UNIVERSITY OF CAPE TOWN

POSTNATAL CLUBS: IMPLEMENTATION OF A DIFFERENTIATED AND INTEGRATED MODEL OF CARE FOR MOTHERS LIVING WITH HIV AND THEIR HIV-EXPOSED UNINFECTED BABIES

AURELIE NELSON

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Supervisor: Prof Landon Myer

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PREAMBLE

Declaration

I, Aurelie Nelson (NLSAUR001), hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Abstract

Background

Despite the reduction in the HIV mother-to-child transmission (MTCT) rate in South Africa, there are ongoing concerns in the breastfeeding period, linked to poor retention in care. To improve this retention, Postnatal Clubs (PNC) were created as an integrated, differentiated model of care providing psychosocial support and comprehensive care for the mother-infant pairs (MIP). We describe the implementation of PNC and examine its health outcomes in a peri-urban primary health care setting in Cape Town, South Africa.

Methods

In this cohort study, conducted between June 2016 and December 2019, MIPs were recruited into PNC between 6 weeks and 6 months of age and followed-up until 18 months of age. PNC MIPs were compared to a historical control group from the same setting. Outcomes included maternal Viral Load (VL), HIV testing at 9 and 18 months of age, and other maternal and child health outcomes.

Results

During the implementation of PNC study period, 484 MIP were recruited with 84% overall attendance, 95% overall viral load suppression, and 98% overall uptake of HIV infant testing. Compared to historical controls, the PNC infant rapid test completion was 1.6 times higher (95% CI: 1.4-1.9) at 9 months and 2.0 times higher at 18 months (95% CI: 1.6-2.6). Through 12 months and between 12-18 months, maternal VL completion was higher in the PNC group compared to the historical control by 1.5 times (95% CI: 1.3-1.6) and 2.6 times (95% CI: 2.1-3.2), respectively, with similar maternal VL suppression. Of 105 infants attending the 12 months visit, 99% were fully vaccinated by one year.

Conclusion

MIP in the PNC showed better PMTCT outcomes than historical controls with high levels of retention in care. Other outcomes such as immunisation results suggest that integration of services, such as in the PNC, is feasible and beneficial for MIPs.

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List of abbreviations

ART	Antiretroviral Therapy
BTC	Back to Clinic
cCMV	Congenital Cytomegalovirus
CDU	Central Dispensing Unit
CI	Confidence Interval
CCT	City of Cape Town Health
DNA	Did Not Attend
ECD	Early Childhood Development
FPD-REC	Foundation for Professional Development-Research Ethics Committee
GCP	Good Clinical Practice
HR	Hazards Ratio
HREC	Human Research and Ethics Board
HIV	Human Immunodeficiency Virus
IPV	Intimate Partner Violence
IUCD	Intrauterine Contraceptive Device
LTFU	Loss to Follow Up
LMIC	Low to Middle Income Countries
M2m	Mothers 2 mothers
MCH	Maternal and Child Health
MIP	Mother Infant Pair
MSF	Médecins Sans Frontières (Doctors Without Boarders)
MTCT	Mother to Child HIV Transmission
NGO	Non-Governmental Organization

NIDS	National Indicator Data Set
NHLS	National Health Laboratory System
Pap smear	Papanicolaou smear
PEPFAR	President Emergency's Plan for AIDS Relief
PMHP	Perinatal Mental Health Project
PCR	Polymerase Chain Reaction
PMTCT	Prevention of Mother to Child HIV Transmission
PNC	Post Natal Clubs
RIC	Retention In Care
SDG	Sustainable Development Goals
SRH	Sexual and Reproductive Health
TB	Tuberculosis
TFO	Transfer Out
UCT	University of Cape Town
UNICEF	United Nations International Children's Emergency Fund
USAID	United States Agency for International Development
VEID	Very Early Infant Diagnosis
VL	Viral Load
WCP	Western Cape Province
WHO	World Health Organisation

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PART A: RESEARCH PROTOCOL

Protocol Synopsis

In South Africa, mother to child HIV transmission (MTCT) has significantly dropped from 15% in 2009 to 4.3% at 18 months in 2018 (1–3). Most of the transmission now happens postnatally (1,4). Postnatal HIV transmissions are due to poor retention in care of mothers living with HIV as well as incident maternal HIV infections during breastfeeding (1,5,6). Disengagement in care applies to mothers living with HIV but also to their HIV-exposed children, with poor HIV testing uptake at 9 months and 18 months (7–10). Access to postnatal services generally remains low in South Africa (11). At the time postnatal clubs (PNCs) were created, there were a limited number of interventions to improve retention in care of the mother infant pair, including recommended integration of maternal and children health services (12). In 2016, postnatal clubs were designed and implemented as an adaptation of adult antiretroviral therapy (ART) adherence clubs to cater for mothers living with HIV and their HIV-exposed infants, providing psychosocial support, focusing on the first thousand days (early childhood development activities, mental health screening, breastfeeding support etc.) as well as providing integrated health care for the mother and the infant.

The aim of the proposed study is to evaluate the integration of maternal and child health interventions delivered through an adapted ART adherence club (PNC) by describing PMTCT outcomes and other maternal and child health services (vaccination, sexual and reproductive health -SRH- services) outcomes.

The proposed study is a secondary analysis of data collected during an observational cohort study of the PNC intervention from June 2016 to March 2019 in one primary care clinic in Khayelitsha, Western Cape Province, South Africa. Participants eligible for the PNC are any HIV-positive mothers and their HIV-exposed infants presenting at Town 2 clinic with infants of less than 6 months. Exclusion criteria include mothers with active pulmonary tuberculosis, mothers refusing to transfer their ART care to the same clinic as the child and HIV-positive children. HIV-positive mothers under 18 years old will be accepted into the PNC but their data won't be used for this study. Participants were recruited when coming to the clinic for their first postnatal visit by City of Cape Town (CCT) nurse and/or m2m (mothers2mothers) mentors (usually the infant's fist clinic visit either at two weeks post birth or at 6 weeks postnatally for their first vaccination).

Individual informed consent was not obtained as this is secondary analysis of data captured under the FPD REC and Stellenbosch HREC approval protocols.

Risks to the study participants are minimal as the study involves secondary analysis of already collected data. There were some indirect risk of breaking patient confidentiality when collecting the data. However, this risk was kept to a minimum by anonymizing data when capturing it. Participants in the study are identified by a unique identifier. Furthermore, no individualised data will be presented or reported in any forum. Quantitative data was collected by MSF data capturers from folders and registers into the electronic data system, using REDCap and stored anonymously using unique identifiers. A list of matching names and unique identifier are kept separately. Maternal data was captured using an adapted adult ART club register (approved by CCT) with one register per PNC for all visits and using the electronic system PREHMIS when needed. For the child, data was captured from the electronic system (PREHMIS). All data capturers from MSF have signed patient confidentiality agreements before capturing data and undergone good clinical practice (GCP) course. Data in REdCAP will be analysed using STATA version 14 (StataCorp (2015) Statistical Software: Release 14. College Station,Texas StataCorp LP).

Being part of the PNC is of direct benefit to the PNC participants. Through the PNC group session, mothers and infants will meet peers with children of similar ages, establishing support amongst peers. They also receive health education on HIV and non-HIV topics, as well as support for breast feeding. They are alerted to the possibility of postnatal depression and screened for it with rapid referrals when needed. Early childhood development activities run during the group sessions. Through the integrated clinical visit, mothers and infants are able to access their individual health needs at once, with the aim of reducing the number of times they visit the clinic and providing continuity of care with a sole supplier. All these components hopefully lead to nurturing care and positively affect the first thousand days of the child.

Benefits of collecting and analysing data from PNC are indirect to the mother-infant pair. Dissemination of the study findings will be of direct benefits to the general population and particularly to HIV-positive women of child bearing age. This adapted differentiated model of care for postnatal women living with HIV and their HIV-exposed infants could impact their retention in care and health outcomes in the first two years of life. This will inform policy at the national and international level.

1.Introduction

1.1 Background

In 2018, there were 160,000 new paediatric HIV infections worldwide, a 41% reduction compared to 2010, thanks to major progress in prevention of mother to child (MTCT) HIV transmission. In South Africa, where the number of vertical HIV transmissions decreased by over 76% between 2009 and 2014, there were 2,600 new paediatric infections in 2018 (1). Since the introduction of lifelong ART for all mothers living with HIV, as well as the previous introduction of early infant diagnosis testing and infant prophylaxis, MTCT has dropped from 15% in 2009 to 4.3% in 2014 (2,3). Whilst before the era of ART, most of the transmission used to be intrapartum, most of the vertical HIV transmission is now postnatal in Southern Africa (1,4).

Postnatal transmissions are due partly to poor retention in care of mothers living with HIV resulting in poor adherence to treatment and partly to incident HIV infections during breastfeeding. Recent data shows an intrauterine transmission of 0.9% in South Africa (2016) and an increase from 55% to 75% breast-feeding HIV transmission between 2009 and 2019 (5,6). At every step of the PMTCT cascade, there is attrition resulting in loss to follow up of mother-infant pairs (MIP). A systematic review looking at retention in care in Sub-Saharan Africa showed that an overall 70% of pregnant women received ART but only 64% of HIV-exposed infants had 6 weeks HIV-PCR, and only 55% of infants were tested between 12 and 18 months (4). More recent studies have shown that disengagement in care for pregnant women/mothers is twice more likely in the postnatal period than in the antenatal period, resulting in 25-50% dropouts (7–9). As a result of disengagement in care, ART adherence becomes suboptimal resulting in high maternal viral loads and high chances of MTCT. Reasons for disengagement are multiple and can be attributed to the health-system (e.g. long waiting clinic times, high patient volumes, negative experience with healthcare workers as well as difficult transition from postnatal care to ART care). Other reasons are linked to social determinants of health and include stigma and non-disclosure of HIV, regimen fatigue, lack of partner involvement, poor knowledge of postnatal MTCT as well as travel costs, work demands and the stresses of motherhood (9–15). Motherhood (particularly for first time mothers) comes with high emotional and logistical demands, compounded for mothers living with HIV by their (often) new HIV diagnosis (16). Logistical demands include the many clinic visits required for under five year olds, particularly if the mother and child's visits are on different days or in different clinics (17).

Disengagement in care applies to mothers living with HIV but also to their HIV-exposed children which is of concern particularly with the extension of the WHO breastfeeding recommendation to 24 months of age (17). Although the uptake of early infant diagnosis testing is good in South Africa (93% of infants tested at birth and about 90% tested at 6-8 weeks), HIV tests later on in the MTCT cascade (at 9 months and at 18 months) are seldomly done (6,18–20). As a result, over 50% of children living with HIV are not being diagnosed under two years of age (18). Reasons for this poor retention in care are similar to the ones mentioned for the mothers. As well, potential reasons include the mobility of children between carers resulting in geographical mobility and clinic transitions, inadequate HIV information in the Road to Health booklet and poor reporting of the rapid test results (20,21). Of note, access to postnatal services, outside the HIV context, seems to be problematic as well. A systematic review in low and middle income countries (LMIC) found that postnatal care coverage was poorer than other maternal and infant services' coverage. Postnatal care coverage was negatively affected by low socioeconomic status, low level of education, the partner's level of education, but positively associated with urban compared to rural areas (22).

1.2 Rationale of the study

Strategies to improve general postnatal care and postpartum HIV care include integration of services. For more than ten years, disease-specific programs (TB, HIV, etc) have been used in many countries, including in South Africa, and particularly for PMTCT where programs were focused on specific components of MCH services, dictated by the funders (23). Albeit making a significant contribution to controlling the burden of HIV disease, vertical programs have been more intensely criticised in recent years due to the perception that they create parallel systems and that some level of integration is necessary (24). In 2011, USAID recommended integration of PMTCT with maternal, newborn and child health services (25). South Africa produced a national PMTCT integrated model in 2011, recommending "integration of PMTCT into the existing maternal and child health interventions such as basic antenatal care, integrated management of childhood illnesses, expanded programme on immunisation and sexual and reproductive health, and to ensure that HIV infected mothers and babies are appropriately referred to HIV and AIDS services for continued treatment, care and support" (26). The implementation of this PMTCT integrated model has been variable (27).

To cope with the high number of ART patients in South Africa, differentiated models of care, such as adherence ART clubs, were created and were rolled out nationally (28,29). Some of the clubs' advantages include decongesting health facilities, saving time as well as providing peer support to patients on ART (14). A retrospective observational study in a similar setting as our proposed study showed that by enrolling into ART adherence clubs, patients were 57% less likely to be lost to follow up (LTFU) (hazard ratio (HR) 0.43, 95% CI=0.21-0.91) and 67% less likely to have a high viral load (HR0.33, 95%CI=0.16-0.67) than standard of care (28). This study and others showed that clubs are an effective way to retain ART patients in care (30–32). Furthermore, qualitative studies on ART clubs as well as studies on peer support in PMTCT interventions showed that peer support was very valuable and led to a decrease in stigma (33,34). This suggests that by using peer support in the ART club model, patients' biopsychosocial needs are being addressed and not just their biomedical needs (35). Other differentiated models of care, such as community-based adherence clubs, have also been assessed and showed good adherence and retention in care (36). In view of the good results of ART clubs as well as of the high number of ART patients in Sub Saharan Africa needing to access care (particularly in South Africa), recent recommendations from the WHO recommended that "stable" pregnant and postpartum women stayed or joined differentiated models of care (17). The WHO however recommends that newly diagnosed HIV positive pregnant patients and mothers who acutely seroconverted postnatally wait to join ART clubs until being "stable" on ART. In parallel, UNICEF recommendations are to focus on "unstable" mothers (who interrupted ART or whose diagnosis was late in pregnancy or whilst breastfeeding) to reach elimination of MTCT (16).

On the child side, although HIV-exposed children have a higher mortality risk compared to unexposed children, children's mortality has declined overall in South Africa (37). This has led global and national policymakers to focus more on the development of children to reach the Sustainable Development Goals of "No child (…) left behind" and to support particularly "the first 1000 days" (38,39). "The first 1,000 days" are the days of pregnancy and first two years of a child's life. This period has been shown to be fundamental in influencing long-term outcomes of the child from a neurodevelopmental, health, education, economics and social aspects and is a window of opportunity. For example, nutrition in that period has been shown to impact not only the child's growth but also his future cognition and school capacity as well as his risk for future chronic diseases. Based on the extensive research done on the first 1,000 days, a few key components have been identified as essential to "nurturing care". These

components include good health, balanced nutrition (with a strong focus on breastfeeding), early childhood development activities, love and nurturing as well as a secure and safe environment (39).

Taking all this into consideration, Doctors Without Boarders (MSF) in partnership with mothers2 mothers (m2m) and City of Cape Town designed and implemented Postnatal Clubs (PNC) in a primary care clinic in Khayelitsha. The intervention is an adaptation of adult ART adherence clubs to cater for all mothers living with HIV and their HIV-exposed infants, providing psychosocial support, focusing on the first thousand days (early childhood development activities, mental health screening, breastfeeding support etc.) as well as providing integrated health care for the mother and the infant (40). By doing a prospective observational cohort study of the PNC intervention, we aim to describe the implementation of PNC and its outputs to inform policy making decision on the implementation of PNC at a bigger scale nationally and internationally.

2. Aims and objectives

2.1 Aim

The aim of the proposed study is to evaluate the integration of maternal and child health interventions delivered through an adapted ART adherence club (called PNC) between June 2016 to March 2019 in one primary care clinic in Khayelitsha, Western Cape Province, South Africa by describing PMTCT outcomes and other maternal and child health services (vaccination, sexual and reproductive health -SRH- services) outcomes.

2.2 Objectives

1) To determine and compare PMTCT results of MIP in PNC in the first 18 months after delivery (from June 2016 to March 2019) to a historical cohort (from November 2015 to December 2018) in Khayelitsha, looking specifically at:

a) HIV-exposed children rapid tests completion and positivity at 9 months and 18 months

b) ART adherence of mothers living with HIV (measured through viral load completion and suppression) in the first 12 months and between 12-18 months after delivery

c) number of MTCT transmission by 18 months after delivery

2) To describe the PMTCT results of MIP in the PNC over time (from joining the PNC to exiting the PNC at 18 months after delivery) in one primary care clinic in Khayelitsha between June 2016 to March 2019 specifically focusing on:

a) retention in care of the MIP

b) VL completion and suppression for mothers living with HIV at 6 months, 12 months and 18 months post delivery

c) HIV-exposed children rapid tests completion and positivity at 9 months and 18 months

d) number of MTCT transmission by 18 months

e) number of "high risk" MIP[1] over the different timepoints

[1] [1] "High risk" MIP are mothers and infants who have at least one of the risk factors described by the Western Cape Department of Health Provincial guidelines, 2016 (50):

"-VL ≥1000 copies/ml after 28 weeks gestation

- Mother initiated ART <12 weeks before delivery

- Mother defaulted ART for at least one month at any stage during pregnancy

-Mother newly diagnosed HIV-positive after 28 weeks gestation, or in labour / immediately postpartum

- Mother with newly diagnosed or untreated TB, or received TB treatment at any point during pregnancy

- Mother with newly diagnosed or untreated Syphilis

- Chorioamnionitis

- Any sick HIV-exposed newborn requiring more than routine neonatal care [for example but not limited to, congenital syphilis, congenital Cytomegalovirus (cCMV) infection etc.]

- Spontaneous preterm labour (<37 weeks gestation) irrespective of maternal viral load.

- Prolonged rupture of membranes > 18 hours irrespective of maternal viral load

-Abandoned newborns / orphans (HIV- exposure confirmed with Rapid Determine."

3) To describe the immunisation rates of children in the PNC cohort by 12 months of age in one primary care clinic in Khayelitsha between June 2016 to March 2019

4) To describe the uptake of SRH services (pap smear and IUCD) for the mothers in the PNC cohort in one primary care clinic in Khayelitsha between June 2016 to March 2019

5) To describe the positivity rate of mental health screening of mothers in the PNC cohort in one primary care clinic in Khayelitsha between June 2016 to March 2019

2.3 Research questions

1) What are the PMTCT results (children rapid HIV tests completion and positivity, maternal adherence to ART - measured through VL completion and suppression, number of MTCT) of PNC members (June 2016-March 2019) compared to a historical cohort in Khayelitsha (November 2015-December 2018) ?

2) What are the PMTCT results (retention in care, maternal VL completion and suppression, children rapid HIV tests completion and positivity, number of MTCT, number of "high risk" MIP) of the PNC cohort over time (from joining the PNC to exiting at 18 months post-delivery) in one primary care clinic in Khayelitsha between June 2016 to March 2019?

3) What are the immunisation rates of children in an integrated model of healthcare delivery in the PNC cohort by 12 months of age at one primary care clinic in Khayelitsha between 2016 to 2019?

4) What is the uptake of SRH services (pap smear, contraception) by HIV-positive mothers in an integrated model of healthcare delivery in the PNC at one primary care clinic in Khayelitsha between 2016 to 2019?

5) What is the positivity rate of maternal mental health screening done at the PNC club every 6 months in one primary care clinic in Khayelitsha between June 2016 to March 2019?

3. Methodology

3.1 Study design

A prospective observational cohort study will be conducted in a primary care clinic (Town 2) in Khayelitsha from June 2016 (when the implementation of PNC will start) to March 2019 (when MSF will exit the implementation process). A historical control cohort will be used for comparison and is a group of mothers living with HIV and their HIV-uninfected exposed infants who were recruited at birth into another study-called VEID study- from November 1st, 2015 to June 1st, 2016 at a primary care clinic nearby, with similar demographics (20)

3.2 Study setting

Khayelitsha is a peri-urban informal settlement on the outskirts of Cape Town, with a total population estimated at 500,000-1,000,000 people (41). The HIV antenatal prevalence is high (about 30%) compared to the rest of the Western Cape Province (5%) (42). In 2015, the antenatal HIV prevalence was 33.1% and MTCT rate at 6/10 weeks was 0.8%, unknown at 9 months and 18 months with an 18 months rapid test uptake of 34% (43). Town 2 is a primary care clinic run by City of Cape Town Health department (CCT). With the planning of the implementation of the PNC intervention, mothers2mothers (m2m) became the community-based organisation involved at Town 2 (44–46). Recruitment for PNC started in May 2016. The PNC were designed, planned and implemented in partnership between MSF, CCT and m2m. Between 2015 and 2019, there were changes in the national PMTCT guidelines. However, the changes did not affect the outcomes looked at in this paper (maternal VL completion interval, 9 months and 18 months infant test). The changes affecting the 9 months infant testing to 6 months were only approved in the Western Cape in 2020 (47).

3.3 Inclusion criteria and recruitment

Participants eligible for the PNC are any HIV-positive mothers and their HIV-exposed infants (including “high risk” MIP) presenting at Town 2 clinic with infants of less than 6 months.

Exclusion criteria are: mothers with active pulmonary TB, mothers refusing to transfer their ART care to the same clinic as the child (Town 2) and HIV-positive children. HIV-positive mothers with HIV-positive children will be excluded from the PNC, as their needs are seen as being very different, and will be seen at the routine clinical services at Town 2 clinic. HIV-

positive mothers under 18 years old will be accepted into the PNC but their data won't be used for this study.

Participants will be recruited when coming to the clinic for their first postnatal visit by CCT nurse and/or m2m mentors (usually the infant's fist clinic visit either at two weeks post birth or at 6 weeks postnatally for their first vaccination). In the first 6 months of the implementation, to speed up the implementation, mothers with children under 6 months of age will be accepted into PNC. Enrolment into the PNC is estimated at maximum 30 MIP per month. Mothers will be asked to sign a consent retrospectively at their 18 months visit, as per the FDP Ethics review[2]. For mothers who become LTFU before their 18 months visit, routine data from their visits will be used as per the FPD amendment[2].

3.4 PNC operations

The target size for each PNC group will be between 3 to 15 MIP. Under 3 MIP was too small to make the necessary logistical adjustments to run a club. Over 15 MIP exceeded the maximum number to ensure the emotional and psychological peer support and ECD activities can be carried out in an appropriate way. Each PNC session will be composed of a predefined peer support session, facilitated by the m2m mentor mother (called PNC facilitator), followed by an integrated clinical visit. Each peer support session will provide ART adherence support and HIV education as well as 1000 days topics (breast feeding support, mental health screening followed by early childhood development (ECD) activities). The peer support group will happen in the existing ART club room at Town 2 clinic. The PNC nurse (a CCT nurse running the PNC) will then provide integrated clinical care for the mother (ART adherence and follow up, SRH services) and for the child (PMTCT as well as immunisations and other interventions as per the Road to Health booklet checklist in a separate private clinical room (48).

MIP will join PNC at 10 weeks of age, meet monthly for the first 6 months and then 3 monthly until their 18th month visit. Mothers will be asked to attend all visits when VL are taken (baseline/10 weeks, 6 months, 12 months, 18 months) or when infant testing happens (baseline/10weeks, 9 months, 18 months). In the interim visits, buddy will be permitted although mothers attendance is encouraged (especially when breastfeeding). If the mother (or buddy) do not attend a visit, they will be recalled on the phone by PNC facilitators twice and

[2] See Annex C

if not presenting to the facility within 5 days, a home visit will be carried out. If the mother did not present to the facility within 2 weeks of being recalled, she will be deemed as a "Do Not Attend" (DNA). She will however be allowed to come back to the PNC to try to encourage retention of "high risk" mothers.

At the 18 months visit, the MIP will "graduate" back to standard of care. Mothers will be encouraged to stay in ART club and HIV-exposed infants to go back to the clinic services.

3.5 Data collection

Quantitative data will be collected by MSF data capturers from folders and registers into the electronic data system, using REDCap and stored anonymously using unique identifiers. A list of matching names and unique identifier will be kept separately. Maternal data will be captured using an adapted adult ART club register (approved by CCT) with one register per PNC for all visits and using the electronic system PREHMIS when needed. For the child, data will be linked to their mothers' on the ART club register and will be captured from the electronic system (PREHMIS). All routine data from the MIP standard of care will be collected. This includes HIV-related data from NHLS (mother's VL results, PCR test results) as well as from paper clinic records (HIV rapid test results). Every 6 months, data from the mental health screening questionnaire will also be collected. This questionnaire was developed by the Perinatal Mental Health Project and is now part of the South African maternity case record (p9)(48,49). All data capturers from MSF will have signed patient confidentiality agreements before capturing data and undergone good clinical practice (GCP) course.

3.5.1 Historical controls

As historical controls, we will use a group of HIV-uninfected exposed infants who were recruited at birth into another study-called VEID study- from November 1st, 2015 to June 1st, 2016 at a primary care clinic nearby, with similar demographics (20). Data management activities for the VEID cohort are described in the Nelson et al paper (20).The infants were tested at birth for HIV (PCR), the mothers received extra counselling on subsequent infant testing and they were all referred back into standard of care. Results of the infants' subsequent tests and of the maternal viral loads were followed up with no additional intervention than monitoring the results, and tracing (results of the tracing are not included in

this analysis). Infants with a positive HIV birth or 6-week PCR were excluded from this control cohort

3.6 Data analysis and management plan

Data in REdCAP will be analysed using STATA version 14 (StataCorp (2015) Statistical Software: Release 14. College Station,Texas StataCorp LP). Descriptive statistics will be used to describe the categorical variables. Risk ratios and confidence intervals were calculated using generalised linear models in Stata. There is no sample size estimation calculated as this is operational research.

3.6.1 Exposures of interest

3.6.1.1 Objective one

For the exposure of interest for objective one, detailed in section 2.2, we will use only MIP joining PNC between June 1st, 2016 and 31st December 2018 and joining before 10 weeks after delivery so that there is the same starting time in the PNC for all MIP, as to not bias the results .

3.6.1.2 Objective two, three, four and five

For the exposure of interest for objectives 2, 3, 4 and 5 (as described in section 2.2), we will use the PNC cohort only, which is defined as all MIP joining PNC within 6 months after delivery between June 1st, 2016 and 31st March 2019 and they will be followed over time. As a result the number of MIP due for visits will decrease over the different timepoints. For "high risk" MIP, we will use the 2016 WCP PMTCT definition of high risk to determine who is high risk over time. However, postnatally after 10 weeks, this list can be simplified mostly to mothers with VL>1,000cp/ml (51). VL can be captured from NHLS. Mental health screening will be done by the PNC facilitator administering the PNMP questionnaire every 6 months.

3.6.2 Outcomes of interest

The outcomes of interest will be the PMTCT results, immunisation results and uptake of SRH services. For the PMTCT results, the outcomes of interest will be:

- *retention in care of the MIP* defined as the proportion of MIP attending each PNC visit (for the PNC cohort only). Retention in care analysis will be conducted among MIP who joined a club at week 10 and using as denominator the number of MIP with enough follow-up time to be due for the visit at each time point. Do not attend (DNA) will be defined as MIP not attending a particular PNC session. LTFU will be defined as MIP not attending more than 2 subsequent PNC visits. Back to clinic (BTC) will be defined as MIP who chose to go back to standard of care treatment at the clinic. Transfer out (TFO) will be defined as mother or infant attending care elsewhere, based on the caregiver's report.

- *maternal viral load completion and suppression* (VL<400cp/ml) . The timelines of viral load completion will differ between the primary objective and secondary objective. In the primary objective, where VL completion is compared between PNC and a historical control, we will look at VL completion in the first 12 months (7-365 days after delivery) and between 12 and 18 months (12-18 months after delivery). Furthermore, for the primary objective analysis, VL will be looked at for all the mothers in the PNC cohort (including the ones not attending the PNC) to account for mothers in the VEID cohort who might be LTFU or TFO. For the secondary objective, VL completion will be calculated at 6 months (7-180 days), 12 months (181-365 days), and 18 months (12-18 months) for the MIP attending those PNC visits.

- *rapid test uptake and positivity for the children at 9 months (8-10 months old) and 18 months (17-19 months old)* for the children attending those particular PNC visits. These test results will be extracted from the counsellors' registers for PNC and from folder reviews for VEID. Children who seroconvert will be excluded from subsequent testing denominators.

- *number of vertical transmission of HIV* defined as the number of positive rapid tests conducted between 9 months and 18 months (if necessary confirmed by a positive PCR test). After the study will be completed, as search will be done for all LTFU infants (including for the VEID historical cohort) on NHLS to see if they had become HIV positive. A positive HIV PCR test or a CD4 count done will be used as proxy for HIV positive result.

-*High risk MIP* was defined as having one of the "high risk" criteria defined by the 2016 WCP PMTCT guidelines (50). These criteria can be simplified postnatally to include only mothers with VL>1,000cp/ml (the other criteria become irrelevant past 6 weeks postpartum).

For the immunisation outcomes, the definition of full immunisation at 12 months of age will be based on the national NIDS definition of immunisation under one year which states "a child under one year who has had all primary course of immunisation vaccination"(52). Vaccination coverage will be checked on the electronic system (PREHMIS) and if discordant by auditing folders.

For SRH outcomes, outcomes such as insertion of intrauterine contraception device will be based on the nurses' own register. Pap smear completion will be based on electronic records on NHLS. Any patient who had not completed their Pap smear 3 year prior to enrolment into PNC will considered eligible as per the national guidelines (53).

For the mental health outcomes, outcomes will be based on the number of mothers who screened positive on the PNMH questionnaire over the total number of mothers who were screened over time.

4. Ethical considerations

This study will be conducted in accordance with the Good Clinical Practices (GCP) and the declaration of Helsinki. The overall study was already approved by the Foundation for Professional Development (FPD) Ethics Board (FPD REC clearance certificate 5-2017) and by the CCT Research Board (ID number 7899).

The VEID study (historical controls) was conducted according to GCP and the Declaration of Helsinki, with the approval of Stellenbosch University Ethics committee (HREC N14/06/060), the Western Cape Provincial Health Research Committee and the MSF-Ethics Review Board.

4.1 Informed consent

Individual informed consent will not be obtained for the PNC cohort as the data captured is data routinely captured into the CCT system or NHLS system. The FPD REC granted authorisation to collect routine data without informed consent, such as NHLS data (VL, PCR), MTCT data from paper clinic records (eg rapid test results) as well as data related to

postnatal club attendance and maternal and child service delivery on the CCT electronic system (PREHMIS).

4.2 Benefits

Being part of the PNC will be of direct benefit to the PNC participants. Through the PNC group session, mothers and infants will meet peers with children of similar ages, hopefully establishing support amongst peers. They will also receive health education on HIV and non-HIV topics, as well as support for breast feeding. They will be alerted to the possibility of postnatal depression and screened for it with rapid referrals when needed. Early childhood development activities will be implemented and taught to the mothers. All these components will hopefully lead to nurturing care and positively affect the first thousand days of the child.

Through the integrated clinical visit, mothers and infants will be able to access their individual health needs at once, hopefully reducing the number of times they visit the clinic and providing continuity of care with a sole supplier. By allowing "high risk" MIP into the PNC, they will hopefully benefit from the same points mentioned above and particularly from the peer support.

Benefits of collecting and analysing data from PNC are indirect to the MIP. Dissemination of the study findings will be indirect benefits to the general population and particularly to HIV-positive women of child bearing age. This will inform policy at national and international level and hopefully lead to the creation of a new differentiated model of care, particularly applicable to postnatal women. This new model of care will hopefully impact retention in care of HIV-positive mothers and their HIV exposed infants in the first two years of life.

4.3 Risks

Risks to the study participants will be minimal as the study will involve analysis of routinely collected data. There will be some indirect risk of breaking patient confidentiality when collecting the data. However, this risk will be kept to a minimal by anonymizing data when capturing it. Participants in the study will be identified by a unique identifier. Furthermore, no individualised data will be presented or reported in any forum.

4.4 Dissemination of findings

Dissemination of findings will include submission as a mini dissertation as part of a Master in Public Health at the University of Cape Town (UCT) (accessible in the UCT Institutional Repository (Open UCT)) as well as publication in a peer reviewed journal. The findings will also be presented at national and international conferences.

4.5 Strengths and limitations

Strengths of this study include being an implementation study, done in a real life setting with no participants' reimbursement or study procedures. Furthermore, it was designed and implemented collaboratively with other stakeholders in the health system (CCT, m2m) which will likely result in better buy-in of the intervention by other actors of the health system. The implementation process allows for flexibility in the model which could be adapted to other settings, such as other provinces or other countries.

Limitations include the fact that this study was done in one clinic only which might affect the generalisability of the findings. Other limitations include the fact that although done in a real life setting, there was support from an exterior independent NGO during the implementation process.

4.6 Timeframe

Table 1: Proposed timetable from start to end of the study

	2021												**2022**											
Research phases	**Jan-Mar**			**Apr-Jun**			**Jul-Sept**			**Oct-Dec**			**Jan-Mar**			**Apr-Jun**			**Jul-Sept**			**Oct-Dec**		
Protocol development																								
Department protocol approval																								
Ethical committee submission (secondary data																								

analysis)																							
MSF Data acquisition process																							
Data management																							
Data analysis																							
Manuscript write-up																							
Submission for examination																							
Addressing Examiners comments																							

4.7 Budget

The implementation of the PNC will be funded by MSF and by m2m. Data collection and management will be funded by MSF. Data analysis will be done in partnership between the primary author and MSF. Dissemination of findings will be funded by MSF. The rest of the other research activities will be self-funded by the primary author.

5. References

1. UNAIDS. Communities at the centre. Defending rights, breaking barriers, reaching people with HIV services. 2019 . Available from: https://rstesa.unaids.org/publications/global-publications/2019/item/209-global-aids-update-2019-communities-at-the-centre (Accessed October 10, 2021)

2. UNAIDS. Joint United Nations Programme on HIV/AIDS (UNAIDS. Unaids. 2015;11(3):1–88. Available from: http://www.unaids.org/sites/default/files/media_asset/JC2774_2015ProgressReport_GlobalPlan_en.pdf%0Ahttp://www.unaids.org/sites/default/files/media_asset/JC2774_2015ProgressReport_GlobalPlan_en.pdf%0Ahttp://www.ncbi.nlm.nih.gov/pubmed/27355509%5Cnhttp://w (accessed October 10, 2021)

3. Goga AE, Lombard C, Jackson D, Ramokolo V, Ngandu NK, Sherman G, et al. Impact of breastfeeding, maternal antiretroviral treatment and health service factors on 18-month vertical transmission of HIV and HIV-free survival: Results from a nationally representative HIV-exposed infant cohort, South Africa. J Epidemiol Community Health. 2020;74(12):1069–77.

4. Wettstein C, Mugglin C, Egger M, Blaser N, Salazar L, Estill J, et al. Missed Opportunities to preventi Mother-to-Child-Transmission in sub-Saharan Africa : Systematic Review and Meta-Analysis. Aids. 2013;26(18):2361–73.

5. Perez K (UNAIDS). Personal Communication. 2019.

6. Goga A, Chirinda W, Ngandu NK, Ngoma K, Bhardwaj S, Feucht U, et al. Closing the gaps to eliminate mother-to-child transmission of HIV (MTCT) in South Africa: Understanding MTCT case rates, factors that hinder the monitoring and attainment of targets, and potential game changers. South African Med J. 2018;108(3):S17–24.

7. McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): Effectiveness results from the pilot phase of a pragmatic open-label randomised trial. Lancet . 2016;387(10013):53–60.

8. Etoori D, Rice B, Reniers G, Gomez-Olive FX, Renju J, Kabudula CW, et al. Patterns of engagement in HIV care during pregnancy and breastfeeding: findings from a

cohort study in North-Eastern South Africa. BMC Public Health. 2021;21(1):1–12.

9. Phillips T, Thebus E, Bekker L, Mcintyre J, Abrams EJ, Myer L. Disengagement of HIV-positive pregnant and postpartum women from antiretroviral therapy services : a cohort study. 2014;1–10.

10. Nachega JB, Hislop M, Dowdy DW, Lo M, Omer SB, Regensberg L, et al. Adherence to Highly Active Antiretroviral Therapy Assessed by Pharmacy Claims Predicts Survival in HIV-Infected South African Adults. JAIDS J Acquir Immune Defic Syndr. 2006;43(1):78–84.

11. Clouse K, Schwartz S, Van Rie A, Bassett J, Yende N, Pettifor A. "What They Wanted Was to Give Birth; Nothing Else." JAIDS J Acquir Immune Defic Syndr. 2014;67(1):e12–8.

12. Phillips T, McNairy ML, Zerbe A, Myer L, Abrams EJ. Postpartum transfer of care among HIV-infected women initiating antiretroviral therapy during pregnancy. J Acquir Immune Defic Syndr. 2015;70(3):e102–9.

13. Suthar AB, Hoos D, Beqiri A, Lorenz-Dehne K, McClure C, Duncombe C. Integrating antiretroviral therapy into antenatal care and maternal and child health settings: a systematic review and meta-analysis. Bull World Health Organ. 2013;91(1):46–56. Available from: http://www.who.int/entity/bulletin/volumes/91/1/12-107003.pdf (accessed October 10, 2021)

14. Wilkinson LS. ART adherence clubs: A long-term retention strategy for clinically stable patients receiving antiretroviral therapy. South Afr J HIV Med. 2017;14(2):48–50.

15. Richard Wilkinson and Michael Marmot. Determinants of Health the Solid Facts. World Health. 1999;2:1–33. Available from: http://www.euro.who.int/__data/assets/pdf_file/0005/98438/e81384.pdf (accessed October 10, 2021)

16. UNICEF. Evidence-based practices for retention in care of mother-infant pairs in the context of eliminating mother-to-child transmission of HIV in Eastern and Southern Africa: A summary with guidance for scale up. 2019.

17. World Health Organization. Key considerations for differentiated antiretroviral therapy

delivery for specific populations: children, adolescents, pregnant and breastfeeding women and key populations. 2017; Available from: https://apps.who.int/iris/bitstream/handle/10665/258506/WHO-HIV-2017.34-eng.pdf?sequence=1 (accessed October 10, 2021)

18. Johnson LF, Patrick M, Sa DCH, Sa F, Stephen C, Sa DCH, et al. Steep declines in pediatric AIDS mortality in South Africa, despite poor progress towards pediatric diagnosis and treatment targets. Pediatr Infect. 2020;39(9):843–8.

19. Kalk E, Kroon M, Boulle A, Osler M, Euvrard J, Stinson K, et al. Neonatal and infant diagnostic HIV-PCR uptake and associations during three sequential policy periods in Cape Town, South Africa: a longitudinal analysis. J Int AIDS Soc. 2018 Nov 1;21(11).

20. Nelson AK, Cassidy T, Duran LT, Cox V, Wedderburn CJ, Giddy J, et al. An analysis of the HIV testing cascade of a group of HIV-exposed infants from birth to 18 months in peri-urban Khayelitsha, South Africa. PLoS One. 2022 Jan 1;17(1):e0262518.

21. Ramraj T, Goga AE, Larsen A, Ramokolo V, Bhardwaj S, Chirinda W, et al. Completeness of patient-held records: observations of the Road-to-Health Booklet from two national facility-based surveys at 6 weeks postpartum, South Africa. J Glob Health. 2018;8(2):1–13.

22. Langlois É V, Miszkurka M, Zunzunegui MV, Abdul G, Daniel Z, Igor K. Systematic reviews Inequities in postnatal care in low- and middle-income countries : a systematic review and meta-analysis. Bull World Health Organ. 2015;93(January):259–70.

23. Aizire J, Fowler M, Coovadia H. Operational Issues and Barriers to Implementation of Prevention of Mother-to-Child Transmission of HIV (PMTCT) Interventions in Sub-Saharan Africa. Curr HIV Res. 2013;11(2):144–59.

24. Rao KD, Ramani S, Hazarika I, George S. When do vertical programmes strengthen health systems ? A comparative assessment of disease-specific interventions in India. 2013;1–11.

25. Lindegren M, Kennedy C, Bain-Brickley D, Azman H, Creanga A, Butler L, et al. Integration of HIV /AIDS services with maternal, neonatal and child health, nutrition, and family planning services (Review). Cochrane Libr. 2012;(9):1–136.

26. Department of Health; Republic of South Africa. The National Integrated Prevention

of Mother-To-Child Transmission (PMTCT) of HIV Accelerated Plan at a Glance. 2011;

27. UNAIDS. 2015 Progress report on the global plan towards the elimination of new HIV infections among children and keeping their mothers alive [Internet]. Vol. 11, Unaids. 2015. p. 1–88. Available from: http://www.unaids.org/sites/default/files/media_asset/JC2774_2015ProgressReport_GlobalPlan_en.pdf (accessed October 11, 2021)

28. Luque-Fernandez MA, Van Cutsem G, Goemaere E, Hilderbrand K, Schomaker M, Mantangana N, et al. Effectiveness of Patient Adherence Groups as a Model of Care for Stable Patients on Antiretroviral Therapy in Khayelitsha, Cape Town, South Africa. Dowdy DW, editor. PLoS One. 2013 Feb;8(2):e56088.

29. World Health Organization (WHO). Everybody's business :strengthening health systems to improve health outcome. WHO s Framework for Action. 2007.

30. Campion EW. Treating Millions for HIV: The Adherence Clubs of Khayelitsha. N Engl J Med. 2015;372(4):301–3.

31. Wilkinson LS. ART adherence clubs: A long-term retention strategy for clinically stable patients receiving antiretroviral therapy. South Afr J HIV Med. 2013;14(2):48–50.

32. Flämig K, Decroo T, van den Borne B, van de Pas R. ART adherence clubs in the Western Cape of South Africa: what does the sustainability framework tell us? A scoping literature review. J Int AIDS Soc. 2019 Mar 1;22(3).

33. Venables E, Towriss C, Rini Z, Nxiba X, Cassidy T, Tutu S, et al. Patient experiences of ART adherence clubs in Khayelitsha and Gugulethu, Cape Town, South Africa: A qualitative study. PLoS One. 2019;14(6):1–18.

34. Akinde Y, Groves AK, Nkwihoreze H, Aaron E, Alleyne G, Wright C, et al. Assessing the Acceptability of a Peer Mentor Mother Intervention to Improve Retention in Care of Postpartum Women Living with HIV. Heal Equity. 2019;3(1):336–42.

35. Engel G. The Need for a New Medical Model : A Challenge for Biomedicine Author (s): George L . Engel Published by : American Association for the Advancement of Science Stable

36. Grimsrud A, Sharp J, Kalombo C, Bekker L-G, Myer L. Implementation of community-based adherence clubs for stable antiretroviral therapy patients in Cape Town, South Africa. J Int AIDS Soc. 2015 Jan;18(1):19984.

37. Brennan AT, Bonawitz R, Gill CJ, Thea DM, Kleinman M, Useem J, et al. A meta-analysis assessing all-cause mortality in HIV-exposed uninfected compared with HIV-unexposed uninfected infants and children. AIDS. 2016 Sep 24;30(15):2351–60.

38. UNDP. SDG. Available from: https://www.undp.org/content/undp/en/home/sustainable-development-goals.html#:~:text=The Sustainable Development Goals %28SDGs%29%2C also known as,all people enjoy peace and prosperity by 2030. (Accessed September 15, 2021)

39. Bamford L. The first thousand days. Ensuring mothers and infants thrive. South African Child Gauge 2019; p71.

40. Western Cape Government. First 1000 days. 2021. Available from: https://www.westerncape.gov.za/first-1000-days/ (accessed September 18, 2021)

41. City of Cape Town. 2011 Census Suburb Khayelitsha. 2013;(2011 Census):1–7.

42. Shisana O, Rehle T, LC S, Zuma K, Jooste S, Zungu N, Labadarios, D, Onoya DEA. South African National HIV Prevalence, Incidence and Behaviour Survey, 2012. HSRC Press. 2014;194.

43. Pieters P. Personal communication. 2015.

44. MSF. MSF in South Africa. Available from: https://www.msf.org/south-africa (accessed September 10, 2021)

45. City of Cape Town. City Health Department. 2021. Available from: https://www.capetown.gov.za/Departments/City Health Department (accessed September 10, 2021)

46. m2m. mothers2mothers organisation. Available from: https://m2m.org/ (accessed September 10, 2021)

47. The Western Cape Government. The Western Cape Consolidated Guidelines for HIV Treatment: Prevention of Mother-to-Child of HIV (PMTCT), Children, Adolescents

and Adults. 2020

48. South African Department of Health. Road to Health Booklet. 2018;1–45. Available from: https://www.westerncape.gov.za/assets/departments/health/rthb_booklet.pdf

49. PNMP. Maternal mental health screening tool. Available from: https://pmhp.za.org/wp-content/uploads/Western-Cape-Maternity-Case-Record-Version-19-June-2018.pdf (accessed September 11, 2021)

50. PMHP. Perinatal Mental Health Project: resources for service providers [Internet]. 2021. Available from: https://pmhp.za.org/resources/for-service-providers/ (accessed September 10, 2021)

51. The Western Cape Government. The Western Cape Consolidated Guidelines for HIV Treatment: Prevention of Mother-to-Child of HIV (PMTCT), Children, Adolescents and Adults. 2016;2016. Available from: https://www.westerncape.gov.za/assets/departments/health/wcgh233_hiv_pmtct_guidelines_03102016.pdf (accessed September 11, 2021)

52. KZNHealth. Annual performance plan 2018/9-2020/21 Indicator descriptions. Available from: http://www.kznhealth.gov.za/app/APP-1819-Indicator-Descriptions.pdf (accessed September 10, 2021)

53. South African National Department of Health. Cervical Cancer Prevention and Control Policy. 2020. Available from: https://www.westerncape.gov.za/text/2020/February/cervical_cancer_prevention_and_control_policy.pdf (accessed September 10, 2021)

PART B: MANUSCRIPT

Postnatal Clubs: implementation of a differentiated and integrated model of care for mothers living with HIV and their HIV-exposed uninfected babies in Cape Town, South Africa

Aurelie Nelson[3*],

Affiliation:

[1] Division of Epidemiology and Biostatistics, School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town, Western Cape, South Africa.

[*]Corresponding author

Division of Epidemiology and Biostatistics, School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town, Western Cape, South Africa.

Email: aurelie.nelson@gmail.com

Key Words: Human Immunodeficiency Virus, Prevention of Mother to Child Transmission, Integrated care, South Africa

[3] The targeted journal chosen to format this manuscript was **PlosOne.** Its publication guidelines are included in Appendix C. As per the MPH dissertation guidelines, the other co-authors are not listed in the main manuscript but they are listed and their contributory role explained in the Acknowledgment section of this dissertation

Abstract

Background

Despite the reduction in the HIV mother-to-child transmission (MTCT) rate in South Africa, there are ongoing concerns in the breastfeeding period, linked to poor retention in care. To improve this retention, Postnatal Clubs (PNC) were created as an integrated, differentiated model of care providing psychosocial support and comprehensive care for the mother-infant pairs (MIP). We describe the implementation of PNC and examine its health outcomes in a peri-urban primary health care setting in Cape Town, South Africa.

Methods

In this cohort study, conducted between June 2016 and December 2019, MIPs were recruited into PNC between 6 weeks and 6 months of age and followed-up until 18 months of age. PNC MIPs were compared to a historical control group from the same setting. Outcomes included maternal Viral Load (VL), HIV testing at 9 and 18 months of age, and other maternal and child health outcomes.

Results

During the implementation of PNC study period, 484 MIP were recruited with 84% overall attendance, 95% overall viral load suppression, and 98% overall uptake of HIV infant testing. Compared to historical controls, the PNC infant rapid test completion was 1.6 times higher (95% CI: 1.4-1.9) at 9 months and 2.0 times higher at 18 months (95% CI: 1.6-2.6). Through 12 months and between 12-18 months, maternal VL completion was higher in the PNC group compared to the historical control by 1.5 times (95% CI: 1.3-1.6) and 2.6 times (95% CI: 2.1-3.2), respectively, with similar maternal VL suppression. Of 105 infants attending the 12 months visit, 99% were fully vaccinated by one year.

Conclusion

MIP in the PNC showed better PMTCT outcomes than historical controls with high levels of retention in care. Other outcomes such as immunisation results suggest that integration of services, such as in the PNC, is feasible and beneficial for MIPs.

Introduction

About 90% of the global women living with HIV reside in 22 countries, mostly in Sub-Saharan Africa. Since the implementation of the Global Plan towards the elimination of mother-to-child HIV transmission (MTCT) in 2011, most of these countries have significantly reduced their MTCT rate, with South Africa achieving a 76% decrease in new vertical HIV infections between 2009-2014 (1). Although MTCT has drastically decreased in South Africa from 15% in 2009 to 3.9% in 2019, there still remain significant challenges to reach elimination of MTCT (2). Whilst MTCT used to be mostly intrapartum, the good uptake and availability of triple antiretroviral therapy for pregnant women have led to a very low intrauterine transmission in South Africa (0.9% nationally in 2016) (3). The postnatal period is now the highest risk period to lose mothers from HIV care, resulting in the majority of new HIV infections occurring in children older than six weeks of age, and breast-feeding transmission increasing from 55% to 75% (2009- 2019) (3–6).

Postnatal retention in care (RIC) of mothers living with HIV is problematic in Southern Africa with disengagement being twice as likely postnatally than antenatally, and resulting in 25-50% drop outs postnatally (7,8). Disengagement from care translates into poor adherence, high viral loads and ultimately a higher chance of MTCT (9). Some of the reasons highlighted for disengagement are health-system related such as: long waiting times at the clinic, high patient volumes, negative experiences with health care workers and difficult transition from postnatal care to ART care. Other individual- and societal-related reasons are: stigma and non-disclosure of HIV status, travel costs, regimen fatigue, lack of partner involvement, demands of work, and inadequate knowledge of postnatal MTCT (10–15). Furthermore, the stresses of motherhood make treatment adherence more difficult, due to the added logistical and emotional demands of being a mother as well as the many health visits required for children under five years old, especially if the mother and child's clinic (and clinic days) are different (16). These challenges arise in part from a "one size fits all" approach of ART distribution and may be addressed by differentiated models of care accommodating different populations (16).

Added to the poor retention in care of mothers living with HIV postnatally, is the poor retention in care of children in HIV services postnatally, particularly concerning with the latest WHO recommendation to extend breastfeeding to two years of age (16). In South Africa, although early infant diagnosis testing is effective (93% of infants tested at birth) the

provincially recommended 9 months and 18 months HIV tests have a poor uptake (17), resulting in more than 50% of children living with HIV under two years of age not being diagnosed (18). Reasons for this disengagement are similar to the ones mentioned for the mother, as well as increased mobility of children between clinics and health districts as well as difficult tracing of the rapid test results ((3,19). Of note, a recommended strategy to improve retention in care of MIP is integration of PMTCT services with neonatal, maternal and child health, but its implementation has been variable (20,21).

In the last five years, ART adherence clubs have been adopted nationally (and internationally) for stable HIV patients as a differentiated model of care with the dual objective of decongesting health facilities as well as providing holistic care to ART patients (22,23). ART clubs have shown good retention in care and virological suppression compared to standard of care (22). Qualitative studies have shown, amongst other reasons, that peer support was very valuable to the ART club members, leading to a decrease in stigma (24). By using peer support, these clubs address biopsychosocial needs of patients, not just focusing on a biomedical approach (25). The WHO recently recommended that "stable" pregnant and breastfeeding women stay or join adult ART adherence clubs (16). However, for women who are diagnosed with HIV during pregnancy, the WHO recommends waiting until they are stable on ART before joining ART clubs. On the other hand, to reach elimination of MTCT, UNICEF recommends focusing on mothers who interrupted ART and mothers diagnosed late in pregnancy with HIV, amongst other recommendations (6). The WHO recommendation for ART clubs excludes all of these high-risk categories and there is a need for a new model to cater for them.

Based on these observations, postnatal clubs (PNC) were created and implemented at a primary care clinic in Khayelitsha. This holistic patient-centred model of care is an adaptation of adult ART clubs for all mothers living with HIV and their HIV-exposed infants, with integration of healthcare services as well as focusing on the first 1000 days of the child (26). In this paper, we describe the implementation of PNC and examine its MTCT, maternal and child health outcomes. Our first objective was to compare PMTCT results between the PNC cohort and historical control cohort in the first 18 months of life. Our second objective was to describe PMTCT results of the PNC cohort only. Our third objectives were to look at more integrated care by looking at the child's full 12 months immunisation completion as well as sexual and reproductive health outcomes for the mother (IUCD insertion, pap smear completion).

Material and methods

Study design and setting

The implementation of PNC was conducted in a single primary care clinic in Khayelitsha, Cape Town from June 2016 to March 2019. Khayelitsha, a peri-urban informal settlement close to Cape Town, South Africa, has an estimated population of over 500,000 and a high antenatal HIV prevalence (33%) with a mother to child transmission rate estimated to be <1% at 6-10 weeks; data on subsequent MTCT are not available but the uptake of the 18 months rapid test is approximately 34% (27)

Description of the implementation of the intervention

The PNC model is a differentiated and integrated model of care for all mothers living with HIV and their HIV-exposed infants, providing peer-led psychosocial support to the women followed by a clinical visit addressing the HIV (and non-HIV) medical needs of the mother and infant.

Setting and partners

The planning, design and implementation of PNC were done in partnership with Doctors Without Borders (MSF), mothers2mothers (m2m) and City of Cape Town Health department (CCT) (28–30). Recruitment for PNC started in May 2016 and the first PNC happened in June 2016. PNC was handed over to CCT and m2m in February 2019.

Participants and recruitment

Participants eligible for the PNC were any mothers living with HIV and their HIV-exposed infants presenting at the clinic when the infants were less than 6 months old. “High risk mothers” (according to the local PMTCT guidelines (31)) were also included. Mothers with active pulmonary tuberculosis (TB), mothers refusing to transfer their care to the same clinic as their infants and children living with HIV were excluded from the PNC.

HIV-exposed babies from 6 weeks of age until 6 months of age and their mothers were recruited into PNC. Mother-infant pairs (MIP) were usually recruited at their first postnatal

visit at the clinic (6 weeks post-delivery). Most of the recruitment was done by the PMTCT nurse, assisted by the PNC facilitator. The PNC facilitator used a recruitment schedule and gave the first PNC date to the mother. Infants were recruited into PNC clubs according to their dates of birth and all infants in one club were within 2 weeks of age of each other.

PNC Operations

Each PNC contained between 3 to 15 MIP. At each PNC visit, there was a group counselling session followed by a clinical visit for the MIP. After weighing the MIP and TB symptom screening, the PNC facilitator led a group session on HIV-related topics (such as adherence, disclosure) as well as non-HIV related topics (contraception, gender based violence) and child health as per the first thousand days campaign (e.g. breastfeeding support, mental health education and screening, early childhood development -ECD- education and activities) (26). Mothers were screened for depression every 6 months with a mental health questionnaire developed by the Perinatal Mental Health Project (32). After the group session, the MIP saw the PNC nurse who provided integrated care for the mother and infant. A summary of the components for each session is described in S1 Annex.

PNCs met in a large room at the facility (used for other groups such as the ART adherence clubs), with a clinical room attached. PNC met monthly for the first 4 sessions (until the infant was 6 months of age), for close monitoring of the infant, and then met three monthly as per locally prescribed child health visits from 6 months until 18 months of age. Due to the sparse availability of the club room, a complex schedule was designed.

The PNC nurse wrote ART prescriptions for PNC mothers a week before each PNC. The PNC facilitator collected prepacked ART on the day of the club. During the Christmas holiday, pre-packing increased to 4 months' supply.

Mothers were asked to attend club sessions that included scheduled 6 monthly Viral Load (VL) testing but were allowed to send someone else (called a buddy) with the baby in her stead on most other visits. If the MIP did not attend a PNC session, the PNC facilitator was responsible for recalling the mother within 2-3 days and when possible, did a home visit. If the patient did not present to care within 2 weeks of the recall, she was considered as a Did Not Attend (DNA). She would however be accepted back into the PNC if she came back at a later stage, in an effort to retain the "high-risk mothers" in PNC care.

"High risk mothers" (according to the local PMTCT guidelines (31) were encouraged to be part of PNC and received extra support with monthly visits to the PNC nurse, enhanced counselling support, three monthly VL and adequate prophylaxis and monitoring for the children, according to local PMTCT guidelines (31). If after three months VL was not suppressed, the mother was referred to a doctor.

When the child reached 18 months of age, the MIP "graduated" from the PNC. When possible, the PNC mothers transitioned as a group into an adult ART club to keep the created peer support. The children went back to standard of care services.

Monitoring and evaluation

Quantitative data were routinely captured from folders and registers into the REDCap electronic data system, and stored anonymously using unique identifiers. Maternal data was captured in a paper register with one register per PNC. At each PNC, the weight of the mother and TB symptoms screen results were entered. The child's information was recorded in the child's folder at every visit and captured into the CCT's electronic medical records (EMR). Both the mother's and child's folders had a PNC sticker on the front cover and were kept separately from other clinic's folders as a unit in a crate for ease of retrieval when attending the PNC. For vaccination status, when children appeared not vaccinated according to the EMR, the child's folder was retrieved, and the information checked. Data were analysed using Stata 14 (StataCorp (2015) Statistical Software: Release 14. College Station, Texas StataCorp LP) (33).

Human resources and management

From May 2016 to February 2019, supervision and mentoring at the clinic level was done by MSF. The PNC model relied mainly on two cadres, the PNC nurse and the PNC facilitator. The PNC nurse was a professional nurse, trained in child and woman's care as well as trained in the initiation and management of ART. The PNC nurse's specific responsibilities included: scripting ART for the mothers, providing integrated clinical care to the MIP and overseeing the recruitment and functioning of the PNC. For "high-risk" mothers, they provided extra support.

The PNC facilitator received basic training by m2m on PMTCT and facilitation as well as further training by MSF on PNC. The PNC facilitator's specific responsibilities included: preparing for the PNC, leading the group sessions, distributing prepacked ART, completing

the club register, administering the mental health screening questionnaire to mothers 6 monthly (34), checking maternal VL and child's polymerase chain reaction (PCR) results as well as tracing patients who did not come to the PNC session. For "high-risk" mothers, they also provided extra psychosocial support as needed.

Other cadres from the clinic involved in the running of the PNC included: a pharmacy assistant (responsible for ensuring timely ART prescriptions and ART pre-packing); a clerk (responsible for capturing the PNC data into EMR, ensuring adequate storage of PNC folders and printing clinical results); a doctor (to manage more complex cases) and a clinic manager (overseeing the smooth running of the PNC). PNC scheduling was also supported by the CCT ART club champion at the district level. No additional funding was required to run the PNCs.

Implementation strategy

Based on observations made whilst working in PMTCT at a primary care clinic in Khayelitsha and on previous work on ART clubs for other vulnerable populations, the concept of PNC was created by MSF in partnership with m2m and CCT.

Before starting the intervention at the clinic, the MSF team reviewed the clinic flow and worked with the clinic team to adapt it to integrate PNC. To get buy-in from the clinic, the PNC model was presented to the clinic management and to the whole clinic, several times. The clinic management selected a team from Town 2 clinic to be trained and to run the PNC. This team, as well as m2m mentors, did a three-day training on PNC, led by the MSF team. Over time, the PNC team received further trainings on ECD and on mental health. After the initial training, the MSF team was initially heavily involved in running the PNC and later, in mentoring and coaching the CCT and m2m teams on the ground. The model evolved along the way through a participatory process with the clinic team (with monthly meetings, review workshop) to finally be handed over to the clinic team in February 2019 through a handover workshop (with agreed targets).

Historical controls

For the purpose of comparing the PNC MIP outcomes, a group of historical controls was defined as a group of HIV-uninfected exposed infants who were recruited at birth into another study, from November 2015 to June 2016, at a primary care clinic nearby with similar demographics (17). The infants were tested at birth for HIV (PCR), the mothers

received extra counselling on subsequent infant testing, and the infants were referred back into standard of care. Results of the infants' subsequent tests and of the maternal viral loads were followed up with no additional intervention other than monitoring the results, and tracing (results of the tracing are not included in this analysis). Infants with a positive HIV birth or 6-week PCR were excluded from this control cohort.

Analysis

Data were analysed using STATA version 14 (StataCorp (2015) Statistical Software: Release 14. College Station,Texas StataCorp LP) (25). Descriptive statistics were used to describe the categorical variables. There were no sample size or estimation calculated as this was operational research. The primary analysis was a comparison of PMTCT results between the PNC cohort and historical control cohort in the first 18 months of life. Data was accessed for PNC between 2016 and 2019 and for the historical controls at the time of the study (between 2015-2018). For this particular part of the analysis, we excluded MIP joining the PNC after 10 weeks of delivery because if they joined later, their follow up time would have been different and their time in PNC different, which would bias the analysis. We only included MIP who joined PNC from November 1st, 2015, to December 31st, 2018. Children who seroconverted were excluded from subsequent testing denominators. The PMTCT results included: children rapid test completion and positivity at 9 months (8-10 months old) and 18 months (17-19 months old); maternal viral load completion and suppression (VL<400cp/ml) in the first 12 months and between 12 and 18 months. For VL completion, PNC mothers who did not attend PNC that day were included in the analysis.

The secondary analysis was a description of PMTCT results PNC cohort only. All MIP joining PNC between June 1st, 2016, and March 31st, 2019, were included in the analysis. Retention in care analysis was conducted among MIP who joined a club at week 10 and using as denominator the number of MIP with enough follow-up time to be due for the visit at each time point. Back to clinic (BTC) was defined as mothers going back to the standard of care. Did not attend (DNA) was defined as MIP not attending or if the mother did not attend, DNA only for the mother. Loss to follow up (LTFU) was defined as MIP not attending more than two subsequent visits in a row and were included in the analysis. Transfer out (TFO) was defined as self-report of MIP attending care elsewhere and were excluded from the analysis, but reported on. For maternal VL completion, the timepoints used were 6 months (7-180 days after delivery), 12 months (181-365 days after delivery) and 18 months (12-18 months after

delivery). The number of "high risk" MIP (based on the 2016 WCP PMTCT definition) was described over 6 monthly timepoints (35). After the study was completed, a search was done for HIV-positive results for all LTFU infants (looking for positive HIV PCR test or a CD4 count).

For tertiary outcomes, the definition of full immunisation at 12 months of age was based on the national definitions of immunisation (36). Vaccination coverage was checked on EMR, and if discordant, by auditing folders. Other outcomes such as the insertion of an intrauterine contraception device (IUCD) was based on the nurses' own register. Pap smear completion was based on the electronic register. Any patient who had not completed their Pap smear 3 years prior to enrolment into PNC was considered eligible as per the national guidelines (37).

Ethics

Ethical review and approval were provided by the Foundation for Professional Development Research Ethics Committee (FPD REC clearance certificate 5-2017) and University of Cape Town (UCT) Ethics Review Boards (ref 314/2022). The intervention was approved by City of Cape Town (CCT) Research Board (ID number 7899). Because anonymised routine data were used, no individual written consent was obtained from PNC participants. The historical controls data collection was conducted in accordance with the approval from Stellenbosch University Ethics committee (HREC N14/06/060), the Western Cape Provincial Health Research Committee and the MSF-Ethics Review Board.

Results

As detailed in Table 1, infant testing as well as maternal VL completion and suppression was compared between the PNC cohort and historical controls. As shown in this table, the 9 months rapid test completion was 1.6 times higher for the infants in the PNC (95% CI 1.4-1.9) and 2 times higher at 18 months (95% CI 1.6-2.6). Both at 0-12month and at 12-18 months, maternal VL completion was higher in the PNC group compared to the historical cohort by 1.5 times (95% CI 1.3-1.6) and 2.6 times (95% CI 2.1-3.2) respectively. Maternal VL suppression was equivalent at 0-12 month and at 12-18 months between the two groups. One infant seroconverted at one year of age in the PNC group after becoming LTFU past the 9 months visit when the infant had a negative rapid test; at 6 months his/her mother had a suppressed VL. In the historical cohort, two infants seroconverted before 18 months of age.

Table 1: Maternal Viral Load (VL) completion and suppression and infant testing in postnatal clubs (PNC) and historical controls (38)

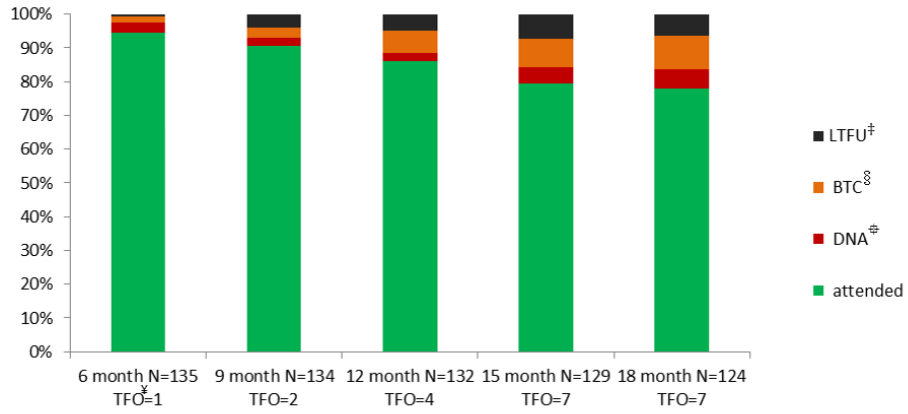
	Historical controls n=221	**Postnatal clubs (PNC) n=141**	**Risk ratio (95% CI) [PNC/controls]**
Infants			
9 months rapid completion (8-10mth)	112/221 (51%)	114/141 (81%)	1.6 (1.4-1.9)
18 months rapid completion (17-19mth)	70/220 (32%)	90/140 (64%)	2.0 (1.6-2.6)
Seroconversions*	2	1	
Mothers			
0-12 months VL completion	149/221 (67%)	140/141 (99%)	1.5 (1.3-1.6)
0-12 months VL suppression	141/149 (95%)	134/140 (96%)	1.0 (0.96-1.1)
12-18 months VL completion	65/221 (29%)	107/141 (76%)	2.6 (2.1-3.2)
12-18 months VL suppression	63/65 (97%)	101/107 (94%)	0.97 (0.9-1.0)

*Control group: two infants seroconverted before 18 months. PNC cohort: one infant seroconverted after exiting the PNC before their 18 months test

Looking at the PNC cohort only
Retention in care and PMTCT results

During the implementation of PNC, n= 484 (3 sets of twins) MIP were recruited into PNC at 10 weeks (baseline). Of those, respectively 353, 238 and 159 MIP were due for their 6, 12 and 18 months follow up. At 6 months, (318/353) 90% attended. At 12 months, (195/238) 82% attended. At 18 months, (127/156) 81% attended, as shown in Figure 1.

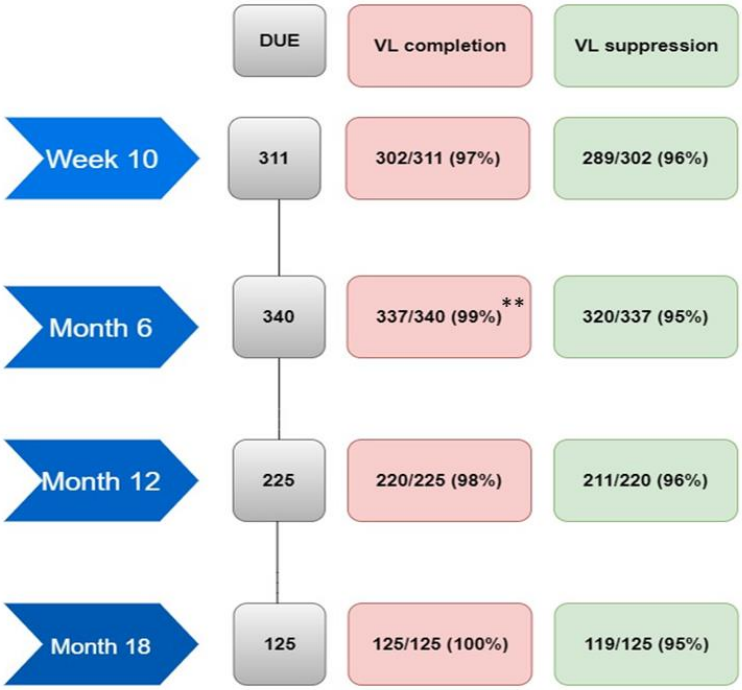
Title: Figure 1: Retention in care of mother and infant pairs (MIP) in PNC.



Legend: †Denominator at each point includes MIP with enough follow-up time to be due for the visit. Only those who joined PNC at week 10 are included ‡LTFU: Loss to Follow Up §BTC: Back to Clinic ¥TFO: Transferred Out ⌗DNA: Did Not Attend

As shown in Figure 2, for the mothers attending their PNC visits, maternal viral load completion and suppression at baseline (week 10) were respectively 97% and 96%. At month 6, it was 99% and 95%; at month 12, it was 98% and 96% and at month 18, it was 100% and 95%.

Title: Figure 2: Maternal viral load (VL) completion and suppression



** Denominator at 6 months is higher than at week 10 because of the first 6 months of implementation when MIP could join up to 6 months of age.

As shown in Table 2, of those attending the 9 months and 18 months visits, 98% (259/263) had 9 months rapid done and 99% (126/127) had 18 months rapid done. There were no positive HIV results amongst the children attending the PNC.

Table 2: Uptake of infants' 9 months and 18 months HIV rapid tests (of those attending 9- and 18-months visits) and HIV positivity

Visit month	Test uptake/ Total attending visit	Uptake percentage	HIV-positive
Month 9	259/263	98%	0%
Month 18	126/127	99%	0%

As shown in Table 3, the percentage of high-risk MIP was consistent throughout the PNC: from 6% at baseline to 4-5% at the other timepoints.

Table 3: High risk mothers at start of PNC, 6 months, 12 months and 18 months (of those due to attend 10 weeks, 6, 12 and 18 months visits)

Visit month	High risk mothers/ Total due to attend visit	High risk percentage
Baseline	30/484	6%
Month 6	17/340	5%
Month 12	9/225	4%
Month 18	6/125	5%

Vaccination results

Out of a total of 105 infants attending the 12 months visit, 99% were fully vaccinated by one year.

Sexual Reproductive Health (SRH) and mental health results

Part of the integration of PNC was to encourage integration of SRH services for the mother. All women were offered family planning at every visit, as part of standard of care. Of the 155 mothers who completed the 18 months visit, 125 mothers had Pap smear data available and of those, 31 were not due for Pap smear and of the ones due, (50/94) 53% had their Pap smear done during PNC. Of the 201 women who had an IUCD inserted at the clinic between 2016-2018, 16% (32/201) were part of the PNC. Of those 32, 75% had the IUCD inserted within their first 6 months of the PNC.

Of the PNC mothers who were screened for depression, 18% (78/423) overall screened positive at one point for depression on the mental health screening questionnaire.

Discussion

Looking at a comparison between MIP in the PNC and historical controls, VL completion for the mothers between 0-12 months and 12-18 months in PNC was 99% and 76% compared to 67% and 29%, respectively, for historical controls. High VL completion in PNC suggests that retention in care of mothers living with HIV and their HIV-exposed infants was better in PNC than in historical controls. VL suppression was comparable between PNC and historical controls (at 0-12 months 96% and 95% respectively; at 12-18 months: 94% and 97% respectively). Uptake of the 9 months and 18 months rapid tests for the infants in PNC was 81% and 64% respectively compared to 51% and 32% for historical controls. One child seroconverted (after becoming LFTU to PNC) in the PNC group compared to 2 children seroconverting in the historical control group.

Looking at the PNC cohort only, at 18 months, 81% of the mothers and infants who had started PNC attended. Of the mothers who attended their 18 months visit, 100% had a VL done and 95% had VL suppressed. 99% of the infants who attended the session had an 18 months rapid test done. All rapid tests were negative. This combined with a 95% full immunization coverage at one year suggests that integration of HIV care and other services is

possible for children. Furthermore, although the results for Pap smear and IUCD insertion are difficult to interpret, they also suggest that integration of HIV care and non-HIV care for mothers is possible. These results are suggestive that it is possible to "doubly" integrate maternal and child health (as well as HIV and non-HIV care) and may even lead to better retention in care.

When looking at retention in care of the MIP, both the comparative results between PNC and historical controls and the results of the PNC cohort suggest better retention in care of the MIP in PNC than what would be observed in the standard of care. This is in agreement with another study done locally, the MCH-ART randomized controlled trial, which showed higher RIC of mothers in integrated maternal and child health (MCH) care compared to standard of care (absolute risk difference: 0.21; 95% CI: 0.12-0.30) (39). Recently, meta-analyses have been looking at RIC of women living with HIV postnatally (40–42). They have all identified integrated care as a factor in improving RIC. The impact of other factors such as peer support, mhealth interventions, and cash transfers are more variable. There are potential multiple reasons for the observed improved retention in care of MIP in PNC. Duviviers et al's qualitative study of the PNC suggests that mothers enjoyed the strong peer support they received in the PNC as well as the comprehensive care for themselves and their infants (43). The mothers felt that the peer support decreased HIV stigma, allowing easier disclosure to family or partners. They also saw the PNC as timesaving by limiting their trips to the clinic. This is in agreement with a qualitative study done for adult ART adherence clubs as well as studies done in PMTCT on peer support (24,44). Britain's meta-analysis found that peer-led support did not improve RIC but continuity of care with one provider did (41). Because our study included integration of care as well as continuity of care with one clinical provider and peer support, it is likely that all these factors played a role in improving RIC of the MIP.

Integration of care in the PNC also led to a better uptake of vaccination of children and relatively good uptake of reproductive and sexual services, as reported by City when compared to their other clinics data (45). Although the data on IUCD insertion and family planning is limited in this study (with likely some under reporting of IUCD insertion), unmet contraceptive needs is a challenge in South Africa and any attempts to encourage postpartum family planning is welcome to try to space out pregnancies (46). Other studies in Sub-Saharan Africa looked at integrating postpartum family planning with immunization and also reported it was feasible and welcomed by mothers (46,47). Of note, it is part of standard of care for women accessing ART services to be offered family planning, so data was not

collected on this. There is also very little literature on the uptake of family planning in ART clubs, except to point out that it is integrated with the services (48).

A major difference from the ART clubs recommended by the WHO for pregnant/breastfeeding women is that PNC includes "unstable" or "high risk" women. Although "high risk" women in the PNC received specific interventions (such as extra visits in between PNC visits and ART adherence counselling), the results do not show improvement in the number of "high risk" mothers overtime. More research is needed into understanding why the women become "high risk" and how to best support them. Studies in a neighbouring clinic suggested that one third of postpartum women had suffered from intimate partner violence (IPV), associated with a high VL postnatally (49). Although there were anecdotal reports of IPV by the PNC mothers, and although gender-based violence was discussed in the PNC group session, the PNC intervention did not specifically focus on IPV. As part of the first 1000 days component of the PNC, mothers were screened regularly for mental health issues, as well as discussing depression in the group session. Although the number of women screening positive on the mental health questionnaire was lower than expected at 18.4%, it is well known that pregnant/breastfeeding women with HIV are at high risk of mental health illness and recommendations have been made globally to address the issue (50,51). More in-depth analysis of risk factors for "high risk" women is needed to better tailor interventions to accommodate them. The number of "high risk" mothers being small, it is difficult to draw conclusions from these results. It suggests however that it is possible to have a more flexible type of club, like the PNC, where "high risk" mothers can be catered for. This will hopefully lead to better RIC of "high risk" mothers and contribute to lowering MTCT in the breastfeeding period.

Looking at the cost-effectiveness of this intervention, we can compare it to the MCH-ART study, which found that integration of maternal and child health in one location was cost-effective and improved the MIP outcomes (52). Duviviers's qualitative study suggested that the implementation process of PNC was feasible to staff, despite initial heavy involvement from the MSF staff (43).

When interpreting these results, there are some strengths and limitations to be considered. Strengths of this study is that it was implementation science, done in a "real life" setting with no reimbursements or financial incentives used, as well as working with the existing team and infrastructure. Furthermore, the intervention was designed and implemented collaboratively with important stakeholders in the health system, such as CCT and m2m. This

is likely to have contributed to the good buy-in of the intervention from other clinics and other stakeholders in the health department. Some limitations include the fact that the results presented in this paper are from one peri-urban clinic only and in the Western Cape Province. Although outcomes are generally better in Western Cape Province than in other provinces and resources are usually more accessible, its HIV prevalence is comparable to the rest of South Africa (53). After the study ended, the PNC model was tried out in two more clinics in Khayelitsha with results on RIC of MIP still pending. Another limitation is that the description of the implementation of PNC corresponds to the period when PNC was implemented by Department of Health staff with MSF staff mentoring. Longer study period without MSF's support would be advisable to see if the outcomes remain significantly better than standard of care.

Other limitations included using a historical cohort for comparison to the PNC MIP. We were not able to compare the baseline characteristics, including maternal ART regimen, of the two groups as they were not collected and this is a potential bias in the comparison. Although using a retrospective cohort brings inherent bias, the PMTCT results from this cohort are very similar to what is reported elsewhere (54). Other limitations in the study included collection methods of the mental health data. Although the PNC facilitators received initial mental health training, they did not have further mentoring or coaching and this could have affected their confidence in administering the questionnaire, as suggested by other studies in similar context (55). This could have resulted in a lower positivity rate on the mental health screening questionnaire than expected, compared to studies in similar settings suggesting 25%-57% of women screening positive for postpartum depression (51,56).

Looking at the generalisability of PNC, the model described here has been adapted to different contexts and different components have been added or subtracted. This allowed the model to be piloted by MSF in other Sub-Saharan African settings such as in Mozambique and eSwatini. In South Africa, the PNC model was adopted by the National Department of Health as a "best case scenario" and included in the national PMTCT guidelines (57). It was then rolled out by PEPFAR, including in Johannesburg and more research is awaited to comment on the results of this roll out (58).

Conclusion

The PNC model showed good retention in care of MIP, with good VL completion and suppression of the mothers as well as good uptake of the HIV testing of infants. Vaccination uptake for the children was also good. These results as well as the integration of care of the MIP, support of the first 1000 days campaign and peer support have made this intervention desirable to be rolled out at the national level to work towards the elimination of MTCT. Further adaptation of the PNC model is possible for use in different contexts and more research is awaited on those outcomes.

References

1. UNAIDS. Joint United Nations Programme on HIV/AIDS. 2015;11(3):1–88. Available from: https://www.unaids.org/sites/default/files/media_asset/JC2774_2015ProgressReport_GlobalPlan_en.pdf (Accessed July 10, 2022)

2. Thembisa model. https://www.thembisa.org/downloads (Accessed July 10, 2022)

3. Goga A, Chirinda W, Ngandu NK, Ngoma K, Bhardwaj S, Feucht U, et al. Closing the gaps to eliminate mother-to-child transmission of HIV (MTCT) in South Africa: Understanding MTCT case rates, factors that hinder the monitoring and attainment of targets, and potential game changers. South African Medical Journal. 2018;108(3):S17–24.

4. Nelson A, Duran LT, Cassidy T, Cutsem G van, Steele S jane, Cotton M, et al. Impact of Birth PCR on Retention in Care of HIV Exposed Infants in Primary Care. CROI Conference, Abstract 791. 2017;

5. Kuhn L, Kroon M. Breastfeeding and the 2015 South African guidelines for prevention of mother-to-child transmission of HIV. South Afr J HIV Med. 2017;16(1):1–5.

6. UNICEF. Evidence-based practices for retention in care of mother-infant pairs in the context of eliminating mother-to-child transmission of HIV in Eastern and Southern Africa : A summary with guidance for scale up. Unicef. 2019;(March 2019):29.

7. McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): Effectiveness results from the pilot phase of a pragmatic open-label randomised trial. The Lancet. 2016;387(10013):53–60

8. Etoori D, Rice B, Reniers G, Gomez-Olive FX, Renju J, Kabudula CW, et al. Patterns of engagement in HIV care during pregnancy and breastfeeding: findings from a cohort study in North-Eastern South Africa. BMC Public Health. 2021;21(1):1–12.

9. Brittain K, Remien RH, Mellins CA, Phillips TK, Zerbe A, Abrams EJ, et al. Determinants of suboptimal adherence and elevated HIV viral load in pregnant women already on antiretroviral therapy when entering antenatal care in Cape Town , South

Africa women already on antiretroviral therapy when entering antenatal care in Cape. 2018;0121.

10. Phillips T, Thebus E, Bekker LG, Mcintyre J, Abrams EJ, Myer L. Disengagement of HIV-positive pregnant and postpartum women from antiretroviral therapy services: a cohort study. J Int AIDS Soc. 2014;17:19242.

11. Suthar AB, Hoos D, Beqiri A, Lorenz-Dehne K, McClure C, Duncombe C. Integrating antiretroviral therapy into antenatal care and maternal and child health settings: a systematic review and meta-analysis. Bull World Health Organ. 2013;91(1):46–56.

12. Hodgson I, Plummer ML, Konopka SN, Colvin CJ, Jonas E, Albertini J, et al. A systematic review of individual and contextual factors affecting ART initiation, adherence, and retention for HIV-infected pregnant and postpartum women. PLoS One. 2014;9(11).

13. Nachega JB, Uthman OA, Anderson J, Peltzer K, Wampold S, Cotton MF, et al. Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: A systematic review and meta-analysis. Aids. 2012;26(16):2039–52.

14. Clouse K, Schwartz S, Rie A van, Bassett J, Yende N, Pettifor A. " What They Wanted Was to Give Birth; Nothing Else " : Barriers to Retention in Option B+ HIV Care Among Postpartum Women in South Africa. J Acquir Immune Defic Syndr. 2014;67(1):12–8.

15. Phillips T, McNairy ML, Zerbe A, Myer L, Abrams EJ. Postpartum transfer of care among HIV-infected women initiating antiretroviral therapy during pregnancy. J Acquir Immune Defic Syndr (1988). 2015;70(3):e102–9.

16. World Health Organization. Key considerations for differentiated antiretroviral therapy delivery for specific populations: children, adolescents, pregnant and breastfeeding women and key populations. 2017; Available from: https://apps.who.int/iris/bitstream/handle/10665/258506/WHO-HIV-2017.34-eng.pdf?sequence=1 (Accessed July 10, 2022)

17. Nelson AK, Cassidy T, Duran LT, Cox V, Wedderburn CJ, Giddy J, et al. An analysis of the HIV testing cascade of a group of HIV-exposed infants from birth to 18 months in peri-urban Khayelitsha, South Africa. PLoS One. 2022 Jan 1

18. Johnson LF, Patrick M, Sa DCH, Sa F, Stephen C, Sa DCH, et al. Steep declines in pediatric AIDS mortality in South Africa, despite poor progress towards pediatric diagnosis and treatment targets. Pediatr Infect. 2020;39(9):843–8.

19. Ramraj T, Goga AE, Larsen A, Ramokolo V, Bhardwaj S, Chirinda W, et al. Completeness of patient-held records: observations of the Road-to-Health Booklet from two national facility-based surveys at 6 weeks postpartum, South Africa. J Glob Health. 2018;8(2):1–13.

20. Ml L, Ce K, Azman H, Aa C, Lm B, Horvath T, et al. Integration of HIV / AIDS services with maternal, neonatal and child health , nutrition , and family planning services (Review). 2012;(9).

21. UNAIDS. 2015 Progress report on the global plan towards the elimination of new HIV infections among children and keeping their mothers alive. Vol. 11, Unaids. 2015. p. 1–88. Available from: http://www.unaids.org/sites/default/files/media_asset/JC2774_2015ProgressReport_GlobalPlan_en.pdf (Accessed July 10, 2022)

22. Luque-Fernandez MA, van Cutsem G, Goemaere E, Hilderbrand K, Schomaker M, Mantangana N, et al. Effectiveness of Patient Adherence Groups as a Model of Care for Stable Patients on Antiretroviral Therapy in Khayelitsha, Cape Town, South Africa. Dowdy DW, editor. PLoS One. 2013 Feb;8(2):e56088.

23. Wilkinson LS. ART adherence clubs: A long-term retention strategy for clinically stable patients receiving antiretroviral therapy. South Afr J HIV Med. 2017;14(2):48–50.

24. Venables E, Towriss C, Rini Z, Nxiba X, Cassidy T, Tutu S, et al. Patient experiences of ART adherence clubs in Khayelitsha and Gugulethu, Cape Town, South Africa: A qualitative study. PLoS One. 2019;14(6):1–18.

25. Engel G. The Need for a New Medical Model : A Challenge for Biomedicine Author (s): George L . Engel Published by : American Association for the Advancement of

Science Stable URL : http://www.jstor.org/stable/1743658 . Science, New Series. 1977;196(4286):129–36.

26. Western Cape Government. First 1000 days. 2021. Available from: https://www.westerncape.gov.za/first-1000-days/ (Accessed July 10, 2022)

27. Pieters P. Personal communication. 2015.

28. City of Cape Town. City Health Department. 2021. Available from: https://www.capetown.gov.za/Departments/City Health Department (Accessed July 10, 2022)

29. m2m. mothers2mothers organisation. 2021. Available from: https://m2m.org/ (Accessed July 10, 2022)

30. MSF. MSF in South Africa. Available from: https://www.msf.org/south-africa (Accessed July 10, 2022)

31. PMHP. Perinatal Mental Health Project: resources for service providers. 2021. Available from: https://pmhp.za.org/resources/for-service-providers/ (Accessed July 10, 2022)

32. Western Cape Department of Health. The Western Cape Consolidated Guidelines for HIV Treatment: Prevention of Mother-to-Child Transmission of HIV (PMTCT), Children, Adolescents and Adults; 2015.

33. Olayo R, Wafula C, Aseyo E, Loum C, Kaseje D. A quasi-experimental assessment of the effectiveness of the Community Health Strategy on health outcomes in Kenya. BMC Health Serv Res. 2014;14(SUPPL.1):1–13.

34. PNMP. Maternal mental health screening tool. Available from: https://pmhp.za.org/wp-content/uploads/Western-Cape-Maternity-Case-Record-Version-19-June-2018.pdf (Accessed July 10, 2022)

35. The Western Cape Government. The Western Cape Consolidated Guidelines for HIV Treatment: Prevention of Mother-to-Child of HIV (PMTCT), Children, Adolescents and Adults. 2016;2016. Available from: https://www.westerncape.gov.za/assets/departments/health/wcgh233_hiv_pmtct_guidelines_03102016.pdf (Accessed July 10, 2022)

36. KZNHealth. Annual performance plan 2018/9-2020/21 Indicator descriptions. Available from: http://www.kznhealth.gov.za/app/APP-1819-Indicator-Descriptions.pdf (Accessed July 10, 2022)

37. South African National Department of Health. Cervical Cancer Prevention and Control Policy. 2020. Available from: https://www.westerncape.gov.za/text/2020/February/cervical_cancer_prevention_and_control_policy.pdf (Accessed July 10, 2022)

38. K. Lebelo, T. Cassidy, L.T. Duran, V. Bhardwaj, N. Mantangana, L. Mdani, N. Malabi, K. Buchanan, L. AN. Integrated postnatal clubs show improved maternal viral load completion and infant testing uptake compared to historical controls in Khayelitsha, South Africa. AIDS conference. 2020.

39. Myer L, Phillips TK, Zerbe A, Brittain K, Lesosky M, Hsiao NY, et al. Integration of postpartum healthcare services for HIV-infected women and their infants in South Africa: A randomised controlled trial. PLoS Med. 2018;15(3):1–21.

40. Vrazo AC, Firth J, Amzel A, Sedillo R, Ryan J, Phelps RB. Interventions to significantly improve service uptake and retention of HIV-positive pregnant women and HIV-exposed infants along the prevention of mother-to-child transmission continuum of care: systematic review. Trop Med Int Health. 2018;23:136–48.

41. Brittain K, Teasdale CA, Ngeno B, Odondi J, Ochanda B, Brown K, et al. Improving retention in antenatal and postnatal care: a systematic review of evidence to inform strategies for adolescents and young women living with HIV. J Int AIDS Soc. 2021;24(8):1–18.

42. Puchalski Ritchie LM, van Lettow M, Pham B, Straus SE, Hosseinipour MC, Rosenberg NE, et al. What interventions are effective in improving uptake and retention of HIV-positive pregnant and breastfeeding women and their infants in preventio mother to child transmission care programmes in low-income and middle-income countries? A systematic review . BMJ Open. 2019 Jul 1;9(7).

43. Duvivier H, Decroo T, Nelson A, Cassidy T, Mbakaz Z, Duran LT, et al. Knowledge transmission, peer support, behaviour change and satisfaction in post Natal clubs in Khayelitsha, South Africa: A qualitative study. Reprod Health. 2020;17(1):1–11.

44. Rollins NC, Essajee SM, Bellare N, Doherty M, Hirnschall GO. Improving retention in care among pregnant women and mothers living with HIV: Lessons from INSPIRE and implications for future WHO guidance and monitoring. J Acquir Immune Defic Syndr (1988). 2017;75:S111–4.

45. Beth Harvey, personal communication (2019)

46 Chersich MF, Wabiri N, Risher K, Shisana O, Celentano D, Rehle T, et al. Contraception coverage and methods used among women in South Africa: A national household survey. South African Medical Journal. 2017;107(4):307–14.

47. Dulli LS, Eichleay M, Rademacher K, Sortijas S, Nsengiyumva T. Meeting postpartum women's family planning needs through integrated family planning and immunization services: Results of a cluster-randomized controlled trial in Rwanda. Glob Health Sci Pract. 2016;4(1):73–86.

48. Hoyt J, Krishnaratne S, Hamon JK, Boudarene L, Chantler T, Demissie SD, et al. "As a woman who watches how my family is… I take the difficult decisions": a qualitative study on integrated family planning and childhood immunisation services in five African countries. Reprod Health. 2021;18(1):1–13.

49. Wilkinson L, Harley B, Sharp J, Solomon S, Jacobs S, Cragg C, et al. Expansion of the Adherence Club model for stable antiretroviral therapy patients in the Cape Metro, South Africa 2011–2015. Tropical Medicine & International Health. 2016 Jun 1;21(6):743–9.

50. Bernstein M, Phillips T, Zerbe A, McIntyre JA, Brittain K, Petro G, et al. Intimate partner violence experienced by HIV-infected pregnant women in South Africa: A cross-sectional study. BMJ Open. 2016;6(8).

51. Stringer EM, Meltzer-Brody S, Kasaro M, Stuebe AM, Wiegand S, Paul R, et al. Depression, pregnancy, and HIV: The case to strengthen mental health services for pregnant and post-partum women in sub-saharan africa. Lancet Psychiatry. 2014;1(2):159–62.

52. Id IM, Nattey C, Jinga N, Mongwenyana C, Fox P, Id DO. Prevalence and predictors of postpartum depression by HIV status and timing of HIV diagnosis in Gauteng , South Africa. 2019;288:1–15.

53. Dugdale CM, Phillips TK, Myer L, Hyle EP, Brittain K, Freedberg KA, et al. Cost-effectiveness of integrating postpartum antiretroviral therapy and infant care into maternal & child health services in South Africa. PLoS One. 2019;14(11):1–18.

54. Shisana, O, Rehle, T, Simbayi LC, Zuma, K, Jooste, S, Zungu N, Labadarios, D, Onoya DEAl. South African National HIV Prevalence, Incidence and Behaviour Survey, 2012. HSRC Press. 2014;194.

55. Phelanyane F. Prevention of mother-to-child-transmission (PMTCT) of HIV in Khayelitsha, South Africa: A contemporary review of the service 20 years later. In: AIDS. San Francisco; 2020.

56. Petersen I, Fairall L, Bhana A, Kathree T, Selohilwe O, Brooke-Sumner C, et al. Integrating mental health into chronic care in South Africa: The development of a district mental healthcare plan. The British Journal of Psychiatry. 2016 Jan 1;208(s56):s29–39.

57. Sudfeld CR, Kaaya S, Gunaratna NS, Mugusi F, Fawzi WW, Aboud S, et al. Depression at antiretroviral therapy initiation and clinical outcomes among a cohort of Tanzanian women living with HIV. Aids. 2017;31(2):263–71.

58. South African National Department of Health. Guideline for the Prevention of Mother to Child Transmission of HIV and other Transmittable Infections. 2018;

59. Makina-Zimalirana N, Dunlop J, Jiyane A, Bartels SM, Struthers H, Mcintyre J, et al. Postnatal Clubs for Integrated Postnatal Care in Johannesburg, South Africa: A Qualitative Assessment of Implementation. 2022

Supporting information

S1 Figure 1: Program for the PNC activities and clinical care

PNC Session Part 2: Activities & Clinical Care

Sessions*	Counsellor-led**		Nurse-led	
	Activities	Topic /ECD	Mother	Infant
6 weeks	Recruitment into PNC			
10-12 weeks	Mental Heath Q weight, register, ART (1m)	Infant Feeding/ Mental Health Tummy time/ Felt mobile	Clinical visit, FP, VL, risk stratification	PCR, immunisations, growth, PMTCT, (IMCI)
14-16 weeks	weight, register, ART (1m)	Child health Tummy exercise/ Make rattle	Pap smear, FP	Growth, immunisations, neurodevelopment, PMTCT, (IMCI)
18-20 weeks	weight, register, ART (1m)	Family planning Sitting with support/ Song	FP	Growth, PMTCT, (IMCI)
22-24 weeks	weight, register, ART (1m)	Disclosure/ Viral load Early conversations/ Song	FP	Growth, PMTCT, (IMCI)
6 months	Mental Health Q weight, register, ART (3m)	Complementary feeding/ Mental health Early milestones/ Stacking	Clinical review, FP, VL	Growth, immunisations, vitA, neurodevelopment, PMTCT, (IMCI)
9 months	Child rapid HIV test*** weight, register, ART (3m)	Sexual and intimate partner violence/Pre-test information Motor games/Hide & Seek, Clap with me	FP	Growth, Immunisations, neurodevelopment, PMTCT, (IMCI)
12 months	Mental Health Q weight, register, ART (3m)	Infant feeding- nutrition for children Language /Read magazine	Clinical, FP, VL	Growth, immunisations, deworming, vit A, PMTCT (IMCI)
15 months	weight, register, ART (3m)	Caregiver child relationship/ Intro adherence club	FP	Growth, PMTCT, (IMCI)
18 months	Child rapid HIV test*** Mental health Q	Pre-test information/ Graduation ceremony Refresher/ Graduation activity	Clinical, FP, VL	Growth, immunisations, deworming, Vit A, neurodevelopment, PMTCT, (IMCI)

*These visits should be attended by the mother (as opposed to a buddy) with the baby, as they involve more intensive clinical interventions for the mother and baby.
**IMCI: Integrated management of childhood illness
***Currently m2m mentors done by facility counselor

Acronyms:

PCR= polymerase chain reaction (HIV test)
Q= questionnaire
ART= antiretroviral therapy
FP= family planning
VL= viral load
PMTCT= prevention of mother to child transmission (medications)
IMCI= integrated management of childhood illness
vit A= vitamin A

(see PNC Toolkit_web version_spread (1).pdf (differentiatedservicedelivery.org)

for more information)

PART C APPENDICES

Acknowledgments

I would like to acknowledge my supervisor Professor Landon Myer for his patience and guidance through many years of juggling work-study-life balance and encouraging me to persevere through, as well as for his guidance on selecting my dissertation topic and guiding me to the finish line. Professor Myer also reviewed and gave input on the manuscript for its finalisation towards publishing.

I would like to thank the non-governmental organisation Médecins Sans Frontières (MSF) for first believing in the concept of Postnatal Clubs and allowing me to develop it from an idea to a full fledge operational activity. A special thanks to Dr Laura Trivino Duran for helping develop the model and analysis as well as for providing insightful comments on the manuscript. Thank you to Suhair Solomon and Kate Buchanan for helping refine the model and trouble-shooting implementation barriers along the way, and for providing input on the final manuscript. I would like to thank and acknowledge the MSF data team for collecting and keeping track of the data, with a special thanks to Tali Cassidy and Keitumetse Lebelo for their help in analysing the data, providing support on the manuscript's structure and input on the content of the manuscript. Thank you to Damian Hacking for many hours spent sorting out the schedule of the PNC and thank you to Vinayak Bhardwaj and Damian for looking at the cost analysis of PNC and providing very helpful comments on the final manuscript.

I would also like to thank and recognise the important role played by the City of Cape Town Health Khayelitsha managerial team (Shariefa Patel-Abrahams, Dr Virginia de Azevedo, Dr Beth Harvey) in supporting and helping develop the concept of PNC as well as in providing inputs on the final manuscript. With her wealth of knowledge of clubs and schedules, Beth also provided invaluable support in developing the PNC schedule.

I would like to thank mothers2mothers for their collaboration in developing the concept of PNC and particularly Clare Hofmeyr and Kathrin Schmitz for their input on the final manuscript.

A special thanks goes to the PNC implementing team on the ground from MSF (sis Mpumi Mantangana, sis Letti Mdani, Nikiwe Mlabi -who also reviewed the manuscript-), City of Cape Town nurses (Sr Letsoma, Sr Bonanto) and m2m mentors for their incredible work and passion working with mothers. I would like to also recognise and thanks the mothers and babies who were part of the initial PNCs who also helped mould its structure.

Finally, I would like to thank my family and friends for their unconditional support whilst I was completing my master and throughout all these years of hard work.

Appendix 1: UCT-HREC APPROVAL DOCUMENT

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UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 45 E-52-E-Floor- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

02 June 2022

HREC REF: 314/2022

Prof L Myer
School of Public Health & Family Medicine
FHS
Email: Landon.myer@uct.ac.za
Student: NLSAUR001@myuct.ac.za

Dear Prof Myer

PROJECT TITLE : POSTNATAL CLUBS: IMPLEMENTATION OF A DIFFERENTIATED AND INTEGRATED MODEL OF CARE FOR HIV-POSITIVE MOTHERS AND THEIR HIV EXPOSED UNINFECTED BABIES-
(MASTERS CANDIDATE-DR AURELIE NELSON)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19. Please refer to guidance letter dated 02 February 2022 on our website:
http://www.health.uct.ac.za/fhs/research/humanethics/forms

Approval is granted for one year until the 30 June 2023.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Dr Aurelie Nelson will also be involved in this study.

Please quote the HREC REF 314/2022 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

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Yours sincerely

Signed by candidate

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637. Institutional Review Board (IRB) number: IRB00001938 NHREC-registration number: REC-210208-007
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2020), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

3

HREC/ref314.2022

Appendix 2: City Health approval

CITY OF CAPE TOWN
ISIXEKO SASEKAPA
STAD KAAPSTAD

CITY HEALTH

Dr Hélène Visser
Manager: Specialised Health

T: 021 400 3981 F: 021 421 4894 M: 083 298 8718
E: Helene.Visser@capetown.gov.za

2017-10-16

Re: Research Request: Effects of Postnatal Club and Mentor Mother Interventions on Adherence and Retention-in-Care among HIV-Positive Postnatal Clients Receiving Prevention of Mother-to-Child Transmission Services, in Town 2 Clinic, Western Cape (7899)

Dear Dr Jude Igumbor,

Your research request has been approved to include Dr Ivan Tom's clinic as a` control', in addition to Town Two which is the intervention site:

Khayelitsha & Eastern	Town Two CDC, Dr Ivan Toms Clinic
Contact Person:	Dr V de Azevedo (Area Manager)
	Tel/Cell: (021) 360-1258/ 083 629 3344

Please note the following:

1. All individual patient information obtained must be kept confidential
2. Access to the clinics and clients must be arranged with the relevant Managers such that normal activities are not disrupted
3. A copy of the final report must be sent to the City Health Head Office, PO Box 2815 Cape Town 8001; within 6 months of its completion (which is currently scheduled for July 2018) and feedback must also be given to the clinics involved.
4. Your project has been given an ID Number 7899; please use this in any future correspondence with us
5. No monetary incentives to be paid to clients on the City Health premises.

Thank you for your co-operation and please contact me if you require any further information or assistance.

Yours sincerely

Signed by candidate

DR G H VISSER
MANAGER: SPECIALISED HEALTH

cc. Dr V de Azevedo
Dr K Jennings

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Appendix 3: Initial PNC protocol FPD approval

FPD

www.foundation.co.za

26 June 2017

Dr Jude Igumbor,
Mothers-to-Mothers

Dear Dr Igumbor

APPROVAL: Protocol – An Evaluation of a "Postnatal Club" Intervention to Promote Adherence and Retention-in-Care to Prevention of Mother-to-Child Transmission Services amongst HIV-Positive Postnatal Clients, in Town 2 Clinic, Western Cape.

Your revised application for ethical evaluation of the above mentioned study was considered by the Foundation for Professional Development Research Ethics Committee (FPD REC) on 19 June 2017.

The FPD REC is registered with the registered with the National Health Research Council for consideration of research projects that involve minimal risk to human participants. (Registration No REC-03711-033-RA Level 1)

FPD REC follows the standards adopted by the latest version of Guidelines for Good Clinical Practice; and conforms to the guidelines laid down by the World Medical Association, in particular, the Declaration of Helsinki, the Belmont Report, the National Department of Health and the Health Research Policy in South Africa.

The following members participated in this review:

Name	Gender	Occupation	Employer
David Cameron	M	Family Physician	Private sector
Nishana Ramdas	F	Pharmacist	Foundation for Professional Development
Braam Volschenk	M	Legal Advisor	That's It Project
Dawie Olivier	M	Evaluation Advisor	Foundation for Professional Development
Simukai Shamu	M	Epidemiologist	Foundation for Professional Development
Locadiah Mlambo	F	Biostatistician	Foundation for Professional Development
Zimasa Sobuza	F	Community	Foundation for Professional Development

The following documents were reviewed:

1. **"Postnatal Club" Intervention** Research Ethics Proposal V2.docx
2. Consent form.docx
3. Feedback to researcher.pdf

Please note the following:

- The approval is valid for 1 year.
- Please use your study number 5/2017 on correspondence and documents with the FPD REC.

Resolution

The committee resolved that all aspects of the protocol for this research complied with the standards of ethical research as outlined in guidelines and policies mentioned above. Ethics approval is subject to the following: (1) The approval is conditional on the receipt of 6-monthly written progress reports, and (2) The approval is conditional on the research being conducted as set out in the document submitted

1

to the FPD REC. Please notify the FPD REC in writing if any changes are made to the investigators, the methods or any aspects, such changes must be submitted as an amendment for approval to the FPD REC.

Yours sincerely,

Signed by candidate

Braam Volschenk
B Iuris LLB AHMP (FPD/YALE)
Chairperson, FPD Research Ethics Committee
Research Project Manager, FPD
E-mail: braamv@foundation.co.za
Tel: 082-821-2786

Secretariat: Ria Schoeman
rias@foundation.co.za
012-816-9163

Appendix 4: Approval of the amendment of the initial PNC protocol

FPD
www.foundation.co.za

30 August 2018

Dr Jude Igumbor,
Mothers-to-Mothers

Dear Dr Igumbor

APPROVAL: Protocol – An Evaluation of a "Postnatal Club" Intervention to Promote Adherence and Retention-in-Care to Prevention of Mother-to-Child Transmission Services amongst HIV-Positive Postnatal Clients, in Town 2 Clinic, Western Cape.

Your revised application for ethical evaluation of the above-mentioned study was considered by the Foundation for Professional Development Research Ethics Committee (FPD REC) in July 2018 and the amended protocol has been approved.

Please note the following:

- The approval is valid for 1 year.
- Please use your study number 5-2017 on correspondence and documents with the FPD REC.

Resolution
The committee resolved that all aspects of the protocol for this research complied with the standards of ethical research as outlined in guidelines and policies mentioned above. Ethics approval is subject to the following: (1) The approval is conditional on the receipt of 6-monthly written progress reports, and (2) The approval is conditional on the research being conducted as set out in the document submitted to the FPD REC. Please notify the FPD REC in writing if any changes are made to the investigators, the methods or any aspects, such changes must be submitted as an amendment for approval to the FPD REC.

Yours sincerely,

Signed by candidate

Braam Volschenk
B Iuris LLB AHMP (FPD/YALE)
Chairperson, FPD Research Ethics Committee
Research Project Manager, FPD
E-mail: braamv@foundation.co.za
Tel: 082-821-2786

Secretariat: Ria Schoeman
E-mail: rias@qode.healthcare
Tel: 0827893096

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Appendix 5 VEID protocol approval

UNIVERSITEIT·STELLENBOSCH·UNIVERSITY
jou kennisvennoot • your knowledge partner

Ethics Letter

28-Sep-2017

Ethics Reference #: N 14/06/060

Title: Clinical impact, performance and feasibility of very early, point of care infant diagnosis and initiation of antiretroviral therapy in HIV-infected infants at primary health care.

Dear Dr J Maritz,

Your application dated 25 May 2017 refers.

The Health Research Ethics Committee (HREC) approved the following documentation pertaining to the abovementioned study:

- Protocol Amendment 2 dated 25 May 2017

Kindly note that all blood draws must be in accordance with the HREC Guideline for Paediatric Blood Volume for Research Purposes. Details available on our website.

Federal Wide Assurance Number: 00001372
Institutional Review Board (IRB) Number: IRB0005240 for HREC1
Institutional Review Board (IRB) Number: IRB0005239 for HREC2

The Health Research Ethics Committee complies with the SA National Health Act No. 61 of 2003 as it pertains to health research and the United States Code of Federal Regulations Title 45 Part 46. This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki and the South African Medical Research Council Guidelines as well as the Guidelines for Ethical Research: Principles, Structures and Processes 2015 (Departement of Health).

Yours sincerely,

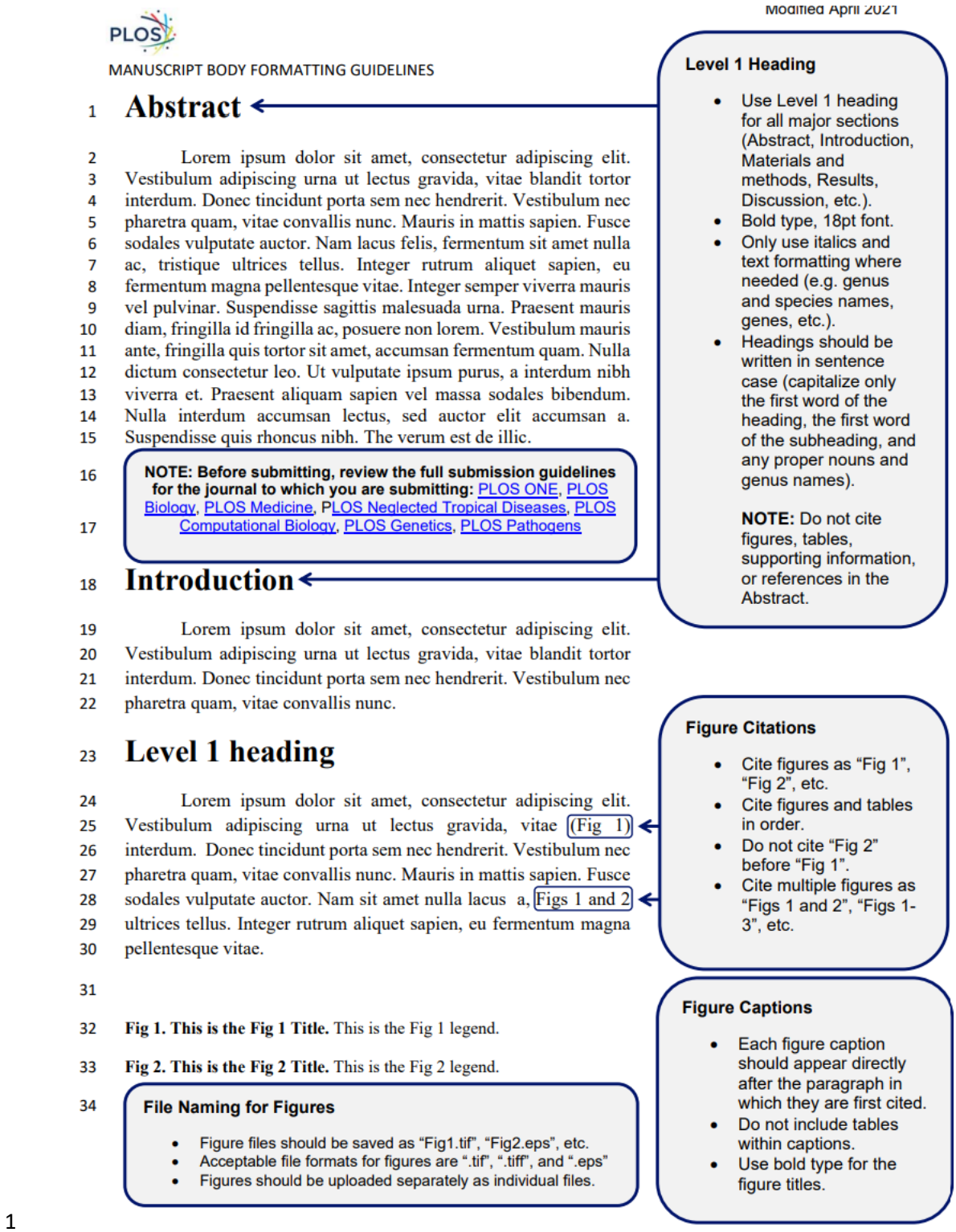
Franklin Weber,
HREC 1 Coordinator

Fakulteit Geneeskunde en Gesondheidswetenskappe
•
Faculty of Medicine and Health Sciences

Afdeling Navorsingsontwikkeling en -Steun • Research Development and Support Division

Posbus/PO Box 241 • Cape Town 8000 • Suid-Afrika/South Africa
Tel: +27 (0) 21 938 9677

Appendix 6: Instructions for authors PlosOne submission



Modified April 2021

PLOS

MANUSCRIPT BODY FORMATTING GUIDELINES

Abstract

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NOTE: Before submitting, review the full submission guidelines for the journal to which you are submitting: PLOS ONE, PLOS Biology, PLOS Medicine, PLOS Neglected Tropical Diseases, PLOS Computational Biology, PLOS Genetics, PLOS Pathogens

Introduction

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Level 1 heading

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Fig 1. This is the Fig 1 Title. This is the Fig 1 legend.

Fig 2. This is the Fig 2 Title. This is the Fig 2 legend.

File Naming for Figures

- Figure files should be saved as "Fig1.tif", "Fig2.eps", etc.
- Acceptable file formats for figures are ".tif", ".tiff", and ".eps"
- Figures should be uploaded separately as individual files.

Level 1 Heading

- Use Level 1 heading for all major sections (Abstract, Introduction, Materials and methods, Results, Discussion, etc.).
- Bold type, 18pt font.
- Only use italics and text formatting where needed (e.g. genus and species names, genes, etc.).
- Headings should be written in sentence case (capitalize only the first word of the heading, the first word of the subheading, and any proper nouns and genus names).

NOTE: Do not cite figures, tables, supporting information, or references in the Abstract.

Figure Citations

- Cite figures as "Fig 1", "Fig 2", etc.
- Cite figures and tables in order.
- Do not cite "Fig 2" before "Fig 1".
- Cite multiple figures as "Figs 1 and 2", "Figs 1-3", etc.

Figure Captions

- Each figure caption should appear directly after the paragraph in which they are first cited.
- Do not include tables within captions.
- Use bold type for the figure titles.

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NOTE: This document is presented in single-space paragraph format for ease of use. Please submit your manuscript in double-space paragraph format.

Display/Numbered Equation

- Format display equations in Mathtype or Equation Tools.
- Do not use Graphic Objects.

Inline Equation

- Format in regular text or as an inline equation in Mathtype or Equation Tools.
- Do not use Symbol Font.
- Do not use Graphic Objects.

Level 2 Heading

- Use Level 2 headings for sub-sections of major sections.
- Bold type, 16pt font.
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- Use sentence case.

Level 3 heading

- Use Level 3 headings for sub-sections within Level 2 headings.
- Bold type, 14pt font.
- Only use italics and text formatting where needed.
- Use sentence case.

Level 1 heading

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Vestibulum adipiscing urna ut lectus gravida, et bland Table 1 Donec tincidunt porta sem nec hendrerit. Vestibulum nec pharetra quam, vitae convalli. Fido nemo.

Table 1. This is the Table 1 Title.

	Chemical W	Chemical X	Chemical Y	Chemical Z
Chemical 1	Reaction 1W	Reaction 1X	Reaction 1Y	Reaction 1Z
Chemical 2	Reaction 2W	Reaction 2X	Reaction 2Y	Reaction 2Z
Chemical 3	Reaction 3W[a]	Reaction 3X	Reaction 3Y[b]	Reaction 3Z
Chemical 4	Reaction 4W	Reaction 4X	Reaction 4Y	Reaction 4Z
Chemical 5	Reaction 5W	Reaction 5X	Reaction 5Y	Reaction 5Z

This is the Table 1 legend.
[a]Table footnotes belong here.
[b]Footnotes should have corresponding symbols in the table.

Tables and Table Citations

- Tables should be cited as "Table 1", "Table 2", etc.
- Cite multiple tables as "Tables 1 and 2", "Tables 1-3", etc.
- Tables should be included directly after the paragraph in which they are first cited.
- Tables must be cell-based in Microsoft Word or embedded with Microsoft Excel.
- Do not use empty rows to create spacing.
- Do not include graphic objects, images, or colored text.

Conclusion

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Reference Citations

- Cite references in brackets (for example, "[1]" or "[2-5]" or "[3,7,9]").
- References must be cited in order at first mention.

Supporting Information Citations

- Format Supporting Information Citations as "S1 Fig", "S1 Table", etc.
- Cite multiple files as "S1 and S2 Figs", "S1-S3 Figs", etc.
- It is not required to cite each Supporting Information file.
- Supporting information should be uploaded separately as individual files.

Acknowledgments

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Acknowledgments

- Do not include funding or competing interests information in Acknowledgments.

References

1. Doe J, Data A, van Stats J, Testperson M, Ribosome D Jr, McBio GHT, et al. This is the article title. PLoS ONE. 2017;12(12):e00000. doi: 10.1371/journal.pone.0000000
2. Doe J, Data A, van Stats J, Testperson M, Ribosome D Jr, McBio GHT, et al. Bunny dynamics in cartoon landscapes. PLoS ONE. Forthcoming 2017.

References

- References should be listed after the main text, before the supporting information.
- References with more than six authors should list the first six author names, followed by "et al."
- References should be formatted according to the NLM/ICMJE style: https://www.nlm.nih.gov/bsd/uniform_requirements.html

Supporting information

S1 Fig. This is the S1 Fig Title. This is the S1 Fig legend.

S2 Fig. This is the S2 Fig Title. This is the S2 Fig legend.

S1 Table. This is the S1 Table Title. This is the S1 Table legend.

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S1 File. This is the S1 File Title. This is the S1 File legend.

Supporting Information Captions

- List Supporting Information captions at the end of the manuscript in a section titled "Supporting information".
- Use a Level 1 heading.
- Use bold type for the titles.
- Supporting Information files do not require full captions; only labels ("S1 Fig") are fully required.

File Naming for Supporting Information

- Supporting Information files should be saved as "S1_Fig.tif", "S1_File.pdf", etc.
- All file types are supported.

Before submitting, review the full submission guidelines for the journal to which you are submitting: PLOS ONE, PLOS Biology, PLOS Medicine, PLOS Neglected Tropical Diseases, PLOS Computational Biology, PLOS Genetics, PLOS Pathogens