster male involvement in services.

Both experts and FHCWs emphasized the need for more efforts to bring in partners to services to improve PMTCT.

> *"Male integration is something else we didn't do well and it needs to be improved a bit…and our health services are female oriented and male staff and partners of our women clients are to (should) be more involved"* – Expert 3.

FHCWs found male support and collaboration difficult to gain:

> *"Other contributions were involving other… allowing people to be involved from outside, especially the men, because our African men don't go to antenatal….to promote the partners to come with"* – FHCW 3.

5. Community health workers' involvement

While there is a long history of CHW involvement in PHC, the advent of HIV and of treatment for HIV and tuberculosis in South Africa led to a major increase in the numbers and visibility of CHWs such as lay counsellors. Many were employed by NGOs and funded by external donors but working in close collaboration with public health facilities (Tsolekile et al., 2018). For experts, CHWs were a cornerstone for linking communities and health systems, addressing stigma and discrimination at family and community level, and for supporting medication adherence. They emphasised the need to establish or enhance community-based services (CBS) with CHWs engagement and full collaboration with health systems.

> *"They (CHWs) are more available than other health workers in the clinics….and if you go back to the HIV story again, I mean, using CHWs is all about bringing HIV care back to the community as they are in charge of what they call community-based club,…. and this gives more room for those nurses and others in clinics to deal with more urgent issues, because*

they are overcrowded now. It (the club) gives them that repeated contact and a lot of those redundant tasks can obviously be shifted nicely to a community health worker who is trained and accessible, and then that eases the pressure on the clinic" – Expert 4.

Experts valued the contributions of CHWs, especially in responding to HIV and in facilitating PMTCT implementation. Increased training and appropriate payments for CHWs were suggested by experts, to ensure that they are motivated and are able to support communities in partnership with local health facilities. Experts experience was that, despite intentions that NGOs provide adequate training, supervision and payment, this was done so inconsistently.

"That systems of peers and CHWs, they need to be properly trained and paid, that's my opinion…When they are trained and offer their services, they have to be paid" – Expert 3.

FHCWs also recognised the importance of CHWs at different fronts to link local health facilities and the communities. Three FHCWs stated they had reservations about the involvement of CHWs but acknowledged that they are useful in ensuring follow-up of women and continuous PCR testing and immunisation for babies. Some CHWs were thought not to have the required education to support community members. This meant that continuous training and supervision by the designated clinic nurse or midwife was required to ensure that the right information and quality services were delivered by CHWs as suggested by one clinic manager:

"….because I need first somebody to train them, or maybe somebody senior to them to listen to what they are saying, because people they start to ask questions. We also see that as an option and then some of them don't even have grade 12, so, those kinds of things. So, we try to control it…" – FHCW 2.

However, most FHCWs described collaboration with CHWs as critical to the success of the PMTCT programme and facilitating its reach into the surrounding communities. CHWs supported

the delivery of health education for a range of health issues, located mothers for appointments if they could not be reached via phone and organised HIV/AIDS support groups at antenatal clinics.

> *"I will say they are helpful, because we use them as the bridge just to get to the communities, because they go the extra mile in this way that they go inside those houses; then they will go there and give talk…So we work hand in hand with them"* – FHCW 5.

6. Clinical training and retraining for nurses

Given the challenge of doctors providing treatment to a large number of people living with HIV, South Africa has adopted a decentralised approach, allowing other health professionals to prescribe treatment. The Nurse Initiated and Managed Anti-Retroviral Therapy (NIMART) training programme was established as an effective task-shifting strategy, following the conclusion of the Streamlining Tasks and Roles to Expand Treatment and Care for HIV (STRETCH) study in South Africa in 2010 by Fairall L. et al. (Fairall et al., 2012). Its role was to train nurses to not only test HIV, but prescribe ART support to pregnant women living with HIV. It was regarded as successful by both experts and FHCWs but they described several challenges in the roll-out of this programme. The shortage of NIMART trained nurses and midwives was thought to result in high workload for those trained and was linked to long waiting hours in the queues and poor-quality services.

> *"Well, I think in the facilities where you've got enough NIMART trained nurses, there isn't a problem…"* – Expert 5.
>
> *"We wanted all the midwives to be NIMART trained, so they would be able to initiate, so they don't send the patients from pillar to post. Then they get tired and don't start their medication because they must wait in other queues"* – FHCW 3.

"Because I do BANC [basic antenatal care] and most of the time… I don't have the HIV course, so I must run around and asking those sisters there for my patients all the time; if they would send me for HIV, then it's going to be okay…" – FHCW 6.

Frequent changes in PMTCT and ART guidelines also presented challenges in ensuring all staff members understood and were implementing updated guidelines.

"I think it is still challenging, particularly when we have to implement new guidelines, because we've got to go through a whole process of training and retraining. And the trouble is with the whole HIV and PMTCT field, is evidence evolves and guidelines change rapidly or consecutively in close succession, so we need to keep retraining groups of people" – Expert 1.

In particular, several experts and FHCWs mentioned changes in the guidelines about breastfeeding. While HIV mothers were previously recommended to formula feed, mothers who have a supressed viral load are now being asked to breastfeed consistently. This has resulted in confusion for both staff members and mothers.

"The other challenge was consistent messaging, because you know, different people were saying different things, and there was a lot of confusion about infant feeding" – Expert 1.

7. Persistent barriers to PMTCT integration

Like other complex health programmes, PMTCT rollout has faced challenges in South Africa (**Table 6**). Experts mentioned attitudinal issues from facility-based health care workers and lack of accountability and bureaucracy at all levels of management in the health system. They also discussed how poor communication and inconsistencies in the fidelity to the clinical algorithm and practice guidelines reduced the overall quality of care, in some facilities.

"I think it's due to a lack of accountability and a lack of good management at all levels…And currently, there's no great communication between primary level and hospital level generally, referral both ways" – Expert 6.

Table 6: **Persistent barriers to PMTCT integration**

According to experts	Common to both experts and FHCWs	According to FHCWs
• Bureaucratic slowness • Lack of managerial accountability • Poor quality of care including suboptimal fidelity to algorithms • Poor training of staff • Attitudinal issues among health care workers in the facilities • Discrimination, stigma • Lack of national health information systems and issues relating to electronic records	• Loss to follow-up • Socio-economic issues for women • Women migration • Lack of unique patient identifiers • Resistance to change	• Small working spaces and other infrastructure related challenges like poor ventilation, congestion, among others • Shortage of personnel and work overload • High staff turnover • Guideline changes • Too much paperwork for managers

Experts suggested that a single health information system has the potential to improve efficiency in patient identification, follow up and reporting and take its integration to a new stage.

"So, we know patients are nomadic… we need linked electronic patient records, and the problem is for HIV care for example in this city, they have three different systems" – Expert 5.

FHCWs also expressed frustration regarding the lack of communication between clinics and their referral hospitals and the lack of a national-wide system of unique identifiers for all patients.

"If we transfer them, they must take over everything, but the problem is, if the patient went to a hospital, even if she went to our Khayelitsha District hospital, if they give them medication there, it doesn't appear, because we don't know where they captured them. So, they appear to us as defaulters, up until we must phone them" – FHCW 8.

FHCWs discussed how their heavy workload, inadequate training, staff shortages and high staff turnover affect the quality and outcomes of service delivery in their health settings.

"It was not all smooth sailing, due to staff turnover…..I had, like almost, six, seven nurses who were basic antenatal care [BANC] trained, who can do all for the pregnant mother… from the time that their patient is pregnant until the baby is born, and still look after the baby, but then with the staff turnover, they left and it was tough, terrible! I've got only two people who are BANC trained, and these people, it's not like the only thing that they must do. They were doing other things as well, and not only focussing on this [PMTCT]" – FHCW 1.

Discussion

Political support of AIDS denialism at national level resulted in the deaths of many mothers and children, and delayed South Africa's adoption of PMTCT until 2002 (Burton et al., 2015). Since then, South Africa has been leading the development of PMTCT integrated into PHC in order to address broader maternal and child health care. This study adds to the limited literature on what has enabled, and challenged, the integration of PMTCT from the perspectives of both FHCWs and experts.

The interviews highlighted that commitment and ground level collaborations between different stakeholders, including policy, research and activist groups, FHCWs and women from the broader community were essential to navigating around the political climate to ensure the integration

of PMTCT services. Considering health system and community elements and their interactions is key to the success of interventions or programmes and should be looked at in terms of degree of interrelatedness and actors from health system structures, their understanding and functions (Kannampallil et al., 2011) as demonstrated in the study conceptual framework . While the rollout of PMTCT was met with resistance early on from FHCWs, they slowly joined the efforts to integrate, agreeing with experts on the importance of PMTCT integration within existing services, especially those related to MCH. As PMTCT care was incorporated into well-equipped facilities where trained doctors and nurses were available, NIMART training contributed to a decentralised approach with a special focus on women and children from general HIV care. As the task-shifting model aimed to overcome issues of low doctor/patient ratio, PMTCT integration was seen as relatively successful by all participants. However, consistent with what happens in other countries, FHCWs argued that beyond focused training on PMTCT algorithms, workload and infrastructure constraints have impeded work towards full integration and eliminating MTCT in South Africa (Davies et al., 2013; Jones & Cameron, 2017; Sanne et al., 2010). Apart from NIMART that has not been offered to all nurses due to many not reaching the qualification threshold, PMTCT protocols have continued to evolve and require compulsory both off-and on-the-job training – which not all FHCWs are able to attend, resulting in PMTCT integration in some local facilities being limited.

The need to involve other groups outside of the health system from the outset for training, treatment, advocacy and community mobilisation (such as MSF, TAC, M2M or other well-equipped NGOs) to reinforce PMTCT services integration was acknowledged by all study participants. Such collaborative initiatives were required from the very beginning to manage the health needs of pregnant women and their babies (Uwimana et al., 2012a). NGOs and partnering local community groups supplemented overwhelmed FHCWs to implement various programmes at local health facilities. Despite the criticism of competition for funding rather than cooperation with national, provincial and

district health departments (Mate et al., 2013), this experience of collaboration was positively regarded by all study participants. Mother to mother services were highlighted by both experts and FHCWs as a way to reduce MTCT and strengthen community-based support. Participants credit M2M efforts and services with establishing links between PMTCT mothers and their local PHC facilities, and maintaining them through the many elements of the PMTCT cascade (SOUTH AFRICA|m2m.org, 2020). A study conducted in Zimbabwe by Shroufi, A. et al. (Shroufi et al., 2013) has similarly found that M2M increases retention in PMTCT, owing to their community-based approach. The three M2M core objectives of 1) reducing the number of babies infected with HIV during or after delivery; 2) promoting the health of pregnant women and new mothers and increasing their opportunities to access and effectively use health and life-sustaining ART; and, 3) supporting disclosure and fighting stigma and discrimination (Baek et al., 2007) have been generally achieved in the SA context (Baek et al., 2007; Lazarus et al., 2010; Nieuwoudt et al., 2019; Schunder et al., 2020).

Participants in this study explained how and why the CHWs are increasingly accepted into PHC. CHWs have emerged as key players in response to HIV/AIDS, tuberculosis and the Ebola virus, among other health problems – particularly in overwhelmed health systems like in South Africa (Gautier et al., 2017; Mwai et al., 2013; Rachlis et al., 2016; Schneider et al., 2008). In case of PMTCT services, the CHWs' role has evolved to improve health for both mothers and their infants, as well as for other family members in the households in different areas of health priority such as disease prevention, hygiene, nutrition, family planning, social support and domestic abuse (Bhutta et al., 2010; Futterman et al., 2010; Lewin et al., 2010; Perry et al., 2014; Shetty et al., 2008). Even though critical, investment in CHWs in South Africa has to date been through NGOs partnerships and have not yet been formally institutionalised nor thoroughly documented despite being considered as a key element of PHC re-engineering strategy, launched almost a decade ago (National Planning

Commission, 2012; Pillay & Barron, 2011; Schneider et al., 2008). This situation does not motivate nor facilitate the development of CHWs, who are mostly from a low social-economic background, in their commitment to advance health care services in communities and at the local facilities. Continuous in-service training, adequate supervision, proper financial incentives and other benefits could bridge the gaps in CHW's knowledge and ability to work closely with PHCs – issues that currently can raise ethical questions in relation to quality of care (Ormel et al., 2019).

Both experts and FHCWs were enthusiastic about the positive results already achieved by PMTCT but were dismayed by HIV stigma and discrimination, small and insufficient spaces and other infrastructure related challenges in the facilities. They did, however, diverge on experiences regarding other health system challenges that impede the full integration of PMTCT within PHC and consequently the virtual elimination of MTCT in South Africa. Experts insisted on bureaucratic slowness and lack of managerial accountability, poor quality of care, including suboptimal fidelity to algorithms and remnant attitudinal issues in the facilities as obstacles. FHCWs expressed concerns with work overload, high staff turnover, loss to follow-up of women, shortage and poor training of staff. These challenges, among others, are well documented to have historically affected the quality of health care that is a constitutional obligation in South Africa (Maphumulo & Bhengu, 2019; Stuckler et al., 2011) and have indeed slowed down the progress with regard to PMTCT integration and virtual MTCT elimination in the country (Goga et al., 2018; Sprague et al., 2011). Participants from both groups suggested approaches and initiatives to address these complex common issues faced by health systems in South Africa and in other LMICs as illustrated in this study conceptual framework. These measures include investment in infrastructures, adequate training of workforce in various capabilities, use of electronic unique patient identifiers and health information technology, social assistance to facilitate transportation, as well as increased investment in the fight against hunger and addressing a number of social factors contributing to HIV-related stigma and discrimination in

which influence non-disclosure and low adherence rates (Chersich et al., 2018; Etoori et al., 2018; Goga et al., 2019; Mahy et al., 2010; Rodriguez et al., 2017). This would be a tremendous step towards fully integrated PMTCT especially in the introduction of WHO recommended option B+ adopted in South Africa, in which all positive tested women are initiated to ART regardless of their CD4 cell count (Chersich et al., 2018; Etoori et al., 2018). Once achieved, full integration of PMTCT would serve as a PHC model to adequately deal with multimorbidity epidemics among ageing populations, including women living with HIV (Luijks et al., 2016; Sturmberg et al., 2016; Trickey et al., 2017). With more investment from stakeholders and consistent changes in bureaucracy and greater accountability from National Department of Health, PMTCT integration within other basic health services might be revamped and more fully reported on in South Africa (Burton et al., 2015; Nicol et al., 2016).

Strengths and limitations of the study

Strengths

This study recaptured the history of PMTCT implementation at local PHC facilities and documented lost lessons or failures, as well as successes, that could be relevant for the integration of other interventions into routine primary care. It also included both experts and FHCWs who had different perceptions. Participants also ranged in their years of involvement in PMTCT implementation, and included those who had been involved in pre-2008 PMTCT services.

Limitations

Despite these strengths, this study also had limitations. Social desirability may have influenced responses and additional challenges may not be captured. Experts were from different

areas, including policy, research, advocacy among others and this may have impacted their shared perspectives and experiences. The Western Cape and Cape Town have the best health systems and had hosted the first PMTCT pilot sites in the country - therefore, the practices and experiences of FHCWs working in this region may vary substantially from those of other provinces in South Africa. This study used a small sample size, and may not be representative of the experiences of experts and FHCWs across South Africa.

Conclusion

While the integration of PMTCT into PHC has been hailed as a success, this research identified ongoing challenges in the integration process for HIV/PMTCT from both the perspectives of experts and FHCWs. Existing issues in bureaucracy and accountability presented barriers to full integration of PMTCT. For FHCWs, concerns of heavy workload and infrastructure constraints, and ongoing issues with training and high staff turnover created challenges in the care of both mother and child. South Africa has prioritised eMTCT – addressing such challenges in the integration of PMTCT into PHC will enable South Africa to achieve this.

Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ART	Anti-Retroviral Therapy

AZT	Azidothymidine or Zidovudine
CDC	Centers for Disease Control
COREQ	COnsolidated criteria for REporting Qualitative research
FHCWs	Frontline Health Care Workers
GFATM	Global Fund to fight against AIDS, TB and Malaria
HAART	Highly Active Anti-Retroviral Therapy
HIV	Human Immunodeficiency Virus
IQR	Inter Quartile Range
LMICs	Low- and Middle-Income Countries
MCH	Maternal and Child Health
MSF	Médecins Sans Frontières
MTCT	Mother-To-Child Transmission
M2M	Mother-to-mother
NGOs	Non-Governmental Organisations
NIMART	Nurse Initiated and Managed Anti-Retroviral Therapy
PCR	Protein-Chain Reaction
PEPFAR	President's Emergency Plan for AIDS Relief
PHC	Primary Health Care

PMTCT	Prevention of Mother-To-Child Transmission
SD	Standard Deviation
SSA	Sub-Saharan Africa
TAC	Treatment Action Campaign
USAID	United States Agency for International Development
WHO	World Health Organisation.

Declarations

Ethics approval and consent to participate

The study was approved by the Human Research Ethics Committee at the Faculty of Health Sciences, University of Cape Town (HREC REF: 946/2014) and the Centre de Recherche du Centre Hospitalier de l'Université de Montréal (2018-6690, 17.044 - ID). Written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analysed during the current study are not publicly available to preserve participant anonymity.

Competing interests

JCM, CG, LM, LJW, SN, KM, NL, HT and CZ declare no competing interests.

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Authors' contributions

JCM, CZ, and HT designed the study. JCM conducted interviews, data analysis and wrote the first manuscript under the supervision of CZ and HT. CG, LM, LJW, SN, KM, NL, HT and CZ critically revised versions of the manuscript. All authors read and approved the final manuscript for publication.

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Additional files

File 1. COREQ checklist

COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	10
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	36
Occupation	3	What was their occupation at the time of the study?	1, 36
Gender	4	Was the researcher male or female?	10
Experience and training	5	What experience or training did the researcher have?	10
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	9-10
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	9-10
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	9-10
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	8-9, 11
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	9
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	9-10
Sample size	12	How many participants were in the study?	9-10
Non-participation	13	How many people refused to participate or dropped out? Reasons?	9-10
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	10
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	10
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	10
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	10-11
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	N/A
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	11
Field notes	20	Were field notes made during and/or after the inter view or focus group?	11
Duration	21	What was the duration of the inter views or focus group?	10
Data saturation	22	Was data saturation discussed?	10-11
Transcripts returned	23	Were transcripts returned to participants for comment and/or	N/A

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
Data analysis			
Number of data coders	24	How many data coders coded the data?	11
Description of the coding tree	25	Did authors provide a description of the coding tree?	11-13
Derivation of themes	26	Were themes identified in advance or derived from the data?	11
Software	27	What software, if applicable, was used to manage the data?	11, 12
Participant checking	28	Did participants provide feedback on the findings?	N/A
Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	14-26
Data and findings consistent	30	Was there consistency between the data presented and the findings?	13-26
Clarity of major themes	31	Were major themes clearly presented in the findings?	12-26
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	N/A

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.

*Page numbers in this tool appear as they were included in the published article.

File 2. Interview guide for experts and FHCWs

Integrating the prevention of mother-to-child transmission of HIV into primary healthcare services after AIDS denialism in South Africa: Perspectives of experts and health care workers - A qualitative study

Interview guide for experts and FHCWs

1. **Introduction**

Thank you for agreeing to be interviewed today. We appreciate your time. The reason why we have asked you to come today is because we want to learn out more about your experiences with the PMTCT programme and the care received by women with gestational diabetes at the clinic during ANC and post-partum.

There are no right or wrong answers to our questions. Different opinions and experiences are valuable to us and we hope you feel comfortable enough to be honest with us. If you have any negative comments or feedback you would like to give us, that is fine.

The information you share with us today is completely confidential. Your responses will not have any identifying information. Your responses will only be shared with members of the study team and will be compiled with other responses from various participants. We would like to tape our discussion because I cannot write down everything you say, but this will also remain confidential.

Before we start, we need to ask you to give us your consent. This means that this discussion is voluntary and you are free to withdraw at any time without having to give a reason.

Do you have any questions about the interview? Is there anything that is worrying you?

Do you have any *other* questions before we start the interview?

2. **Demographic information**

Names:

Age:

Sex:

Institution:

Position:

Years of experience:

Contact details:

3. **Interview guide**

1. We are interested in understanding how PMTCT has moved from being a vertical program, to one that is integrated into PHC. Can you share your perspectives of the key points, successes, and challenges with the integration history or process in South Africa?
2. We are hoping to learn from the PMTCT integration experience in order to help support integrated care for other health problems, including diabetes, hypertension, and others into PHC. Can you share your perspectives on whether and how other health problems or issues are managed or integrated in the guidelines and into the PMTCT services?
3. We would very much appreciate to hear your perspectives on how these processes are actually playing out on the ground in individual facilities and communities. From your engagement with the clinics, with the clinic manager (s), with the nurses/midwives or other health care providers, please can you describe your views of:

- How the clinic(s) are functioning in terms of PMTCT integration?
- Which have integrated PMTCT, at which level (extent) and why?
- How is postnatal care managed?

- What is/are the role of clinic manager (s)?
- What the role health care providers (Nurses and CHWs) are playing?
- What are the challenges and successes for integrating other health problems such as diabetes in post-partum for women under PMTCT programs? Probe: Whether the management of the clinics in jurisdictions are changing to integrate the care of these diseases, whether the GDM is specifically managed in PMTCT program and whether there is a planned post-partum follow up for women with subsequent GDM.

4. Finally, is there anyone in particular you think we should talk to next or any important documents or guidelines that we should consult?

Paper 3 – Integrating gestational diabetes and type 2 diabetes care into primary health care: lessons from prevention of mother-to-child transmission of HIV in South Africa - A mixed methods study

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Status: This mixed methods study was published in PLOS One journal (January 2021). (Mutabazi et al., 2021). http://dx.doi.org/10.1371/journal.pone.0245229

Abstract

Background: Implementation of Prevention of Mother to Child Transmission of HIV (PMTCT) programs into antenatal care over the last three decades could inform implementation of interventions for other health challenges such as gestational diabetes mellitus (GDM). This study assessed PMTCT outcomes, and how GDM screening, care, and type 2 diabetes (T2DM) prevention were integrated into PMTCT in Western Cape (WC), South Africa.

Methods: A convergent mixed methods and triangulation design were used. Content and thematic analysis of PMTCT-related policy documents and of 30 semi-structured interviews with HIV/PMTCT experts, health care workers and women under PMTC diagnosed with GDM complement quantitative longitudinal analysis of PMTCT implementation indicators across the WC for 2012-2017.

Results: Provincial PMTCT and Post Natal Care (PNC) documents emphasized the importance of PMTCT, but GDM screening and T2DM prevention were not covered. Data on women with both HIV and GDM were not available and GDM screening was not integrated into PMTCT. Women who attended HIV counselling and testing annually increased at 17.8% (95% CI: 12.9% - 22.0%), while women who delivered under PMTCT increased at 3.1% (95% CI: 0.6% - 5.9%) annually in the WC. All 30 respondents favour integrating GDM screening and T2DM prevention initiatives into PMTCT.

Conclusion: PMTCT programmes have not yet integrated GDM care. However, Western Cape PMTCT integration experience suggests that antenatal GDM screening and post-partum initiatives for preventing or delaying T2DM can be successfully integrated into PMTCT and primary care.

Key words: Integration, primary health care, Prevention of Mother-to-Child Transmission of HIV, Gestational diabetes, Type 2 diabetes, South Africa.

Abbreviations

ANC	Ante-Natal Care
ART	Anti-Retroviral Therapy
CHWs	Community Health Workers
CI	Confidence Interval
DOH	Department of Health
GDM	Gestational Diabetes Mellitus
GSH	Groote Schuur Hospital
HCT	HIV Counselling and Testing
HIV	Human Immunodeficiency Virus
MCH	Maternal and Child Health
MMAT	Mixed Methods Appraisal Tool
NGOs	Non-Governmental Organisations
NCDs	Non-communicable diseases
PCR	Protein-Chain Reaction
PHC	Primary Health Care
PLHIV	People Living with HIV
PMTCT	Prevention of Mother-To-Child Transmission

PNC	Post Natal Care
REML	Restricted maximum likelihood
SA	South Africa
T2DM	Type 2 Diabetes Mellitus
WC	Western Cape
WHO	World Health Organisation

Background

South Africa (SA) has extensive programs for HIV counselling and testing (HCT) and lifelong antiretroviral therapy (ART) aimed at achieving national and global HIV control targets (Abuogi et al., 2018; Barron et al., 2013b). These include integrated primary health care (PHC) based post-partum follow-up for both mothers and their babies, who undergo early diagnosis using HIV polymerase chain reaction (PCR) testing (Abuogi et al., 2018; Dunning et al., 2017). With the implementation of Prevention of Mother-to-Child Transmission (PMTCT) of HIV, and its subsequent integration into existing primary health care services, coverage has increased over time, especially in the wake of the initiation of lifelong ART immediately after diagnosis, regardless of CD4 count or clinical staging (Etoori et al., 2018; Muyunda et al., 2020; WHO, 2020). This approach, known as Option B+ for PMTCT, was included in national policies and implemented in more than 95% of countries worldwide, resulting in the considerable reduction of infections in children (Etoori et al., 2018; Muyunda et al., 2020; WHO, 2020). In a country with a high HIV prevalence among pregnant women, ranging from 30% to 50% in some areas (SANAC, 2017), the effectiveness of an integrated PMTCT cascade has influenced other services, especially those available within ante-natal care (ANC) in all local health settings in SA. Although the impact of PMTCT integration has not been quantified in terms of health indicators and economic output, evaluations indicate that integration has helped to revitalise PHC (Both & van Roosmalen, 2010; Mutabazi et al., 2017). However, influence on other programmes in primary care has not included screening and managing non-communicable diseases (NCDs), like gestational diabetes mellitus (GDM), which are on the rise among pregnant women and their offspring in low- and middle-income countries like SA (Hussein, 2017). GDM is defined by the World Health Organisation (WHO) as “any degree of glucose intolerance with onset or first recognition during pregnancy” (American Diabetes Association, 2004; Metzger, 1998). It occurs in 2 to 9% of all pregnancies and increases pregnancy or delivery complications and long term

risks of developing T2DM for both mothers and their babies, even though up to 95% of women with GDM revert to normal glucose levels after delivery (Crowther et al., 2005; Gilmartin et al., 2008; Hoffman et al., 1998). GDM prevalence in SA is not exactly known but was estimated at 9.1% in a study conducted in 2018 (Macaulay et al., 2018). Women who are diagnosed with GDM in SA are referred from their primary care clinics to receive ante-natal care and delivery services at the nearest tertiary facility. While those who are HIV positive return to their PHC facility for follow-up after delivery, there is no follow up intervention other than a referral letter for a six-week post-partum oral glucose tolerance test for women who had GDM, despite their well monitored ANC and delivery (Adam & Rheeder, 2017b; Muhwava et al., 2018). Regardless of how other women's health problems are treated, ART after delivery is consistently offered and monitored. Integrating GDM screening and T2DM prevention through PMTCT might be an innovative approach that could further improve health services for this same population (HIV positive women and their babies) and strengthen health systems in SA.

The PMTCT cascade begins with HCT, continues after delivery and has been universally integrated into ANC and postnatal care for both women and their exposed babies (Delobelle, 2013; Turan et al., 2015). Through PMTCT, many lessons have been learned in SA on how to adequately provide and maintain treatment for women during and after pregnancy - more so than for other people living with HIV (PLHIV) who are not as closely supported (Abuogi et al., 2018; National Department of Health (NDoH), 2016). Women under PMTCT learn to navigate the health system and to prioritise protecting their health post-partum. This reinforces their adherence to ART and leads to virtual elimination of mother-to-child transmission of HIV (National Department of Health (NDoH), 2016; Okafor et al., 2014) and could create opportunities for other linkages. In addition, due the high prevalence of HIV and increasing prevalence of GDM among pregnant women in SA (Barron et al.,

2013b; Mamabolo et al., 2007), the PMTCT integration experience offers opportunities and lessons for integrating GDM screening and T2DM prevention initiatives into existing PHC services.

This study aimed to assess PMTCT implementation outcomes, and how GDM screening and care and T2DM prevention were integrated into PMTCT in Western Cape Province (WC), SA. It also explored how the PMTCT experience might bridge gaps in screening GDM and preventing T2DM for women and their exposed babies at the primary level of care in SA.

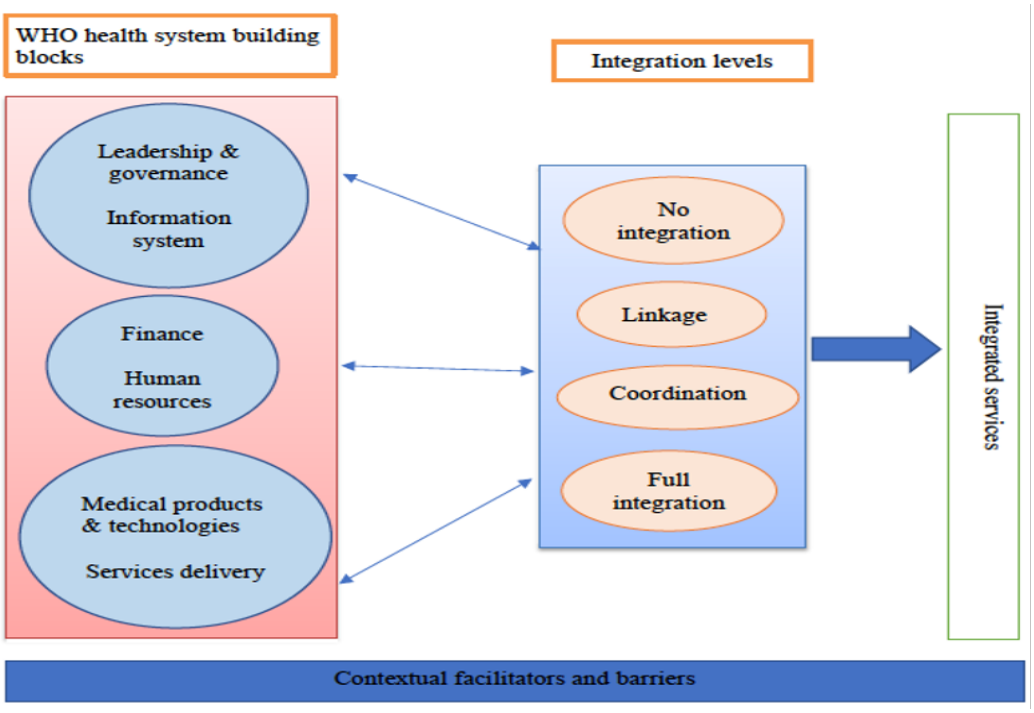
Study framework

This study framework draws from the WHO "six building blocks" model (WHO, 2015), as well as the health systems integration framework proposed by Atun et al. (Atun et al., 2010b; Shigayeva et al., 2010a). In the latter, a "levels of integration" framework, analysis of interactions between programmes and interventions in health systems facilitates the determination and understanding of different integration levels. Possible levels of integration include **no integration**, when there is no formal interaction between programmes, **partial integration** ranging from (1) ***linkage***, or unstructured interactions, to (2) ***coordination*** with a committee to oversee their goal-oriented interchanges, but keeping separate structures, and finally to **full integration,** in which two programmes are merged in both their structural (funding, human resources, information systems) and functional elements (strategic planning, resource allocation, intervention delivery) (Atun et al., 2010a; Shigayeva et al., 2010a).

The six WHO health system building blocks (WHO, 2015) that contribute to the strengthening of health systems, in conjunction with health service integration are: 1) leadership and governance, 2) health information systems, 3) health financing, 4) human resources for health, 5) essential medical products and technologies, and 6) service delivery. Once access, coverage, quality and safety are ensured, improved health (in terms of level and equity), responsiveness, social, and financial risk protection and improved efficiency would follow.

The contexts in which health interventions are implemented differ and are likely to pose diverse facilitators and barriers to the process of integration. It is therefore important to bring together both key structural components of health systems and the processes related to interaction and integration of health programmes in a given context in order to arrive at a framework for analyzing and implementing integrated services.

While our adapted framework included "no integration" and "full integration" as theoretical possibilities for eventual integration of GDM and T2DM management with PMTCT services, earlier formative research suggested that there was openness to and perceived feasibility of partial integration among health system actors (Muhwava et al., 2018). The study therefore concentrated on this middle option. The adapted framework (Atun et al., 2010a, 2010b; Shigayeva et al., 2010a; WHO, 2015), proposed for this study is outlined in **Figure 7**.



WHO health system building blocks and integration levels.
(Atun et al., 2010a, 2010b; Shigayeva et al., 2010a; WHO, 2015).

Methods

Study design, setting and participants

A mixed method research strategy with a convergence design and data source triangulation was used (Carter et al., 2014; Creswell & Clark, 2017). Having diversified data sets collected from various sources helped to strengthen our internal validity through triangulation (Yin, 2013). This study contributes to and draws on an ongoing complex intervention implementation research project, IINDIAGO, aiming to integrate improved post-partum follow up for women with GDM into PHC and thus to contribute to prevention of T2DM in women with GDM in two South African provinces (WC – focus on Cape Town, and Gauteng – focus on Soweto township in Johannesburg). The overall research process was checked against the methodological quality criteria of the Mixed Methods Appraisal Tool (MMAT), version 2018 (Hong et al., 2018). The methods and data sources included 1) documentary analysis of PMTCT and postnatal care policies; 2) semi-structured in-depth qualitative interviews with experts, health workers and women diagnosed with GDM while under PMTCT; and 3) quantitative longitudinal analysis of PMTCT implementation indicators across the WC for 2012-2017. A sub-analysis of outcomes for women with GDM under PMTCT and included in the PMTCT database was planned.

With regards to qualitative interviews, three groups of respondents were interviewed. The first were experts involved in research, programme development or evaluation related to integrating PMTCT into primary care at both national and provincial levels. The second were health workers drawn from public PHC facilities in Cape Town, WC Province, in order to inform the Cape Town arm of the ongoing IINDIAGO intervention study. The third were women with both GDM and HIV who were followed in PMTCT services in Cape Town. Respondents for all three groups of participants for semi-structured interviews were purposively selected.

Qualitative data collection and analysis

Two policy documents; 1. *The Western Cape Consolidated Guidelines for HIV Treatment: Prevention of Mother-to-Child Transmission of HIV (PMTCT), Children, Adolescents and Adults – Amended version (Provincial Government of the Western Cape, 2015), and 2. The Western Cape Postnatal Care Policy (Provincial Government of the Western Cape, 2016)*, developed by the WC Department of Health (DOH) experts, on the basis of national and international guidelines, were obtained as public records (O'Leary, 2014). Content analysis (Bowen, 2009) of the two documents was conducted to understand the PMTCT and postnatal care practices in SA and provide contextual information relevant to interpreting qualitative and quantitative data (Bowen, 2009).

Interviews:

Experts: Eligibility criteria included experience in research, programme development or evaluation related to integrating PMTCT into primary care at both national, provincial and international levels. Three of the 13 experts contacted by email were unable to attend the interview due to schedule constraints, leaving a final sample of 10.

Health workers: Clinic managers, PMTCT nurses and midwives in clinics under the DOH of the city of Cape Town or WC province, with experience in organising PMTCT and ANC services were included in the study. Two of 12 health workers contacted by introductory email and a follow-up telephone were not available due to conflicting agendas and urgent matters to attend to in their facilities.

Patients: HIV+ women, aged 18 years and above, who were diagnosed with GDM while participating in the PMTCT programme during their ANC, and who delivered at a tertiary facility, were included. These women were interviewed about their satisfaction with PMTCT integrated services, and their perspectives on the desirability, facilitators, and barriers to GDM screening and T2DM prevention at PHC level. Recruitment took place between June 2016 and September 2016 for health workers, and

was extended up to October 2017 for experts, and up to May 2018 for participating women. A total of 30 participants (n=30) was reached for this study. All participants spoke English, but women who could not easily express themselves in that language were invited to take the interview in Xhosa through a fluent research assistant. Participants from the "patients" category were reimbursed for travel costs and received a 100 Rand (around 7 US dollars) voucher for appreciation to buy food or airtime, upon completion of the interview.

Interviews took place at the workplace or any other quiet setting suggested and agreed upon by both the interviewer and interviewee. Interview guides developed and tested for each category of participants were used, notes were taken during every interview, and all interviews were audio-recorded and transcribed. Interviews were conducted by a trained researcher (JCM) under the supervision of experienced qualitative researchers (KM and CZ). The researcher (JCM) introducing himself as a doctoral student and briefly interacted with the participants about the study before commencing the interviews. Each interview lasted between 45 and 90 minutes and interviews were conducted until no new information was obtained. By the end of all planned interviews, thematic saturation was achieved within each interview, and for all three groups of study participants. A coding system was hierarchically developed by JCM in collaboration with CZ using an inductive/deductive approach, and all discrepancies in the coding process were resolved through discussions between these two investigators. Content analysis was used for policy document while thematic analysis was used for interviews (Paillé & Mucchielli, 2016; Vaismoradi et al., 2013). ATLAS.ti software was used to assist data analysis and management. Interpretation of data was further supported through IINDIAGO team discussions and in relation to other research findings of the project, some of which have already been published (Muhwava et al., 2018, 2019). Characteristics of participants were analyzed by JCM using SPSS version 24.0.

Quantitative data collection and analysis

Panel and spatial data were analyzed using the annual number of women tested for HIV and the proportion of HIV+ women among women screened and the annual number of deliveries registered within the framework of the PMTCT program. The data used were annual series for each of the 25 subdistricts of the WC Province. For deliveries registered under the PMTCT program, the data series covered the period 2012-2017 while for the other two series, data were available for the period 2014-2016. To analyze the trend over time, a multilevel modeling approach was used. For each panel, a two-level linear hierarchical model with random intercept and slope (Commenges & Jacqmin-Gadda, 2015; Steele, 2014) has been estimated. Level 1 captures the evolution over time of each panel dependent variable using a growth curve of equation $Y_{ti} = \pi_{0i} + \pi_{1i}*(TIME_{ti}) + \varepsilon_{ti}$. Where i=1……25, t=0…2 (for the two panel dependent variable related to HIV testing) or t=0…..5 (if the panel dependent variable was the number of women who gave birth under the PMTCT program). The variable Y_{ti} is the value of the dependent variable in subdistrict i at time t, π_{0i} is the initial value (TIME = 0) in subdistrict i, π_{1i} is the rate of growth per unit of time in subdistrict i and the term ε_{ti} represents the residue which captures the unexplained variation of the evolution over time in the subdistrict i (ε_{ti} ~N (0, σ_ε^2). The equations of the level 2 model materialize the variability of the intercept (π_{0i}) and slope (π_{1i}) due to the specifics of each subdistrict. The equations of level 2 which have been considered are indicated below: $\pi_{0i} = \beta_{00} + r_{0i}$ et $\pi_{1i} = \beta_{10} + r_{1i}$. In these equations, β_{00} represents the general average at the initial time, r_{0i} is the random effect which corresponds to the deviation from the initial value π_{0i} of each subdistrict to the general average β_{00} (r_{0i} ~N (0, σ_0^2), β_{10} is the average growth rate per time unit and r_{1i} is the random effect which corresponds to the difference between the growth rate in each subdistrict and the average growth rate β_{10} (r_{1i} ~N (0, σ_1^2). The final equation obtained by combining the equations of the two hierarchical levels is written $Y_{ti} = \beta_{00} + \beta_{10}*TIME_{ti} + r_{0i} + r_{1i}*TIME_{ti} + \varepsilon_{ti}$. To make the distributions of the dependent variables approximately normal, a basic logarithmic transformation was performed. The models were estimated using Restricted

maximum likelihood (REML), which is recommended for small samples (Commenges & Jacqmin-Gadda, 2015; Steele, 2014). The unstructured option was chosen to specify variance-covariance structure of the random effects. In addition, spatial autocorrelation of annual growth rates between subdistricts was analyzed using Moran I global index and Moran I local index (Anselin, 1995; Feuillet, 2018; Griffith, 1983; Moran, 1950). The values of these two indices generally vary between -1 and 1. The spatial autocorrelation is all the stronger as these indices are close to 1 or -1. Positive values translate positive autocorrelation and negative values translate negative autocorrelation. To test the statistical significance of these two indices, the spatial weight matrix was determined from the inverse of the distances between the different geographic units (Drukker et al., 2013). Spatial data were obtained from GADM (https://gadm.org/data.html). All statistical analyzes were carried out with the software STATA/SE 14.2.

Ethics approval and consent to participate in the study

Ethics approval was obtained from the Human Research Ethics Committee, Faculty of Health Sciences, University of Cape Town (HREC REF: 946/2014), SA; and Comité d'éthique de la recherche (an accredited Research Ethics Board) du Centre Hospitalier de l'Université de Montréal (CHUM), (2018-6690, 17.044 - ID), Canada. Written informed consent was obtained from each participant prior to the interviews, and filed for safekeeping. The anonymity of all study participants has been maintained throughout this research process.

Results

The 3 groups of participants included: 10 pregnant women with HIV under PMTCT, diagnosed with GDM, 10 experts and 10 health workers - 3 (15%) clinic mangers, and 7 (85%) PMTCT nurses and midwives. **Table 7** shows the characteristics of experts and health workers who participated in this study.

Table 7: **Characteristics of experts and Frontline health workers participants**

Factor	Level	Value
N		20
Category of participants	Clinic managers	3 (15%)
	Nurses and midwives	7 (35%)
	Experts/KIs	10 (50%)
Gender	F	16 (80%)
	M	4 (20%)
Age mean and SD	Experts	49.8
	FHCWs	40.1
	Overall mean (SD)	44.9 (8.2)

FHCWs: Frontline health workers; SD: Standard deviation

The synthesised results from policy documents, interviews, and PMTCT data in the WC are presented under the following three main headings, each with sub-headings: 1) current revised PMTCT and PNC guidelines; 2) integration of PMTCT and navigating systems for women with HIV and GDM; and 3) collaboration initiatives to enhance integration of programmes and retention of women.

1. **Current revised PMTCT and PNC guidelines**

Health system leadership is expressed in part through health policies, their dissemination, and implementation, as demonstrated in this study framework (Atun et al., 2010b; Shigayeva et al., 2010a; WHO, 2015). Interviewed experts explained that the policy documents and guidelines analysed in this study were developed by a team of provincial DOH-approved experts in relevant domains, e.g., HIV/PMTCT, maternal and child health (MCH), and health systems and in relation to provincial DOH priorities and the social, epidemiological and health system context. They were formulated based on the South African national consolidated PMTCT guidelines, that have themselves been drawn from the WHO consolidated guidelines. From time to time, protocols were revised to adjust to changing local circumstances. After amending the guidelines for PMTCT in 2015, covering HIV care for children, adolescents, and adults (Provincial Government of the Western Cape, 2015), the WC

Department of Health initiated the postnatal care policy in 2016. This policy covers the first 1000 days of life, which includes pregnancy and two years after delivery (Provincial Government of the Western Cape, 2016). Both policy documents have called for comprehensive ANC, including HIV counseling and testing, treatment initiation, and postnatal follow-up, to ensure adherence to PMTCT services. To achieve that, an integrated approach was recommended in the guideline amendments, but there was no mention of how it could be structured and implemented. Screening and care of GDM and other important NCDs whose rates are rising in the same population were not covered in the basic antenatal care documents that focused on elimination of vertical transmission of HIV (Ebonwu et al., 2018; Pattinson, 2007). In addition to HCT and ART for women during ANC and for women with their babies after delivery, only two HIV opportunistic diseases - tuberculosis and cryptococcal meningitis - were included in the PMTCT policy document. The many other possible HIV co-morbidities were not mentioned.

Detailed but less inclusive PNC policies

Although the PNC policy laid a foundation for integrated care at the provincial level – with guidance for improving wellbeing of mothers and their babies in post-partum and beyond, such as HIV, contraception, domestic violence, and alcohol, or drug use – it did not include major NCD conditions. The increasing NCDs among pregnant women, such as diabetes, hypertension, other cardio-vascular conditions, and cancers, with harmful consequences to women and their babies – did not appear at all in this important document, nor were their screenings or treatments.

Human resources and training to implement integrated PMTCT

The implementation of health policy into practice depends on the way that guidelines are disseminated to health services and settings, available human and other resources such as medical products and technologies, as well as underlying contextual facilitators and barriers. Both experts and

health workers discussed the implementation of the guidelines analysed above, in terms of service delivery. Their perspectives and comments reflected their differing roles and positions and hence experiences with these guidelines and practices (see key findings and illustrative quotes in **Table 8**).

Experts who researched PMTCT policies and their implementation – some of whom had played a role in their development – explained how guidelines were integrated, in part to cover some MCH areas. They reported that amendments made by the DOH to adapt health systems to changing health needs, and increasing rates of NCDs like GDM, brought about other challenges; e.g., the need for more resources in terms of personnel and their training, supplies and medicines. An expert from PMTCT leadership in the province insisted on the need for more trained nurses through nurse-initiated and managed antiretroviral therapy and other continuous training schemes to ensure a fully integrated PMTCT, before considering it as an example for integrating other interventions.

Table 8: **Results from interviews with experts and health workers by themes and illustrative quotes**

Key findings	Quotes from experts and health workers
Theme 1: **Current revised PMTCT guidelines**	
Human resources and training to implement integrated PMTCT	*"The guidelines have been aligned and the Integrated Management of Child Illness (IMCI) guidelines now incorporate HIV, ARVs and PMTCT Guidelines, now referred to as the Child Health Guidelines. On the ground, at facility level, there is always integration…..At the beginning it was challenging and it is still challenging, particularly when we have to implement new guideline because we've got to go through a whole process of training and retraining. The trouble with the whole HIV and PMTCT field is that it evolves and guidelines change rapidly or consecutively in close succession, so we need to keep retraining groups of people"* (Expert 1). *"I think in clinics where there are enough NIMART trained nurses it's going well. You know, we have to do regular in-service training every time the guidelines change, make sure they are using the registers properly. There's a PMTCT coordinator at the sub-structure district level who goes around, looks at the registers and does top-up training,…"* (Expert 3). *"I send the staff to the trainings on PMTCT, on BANC, and so on, and I think the sisters [nurses] are well equipped. It is part of my role to see who is running short and you can see I have that training record there and I can see who's not trained on this or that, and then when there's a space, I know that and I have to send her on this type of training. Regarding NIMART training, we have the help of MSF. MSF have been helping us and whenever we really run short of trained nurses through NIMART, then MSF just arrange their training, even if it's only one sister. They conduct a class of one*

	nurse and then make a follow-up. They would come to make a follow-up to that trained staff and make sure that she's competent on what she was trained on,…" (Health care worker 1).
Uneven PMTCT implementation and better WC quantitative outcomes	*"We wanted every pregnant woman to have an HIV test. So that's the first PMTCT success [to identify HIV positive pregnant women]. The second success is to get them into treatment, and the third success is the baby is not infected. I started… What I say is that, I started off my career seeing babies die in their hundreds because of HIV, and now when I see what we did in 15, 16, years, babies are living. We've managed paediatric HIV, so I see it as the most beautiful thing in the world to see what this country has done…. But as you know, it's still hard, because we still have more people with HIV than anywhere else in the world, and we still don't even know who they all are; and we still have to find them and put them on to treatment….., in Kwazulu Natal, it's just spiralling out of control. It's not stopping. It's the epicentre. It's where the fire is and we don't know how to put off that fire"* (Expert 4). *"I'm just thinking back, in general and for Cape Town in particular, it's a bit different from that of the broader South Africa. We basically received global funding, and in 2006, we appointed quite a number of PMTCT coordinators and with the trained PMTCT registered professional nurses within the MOU and PHC settings, as a means* of offering integrated ANC, ART and TB screening *into the broader PHC platform. So, a lot work has been done to close the PMTCT implementation loopholes* (Health worker 2).
Theme 2: Integrated PMTCT and navigating systems for GDM care	

Partial integration of PMTCT and challenges to access unintegrated services	*"I don't think it's fully integrated yet, but I think we've come a long way since when we started……We had a bit of a hiccup when the immunisation was not really integrated into the HIV testing programme, and I think that is probably the one place where we still have a little bit of verticalisation on the whole issue of infant testing*" (Expert 1). *"So, my main objective within the PMTCT scope is to identify the patient when they come in. So, all patients who are HIV positive, I or my colleague chat with them and get them to see the counsellors as well. We make sure that they always have medication. We try to educate them regarding any side-effects and the obvious things like safer sex and the importance of adherence. We try to see where we can help them practically…. If there is any TB, other co-morbidities, if they have HIV and cardiac disease, we obviously see a lot of GDM. If there are any of these issues, then we will refer them to other departments within the hospital"* (Health worker 3).
Efforts to keep women into integrated PMTCT	*"….You know what, the last mile is the mile of stigma and discrimination. It's how we address that. So what happens is that we discriminate against HIV infected people, even in pregnant women in the hospital, so when I've looked at treatment failures, so why did children get HIV infected, it's all around stigma. So the woman hasn't disclosed her status to her family and she didn't take the drugs, so she affects her baby….."* (Expert 4). *"So, you know, we have families that chase their loved ones away. If you're gay or a lesbian, we have families that beat you up. So, if we want to do true integration, you have to get rid of stigma and*

	discrimination and shame, and the way one human being treats another human being, and so that's our problem" (Expert 4).
Theme 3: Collaboration initiatives to enhance integration and retention of women	
NGOs engagement	*"Mothers to Mothers services which is well supporting the mothers who are pregnant and those after delivery, so they work hand in hand with antenatal labour ward as well as Child Health for continuity of care. So it has improved a lot based on other NPOs (non-profit organisational staff) that assist us if we have a problem with… We can't find person, a patient, then mothers trace them, or the NPOs do trace them"* (Health worker 4). *".....Another example which I'm personally familiar with is MomConnect, started two years ago to try and get pregnant women hooked up to a mobile health messaging, and quite quickly we achieved a 60%, currently running at about 60%, 60, 70% of all pregnant women are being registered on the system"* (Expert 2).
Continuity of care in a context of migration	*"Some go back to the Eastern Cape, I'm making now an example. So you don't know, do they really rock up there and think that must be the same? If we have a system in place where if she goes to Jo'burg, when they punch in, say for instance, that folder number, here everything comes up. I'm just talking just health-wise, not in everybody's eyes, but health-wise"* (Health worker 5). *"It is a problem with follow ups so, patients do move around, and if you don't have an identifier can you can use across the country then it is difficult to trace. So, we deal mostly with patients that do return for care. Those that gets lost to follow-up, it's difficult to get hold of because you don't know where she went, what happened to her"* (Expert 5).

Possibility of integrating GDM and other NCDs	*"So, things can be scaled up very quickly if there is leadership from the national department and a willingness. So, the PMTCT system is such that people do take new interventions and can run with them quickly. So, that is something you could bear in mind for this Gestational Diabetes if it is seen to be a priority"* (Expert 4). *"I guess in terms of success, we see it very clearly, in terms of the number of lives saved. I guess all recent statistics have been consistently suggesting that in South Africa, the early life mortality due to HIV has reduced significantly, and this is essentially a result of the significant reduction of mother to child transmission….. the framework of prevention of mother to child transmission is a good setting, for instance, to provide good antenatal care and also good postnatal care, is an example for you of integration"* (Expert 5). *"…Even if the laboratory attached to the HIV Clinic, or to the Postnatal Clinic, it should provide, not only for the HIV, but for the screening of the risk of other conditions"* (Expert 6).
Liaising with the communities	*"I will say that they are helpful, because we use them as the bridge just to get to the communities, because they go the extra mile, in this way that they go inside those houses; then they will go there and give talk… For instance, when I was working in the TB Room, the CHWs will go and check if the patient is taking the medication correctly; or sometimes they will help them to take the treatment from us to them. So, sometimes they even help us to check, how is the condition of the room where the patient is staying in? Was there sanitation? Was there running water, and all that? So, they go deeper into the community whereas we are here in the facility. So, we use them in those terms, and also when we're looking for the crèches, they know where are the crèches in the community, and how we go about getting in touch with the principal of those*

	crèches? So, we use them for that. So, we work hand in hand with them" (Health worker 4). *"For our HIV programmes, we have clinic-based counsellors and CHWs who are key part to the services….in past I remember some suggested, the diabetic patients can benefit on that notion of peers helping others as well and CHWs. That systems of and CHWs, they need to be train, they need to be paid, that's my opinion…When they are trained and offer their services, they have to be paid"* (Expert 6).

Nurses discussed their training needs and expressed their interest in more specific training sessions beyond PMTCT, using different strategies in cooperation with various actors within and outside health systems, so that they could cope with the rising health needs requiring integrated services in their local clinics. One clinic manager, who runs a facility that received the health department's award for reaching zero mother-to-child transmission of HIV in 2018, praised the role of trained nurses in HCT, treatment initiation and follow-up to monitor HIV viral load and to encourage and ensure adherence to ART, as key components of the successful PMTCT integration into PHC in the country. Training sessions to reinforce knowledge and best practices on these elements have been conducted in coordination with Médecins Sans Frontières, one of the non-governmental organisations (NGOs) that supports local health facilities in their efforts to deliver integrated HIV services into PHC in SA.

Since interviewed women were not involved in PMTCT guideline development or implementation, they did not share anything about policy documents, beyond expressing their wish for integrated services within the PMTCT program. They expressed their desire to avoid navigating different facilities when they are screened for GDM or any other condition while under the PMTCT program.

One participant listed three facilities she visited in her journey for care, after she was diagnosed with GDM:

"I booked at KTC Gugulethu, then they transferred me to Mowbray, after Mowbray, I came here [*Groote Schuur Hospital*]*".* (Women under PMTCT with GDM, Gugulethu 1).

When asked whether she would prefer to have integrated services and follow-up for her and her baby at the local clinic, instead of navigating between her local facility and hospitals, she replied with these words:

"I know, it's for me, I know I am just going to get that medication for me, I must also go and take medication for my baby; because sometimes you don't go to the same clinic or we don't have the same appointments….It would be easier for me if it's the same clinic, and that is according to distance and people I am used to…". (Women under PMTCT with GDM, Gugulethu 1).

Uneven PMTCT implementation and better WC quantitative outcomes

Even though the scale-up of PMTCT within PHC was carried out in all South African provinces, facilitators and barriers were not the same everywhere, and hence there have been different outcomes (Burton et al., 2015; Weiss et al., 2014). This situation is similar for GDM-related and other NCD services. Most provinces generally succeeded to reduce and control vertical transmission but some, and regions within provinces, still struggle in terms of some PMTCT indicators, due to historical health system inequities, and are considered a setback to the country's overall good PMTCT performance (McIntyre et al., 2002; Woldesenbet et al., 2017). The WC province is one of the highest-performing provinces in SA across most health care indexes, especially HIV-related indicators (Neethling et al., 2019; Ngobeni et al., 2020; Woldesenbet et al., 2019). The WC data revealed significant positive outcomes over the period of implementation of the PMTCT policies and guidelines since its initial rollout in 2002 but especially with the 2015 guidelines. The WC hosted the

two first PMTCT trial sites in the country (pilot sites in Khayelitsha) in 1999 (Burton et al., 2015; Stinson et al., 2014) and its Government has since been working with local authorities, teaching institutions and NGOs, to mobilise resources towards integration of PMTCT services into all local health facilities (Stinson et al., 2014).

According to the results of the estimation of the growth model (**Table 9**), there was generally a significant annual increase of 17.8% (95% CI: 12.9% - 22.0%) in the number of women screened for HIV between 2014 and 2016. Moran's I global autocorrelation index is close to 0 and is not statistically significant (I= -0.039, p = 0.953). Thus, there is no spatial correlation between the subdistricts regarding the average annual growth rate of the number of women tested for HIV between 2014 and 2016. However, according to Moran's I local spatial autocorrelation index, there is a negative spatial correlation between some of the subdistricts (**Table 10**). Indeed, the average annual growth rate of the number of women tested for HIV is relatively higher in one subdistrict (Beaufort West) compared to many neighboring subdistricts (**Figure 8**).

Regarding the proportion of HIV + women among women tested, on average, a non-statistically significant annual decrease of 1% (95% CI: -7.0% - 5.5 %) was recorded (**Table 9**). Furthermore, the data do not show a partial correlation overall (I = -0.026, p = 0.687). However, a negative spatial correlation between the Laingsburg subdistrict and neighboring subdistricts has been highlighted (I = -0.470, p <0.001). This subdistrict recorded a significant drop in the proportion of women testing HIV positive compared to neighboring subdistricts (**Figure 9**).

Table 9 : **Results of the estimation of hierarchical linear models with random intercept and slope**

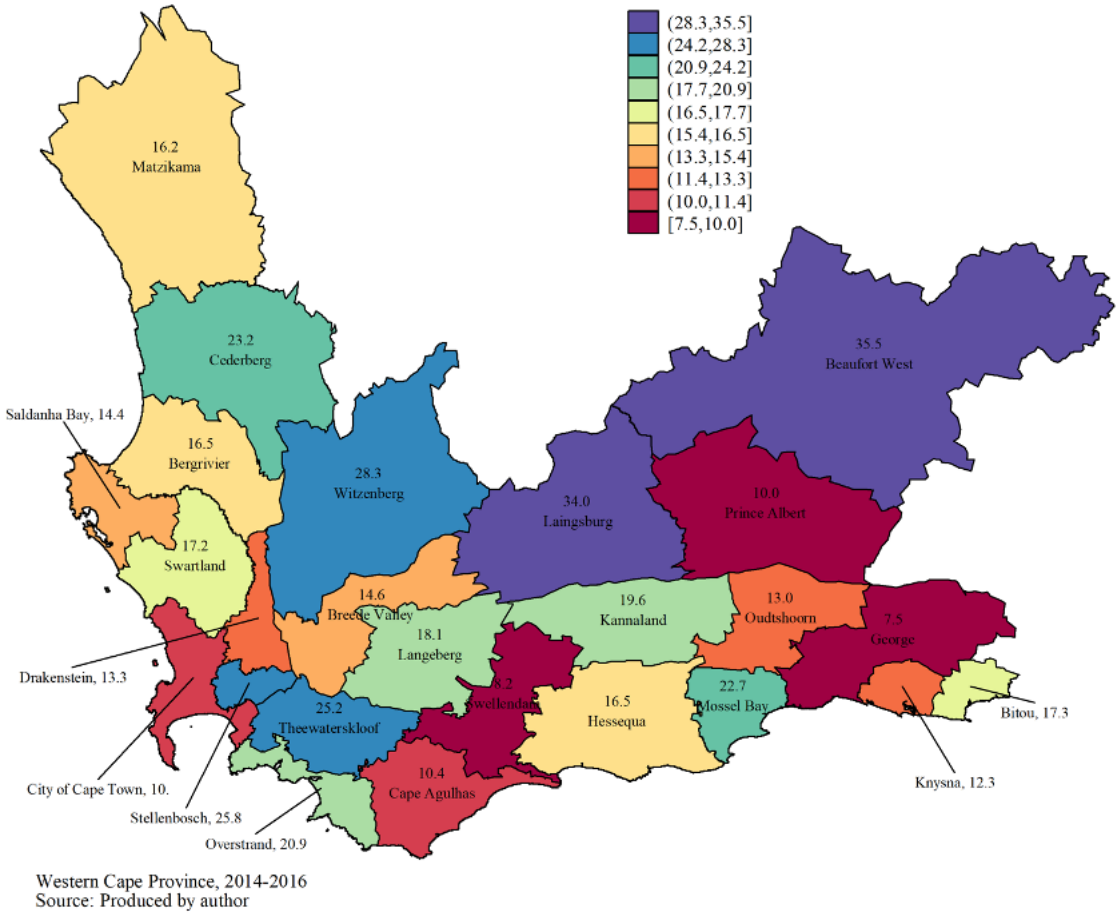
Variables	**Dependent variables**					
	Natural logarithm of the number of women tested for HIV		Natural logarithm of the proportion of HIV+ women among women tested		Natural logarithm of the number of women delivering on the PMTCT program[⊥]	
	Coefficient (95% CI)	**p**	**Coefficient (95% CI)**	**p**	**Coefficient (95% CI)**	**p**
Time (in years)	**0.164[‡] (0.121 - 0.207)**	**0.000**	-0.010[‡] (-0.073 - 0.054)	0.761	**0.031[‡] (0.006 - 0.057)**	**0.016**
Intercept	9.049 (8.627 - 9.472)	0.000	1.020 (0.787 - 1.253)	0.000	4.685 (4.066 - 5.305)	0.000
Random-effects Parameters	**Estimate (95% CI)**		**Estimate (95% CI)**		**Estimate (95% CI)**	
Between-subdistrict variance	1.154 (0.653 - 2.041)		0.324 (0.175 - 0.601)		2.378 (1.326 - 4.262	
Slope variance	0.007 (0.002 - 0.020)		0.009 (0.001 - 0.064)		0.001 (0.000 - 0.008)	
Intercept-slope covariance	-0.023 (-0.071 - 0.026)		-0.011 (-0.052 - 0.030)		0.013 (-0.028 - 0.053)	
Within-subdistrict variance	0.010 (0.006 - 0.018)		0.034 (0.020 - 0.060)		0.045 (0.034 - 0.060)	

[⊥]Data was not available for the Bitou subdistrict.

[‡]Since the dependent variable has been transformed using the natural logarithm, this value corresponds to annual percentage increase /decrease of (e^{beta}-1)*100. So we have 17.83% for beta = 0.164; -1.00% for beta = -0.010 and 3.15% for beta = 0.031.

Table 10: **Moran's I local spatial autocorrelation index**

Subdistrict	Indicators					
	Average annual growth rate (in %) of the number of women screened for HIV		Average annual growth rate of the proportion of HIV + women among women tested		Average annual growth rate of the number of women delivering on the PMTCT program	
	I	p-value	I	p-value	I	p-value
Beaufort West	**-0.435**	**0.000**	-0.023	0.873	0.087	0.341
Bergrivier	-0.008	0.826	0.003	0.774	-0.017	0.873
Bitou	0.030	0.744	-0.020	0.922	//	//
Breede Valley	-0.040	0.988	-0.008	0.808	-0.013	0.842
Cape Agulhas	-0.037	0.973	0.127	0.211	0.075	0.426
Cederberg	-0.002	0.758	0.004	0.738	-0.067	0.873
City of Cape Town	-0.153	0.537	0.012	0.768	0.074	0.527
Drakenstein	-0.054	0.937	-0.006	0.826	0.024	0.693
George	0.207	0.281	0.003	0.844	-0.068	0.917
Hessequa	0.009	0.688	-0.074	0.805	-0.100	0.701
Kannaland	0.004	0.710	-0.009	0.801	**-0.518**	**0.001**
Knysna	0.229	0.268	0.001	0.861	-0.000	0.858
Laingsburg	-0.211	0.093	**-0.470**	**0.000**	0.014	0.659
Langeberg	-0.001	0.765	0.009	0.721	0.026	0.654
Matzikama	-0.021	0.845	-0.034	0.946	0.020	0.635
Mossel Bay	-0.113	0.606	-0.036	0.966	-0.043	0.997
Oudtshoorn	0.054	0.523	0.007	0.750	-0.143	0.555
Overstrand	0.010	0.758	0.017	0.728	0.128	0.332
Prince Albert	-0.098	0.664	0.006	0.726	0.132	0.252
Saldanha Bay	-0.005	0.821	-0.020	0.894	-0.029	0.934
Stellenbosch	-0.183	0.433	-0.169	0.484	0.105	0.424
Swartland	0.007	0.758	-0.020	0.890	**-0.412**	**0.028**
Swellendam	-0.070	0.820	0.132	0.187	-0.004	0.789
Theewaterskloof	-0.052	0.948	0.026	0.677	0.085	0.450
Witzenberg	-0.048	0.952	-0.111	0.539	-0.019	0.853
// Data not available						

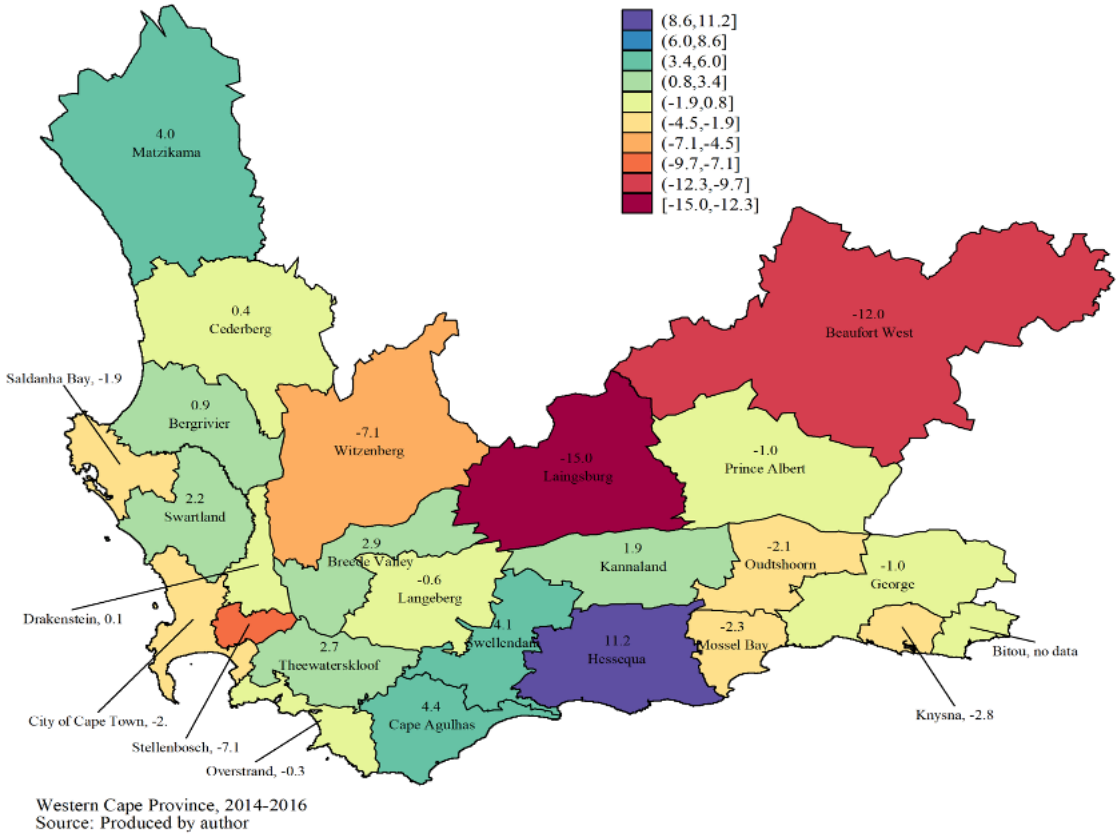


Average annual growth rate (in %) of the number of women screened for HIV between 2014 and 2016.

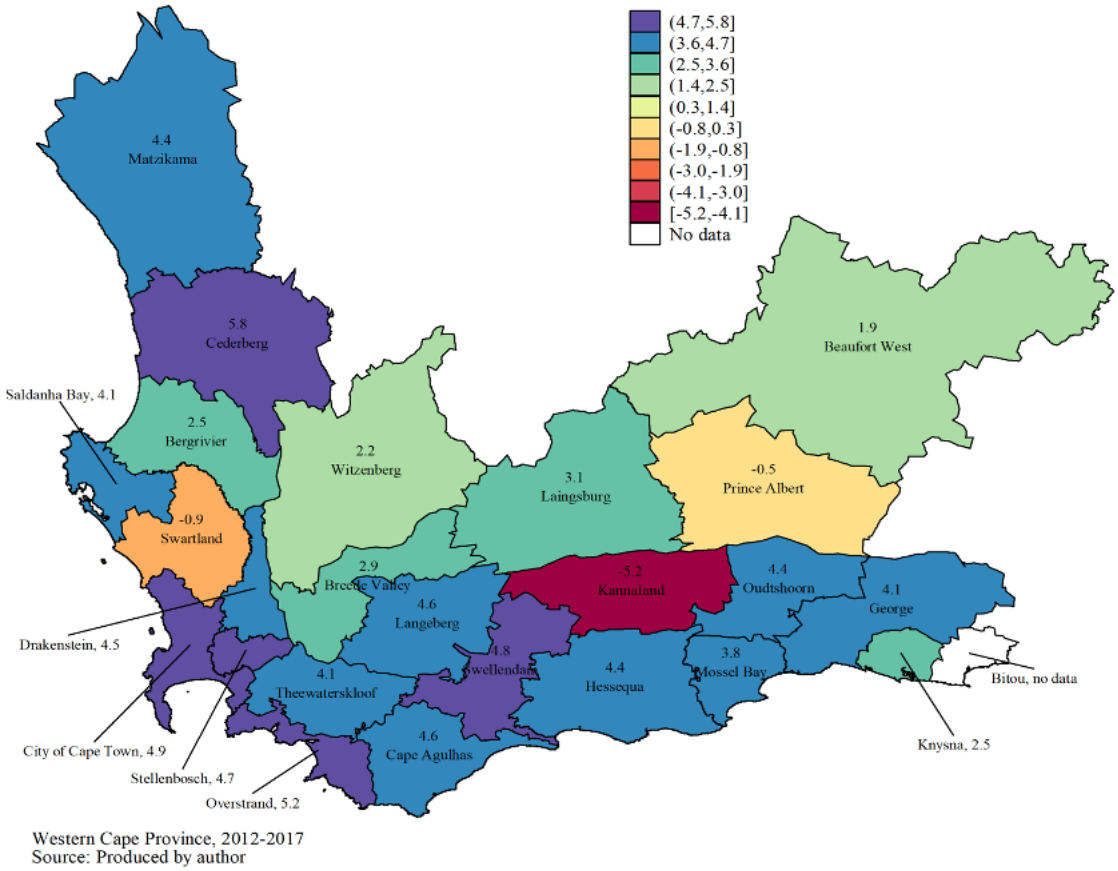
The results of the growth model estimate recorded in **Table 9** indicate that there was generally a significant annual increase of 3.1% (95% CI: 0.6% - 5.9%) in the number of births recorded within the PMTCT programme between 2012 and 2017. Moran's I global autocorrelation index is close to 0 and is not statistically significant (I= -0.028, p = 0.659). So, there is no spatial correlation between the subdistricts regarding the average annual annual growth rate of the number of women delivering on the PMTCT program between 2012 and 2017. However, according to Moran's I local spatial autocorrelation index (**Table 10**), there is a negative spatial correlation between the Kannaland subdistrict (I = -0.518, p=0.001), Swartland subdistrict (I = -0.412, p=0.028) and their neighboring

subdistricts. Compared to neighboring districts, a decrease in the number of women who gave birth under the PMTCT program was observed in these two districts (**Figure 9**).

No data were available about women in PMTCT who also had GDM.



Average annual growth rate (in %) of the proportion of HIV + women among women tested between 2014 and 2016.



Average annual growth rate of the number of women delivering on the PMTCT program between 2012 and 2017.

2. Integration of PMTCT and navigating systems for women with HIV and GDM

Experts and health workers discussed different aspects of PMTCT integration into existing PHC services. Both agreed that PMTCT was partially integrated, which means that linkages and coordination were created between programmes and services available in every facility, as discussed in the study framework (Atun et al., 2010b; Shigayeva et al., 2010a; WHO, 2015).

Partial integration of PMTCT and challenges to access unintegrated services

Although PMTCT results were praised with respect to integration into PHC services by all study participants, women who were diagnosed with GDM while under PMTCT said that they have struggled in their pursuit of care. In addition to their PMTCT program, they were also required to

visit tertiary health care facilities for pregnancy follow-up and delivery, because of their GDM diagnosis. Since the guidelines to screen and address such diseases within PMTCT do not exist, the women who were diagnosed with GDM while enrolled into PMTCT face barriers vis-à-vis transportation and safety issues, while going to the hospital for GDM follow-up. Taking medicines for both health problems, and exploring lifestyle changes are other challenges. Six out of ten women who continued their ART in the PMTCT program at their clinics, wished to have their NCDs screened and managed within PMTCT at their local health settings. These women also spoke of the challenges in adhering to treatment and recommended lifestyle modifications, including challenges such as work stoppage with concurrent loss of income, and increased expenses for healthy food or a changing diet. However, one of the most inconveniencing experiences reported by these women was their separation from their usual local health care team while attending tertiary health facilities for their GDM care. One woman shared how she missed the PMTCT health team she was used to at her local clinic, while attending diabetic clinic at tertiary hospital:

> *"....That doctor, that is why I said he is like our father, you see? When you come to his room, when you go out you just have that hope… You can't explain it, but you just have that hope…, I can't lie, even the nurses there they know how to treat us. They don't shout out, they just tell us we have to do this, even if you tell them the truth, the way you eat. They call the dietician to guide you,…"* (Women under PMTCT with GDM, Langa 7).

After a couple of visits to tertiary hospitals (Groote Schuur Hospital (GSH) and Tygerberg Hospital in the Cape Town metropolitan context), however, women reported that they adjust their routines and come to appreciate and recommend the high quality of services they receive there. One of the women who attended GSH for her GDM while under PMTCT explained:

"I was scared to ask them [*nurses*] *and because they were talking and treating us, I thought that this is the special hospital. Then I did ask the doctor and he said that this is the special hospital and that they are very good to treating Diabetes…..That's what I experienced here* [*GSH*]. *Now, when someone is pregnant, I tell them that if you will be treated in GSH, you will be fine"* (Women under PMTCT with GDM, KTC)

Efforts to keep women in integrated PMTCT

Despite their commitment to navigate a complex and fragmented health system in order to protect their own and especially their baby's health during pregnancy, the issues raised above can cause retention problems in the long run, as some women default the programme or fail to take their regular medication. This is the reason why the DOH has recently requested that the lower level facilities also hand over their PMTCT services to the tertiary hospital for all referred GDM patients. This approach helped to fully integrate care for all co-morbidities during the pregnancy at well-equipped tertiary hospitals. GSH and Tygerberg hospitals have all the required critical services for mothers and their babies during pregnancy, during labour, and after delivery. They have trained nurses and midwives to care for these HIV positive individuals with GDM, and other co-morbidities. After delivery, these women go back to their local clinics for their ART and early infant diagnosis and immunisation services for their babies (Dunning et al., 2017). However, there are no follow-up initiatives to prevent or delay T2DM for women with a previous GDM diagnosis, and the interviewed health workers said their role ends with the PMTCT cascade, and PNC packages that do not include NCDs. PMTCT coordinators were assigned at each sub-district level in the province to ensure that everything regarding PMTCT is implemented, monitored and evaluated. However, their mandate is solely for PMTCT services, and this stance shows how partial its integration has been. All ten experts emphasised the successful results, and various benefits of partially integrated PMTCT into PHC throughout the country, and suggested approaches to move it to the next stage: full integration. They

also discussed the journey that lies ahead, before the complete success of PMTCT programme could be achieved. They explained that discrimination and stigma became obstacles to the integration process because of psycho-social and health effects, with consequences to individuals, families and health care systems. While highlighting most of the persisting barriers like bureaucracy, poor management, lack of sufficient infrastructure and other resources at local facilities and provincial, or national health systems, 7 out of 10 experts firmly concluded that PMTCT has not been fully integrated and that this has complicated retention of these women. They based this conclusion on the failure to consider and include some MCH programmes that are very important for both women and their babies such as GDM screening and immunisation.

3. Collaboration initiatives to enhance integration and retention of women

Both experts and health workers who participated in this study discussed different collaboration initiatives and the underlying facilitators and barriers that led to PMTCT integration into existing PHC services. For cooperation efforts towards integrated PMTCT in policies and practice, various components from WHO building blocks and integration levels were mobilised, as discussed in the study framework (Atun et al., 2010b; Shigayeva et al., 2010a; WHO, 2015).

NGO engagement

Integrated care of PMTCT and other health conditions that women face during pregnancy could not be achieved without the collaboration of different actors in health systems, NGOs and in communities. Experts and health workers stressed that NGOs such as Momconnect, Mothers to Mothers, and Médecins Sans Frontières have made substantial contributions to PMTCT implementation, and that this is reflected in the tangible results documented for PMTCT services. These organisations actively participated in key activities essential to the success of this programme, activities such as health education, home visits and sometimes intervening at the facilities,

accomplished by trained members of the community who are supervised and incentivised by professionals working for these NGOs. These collaboration initiatives have been supplementing Governmental efforts to enhance HCT, initiate ART, keep women on treatment and trace the defaulters and all participants appreciated their roles.

Continuity of care in a context of migration

Tracing all women who default from treatment has been consistently difficult, as some had moved out of the province and could not be reached at all. Some women from other provinces come to work in Cape Town and book for PMTCT and ANC follow-up in the local facilities in Cape Town's informal settlements. Some among them leave before or after delivery, returning mostly to the neighbouring Eastern Cape Province, but also elsewhere outside of the provincial boundaries. Experts and health workers recommended a nation-wide health information system, with unique identifiers that could help to trace women or other patients, wherever they book. With a nationally interconnected health system, women with co-morbidities could attend any health facility, have their health problems addressed and their medical reports stored and accessible for further visits or interventions elsewhere. Women who were interviewed in this study and who themselves navigated health systems for testing and treatment for multiple conditions could not offer any insights on this issue and have been relying on "Road to Health" booklets or transfer letters. Without health information system managing and transmitting electronic records at national level, some patients like these women may be lost or forgotten and when they migrate or attend a different facility, their diagnoses and medications are not known and this hinders the continuity of care. The use of unique identifiers through functioning health information systems could be a feasible and sustainable solution to this situation, as reported by experts who participate in this study.

Possibility of integrating GDM and other NCDs

Experts said that increasing the number of women benefiting from integrated HCT and delivering under PMTCT should not only be seen as a success story, but also as a window of opportunity for universal GDM or NCD screening, and subsequently initiating preventive measures for T2DM for both women and their babies. Most experts (80%) and clinic staff (70%) agreed on the feasibility of GDM and T2D integration but, unfortunately, without a clear policy and proper guidelines to include them into PHC based services like PMTCT, implementation of that integration is not likely possible in the current national and provincial context. According to the study respondents, prioritising health problems of such magnitude to this particular population, by authorities in national, provincial and municipal health departments, has to be the first step in the process of integrating them. Through PMTCT services, good results have been obtained and most of the interviewed experts asserted that it would be the logical and the right thing to do to integrate GDM screening and T2DM prevention measures with this important programme for women and their babies**.**

Liaising with the communities

The PMTCT cascade has the opportunity to integrate not only with other health services, but also within communities themselves. The existence of a well-functioning network within communities, and the trust that PMTCT has built over time, especially in liaising with the community health workers (CHWs) to follow-up with women, their babies, and their families, present an opportunity for screening and care of other health problems. The extensive role of CHWs has been recognized by each of the groups interviewed for this study: experts, health workers and women with GDM under PMTCT. They all emphasized the many important accomplishments health services integration achieved by CHWs, at clinics, and in communities. Before being transferred to the tertiary hospital for follow-up and delivery, one woman diagnosed with GDM while in the PMTCT

programme at her clinic was asked about CHWs and their role in her pursuit of care. She immediately replied as follows:

"I even have their cell numbers". She continued to say that CHWs assist women and their families in every situation, and ensure they attend the clinics or hospitals for regular administration of medication and follow-ups.

"So, if maybe your date is tomorrow, they have to Whatsapp you, don't forget about tomorrow".

She then elaborated, when asked whether CHWs only remind women about their appointments:

> *"No, they're dealing with the child that's going to that clinic. They just remind us about our dates. Sometimes, they visit. Most of the time the people there have tuberculosis. Ja, they are good. They are doing good jobs, you see, sometimes if someone does not have the power to wash themselves, you know those people are very sick, they help and wash them or just to give them their breakfast".* (Women under PMTCT with GDM, Langa 20).

Health workers interact with CHWs at the clinics, especially when there are many patients and queues to manage or when they are needed to give health talks, and their help is routinely sought to liaise with patients in the communities. All health workers agreed that CHWs are the key to successful interactions with women and other patients in the community. Experts praised the CHWs and added their voices to those of the health workers regarding the importance of the CHWs, adding that the CHWs could be more efficiently used to improve the overall PHC services. Experts noted that CHWs have played a critical role in other countries like Ethiopia, Rwanda and others and that they not only help at the clinics but also in assisting to deal with health problems of individuals and families in the communities. Experts encouraged offering training, supervision and payment to CHWs. This would motivate and give them the sense of responsibility, equip them with sufficient knowledge and, in fact help to resolve occasional cases of ethical concerns such as breach of

confidentiality, issues regarding privacy and informed consent among others, as raised by some nurses closely working with them.

Discussion

WHO's "six health system building blocks" model and a health systems integration framework by Atun et al. (Atun et al., 2010b; Shigayeva et al., 2010a; WHO, 2015), constituted the adapted framework for this study and each main result heading was conceptualised based on either or both components of this adapted framework. Components from the WHO building block model were used to review the current revised PMTCT and PNC guidelines, the health system integration framework was applied to the integration of PMTCT and navigating systems for women with HIV and GDM while components from both models were considered to elucidate the collaboration initiatives to enhance integration and retention of women.

The significant health and societal gains from PMTCT and extended HIV policies in SA have shown that an integrated approach can bridge structural gaps in service delivery across antenatal, intrapartum and postnatal care. PMTCT has been consistently implemented throughout the country, but concerns were raised by experts about the postnatal care that has not received the attention it is due, at both national and provincial levels, compared to antenatal and intrapartum care (Larsen et al., 2017). The question we have addressed was how PMTCT integrated into PHC is perceived by key stakeholders and reflected in policy and in empirical data, and specifically how women with both GDM and HIV are followed in PMTCT, in order to explore how the PMTCT experience might bridge gaps in screening GDM and preventing T2DM for women and their exposed babies at the primary care level in South Africa. Our hypotheses were two-fold: that the successful implementation and integration of PMTCT in the WC would offer lessons for integrating other important conditions, notably GDM; and that women with GDM would be reasonably well integrated into seamless care within the PMTCT programme because the lessons already learned about the value of PMTCT

integration would have already been generalized to women with GDM. This study provides evidence in support of the first hypothesis, including widespread and strong support across stakeholder groups (experts, health workers and patients) for integration of GDM into PMTCT and into PHC. However, we found that women with GDM are poorly supported in integrated PMTCT – except if they are referred to have all of their ante-natal and delivery care at a tertiary facility.

PMTCT outcomes have been quantitatively assessed during the study period and the calculated number of women who attended HCT annually increased at 17.80%, while women who delivered under PMTCT increased at 3.1% annually in the WC, SA. These quantitative results corroborated the views of this study respondents regarding the integrated PMTCT services in the province and at national level.

Secondly, although there were no provincial data for women diagnosed with GDM while under PMTCT, the study participants suggested that the lessons from PMTCT should and can be extended, especially for interventions targeting the same population. This could apply beyond HIV care, notably in GDM and other NCD screenings and T2DM prevention, for which continuous testing, lifelong medication, behavioural change, and follow-up, as well as monitoring and evaluation would be needed. Integrating interventions like PMTCT into PHC has not been a simple or single step initiative, but rather a very complex intervention with multiple components. PMTCT has evolved from using a single dose of Nevirapine, to the combined regimens for eligible women (Mandala et al., 2009), and to option B+ and to the PMTCT cascade extending from HCT, through pregnancy and delivery, post-partum care of mothers and infants, and lifelong ART for women. It has progressively been successfully integrated into PHC, due to enhanced training for nurses and closer monitoring and evaluation of services they provide. The positive assessments of the PMTCT programme by all categories of respondents as well as the quantitative data showing increased uptake of HCT, treatment initiation and subsequent long-term retention of women in ART, followed by reduction in HIV

positivity rate, suggests that the integration approach can work well in the SA context. The experience has the potential to offer constructive ideas for planning other health interventions, especially those targeting the same population. Apart from a cohort study on selective screening strategies for Gestational Diabetes by Adam, S. and Rheeder, P. (Adam & Rheeder, 2017a) in 2017, that included a limited assessment of HIV effect on the GDM incidence in the high HIV burdened South Africa, to our knowledge there is no other study that examined integrated GDM screening and subsequent follow-up for women under PMTCT. Our study suggests that GDM screening and T2DM prevention would ideally start with women who are already under PMTCT programme and then be expanded within PHC services.

Thirdly, GDM and T2DM have emerged as conditions increasingly affecting women in SA (Chivese et al., 2019; Macaulay et al., 2018), and their integration into this well-grounded PMTCT program is seen as desirable, although with caveats. Dias et al in their recent study (Dias et al., 2019) highlighted that there are no compelling means to implement and integrate GDM screening and management into the existing MCH services and integrating it into PMTCT would therefore be one of the viable solutions to deal with it. PMTCT acceptability and adherence to treatment by women has generally increased over time, and has been the key to the success of the integrated PMTCT services in different contexts, despite pending socio-cultural, economic and leadership challenges (Aizire et al., 2013; Akinleye et al., 2017; Okoli & Lansdown, 2014), and would make integrated GDM screening and T2DM prevention feasible. This study found that women appreciate having the key health services they need in facilities that are accessible to their communities during pregnancy, and for their babies after delivery. Worries and fear expressed by women about GDM and the T2DM onset soon or later after delivery are similar to what they felt when tested positive to HIV and this could mean that they would abide to services for screening and treating GDM, and would initiate lifestyle changes to prevent T2DM, especially through its integration within PMTCT.

PMTCT owes its success, in part, to the supportive networks it enjoyed not only among donors and health systems but also from community actors whose contributions would also be relevant for other conditions affecting this same population, including GDM, T2DM and other NCDs. Working with community-based organisations has helped to empower HIV positive women, and reduced stigma and discrimination (Kontomanolis et al., 2017; WHO, 2013a) through providing information and counselling to patients and educating families and communities. The CHWs who are appreciated by all interviewed participants have emerged as an important force for supporting adherence, an important issue that surrounded PMTCT rollout (Mepham et al., 2011; Moosa et al., 2019). CHWs could under supervision contribute towards the integration of GDM screening and T2DM prevention into the PMTCT cascade, and other PHC services for the same population.

Finally, there are barriers to integrating the screening and care of GDM and prevention of T2D in SA, and as during PMTCT implementation, they could be progressively dealt with. From integrated GDM screening and follow-up during ANC, a period when HIV positive women are motivated to do whatever it takes to save their pregnancy and their babies (Ekama et al., 2012), it could be feasible to retain them and their babies into postpartum care and follow-up. Using the PMTCT model of keeping previously pregnant women and their babies under care after delivery would bridge gaps within PNC, and follow-up with women who had GDM, along with their infants, for lifestyle change initiatives to prevent or delay T2DM onset and lessen the burden of tertiary care. This will however require changes in health policy, extra efforts in terms of training local health care providers, and attempting innovative approaches like integration in other well-implemented services, especially in public health facilities with limited resources (Jayanna et al., 2019; Kachimanga et al., 2017).

Without including the necessary screening programmes and care for GDM or subsequent T2DM prevention among other NCDs in the policy guidelines, a gap in practice would remain, and impact the results of PHC services. Prioritisation of GDM by the DOH and mobilisation of decision makers

against this increasingly common chronic condition, that not only affect mothers, but also their babies, and their communities, is the key for its successful integration. However, integrating GDM management and initiatives to prevent or delay T2DM would add a significant layer of complexity to PHC. This goes beyond the relatively simple needs addressed through PMTCT during ANC, assessing viral loads and conducting PCR tests after delivery - it extends to teaching women to monitor their blood glucose levels, to modify their lifestyle and regularly visit the health facility to ensure their control is adequate or identify the need to refer for specialist care. Although this study provides a useful exemplar and protocol for future studies, there may be differences across the provinces and it may not be generalizable across SA.

Conclusion

PMTCT programmes have not yet integrated the management of NCDs, notably GDM. However, there is significant learning from the PMTCT integration experience to suggest that GDM screening and care could be successfully integrated into PMTCT and PHC during ANC and initiate initiatives for preventing or delaying T2DM in postpartum. Key research is now needed in this area of integration to evaluate its effectiveness.

Declarations

Ethics approval and consent to participate

The study was approved by the Human Research Ethics Committee at the Faculty of Health Sciences, University of Cape Town (HREC REF: 946/2014) and the Centre de Recherche du Centre Hospitalier de l'Université de Montréal (2018-6690, 17.044 - ID). Written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analysed during the current study are not publicly available to preserve participant anonymity.

Competing interests

JCM, PREB, LJW, SN, KM, NL, HT and CZ declare no competing interests.

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Authors' contributions

JCM, CZ, and HT designed the study. JCM conducted interviews, data analysis and wrote the first manuscript under the supervision of CZ and HT. PREB conducted quantitative analysis in collaboration with JCM. PREB, LJW, SN, KM, NL, HT and CZ critically revised versions of the manuscript. All authors read and approved the final manuscript for publication.

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Additional files

File 1 - Mixed Methods Appraisal Tool (MMAT), version 2018

Integrating gestational diabetes and type 2 diabetes care into primary health care: lessons from prevention of mother-to-child transmission of HIV in South Africa: - A mixed methods study

Category of study designs	Methodological quality criteria	Responses			
		Yes	No	Can't tell	Comments
Screening questions (for all types)	S1. Are there clear research questions?	√			
	S2. Do the collected data allow to address the research questions?	√			
	Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative	1.1. Is the qualitative approach appropriate to answer the research question?	√			
	1.2. Are the qualitative data collection methods adequate to address the research question?	√			
	1.3. Are the findings adequately derived from the data?	√			
	1.4. Is the interpretation of results sufficiently substantiated by data?	√			
	1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?	√			
2. Quantitative randomized controlled trials	2.1. Is randomization appropriately performed?				
	2.2. Are the groups comparable at baseline?				
	2.3. Are there complete outcome data?				
	2.4. Are outcome assessors blinded to the intervention provided?				
	2.5 Did the participants adhere to the assigned intervention?				
3. Quantitative non-randomized	3.1. Are the participants representative of the target population?				
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?				
	3.3. Are there complete outcome data?				
	3.4. Are the confounders accounted for in the design and analysis?				
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?				
4. Quantitativ	4.1. Is the sampling strategy relevant to address the research question?	√			
	4.2. Is the sample representative of the target population?	√			

e descriptive	4.3. Are the measurements appropriate?	√			
	4.4. Is the risk of nonresponse bias low?	-			
	4.5. Is the statistical analysis appropriate to answer the research question?	√			
5. Mixed methods	5.1. Is there an adequate rationale for using a mixed methods design to address the research question?	√			
	5.2. Are the different components of the study effectively integrated to answer the research question?	√			
	5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?	√			
	5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?	√			
	5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?	√			

File 2. Interview guide for key informants and clinic managers/nurses

Integrating gestational diabetes and type 2 diabetes care into primary health care: lessons from prevention of mother-to-child transmission of HIV in South Africa - A mixed methods study

Interview guide for the key informants and clinic managers/nurses

INTRODUCTION

Thank you for agreeing to be interviewed today. We appreciate your time. The reason why we have asked you to come today is because we want to learn out more about your experiences with the PMTCT programme and the care received by women with gestational diabetes at the clinic during ANC and post-partum this area in general and compared to other jurisdictions in South Africa.

There are no right or wrong answers to our questions. Different opinions and experiences are valuable to us and we hope you feel comfortable enough to be honest with us. If you have any negative comments or feedback you would like to give us, that is fine.

The information you share with us today is completely confidential. Your responses will not have any identifying information. Your responses will only be shared with members of the study team and

will be compiled with other responses from various participants. We would like to tape our discussion because I cannot write down everything you say, but this will also remain confidential.

Before we start, we need to ask you to give us your consent. This means that this discussion is voluntary and you are free to withdraw at any time without having to give a reason.

Do you have any questions about the interview? Is there anything that is worrying you?

Do you have any *other* questions before we start the interview?

DEMOGRAPHIC INFORMATION

Names:

Age:

Contact details:

Institution:

Position:

INTERVIEW GUIDE

Main question: Please can you tell us what used to happen in this clinic before and after the PMTCT programme was integrated in this clinic?

Once the clinic managers have said what is on their minds, we will then ask the following specific questions:

- Can you tell us what have been your main activities since PMTCT was integrated?
- Have these activities changed from the previous experience (before integration)? Why did you make these changes?
- How is postnatal care managed and what works well and not so well?
- Let's discuss each of those activities in detail. (also ask to see card system how and how it is working)
- Can you tell me about particular successes you have had in the last year or last few months?

- Can you tell me about particular problems or challenges you have had?
- Tell us about how the clinic has been handling women under PMTCT who are diagnosed with GDM. (How do you identify them? What do you do for them in ANC and post-partum?)
- Tell us about how the clinic has been functioning this last year (regarding PMTCT and GDM management).
    - Major/ notable events;
    - Shortage of nurses/patient load/ appointments;
    - drugs/ equipment/ other CHWs;
    - atmosphere between staff, between staff and women/patients;

To prompt with the following if topics don't come in conversation:

- Practical issues like patient flow
- Follow up of patients
- Post-natal care – for women and for babies
- What if patients have multiple problems – ANC or PNC plus other conditions (chronic, like T2D, or acute)
- Performance of nurses and other staff members;
- Nurses taking initiative;
- Nurses responding to problems;
- Activities are co-evolving
- Engagement between CHWs and women
- Engagement between CHWs and nurses;

Finally, is there anyone in particular you think we should talk to next or any important documents or guidelines that we should consult?

Interview with women about PMTCT and GDM

INTRODUCTION

Thank you for agreeing to be interviewed today. We appreciate your time. The reason why we have asked you to come today is because we want to learn out more about your experiences with the PMTCT programme and the care you received for diabetes at the clinic during ANC and post-partum. There are no right or wrong answers to our questions. Different opinions and experiences are valuable to us and we hope you feel comfortable enough to be honest with us. If you have any negative comments or feedback you would like to give us, that is fine.

The information you share with us today is completely confidential. Your responses will not have any identifying information. Your responses will only be shared with members of the study team and will be compiled with other responses from various participants. We would like to tape our discussion because I cannot write down everything you say, but this will also remain confidential.

Before we start, we need to ask you to give us your consent. This means that this discussion is voluntary and you are free to withdraw at any time without having to give a reason.

Do you have any questions about the interview? Is there anything that is worrying you?

Do you have any *other* questions before we start the interview?

DEMOGRAPHIC INFORMATION

Names:

Age:

Contact details:

Pregnancies:

No of children:

Health status:

Medication and current clinic visits:

INTERVIEW SCHEDULE

(A) Women's experiences of PMTCT and other health services

1. First of all, we would like to talk about your experiences with the care you received from the PMTCT programme while you were pregnant. Would that be okay?

Prompt: Where did you go for care? – Describe what care you received – what aspects were you satisfied with/unsatisfied with (what was good and not so good) – how was the delivery? – What care did you receive post-partum?

(B) About GDM

2. Now we would like us to talk about the diabetes you had during pregnancy.

   - **Diagnosis**: When and how were you diagnosed with GDM? – How did you feel when you were diagnosed? – did they explain to you, what diabetes was? What do you understand about GDM? The risks to you and the baby?
   - **GSH:** What was your experience at GSH like? What were you satisfied/unsatisfied with? Were you given any information/support/counselling about how to manage your diabetes? (by whom, what info) In your view, how well controlled was your diabetes in pregnancy? What concerns did you have?

Prompt: How was the delivery? What happened post-delivery? Were you advised to get another test 6 weeks later? Did you go for this test? Why or why not? Was it ever explained to you that after GDM, you can develop T2D? How do you feel about being at greater risk of developing type 2 diabetes?

Integration: Did you have to continue going to 2 separate clinics? How was that? Would you have preferred going to one place for all your ANC and PNC? Please explain why….**WBC:** Did you take your baby to the WBC for immunisations? Tell us about your experience at WBC.

(C) Women's experiences around lifestyle modification/health behaviour change

3. Now we would like to understand more about the lifestyle changes you made after the GDM diagnosis

Prompt: Tell us about what motivated you to make these changes. Did your PMTCT adherence facilitate/complicate this? Tell us about what were the difficulties you experienced (barriers and/or facilitators and how you dealt with them)? How did you feel about your weight gain during PMTCT cascades and in pregnancy?

(D) Views on proposed intervention

First explain the proposed intervention.

4. Now I would like to understand your opinion about this intervention.

Prompt: Would you be interested in participating in such intervention? Why/why not? Tell us what you think our project should do to help women at risk of type 2 diabetes. Would you have preferred individual counselling/group counselling, health education materials or all of the above? Who would you prefer to deliver the intervention?

5. **CHW**: What is your experience with CHWs regarding their role for your PMTCT, GDM care and overall health services?

Is there anyone else who you think we would need to speak to as part of this study?

After this discussion, do you have any questions?

Thank you for time and valuable insights. We may contact you in future for follow up or feedback.

Paper 4 – Integrating type 2 diabetes mellitus prevention after gestational diabetes into community based PHC services: health care providers' experience and women knowledge in South Africa – Mixed methods study

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Status: This mixed methods study was submitted to the International Journal of Integrated Care (IJIC) (August 2020).

Abstract

Background: Despite high gestational diabetes mellitus (GDM) prevalence in South Africa (SA) (9.1% in 2018), its screening and management are poorly linked to post-GDM prevention of type 2 diabetes mellitus (T2DM) in SA's fragmented health system. This study explored the integration of GDM screening and prevention of T2DM post-GDM within community-based primary health care (PHC) in SA.

Methods: Our mixed method, sequential exploratory study included 18 semi-structured interviews with health care providers (HCPs), 5 in-depth interviews with key informants (KIs), 2 focus group discussions (FGDs) with Community Health Workers (CHWs n=15), 4 FGDs with women with GDM attending a hospital GDM clinic in Cape Town (n=35) and individual exit interviews with these 35 women. Thematic analysis of qualitative datasets and descriptive statistical analysis of quantitative data were undertaken, drawing on the Behaviour Change Wheel (BCW) framework.

Results: Shortage of well-trained staff in PHC, ill-equipped clinics and lack of knowledge among women were reported to be the major barriers to successful integration of GDM screening and postnatal interventions to prevent or delay T2DM onset in SA. Only 51% of women were aware that they have to reduce sugar intake and only 43% reported having received advice about all 4 recommended actions (improve diet, reduce sugar intake, physical exercise and regularly taking medication) to manage GDM and prevent T2DM.

Conclusion: GDM and post-GDM prevention of T2DM are poorly integrated into PHC. Integration is desired and may be feasible if PHC resource and training constraints and women's socio-economic barriers are addressed.

Key words: Integration, primary health care, Gestational diabetes, GDM, Type 2 diabetes, T2DM, South Africa.

Abbreviations

ADA	American Diabetes Association
ANC	AnteNatal Care
ART	Anti-Retroviral Therapy
BANC	Basic ANtenatal Care
BCW	Behaviour Change Wheel
CHWs	Community Health Workers
DPSG	Diabetes Pregnancy Study Group
EASD	European Association for the Study of Diabetes
GDM	Gestational Diabetes Mellitus
GSH	Groote Schuur Hospital
HCPs	Health Care Providers
HIV	Human Immunodeficiency Virus
IADPSG	International Association of Diabetes and Pregnancy Study Groups
IGT	Impaired Glucose Tolerance
IINDIAGO	Integrated INtervention for DIAbetes rIsk after GestatiOnal diabetes
IQR	InterQuartile Range
KIs	Key Informants

LMICs	Low and Middle-Income Countries
MMAT	Mixed Methods Appraisal Tool
MOU	Midwife and Obstetrics Unit
NCDs	Non-communicable diseases
NDDG	National Diabetes Data Group
NIMART	Nurse -Initiated Management of AntiRetroviral Therapy
OGTT	Oral Glucose Tolerance Test
PHC	Primary Health Care
PICT	Provider-initiated counselling and testing
PMTCT	Prevention of Mother-To-Child Transmission
PNC	Post Natal Care
SA	South Africa
SD	Standard Deviation
SSA	Sub-Saharan Africa
T2DM	Type 2 Diabetes Mellitus
WC	Western Cape.

Background

A 2018 prevalence study conducted in SA has assessed GDM prevalence at 9.1% and warned of subsequent T2DM for these women and their children along with more complications, reduced longevity and impacts on the national health care system (Macaulay et al., 2018). GDM is defined by the World Health Organisation (WHO) as "any degree of glucose intolerance with onset or first recognition during pregnancy" (American Diabetes Association, 2004; Metzger, 1998) and was defined by American Diabetes Association (ADA) as "diabetes diagnosed during pregnancy that is not clearly overt diabetes" (American Diabetes Association, 2014). T2DM, formerly known as non-insulin-dependent diabetes mellitus, is a chronic metabolic disease resulting from interactions between genetic, environmental, socio-economic and behavioral risk factors; leading to severe health complications (Chen et al., 2011; Maitra & Abbas, 2005; Olokoba et al., 2012; The National Institutes of Health (NIH), U.S. Department of Health and Human Services, 2011; UK Prospective Diabetes Study (UKPDS) Group, 1998b, 1998a).

Given that between 10 and 31% of T2DM cases among women are reported to be associated with previous GDM and that the risk of developing T2DM is increased more than 7 fold for women who had GDM compared to those who did not (Bellamy et al., 2009; Cheung & Byth, 2003), GDM screening for all pregnant women has since been strongly recommended by ADA and other professional bodies (Blatt et al., 2011; Daneshmand et al., 2019). However, only a minority of women are screened for GDM (Blatt et al., 2011) , using many GDM testing and diagnostic criteria that have not been standardised despite efforts to do so (Daneshmand et al., 2019). (**Table 11**).

Table 11 : **Different diagnostic criteria for GDM**

Different diagnostic criteria to diagnose GDM		
Group/Organisation level thresholds	Screening test	Diagnostic criteria: blood glucose
American Diabetes Association (American Diabetes Association, 2013, 2014)	One step: 2 hr 75 g OGTT	At least one of the following must be met: Fasting: ≥5.1 mmol/l (92 mg/dl) 1 hr: ≥10.0 mmol/l (180 mg/dl) 2 hr: ≥8.5 mmol/l (153 mg/dl)
	OR Two step: 1) 1 hr 50 g (non-fasting) screen 2) 3 hr 100 g OGTT	OR If 1 hr: ≥10.0 mmol/l (180 mg/dl) proceed with step 2 3 hr: ≥7.8 mmol/l (140 mg/dl)
Carpenter and Coustan (Carpenter & Coustan, 1982)	3 hr 100 g OGTT	At least two of the following must be met: Fasting: ≥5.3 mmol/l (95.4 mg/dl) 1 hr: ≥10.0 mmol/l (180 mg/dl) 2 hr: ≥8.6 mmol/l (154.8 mg/dl) 3 hr: ≥7.8 mmol/l (140 mg/dl)
Diabetes Pregnancy Study Group (DPSG) of the European Association for the Study of Diabetes (EASD) (The Lancet, 1988)	2 hr 75 g OGTT	Fasting: >5.2 mmol/l (93.6 mg/dl) OR 2 hr: >9.0 mmol/l (162 mg/dl)

	2 hr 75 g OGTT	At least one of the following must be met:
International Association of Diabetes and Pregnancy Study Groups (IADPSG) (International Association of Diabetes and Pregnancy Study Groups consensus panel, 2010)		Fasting: ≥5.1 mmol/l (92 mg/dl) 1 hr: ≥10.0 mmol/l (180 mg/dl) 2 hr: ≥8.5 mmol/l (153 mg/dl)
	3 hr 100 g OGTT	At least two of the following must be met: Fasting: ≥5.8 mmol/l (105 mg/dl) 1 hr: ≥10.6 mmol/l (190 mg/dl) 2 hr: ≥9.2 mmol/l (165 mg/dl) 3 hr: ≥8.0 mmol/l (145 mg/dl)
National Diabetes Data Group (NDDG) (1979) (National Diabetes Data Group, 1979)	2 hr 75 g OGTT	Fasting: ≥7.8 mmol/l (140 mg/dl) OR 2 hr: ≥7.8 mmol/l (140 mg/dl)
World Health Organisation (1985) (WHO, 1985)	2 hr 75 g OGTT	Fasting: ≥7.0 mmol/l (126 mg/dl) OR 2 hr: ≥7.8 mmol/l (140 mg/dl)
	2 hr 75 g OGTT	At least one of the following must be met: Fasting: 5.1–6.9 mmol/l (92–125 mg/dl)

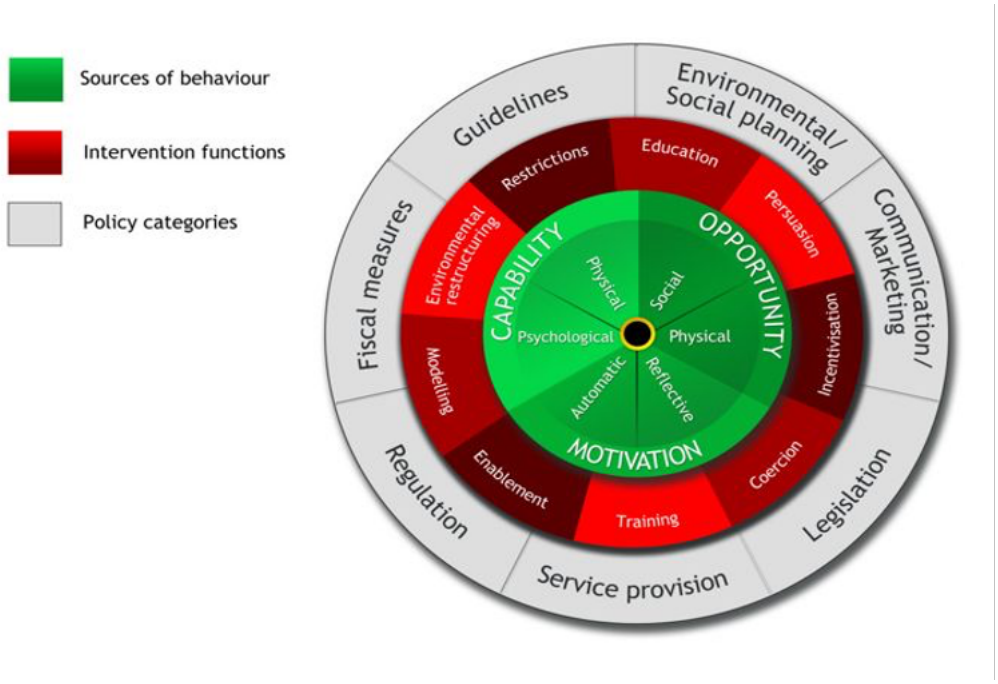
World Health Organisation (1999) (WHO, 1999)		1 hr: ≥10.0 mmol/l (180 mg/dl) 2 hr: 8.5–11.0 mmol/l (153–199 mg/dl)
World Health Organisation (2013) (IDF, 2013)		

In SA, women attending ante-natal care (ANC) are screened for GDM based on the presence of risk factors (Adam & Rheeder, 2017b; Dias et al., 2019; Muche et al., 2019). Those who are diagnosed with GDM are then referred to tertiary hospitals for their pregnancy follow-up and delivery, but only a small proportion of these women with recent GDM return for postpartum assessment, including an oral glucose tolerance test (OGTT), and management (Benatar, 2013; Muhwava et al., 2018). This gap between antenatal and postnatal care is being investigated in high income settings where many women report intentions to change their lifestyle post GDM to prevent T2DM onset, even though they find that effort challenging (Nielsen et al., 2014; Shih et al., 2013), with a high attrition rate for the postpartum OGTT (Bennett et al., 2012). As GDM can have devastating maternal and child effects and is known to increase the risk of developing subsequent T2DM (Ben-Haroush et al., 2004; Herring & Oken, 2011; Kim et al., 2011), experts are increasingly calling for universal screening and integration of GDM and post-GDM care into routine public health services in low and middle-income countries (LMICs). This study aimed to explore the integration of GDM screening and prevention of T2DM post-GDM within routine, community-based PHC services in SA.

Methods

Study framework

The Behaviour Change Wheel (BCW) framework (Michie et al., 2015) (**Figure 11**), was used for this study. BCW has been effectively applied to planning and evaluating interventions targeting individuals, groups, programmes and behaviours (Michie et al., 2013; Ware et al., 2019). While motivation, capability and opportunity from the model's inner circle are seen as the enablers for both individual and collective behaviour change, they must be assessed in relation to programme implementation, its mechanism and context (Michie et al., 2011; Moore et al., 2015a). In this study, the BCW was used to understand the *policies, practices and barriers to change* among health workers and women.



Behavioural Change Wheel framework

(Michie et al., 2015) (Figure used with permission of Prof. Susan Michie).

Study design and settings

A mixed method, sequential exploratory design was used, applying the Mixed Methods Appraisal Tool (MMAT), version 2018 (Creswell & Clark, 2017; Hong et al., 2018).

This study contributes to the process evaluation of an ongoing complex intervention implementation research project, IINDIAGO (an Integrated health system INtervention aimed at reducing type 2 DIAbetes risk in women after GestatiOnal diabetes in South Africa, Trial ID: PACTR201805003336174), which aims to integrate improved post-partum follow up for women with GDM into PHC and thus contribute to T2DM prevention in two South African cities: Cape Town, Western Cape province and Soweto township in Johannesburg, Gauteng province). The IINDIAGO trial was in the recruitment stage among women from disadvantaged communities in Cape Town and Soweto, South Africa, when data were collected for this paper.

Data sources and eligibility criteria

The data sources included: 1) semi-structured in-depth qualitative interviews with key informants (KIs) (N=5) and health care providers (HCPs) (N=18); 2) focus group discussions (FGDs) with women diagnosed with GDM (N=35) and community health workers (CHWs) (N=15); and 3) exit interview questionnaires with the 35 women who participated in FGDs.

The KIs included researchers, policy makers and clinicians who have been involved in DM policies and care, especially for GDM and T2DM patients at national and provincial levels. They were interviewed about GDM policies and their experiences and perspectives on integrated GDM screening and T2DM prevention within PHC services. HCPs included managers, nurses or midwives from the public health sector in Cape Town (WC province), South Africa. They were interviewed about their practices or processes for GDM screening and care in facilities, including referral pathways. Drawn from these same local facilities, CHWs were recruited to FGDs to share their experiences and roles working with patients including those who had GDM and T2DM. Women with GDM referred by different clinics in Cape Town and attending the Groote Schuur Hospital (GSH) for their GDM follow-up and delivery, were identified from hospital records, contacted and recruited to participate in the FGDs and share their GDM knowledge and the challenges they face while seeking

care. These women also completed brief exit interviews using questionnaires, regarding their background and how their own GDM is being managed. All research participants discussed their views of whether and how integrated health services such as those proposed in the IINDIAGO trial could help with GDM screening and initiatives for T2DM prevention among women in SA.

Participants aged more than 18 years without any cognitive disabilities were included in this study. All were able to communicate in English. In cases of women with GDM and CHWs who did not speak English well, participants were encouraged to express themselves in isiXhosa or Afrikaans and their responses were contemporaneously translated into English by the research assistant who was fluent in these local languages. The KIs and HCPs were offered no compensation upon completion of interviews. Women with GDM who participated in this study were provided with a R100 ZAR (around $7 USD) voucher while CHWs shared refreshments after FGDs. Fieldwork was conducted between March 14th, 2018 and August 24th, 2018.

Study sample and data collection

Beginning with two experts recommended by the IINDIAGO principal investigators, sequential referral snowball sampling (Atkinson & Flint, 2001) was used to identify and recruit other KIs, who were then approached and recruited for this study. Criterion sampling (Patton, 2002; Suri, 2011) was used to identify all other respondents depending on their occupations or their GDM diagnosis and referral to GSH. Managers and nurses or midwives involved in GDM screening at the clinics, CHWs who (in coordination with the local facilities) deliver services to women with different health problems in the community and assist at the clinics when called upon, were selected using this sampling strategy.

Interview/FGD guides and exit interview questionnaires were respectively used as tools to collect qualitative and quantitative data. KIs were interviewed in their offices at the hospital, clinic or research facilities. The two FGDs conducted with CHWs were organised in collaboration with

the two local clinics with which they were affiliated. The four patient FGDs included 6-10 women diagnosed with GDM and receiving care at GSH (N=35), followed by individual exit interview questionnaires that took place in a room provided by the maternity ward at GSH. All interviews and FGDs were conducted by a trained researcher (JCM), assisted by a trained research assistant (SK) fluent in local languages, under the supervision of experienced qualitative researchers (KM and CZ). The researcher (JCM) introduced himself as a doctoral student and briefly interacted with the participants about the study before commencing the interviews and FGDs. Interviews with HCPs and 2 FGDs (N=15) with CHWs took place at the clinics, in their clinic offices for HCPs and in the rooms provided by the local clinics for CHWs. Each interview lasted between 30 and 45 minutes. FGDs lasted between 45 minutes and 1 hour. The Exit interviews lasted between 10 and 15 minutes. All interviews and FGDs were audio recorded and ATLAS.ti software was used to assist data analysis and management.

Data analysis

The interviews and FGDs were transcribed and a coding system was developed by JCM in collaboration with CZ using an inductive/deductive approach. All discrepancies in the coding process were discussed and resolved between these two investigators. Thematic analysis was generally used but content analysis was applied on a few occasions in order to check the frequency of important codes (Paillé & Mucchielli, 2016; Vaismoradi et al., 2013). For statistical analysis of the 35 exit interviews questionnaires, categorical variables were summarized using absolute frequencies and relative frequencies, while continuous variables were synthesized using central trend statistics (mean, median) and dispersion statistics (standard deviation (SD), interquartile range (IQR)). To measure the correlation between qualitative variables, we used Cramér's V coefficient which is interpreted as follows : from 0.0 to <0.1 negligible association, from ≥0.1 to <0.3 weak association, from ≥0.3 to

<0.5 moderate association and ≥0.5 strong association (Cohen, 2013). This analysis has also contributed to the ongoing process evaluation of the IINDIAGO study.

Ethical approval

Ethical approval was obtained from the Human Research Ethics Committee, Faculty of Health Sciences, University of Cape Town (HREC REF: 946/2014), the City Health Department, Cape Town and the Department of Health, Western Cape, South Africa; and comité d'éthique de la recherche en sciences et en santé (CERSES), Université de Montréal (CERSES-19-058-D), Canada. Written consent was given for all interviews and the anonymity of participants was maintained throughout the research process.

Results

In total, 73 individuals participated in this study. Participants in the in-depth individual interviews (N=23), included 4 (17%) clinic managers and 14 (61%) nurses and midwives and 5 expert KIs (22%). Of these 23 respondents, 19 (83%) were female, with a mean age of 42 years and mean of 16 years' experience in health care (see **Table 12**). Participants in FGDs (N=50) included women with GDM and CHWs and were all female.

Table 12 : **Characteristics of KIs and HCPs**

Factor	Level	Value
N		23
Gender	F	19 (83%)
	M	4 (17%)
Age (in years)	mean (SD)	42.7 (10.6)
	median (IQR)	41.0 (35.0, 47.0)
Experience (in years)	mean (SD)	16.1 (11.0)
	median (IQR)	12.0 (7.0, 23.0)
Category	Clinic managers	4 (17%)
	Nurses and midwives	14 (61%)
	KIs	5 (22%)

The four thematic categories that emerged from the analysed data were interpreted using three BCW layers from outer to inner: policy categories, intervention functions and sources of behaviour respectively. Each category was linked to a specific layer except the third and the fourth categories that were classified using the same "inner" layer (**See Table 13**).

Table 13: **Categories and BCW layers**

Category		**BCW layer and main content, from outer to inner**
I.	Existing guidelines, services and current practices in the clinics	Outer layer: policy categories
II.	Effective antenatal referral procedures but lack of follow-up after delivery	Middle layer: intervention functions
III.	IINDIAGO, an intervention with potential to bridge the gaps	Inner layer: sources of behaviour
IV.	Encouraged role of CHWs involvement toward community based T2DM prevention intervention	Inner layer: sources of behaviour

Each category had different themes with each illustrated by a single quote from one of the participant groups. More illustrative quotes from various participants are depicted in **Table 14**.

Table 14: **Categories and illustrative quotes**

Key findings and illustrative quotes
Category 1: **Existing guidelines, services and current practices in the clinics** **1. Current GDM screening/care guidelines and its poor implementation** *"So, what we basically do in our facility, so we go according to the BANC protocol. We have our own protocol. If a mother comes in the morning for an antenatal booking, then we test her urine…".* **HCP 1.**

2. **From no testing to the risk-based screening of GDM at the clinics**

i. Risk factors assessment

"There are two Community Centres in Gugulethu, the, and then it's us, the mobile Baby Clinic. In our clinic it's basic antenatal care, so the people who have a history with parents who are diabetic, usually we send them to the MOU, they are screened that side. We don't do screening in our clinic. We don't actually do that". **HCP 3.**

"*Not every mum, but if she presents risk factors such as a family history of diabetes, the mum had a previous history with Gestational Diabetes, she has an exceeding Body Mass Index (BMI) and then if we tested the random blood sugar and found that it was above 7.8, then we will give the mother a Gestational Diabetes check…".* **HCP 4.**

"So we do a random blood glucose at the facility, and depending on that result, we will then follow the necessary steps. There is obviously a screening in terms of family history, and have you had Diabetes before, or do you currently have Diabetes….". **KI 6.**

ii. Process of GDM testing and referring women with GDM

"the procedure for screening, we've got a list of indications for doing Glucose Tolerance Test (GTT): family history of diabetes from her mother, her father or her siblings, BMI of 35 and above, history of big babies, persistent Glycosuria; for three consecutive visits. She has to come in the morning, fasting, her last meal the previous night around 10 o'clock. So, when she comes, we do the prick. If the sugar is 7 and above, we don't continue, but if it is less than 7, we take the fasting blood and we give her 75 grams of glucose, and we take the second blood after two hours. So, they come after one week for the results. If it's an IGT, we refer to Mowbray not Groote Schuur, but if it's GDM, then we refer to Groote Schuur". **HCP 2.**

"when they come here for the first time, we do the IGT (Impaired Glucose Tolerance) test or sugar test, and then if there is family history like the mother was diabetic, then we do the OGTT test, which is the fasting glucose, but we don't do it here. I have to book for them in Gugulethu, and then they are going to give me the date when the patient can go there. Otherwise we have the forms that we use. We just take… I'm going to show you later the forms, and then we take, if the patient has already diabetes and she does not qualify to book here at the clinic, so I refer the patient straight to Gugulethu MOU". **HCP 5.**

3. Barriers to GDM screening into PHC

"You know, unfortunately a lot of the patients are picked up a bit later. The patients we pick up earlier of course, are those who previously diabetes, which is a different ballgame. So those get to come in early, but the majority of the patients come in at a later time…". **KI 3.**

"The only challenge is that when you give an appointment for the lady to come to do bloods, then she doesn't come. Then it will be picked up because they are supposed to do it before they are 28 weeks; or if you do it at 28weeks then you have to repeat it. If it was borderline then you have to repeat, so then you don't have that chance of checking if you pricked them already at seven months or close to eight months, so you don't have that chance of checking, then you are going to refer them, because they are already late in pregnancy". **HCP 6.**

"….The presentations are varied, and 50% of patients that are currently diabetic don't know yet that they have Diabetes. So I think anyone allied to the healthcare should be thinking about screening and actually being able to screen….". **KI 1.**

"I don't think it's okay, because sometimes we miss them, because maybe, it depends, maybe the family doesn't have diabetes and the person can develop Diabetes during pregnancy. So sometimes, if it's not picked up in the urine, and we don't often do the diabetes test every time, it's not like Hypertension, it's not… I don't think we are doing a good job in this case. There are no signs you know, if it's high….". **HCP 2.**

"We don't have time to talk individually, but at times when we give the Health Talk, we do explain to them…". **HCP 4.**

"At the moment I think we have got one glucometer in the whole clinic, you understand? Sometimes we don't know where it is and it is difficult to find it, you see…". **HCP 2.**

"She must bring her own food, because we do not have glucose to eat. She goes and has breakfast, and then two hours later we re-prick…". **HCP 1.**

"You call an ambulance to pick up the clients to take to the MOU, or Mowbray, depending on where the pathway is. Now we send the letter. On the letter there is a sleeve that is supposed to come back to us, but that has never happened. I have been here for more than eight years now, I have never seen that sleeve coming back...". **HCP 7.**

Category 2: **Effective antenatal referral procedures but lack of follow-up after delivery**

i. On-site integrated hospital services

"she gets referred to Groote Schuur Hospital's antenatal clinic where they will do what we call OPD (Out-Patients Department) spreads, and then they will start treatment; but the first line treatment for any diabetic is diet, and so she will see the dietician, lifestyle changes, and then she will start treatment…". **HCP 8.**

"nurses play an indispensable role in managing these patients, bearing in mind that the maternal and foetal wellbeing will be first assessed by nurses, and also nurse will also help in providing anthropometric measurements, they help to also reduce the time-lapse in some of these patients to spend a very long time waiting for doctors. So basically, nurses play a role in monitoring of the mother and the baby, as well as even sometimes in diagnosis and also in management". **KI 5.**

We all have our specialities, so the registrar that would be looking after the patient is somebody that is rotated through the whole block, so they've seen cardiac, they've seen eclamptic patients, they've done diabetes; but if there is a specific problem, then we are in the fortunate position where we have the resources where we can get infectious disease people out, instead of struggling with that, or we can get the endocrinologist out, and say listen, we have now hit a wall, how do we go forward, but that is within our setting". **HCP 8.**

ii. Socio-economic boundaries to healthy antenatal and postnatal initiatives

".... sometimes when you check in, they say you must come without eating to the clinic and then they take a long time to check your sugars, and then you get tired, you are hungry. You know how you are when you're hungry, you seriously want to". **Participant in FGD 1.**

"*.... Like delays, and it's now the strike, so there are no busses, so the trains are full; taxis you have to wait in line, and you know when you are pregnant, to stand for a long time in line, it also causes back pains; like now, I've got a huge back pain from standing in the line".* **Participant in FGD 4.**

".... Sometimes you just want to ask a small question and the sister goes to levels like (she gets upset and shout). She doesn't even know the question that you want". **Participant in FGD 1.**

" ...You come from work, even if you get your day off, you are tired, thinking about exercising, even if you want to, but your body doesn't allow you to do so, because you are tired". **Participant in FGD 3.**

"...For me it's very tough, to change my diet, because I'm used to eating. For me it's really... and it's not easy; that is why I'm cheating sometimes. **Participant in FGD 2.**

iii. Confusion or little knowledge of women on GDM and lifestyle changes

"…this is my second child, I didn't have sugar. Nobody in my family has sugar. I find out my sugar is high in my blood, so the doctor explained to me I must go on the Insulin, because otherwise I can have a miscarriage; and I don't understand actually, maybe can it be, or what….". **Participant in FGD 2.**

iv. Poor communication and inexistent plans for postnatal follow-up

We don't have a six week visit. We don't have a six week visit. When six weeks postnatally, the baby is six weeks, so at six weeks they go to the Baby Clinic, so they don't come back to us, that's the thing. **HCP 9.**

"There is no strict channel. Obviously, there is very detailed discharge information about what the diagnosis is, what the implications are, and what needs to be done in the interim. But as to whether people phone and follow up…? You know, there isn't that, and there needs to be; not only in the management of GDM, but in the management of a lot of patients that we see for whatever medical reason…". **KI 3.**

"So, I think firstly the doctors and nurses don't always have enough time, and also, they're not very knowledgeable, and then even the dieticians are sometimes giving the wrong messages because of this whole debate internationally. So, I think those things are a problem, and then there is also the issue of healthy foods being expensive in townships, and the issue of exercise is difficult. I mean, if women get up at five o'clock, go to work in the town, go back, don't get home till seven, you know, their lifestyles aren't conducive to exercise". **KI 4.**

"The maternity sisters do not communicate with the local clinic sister for follow-up on these clients about medication after delivery and then we don't know. So, maybe they got letters from hospital that you must follow up at this clinic to get your medication that is going to control you but mothers don't follow up, as I have noted, they don't follow up, they only focus on the baby after delivery, they focus on the baby. They don't go for that follow up appointment and the medication, especially after they are coming from

Maternity. But if there is a problem, then the doctor prescribes when discharging them but they will never mention it to us at the clinic…And then, if they are with the person who didn't see them when pregnant, you won't know if the client had a problem with the glucose". **HCP 10.**

"I mentioned earlier about the six weeks postnatal visit that needs to take place, and our nurses are overworked and understaffed, and I can attest to that. On any given day it is hectic in front, and staff shortages and absenteeism and people not adequately trained. People get pulled from one department to another to go and help out, and so all in all, what I'm trying to say is the six weeks postnatal visit, I don't think to my knowledge that it is actually happening, that is, not in our facility". **KI 6.**

Category 3: **IINDIAGO, an intervention with potential to bridge the gaps**

"It is now policy. We had it two or three years ago, we wrote a postnatal care policy for the Western Cape, and I was involved in writing it, and it's agreed, it's just no-one has implemented it. So, it has to be implemented…. So, I do think it needs to be resourced. You need another nurse, and you need a particular training to give that nurse the referral route. So, what does she do with a person who's depressed at six weeks? What does she do with the one who had GDM and they've checked her sugar now and it's normal? What do they do with her? So, I think it needs almost a little bit of a syllabus for what the nurse does, you know?". **KI 4.**

We see it with IGT patients who are very well counselled and can actually reverse the whole and become normal. So, I think it's feasible. I think it's good that it (IINDIAGO) will give you raw data that you can then present to policymakers and say, listen, although we knew this, this is the hard data, done in a methodologically robust manner, and that no-one can argue with. And once faced with that, then one will have to change policies, and be forced to change the infrastructure and the way the infrastructure is set up to deal, not only with Type 2 Diabetes but with many other problems. **KI 3.**

"I think if we can implement it (IINDIAGO) at the Well Baby Clinics for instance if they have enough staff and they are well-trained, I think it would make a big difference,

because as a mother sometimes you are more worried about your baby, so then you are more likely to access that service; and then I think, like I said earlier, a continuation of care is better… So, if she has that continuous support at the Well Baby Clinic, because that is a place where she will be accessing the services quit e frequently, so she will be able to build a bond or a type of relationship with that caregiver on that side as well". **HCP 8.**

"It (IINDIAGO) is a good thing, because we such type of intervention we will normally check if everything is good when they come for post-delivery. We now just focus on breastfeeding and not in that side. We don't go on the Diabetes side and Hypertension and all those things". **HCP 6.**

Category 4: **Encouraged role of CHWs involvement toward community based T2DM prevention intervention**

"You see, I think because the women with GDM after pregnancy, most of them don't have any medical problem, the doctor or nurse will think they are wasting their time at the clinic, so, actually the initiative should be a community based one through lifestyle, and I think the community health workers are most important…but I don't know the answers about the scope of a community health worker". **KI 4.**

"We also have health care workers that are not based in the clinic, but they report. Those are the people that are helping us work or supervising the ART or TB treatment for the people that are placed in the community to take their treatment. They visit. Even with the immunisation that is really not doing so well, they are able to the visits, the home visits. They are in contact with the community, so they also can help in this intervention (IINDIAGO)". **HCP 10.**

"…they also help us with recalling the mothers for other things. I think they can also play a role in this intervention (IINDIAGO)". **HCP 11.**

"For me, I think that the community workers are people from the community, so, the patients trust them more than coming to a sister in a hospital they can only see once.… so, the community knows them. If they do the screens and stuff they tend to trust them more than us some times. Yes, I think they need to be trained, because the last time I said they even need to be trained in doing prognostics for us, then they can do the diabetic screening at the same time, different screenings; because they are there in the house with ten people around them, so they can do all of that, and then they catch them early, even the blood finger prick". **HCP 4.**

"We have this form called household chart, here is a copy. So, inside house with the members of the household, and then you ask all these questions. Maybe there is someone who has symptoms of TB, who is HIV Positive, who is interested to test, then you advise to go and test. I give some card that we write in for follow-up on that date, referral cards. You tell them go to Crossroads if you are feeling that you are hypertensive and get your medication there. Diabetics, they talk a lot like I am drinking a lot of water. I am always tired, they talk about all those symptoms to you when you get there, so you record them and you check all the symptoms…You advise them about immunisation, Vitamin A, etc". **Participant in 1, FGD 1.**

"And even if it's difficult, and they don't want to come to the clinic, you as a CHW, you help her to start medication again. You educate people about their health, you tell them what is going to happen to them if they keep doing this or that? For example, you say to the patient that if you don't go there and take your medicine, this is going to happen to you". **Participant 1, FGD 2.**

"Me, I love the job that I am doing because I don't have a problem with people, and I can convince them but if someone is not doing well, I report her to the supervisor who will then intervene". **Participant 3, FGD 1.**

"My challenge is work load. We have to record. We have to be ready to give weekly and monthly statistics for our work. It's a challenge, because there is a lot of work. We have to visit the clients, rain or shine, you have to visit them. You must have the minimum

six to eight, and then each and every day you must have something to write down as proof of what you have done for the day. We must also cover many households at a long distance and reach target…. **Participant 5, FGD 1.**

"Sometimes when we arrive at a patient, we see a number of men smoking. The whole house is like snow, so I am afraid of entering that house fearing what could happen to me when I enter that house". **Participant 3, FGD 2.**

"Challenges also include robberies in the community and even here at the clinic, they just come and attack you at the clinic's gate and sometimes we are not working with our cell phones because we are afraid of robbery by the gangsters. And sometimes, even in the houses that they are going to do the pill counts in, they mustn't go alone. We must therefore be two or three but it is not easy to get that one to make a friend and go together to avoid those incidents". **Participant 4, FGD 2.**

I. The existing guidelines, services and current practices in the clinics

The BCW's policy categories or outer layer (Michie et al., 2011) was used to assess the process of policy development, analyse its implementation and interpret insights from the KIs and the HCPs regarding the existing guidelines, services and current practices in the clinics regarding GDM screening, care and post-partum T2DM prevention initiatives. Perspectives and experiences of CHWs and women who participated in FGDs mostly referred to services they received and the practices in the clinics they attended. The results for this thematic category were subsequently grouped into 3 headings: 1. Current GDM screening/care guidelines and their poor implementation; 2. From no testing to risk-based screening of GDM; and 3. Barriers to GDM screening in PHC.

1. Current GDM screening/care guidelines and their poor implementation

Both National and Western Cape departments of health have put in place guidelines developed by experts based on international protocols to screen, diagnose and treat GDM (Muhwava et al.,

2018), but challenges arise in their implementation at local facilities. While discussing how GDM is diagnosed within ANC, KIs and HCPs reported that GDM screening guidelines have been poorly implemented at primary care level, resulting in missing some women with potential GDM. The "Basic antenatal care (BANC) protocol" was identified as the main tool used in most of Cape Town clinics but as it is a complex guideline with many components, the decision to screen GDM or not lies with the nurses in line with the facility plan instead of the protocol itself.

> *"We have screening protocols, and the South African Endocrinology Society has put out screening guidelines [for GDM]. Unfortunately, I think our screening is poor. We don't screen widely enough, and there are many risk factors that aren't screened…."*. **KI1**

2. From no testing to risk-based screening of GDM

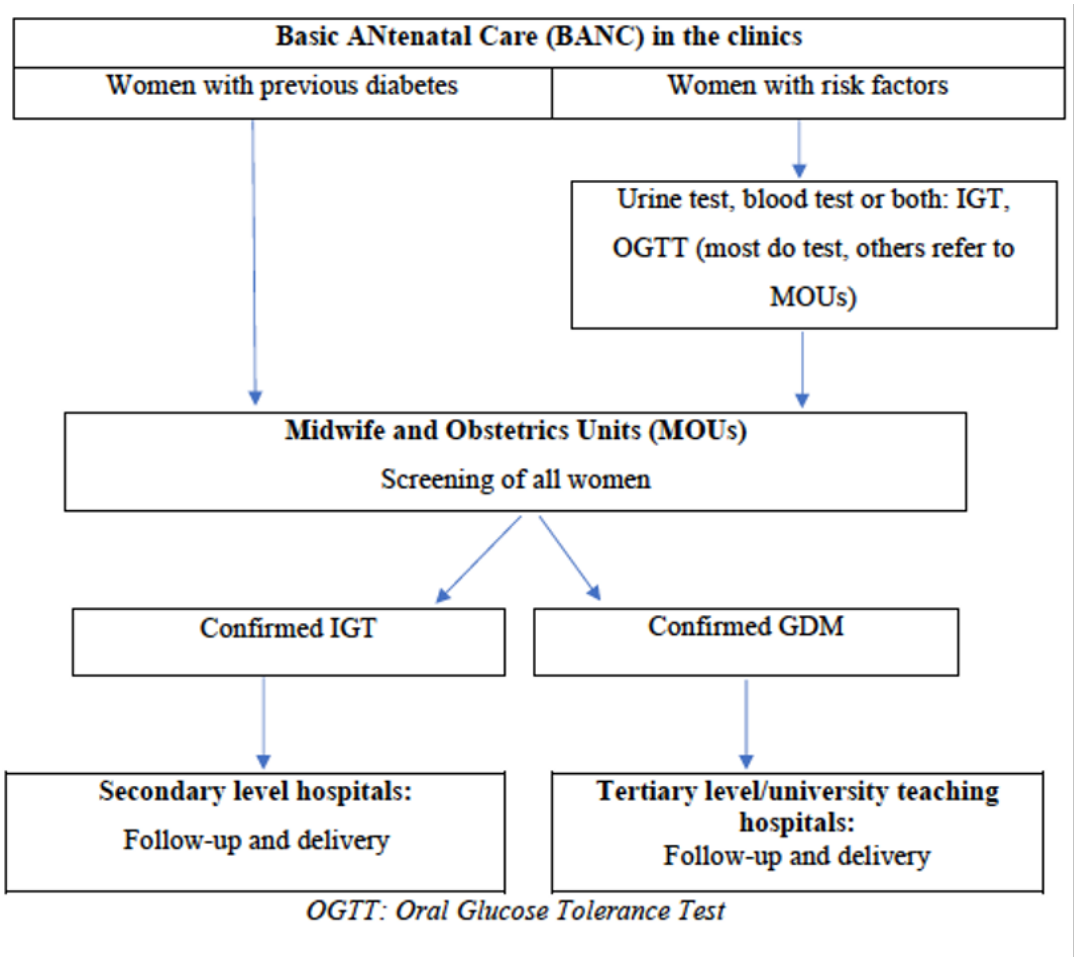
i. Risk factors assessment

Based on the current guidelines, screening for GDM was supposed to be included in all ANC services and uniformly conducted in all local facilities. However, clinics approach GDM screening for pregnant women in different ways; some only test urine and then refer those with glycosuria, while others conduct confirmatory blood glucose tests before referring women to the next level of care. HCPs emphasised that it all depends on the risk factors that women present with during their ANC visits. Thus, not all women who attend ANC are tested for GDM in all clinics despite the ANC guidelines.

> *"Firstly, I think I should explain that we are doing basic antenatal care. We then are taking care of women who don't have any high risks, or just a normal pregnancy. If one is found to have sugar that is, glucose actually, that is evident in the urine, then we refer them, because we don't even do them, the fasting stuff, so we will refer them to Gugulethu MOU, that's where all the screening gets done. So, we take care of just the normal without any risk antenatal patients".* **HCP 1.**

ii. Process of GDM screening and referring women diagnosed with GDM

The process of diabetes screening during pregnancy based on current guidelines in the local facilities in Cape Town is summarized in **Figure 12**.



Process of diabetes screening during pregnancy in Cape Town

Referral starts from BANC, to Midwife and Obstetrics Units (MOU), to secondary level specialised maternity hospitals in case of impaired glucose tolerance (IGT - in which plasma glucose levels were above normal but below those defined as diabetes) (Alberti & Zimmet, 1998; American Diabetes Association, 2018), to tertiary hospitals (GSH or Tygerberg hospital depending on jurisdiction of the MOU) for cases meeting local criteria for GDM.

"the procedure for screening, we've got a list of indications for doing Glucose Tolerance Test (GTT): family history of diabetes from her mother, her father or her siblings, BMI of 35 and above, history of big babies, persistent Glycosuria; for three consecutive visits. She has to come in the morning, fasting, her last meal the previous night around 10 o'clock. So, when she comes, we do the prick. If the sugar is 7 and above, we don't continue, but if it is less than 7, we take the fasting blood and we give her 75 grams of glucose, and we take the second blood after two hours. So, they come after one week for the results. If it's an IGT, we refer to Mowbray not Groote Schuur, but if it's GDM, then we refer to Groote Schuur". **HCP2.**

3. Barriers to GDM screening in PHC

"Well, the current practice is to try and identify them from women who attend antenatal care. That obviously means, the people who don't attend, we wouldn't pick it up…" **KI 2.**

Respondents identified several barriers to screening. First of all, socio-economic factors impede the timely access of many women to BANC and to GDM screening. Secondly, some may be diagnosed late when symptoms or consequences of GDM are already present; this becomes a reason for immediate referral to the hospital for follow-up. Thirdly, there is no way to identify and screen some women as they do not attend ANC at the clinics at all. Fourthly, as many women, like other patients, do not know or suspect that they might have diabetes, they do not proactively seek any screening during their pregnancy or clinic visits, which is why the provincial guidelines mandate that screening be initiated by the provider. Finally, lack of time due to work overload, shortage or ineffective utilisation of key equipment and other resources for GDM screening, and poor communication between facilities, were also included among other documented health system issues preventing consistent GDM screening in PHC.

II. Effective antenatal referral procedures but lack of follow-up after delivery

Themes in this category were appraised in the light of BCW's intervention functions or middle layer (Michie et al., 2011), regarding services offered to women diagnosed with GDM while attending a diabetic clinic at hospital for follow-up and delivery.

i. On-site integrated hospital services

Upon arrival at the respective hospital to which they are referred, women with GDM benefit from hospital level integrated care under the coordination of the diabetic clinic of the maternity department. Integrated services at referral hospitals include regular blood glucose monitoring, investigations for other health problems, medical care for GDM and other health problems beyond GDM, as well as diet and lifestyle change interventions.

> *"We all have our specialities, so the registrar that would be looking after the patient is somebody that is rotated through the whole block, so they've seen cardiac, they've seen eclamptic patients, they've done diabetes; but if there is a specific problem, then we are in the fortunate position where we have the resources where we can get infectious disease people out, instead of struggling with that, or we can get the endocrinologist out, and say listen, we have now hit a wall, how do we go forward, but that is within our setting"*. **HCP 3.**

Counselling sessions regarding lifestyle changes to deal with diabetes and its devastating consequences were said to be routinely scheduled at the diabetic clinic of GSH's obstetrics unit, but the implementation of these sessions was problematic: the crowded and busy conditions in the clinic, observed by the researchers and reported by respondents, was not conducive to effective group sessions and made individual counselling sessions almost impossible.

ii. Socio-economic barriers to challenges to healthy antenatal and postnatal initiatives

Women diagnosed with GDM at primary care and referred to tertiary hospital (GSH) (N=35) discussed barriers they faced in their long road to care from families/communities, local facilities and

up to referral hospitals, with many visits both during and after pregnancy. For many women the transport costs to attend care and the extra cost of healthy food contributed to depleting their already constrained economic resource.

"…The diet food is actually very expensive compared to junk food. So, when I had to change, it was actually very hard, because I now have to spend much on my budget when it comes to my groceries, because of my diet and other food stuff for my boyfriend who is not diabetic". **Participant 3 in FGD 4.**

iii. Confusion or little knowledge about GDM and lifestyle changes

Apart from the socio-economic issues that women have to deal with in their daily lives, many have shown confusion or limited understanding of what GDM is and the behavioural/lifestyle changes required to manage GDM and prevent or delay future T2DM for themselves and long-term metabolic problems for their babies. Some women could not explain clearly what GDM was or why a particular treatment was prescribed to them while others struggled to name GDM consequences for themselves and their babies.

"I also think GDM is when you are diabetic, they find out when you are pregnant, and then it's not going to be seen after birth, but I was thinking like that before, but I have never actually known…that's an impression, but I'm just assuming, I'm not sure". **Participant 1 in FGD 4.**

Women's understanding about GDM as discussed in the FGDs was compared to the results from exit interview questionnaires. Despite the time they spent throughout the diagnosis and referral process at lower levels of health care, and after attending the diabetic clinic at GSH for their GDM care many times, only 43% reported having received advice about all four recommended actions (improve diet, reduce sugar intake, physical exercise and regularly take prescribed medication) to improve their GDM and prevent T2DM. However, women reported being satisfied with the information they had received, despite this lack of alignment with recommendations. Only half (51%)

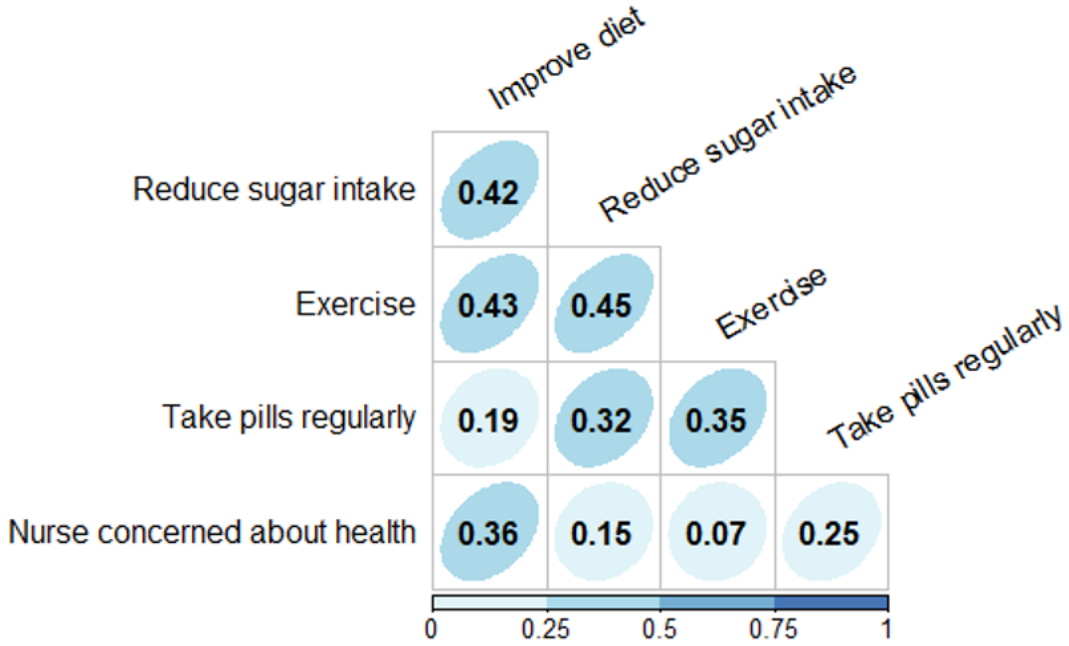
of the respondents were aware of the importance of reducing sugar intake, while 69% recalled being advised to exercise, 86% to improve their diet and 83% to take pills regularly. The contrast of improving diet (86%) and reducing sugar intake (51%) suggests incomplete and/or ineffective lifestyle change education. **Table 15** shows that, in contrast to the barriers reported by respondents regarding selective and late screening practices at primary care level, 94% kept their appointments at the referral hospital (GSH), 49% had already been tested in the morning before the FGDs were conducted, and 77% felt that nurses were interested or concerned about their health. Women who felt that nurses have empathy and time for them easily engaged with the nurses to ask about their GDM and general health, trusting their advice to change their lifestyle during pregnancy and postpartum to prevent or delay T2DM onset. The multiple correlations between the advice that women with GDM received and their view on whether nurses were interested or concerned about their health, generally established a negligible, weak or moderate association as none reached 0.5. Taking pills regularly was, for example, supposed to work well in stabilising GDM and preparing women for postpartum initiatives to prevent T2DM when combined with diet improvement but it showed a weak correlation of 0.19, and this trend appears among all other advice.

***Table 15*: Descriptive statistics**

Factor	Level	Value
N (sample size)		35
Age (in years)	mean (SD)	33.7 (4.6)
	median (IQR)	34.0 (30.0, 37.0)
How long have you been attending diabetic clinic for your GDM care? (in days)	mean (SD)	106.9 (52.3)
	median (IQR)	120.0 (90.0, 120.0)
OGTT or blood glucose measured today?	Yes	17 (49%)
	No	9 (26%)
	Missing value	9 (26%)
Receive a SMS or a phone call to come to clinic?	Yes	1 (3%)
	No	33 (94%)
	Missing value	1 (3%)
Advices to reduce sugar intake?	Yes	18 (51%)
	No	17 (49%)
Advices to exercise?	Yes	24 (69%)
	No	11 (31%)
Advices to take my pills regularly?	Yes	29 (83%)
	No	6 (17%)
Advices to improve my diet?	Yes	30 (86%)
	No	5 (14%)
Number of advices received	One	8 (23%)
	Two	3 (9%)
	Three	9 (26%)
	Four	15 (43%)
The nurse was interested/concerned about your health?	No concerned	2 (6%)
	Somewhat concerned	6 (17%)
	Appropriately concerned	27 (77%)
Is there any medication that the nurse should have given you, but it is out of stock?	Yes	4 (11%)
	No	30 (86%)
	Missing value	1 (3%)
When is your return date?	1 Week	15 (43%)
	2 Weeks	12 (34%)
	1 Month	5 (14%)
	2 Months	1 (3%)
	Other	2 (6%)

IQR: interquartile range; **SD:** Standard deviation

The multiple correlations between the advice that women with GDM received and their view on whether nurses were interested or concerned about their health, generally established a negligible, weak or moderate association as none reached 0.5. (**Figure 13)**.



*All variables have two categories "Yes" vs. "No", except variable Nurse concerned about health whose two categories are "No concerned/Somewhat concerned" vs. "Appropriately concerned",

Multiple correlation between advices received by patients and their views on nurses' interest in their health*

iv. Poor communication and non-existent plans for postnatal follow-up

Even though integrated services including ANC and GDM were generally appreciated at referral hospitals, there was no follow-up for women and their babies after delivery. When women and their babies were back in their community after delivery, it was reported that they were seen at their local facilities exclusively for babies' check-up and immunisation and that women did not have access to any specific programme that provided follow-up. Upon discharge, the details about their health were written up in their antenatal record (Road to Health booklet), but according to women and HCPs, the hospital does not consistently give or send a referral letter, nor call or communicate in other ways with local clinics regarding postnatal care. This is despite the guidelines indicating that a referral letter recommending a 6 week postpartum OGTT and follow up at a local clinic should always be handed to women at discharge. Both KIs and HCPs reported that, once back at the clinics, the

women who did receive follow-up letters and medication from hospital tend to focus on their babies and forget or ignore to look after their own health. The few women who had approached the nurses at the primary care clinic regarding their postnatal check-up reported that they had not been successful in getting screened for diabetes.

> *"The maternity sisters do not communicate with the local clinic sister for follow-up on these clients about medication after delivery and then we don't know. So, maybe they got letters from hospital that you must follow up at this clinic to get your medication that is going to control you but mothers don't follow up, as I have noted, they don't follow up, they only focus on the baby after delivery,..... But if there is a problem, then the doctor prescribes when discharging them but they will never mention it to us at the clinic…And then, if they are with the person who didn't see them when pregnant, you won't know if the client had a problem with the glucose".* **HCP 3.**

III. IINDIAGO, an intervention with potential to bridge the gaps in postnatal follow-up

The BCW's sources of behaviour or inner layer (Michie et al., 2011) was used to map and interpret failures in postnatal follow-up for mothers with previous GDM and their babies, a problem identified by all KI and HCPs approached for this research. This reported gap in postnatal care for women with GDM was also seen as an implementation vacuum that the newly approved WC postnatal policy aimed to solve (Provincial Government of the Western Cape, 2016) but respondents considered that the policy fell short in terms of follow-up for women who had GDM. The ongoing IINDIAGO study that aims to integrate post-partum follow up for women post-GDM into PHC was presented to respondents at the end of the interview, in order to explore the perceived relevance and feasibility of such an intervention. The idea was welcomed and seen as feasible by all respondents including women.

Well, the issue about IINDIAGO is that you are actually addressing the exact problem. I think it's feasible, given the right funding. I have no doubt, you know, things like weight reduction and proper dietary counselling etc. can prevent the development of Type 2. **KI 3.**

IV. Appreciation of CHWs involvement in community based T2DM prevention intervention

The BCW's sources of behaviour or inner layer (Michie et al., 2011) was applied to help understand the changes that need to take place in the community in order to prevent or delay T2DM. Since the overwhelmed clinics do not intervene much, if at all, in T2DM prevention efforts, CHWs were considered to be the best-placed health workers to successfully contribute to implementation of activities in the family and community. CHWs in South Africa have greatly assisted (Clarke et al., 2008; Uwimana et al., 2012a) in other community-based interventions to improve health, principally in the areas of maternal and child health and HIV care. Existing policy also gives them a role to play in non-communicable diseases (NCDs) (Tsolekile et al., 2018). All participants (KIs, HCPs, Women) commended CHWs and suggested that they get involved in T2DM prevention once trained and working under clinic supervision. KIs suggested that their involvement could bring some clinical services like NCDs screening, counselling, health education, and implementation of specific preventive measures to the patients and family members within communities.

Reflecting on their experiences with HIV and tuberculosis, the CHWs who participated in this study responded positively to the idea of getting involved in such innovative and integrated approach towards T2DM prevention for women who had GDM. CHWs explained how their visits to the families within community are more inclusive and go beyond the single patient they are scheduled to visit, covering a range of health problems of all present family members. Equipped with their household charts, they reported that they conduct a complete surveillance of the family and refer family members with particular health problems to the right health facility for further diagnosis and

care. CHWs emphasised their visiting and educating roles would align well with the tasks they would handle in T2DM prevention efforts. These positive comments were made despite reporting challenges they face in their daily activities like limited training; low and irregular payments; very busy clinics that sometimes fail to follow up the patients they refer to them. CHWs expressed commitment to their cause and engagement in their mission within the community.

> *"Me, I love the job that I am doing because I don't have a problem with people, and I can convince them but if someone is not doing well, I report her to the supervisor who will then intervene".* **CHW participant 3, FGD 1.**

Discussion

In the face of increasing GDM prevalence in Africa (Chivese et al., 2019) and despite calls for universal screening, the guidelines in most countries recommend selective screening to diagnose and manage GDM and its sequelae (Ferrara, 2007; Teh et al., 2011). Risk factor-based screening has been the main approach adopted in South Africa. Even though current GDM screening guidelines in South Africa now meet international standards, respecting the value thresholds as recently discussed by Adam S. and Rheeder (Adam & Rheeder, 2017b), they are still ineffectively applied.

Documented challenges in GDM testing at primary care level were a sign but also a cause of poor screening practice. Universal screening of GDM cannot be successful if concurrent barriers are not addressed. These challenges to GDM screening in PHC include but are not limited to shortages of well-trained HCPs and ill-equipped clinics to test and deal with NCDs based on the available guidelines (Bhavadharini et al., 2016). Multiple barriers impeding proper GDM screening and follow up post-GDM have been documented in other studies and this study's findings corroborate many, including: weaknesses at different health system levels; poor understanding of postpartum GDM risks of T2DM development for both women and their babies; and various patient, community and health

service level barriers for women when they are referred back into PHC for follow-up after delivery (Bennett et al., 2011a; Nielsen et al., 2012, 2014). Our findings further suggest that the expertise and knowledge required of both nurses and women are insufficient to make a risk factor-based approach effective in South Africa.

It has never been easy for women to navigate health systems to access obstetric care in sub-Saharan Africa due to multiple individual and family socio-economic barriers such as low household income, illiteracy, lack of transport means and its cost, and cultural beliefs/practices, among others as reported in recent systematic reviews (Geleto et al., 2018; Kyei-Nimakoh et al., 2017). Despite these issues, women receive integrated and highly appreciated antenatal and perinatal care at the tertiary level. Women with GDM who participated in this study confirmed this. However, women who strived to protect their babies from the adverse effects of GDM feel relieved after delivery and this is reinforced after their glucose levels return to the normal range. Additionally, the lack of structured postnatal care for these women does not foster the implementation of T2DM prevention initiatives.

Our findings suggest that this could be at least partially mitigated with clear and consistent discussions about GDM and its long-term consequences for both women and their babies throughout ANC, perinatal and post-partum services. Health education may encourage these women to follow-up with postnatal testing and lifestyle change measures at the clinic and in the community. Referral hospitals must first communicate with the local facilities regarding follow-up for these women and, in return, the clinics need to continue surveillance and initiate integrated postnatal behavioural change interventions for T2DM prevention. Such interventions would be useful for other NCDs and broader health care needs beyond the immediate aim of dealing with IGT, T2DM or diabetes related health issues but to achieve this, nurses need appropriate training and more resources in the facilities.

The IINDIAGO project is exploring whether such postnatal follow-up could be linked to the babies' immunisation, which normally starts soon after delivery and discharge from hospital. HCPs showed willingness to add this programme to their workload after receiving proper guidelines and adequate training on their side. Women also expressed support for this kind of intervention after discussing its dual benefits, for them and for their babies. Engaging policy makers to change guidelines on the one hand and appropriately train frontline healthcare workers including CHWs on the other has succeeded in other trials and interventions in PHC for the same populations. Here, Prevention of Mother-to-Child Transmission of HIV (PMTCT) which continues from ANC into postnatal care with lifelong services within the facility and in the community (Fairall et al., 2016, 2018; Fairall & Bateman, 2017) could serve as a case study.

Conclusion

Many women are diagnosed late in pregnancy and postnatal follow-up is almost non-existent. An innovative strategy of integrating universal GDM screening in local health facilities with postnatal follow-up of these women and their babies in the community based PHC services is considered desirable and feasible. Women, health workers, and experts added that this integration would work well if the resource and training constraints facing PHC as well as socio-economic barriers to women are addressed.

Declarations

Ethics approval and consent to participate

The study was approved by the Human Research Ethics Committee at the Faculty of Health Sciences, University of Cape Town (HREC REF: 946/2014) and the Centre de Recherche du Centre Hospitalier de l'Université de Montréal (2018-6690, 17.044 - ID). Written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analysed during the current study are not publicly available to preserve participant anonymity.

Competing interests

JCM, PREB, HT, LJW, SN, KM, NL and CZ declare no competing interests.

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Authors' contributions

JCM, CZ, and HT designed the study. JCM conducted interviews, data analysis and wrote the first manuscript under the supervision of CZ and HT. PREB, LM, LJW, SN, KM, NL, HT and CZ critically revised versions of the manuscript. All authors read and approved the final manuscript for publication.

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Additional files

File 1 - Mixed Methods Appraisal Tool (MMAT), version 2018

Integrating type 2 diabetes mellitus prevention after gestational diabetes into community based PHC services: health care providers' experience and women's knowledge in South Africa – Mixed methods study

Mixed Methods Appraisal Tool (MMAT), version 2018

Category of study designs	**Methodological quality criteria**	**Responses**			
		Yes	No	Can't tell	Comments
Screening questions (for all types)	S1. Are there clear research questions?	√			
	S2. Do the collected data allow to address the research questions?	√			
	Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative	1.1. Is the qualitative approach appropriate to answer the research question?	√			
	1.2. Are the qualitative data collection methods adequate to address the research question?	√			
	1.3. Are the findings adequately derived from the data?	√			
	1.4. Is the interpretation of results sufficiently substantiated by data?	√			
	1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?	√			
2. Quantitative randomized controlled trials	2.1. Is randomization appropriately performed?				
	2.2. Are the groups comparable at baseline?				
	2.3. Are there complete outcome data?				
	2.4. Are outcome assessors blinded to the intervention provided?				
	2.5 Did the participants adhere to the assigned intervention?				
3. Quantitative non-randomized	3.1. Are the participants representative of the target population?				
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?				
	3.3. Are there complete outcome data?				
	3.4. Are the confounders accounted for in the design and analysis?				

	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?				
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the research question?	√			
	4.2. Is the sample representative of the target population?	√			
	4.3. Are the measurements appropriate?	√			
	4.4. Is the risk of nonresponse bias low?	-			
	4.5. Is the statistical analysis appropriate to answer the research question?	√			
5. Mixed methods	5.1. Is there an adequate rationale for using a mixed methods design to address the research question?	√			
	5.2. Are the different components of the study effectively integrated to answer the research question?	√			
	5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?	√			
	5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?	√			
	5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?	√			

File 2. Interview/FGDs guides for key informants, clinic managers/nurses, CHWs and women and questionnaire for exit interview with women

Integrating type 2 diabetes mellitus prevention after gestational diabetes into community based PHC services: health care providers' experience and women's knowledge in South Africa – Mixed methods study

Interview Guide for key informants and clinic managers/nurses

Thank you for agreeing to be interviewed today. The information you share with us today is completely confidential. You will be assigned (or you can give us one!) a pseudonym and your responses will not have any identifying information. Your responses will only be shared with members of the study team and will be compiled with other responses from various participants. I'm going to ask you questions about your experience as manager/nurse of/at this clinic regarding GDM screening and management at PHC level.

Main question: Can you please share with me what happens regarding GMD screening, management and follow-up of GDM women before and after delivery before you heard this intervention?

Prompt:

- Tell us about how the clinic has been handling women who are diagnosed with GDM. (How do you identify them? What do you do to identify them & look after them in ANC and in post-partum?)
- How is postnatal care managed and what works well and not so well?
- Let's discuss each of those activities in detail.... (also ask to see card system how and how it is working)
- Can you tell me about particular successes you have had in the last year or last few months?
- Can you tell me about particular problems or challenges you have had?

- Tell me about how the clinic has been functioning this last year (regarding GDM management).
    - Major / notable events;
    - Shortage of nurses/patient load / appointments;
    - Medicine/ equipment/ other CHWs;
    - Atmosphere between staff, between staff and women.

To prompt with the following if topics don't come in conversation:

- Practical issues in screening GDM
- Follow up after diagnosis
- Post-natal care – for women and for babies
- What if patients have multiple problems – ANC or PNC plus other conditions (chronic, like T2D, HIV or acute like malaria, TB, diarrhea)
- Performance of nurses and other staff members;
- Nurses taking initiative; responding to problems;
- Engagement between nurses and CHWs
- Engagement between CHWs and women.

Finally, is there anyone here at this clinic in particular you think we should talk to next or any important documents or guidelines that we should consult?

<u>Guide for FGDs with women diagnosed with GDM</u>

Thank you for agreeing to be part of this group discussion today. The information you share with us today is completely confidential. You will be assigned (or you can give us one!) a pseudonym and your responses will not have any identifying information. Your responses will only be shared with members of the study team and will be compiled with other responses from various participants.

The focus group discussion will be guided to cover the following topics:

- Understanding of GDM and T2D
- What are the problems women with GDM do face when getting to the clinic or hospital?
- Experience of using clinics – how well does it work to have some activities integrated into the well-baby clinics; what about other health problems (probe: "one stop shop" – is it desirable, feasible? Integration of care vs distinct facilities or days for different problems or people)
- What are the other health problems women with GDM do face/report at the clinic (e.g. HIV, TB, Hypertension, etc.?)
- How do you feel about changing your diet and starting taking a walk or other physical activities? What are challenges you see in doing so?
- Is there anything you would like to see change in the way your clinic looking after you for your GDM and other health needs and for your kids at WBC (if any)?
- Is there anything else you want to discuss?

Guide for FGDs with community health workers

Thank you for agreeing to be interviewed today. The information you share with us today is completely confidential. You will be assigned (or you can give us one!) a pseudonym and your responses will not have any identifying information. Your responses will only be shared with members of the study team and will be compiled with other responses from various participants.

- What activities do you normally do?
- What type patients do you normally see?
- What services do you provide?
- For patients such as women with HIV and GDM/GDM, where it is important to visit the clinic on regular basis and take medication or for counseling sessions.....What are the problems that patients do face in doing that?....What could be helpful for them?

- How long is the distance do you manage to cover in a day when you are in your CHW activities? Walking / taxi?
- Who do you report to? Please describe the NGO, if any?
- How do you work with the manager and nurses in the clinic? Do you go at the clinic every working day? Do you daily/periodically talk to the nurses about patients? Please explain how this works
- Do you ever visit people just to remind them to come to the clinic?
- Do you deliver medicines/messages from the clinic to patients?
- What challenges do you face in your work?
- Is there anything else to share?

Questionnaire for women with previous GDM exit interviews – (quantifiable answers)

GSH diabetic clinic

Date:

Fieldworker:

1) Name of the participant:
2) Age:
3) Local clinic:
4) How long have you been attending diabetic clinic for your GDM care?
5) Was your OGTT or Blood glucose measured today? (we will know this from clinic link?)
6) Did you receive an SMS or a phone call to come to the clinic?
7) If yes, was the SMS helpful in reminding you to come to the clinic?
8) What advices were you given? (multiple answers)
    a) Reduce sugar intake
    b) To exercise

c) To take my pills regularly

d) To improve my diet

9) Did you feel the nurse was interested / concerned about your health? (single answer)

a) Not concerned

b) Somewhat concerned;

c) Appropriately concerned;

10) Is there any medication that the nurse should have given you, but it is out of stock? Yes / No

11) When is your return date (none; 1 day, 1 week, 1 month, 2 months, 3 months)

12) Is there anything else you would like to say?

CHAPTER 6: A SYSTEMATIC REVIEW - INTEGRATING DM WITHIN INTERVENTIONS FOR MULTI-MORBIDITIES

Paper 5 – Integrated T2DM and GDM in multimorbidity: SR protocol

Integrated management of type 2 diabetes and gestational diabetes within multi-morbidity conditions in Africa: A systematic review protocol

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Abstract

Introduction: Multi-morbidity, defined as the co-existence of more than one chronic condition in one person, has been increasing due to comorbid non-communicable and infectious chronic diseases (CNCICDs). Type 2 diabetes mellitus (T2DM) and gestational diabetes mellitus (GDM) incidences within the CNCICDs conditions are increasing and overwhelming already weak and under-resourced health care systems in Africa. There is then an urgent need for the integrated management of CNCICDs. We aim to review the integrated management of T2DM and GDM within multi-morbidity conditions in Africa.

Methods: Studies that have assessed the integrated management of T2DM and GDM within multi-morbidity conditions in Africa will be considered based on the PICO method: Population (adult diagnosed with T2DM and GDM, who also have other diseases, non-communicable diseases (NCDs) and infectious, in public primary and secondary health care facilities in Africa); Intervention (integrated management of T2DM and GDM, also suffering from other diseases in Africa), Comparator (Unintegrated management of T2DM and GDM in Africa) and Outcomes (integrated management of T2DM and GDM in Africa). The following databases Cochrane Library, MEDLINE, PubMed and SCOPUS, the WHO International Clinical Trials Registry Platform, among others will be searched. Two reviewers (JCM, MW) will independently screen, select eligible studies, and extract data. Discrepancies will be resolved by consensus or by a discussion with the third author (AR). Quality of included studies will be assessed using both the newly developed tool, "the Cochrane Collaboration Risk of Bias Tool (CCRBT)" and "Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I)". A narrative synthesis of extracted data and meta-analysis, if necessary will be conducted and then reported according to the preferred reporting items for systematic review and meta-analysis (PRISMA).

Ethics consideration and dissemination: By only using the published data, there is no ethics approval required for this study. This systematic review will be included in JCM's PhD thesis and its findings will also be disseminated through peer-reviewed publication and conference presentation.

Systematic review registration: PROSPERO CRD42016046630

Keywords: Type 2 diabetes, gestational diabetes, multi-morbidity, integrated care, Africa.

Strengths and limitations of this study

Substantial search strategy to identify relevant studies will be adopted, a large number of online databases will be searched, public health websites will be manually searched and credible experts will be consulted. Study results will be assessed and reported in accordance with relevant guidelines for quality assessment of systematic reviews. Scarcity of eligible studies for selection and inclusion is expected. Reviewers will not be blinded during data extraction and quality assessment stages.

Introduction

The World Health Organisation (WHO) global report in 2016 estimated that 415-422 million adults worldwide had diabetes in 2014-2015 and that diabetes caused 5 million deaths in 2015, with an estimated 673 billion USA dollars of total global health expenditure in diabetes care (Ogurtsova et al., 2017; WHO, 2016b). In the Africa region there were an estimated 14.2 million people with diabetes in 2015 increasing to 34.2 million in 2040 (Day, 2016; WHO, 2016b). With the expected rural depopulation causing increased exposure to urban environments and diabetogenic lifestyles such as inactivity, obesity, depression, smoking among others, diabetes cases are expected to increase by 54% to 642 million worldwide by 2040 (Aguiree et al., 2013; Dalal et al., 2011; Day, 2016).

Globally, the burden of non-communicable diseases (NCDs) is rising. Low and middle-income countries (LMICs) are most affected by changes in patterns of population age distributions, fertility, life expectancy, morbidity and mortality, known as the "epidemiological transition" (McKeown, 2009). In Africa, especially in sub-Saharan Africa, this is occurring against a background of continuing infectious disease epidemics (i.e., HIV and tuberculosis), increasingly becoming a coinfection epidemic that requires an integrated response (Howard & El-Sadr, 2010). Consequently, multi-morbidity defined as the co-existence of more than one chronic condition in one person, has been increasing due to comorbid non-communicable and infectious chronic diseases (CNCICDs) (McKeown, 2009). Given the risk factors and complex care needs of multi-morbidity, there is a need to integrate healthcare systems, particularly between primary and secondary health care.

The current approaches to surveillance, prevention and treatment of CNCICDs appear to be insufficient to provide for the long-term health needs of this convergence especially in the context of human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) era, antiretroviral therapy (ART) linked concomitant metabolic complications and HIV/AIDS allied opportunistic infectious diseases (Levitt et al., 2011). To address this, the WHO developed the

Innovative Care for Chronic Conditions (ICCC) Framework to provide a healthcare systems roadmap that would meet the increasing needs of chronic disease care within this growing multi-morbidity context. This framework incorporates community, patient, healthcare and policy environment perspectives, and has been adopted by different healthcare systems. However, it does not clearly include the infectious diseases within the context of multi-morbidity (Oni et al., 2014) and it is then necessary to reorganise health care services and systems to tackle this growing public health problem (Levitt et al., 2011; Oni et al., 2014).

The 2016 global diabetes report (WHO, 2016b) emphasizes the need to reach better outcomes of diabetes management through an integrated management, especially with NCDs such as cardiovascular diseases as well as tuberculosis and/or HIV/AIDS. This is especially important where the prevalence of these diseases is high. Despite calls for a shift in approach from disease-specific interventions to the integrated delivery model (Fleury, 2006), health care systems in Africa are weak and under-resourced to provide care for the increasing number of patients with multi-morbidities including diabetes, especially compared to high-income settings (Iwelunmor et al., 2016).

Two types of diabetes commonly identified during adulthood are type 2 diabetes (T2DM), that is insulin resistance linked diabetes, and gestational diabetes (GDM), known as a glucose intolerance with onset or first recognition during pregnancy. T2DM can be prevented or delayed for women with previous GDM (Alberti & Zimmet, 1998; Buchanan et al., 2007; Ruchat & Mottola, 2013; Tuomilehto et al., 2001). The established connection between T2DM and GDM (Levitt et al., 2011) does not determine how GMD is managed. It can either be managed alone in a diabetic clinic or preferably within integrated care at ANC and postnatal clinics, which is a right approach for increasing multi-morbidity (Fealy et al., 2017; Struckmann et al., 2018).

The treatment pathway for women with GDM is through accessing antenatal care (ANC) at the nearest health facility for their pregnancy follow-up and delivery. In contrast, only a small

proportion of women with recent GDM return for postpartum oral glucose tolerance test, assessment and management (Ben-Haroush et al., 2004; Bennett et al., 2011b; Hartling et al., 2012, 2013; Nicklas et al., 2011). The main challenge is that GDM women must navigate fragmented health systems for their care and care of their babies and this situation supports calls for integrated health systems and services that are easy for patients to navigate (Kugel, 2001).

Disease-specific or vertical programmes can be used to manage specific diseases and health problems while strengthening fragmented health systems in Africa (Van Damme et al., 2011). However, disease-specific or stand-alone interventions are criticized for not promoting equity and sustainability of their outcomes (Atun et al., 2008), and therefore integrated programmes to address various NCDs such diabetes in comorbid conditions are recommended (Haregu et al., 2015; Levitt et al., 2011).

Integrated care is "*combining parts so that they work to form a whole (i.e., integration) in order to optimise care and treatment to people where fragmentations in care have led to a negative impact on their care experiences and outcomes*" (Goodwin, 2013, p. 1). It describes a range of organizational arrangements with variable nature and intensity and comprises two main concepts: a) an organizational structure focused on economic benefits (cost-effectiveness), or b) a way of organizing service delivery (Shigayeva et al., 2010a; Tudor Car et al., 2011). We conceptualized integration based on dynamic interactions in which formal governance is arranged, responsibilities are shared and resources are pooled (Messeri et al., 2003; Shigayeva et al., 2010a), regardless of many other existing integration level models such integrated care typologies used in a recent systematic review that studied the integration of cardiovascular diseases, hypertension and diabetes with HIV services (Haldane et al., 2017).

The analysis of interactions in health systems enables us to understand the levels of integration. They include partial integration initiatives ranging from (1) the linkage or unstructured

interactions; (2) the coordination with a committee to oversee their goal-oriented works but keeping the separated structures; and, (3) full integration in which two programmes are merged in their structures (funds, human resources, informational system) and functional elements (strategic planning, resources allocation, interventions delivery) (Atun et al., 2010b; Shigayeva et al., 2010a). Integrated health care systems have advantages such as being associated with more accessibility of care, improved quality and safety of care, health care cost reductions and economic benefits for both providers and families (Coddington et al., 1994; Henke, 2006). This integrated management approach including partial and full integration initiatives, will play a key in responding and providing the appropriate health care services to the increasing cases of multiple conditions (Haldane et al., 2017).

We aim to provide a systematic review on integrated management of T2DM and GDM within the CNCICDs conditions in Africa. The ultimate goal is to describe the emerging practices and lessons learned from integrated management of GDM and T2DM within comorbidity conditions in Africa and the different research gaps to GDM and T2DM integration within management of other non-communicable and infectious chronic diseases. This systematic review aims to answer the following research questions: 1) What are the existing integrated interventions and services delivery models for managing T2DM including GDM within multi-morbidity conditions in Africa? and, 2) What are the successes and challenges of the existing integrated management of T2DM including GDM within multi-morbidity conditions?

Methods

The Cochrane Handbook and systematic review study protocol (Higgins & Altman, 2008) published by the Cochrane Collaboration Methods Groups that provides the methodological framework in designing and conducting this systematic review to enable critical appraisal and replication. We did register this protocol online on PROSPERO, the International prospective register

of systematic reviews, found at (https://www.crd.york.ac.uk/prospero/, registration no. CRD42016046630).

Study design

This systematic review will only include studies of good quality based on the developed inclusion and exclusion criteria.

Patient and public involvement

There will be no patient and/or public involvement in this study.

Search strategy for the identification of relevant studies

Our search strategy will use the controlled terms (MeSH: Medical subject heading) and free texts. The following databases will be searched: Cochrane Library, MEDLINE, PubMed and SCOPUS. Other database resources such as the WHO International Clinical Trials Registry Platform, Clinicaltrials.gov, Pan African Clinical Trials Registry (PACTR) and HINARI (Health InterNetwork Access to Research Initiative) will also be searched. Additional search will be conducted in Google scholar.

Our research will focus on articles published and gray literature in English and French languages. Upon the extraction of interesting articles in other languages without any English or French abstracts, we will then include them or get assisted by a researcher who is fluent in those languages. Since there were not many articles regarding our review topic in our preliminary search, there will be no starting time limits in our search but our focus will be limited to all fifty-four African countries. However, the search will be conducted from the start of each database until the 31st December to include as many relevant studies as possible. Search Strategy will be validated with the assistance of a Librarian.

Our search for articles will be based on the following Population, Intervention, Comparator and Outcome (PICO) method (Counsell, 1997) describing the population, intervention, comparator and outcome (see **the table 16** below).

Table 16: PICO description table

Population	**Intervention**	**Comparator**	**Outcomes**
Adults diagnosed with T2DM and women diagnosed with GDM, who have other diseases in public primary and secondary health care facilities in Africa	Partial or full Integrated management of T2DM in adults and GDM in pregnant women who have other diseases in Africa	Unintegrated management of T2DM and GDM in public primary and secondary healthcare facilities in Africa.	Utilisation and effectiveness of Integrated management of T2DM and GDM in public primary and secondary healthcare facilities within multi-morbidity conditions in Africa

Criteria for considering studies for this review

Studies that have assessed the integrated management of T2DM and GDM within multi-morbidity conditions in Africa will be considered, including randomised controlled trials (RCTs), non-RCTs, quasi-randomised controlled trials (QCTs) and observational studies.

Studies will be all kinds of interventions with different targeted participants from all ethnicities, genders, socioeconomic, educational backgrounds and in all countries in Africa who were diagnosed with T2DM and GDM as one disease of the multi-morbidity using standard diagnostic criteria will be eligible for inclusion. The patients who had T2DM including GDM before and after the occurrence of other diseases and the interventions to handle both diseases will be included in this review. Interventions carried out or facilitated by healthcare providers including community health workers

in public health facilities will also be included, providing that the focus of the intervention is to treat diseases in which one is diabetes, specifically T2DM and GDM. Studies that separately evaluated interventions or assessing vertical programmes of T2DM, GDM and other diseases, will be excluded.

Reference lists

Manual-search by (MJC and MW) lists of references of included studies, tables of contents of relevant journals and conference abstracts for the relevant material will be conducted. A grey literature search strategy by (JCM and MW) will be developed to conduct web-based searches to obtain key unpublished sources in our stated search languages.

Selection of studies

Full copies of articles identified by the search, and considered to meet the inclusion criteria, based on the title and abstract will be obtained for data synthesis. Initially, studies will be screened using predefined inclusion and exclusion criteria. Two reviewers (JCM and MW) will apply the criteria independently to the results of the searches, based first on titles and abstracts only. At least two reviewers (JCM and MW) will proceed independently with the articles selection at the same time based on our described inclusion criteria into two steps: 1) examining the title and abstract, and then, 2) reviewing the full texts. Study authors of eligible articles for which the full text copies are not freely accessible will be contacted to obtain their access and additional information about them will also be requested if required. The inclusion of an article will be made by consensus. In case the two (JCM and MW) do not reach consensus, the decision from a third person (AR) will be required and reasons for exclusion will be recorded. All studies which initially appear to meet inclusion criteria but on closer inspection do not meet the inclusion criteria will also be detailed in the table of "characteristics of excluded studies". The preferred reporting items for systematic review and meta-analysis (PRISMA) flow chart will be produced to facilitate transparency of the process (see Figure 1 in supplementary files)

Types of outcome measures

Studies reporting at least one of the following outcomes will be included:

Primary outcomes

Two primary outcomes will be considered: 1) Integrated care outcome and 2) cost-effectiveness outcome. For the integrated care outcome, the focus will be on patients screened and/or treated for both T2DM and GDM in the course of treatment of other major diseases (e.g. HIV, tuberculosis, cardiovascular diseases, etc.) in what is known as multi-morbidity conditions. For cost-effectiveness outcome, the focus will be on approach to integrated diagnosis and treatment of T2DM and GDM within comorbidity conditions, which simplifies the workload and saves means of depleted health systems in Africa and helps the patients to do not navigate different levels of health systems for their comorbidities that positively impacts the family economies.

Secondary outcomes

We will also consider early diagnosis through the integrated management of other diseases as this improves clinical outcomes and strengthens health systems for the long-term results of the integrated management of T2DM diabetes including GDM within comorbidity conditions.

Quality assessment

The quality of articles selected will be assessed using the newly developed tool, "the Cochrane Collaboration Risk of Bias Tool (CCRBT)" and "Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I)" (Higgins et al., 2011; Sterne et al., 2016). The CCRBT is an appropriate quality assessment tool for RCTs and QCTs (Moher et al., 2009; Werfalli et al., 2014). Since the quick preliminary search shows that there are few RCTs and QCTs to be included in this study, this single tool will not be enough and the ROBINS-I will be used to assess the quality of non-RCTs and observational studies (Sterne et al., 2016). These quality assessment tools encompass all aspects needed to appraise the quality of any studies that will be selected for inclusion. Two reviewers (JCM

and MW) will independently assess the risk of bias in the included studies and cross-checked by a third reviewer (AR).

The following individual quality elements recommended in the modified Cochrane Collaboration tool to assess the risk of bias for RCTs (high, low, or unclear) as a judgment for individual elements from six domains (selection, performance, attrition, reporting, and other) (Higgins et al., 2011), will be assessed for RCTs and QCTs. Likewise, the elements recommended in the ROBINS-I to assess risk of bias for non-RCTs and observational studies (low, moderate, serious and critical) as a judgement for individual categories from six domains of bias (bias due to confounding, bias in selection of participants into the study, bias in classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes and bias in selection of the reported result) (Sterne et al., 2016) will also be assessed. Any disagreements over bias between two reviewers will be settled by involving the third review author and each bias in these domains for each study will be separately presented in a table in the final review publication.

Data extraction and management

As above discussed, the selected citation titles and abstracts will be exported from the search engines to Endnote X8.2 and duplicates will be removed automatically and a search will be conducted manually to check any missed duplicates. Eligible citations will be retrieved after the screening of titles and abstracts and full texts be sought and imported.

JCM and MW will extract data on: study ID, author's name, country, year, type of paper/report, form of publication, study design, comorbidity, description of the intervention (including process, cost-effectiveness and outcomes), context of integrated intervention (i.e., PHC, hospitals), details about participants (including number in each group, baseline health information, demographic characteristics), length of intervention and follow-up.

Data analysis and synthesis

We will first undertake a narrative synthesis to summarize and discuss the findings of the included studies. We will then present findings through primary and secondary outcomes. We will use tabular summary to synthesize individual studies characteristics and results (intervention effects). The data synthesis will be conducted through the measurements of effect for continuous outcomes of the included studies. Studies reporting multiple outcomes and outcome measures will be categorised according to definitions outlined in section types of outcome measure above.

A predetermined order of preference for extracting multiple outcome measures will be used where data is available in several formats. For RCTs preference will be to extract data that requires the least manipulation by authors or inference by review authors. Raw values (e.g., Means and standard deviations) rather than calculated effect size will be extracted. For studies reporting both final values and changes from baseline for outcomes, preference will be to extract the former. In the case of cluster-RCTs, the preference will be (i) extract adjusted estimates reported by the study, or (ii) use raw data and inflated the standard error (SE) data using weighting.

In case of missing data in some eligible studies, efforts will be made to contact corresponding authors to request for clarification of all relevant information. For ongoing studies trial authors will be contacted for further information and updates.

Statistical analysis and subgroup analysis and investigation of heterogeneity

Heterogeneity between studies will then be assessed using both x^2 and I^2 and Q statistics where appropriate. The I^2 statistic estimates the percentage of total variation across studies due to a true difference rather than chance. In general, I^2 values greater than 60–70% indicate the presence of substantial heterogeneity. We will explore sources of heterogeneity by comparing the pooled study estimates between subgroups defined by study-level characteristics. Subgroup analysis will be performed where heterogeneity is statistically significant. Sensitivity analyses will be conducted to

determine the potential sources of heterogeneity. Two additional sensitivity analyses will be conducted to: (i) evaluate the effect of excluding studies unable to meet each quality criterion affect the overall estimate; and, (ii) evaluate the change in the results if only high-quality studies where included.

In case the identified studies are of substantial heterogeneity and where statistical pooling is impossible, the findings will be summarised in a narrative form by tables and figures to facilitate in effective data presentations. Two reviewers will write the narratives independently and later checked by other reviewers. Decisions on any disagreements will be resolved through discussions and consensus by all reviewers in the team. We will assess the presence of publication bias by using a funnel plot and the Egger test of bias (Ukoumunne et al., 1999) . Subgroup and sensitivity analyses will be conducted to look at the effects of certain factors on for example: geographic region, age and gender and diabetes type of participating patients.

Reporting of this review

This protocol complies with the requirements of Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocol (PRISMA-P), which is included as a supplementary file 1. The systematic review results will be reported according to preferred reporting items for systematic review and meta-analysis (PRISMA) (see Figure 1 in supplementary files) (Moher et al., 2009).

Ethics and dissemination

Given that this is a protocol for a systematic review only using the published data, there is no ethics approval required for this study. This systematic review will be included in JCM's PhD thesis, a research supervised by Christina Zarowsky (CZ) and Helen Trottier (HT). Its findings will also be disseminated through peer-reviewed publications and conference presentations.

Additional files

Figure 1 in supplementary files: The preferred reporting items for systematic review and meta-analysis (PRISMA) flow chart

Figure 2 in Supplementary files: PRISMA-P 2015 Checklist. The Preferred Reporting Items for Systematic Reviews and Meta-analyses for Protocols 2015 (PRISMA-P 2015) checklist was used in development of this protocol. Items 1b, 2, 4, 5b, 5c, 15d, 16 and 17 were not applicable.

Abbreviations

AIDS: Acquired Immunodeficiency Syndrome

ANC: Antenatal Care

ART: Antiretroviral Therapy

CCRBT: Cochrane Collaboration Risk of Bias Tool

CNCICDs: Comorbid Non-Communicable and Infectious Chronic Diseases

EPHPP: Effective Public Health Practice Project

GDM: Gestational Diabetes Mellitus

HINARI: Health InterNetwork Access to Research Initiative

HIV: Human Immunodeficiency Virus

ICCC: Innovative Care for Chronic Conditions

LMICs: Low and Middle-Income Countries

MeSH: Medical subject heading

NCDs: Non-Communicable Diseases

PACTR: Pan African Clinical Trials Registry

PICO: Population, Intervention, Comparator and Outcome

PRISMA: Preferred Reporting Items for Systematic review and Meta-Analysis

QCTs: Quasi-randomised Controlled Trials

RCTs: Randomised Controlled Trial

ROBINS-I: Risk Of Bias In Non-randomized Studies - of Interventions

SE: Standard Error

T2DM: Type 2 Diabetes Mellitus.

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Availability of data and materials

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Author contributions

MJC, and MW designed the study. MJC wrote the first manuscript of the review. MJC, MW, AR, EM, KM, SN, HT, NL and CZ critically revised the review. All authors read and approved the final manuscript.

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MJC is an MHA, MSc, MA, MPhil and PhD candidate in Public Health-Global Health. MW is an MD, MPH and PhD candidate in Public Health. AR is an MPH and PhD in Healthcare and Epidemiology-Global Health. EM is an MBBS and Fellow of West African College of Physicians (FWACP) in Internal Medicine-Endocrinology. KM is a BA, HDE, PGDip. in Health Promotion and PhD in Public Health. HT is an M.Sc and PhD in Epidemiology. NL is MBChB, MD and Fellow of College Physicians of South Africa (FCP-SA)-Endocrinology/Diabetology. CZ is an MD, MPH and PhD in Medical Anthropology.

Competing interests

MJC, MW, AR, EM, KM, SN, HT, NL and CZ declare no competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

Not applicable.

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Additional files

Figure 1: PRISMA flow chart

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

Fig. 2 - Checklist of items to include when reporting a systematic review or meta-analysis

Figure 2: PRISMA-P 2015 checklist

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: **Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1**

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	☒	☐	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	☐	☐	
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	☒	☐	3, 8
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	☒	☐	1, 17-18
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	☒	☐	17
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	☐	☐	
Support					
Sources	5a	Indicate sources of financial or other support for the review	☒	☐	17 (No funder)
Sponsor	5b	Provide name for the review funder and/or sponsor	☐	☐	
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	☐	☐	
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	☒	☐	4-7

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	☒	☐	7-8
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	☒	☐	9
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	☒	☐	8
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	☒	☐	8-9
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	☒	☐	13
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	☒	☐	10
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	☒	☐	9-11
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	☒	☐	9-11
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	☒	☐	11-12
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	☒	☐	12-13
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	☒	☐	13-15

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2, Kendall's tau)	☒	☐	13-15
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	☒	☐	13-15
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	☐	☐	
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	☐	☐	
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	☐	☐	

*Page numbers in this tool appear as they were included in the published article.

Paper 6 – Integrated management of type 2 diabetes and gestational diabetes in the context of multi-morbidity in Africa: a systematic review and meta-analysis

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Abstract

Introduction

Many adults diagnosed with gestational diabetes mellitus (GDM) and type 2 diabetes mellitus (T2DM) also suffer from other known or unknown comorbid conditions. The rising prevalence of GDM and T2DM within multimorbidity can best be addressed through an integrated management response, instead of stand-alone programs targeting specific infectious and/or chronic diseases.

Aim

To describe GDM and T2DM screening, care and cost-effectiveness outcomes in the context of multimorbidity through integrated interventions in Africa.

Methods

A systematic review and meta-analysis of all published studies conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Risk Of Bias in Non-randomised Studies of Interventions (ROBINS-I) was used to assess risk of bias. Data synthesis was conducted using narrative thematic synthesis for studies and random effects models.

Results

A total of 9 out of 13 included studies reported integrated diabetes mellitus (DM) screening, 7 included integrated care and 9 studies addressed the cases of newly detected DM who were asymptomatic in pre-diabetes stage. The pooled proportion of participants screened for DM during the integrated screening outcome was 0.10 (95% CI 0.07 to 0.13, n=9 studies), the pooled proportion of participants who received integrated care was 0.26 (95% CI 0.14 to 0.39, n=7 studies) and the pooled proportion of those who had early detection of DM because of integrated care was 0.45 (95% CI 0.08 to 0.83, n=8 studies). Significant heterogeneity across studies was calculated at (I^2=99.5%, p=<0.01) for the first two outcomes and at (I^2=99.9%, p=<0.01), for the third outcome. Only one study clearly analysed cost-effectiveness in home-based care while other five did not evaluate cost-

effectiveness but rather discussed some potential cost benefits of integrated approach to DM screening and care. Compared to partial integration, only two fully integrated interventions yielded tangible results in regarding DM screening, care and early detection of cases despite many reported barriers to its sustainability.

Conclusion

Though few, integrated interventions for screening and/or care of DM in the context of multimorbidity, within available resources in health systems throughout Africa suggest that this approach is possible and could improve health outcomes.

Key words: integrated care, diabetes mellitus, type 2 diabetes, gestational diabetes, multimorbidity, syndemic, health systems.

Background

GDM and T2DM comprise more than 90% of global diabetes cases (Cho et al., 2018; Saeedi et al., 2019). Their prevalence has been rising worldwide, especially in the context of multiple co-morbidities and risk factors in LMICs, despite the history of underdiagnosis and low reporting in those countries (International diabetes federation, 2015; Jaacks et al., 2016; Leone et al., 2012; Luppens et al., 2014; McMurry et al., 2019; Mendenhall et al., 2014; Vellakkal et al., 2015). Several factors contribute to this increasing burden. First, some women with T2DM are diagnosed for the first time during their pregnancy and are included among women with GDM (Mirghani & Doupis, 2017). For those diagnosed with GDM and not unknown T2DM and their children are at high risk to develop T2DM in the long term (Damm et al., 2016; Mirghani & Doupis, 2017). Secondly, triggered by genetic and environmental factors through epigenetic mechanisms (Unnikrishnan et al., 2017), both GDM and T2DM occur later in life, in a population that increasingly becomes vulnerable to various other risk factors and complications (Bellamy et al., 2009; Damm et al., 2016; Gunderson et al., 2014; Kim et al., 2002). Thirdly, adults diagnosed with GDM or T2DM may remain unaware that they are diabetic and may also suffer from other known or unknown comorbid conditions. Co-morbid conditions could include cardio-vascular diseases (e.g., hypertension) and/or infectious diseases (e.g., tuberculosis, Hepatitis B, HIV/AIDS) and/or vector borne diseases (e.g., malaria) (Valderas et al., 2009). Treatment of some of these diseases - such as antiretroviral therapy (ART) for HIV - may increase the likelihood of concomitant metabolic complications, opportunistic infections among others (Alexander et al., 2019; American Diabetes Association, 2019; Archambault et al., 2014; Dunachie & Chamnan, 2019; Gunderson et al., 2014; Kalra et al., 2011; Kendir et al., 2017; Lao et al., 2007; Li et al., 2018; Mirghani & Doupis, 2017; Prioreschi et al., 2017; Restrepo et al., 2007; Soepnel et al., 2017; Wu, 2019), necessitating more complex and costly clinical management (Valderas et al., 2009). The multimorbidity caused by comorbid non-communicable and infectious

chronic diseases (Oni et al., 2014), which include GDM and T2DM, have not been well studied, especially their integrated management into primary health care (PHC) in LMICs like Africa. Fourthly, the diagnosis of GDM or T2DM among some patients with multiple diseases has to be conducted along with diagnosis of these other multiple diseases, a situation that causes challenges in terms of cost and logistics for adequate testing and management, especially in the context of struggling health systems. Hence, the rising prevalence and burden of GDM and T2DM (Ferrara, 2007; Saeedi et al., 2019; Zhu & Zhang, 2016), can best be addressed through an integrated management response instead of more easily delivered and less costly stand-alone programmes targeting specific diseases (Hörnsten et al., 2011; Oni et al., 2014; Pantalone et al., 2015; Rijken et al., 2018; Simmons et al., 2016).

Syndemic theory is increasingly being used as a framework to not only understand but to also design interventions for complex multiple diseases affecting disadvantaged populations, especially in low- and middle-income countries (LMICs). LMICs in Africa and beyond are facing epidemiological transitions (Mendenhall et al., 2017; Omran, 2005), that overwhelm already weak health systems dealing with more complex health problems rather than a single disease or isolated risk factors (McKeown, 2009). A syndemic framework assesses and addresses interacting population health problems where underlying biological, cultural, socioeconomic and environmental dimensions lead to health inequities (Mendenhall et al., 2017; Singer, 2009). It also goes beyond conventional approaches to co-morbidity and multimorbidity (Hart & Horton, 2017) such as disease-specific, stand-alone or vertical programmes for targeted infectious, non-communicable, acute or chronic conditions and specific co-morbidities. It instead suggests that integrated management of multiple conditions, though not simple, is necessary for better health services delivery (Haldane et al., 2017).

This study aimed to review the literature on integrated management of T2DM and GDM in the context of multimorbidity in Africa to identify emerging good practices, lessons and advantages including cost-effectiveness of integrated rather than vertical or targeted interventions. Additionally, we identified research gaps related to GDM and T2DM integration within management of other chronic and infectious diseases.

This systematic review answers the following research questions: 1) What are the existing integrated interventions and service delivery models for managing T2DM including GDM in the context of multi-morbidity in Africa? and, 2) What are the successes and challenges of the existing integrated management of T2DM including GDM in the context of multi-morbidity in Africa?

Methods

Protocol

The protocol for this study was developed based on the Cochrane Handbook for Systematic Reviews (Higgins & Wells, 2011) and registered with PROSPERO: (https://www.crd.york.ac.uk/prospero/), registration no. CRD42016046630. The systematic review methods were described in our previously published protocol (Mutabazi et al., 2019).

Study design and search strategy

For this study, the PRISMA guideline was followed during the review and meta-analysis (Shamseer et al., 2015). Published studies were searched using controlled terms (MeSH: Medical subject heading) and free texts. The following databases were searched: Cochrane Library, MEDLINE, PubMed, Embase, SCOPUS, AIDS journal and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). Additionally, a manual search was conducted in Google scholar, ClinicalTrials.gov (*ClinicalTrials.gov) and relevant journals for additional studies*. The target population, the intervention of interest, the comparator intervention, key outcomes and time (PICOT) approach (Thabane et al., 2008) was used as a framework for the identification and selection of studies

for inclusion. This study was limited to all fifty-four African countries. Since there were not many articles regarding our review topic in our preliminary search, there were no starting time limits till the search date on February 2019 but two full papers published later in 2019 were extracted after their conference abstracts were initially included in the selection. The search strategy used is shown **in table 17**.

Table 17: Search strategy

(integrat* OR linkag* OR combin* OR amalgamat* OR coordinat* OR unificat* OR manag* OR comprehensive* OR "co-ordinated" OR "disease control" OR care deliver* OR "healthcare deliver*" OR "health care deliver*" OR "collaborative care" OR "intersectional collaborat*" OR "interagency collaborat*" OR "care partner*")	AND	(diabet* OR diabetes mellitus, type 2/ OR diabetes, gestational/)	AND	(comorbid* OR co-morbid* OR multimorbid* OR multi-morbid* OR polymorbid* OR poly-morbid* OR codisease* OR co-disease* OR multidisease* OR multi-disease* OR polydisease* OR poly-disease* OR coillness* OR co-illness* OR multiillness* OR multi-illness* OR polyillness* OR poly-illness* OR copatholog* OR co-patholog* OR multipatholog* OR multi-patholog* OR polypatholog* OR poly-patholog* OR codisorder* OR co-disorder* OR multidisorder* OR multi-disorder* OR polydisorder* OR poly-disorder* OR cocondition* OR co-condition* OR multicondition* OR multi-condition* OR polycondition* OR poly-condition* OR cosyndrom* OR co-syndrom* OR multisyndrom* OR multi-syndrom* OR polysyndrom* OR poly-syndrom* OR ((coexisting OR co-existing OR multiple) W0 (morbidit* OR disease* OR illness* OR patholog* OR disorder* OR	AND	Africa/ OR "Africa South of the Sahara"/ OR "Sub-Saharan Africa"/ OR north Africa/ OR Africa, Northern/ Egypt or Libya OR Tunisia OR Algeria OR Morocco OR "Western Sahara" OR Angola/ OR Benin/ OR Botswana/ OR Burkina Faso/ OR Burundi/ OR Cameroon/ OR Cape Verde/ OR Central African Republic/ OR Chad/ OR Comoros/ OR Congo/ OR Brazzaville/ OR Cote d'Ivoire/ OR Djibouti/ OR Equatorial Guinea/ OR Eritrea/ OR Ethiopia/ OR Gabon/ OR Gambia/ OR Ghana/ OR

				condition* OR syndrom*)) OR ((Charlson* OR Elixhauser*) W0 (index* OR score*))) OR OR "noncommunicable disease*" OR "non communicable disease*" OR ncd OR ncds OR "non infectious disease*" OR "non infectious illness*" OR "chronic disease*" OR "chronic illness*" OR "cardiovascular disease*" OR "vascular disease*" OR "heart disease*" OR "heart illness*" OR "cardiac disease*" OR "heart attack*" OR stroke* OR "heart failure" OR "heart rupture" OR "cardiac arrest" OR cancer* OR neoplasm* OR "chronic respiratory disease*" OR "chronic airflow obstruction*" OR "chronic obstructive airway disease*" OR "chronic obstructive lung disease*" OR "chronic obstructed pulmonary disease*" OR asthma OR "lung disease*" OR "communicable disease*" OR "infectious disease*" OR "human immunodeficiency virus" OR hiv OR "acquired immunodeficiency syndrome" OR aids OR "opportunistic infectious disease*" OR tuberculosis OR tb OR malaria OR pneumonia OR "diarrheal disease*")		Guinea/ OR Bissau/ OR Kenya/ OR Lesotho/ OR Liberia/ OR Madagascar/ OR Malawi/ OR Mali/ OR Mauritania/ OR Mauritius/ OR Mozambique/ OR Namibia/ OR Niger/ OR Nigeria/ OR Rwanda/ OR Sao Tome e Principe/ OR Senegal/ OR Seychelles/ OR Sierra Leone/ OR Somalia/ OR South Africa/ OR South Sudan/ OR Sudan/ OR Swaziland/ OR Eswatini OR Tanzania/ OR Togo/ OR Uganda/ OR Western Sahara/ OR Zaire/ OR Zambia/ OR Zimbabwe/

Study selection

After systematic searches, the retrieved citations were exported to and managed using Endnote X9. Duplicates were removed automatically and a manual search was conducted to crosscheck and remove any duplicates that escaped the automatic removal. The remaining citations were independently screened for eligibility by two researchers (JCM and EM), in accordance with the inclusion and exclusion criteria of the study. Any disagreements were resolved through discussion between reviewers and with a third author (CT). These citations were assessed in two phases by two researchers (JCM and EM); the titles and abstracts first and then the full-text articles of potential studies for inclusion. Once titles and abstracts were screened, the full text were retrieved and screened to definitely decide whether the study fits the eligibility criteria. The team of three researchers (JCM, EM and CT) discussed and agreed on the final studies included.

Eligibility criteria

Eligible studies were published and unpublished quantitative studies on integrated interventions for management of T2DM and GDM within multi-morbidity conditions in Africa, without language restrictions. Because most of the included studies simply used “diabetes mellitus” (DM) as a classification instead of standardised classification of type 1, type 2, GDM or other specific types of diabetes (American Diabetes Association, 2018; Kuzuya et al., 2002) in the context of multimorbidity, we considered DM instead of T2DM and GDM. We first checked whether the screened and care of DM or its early cases detection were among adult patients without the pre-existing diagnosis of type 1 diabetes. All screenings and subsequent procedures were indicated as conducted for the first time, without prior diagnosis and this made us confident that they would be GDM or T2DM, if standard classifications were applied. For the meta-analysis, only studies that reported number of patients screened, managed or early cases detected of T2DM and GDM within multi-morbidity were included

Data extraction

Data were extracted using a piloted form for this review and the following information describing the extracted studies included: the baseline characteristics of the eligible research reports (author (s), year of publication, country of study, and study setting); study methodology (study design, target population, sampling strategy, total number of participants, and response rate); intervention and facility (diagnosis, other co-morbidities, service providers (Doctor, Nurse, Both), and point of entry/type of facility); study outcomes (integrated screening outcome, integrated care outcome (preventive, treatment and referral services), cost-effectiveness outcome, and early detection of disease outcome); and approach and level of integration (integration through co-location of services (same room or same clinic), integration of two services OR integration into PHC-mainstreaming, partial integration (linkages, coordination), and full integration.

Assessment of risk of bias in included studies

We assessed the methodological quality and risk of bias of the included studies using the ROBINS-I assessment tool.

Data synthesis

Findings from included studies varied extensively and therefore we performed a narrative synthesis to easily compare them (Schwarz et al., 2019).

For each outcome, prevalence was pooled using the *metaprop* package in Stata Statistical Software, version 15. A random effects framework was applied as the data from different studies were expected to be highly heterogenous. In the metaprop package, the prevalence estimates are modelled using the binomial distribution and a Freeman-Turkey double arcsine variance stabilizing transformation is used to normalize the estimates prior to pooling them and then back transformed. For each outcome, computation of the pooled estimates and their confidence intervals was done using the procedure described by DerSimonian and Kacker (Kalra et al., 2011). The Cochrane's Q statistic

and I2 statistic were also computed using the metaprop package in Stata. Heterogeneity was considered to be present if I^2 test statistics results were > 50% and Q test and its respective *P*-value were < 0.05. Forest plots were used to present the prevalence of each outcomes and their 95% confidence intervals (95% CI). Assessment of publication and other systematic biases was done using funnel plots and Egger's statistic (Egger & Smith, 1997).

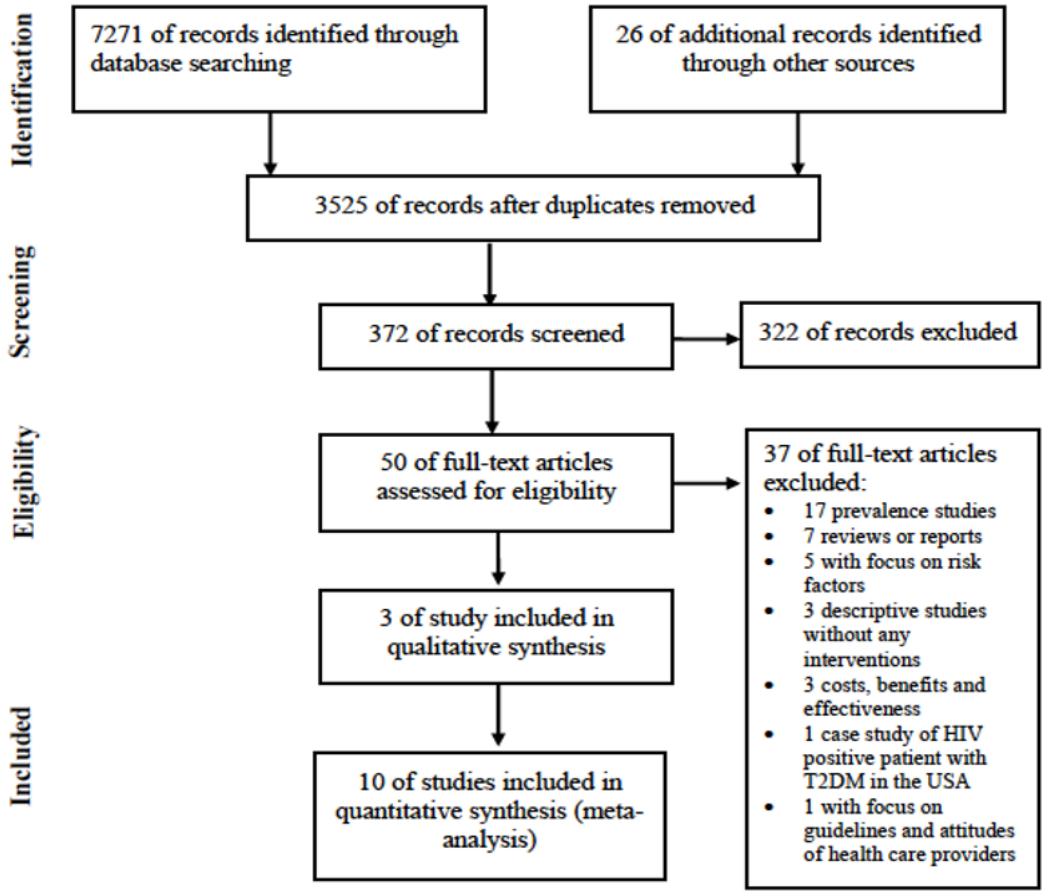
Patient and public involvement

No patients were involved in the development of the research question, the design or the conduct of this study.

Results

Description of included studies

A total of 7297 published articles were retrieved; 3772 duplicate records were removed and 3153 records were excluded after screening title and abstract. A total of 372 full-text articles were screened for eligibility. Of those, 322 full-text articles were excluded, because they failed to fulfill prior eligibility criteria and out of 50 potential studies 37 articles were excluded for cited reasons. Finally, 13 studies were included in the final analysis, 3 for qualitative analysis and 10 for quantitative analysis (**Figure 13).**



Flow diagram of the included studies for the systematic review and meta-analysis of Integrated management of type 2 diabetes and gestational diabetes within multi-morbidity conditions in Africa

Characteristics of the included studies

Only seven African countries were represented in this review. Of thirteen studies included, eight were from Southern African countries - four from South Africa (Almossawi et al., 2019; Golovaty et al., 2018; Govindasamy et al., 2013; Manne-Goehler et al., 2017), three from Malawi (Kachimanga et al., 2017; Pfaff et al., 2018; Wroe et al., 2015) and one from Angola (Segafredo et al., 2019), four were from East African countries; two from Kenya (Pastakia et al., 2017; Venables et al., 2016), one from Ethiopia (Jerene et al., 2017), one from Uganda (Chamie et al., 2012) and one from Central Africa (Cameroon) (Labhardt et al., 2010). Regarding the study design, most studies (9/13) were classified as cross-sectional (Almossawi et al., 2019; Chamie et al., 2012; Golovaty et

al., 2018; Jerene et al., 2017; Manne-Goehler et al., 2017; Pfaff et al., 2018; Segafredo et al., 2019; Wroe et al., 2015), three as cohort (Govindasamy et al., 2013; Labhardt et al., 2010; Pastakia et al., 2017) and one was descriptive (Kachimanga et al., 2017). A total of 27,772 participants were included in this review and some were purposively sampled (Jerene et al., 2017; Labhardt et al., 2010; Pfaff et al., 2018; Segafredo et al., 2019; Venables et al., 2016; Wroe et al., 2015) while others were on voluntary (Govindasamy et al., 2013; Kachimanga et al., 2017; Pastakia et al., 2017), random (Manne-Goehler et al., 2017), quota from an old enrolled cohort (Golovaty et al., 2018), convenience (Almossawi et al., 2019) and community based campaign (Chamie et al., 2012) sampling bases. **Table 18** details the characteristics of the included studies.

Table 18: Study characteristics

Author	**Year**	**Country**	**Study aim**	**Study design**	**Sampling strategy**
Labhardt et al.	2010	Cameroon	To examine the effectiveness of integrating care for HT and T2DM by task shifting to non-physician clinician (NPC) facilities in eight rural health districts in Cameroon.	Cohort	Purposive
Segafredo et al.	2016	Angola	To estimate the double burden of DM, HT and TB and to pilot the integration of the screening for DM and HT in the TB national programs in six TB centers in Luanda.	Cross-sectional or Interventional	Purposive
Wroe et al.	2015	Malawi	To increase access to care for NCD patients, to maximize efficiency given the severe human resource shortages, and to replicate strong HIV outcomes for patients with other chronic conditions.	Cross-sectional	Purposive
Chamie et al.	2012	Uganda	To test the feasibility and diagnostic yield of integrating NCD and other communicable disease services into a rapid, high-throughput, community-based HIV testing and referral campaign for all residents of a rural Ugandan parish, and to determine rates	Cross-sectional	Community based campaign (census)

			and predictors of post-campaign linkage to care by disease.		
Jerene et al.	2017	Ethiopia	To demonstrate the feasibility of integrated care for TB, HIV and DM in a pilot project.	Cross-sectional	Purposive
Almossawi et al.	2019	South Africa	To assess the readiness of the PHC system to provide integrated TB and DM services.	Cross-sectional	Random for patients records, convenience for respondents
Pfaff et al.	2018	Malawi	To describe the experience of this pilot initiative, where all adults accessing care in the HIV clinic are screened and treated for HT and DM during the same visit.	Cross-sectional	Purposive
Pastakia et al.	2017	Kenya	To assess the impact of the implementation of a patient-centered rural NCD care delivery model called Bridging Income Generation through grouP Integrated Care (BIGPIC).	Cohort or Interventional	Voluntary
Govindasamy et al.	2013	South Africa	To determine the yield of newly-diagnosed HIV, TB symptoms, DM and HT, and to assess CD4 count testing, linkage to care as well as correlates of linkage and barriers to care from a mobile testing unit.	Cohort or Interventional	Voluntary
Kachimanga et al.	2017	Malawi	To increase case detection for NCDs in the community, at the facility for acute outpatient care, and at Integrated Chronic Care Clinic (IC3) itself.	Descriptive	Voluntary
Manne-Goehler et al.	2017	South Africa	To assess the relationship between ART use and utilization of health care services for DM and HT.	Cross-sectional	Random
Golovaty et al.	2018	South Africa	To conduct a cost analysis to determine the per-person incremental costs associated with integrating NCD screening and counseling to a home-based HIV counseling and testing program in KwaZulu-Natal.	Cross-sectional	Quota from an old enrolled cohort
Venables et al.	2016	Kenya	To assess patient and health-care worker perceptions and experiences of medicines adherence clubs (MACs) in the urban informal settlement of Kibera.	Cross-sectional	Purposive

Quality appraisal and risk of bias for included studies

All studies reported the results of nonrandomized studies, many biases were recorded while analyzing all studies and only one study was considered to have a low risk (Labhardt et al., 2010) while the remaining twelve had serious risk of bias (Almossawi et al., 2019; Chamie et al., 2012; Golovaty et al., 2018; Govindasamy et al., 2013; Jerene et al., 2017; Kachimanga et al., 2017; Manne-Goehler et al., 2017; Pastakia et al., 2017; Pfaff et al., 2018; Segafredo et al., 2019; Venables et al., 2016; Wroe et al., 2015). Studies with serious either missed or had unclear information on participant selection, classification of interventions, measurement of outcomes, selection of the reported results. Some biases were caused by confounding, deviation from intended interventions or by missing data (**Table 19**).

Table 19: Results of the assessment of risk of bias in included studies by using the ROBINS-I assessment tool

Study ID	1. Bias caused by confounding	2. Bias caused by selection of participants	3. Bias caused by classification of interventions	4. Bias caused by deviations from intended interventions	5. Attrition bias caused by missing data	6. Detection bias caused by measurement of outcomes	7. Reporting bias caused by selection of the reported results	Overall judgement
Labhardt et al. 2010 Cameroon	Low	Low	Low	No information	Low information on reasons for missing data provided)	Low	Low	Low

Segafredo et al. 2016 Angola	Serious	Low	No information	No information	No information	Serious	No information	Serious
Wroe et al. 2015 Malawi	Serious	Serious	No information	No information	Serious	Serious	Serious	Serious
Chamie et al. 2012 Uganda	Serious	Serious	No information	No information	Serious	No information	No information	Serious
Jerene et al. 2017 Ethiopia	Serious	Serious	No information	No information	Low (information on reasons for missing data provided)	No information	No information	Serious
Almossawi et al. 2019 South Africa	Serious	Low	No information	No information	Low (information on reasons for missing data provided)	No information	Low	Serious
Pfaff et al. 2018 Malawi	Serious	Low	Low	No information	Low (information on reasons for missing data provided	No information	No information	Serious
Pastakia et al. 2017 Kenya	Serious	Serious	Serious	Low	No information	Serious	Serious	Serious
Govindasamy et al. 2013 South Africa	Low	Low	No information	No information	No information	No information	No information	Serious

Kachimanga et al. 2017 Malawi	Serious	Serious	No information	No information	No information	No information	No information	Serious
Manne-Goehler et al. 2017 South Africa	Serious	Low	No information	No information	Low (information on reasons for missing data provided	Serious	No information	Serious
Golovaty et al. 2018 South Africa	Low	Low	No information	No information	No information	No information	No information	Serious
Venables et al. 2016 Kenya	Serious	Serious	No information	No information	Serious	No information	No information	Serious

The main study outcomes from included studies in this review were analysed, summarized and were subsequently presented under the following themes (**Table 20**).

Table 20: Study outcomes

1. Integrated DM screening outcomes

Study	Year	Country	Total sample size	Total integrated DM screened
Labhardt et al.	2010	Cameroon	796	144
Segafred et al.	2016	Angola	5890	368
Wroe et al.	2015	Malawi	721	76
Chamie et al.	2012	Uganda	2283	80
Jerene et al.	2017	Ethiopia	435	141
Pfaff	2018	South Afrcia	2979	25
Govindasamy et al.	2013	South Africa	9806	31
Kachimanga et al.	2017	Malawi	4016	716
Pastakia et al.	2017	Kenya*	846	45

*23 had DM and HT comorbidity

2. Integrated DM care outcomes

Study	Year	Country	Total sample size	Total integrated DM care
Labhardt et al.	2010	Cameroon	796	144
Wroe et al	2015	Malawi	721	76
Chamie	2012	Uganda*	80	18
Pfaff et al	2018	South Africa	2979	25
Govindasamy et al.	2013	South Africa**	31	23
Kachimanga et al.	2017	Malawi	716	113
Almossawi et al.	2019	South Africa	836	419

*18 accepted referrals, 11 linked to care within 3 months

**21 repeated glucose test, 14 started medication

3. Early DM detection outcomes

Study	Year	Country	Total sample size	Total integrated DM early detected
Labhardt et al.	2010	Cameroon	144	103
Segafred et al.	2016	Angola	431	370
Chamie et al.	2012	Uganda	80	18
Jerene et al.	2017	Ethiopia	141	136
Pfaff et al.	2018	South Africa	25	13
Govindasamy et al.	2013	South Africa	9806	31
Kachimanga et al.	2017	Malawi	401	113
Pastakia et al.	2017	Kenya*	45	2
Wroe et al.	2015	Malawi**		

*10 had DM and HT comorbidity

**Weekly new DM screening during outreach and at the clinic.

4. Cost effectiveness outcomes and integration levels

Author	Year	Country	Cost-effectiveness outcome	Integration level: Partial*/ Full**
Labhardt et al.	2010	Cameroon	Affordable drugs from the national essential drug list were available and used	Full
Segafredo et al. 2016	2016	Angola	Not measured	Partial
Wroe et al.	2015	Malawi	All patients were seen in one day, at the nearest health center, for all of their chronic conditions.	Full
Chamie G.et al.	2012	Uganda	Cost-effectiveness of adding NCD screening was not the aim of the study but the relatively low cost of $2.41/person makes it likely to be cost-effective.	Partial
Jerene et al.	2017	Ethiopia	Not measured	Partial
Almossawi et al.	2019	South Africa	Not measured	Partial
Pfaff et al.	2018	Malawi	Not measured but its advantages discussed and its evaluative recommended	Partial
Pastakia et al.	2017	Kenya	group care model resulted in 72.4 % of screen-positive participants returning for subsequent care, of which 70.3 % remained in care through the 12 months of the evaluation period.	Partial
Govindasamy et al.	2013	South Africa	Not measured	Partial
Kachimanga et al.	2017	Malawi	Not measured	Partial
Manne-Goehler et al.	2017	South Africa	Not measured	Partial
Golovaty et al.	2018	South Africa	Comprehensive home-based HIV-NCD testing and counseling results in a modest increase in costs with the potential to avert NCD death and disability. The additional time burden of NCD screening and testing was the	Partial

			major driver of costs, emphasizing the need for a targeted approach that bridges to an integrated public health model. 20% increase in testing and counseling time was revealed in time assessment	
Venables et al.	2016	Kenya	MACs allow for the efficient management of co-morbidities and enable large numbers of stable patients to collect their chronic medication efficiently, whilst simultaneously enabling patients to benefit from peer support and health education.	Partial

Partial*: Integration through co-location of services (same room or same clinic)
Full**: Integration of services OR integration into PHC-mainstreaming

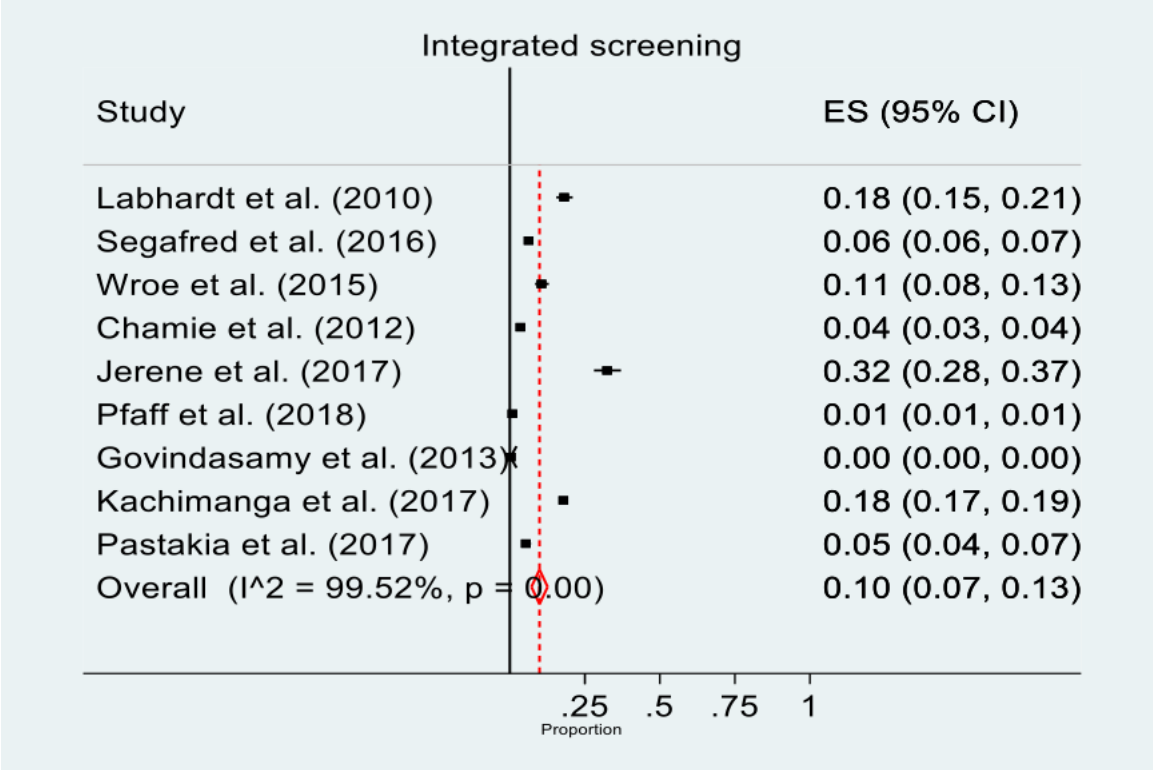
Outcomes from included studies

Included studies have shown that integrated screening and care of DM as well as the early detection of DM cases in the context of multimorbidity is possible, although these studies were few and had significant heterogeneity in its findings. Outcomes regarding the integrated screening, care and early detection of DM cases were shown in the figures 1, 2 and 3. Cost-effectiveness and integration level outcomes from the included studies were analysed, summarized and were subsequently presented under the following themes

Integrated diabetes mellitus screening and care in Africa

One included study clearly mentioned that the type of diabetes was T2DM (Labhardt et al., 2010), while the remaining studies used DM as diabetes diagnosed or treated along with other diseases that patients suffered from. Among twelve studies that reported DM screening among other co-morbidities (Almossawi et al., 2019; Chamie et al., 2012; Golovaty et al., 2018; Govindasamy et al., 2013; Jerene et al., 2017; Kachimanga et al., 2017; Labhardt et al., 2010; Manne-Goehler et al., 2017; Pastakia et al., 2017; Pfaff et al., 2018; Segafredo et al., 2019; Wroe et al., 2015), only nine reported

the exact number of patients who were screened. As expected, the review found that different criteria were used to diagnose DM in routine screening. Applying different criteria was an additional challenge in Africa where lack of clear protocols, limited resources in health facilities and inadequate training for health workers, especially at primary levels of care was widely documented (Almossawi et al., 2019; Labhardt et al., 2010; Wroe et al., 2015). Though integrated DM screening was identified in most retained studies, not all patients who benefited from integrated screening had integrated treatment. The pooled proportion of participants screened for DM during the integrated screening outcome was 0.10 (95% CI 0.07 to 0.13, n=9 studies), with significant heterogeneity (I^2=99.5%, p=<0.01), **figure 15**.

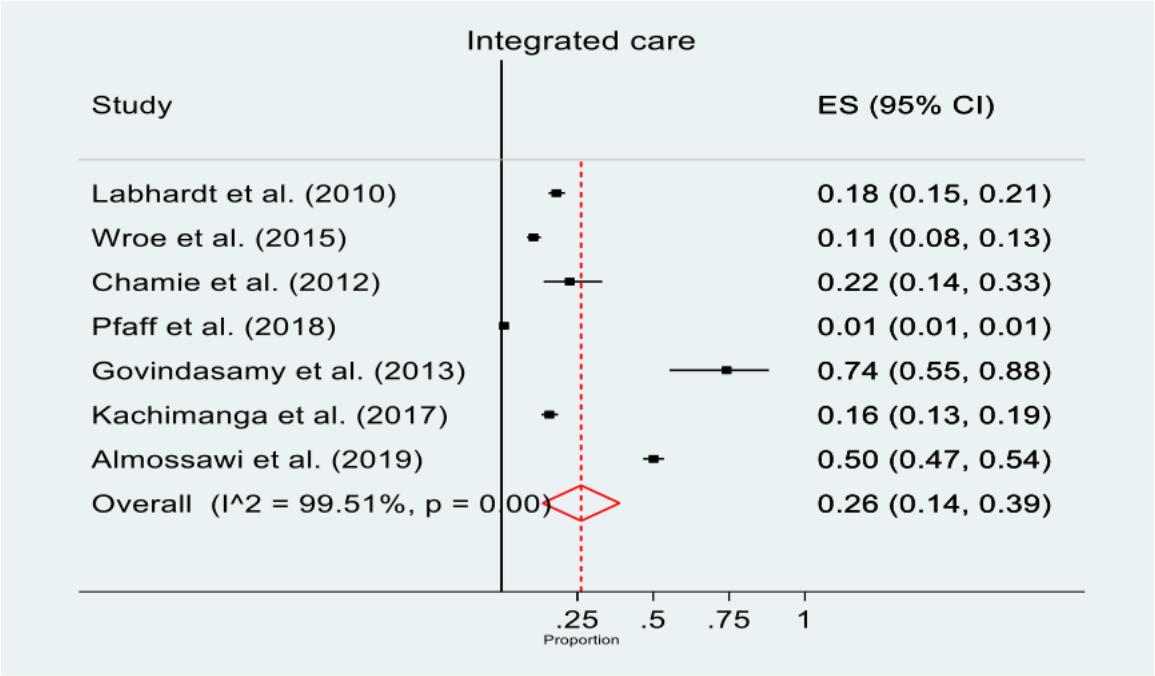


Integrated DM screening outcome.

Integrated care including preventive, treatment and referral services was reported in nine studies (Almossawi et al., 2019; Chamie et al., 2012; Govindasamy et al., 2013; Kachimanga et al., 2017; Labhardt et al., 2010; Manne-Goehler et al., 2017; Pfaff et al., 2018; Venables et al., 2016;

Wroe et al., 2015), out of which seven had a known number of patients in care. DM screening in the reviewed studies was conducted at different venues: four at the clinic or PHC facilities exclusively (Labhardt et al., 2010; Pfaff et al., 2018; Venables et al., 2016; Wroe et al., 2015), three at home or community based infrastructures (Chamie et al., 2012; Golovaty et al., 2018; Pastakia et al., 2017), five at specialised clinics or clinics in close collaboration with hospitals or at hospitals (Almossawi et al., 2019; Jerene et al., 2017; Kachimanga et al., 2017; Manne-Goehler et al., 2017; Segafredo et al., 2019) and one at a mobile clinic (Govindasamy et al., 2013), and by different teams. Health care workers involved in screening and care of DM within multi-morbidities ranged from expert clients or trained patients (Pfaff et al., 2018) and lay counsellors and community health workers (Golovaty et al., 2018; Govindasamy et al., 2013; Jerene et al., 2017; Kachimanga et al., 2017; Manne-Goehler et al., 2017; Pastakia et al., 2017; Wroe et al., 2015) playing limited roles, to nurses and clinicians that lead interventions in all 13 included studies. The expertise and available resources, including equipment and medication in the facilities, were highlighted as key factors for the successful implementation of integrated screening and care of DM and other NCDs. This integration was more easily carried-out when conducted within the existing protocols of well-established programmes like HIV and these were seen as of tremendous impact to its success (Kachimanga et al., 2017; Manne-Goehler et al., 2017; Pfaff et al., 2018; Wroe et al., 2015). In fact, nine integrated DM screening and care interventions included in this study were conducted with HIV as one of the multi-morbidities (Chamie et al., 2012; Golovaty et al., 2018; Govindasamy et al., 2013; Jerene et al., 2017; Kachimanga et al., 2017; Manne-Goehler et al., 2017; Pfaff et al., 2018; Venables et al., 2016; Wroe et al., 2015). Tuberculosis (Almossawi et al., 2019; Chamie et al., 2012; Govindasamy et al., 2013; Jerene et al., 2017; Kachimanga et al., 2017; Segafredo et al., 2019), hypertension (Labhardt et al., 2010; Manne-Goehler et al., 2017; Pastakia et al., 2017; Pfaff et al., 2018) and other NCDs including hypertension, depression, cardiovascular and risks such as tobacco, obesity and alcohol use (Golovaty

et al., 2018; Govindasamy et al., 2013; Kachimanga et al., 2017; Wroe et al., 2015), and malaria (Chamie et al., 2012) were other diseases and risk factors screened or treated along with DM. The pooled integrated DM care outcomes was 0.26 (95% CI 0.14 to 0.39, n=7 studies), with significant heterogeneity (I^2=99.5%, p=<0.01), **Figure 14**.



Integrated DM care outcome.

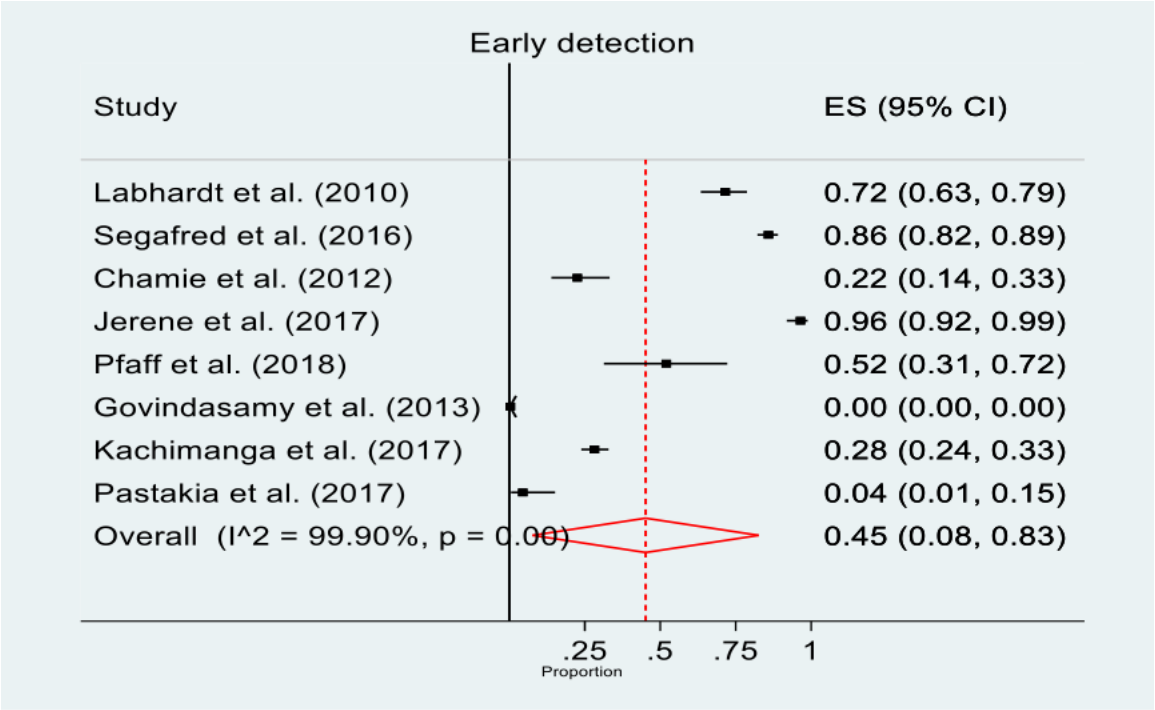
Cost-effectiveness of integrated DM screening and care

The majority of included studies (7/13) did not evaluate cost-effectiveness (Almossawi et al., 2019; Govindasamy et al., 2013; Jerene et al., 2017; Kachimanga et al., 2017; Manne-Goehler et al., 2017; Pfaff et al., 2018; Segafredo et al., 2019). Only one study clearly analysed cost-effectiveness of home-based integrated screening and referral to care of HIV and comprehensive NCDs including DM (Golovaty et al., 2018), other five did not evaluate cost-effectiveness but rather discussed some potential cost benefits of integrated approach to DM screening and care (Dunachie & Chamnan, 2019; Labhardt et al., 2010; Pastakia et al., 2017; Venables et al., 2016; Wroe et al., 2015). Some of the elements addressed throughout different studies that were highlighted and that could relate to cost-

effectiveness were: Patients with multi-morbidities were seen in one day for all their health conditions (Wroe et al., 2015), availability and affordability of essential DM/NCDs drugs (Chamie et al., 2012; Labhardt et al., 2010), efficient collection of DM and other NCDs medication, benefiting from peer support and health education (Venables et al., 2016) and reinforcement of adherence to care (Pastakia et al., 2017).

Early detection of DM cases

Nine studies addressed the cases of newly detected DM who were asymptomatic and those with impaired glucose or in pre-diabetes stage (Chamie et al., 2012; Govindasamy et al., 2013; Jerene et al., 2017; Kachimanga et al., 2017; Labhardt et al., 2010; Pastakia et al., 2017; Pfaff et al., 2018; Segafredo et al., 2019; Wroe et al., 2015). The remaining four studies did not measure this outcome nor include it as one of its results (Almossawi et al., 2019; Golovaty et al., 2018; Manne-Goehler et al., 2017; Venables et al., 2016). The pooled early detection outcome of DM cases was 0.45 (95% CI 0.08 to 0.83, n=8 studies), with significant heterogeneity (I^2=99.9%, p=<0.01), **figure 15**. One study was not included in the meta-analysis as it only mentioned this particular outcome in their weekly integrated screening at the clinic and during outreach but did not share the number of early detected DM cases (Wroe et al., 2015).



Early detection outcome for DM cases.

Integration levels for GM screening and care within multimorbidity

Integration of screening and care of DM within multimorbidity including early detection of DM and cost-effectiveness of interventions were important aspects of this systematic review. Interventions carried out in the included studies were integrated but at different levels based on the study objectives, design or available resources for services delivery. A very small number of two studies were classified as fully integrated (i.e., services offered for two or more diseases were merged in structural and functional aspects or were integrated into and delivered along with other primary care services, also known as mainstreaming). Only two studies: Wroe et al. in Malawi and Labhardt et al. in Cameroon were considered fully integrated (Labhardt et al., 2010; Wroe et al., 2015) and provided DM screening and care following a clear protocol within the package of other services available in the health care facility. The other 11 studies were partially integrated (Almossawi et al., 2019; Chamie et al., 2012; Golovaty et al., 2018; Govindasamy et al., 2013; Jerene et al., 2017; Kachimanga et al., 2017; Manne-Goehler et al., 2017; Pastakia et al., 2017; Pfaff et al., 2018;

Segafredo et al., 2019; Venables et al., 2016), which means that the services were offered through coordination or co-location in the same room or same clinic but each programme kept its structures as separate entities within health care services.

Integration approaches and models of DM screening and care

Most studies included in this review did not apply specific approaches or models to integrate DM screening and care in the context of multimorbidity. However, some details emerged from a small number of reviewed studies that gave limited information regarding intervention approaches or models used to achieve the aimed integration of screening or care of DM. Task shifting to non-physician clinicians (Labhardt et al., 2010), the integrated Chronic Care Clinic, locally called IC3 or "Ice-Cubed" through task shifting and decentralisation (Kachimanga et al., 2017; Wroe et al., 2015), medication adherence clubs (Venables et al., 2016), mobile testing (Govindasamy et al., 2013) were the few documented approaches adopted to integrate screening or care DM in the context of multimorbidity. Other studies strived for integration of screening or managing DM along with other services or available protocols in the facility but without a specified model used for this particular purpose.

Discussion

In most high-income countries, patients with multi-morbidities including NCDs like DM have access to family doctors or general practitioners and health care facilities equipped to provide appropriate integrated care and address multiple health problems (Health Council of Canada, 2012; Martínez-González et al., 2014; Rijken et al., 2017, 2018). In contrast, Africa does not generally possess enough facilities and the required resources to offer integrated care models like ICCC, integrated chronic disease management model, among others (Capelli et al., 2016; Garrib et al., 2019; Mahomed & Asmall, 2015; Oni et al., 2014) for DM. In the context of multimorbidity and severe

resource constraints, few studies included in our review followed well-described integrated care models, as seen in the results.

Only one study of Labhardt et al. on the integrated intervention of hypertension and T2DM into PHC clinics conducted by clinical nurses in rural Cameroon (2010) assessed after two years, had a low risk of bias. We did not identify any RCTs.

The Labhart et al study (60) highlighted that fully integrated management of DM is feasible (Labhardt et al., 2010). The findings (Labhardt et al., 2010) demonstrate that with adequate training and supervision for nurses on T2DM prevention, diagnosis and care and the provision of additional needed equipment and drugs to the existing facilities within national health system framework, successful integration into PHC is possible. Another study conducted under the fully integrated chronic care clinic in Malawi by Wroe et al. (Wroe et al., 2015) in 2015 had similar results. With lessons from a previously failed partial integration intervention, existing HIV platforms were used to benefit NCDs including DM in terms of prevention, diagnosis, care and follow-up to trace the defaulters (Wroe et al., 2015). Both of these fully integrated interventions have shown how tasks to prevent, screen and treat DM and other NCDs could be shifted from doctors to nurses and other health care workers in the clinics and communities (Labhardt et al., 2010; Wroe et al., 2015). Drawing on the experience of scaling up HIV testing and care in Africa, task-shifting could be seen as a good strategy to increase the availability and accessibility of clinical services that are also cost-effective to deal with the rising burden of DM and other major NCDs at primary care (Frieden et al., 2020; Heller et al., 2019; Joshi et al., 2014; Kengne et al., 2009, 2009; Varghese et al., 2019). However, other studies included in this review were of partially integrated interventions that did not assess task shifting or task sharing aspect of services integration and were limited to either DM screening, care or both and other components as above shown in the results section. The main finding in relation to

our study question was that full integrated screening and care have been shown to work well within multimorbidity approaches in PHC, although only two studies covered this.

As one of the main review outcomes, integrated DM screening conducted has led to early detection of unclassified DM in nine studies, and DM would be T2DM and GDM if it were categorised well in those respective studies. These new screened patients were asymptomatic when diagnosed for the first time in the integrated package of services and had an opportunity to be initiated on treatment before complications appear, while those found to be in pre-diabetes stage with impaired glucose had time to change their lifestyle in order to prevent or delay DM onset (American Diabetes Association, 2004, 2016, 2018). While arguing that the early detection of T2DM should align with changes in LMICs' health systems, Narayan et al. recommend an integrated approach to address the rapidly increasing T2DM rates and its associated complications or other NCDs in the most cost-effective way (Narayan et al., 2011).

The last outcome from this review was cost-effectiveness, suggested in seven studies. Only one study conducted by Golovaty et al. in South Africa in 2018 analysed the cost of the home-based integrated screening of NCDs including DM into HIV testing and counselling (Golovaty et al., 2018). Others neither systematically measure the costs, nor the health outcomes (Petitti, 2000) of DM integration as an intervention option within multimorbidity. Desmedt et al. in 2016 did not find any study from African country to include in their research assessing the economic impact of integrated care for patients with NCDs including T2DM (Desmedt et al., 2016). In fact, a study by Pfaff et al. in 2018 included in this review did not find a publication with formal cost-effectiveness of NCDs and HIV, a disease with supported interventions in Africa (Pfaff et al., 2018). HIV programmes, especially in Africa could present an opportunity for measured integration of NCDs, against the always mentioned potential cost-savings of integrated NCD screening and treatment (Hod et al., 2015; Pfaff et al., 2017, 2018).

Strengths and Limitations

Strengths

For this systematic review and meta-analysis, many databases were searched and all identified evidence of integrated management of T2DM and GDM within multimorbidity through-out the continent were analysed, even though few studies qualified for inclusion. To our current knowledge, no other study has comprehensively assessed integrated management of DM within multimorbidity in Africa.

Limitations

Many studies that could have enriched this review did not have integrated DM screening and care interventions but merely focused on prevalence or others aspects that did not meet this study's inclusion criteria. Lack of RCTs to meet the study inclusion has shown the critical paucity of low-bias, rigorous data and highlights the need for breakthroughs in this important health systems domain. No study was found to meet the review inclusion criteria in many sub-regions and countries in the continent hence its findings may not represent or be generalisable to all African regions and countries. GDM as a specific health problem for a particular group of population prone to other diseases or risk factors, that has been increasing in recent years, did not clearly appear in studies included in this review and would be important to consider it for further integrated services.

Conclusions

All included studies demonstrated the feasibility and benefits of integrated management of DM within multimorbidity in PHC and emphasized the importance of integration. Only two studies reported on fully integrated interventions and both were successful. Some studies suggested that the integrated interventions to screen and care for DM in the context of multimorbidity could potentially be cost-effective, although scarce evidence of its formal analysis was noted. More original research

and review studies are needed to analyse integrated management of T2DM and GDM practices within multimorbidity in Africa.

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PART THREE: DISCUSSION AND CONCLUSIONS

CHAPTER 7: DISCUSSION

7.1: Overview

This chapter discusses the main results of this thesis and is structured according to the four study objectives. It also discusses the key messages of this study and the application or relevance of the research findings in public global health. Even though each article discussed its own strengths and limitations, I add some general strengths and limitations of this study.

The overall goal of this thesis was to explore the integration of GDM management and prevention of T2D post-GDM within routine, community-based PHC services in urban South Africa, with a particular interest in whether the experience of PMTCT integration of HIV-positive women and of HCPs may offer insights into how T2DM prevention can be integrated into post-natal primary care. Four specific objectives were formulated to achieve this research goal: 1) Document the history and experience of PMTCT integration into routine primary health care, particularly in South Africa. (Papers One and Two). 2) Analyse how GDM and T2DM are currently managed and integrated within South African PMTCT programmes, and investigate the advantages and disadvantages of integration of PMTCT as perceived by the various stakeholders in the study site (Paper Three). 3) Explore stakeholders' perceptions (CHWs, managers, policy makers, and women) regarding the current and optimal level of integration of GDM and T2DM with antenatal and postnatal PHC (Paper Four). 4) Assess the contextual facilitators and barriers to scale-up and sustainability of an integrated T2DM prevention intervention into routine, community-based PHC services in South Africa and contribute to the process evaluation of the initial phases of the ongoing implementation of the IINDIAGO prevention intervention (Papers Four, Five, Six).

PMTCT is at the forefront of HIV prevention strategies and has been successfully integrated (Vrazo et al., 2018; WHO, 2010a). HIV prevention measures were increasingly initiated in the 1990s, and PMTCT rapidly became a critical WHO strategy for HIV prevention, care and treatment among women and babies. In addition to the clinical elements of the PMTCT cascade, described in Paper 1, WHO guidance for implementing PMTCT at scale identified 7 principal strategic directions: commitment; technical guidance; integration; equitable access; health systems; measurement; and, collaboration (Ainsworth, 1998; Kelly, 1999; Luo et al., 2007; WHO, 2010a). Globally, WHO itself had to partner with various actors at international, regional and nation levels to accelerate PMTCT scale-up in order to deal with the then exploding new HIV infections among children and women (Idele et al., 2017; WHO, 2010a). This mobilisation and increased funding and monitoring of the programme yielded tangible results. It renewed the hope of policy makers and researchers for eliminating MTCT by implementating and integrating PMTCT services into PHC, especially in SSA which accounts for the majority of the world's HIV burden among adolescent girls and young women (Audureau et al., 2013; Mahy et al., 2010; UNAIDS, 2019). PMTCT has progressively gained recognition as an integrated and functioning HIV prevention programme and PMTCT interventions have, in coordination among health authorities, NGOs and local stakeholders, contributed to efficient and effective health services at the primary level of care (Kiragu et al., 2017; Odeny et al., 2013; Pfeiffer et al., 2010; Price et al., 2009; Sweeney et al., 2012). PMTCT integration has also positively influenced MCH services for HCT, uptake and adherence to ART, even though the postnatal care component still faces implementation challenges in many LMIC facilities (Ambia & Mandala, 2016; Herlihy et al., 2015; Turan et al., 2015). Some women (and their infants) looked after throughout the PMTCT cascade suffer from other conditions with serious consequences, notably NCDs including GDM and T2DM (Gowshall & Taylor-Robinson, 2018; Sinha et al., 2018). Unlike PMTCT, women have to navigate complex and often fragmented health systems to access health care services for these

co-morbidities and, as other research has suggested (Levitt et al., 2011; Muhwava et al., 2018; Nyaaba et al., 2017) and this study has found, the gaps in care are significant. I decided to explore how PMTCT was integrated in SSA, especially in South Africa, and whether and how this PMTCT integration experience could help to integrate GDM screening and T2DM prevention initiatives within PHC services.

The following sections of this chapter discuss the findings for these four objectives.

7.2: History and experience of PMTCT integration (Objective 1)

The narrative review, Paper One in the Results section of this dissertation, examined published research on PMTCT, its integration and impact on other PHC services across SSA. The findings it yielded were the foundation for the design of appropriate data collection tools in order to build datasets responding to the empirical research objectives. Findings from this review partially addressed the first objective. They were complemented by the results reported in Paper Two, which explored the perspectives of experts and health care workers at the frontline on the history and outcomes of integration of PMTCT into PHC services after AIDS denialism in South Africa. These two articles offer a big picture of PMTCT integration in general, detailed how the broader context of AIDS denialism politics delayed its initial scale up in South Africa and documented how the South African Government made sustainable efforts towards PMTCT integration in all PHC facilities in the country.

In 2010 the Department of Health revised the National PMTCT Policy and specified the essential components for the PMTCT programme in four categories that were focused at each step of the cascade - antenatal care, labour, delivery and during the postnatal period (Department of Health, Republic of South Africa, 2010). These components were viewed as too complex to be provided simultaneously at scale across clinical units nation-wide and the DoH decided that a more feasible and effective approach to scale up PMTCT, especially in the context of fragmented and overburdened

health systems (Doherty et al., 2009), was to integrate progressively into existing programmes (Department of Health, Republic of South Africa, 2010). Also, South Africa has a history of high ANC attendance (90%) and health professional-assisted delivery at 84% (Day & Gray, 2008). This context facilitated PMTCT integration within MCH and PHC services.

Using the adapted CAS framework, I considered the health system as an open system that interacts with actors in the community and beyond to expedite PMTCT integration (Kannampallil et al., 2011). For example, the PMTCT rollout was initially resisted by frontline health workers, who slowly came to acknowledge its, then joined the efforts to integrate it within existing services. Healthcare workers now take it for granted that PMTCT is integrated into routine public PHC – to the extent that some study participants felt it had always been integrated (Mutabazi et al., 2020). This historical experience is now being repeated to a large extent in screening and management of GDM. Staff report being overwhelmed, and observations support these perspectives as shown in Papers Three and Four, but on reflection health workers are supportive of the idea of integration as proposed in the IINDIAGO project, though this integration is far from being taken for granted.

Nurse-Initiation and Management of ART (NIMART) training was initiated to bridge the gaps in training of nurses, who in return contributed to a decentralised approach, overcoming issues of poor doctor/patient ratios to make PMTCT integration into PHC services successful and sustainable (Mboweni & Makhado, 2019; Nyasulu et al., 2013). Other constraints to full PMTCT integration towards eliminating MTCT in South Africa (Davies et al., 2013; Jones & Cameron, 2017; Sanne et al., 2010) were raised and the CAS framework offers a way to think about further solutions and improvement in health systems, drawing on the experience of developing and implementing NIMART in South Africa's complex political and epidemiological context.

The key messages arising from Papers One and Two are:

- Integration of PMTCT has occurred in Africa, at various levels from partial to full integration;

- Integrated PMTCT has strengthened services and programmes directly related to reproductive health but with less clear findings regarding impact on broader health systems;
- Political context is very important and is perceived differently by policy experts and managers versus frontline workers, and
- Once integration has occurred – after a long and difficult public health and advocacy struggle – it is taken for granted by health workers and faces the same challenges as any other health programme, such as human resources, training, supervision, infrastructure, budgets, and monitoring and evaluation.

The achievements of PMTCT integration in local facilities were agreed upon by all participants in the study described in the second article. This supported the proposal to examine more closely how GDM is screened among women undergoing PMTCT and how PMTCT integration lessons could serve to integrate GDM screening and T2DM prevention interventions.

7.3: GDM screening and care among women in the PMTCT programme (Objective 2)

Integrating HIV/PMTCT within PHC clinics has transformed the way services are provided in health care systems (Mutabazi et al., 2017; Turan et al., 2015; Wiegert et al., 2014). A "one stop shop" model, combining a range of services and providers in *one health setting,* is no longer a dream but a feasible and best practice for strategy of health care delivery in most high income countries but not in many LMICs, including South Africa (Hetrick et al., 2017; Schäfer et al., 2018). With the adapted framework combining WHO's six building blocks and health systems integration (Atun et al., 2010b; Shigayeva et al., 2010a; WHO, 2015) used in Paper Three, I reviewed the current revised PMTCT and post-natal care (PNC) guidelines in the Western Cape, South Africa and analysed how they were implemented to integrate PMTCT. Using previously unanalysed Western Cape Province

PMTCT data and qualitative data from interviews with experts, health care providers and women diagnosed with GDM while undergoing PMTCT, I also assessed how women navigate systems for what proves to be unintegrated HIV and GDM screening and care.

While initiatives and collaboration at health system and community levels helped to enhance integration and retention of women under PMTCT in ANC and PNC, women diagnosed with GDM have no such assistance during pregnancy and are not followed up after delivery. I did not find any records of women with GDM in PMTCT records. The tertiary care facility (Groote Schuur Hospital) realised this failure and appointed a nurse/midwife with training in PMTCT to address the specific health needs of HIV-positive women in the diabetic clinic of the maternity ward, but nothing is planned for them after delivery. Experts, HCPs and patients all supported the integration of GDM within PMTCT and into PHC, a change that would help to deal with post-partum complications for both diseases (PMTCT and GDM) (Martí et al., 2007). PMTCT includes continuous testing, lifelong medication, behavioural change, follow-up of women during ANC and after delivery and monitoring and evaluation of the programme, and these components are directly relevant to integrating GDM and other NCD screening and T2DM prevention.

The key messages arising from Paper Three are:

- GDM screening and care are not integrated into PMTCT and ANC in South Africa and no records of women screened or diagnosed with GDM were available in PMTCT indicators;
- while women diagnosed with GDM under PMTCT receive integrated care in the diabetic clinic of maternity at tertiary care level, they do not get any follow up after delivery;
- integration of GDM into PMTCT and into PHC is supported by experts, health workers and patients;
- PMTCT and PNC policies need to be revised and include GDM screening and follow up of these women after delivery in order to make GDM integration into PMTCT possible.

I therefore suggest, on the basis of these findings and Papers One and Two, that GDM screening and T2DM prevention initiatives could start with women who are already under the PMTCT programme and then be expanded within PHC services. This requires policy changes and the involvement of health policy makers, as has been the case for PMTCT.

7.4: Integration of T2DM prevention after GDM into community-based PHC services (Objective 3)

Africa faces an increasing GDM prevalence (Chivese, Werfalli, et al., 2019), which increases risks of subsequent T2DM for mothers and their offspring (Ferrara, 2007; Teh et al., 2011). GDM screening in PHC is thus a starting point for care and prevention interventions for T2DM, but screening is not mandatory in South Africa's current guidelines or elsewhere. Changing this situation so that GDM screening and follow up are routinely implemented poses a serious challenge for health systems in LMICs, beyond the first essential step of amending policy and guidelines (Bhavadharini et al., 2016). This requires contextualized analysis of multiple and diverse barriers to proper GDM screening and follow up of women with recent GDM including: health system weaknesses at all levels; poor understanding of postpartum GDM risks of T2DM development for both women and their babies; and different patient, community and health service level barriers for women when they are referred back into PHC for follow-up after delivery (Bennett et al., 2011a; Nielsen et al., 2012, 2014). Paper Four highlights structural challenges facing individuals, like low household income, illiteracy, transport issues, cultural beliefs and practices and others (Geleto et al., 2018; Kyei-Nimakoh et al., 2017) that in addition to health system barriers complicate access to and delivery of NCD screening, care and prevention (Heller et al., 2019). In Paper Four, different datasets were triangulated and the integrated findings suggest that several changes in the content, resourcing and implementation of policies are needed to effectively integrate GDM screening and T2DM prevention

interventions in South Africa, including universal screening of GDM, increasing the expertise and knowledge of nurses and educating pregnant women regarding GDM and its risk factors, – in addition to addressing broader social determinants of health. The BCW framework enables examination of these multiple but interconnected issues through the different layers of the framework and shows how health systems might consider many elements and complementary approaches to conceive and implement comprehensive interventions. The key messages arising from Paper Four are:

- GDM screening is not mandatory in the guidelines in South Africa and is therefore not integrated into ANC;
- multiple barriers impede integration of GDM screening, care and follow-up of women with recent GDM for T2DM prevention interventions;
- integration of the proposed universal GDM into ANC and postnatal T2DM prevention initiatives have are favoured by experts, HCPs and patients but clear policies and guidelines as well as ongoing support are needed.

The findings in this Paper show that decision makers, health workers and women all have a role to play in order to arrive at integrating T2DM prevention initiatives into community-based PHC services. The IINDIAGO project underway in Cape Town and Soweto is exploring whether interventions during pregnancy could be strengthened and referral to postnatal follow-up could be linked to babies' immunisation, which normally starts soon after delivery and discharge from hospital, and to community-based peer support. The findings of the IINDIAGO project would take the research reported in this thesis to the next stage.

7.5: Integrated management of GDM and T2DM in the context of multimorbidity in Africa (Objective 4)

Most countries in Africa are not equipped to deal with rising NCDs including GDM and T2DM; integrated interventions are especially lacking (Capelli et al., 2016; Garrib et al., 2019; Mahomed & Asmall, 2015; Oni et al., 2014). The gaps and barriers at all levels of health systems and community are reported in the narrative review and empirical results of Papers One through Four, especially in terms of NCDs compared to PMTCT or other programmes targeting infectious diseases. Patients are often diagnosed with more than one disease, each treated in different ways. The few studies throughout Africa that included DM in the context of multimorbidity show the paucity of integrated interventions, and the finding in Papers Five and Six (published protocol and submitted systematic review) urge for more integrated intervention and research in this domain. Though partially integrated interventions to screen or care for DM along with other disease were preferred, two studies out of thirteen included interventions that were fully integrated and had promising results. Again, the experience of HIV/PMTCT scale-up in Africa using strategies like task-shifting, decentralisation and linkage were shown as good approaches towards increasing the availability and accessibility of cost-effective clinical services to deal with the rising burden of DM and other major NCDs at primary care (Frieden et al., 2020; Heller et al., 2019; Joshi et al., 2014; Kengne, Fezeu, et al., 2009; Kengne, Sobngwi, et al., 2009; Varghese et al., 2019).

As my project evolved, and in the context of co-morbidity and multimorbidity, I began to explore syndemics theory in order to comprehend how many health problems and their underlying factors interact in a population and how complex interventions can address not only more diseases but also shared structural and individual risk factors (Hart & Horton, 2017; Mendenhall et al., 2017). In the same vein as the frameworks I used, syndemics theory offers a broad and useful approach to

considering NCDs like GDM and T2DM while diagnosing, treating and preventing other diseases and health problems and their determinants (Ferlatte et al., 2018; Mendenhall et al., 2017; Tsai, 2018) and may offer an overall framework that is "closer to the ground" than CAS theory and allows better integration of social, behavioural and health systems factors than the WHO building blocks. This framework could be explored in a further analysis of my findings, or in further empirical work.

The key messages arising from Paper Five and Six are:

- There are few studies on the integrated intervention; screening and care of DM in the context of multimorbidity in Africa;
- Most of the included studies were partially integrated (11/13) and only two studies were considered fully integrated and these yielded better results.

The overall message of this thesis is that the integration of health care services and systems is an important but challenging approach that helps to improve access and utilisation of services and thus strengthen health systems. The results presented throughout this thesis have shown how the process towards integration requires a multistage process that includes not only changes in policies but also cooperation of various actors at all levels. A close, iterative and transparent monitoring and evaluation of the process is needed so that the experiences gained in the early implementation stages could lead to further integration in terms of levels or service packages offered.

PMTCT roll-out in South Africa was initially impeded due to national politics during the AIDS denialism era. This changed from the middle of the first decade of the 2000s, and the country worked with various partners and invested significantly into the programme to integrate PMTCT into all PHC services through policies, adequate funding, and training of frontline health workers, managers and a network of CHWs who play key roles in outreach and adherence to ART. PMTCT integration in South Africa, although partial and not perfect, is an inspiring example of how

integration of health services could evolve and help to meet the critical health needs of a population. This PMTCT experience should not be lost or limited to HIV but rather serve as an opportunity to integrate other services for the same population into existing programmes and into PHC more broadly. GDM is a growing health problem and affects many women under PMTCT. Unfortunately, GDM screening and post-partum follow up interventions to prevent T2DM for these women and their babies are not integrated into PMTCT and PHC, despite the many parallels between HIV and GDM/T2DM documented in this thesis.

Based on the experience of PMTCT integration, where comprehensive national and provincial policy guidelines were crucial and eventually implemented, GDM screening and care as well as T2DM prevention interventions should be specifically included in the PHC re-engineering that has been under way in South Africa (Pillay & Barron, 2011), in order to reduce preventable DM related mortalities and morbidities and improve the health of this population. Beyond including them in policy and guidelines, this thesis has shown that attention to the complex details of both the health problem and the health system is essential. GDM and NCD management often require specialist treatment, which is not easily accessible. Women and their families face many socio-economic constraints and barriers to accessing health care as well as the healthy diets, physical activity and social support needed to manage GDM and prevent T2DM. The referral system is complex to navigate, and poor communication between facilities (clinics and hospitals) complicates implementation of such complex integrated interventions. Finally, the historical experience discussed in Paper 2 highlights the importance of sustained, evidence-based advocacy. While the study's key finding that the lessons learned in integrating HIV, and specifically PMTCT, have not been generalized beyond the HIV-focused community, emphasizes that much still needs to be done to break disease-based siloes reinforced by decades of vertical programming and disease-based research. Recognizing and dealing with these challenges and gaps would increase the availability

and improve quality of PHC services in Western Cape and at national level as well as setting an example of good practice for other health systems in LMICs. However, it is still necessary to go deep into the details without losing sight of the big picture in order to achieve this vision.

7.6: Strengths and limitations of the study

7.6.1: Strengths

The major strength of this study is that it combines detailed empirical and literature-based analysis of how one major complex health intervention for women and babies – PMCTC – was integrated into primary health care and empirically explores whether the lessons of integration for this HIV-focused programme have been, and could be, applied to integrate a second major complex health intervention: the management of GDM and prevention of T2DM. The study recognizes the importance of macro and political context as well as micro-level context, implementation and behaviour, and it attempted to apply a multi-level conceptual approach to the challenge of integrating complex interventions into LMIC health systems. This study first documented what was done - advances and approaches in PMTCT integration - by means of a systematised narrative review. The combination of the review (Paper One), an empirical study looking at the history of PMTCT (Paper Two), and an empirical paper examining the outcomes of integrated PMCTC and whether GDM is in return integrated into PMTCT (Paper Three) is innovative and of practical and policy relevance. It retraced the history of PMTCT and challenges surrounding its initial integration as well as the progress recorded over time. Lost lessons or opportunities that could be relevant for the integration of other interventions into community-based PHC were highlighted. This study showed that many of the challenges currently facing integration of universal GDM screening and continuity from ANC to post-partum for T2DM prevention were also faced for HIV. These lessons from HIV and specifically PMTCT have not been well integrated by NCD researchers. The papers published will help bridge

this gap. For the systematic review and meta-analysis, many databases were searched and all identified evidence of integrated management of T2DM and GDM within multimorbidity throughout the continent was analysed, even though few studies qualified for inclusion. To my current knowledge, no other study has thoroughly assessed integrated management of DM within multimorbidity in Africa.

This dissertation included experts, HCPs and women from different backgrounds and with diverse perspectives. Participants ranged in their years of involvement in PMTCT services, included those who had been involved in pre-2008 PMTCT services during AIDS denialism era. Those who participated in policy making and implementation for both PMTCT and GDM screening and care shared their insights regarding facilitators and barriers to integration health services into PHC. Drawing from different conceptual frameworks, the study accessed a larger environment to scrutinise health systems, community and individuals involved in services design, provision, use and evaluation.

This study also contributed to the formative research of IINDIAGO and played a central part in exploring the perceived acceptability and feasibility of women's and the health system's adoption of such an intervention. Process evaluation is a very important part of complex intervention design, implementation and testing (Moore et al., 2015b). It offers opportunities to explain the outcomes of intervention referring to the actors, resources and contextual factors that affect these outcomes, suggest improvement and provide roadmaps for future research and practice (Limbani et al., 2019; Murdoch, 2016). As described in the IINDIAGO protocol, process evaluation in complex intervention implementation research such as the IINDIAGO project includes formative research as well as analysis of context, the implementation itself, and the potential for adoption and scaleup. None of the papers in this thesis are specifically identified as "process evaluation", but collectively they contribute to the study and its ongoing process evaluation. As reported in Papers Three and Four, IINDIAGO

enjoyed support from all participants in this study and its revised protocol is being implemented. Findings from formative research and data collected at the beginning of recruitment period identified areas for adjustment that were made in the trial protocol and questionnaires. Consultations with facility managers and staff members who deal with referred women diagnosed with IGT and GDM, reported in Papers Three and Four, helped to update and finalise the intervention tools. Research team members come together biweekly for debriefings about meetings with other stakeholders, report on progress, and continued implementation of the trial and the ongoing process evaluation. During my fieldwork and data collection periods in Cape Town, I actively participated in those meetings and exchanged with IINDIAGO team members regarding the issues surrounding the trial, barriers encountered and the measures taken to address them. I took notes to track updates in implementation, changes or adaptations and other issues related to the implementation, in order to ensure fidelity to and quality of the planned intervention, and I supported and supervised interns conducting additional elements of process evaluation, after my own thesis fieldwork was completed. Because of numerous delays in implementing IINDIAGO (related to funding agreements and local contextual challenges), this doctoral research contributed directly only in the early periods of the trial, which is still ongoing.

7.6.2: Limitations

Despite these strengths, this study also had many limitations. The reviews were highly complex and included a range of issues such as integration, health services, PMTCT, GDM, T2DM, multimorbidity and many more that could not all be reviewed in only two papers despite rigorous methodology.

Some countries and regions appear less or not at all in published research and I was unable to find out how their health systems work or how health services including PMTCT, GDM screening and other interventions are integrated. Therefore, this study's findings may not represent or be generalisable to all African regions and countries. Many studies that could have enriched this review

did not have a specific integration component and most well-designed and implemented interventions focused on prevalence or others aspects that did not meet the inclusion criteria. Power, positions and partnerships are always different between countries and regions of the continent and this influences how health interventions are funded and reported, a context that shapes what is seen in the research publications.

While the IINDIAGO intervention includes the two major urban areas of South Africa, resource and time constraints limited my empirical health system assessment to Cape Town. This limits its generalisability. Integrating health services is always a complex and context-specific exercise as discussed in the first chapter of this dissertation, As Atun et al. argued, integration is not a binary yes/no function but is instead a difficult and changing process over time (Atun et al., 2010b). Even within the Cape Town setting, I was only able to access a subset of clinics and communities and I could not reach everywhere to document every progress or hear every story that could have been useful for this study. Health care providers in the clinics were dealing with many tasks and some complained of work overload. They sometimes told me that they were running out of time and some details in the discussion could have been forgotten or missed due to this pressure.

Social desirability may have influenced findings that came out of interviews and FGDs conducted with different participants and some practices, lessons as well as issues and challenges may not be captured. The Western Cape and Cape Town have some of the best health systems and had hosted the first PMTCT pilot sites in the country - therefore, the practices and experiences of health care practitioners working in this region may vary substantially from those of other provinces in South Africa. South Africa has its own health systems (national, provincial and district) but it is generally very developed compared to many countries in Africa and other LMICs out of Africa and lessons from this study may not be applicable in those other contexts. Even though different types of participants were involved in this study and rich datasets were triangulated, a relatively small sample

size was used, especially for women diagnosed with GDM while under PMTCT and the findings may not be representative of the all experiences and practices of what happens in South Africa.

Reflecting back on my data collection, it was easy to access information about PMTCT and participants were forthcoming with stories that praised PMTCT integration into PHC, and they demonstrated extensive and accurate knowledge of HIV and PMTCT. The situation was different when discussing GDM and T2DM. Data collection on DM, specifically GDM, came later in my fieldwork and I wished I had more time on the ground to learn more about health workers and women in both their local facilities and communities. I attended and presented papers in various international conferences during this PhD research and did well discussing PMTCT, but the GDM and T2DM components came later in my analysis of datasets. If I had had more information earlier on, about GDM among women under PMTCT and how health systems deal with them, some of the findings regarding both could have been appeared in more of my presentations and helped to bridge the persisting gaps across disease-based research, policy and practice. My personal experience shows how complex, lengthy and challenging the process of applying lessons of integration across HIV and NCDs is in practice.

7.7: Application of the research findings and future directions

Health services and systems form part of social determinants of health (Braveman & Gottlieb, 2014; Labonté & Schrecker, 2007) that need to be considered with as a whole to deal with complex health problems. GDM screening and T2DM prevention initiatives cannot be addressed by health services and systems alone but must be addressed along with other factors. These other factors include policies and political context, socio-economic conditions including the food environment as well as social and built environments, collaborations, community participation, training, and the broader labour relations environment among others.

Nevertheless, health services and systems are an important part of this comprehensive approach to dealing with complex public health problems. This study adds new evidence to the existing body of knowledge on PMTCT/HIV and health systems integration, and it shares this knowledge outside of the community of HIV experts thus bridging across HIV and NCD silos in research and in practice. It gives specific insights on how to learn and use learnt lessons to implement a different programme into PHC services. It identifies facilitators and barriers to GDM screening and T2DM prevention interventions and its integration within PHC based on what is known to have worked or not for the same population. It explored an approach to designing and implementing a new intervention that is very important in public health interventions, not starting from scratch but using available resources. This contextualised study that let the local realities drive data collection and results interpretation, may serve as a case study covering many aspects of global health. Working with multidisciplinary teams on the ground and during analysis, results interpretation and report writing, offered many opportunities for reflexivity, for contributing to teamwork and for initiating or sustaining collaborations. Weaknesses in health systems identified in this study could be addressed and help to improve health outcomes of other interventions. This study's findings could inform other researchers in this domain and lead to further comparative analysis in terms of health services integration into PHC, focusing on PMTCT, diabetes or other NCDs and beyond.

The research reported here demonstrates the breadth and complexity of what is relevant to consider and analyse to move towards health system integration. This discussion has been structured according to the objectives of the study, in order to lay out step by step and in detail what has been learned and might be adapted from the PMTCT experience to the integration of GDM and T2DM interventions in PHC in South Africa. As mentioned above, the PMTCT lessons are complex, and I have only begun to explore in depth how they might specifically inform GDM and NCD integration. The immediate next steps in my own research are to finalize publications and prepare additional

knowledge translation products to help bridge the existing gaps between HIV and NCD research, policy and practice, so that the empirical findings reported here can be more accessible. After that, I believe that a deeper synthesis and analysis of the findings using different frameworks – including health policy analysis (Walt et al., 2008) and, especially, syndemics theory (Hart & Horton, 2017) – would help to make the complex empirical findings and implications easier to address. Finally, I continue to be involved with the IINDIAGO team and will ensure that the lessons from this thesis are integrated in the overall evaluation and recommendations of that ongoing intervention study.

As a thesis in public health (global health specialisation) and based on the findings of this thesis, I offer the following recommendations to:

Public health authorities in Western Cape: integrating PMTCT into PHC services had clear advantages for women and their babies who attend the local facilities and access all HIV related services. Other health services for this population within PHC could build on the PMTCT gains. Women attending ANC get HCT services, those who test positive are immediately initiated to ART regardless of their CD4 count, following the option B+ guideline implemented in the province and countrywide, and they are followed up before and after delivery with their babies. Adherence to ART has been increasing, and the PMTCT programme, as a whole, in all local facilities has been appreciated by women; CHWs; health care providers in the clinics; researchers; and policy makers. As such, PMTCT services offer a window of opportunity for reinforcement towards integrating other health screening and treatment services for both women (during ANC) and their babies in post-partum. DOH could link the implementation of other interventions for this population to the integrated PMTCT services instead of starting over with a different vertical programme. This would facilitate reaching and keeping most of these women and their babies in that intervention, which could be monitored using the existing structures. Therefore, I would suggest starting, where appropriate, with the population under the integrated PMTCT services and expand to others, in a strategy that could

enhance continuity of care for women and their babies. In this context, frontline health care workers including CHWs who participated in this research expressed their support to integrating GDM screening and T2DM prevention interventions into PMTCT and agreed they could play a role on that integration once they are adequately trained.

National health department and international agencies: The outcomes of PMTCT integration in Western Cape could, together with other experiences, offer a foundation for national and global reflection on how to mobilise forces at all levels (international, national, provincial, district and local) to successfully implement and integrate complex interventions of PMTCT magnitude. NCDs such as GDM and T2DM have been categorised as a rising health threat, including for women under PMTCT, and GDM and T2DM screening and management could be integrated into PMTCT cascades and PHC if included in international and national health policies and funding made available. WHO may be able to draw on the published findings and the words and ideas of the women and health workers who participated in this research to encourage and assist African health systems to integrate NCDs into already functioning health interventions within the PHC.

7.8: Conclusion

The overall aim of this thesis was to explore the possible integration of GDM management and prevention of T2DM post-GDM within routine, community-based PHC services, drawing on the lessons learned from integration of PMTCT programmes into PHC in South Africa. Using mixed methods, this study highlights the benefits of integrated screening and management of diabetes among other NCDs while learning from what happened elsewhere and in other programmes, which is the essence of global health. This thesis concludes that although full integration rather than partial integration was not always opted for, due to structural and operational challenges, women, health workers, managers and experts all considered that the full instead of partial integration of health

services to screen, diagnose and care for chronic diseases including GDM and T2DM into routine PHC, following the PMTCT approach, was both desirable and feasible. However, the lessons learned through the history of PMTCT and its integration have not been adapted to this next public health challenge.

As a successful public health intervention to reduce vertical transmission of HIV, PMTCT has influenced other PHC services, especially those delivered to the same population, women and their babies, and has generally been credited not only with reducing pædiatric HIV but also improving MCH in sub-Saharan Africa including South Africa. PMTCT services were documented to have increased the availability, accessibility and utilization of ANC and postpartum services beyond HIV when integrated.

Since 2008, PMTCT was prioritised in South Africa and the Government in partnership with various organisations and actors worked to consistently make it a successful response following the AIDS denialism era in the country. The results included in this thesis recapitulated barriers as well as opportunities to address operational challenges towards full integration of PMTCT and other important health services in local health settings.

PMTCT services do not include GDM screening and care and women under PMTCT who were in parallel diagnosed with GDM in routine ANC were not recorded in PMTCT register as suffering from other co-morbidities like diabetes, hypertension or others. Screening and care of GDM outside of PMTCT negatively affected the quality of services and overall health outcomes for these women and their babies. However, the experience of PMTCT integration in Western Cape leads to the suggestion of feasible integrated antenatal GDM screening and post-partum initiatives for preventing or delaying T2DM into PMTCT and primary care.

Given that many women do not benefit from GDM screening on time and that some are entirely left out of this critical diagnosis due to the current health policies and health system structures

in South Africa, universal GDM screening and postnatal follow-up of these women and their babies in their community based PHC is a desired solution. Although it was considered desirable by women and potentially feasible by HCPs and experts, it would require addressing resource and training issues in PHC as well as socio-economic barriers that women face in their daily lives. Integrating post-GDM prevention initiatives would only be possible if communication is improved between local facilities and referral hospitals where women diagnosed with GDM are referred for pregnancy follow-up and delivery. Proper health education measures to prevent or delay T2DM onset for these women has to be ensured during pregnancy and in PNC in order to increase knowledge about GDM and its consequences for them and their babies. Interventions to support the capacity of women and communities to act on this knowledge are also critical but were not directly explored in this thesis. As was the case when PMTCT was being integrated, guidelines need to be adopted to the alarming situation of GDM screening and follow-up of women with GDM and their infants, and HCPs including CHWs have to be trained, supervised and supported, so that they could play an effective role in GDM screening as well as in T2DM prevention. Additionally, social determinants of health and the social and health inequalities facing the majority of South Africans have to be considered at all times and in all health policies and initiatives.

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APPENDICES

Ethics certificates

Comité d'éthique de la recherche du CHUM
Pavillon R, 900 rue St-Denis, 3e étage
Montréal (Québec) H2X 0A9

Le 11 mai 2017

Docteure Christina Zarowsky
Axe de recherche: santé mondiale

a/s: M. Jean-Claude Mutabazi

Objet :	**17.044 – Approbation initiale-FINALE (CÉR restreint)**
	Exploration de l'intégration des systèmes de santé en Afrique du Sud urbaine: de l'intégration des programmes de prévention de la transmission mère à enfant du VIH, à la prévention du diabète de type 2 après un diabète gestationnel

Docteure,

Nous accusons réception, des documents soumis en vue de l'approbation du projet mentionné en rubrique. Votre projet a été évalué par le CÉR en comité restreint compte tenu qu'il s'agit d'un projet considéré à risque minimal pour les participants. Le CÉR a également procédé à l'évaluation de la qualité et de la pertinence scientifique du projet.

Dans le cadre de notre évaluation nous avons examiné les documents suivants :

- Formulaire de demande d'évaluation éthique d'un projet (formulaire 11)
- Protocole de recherche [date ; 4 mai 2016]
- Autres documents : Full application review decision [date : 2 février 2015]
- Documents destinés aux participants : Draft of data collection instruments
- documents pertinents : Ethics Approval
- documents pertinents : Ethics Extension
- Autres documents
- Soutien Service/Département du CHUM
- Formulaire d'information et de consentement focus groups [date : 01 avril 2017]
- Formulaire d'information et de consentement les gestionnaires et les infirmère [date : 01 avril 2017]
- Formulaire d'information et de consentement les informateurs clés [date : 04 mai 2017]
- Formulaire A [date : 19 avril 2017]
- Formulaire d'information et de consentement IINDIAGO ethics approval with consent forms [date : 04 mai 2017]
- Formulaire d'information et de consentement ethics approval with consent forms [date : 04 mai 2017]

Le tout étant jugé satisfaisant, il nous fait plaisir de vous informer que la présente constitue l'approbation finale de votre projet de recherche, **valide pour un an à compter du 11 mai 2017**. Vous devrez compléter le formulaire de renouvellement que nous vous ferons parvenir annuellement. De même, vous devrez soumettre pour approbation préalable, toute demande de modification ou document de suivi requis par le comité d'éthique conformément à ses Statuts et Règlements et ce via Nagano.

Veuillez noter que le projet de recherche ne pourra débuter avant que vous n'ayez reçu la lettre d'autorisation de réaliser la recherche dans les murs de l'établissement. De même, lorsque cela s'applique à votre situation, le projet ne peut débuter tant que le contrat n'est pas finalisé et dûment signé.

Le comité d'éthique du CHUM est désigné par le gouvernement du Québec (MSSS) et adhère aux règles de constitution et de fonctionnement de l'Énoncé de Politique des trois Conseils (ÉPTC 2) et des Bonnes pratiques cliniques de la CIH.

Pour toute question relative à cette correspondance, veuillez communiquer avec la personne soussignée via NAGANO, ou avec le secrétariat du comité par téléphone ou courriel: ethique.recherche.chum@ssss.gouv.qc.ca – 514 890-8000, poste 14485, ou consulter le fichier «Questions-réponses» au bas de la page d'accueil Nagano**.**

Vous souhaitant la meilleure des chances dans la poursuite de vos travaux, nous vous prions d'accepter, Docteure, nos salutations distinguées.

[redacted]

Me Marie-Josée Bernardi, avocate
Présidente intérimaire
Comité d'éthique de la recherche du CHUM

Université de Montréal

CERSES-19-058-D

Comité d'éthique de la recherche en sciences et en santé (CERSES)

CERTIFICAT D'APPROBATION ÉTHIQUE

Le Comité d'éthique de la recherche en sciences et en santé (CERSES), selon les procédures en vigueur, en vertu des documents qui lui ont été fournis, a examiné le projet de recherche suivant et conclu qu'il respecte les règles d'éthique énoncées dans la Politique sur la recherche avec des êtres humains *de l'Université de Montréal.*

Projet	
Titre du projet	**Exploration de l'intégration des systèmes de santé en Afrique du Sud urbaine : de l'intégration des programmes de prévention de la transmission mère à enfant du VIH, à la prévention du biabète de type 2 après un diabète gestationnel**
Chercheur requérant	**Jean-Claude Mutabazi**, Candidat au doctorat, Ecole de santé publique

Financement
Organisme
Programme
Titre de l'octroi si différent
Numéro d'octroi
Chercheur principal
No de compte

MODALITÉS D'APPLICATION

Tout changement anticipé au protocole de recherche doit être communiqué au Comité qui en évaluera l'impact au chapitre de l'éthique.

Toute interruption prématurée du projet ou tout incident grave doit être immédiatement signalé au Comité.

Selon les règles universitaires en vigueur, un suivi annuel est minimalement exigé pour maintenir la validité de la présente approbation éthique, et ce, jusqu'à la fin du projet. Le questionnaire de suivi est disponible sur la page web du Comité.

[redacted]

Marie-Josée Bernardi, vice-présidente
Comité d'éthique de la recherche en sciences et en santé (CERSES)
Université de Montréal

11 juin 2019
Date de délivrance

1er juillet 2020
Date de fin de validité

1er juillet 2020
Date du prochain suivi

adresse postale
C.P. 6128, succ. Centre-ville
Montréal QC H3C 3J7

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3333, Queen Mary
Local 220-3
Montréal QC H3V 1A2

Téléphone : 514-343-6111 poste 2604
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www.cerses.umontreal.ca

Université de Montréal

Comité d'éthique de la recherche en sciences et en santé (CERSES)

11 juin 2019

Objet: Approbation éthique – « Exploration de l'intégration des systèmes de santé en Afrique du Sud urbaine : de l'intégration des programmes de prévention de la transmission mère à enfant du VIH, à la prévention du biabète de type 2 après un diabète gestationnel »

M. Jean-Claude Mutabazi,

Le Comité d'éthique de la recherche en sciences et en santé (CERSES) a étudié le projet de recherche susmentionné et a délivré le certificat d'éthique demandé suite à la satisfaction des exigences précédemment émises. Vous trouverez ci-joint une copie numérisée de votre certificat; copie également envoyée au Bureau Recherche-Développement-Valorisation.

Notez qu'il y apparaît une mention relative à un suivi annuel et que le certificat comporte une date de fin de validité. En effet, afin de répondre aux exigences éthiques en vigueur au Canada et à l'Université de Montréal, nous devons exercer un suivi annuel auprès des chercheurs et étudiants-chercheurs.

De manière à rendre ce processus le plus simple possible, nous avons élaboré un court questionnaire qui vous permettra à la fois de satisfaire aux exigences du suivi et de nous faire part de vos commentaires et de vos besoins en matière d'éthique en cours de recherche. Ce questionnaire de suivi devra être rempli annuellement jusqu'à la fin du projet et pourra nous être retourné par courriel. La validité de l'approbation éthique est conditionnelle à ce suivi. Sur réception du dernier rapport de suivi en fin de projet, votre dossier sera clos.

Il est entendu que cela ne modifie en rien l'obligation pour le chercheur, tel qu'indiqué sur le certificat d'éthique, de signaler au CERSES tout incident grave dès qu'il survient ou de lui faire part de tout changement anticipé au protocole de recherche.

Nous vous prions d'agréer, Mesdames, Monsieur, l'expression de nos sentiments les meilleurs,

Marie-Josée Bernardi, vice-présidente
Comité d'éthique de la recherche en sciences et en santé (CERSES)
Université de Montréal

c.c. Gestion des certificats, BRDV

p.j. Certificat #CERSES-19-058-D

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[redacted]

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Comité d'éthique de la recherche en sciences et en santé (CERSES)
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Objet: Approbation éthique – « Exploration de l'intégration des systèmes de santé en Afrique du Sud urbaine : de l'intégration des programmes de prévention de la transmission mère à enfant du VIH, à la prévention du biabète de type 2 après un diabète gestationnel »

M. Jean-Claude Mutabazi,

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De manière à rendre ce processus le plus simple possible, nous avons élaboré un court questionnaire qui vous permettra à la fois de satisfaire aux exigences du suivi et de nous faire part de vos commentaires et de vos besoins en matière d'éthique en cours de recherche. Ce questionnaire de suivi devra être rempli annuellement jusqu'à la fin du projet et pourra nous être retourné par courriel. La validité de l'approbation éthique est conditionnelle à ce suivi. Sur réception du dernier rapport de suivi en fin de projet, votre dossier sera clos.

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UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

Form FHS006: Protocol Amendment

HREC office use only (FWA00001637; IRB00001938)			
☑ Approved	☑ Type of review: Expedited	☐ Full committee	
This serves as notification that all changes and documentation described below are approved.			
Signature Chairperson of the HREC	pp T Burgess	Date	23/08/2016

Note: All major amendments must include a local **PI Synopsis** justifying the changes for the amendment. Please note that incomplete amendment submissions will not be reviewed.

Comments from the HREC to the Principal Investigator:
Thank you for this amendment submission. Please note that the HREC consider this a major study amendment. T Burgess
Note: The approval of this protocol amendment does not grant annual approval. Please complete the FHS016 / FHS017 form for annual approval at least one month before study expiration

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	05 August 2016
HREC REF Number	946/2014
Protocol title	Assessing the feasibility and acceptability for an integrated health system intervention aimed at reducing type 2 diabetes risk in disadvantaged women after gestational diabetes in South Africa through formative work
Protocol number (if applicable)	
Principal Investigator	Prof. N.Levitt
Department / Office Internal Mail Address	Endocrinology & diabetes. J-Floor, Old Main Building

FOR HUMAN RESEARCH ETHICS COMMITTEE
- 8 AUG 2016
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

1.1 Is this a major or a minor amendment? (see FHS006hlp) Major (tick box) Minor (tick box)	☐ Major	✓ Minor
1.2 Does this protocol receive US Federal funding?	☐ Yes	✓ No
1.3 If the amendment is a major amendment and receives US Federal Funding, does the amendment require full committee approval?	☐ Yes	✓ No

2. List of Proposed Amendments with Revised Version Numbers and Dates

Please itemise on the page below, all amendments with revised version numbers and dates, which need approval.
This page will be detached, signed and returned to the PI as notification of approval. Please add extra pages if necessary.

In the same process and with the same participants, we intend to add a few questions regarding the experience of prevention of mother-to-child transmission (PMTCT) of HIV that has been successfully integrated in South Africa.

1. **Interviews with HIV positive women who were diagnosed with gestational diabetes mellitus (GDM)**

Given that some HIV-positive women are also diagnosed with GDM and the way it is managed among them in the course of their PMTCT cascades has not been studied, we therefore want to add to our research, a few questions that focus on PMTCT integration and management of GDM during the pregnancy and in the post-partum period. We will need to call those women who are in that category for further interviews about their experience with both PMTCT cascade and GDM (they have taken part in previous interview).
We will first interview them about their experience with the care they received from the PMTCT programme while they were pregnant and diagnosed with GDM. We will then ask them about their experience at well baby clinics to find out whether postnatal care for them and their babies has been integrated.

2. **Interviews with key informants**

We will also add a few PMTCT related questions in all our interview guides for health care workers and key informants. The new key informants on HIV/AIDS care and PMTCT will be added to the participants list and the following questions will be asked to them:

1. We are interested in understanding how PMTCT has moved from being a vertical program, to one that is integrated in PHC. Can you share your perspectives of the key points, successes, and challenges with the integration process in South Africa?

2. We are hoping to learn from the PMTCT integration experience in order to help support integrated care for other health problems, including diabetes, hypertension, etc. Can you share your perspectives on whether and how other health problems or issues are managed or integrated into the PMTCT services?

3. We would very much appreciate to hear your perspectives on how these processes are actually playing out on the ground in individual facilities and communities. From your engagement with the clinics, with the clinic managers and health care providers, please can you describe your views of:

- How the clinics are functioning in terms of PMTCT integration?
- Which have integrated PMTCT, at which level (extent) and why?
- How they are managing GDM for women under PMTCT program?
- What the role clinic managers are playing?
- What the role health care providers (Nurses and CHWs) are playing?
- What are the challenges and successes for integrating other health problems such as diabetes in post-partum for women under PMTCT programs? Probe: Whether the management of the clinics in jurisdictions are changing to integrate the care of these diseases, whether the GDM is specifically managed in PMTCT program and whether there is a planned post-partum follow up for women with subsequent GDM.

All other components and procedures remain unchanged.

UNIVERSITY OF CAPE TOWN
IYUNIVESITHI YASEKAPA • UNIVERSITEIT VAN KAAPSTAD

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS016: Annual Progress Report / Renewal

HREC office use only (FWA00001637; IRB00001938) This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30.11.2018
☐ Not approved	See attached comments		
Signature Chairperson of the HREC		Date Signed	28/11/2017

Comments to PI from the HREC

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	29.09.2017		
HREC REF Number	946/2014	Current Ethics Approval was granted until	
Protocol title	Assessing the feasibility and acceptability for an integrated health system intervention aimed at reducing type 2 diabetes risk in disadvantaged women after gestational diabetes in South Africa through formative research		
Protocol number (if applicable)			
Are there any sub-studies linked to this study?	☐ Yes ☐ No		
If yes, could you please provide the HREC Ref's for all sub-studies? Note: A separate FHS016 must be submitted for each sub-study.			
Principal Investigator	Prof N Levitt		
Department / Office Internal Mail Address	Endocrinology & diabetes. J-Floor, Old Main building		

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

1.1 Does this protocol receive US Federal funding?	☐ Yes	✓ No
1.2 If the study receives US Federal Funding, does the annual report require full committee approval? Note: Any annual approvals for **Full Committee** review MUST be submitted on the monthly HREC submission dates.	☐ Yes	✓ No

If yes in 1.2 please complete section 1.3 below for invoicing purposes	
1.3 Annual Approval for **full committee** review	- R 3420 (inclusive of vat)
For invoicing purposes, please provide:	
Sponsor's name	
Contact person	
Address	
Telephone number	
Email Address	

2. List of documentation for approval

3. Protocol status (tick ✓)

☐	Open to enrolment
☐	Closed to enrolment (tick ✓)
✓	Research-related activities are ongoing
☐	Research-related activities are complete, long-term follow-up only
☐	Research-related activities are complete, data analysis only
☐	Main study is complete but sub-study research-related activities are ongoing
☐	Study is closed → Please submit a Study Closure Form (FHS010)

4. Enrolment

Number of participants enrolled to date	20
Number of participants enrolled, since last HREC Progress report (continuing review)	
Additional number of participants still required	10

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

5. Refusals

Total number of refusals (participants invited to join the study, but refused to take part)	0

6. Cumulative summary of participants

Total number of participants who provided consent	20
Number of participants determined to be ineligible (i.e. after screening)	
Number of participants currently active on the study	
Number of participants completed study (without events leading to withdrawal)	
Number of participants withdrawn at participants' request (i.e. changed their mind)	
Number of participants withdrawn by PI due to toxicity or adverse events	
Number of participants withdrawn by PI for other reasons (e.g. pregnancy, poor compliance)	
Number of participants lost to follow-up. Please comment below on reasons for loss of follow-up.	
Number of participants no longer taking part for reasons not listed above. Please provide reasons below:	

7. Progress of study

Please provide a brief summary of the research to date including the overall progress and the progress since the last annual report as well as any relevant comments/issues you would like to report to the HREC:

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

We completed to conduct interviews with health care workers in the clinics and key informants regarding PMTCT related questions and we still need to enroll and interview women about their experience with the care they receive from PMTCT programme while they were pregnant and diagnosed with GDM. As stated before, we will also ask them about their experience at well baby clinics to find out whether postnatal care for them and their babies has been integrated.

8. Protocol violations and exceptions (tick ✓ all that apply)

✓	No prior violations or exceptions have occurred since the original approval
☐	Prior violations or exceptions have been reported since the last review and have already been acknowledged or approved
☐	Unreported minor violations that have occurred since the last review, as well as significant deviations not yet reported, are attached for review

9. Amendments (tick ✓ all that apply)

☐	No prior amendments have been made since the original approval
✓	Prior amendments have been reported since the last review and have already been approved
☐	New protocol changes/ amendments are requested as part of this continuing review (See note below)

Note: If new protocol changes are being requested in this review, please complete an amendment form (FHS006).
Specific changes in the amended protocol and consent/assent forms must be **bolded**, *italicised* or tracked and all changes must include a rationale.

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

10. Adverse events

10.1 Please provide below or attach a narrative summary of serious adverse events and/ or unanticipated problems since the last progress report. Please indicate changes made to the protocol and informed consent document(s) as a result (if not already reported to the HREC). Please comment on whether causality to any study procedure or intervention could be established.

10.2 Have participants received appropriate treatment/ follow-up/ referral when indicated (e.g. in the case of abnormal or incidental clinical findings, distress or anxiety)?		
☐ Yes	☐ No	✓ Not applicable
If yes, please describe:		

11. Summary of Monitoring and Audit Activities (tick ✓)

11.1 Was this study monitored or audited by an external agency (e.g. MCC, FDA)?		
☐ Yes	✓ No	☐ Not applicable

11.2 Did a Data and Safety Monitoring Board publish a report?		
☐ Yes	✓ No	☐ Not applicable

11.3 If yes, please identify the agency and attach a summary of the findings.					
Agency Name		Report attached	☐ Yes	☐ No	☐ Not applicable
		DSMB report attached	☐ Yes	☐ No	☐ Not applicable

11.4 Has there been any agency, institutional or other inquiry into non-compliance in this study, or any finding of non-compliance concerning a member of the research team?	
☐ Yes	✓ No
If yes, please explain:	

12. Level of risk (tick ✓)

12.1 Considering your experience of this research, please indicate whether the level of risk to participants has:	
☐	Increased

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

Study information and consent form

Study information

Study title: Exploring health systems integration in urban South Africa: from integrating prevention of mother-to-child transmission of HIV to prevention of type 2 diabetes after gestational diabetes

I am researcher from University of Montréal, with the Chronic Diseases Initiative for Africa (CDIA)/IINDIAGO project, doing research on women who have had gestational diabetes (diabetes during pregnancy) and at the same time followed PMTCT cascades. Many of these women recover from the diabetes after the birth of their babies, but they continue their antiretroviral therapy (ARVs) and are at high risk of developing diabetes sometime later. However, with an integrated healthy lifestyle, this diabetes can be avoided or delayed. Through INDIAGO project, CDIA researchers and collaborators want to develop the integrated health services and an education programme for women with previous gestational diabetes that will help them prevent getting diabetes later. For my PhD research, I need to understand what key informants think about PMTCT integration at primary health care and possibly the GDM management during pregnancy and after delivery. We need also to find out whether or not the prevention of T2DM among HIV-positive women with GDM while under PMTCT programme is integrated and see what can be learnt from that experience of PMTCT integration at primary health care and then apply and adapt this experience to overall women population with recent GDM. We would also like to ask key informants what they think of a possible programme which would offer tests, education and counselling at Well Baby clinics.

I am inviting the key informants, clinic managers, nurses and midwives, women diagnosed with GDM under PMTCT who live in Cape Town and Soweto and were involved with PMTCT/GDM policies or programmes and care, GDM diagnosis, care and follow-up during antenatal and postnatal care at district, provincial and national levels.

The discussion will last for approximately one hour in English and will be led by members of the research team. We will record the discussion so that we do not miss any important information.

Risks: As the study involves you voluntarily taking part in discussions with the researchers, we expect minimal risk to you. There is a possibility that you might share some personal information during the discussion or feel uncomfortable with some of the topics being discussed. You may refuse to answer questions you are not comfortable with and you may stop participating in the study at any point without giving reasons.

Benefits: By taking part in this study you will share your experience or viewpoints about integration of PMTCT and GDM and these will be included in this research conclusions and recommendations.

Reimbursement: You will not be provided any incentive to take part in the research.

Confidentiality: Your name will not be used in any of the reports written up about this research without your prior permission.

Please ensure that you have carefully read and understood this information sheet and been given a copy to keep for yourself.

Contact details of researchers: For any questions or concerns, please feel free to contact Mrs Chantal Stuart at our research office or the researchers whose emails are listed below:

Dr Katherine Murphy
Mr MUTABAZI Jean Claude

This study was granted ethical clearance from the Human Research Ethics Committee at UCT. Their contact details are:
The Human Research Ethics Committee
Old Main Building
Groote Schuur Hospital
Floor E52, Room 23
Observatory, 7925.

Informed consent form

Study Title: Exploring health systems integration in urban South Africa: from integrating prevention of mother-to-child transmission of HIV to prevention of type 2 diabetes after gestational diabetes

By signing this document:

I confirm that I have read the above information and understand it.

I confirm that I have had an opportunity to ask questions and I am satisfied with the answers and explanations that have been given to me.

I give my permission for the researchers to use the information I offer in the interview for the purposes of developing an intervention for women with previous GDM learning from the successfully integrated PMTCT programme and for the purposes of academic publication.

I agree to maintain confidentiality of information shared in this focus group.

I understand that my participation in this discussion is voluntary and I am free to withdraw at any time without having to give a reason.

Please tick one of the boxes below:

☐ YES, I would like to take part in this study
☐ NO, I do not wish to take part in this study

Name of research participant: ……. Signature……. Date: …….

Name of researcher: ……. Signature……. Date: ……

IINDIAGO description and registration

Pan African Clinical Trials Registry

South African Medical Research Council, South African Cochrane Centre
PO Box 19070, Tygerberg, 7505, South Africa
Telephone: +27 21 938 0506 / +27 21 938 0834 Fax: +27 21 938 0836
Email: pactradmin@mrc.ac.za Website: www.pactr.org

Trial #: PACTR201805003336174			
Date of Approval:	20/04/2018	**Trial Status:**	Registered in accordance with WHO and ICMJE standards

TRIAL DESCRIPTION	
Public title	IINDIAGO
Official scientific title	An integrated health system intervention aimed at reducing type 2 diabetes risk in women after gestational diabetes in South Africa (IINDIAGO): a randomized controlled trial
Brief summary describing the background and objectives of the trial	Background Women with a history of gestational diabetes (GDM) are at high risk of later development of type 2 diabetes and cardiovascular disease. In South Africa, data from unpublished ongoing studies show that there is a high prevalence of GDM (15%) and a high proportion of women with a history of GDM progress to type 2 diabetes (>40%) in the 5-year period after the pregnancy. IINDIAGO is a health system intervention, which aims to integrate the provision of post-natal care and intervention to prevent progression to T2DM in the mother with the scheduled post-partum care of her baby. Methods IINDIAGO is a convergent parallel mixed methods study with the main component being a phase 2, 2-arm parallel individually randomised controlled trial, which will be carried out at 4 major referral centres and up to 12 well-baby clinics in the Western Cape and Gauteng provinces of South Africa. Participants in the trial will be randomized 1:1 to either intervention or control using standard techniques, 390 participants with GDM (with no history of either type 1 or type 2 diabetes) will be recruited into the study at 32 to 33 weeks¿ gestational age. Data collection will take place between 29 and 33 weeks¿ pregnancy and at 6-8 weeks after delivery and again at 12 months. Each participant will be followed up for 12 months. The intervention will consist of a number of behavioural change components administered at various time points; during the hospital stay or hospital based GDM clinic visits, at Well-Baby clinics and in the community. Controls will receive standard usual care. The primary outcomes for the trial will be the completion of a 2-hour oral glucose tolerance test at 6-8 weeks after the pregnancy and a composite (percentage weight change>5%, percentage change in waist circumference >3%, normoglycaemia) diabetes risk reduction indicator at 12 months. Ethics approval has been granted by UCT, Wits U, Stellenbosch U and at U Montreal.
Type of trial	RCT
Acronym (If the trial has an acronym then please provide)	IINDIAGO
Disease(s) or condition(s) being studied	Nutritional, Metabolic, Endocrine,Pregnancy and Childbirth,type 2 diabetes, gestational diabetes
Sub-Disease(s) or condition(s) being studied	
Purpose of the trial	Prevention
Anticipated trial start date	24/04/2018
Actual trial start date	
Anticipated date of last follow up	31/05/2020
Actual Last follow-up date	
Anticipated target sample size (number of participants)	370
Actual target sample size (number of participants)	
Recruitment status	Recruiting
Publication URL	not yet published

Secondary Ids	Issuing authority/Trial register

STUDY DESIGN					
Intervention assignment	**Allocation to intervention**	**If randomised, describe how the allocation sequence was generated**	**Describe how the allocation sequence/code was concealed from the person allocating the participants to the intervention arms**	**Masking**	**If masking / blinding was used**
Parallel: different groups receive different interventions at same time during study	Randomised	Permuted block randomisation (please state block size and whether or not the block size was variable) and Stratified allocation	Sealed opaque envelopes	Masking/blinding used	Care giver/Provider,Outcome Assessors,Participants

		where factors such as age, gender, centre, or previous treatment are used in the stratification (please specify factors used for stratification)			

INTERVENTIONS						
Intervention type	Intervention name	Dose	Duration	Intervention description	Group size	Nature of control
Experimental Group	Post-partum lifestyle interventions for the prevention of progression to T2DM among GDM women	Brief counseling sessions, of variable duration	1 year	1. Hospital based antenatal intervention: 2 brief, face-to-face counselling sessions. 2. Post-partum clinic based intervention: point of care OGTT at the routine 6-week post-partum visit. 3. Brief behavior change counselling: 4 brief, face-to-face counselling sessions. 4. Community based intervention: Home visits in between the counselling sessions & 3 Peer support group sessions.	185	
Control Group	Control or usual care	Brief lifestyle change advice during hospital stay	1 year	Typically, GDM women receive some health education and advice on lifestyle from healthcare providers during routine antenatal care.	185	Placebo

ELIGIBILITY CRITERIA					
List inclusion criteria	List exclusion criteria	Age Category	Minimum age	Maximum age	Gender
Women who fulfil the following criteria will be eligible for initial inclusion: 1. Diagnosed with GDM using standard criteria (specify) defined by the research team. 2. Currently living in the community served by the clinics included in the study and planning to remain in the area for the next year 3. Participant is willing and able to give informed consent for participation in the study. 4. Able to communicate in one of the predominant official languages spoken in the Western Cape (Cape Town) and Gauteng (Johannesburg) provinces (e.g. English, Afrikaans, isiXhosa, isiZulu and Sesotho)	Women with the following characteristics will not be included in the study: 1. Women who had T2DMM or type 1 diabetes prior to the index pregnancy 2. Post-delivery, women are diagnosed with diabetes at the postpartum OGTT 3. Post- delivery women who have stillbirths or infants who die before 6 weeks		18 Year(s)	60 Year(s)	Female

ETHICS APPROVAL			
Has the study received appropriate ethics committee approval	Date the study will be submitted for approval	Date of approval	Name of the ethics committee
Yes		21/11/2016	UCT HREC

Ethics Committee Address			
Street address	City	Postal code	Country
observatory	Cape Town	7925	South Africa

Has the study received appropriate ethics committee approval	Date the study will be submitted for approval	Date of approval	Name of the ethics committee
Yes		27/03/2017	Human Research Ethics Committee Univ Witwatersrand

Ethics Committee Address			
Street address	City	Postal code	Country
York Road	Johannesburg	2193	South Africa

OUTCOMES		
Type of outcome	Outcome	Timepoint(s) at which outcome measured
Primary Outcome	Completion of the 6-weeks OGTT (yes/no variable)	6-8 weeks post pregnancy
Primary Outcome	The change in diabetes risk at 12 months	12 months after delivery
Secondary Outcome	weight change	12 months after delivery
Secondary	Absolute waist circumference	12 months after delivery

Outcome		
Secondary Outcome	f. T2DM and dysglycaemia measured using fasting and 2-hour OGTT blood glucose	12 months after pregnancy
Secondary Outcome	g. Insulin resistance (HOMA-IR) and 2-hour OGTT insulin	12 months post delivery
Secondary Outcome	Indicators of psychosocial health	12 months post delivery
Secondary Outcome	diet intake	12 months post delivery
Secondary Outcome	blood pressure	12 months post delivery
Secondary Outcome	physical activity	12 months post delivery
Secondary Outcome	breast feeding history	12 months post partum

RECRUITMENT CENTRES

Name of recruitment centre	Street address	City	Postal code	Country
Chris Hani Baragwanath hospital	Soweto	Soweto	1864	South Africa
Tygerberg hospital	Tygerberg	Cape Town	7505	South Africa
Mowbray Maternity Hospital	Mowbray	Cape Town	7700	South Africa
Groote Schuur hospital	Observatory	Cape Town	7925	South Africa

FUNDING SOURCES

Name of source	Street address	City	Postal code	Country
the International Development Research Centre (IDRC), grant number: 108002-001.				

SPONSORS

Sponsor level	Name	Street address	City	Postal code	Country	Nature of sponsor
Primary Sponsor	Chronic Disease Initiative for Africa.	J47, Old Main Building, Groote Schuur hospital, Observatory	Cape Town	7925	South Africa	University

COLLABORATORS

Name	Street address	City	Postal code	Country
Tracey Naledi, South Africa Department of Health	Room T20-06	Cape Town	8000	South Africa

CONTACT PEOPLE

Role	Name	Email	Phone	Street address
Principal Investigator	Naomi Levitt	naomi.levitt@uct.ac.za	0216506541	J47, CDIA, Old Main Building, Groote Schuur hospital, Observatory
City	**Postal code**	**Country**	**Position/Affiliation**	
Cape Town	7925	South Africa	Director, Chronic Disease Initiative for Africa	
Role	**Name**	**Email**	**Phone**	**Street address**
Public Enquiries	Bee Williams	bee.williams@uct.ac.za	0214066572	J47, CDIA, Old Main Building, Groote Schuur hospital, Observatory
City	**Postal code**	**Country**	**Position/Affiliation**	
Cape Town	7925	St. Helena	Manager, Chronic Disease Initiative for Africa	
Role	**Name**	**Email**	**Phone**	**Street address**
Scientific Enquiries	Naomi Levitt	naomi.levitt@uct.ac.za	0216506541	J47, CDIA, Old Main Building, Groote Schuur hospital, Observatory
City	**Postal code**	**Country**	**Position/Affiliation**	
Cape Town	7925	South Africa	Director, Chronic Disease Initiative for Africa	

REPORTING

Share IPD	Description	Additional Document Types	Sharing Time Frame	Key Access Criteria
URL	**Results Available**	**Results Summary**	**Result Posting Date**	**First Journal Publication Date**
Result Upload 1:	**Result Upload 2:**	**Result Upload 3:**	**Result Upload 4:**	**Result Upload 5:**

Results URL Hyperlinks	Link To Protocol
Result URL Hyperlinks	

Changes to trial information					
Section Name	**Field Name**	**Date**	**Reason**	**Old Value**	**Updated Value**
Funding Source	FundingSources List	14/05/2018	Adding address of funder	the International Development Research Centre (IDRC), grant number: 108002-001.	the International Development Research Centre (IDRC), grant number: 108002-001.
Section Name	**Field Name**	**Date**	**Reason**	**Old Value**	**Updated Value**
Trial Information	Trial type	20/04/2018	Modified	CCT	RCT
Section Name	**Field Name**	**Date**	**Reason**	**Old Value**	**Updated Value**
Intervention	InterventionTypeID	09/05/2018	Correcting wrong information	Experimental group	Experimental group
Section Name	**Field Name**	**Date**	**Reason**	**Old Value**	**Updated Value**
Trial Information	Trial phase	05/07/2018	pactr update		Not Applicable
Section Name	**Field Name**	**Date**	**Reason**	**Old Value**	**Updated Value**
Trial Information	Disease(s)	05/07/2018	pactr update	Other	Nutritional, Metabolic, Endocrine, Other
Section Name	**Field Name**	**Date**	**Reason**	**Old Value**	**Updated Value**
Ethics	Ethics List	11/06/2020	edit	TRUE, UCT HREC, observatory, Cape Town, 7925, South Africa, , 21 Nov 2016, , ,	TRUE, UCT HREC, observatory, Cape Town, 7925, South Africa, , 21 Nov 2016, +27214066411, nosi.tsama@uct.ac.za, 3336_2651_4737.pdf
Section Name	**Field Name**	**Date**	**Reason**	**Old Value**	**Updated Value**
Ethics	Ethics List	11/06/2020	update		TRUE, Human Research Ethics Committee Univ Witwatersrand, York Road, Johannesburg, 2193, South Africa, , 27 Mar 2017, +27117171234, Rhulani.Mkansi@wits.ac.za, 3336_11436_4737.pdf
Section Name	**Field Name**	**Date**	**Reason**	**Old Value**	**Updated Value**
Trial Information	Recruitment status	11/06/2020	update	Not yet recruiting	Recruiting
Section Name	**Field Name**	**Date**	**Reason**	**Old Value**	**Updated Value**
Trial Information	Disease(s)	11/06/2020	update request from trialist	Nutritional, Metabolic, Endocrine, Other	Nutritional, Metabolic, Endocrine, Pregnancy and Childbirth, Other