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Prevention of Mother-to-Child Transmission of HIV(PMTCT) Efforts in KwaZulu-Natal, South Africa: Lessons from Botswana

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ABSTRACT

In sub-Saharan Africa (SSA) where mother-to-child transmission (MTCT) of human immunodeficiency virus (HIV) continues to be an ongoing problem, scale up of prevention of mother-to-child transmission (PMTCT) services remains a priority. Between 2001 and 2012 globally, the 52% decline of new pediatric HIV infection was attributed to the expansion of PMTCT services. In December of 2021, the World Health Organization (WHO) announced that Botswana was certified as having attained the silver-tier status in the elimination of mother-to-child transmission of HIV, because it had successfully reduced the MTCT rate to less than 5%, had provided antenatal care (ANC) and antiretroviral therapy (ART) to over 90% of pregnant women, and met the threshold of < 500 HIV cases per 1000,000 live births. This was a significant achievement as Botswana was the first high-burden country to be certified as having achieved this milestone. Hence, Botswana's journey towards elimination of MTCT can help inform and guide decisions surrounding PMTCT program implementation for other SSA countries. The South African province of KwaZulu-Natal may particularly benefit from such knowledge transfer as it has one of the highest prevalence of HIV in the world at 20.6%. The overall objective of this paper is to conduct a case study on Botswana's PMTCT implementation efforts to identify lessons learned from Botswana's success with its PMTCT implementation to improve PMTCT services in KwaZulu-Natal. The two primary aims were to: (1) conduct a scoping review to understand Botswana's journey towards elimination of mother to child transmission of HIV and (2) to identify lessons learned from Botswana to apply to KwaZulu-Natal. The majority of selected papers about Botswana's PMTCT programs emphasized the integration of PMTCT into the broader healthcare system, ANC attendance, HIV testing

coverage, infant feeding practices for breastfeeding among HIV-positive women, and targeted counseling and educational outreach efforts. These strategies can be adapted and applied to regions such as KwaZulu-Natal to reduce the performance gap for PMTCT for especially adolescent and young women. Future research exploring the specific structural and cultural barriers to antenatal attendance and health literacy will be important in maximizing program effectiveness to ensure adherence to the cascade of care. Accurate empirical evidence on the impact of PMTCT integration will guide future evidence-based interventions to eliminate MTCT in KwaZulu-Natal.

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TABLE OF CONTENTS

Abstract	2
Acknowledgements	4
Abbreviations	6
Introduction	7
Methods	18
Results	21
Discussion	32
Conclusion	39
Appendix	41
References	51

ABBREVIATIONS

ANC: antenatal care
ART: antiretroviral therapy
ARV: antiretroviral
AZT: zidovudine
EID: early infant diagnosis
HAART: highly active antiretroviral therapy
HIV: human immunodeficiency virus
MTCT: mother to child transmission
NVP: nevirapine
PMTCT: prevention of mother-to-child transmission
SSA: sub-saharan Africa
UNAIDS: Joint United Nations Programme on HIV/AIDS
UNFPA: United Nations Population Fund
UNICEF: United Nations Children's Fund
WHO: World Health Organization

INTRODUCTION

Elimination of MTCT

Mother-to-child transmission of HIV, or vertical transmission of HIV happens when the virus is transmitted from the mother to her child during pregnancy, childbirth (labor and delivery), or breastfeeding (breastmilk) (NIH, 2023). In 2021, 1.7 million children aged under 15 were living with HIV (U. S. Government, 2022). MTCT accounts for more than 90% of these pediatric infections, given that around 1.3 million pregnant women and girls infected with HIV give birth to children with a rate of transmission that ranges from 15% to 45% in the absence of intervention (Elizabeth Glaser Pediatric AIDS Foundation, 2023; WHO, 2023b). Although there has been a significant decrease of 52% in new HIV infections, from among children aged 0-9 since 2010 which is attributable to the scale-up PMTCT programs which include antiretroviral therapy (ART), there still exists a disproportionately high burden of HIV in SSA (UNAIDS, 2023; UNICEF, 2023). This geographical disparity is concerning, given that in 2021, 88% of children and adolescents living with HIV globally and 67% of people with HIV were located in SSA. Heterosexual relationships and MTCT are two major routes of transmission in this region, which contrasts from regions such as Asia where men who have sex with men, and persons who inject drugs and sex workers are at higher risk of HIV infection. Since interruption of MTCT can result in prevention of virtually all pediatric infections, implementing effective strategies to prevent mother to child HIV infection is a global priority to reduce child mortality and morbidity, especially in SSA.

Integration of PMTCT Interventions

During the 2009 World Health Assembly, UNAIDS called for a collective effort to integrate PMTCT programs into a broader health agenda, highlighting that virtual elimination of MTCT is possible given the availability of ART and committed efforts towards integrated and maintained PMTCT health services (UNAIDS, 2009). Organizations such as UNAIDS, WHO, UNICEF, and UNFPA have adopted this as a main priority, and this global campaign has led to wide implementation of PMTCT in especially low-and middle-income countries with high MTCT rates. According to the WHO principles outlined for effective national PMTCT implementation, integration of HIV testing, care, and treatment into maternal and child health services such as CD4 count testing and ART is a crucial aspect of PMTCT efforts. According to WHO's PMTCT Strategic Vision 2010-2015 in the context of the Millennium Development Goals, the comprehensive PMTCT programme is comprised of four components (WHO, 2010b):

- (1) Primary prevention of HIV infection among women of childbearing age
- (2) Preventing unintended pregnancies among women living with HIV
- (3) Preventing HIV transmission from a woman living with HIV to her infant
- (4) Providing appropriate treatment, care and support to mothers living with HIV and their children and families

This paper will primarily focus on component 3, which is preventing HIV transmission from mothers living with HIV to their children. WHO recommends lifelong ART for both pregnant and breastfeeding women who are test positive for HIV. The relevant components in the PMTCT cascade, a series of key steps to prevent mother to child transmission of HIV, regarding HIV-positive pregnant women include (Jean Claude Mutabazi, 2017; WHO,

2010b):

- CD4+ T-lymphocyte cell assessment (CD4 count)
- Antiretroviral (ARV) prophylaxis for mom and/or baby (for seropositive moms)
- Adherence to ARVs during pregnancy
- Delivery by skilled attendant
- Continuation of adherence to ARVs post delivery
- Follow safe infant feeding practices
- Bring infant for HIV testing

Infant Feeding Recommendations

Infant feeding recommendations in the context of HIV are applicable everywhere including where diarrhea, undernutrition and pneumonia are common causes of mortality. These recommendations are necessary to support maternal, infant and child health targets as described in the Global Strategy for Women's Children's' and Adolescent's Health (2016-2030) and Sustainable Development Goals (WHO, 2023a). In Southern Africa, where there is a high prevalence of MTCT rates, commercialized infant feeding formulas have resulted in increased mortality and morbidity among infants, highlighting the long-term benefits of breastfeeding.

Updates on HIV and Infant Feeding Guidance in 2016

- Mothers living with HIV should breastfeed for at least 12 months and may continue breastfeeding for up to 24 months or longer (similar to the general population) while being fully supported for ART adherence (see the WHO consolidated guidelines on ARV drugs for interventions to optimize adherence).
- National and local health authorities should actively coordinate and implement services in health facilities and activities in workplaces, communities and homes to protect, promote and support breastfeeding among women living with HIV.

Relevant Principles from 2010 Guidelines on HIV and Infant Feeding

- Setting national or subnational recommendations for infant feeding in the context of HIV: national or subnational health authorities should decide whether health services will mainly counsel and support mothers known to be living with HIV to either (1) breastfeed and receive ARV drug interventions or (2) avoid all breastfeeding as the strategy that will most likely give infants the greatest chance of HIV-free survival (remains valid)
- Conditions needed to safely formula feed Mothers known to be living with HIV should only give commercial infant formula milk as a replacement feed to their HIV-uninfected infants or infants who are of unknown HIV status when specific conditions are met: (a) safe water and sanitation are assured at the household level and in the community; and (b) the mother or other caregiver can reliably provide sufficient infant formula milk to support the normal growth and development of the infant; and (c) the mother or caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhea and malnutrition; and (d) the mother or caregiver can exclusively give infant formula milk in the first six months; and (e) the family is supportive of this practice; and (f) the mother or caregiver can access health care that offers comprehensive child health services. These descriptions are intended to give simpler and more explicit meaning to the concepts represented by AFASS (acceptable, feasible, affordable, sustainable and safe)

According to WHO, the elimination of mother to child transmission of HIV is defined as a rate of <50 new pediatric HIV infections per 10,000 live births transmission rate <5% among infants that are breastfeed for a minimum for a year (WHO, 2014). The ambitious

aim outlined by the Global AIDS Strategy of 2021-2016 has set the HIV epidemic control targets as 95-95-95 by 2025 with the emphasis of targeting HIV-infected adolescents and women within the framework of sexual reproductive health and rights (UNAIDS, 2021). This means that 95% of all people living with HIV should be aware of their status; 95% of all people diagnosed with HIV should receive sustained antiretroviral therapy(ART) and 95% of those who are receiving ART should have HIV viral suppression. These targets are aimed to reduce AIDS- related mortality and HIV incidence to achieve HIV epidemic control by 2030.

KwaZulu-Natal

<u>HIV Epidemiology</u>

South Africa is located in Sub-Saharan Africa and has one of the highest prevalence of HIV in the world at 20.6% (SABSSM, 2017). Following the establishment of the national PMTCT program in 2002, South Africa has benefited from the major guidelines changes such as the shift to zidovudine (AZT) monotherapy from single-dose nevirapine (NVP) in 2008 for mothers post 28 weeks of gestation period and administration of NVP prophylaxis within 72 hours of birth (Lilian et al., 2014). By 2012, South Africa experienced an estimation of approximately 10 fold decrease of mother to child transmission of HIV compared to the vertical transmission rate of 23.2% in 2003. In 2015, South Africa implemented the option B+ and PCR testing for infants in 2015. Despite these efforts coupled with effective ART scale up, South Africa had the greatest number of new HIV infections among women between 2009 and 2015 and continues to have high HIV prevalence and incidence rates (Woldesenbet et al., 2021). There is also the challenge of

heterogeneous uptake of PMTCT intervention across various districts in South Africa (Jooste et al., 2021). In 2018, only 62% of the 7.7 million HIV-positive people were accessing ART despite the implementation of universal routine HIV testing and immediate initiation of ART irrespective of CD4 cell count (Goga et al., 2018; National Department of Health South Africa, 2015). Within South Africa, KwaZulu-Natal is the province that has the highest prevalence (27.9%) of HIV (Jooste et al., 2021).

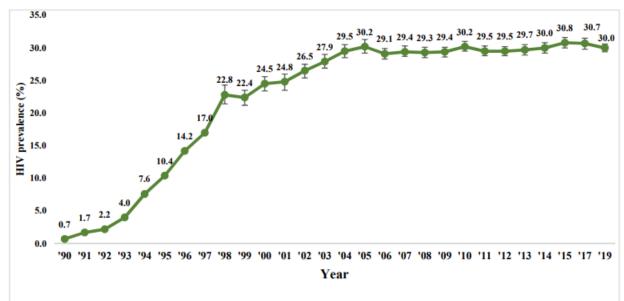


Figure 1. The HIV epidemic curve among antenatal women, South Africa, 1990-2019, Antenatal HIV Sentinel Survey

Both first-ANC-visit attendees and follow-up visit attendess were included in 2015, 2017 and 2019 surveys

Note. Woldesenbet, S.A., Lombard, C., Manda, S., Kufa, T., Ayalew, K., Cheyip M., and Puren, A. (2021). The 2019 National Antenatal Sentinel HIV Survey, South Africa, National Department of Health. Copyright 2021 by National Department of Health

According to the Antenatal HIV Sentinel Survey conducted in South Africa in 2019, which aimed to monitor HIV trends among 15-49 year old pregnant women attending antenatal clinics, KwaZulu-Natal province had the highest HIV prevalence (40.9%, 95% CI: 39.6%–42.3%) (Woldesenbet et al., 2021). This has been the case for the past five years in South Africa. Between 1990 and 2004, KwaZulu-Natal had an increase of HIV prevalence from 1.6% to 40.7%. Starting in 2004, the prevalence remained fairly constant until 2010 followed by a slight decrease to 41% in 2017 and 2019. Within the province, the HIV prevalence ranged from 33.6% (in uMzinyathi) to 44.2% (in Ugu). Overall, the HIV prevalence in KwaZulu-Natal is around 10% higher than the national average (Woldesenbet et al., 2021).

PMTCT Cascade

In KwaZulu-Natal, 98.6% of HIV-positive women are aware of their HIV status which is slightly higher than the national average of 97% (Woldesenbet et al., 2021). Specifically, 76.8% of HIV positive women knew their status before pregnancy, which is also above the national average of 72.7%. Among those who know their positive HIV status, 97.5% women were on ART. By 2018, the UNAIDS 90-90-90 targets were achieved, with 89.9% of people living with HIV aware of their HIV status, 93.8% of those aware of their status on ART, and 94.5% of those on ART virally suppressed (Conan et al., 2022). This was a dramatic improvement compared to 2013 when the corresponding figures were 75%-70%-93%. However, it is important to note that there is a significant variation among different age groups, and the proportion of adolescents and women below the age of 30 years in regards to the awareness of HIV positive states which is between 69.2 and 87.5% (Ntombela., 2022). This shows that structural and individual level barriers may be preventing access to testing services among certain population subgroups in spite that these testing services are widely available through primary healthcare clinics, leading to the broken linkage of care in KwaZulu-Natal.

Furthermore, only 88.9% of HIV+ adolescents who were between ages 14-19 and aware of their HIV positive status were on ART, which is the second target. This has been linked to

the high MTCT rates in this age group due to the lack of timely access to healthcare facilities and inability to achieve viral suppression. Lastly, in regards to the "third target," 95.9% of female adolescents and adult women were virally suppressed among those who had initiated ART and 90.8% of all pregnant women with HIV-positive status were virally suppressed, indicating that this critical target of PMTCT is being met (Ntombela et al., 2022).

Unintended Pregnancies

It is important to note that KwaZulu-Natal has the highest national prevalence of unintended pregnancy at 60.6% in South Africa, with adolescent girls between ages 15-19 years being at highest risk in all districts in the province (Woldesenbet et al., 2021). In addition, more than 75% of single women had unintended pregnancies in all districts, which is significantly higher than the prevalence of unintended pregnancies among married women. In KwaZulu-Natal, where heterosexual sex is the major mode of HIV transmission, women of child-bearing age are at the greatest risk of transmitting HIV to their children during pregnancy, delivery, and breastfeeding (Woldesenbet et al., 2021). Studies have shown that the lack of knowledge of HIV status is a major barrier to effective viral suppression among younger women, and married women are more likely to be virally suppressed, suggesting that married women are more likely to live in supportive environments for testing, treatment and maintenance of ART (Ntombela et al., 2022).

Early ANC Attendance

Almost three quarters (73.7%) of participants in KwaZulu-Natal initiate ANC before 20

weeks of gestation, which is the second highest ANC attendance rate nationally. However, 15-19 years old adolescent girls had the lowest attendance (Woldesenbet et al., 2021). This is also the group with the highest prevalence of unintended pregnancies in the province.

Gaps in PMTCT Services

The sharp reduction in MTCT in South Africa that fell from >20% to 2% over the past decade, has been attributed to increased access to ART and improved infant prophylactic regimens, transitions into Option B+, which gives lifelong ART to all pregnant and breastfeeding HIV-infected women, treats patients with lifelong triple ART irrespective of CD4+ cell count or clinical stage, and gives access to PMTCT programs on a large scale (Moyo et al., 2018; National Department of Health South Africa, 2015). Indeed, the early infant HIV screening program eventually evolved into a robust evidence-based program based on guidelines for routine testing for all exposed neonates at birth using HIV polymerase chain reaction (PCR), and a repeated PCR testing at 10 weeks of age and 6 weeks after cessation of breastfeeding for infants who had previously tested negative (National Department of Health South Africa, 2015). However, the high prevalence of youth pregnancy, accompanied by the discontinuation of PMTCT cascade of care are notable challenges for KwaZulu-Natal (Woldesenbet et al., 2021). Specifically, according to a study published in 2018, 36.3% of HIV positive infants were diagnosed late (during delivery or breastfeeding), and 26.6% received less than 12 weeks of ART prior to delivery (Moyo et al., 2018). There was also a gap in infants receiving ARV prophylaxis. This explains why there are high rates of MTCT in the province despite the availability of PMTCT programs. Ineffective management information systems also contribute to the failure to properly manage MTCT risk groups and the needed continuum of care to address it. It is

important for the overall effectiveness of the PMTCT programme that women with low CD4 counts, whose high viral loads put them at high risk of MTCT, are identified early and started on HAART (highly active antiretroviral therapy) prior to delivery (Horwood et al, 2010).

Infant Feeding Practices

In South Africa, a relatively high maternal HIV prevalence and high level of seroconversion of the offspring during pregnancy and breastfeeding continues to be a public health challenge (Johnson, Stinson, Newell., et al, 2012; National Department of Health, South Africa, 2015). South Africa has a fivefold higher intrauterine infection rate compared to the WHO elimination of MTCT target, which is <50 HIV-infected infants per 100,000 live births and half of the mother to child transmission of HIV occur due to intrapartum and postpartum transmission (Sherman GG, 2016; WHO, 2014). This implies that the lack of access to or delay of ART initiation during pregnancy causes insufficient viral suppression of maternal viraemia during delivery, postpartum and breastfeeding (Dinh, Delaney, Goga et al., 2015).

Since 2010 when the WHO recommended exclusive breastfeeding for the first 6 months of infant's life and mixed feeding until 24 months of age, South Africa had to adapt its PMTCT strategies as new evidence and corresponding guidelines emerged (WHO, 2010a, 2016). Specifically, the South African government recommended and supplied infant formula in 2002, and in 2011 recommended cessation of breastfeeding at 6 months to all babies born to HIV+ women (Department of Health: Republic of South Africa, 2017). However, by 2017, the government changed its recommendations to promote exclusive breastfeeding for 6 months and continued breastfeeding until 24 months of age for women on ART, which was totally aligned

with the most updated WHO infant feeding recommendations in the context of PMTCT (WHO, 2010a, 2016). Despite the clear evidence which shows that breast milk provides necessary nutrients and antibodies for proper infant growth and development among infants born to HIV+ mothers and that breastfeeding is a safe practice in the context of ART, many mothers do not adhere to this recommendation because of fear of transmission and stigma from HIV status disclosure (Tuthill et al., 2014; WHO, 2010a). Hence, it is not surprising that studies have shown that mixed feeding instead of exclusive breastfeeding, is the most prevalent method of infant feeding for infants less than 6 months of age in SSA (Bradley & Mishra, 2008). Specifically in South Africa, identified barriers include: fear of vertical transmission of HIV, employment, financial constraints, stigma, and misguided information from healthcare providers (West et al., 2019).

Given the present challenges of high MTCT rates in KwaZulu-Natal, the goal of this case study was to identify applicable lessons from Botswana's journey of developing PMTCT programs to provide helpful insight for the PMTCT programs in KwaZulu-Natal. Botswana's journey towards elimination of mother-to-child transmission of HIV could serve as an example of future program design and evaluation for the vulnerable populations in KwaZulu-Natal.

METHODS

<u>Objective</u>

The overall objective of this case study was to identify lessons learned from Botswana's success with its PMTCT programs to improve the PMTCT programs in KwaZulu-Natal, South Africa. The first specific aim was to conduct a scoping review to understand Botswana's journey towards elimination of mother-to-child transmission of HIV. The second specific aim was to identify lessons learned from Botswana to apply to KwaZulu-Natal, South Africa, where the PMTCT has been much less successful.

Search Strategy

The databases used for conducting the scoping review to address the first primary aim were Medline, Global Health, Web of Science, and Scopus. The search terms shown in Table 1 were used. The search terms were refined through MeSH terms and synonyms with support from a public health librarian.

Database	Search Terms	
Medline	Botswana.tw AND (PMTCT or vertical transmission HIV or mother to child transmission HIV).tw	
Global Health	((exp vertical transmission/) OR (PMTCT or vertical transmission HIV or mother to child transmission HIV).tw)) AND Botswana.tw	
Web of Science	Botswana AND (PMTCT OR "mother to child transmission HIV" OR "vertical transmission HIV") (Topic)	
Scopus	(TITLE-ABS-KEY (botswana)) AND (TITLE-ABS-KEY (PMTCT OR "mother to child transmission HIV" OR "vertical transmission HIV"))	

Table 1. Databases and Search Terms

Inclusion and Exclusion Criteria

Articles were included if they (1) discussed PMTCT national programs in Botswana; (2) were published since 2000; (3) were available in English; and (4) were peer reviewed. Articles were excluded if they (1) focused on countries other than Botswana; (2) focused on other pre-specified health care services without reference to PMTCT (3) focused on non-national PMTCT programs (4) did not discuss program effectiveness or implementation. Initially 161 articles were identified, and then titles and abstracts were screened before the final set of papers were selected for data extraction (see Figure 1).

Data Analysis and Extraction

Initially, all results identified by the searches were compiled into one electronic file and the duplicates were removed through Covidence with the help of the librarian. All titles and abstracts were screened to identify potentially eligible papers during the primary screening. Then, final retrieval of papers was conducted. The full texts were screened based on the stated inclusion criteria. The following study characteristics were extracted from each of the papers: authors, year of publication, study design, aim of the study or paper, main topics discussed, and main findings.

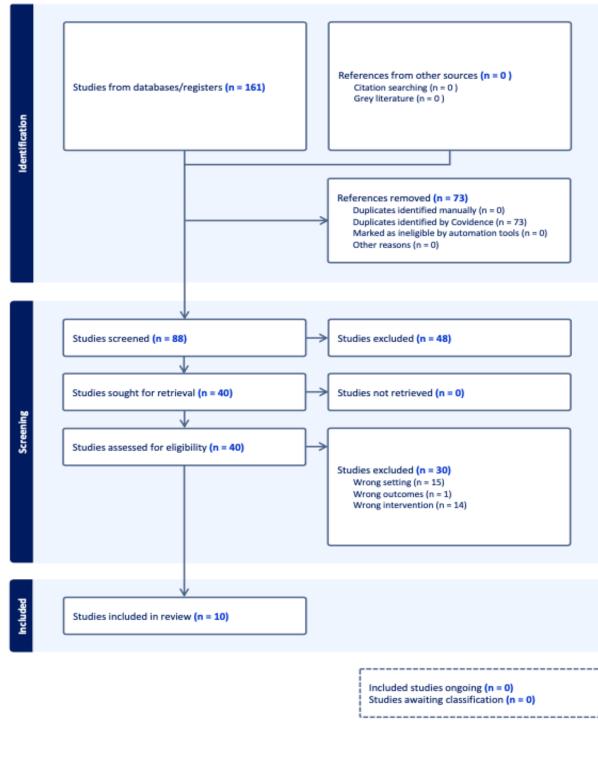


Figure 1. Prisma Flow Chart of a Literature Search of PMTCT Programs in Botswana

27th March 2023

covidence

RESULTS

161 papers (63 from Global Health; 41 from Web of Science; 37 from Scopus; 20 from Medline) were identified through the search strategy. A total of 73 duplicates were removed which resulted in 88 papers for primary screening. Subsequently, 48 studies were removed due to the following reasons: wrong setting (N=15), wrong intervention (N=14), wrong outcomes (N=1). This resulted in a total of 40 papers for full-text review and ultimately 10 papers were identified for final data extraction.

There were consistent findings among the identified papers, such as the necessity of appropriate communication strategies such as dissemination of educational materials and training basic community workers to address cultural stigma and encourage HIV testing among HIV-infected women (Programme Review Team 2002; Mostwere-Chirwa et al., 2014) and the positive effect of increased testing coverage through the implementation of routine HIV testing and addition of on-site rapid testing (Programme Review Team 2002; Creek et al., 2007a; Creek et al., 2007b; Dryden-Peterson et al., 2015). Five papers identified high rates of antenatal services usage as one of the main strengths of the Botswana healthcare system and highlighted importance of integrating PMTCT services to antenatal clinics and supporting early access to antenatal care (Programme Review Team 2002; Creek et al., 2007a; Dryden-Peterson et al., 2015; Ortbald et al., 2022; Zash et al., 2016)). Regarding infant feeding practices, two papers mentioned the lack of breastfeeding as one of the reasons for high mortality among infants with HIV infected mothers within the context of Botswana (Mostwere-Chirwa et al., 2014; Zash et al., 2016) and supported strategies such as early HIV testing and diagnosis for infants and mothers, and Baby

Mother Friendly Hospital Initiative to support breastfeeding in order to minimize the negative spillover effect of formula feeding (Programme Review Team 2002; Mostwere-Chirwa et al., 2014; Zash et al., 2016). Lastly, three papers highlighted that removal of structural barriers such as lack of transportation, insufficient specimen, delay in CD4+ cell count results, delay in HAART referrals, and other service coordination issues would be helpful in successful implementation of PMTCT services (Creek et al., 2008; Mostwere-Chirwa et al., 2014; Dryden-Peterson et al., 2015). **Table 2.** Data extraction of included studies. Review of PMTCT programs in Botswana published since 2000.

		Study		Topics	
No.	Year, Author	Design	Aim	Discussed	Relevant main findings
					1. Pilot program: there are high standards of
					antenatal and delivery services; strong healthcare
					system, low rates of counseling and testing;
	2002 Programme				irregular timing and place of antenatal
	Review Team,				attendance; supporting evidence for program
	PMTCT			HIV treatment;	scale up 2. Infant feeding practices: there are
	Advisory Group			HIV testing;	significant differences in infant feeding practices
	and Infant		Evaluation of 1. pilot	Infant feeding	between infected vs. uninfected mothers and
	Feeding Study		program 2. Infant feeding	practices	known vs. unknown HIV status mothers; clear
1	Group	mixed	practices	(component 3)	lessons learned
					Factors associated with HIV testing among
					pregnant and postpartum women included: being
					interviewed at an urban site, having a high
			Explore reasons for poor		PMTCT knowledge score, knowing someone
			PMTCT program uptake in		receiving PMTCT or ARV therapy, and having a
			relation to perceptions and		partner who had been tested for HIV; lack of
			awareness of PMTCT issues		HIV knowledge and skills among HIV
			among Botswana's pregnant	HIV testing	healthcare providers; support for routine HIV
2	2007 Creek et al.	qualitative	women	(component 3)	testing
			examine the impact of the		
			nationwide introduction of	HIV testing,	Overall success of routine testing shown by
			routine HIV testing in	ANC	substantial increases in participation in PMTCT
			antenatal clinics by	attendance	interventions, ANC attendance, HIV testing, and
3	2007 Creek et al.	mixed	comparing HIV testing rates,	(component 3)	testing coverage

			PMTCT intervention rates,		
			and ANC attendance		
4	2008 Strover et al.	-	Estimate HIV prevalence trend 1980-2007 and effects of treatment and prevention programs by using surveillance, survey and program data	trend, ART	There is major success with PMTCT program: there is over 90% of HIV-positive women receiving antiretrovirals to prevent transmission of HIV to their children; an estimated 10,000 child infections were averted since the program's inception and an estimated 11,000 child AIDS death was averted through the combined effects of the PMTCT program and the child treatment
4	al.	e	program data	program	program
5	2008 Creek et al.	quantitativ e	conduct and assess implementation of large-scale demonstration project by testing HIV-exposed infants using PCR on dried blood spots	Infant HIV diagnosis	Overall success of project: dramatic reduction of 80% infant HIV infections; high effectiveness of PMTCT interventions to reduce HIV transmission rates between mother and infant pairs; feasibility of early infant diagnosis which improves outcome and survival. There is support to nationally implement DBS PCR in Africa
6	2010 Chen et al.	quantitativ e	analyze rates of HIV testing, CD4+ cell count testing, HAART initiation during pregnancy		There is low rates of CD4+ cell count testing and HAART initiation among pregnant women; rapid CD4+ cell count testing and HAART referral is needed for HIV-infected women
7	2014 Motswere-Chirw a et al.	quantitativ e	identify HIV-infected infants in Francistown, Botswana 2005-2012	Infant HIV diagnosis	71% of infants born to HIV-infected women were tested for HIV; survival of HIV-infected infant is low in the absence of early diagnosis, rapid initiation of treatment and retention in care; there is a need to address cultural,

					educational, and structural barriers to improve EID program outcomes
8	2015 Dryden-Peterson et al.	quantitativ e	Evaluate the impact of programmatic transition from Option A to Option B for PMTCT through projected MTCT risk	Option B, MTCT risk	Due to the increased proportion of women receiving no antiretrovirals, that was a 24% increase in projected MTCT during the initial implementation of Option B. However, ongoing surveillance has shown that there was subsequent improvement.
9	2016 Zash et al.	quantitativ e	Determine accurate child mortality rates, accounting for HIV status and infant feeding practices in setting with widespread antiretroviral treatment availability		HIV-exposed and HIV-infected children account for most deaths at 24 months within the programmatic setting of high maternal HIV prevalence and widespread maternal and child ART availability. Excess mortality among HIV-exposed children could be attributable to lack of breastfeeding.
10	2022 Ortblad et al.	quantitativ e	Measure frequency of previously undiagnosed HIV infection and HIV incidence among pregnant women	HIV incidence	Programmatic data from HIV implementation programs can be used to inform HIV prevention programs. Botswana's HIV incidence levels remain above HIV epidemic control (≤1 per 1000 person-years).

In KwaZulu-Natal, factors such as adoption of B+ option, WHO infant feeding recommendations, integration of PMTCT services in the primary health care settings, early infant HIV testing, routine HIV testing have been established on the national policy level but faces implementation challenges (Grimwood et al., 2012; Moyo et al., 2018; Mutabazi et al., 2020; National Department of Health, 2015; Zash et al., 2016). Contextually, it is important to note the political interference due to AIDS denialist views during Thabo Mbeki's presidency from 1999 to 2008 that delayed the effective prioritization of PMTCT implementation and ART services until 2008 (Barron et al., 2013; Kalichman et al., 2010). This most likely affected the effective timing of testing, diagnosis and treatment and led to dramatic increases of the epidemic scope although South Africa has made rapid progress. South Africa is presently established as having the world's largest ART programmes and well-established PMTCT roll-out which has proved its effectiveness by achieving less than 5% MTCT rate and more than 95% ART coverage in 2019 (Astawesegn et al., 2022; National Department of Health, 2015). In South Africa, females between ages 15-24 are the highest age group to acquire HIV (UNAIDS, 2018). In 2019, this population group accounts for approximately 35% of all new HIV infections nationally and the annual HIV-deaths related deaths are estimated to be approximately 3900 per year (Simbayi et al., 2019; UNAIDS, 2018).

Specifically, in KwaZulu-Natal, the major performance gaps are shown in the antenatal care attendance rates and disproportionally high HIV prevalence among adolescent females. High levels of unintended pregnancies among this age group is a major challenge. According to the 2019 South Africa HIV Sentinel Report, KwaZulu-Natal had the second

highest early ANC attendance rate nationally (next to Western Cape) with 73.7% of participants in the province initiating ANC before 20 weeks of gestational age, but this is significantly lower than the Botswana average attendance rate of 97% (Woldesenbet., 2021). In addition, women who had unintended pregnancy in KwaZulu-Natal had lower attendance of ANC (71.4%) compared to women whose pregnancy was intended (79.5%). In general, younger women are less likely to have knowledge of their HIV status, which negatively affects their ART initiation and ability to achieve viral suppression (Ntombela et al., 2022). In all districts, adolescent girls (15–19 years) had the highest level of unintended pregnancy (ranging between 61.8% in Amajuba districts to 85.5% in uMgungundlovu districts) followed by young women (20–24 years: ranging between 50.8% in uMzinyathi to 76.9% in eThekwini districts). Although KwaZulu-Natal has the second highest early ANC attendance compared to other provinces, there are significant disparities between districts (65.4% - 79.7%) and in all districts, adolescent females between ages 15-19 years had the lowest attendance of ANC compared to other age groups (Woldesenbet., 2021).

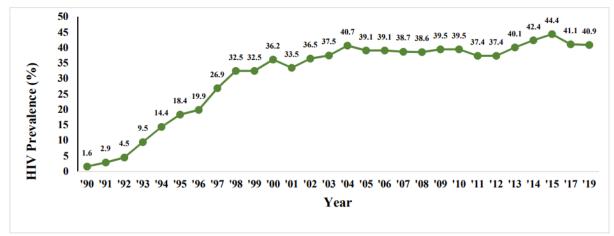
This is significant because this age group with the highest unintended pregnancies, has lower ANC attendance rates and highest HIV prevalence among female adolescents and women, showing that there is a need for age-specific PMTCT intervention strategies in KwaZulu-Natal. In terms of the "first 95 target" for HIV cascade of care, females between ages 15-24 in KwaZulu-Natal range from 69.2% to 87.5%, which also knows the need for health literacy outreach and communication strategies (Ntombela et al., 2022). There is consistent finding across studies conducted in South Africa that adolescent women are less likely to know their HIV status before their first ANC visit compared to adult females, such as the case in Eastern Cape, where more than 75% of adolescent women were unaware of their HIV status compared to the 44.7% of older women. Cultural and structural barriers such as parental consent, lack of health literacy, fear of HIV testing and knowledge of HIV status, and stigma are hindrances to the access of voluntary HIV counseling and testing services, which result in missed opportunities for adolescentes to access PMTCT services (Fatti, et al., 2014; Horwood et al., 2013; Woldesenbet et al., 2015).

Considering the findings regarding Botswana from the scoping review, there are areas of application for KwaZulu-Natal's PMTCT efforts targeting the high risk population of adolescents and young women. Firstly, the ANC attendance among adolescents and young women should be prioritized to ensure a smooth continuum of care. This is a critical step because proven effective approaches of routine HIV testing and early infant diagnosis programs can only be accessed by this population given ANC attendance. Because South Africa's PMTCT services are well integrated with the primary healthcare system, it is critical to expand ANC coverage and usage for a positive outcome, as demonstrated by Botswana's high coverage of HIV testing, diagnosis and treatment by leveraging the established ANC services in the nation (Grimwood et al., 2012; Moyo et al., 2018). In order to do this, training community health workers to counsel pregnant mothers to provide accurate PMTCT knowledge is essential. Specifically, involving of individuals who are receiving PMTCT services or ART during counseling sessions to provide emotional support and encouraging sexual partners to receive HIV testing are critical strategies as proven by Botswana example of including and educating family members into the PMTCT process (Creek et al., 2009; Luo, 2002). Culturally appropriate and targeted communication strategies such as integration of PMTCT information in the school educational systems and usage of easily accessible education materials such as flip charts and radio messages have also demonstrated effectiveness in Botswana, which can be implemented in KwaZulu-Natal for especially 15-19 year old females (Luo, 2002; Ortblad et al., 2022). This approach can additionally include information regarding infant feeding practices, but considering the family pressure among majority formula feeding women within KwaZulu-Natal, it would be critical to also reach the family members of the pregnant mothers to reduce cultural barriers to healthy infant feeding practices compliant with the WHO recommendations (Luo, 2002; WHO, 2016; Zash et al., 2016). For all post-test counseling sessions, the content should be standardized in order to ensure quality care and ARV uptake.

In addition, KwaZulu-Natal can implement rapid testing on site to ensure same day results to reduce structural barriers such as transportation, as shown by Botswana's strategy of combining routine HIV testing with on-site rapid testing which increased testing coverage to 95% (Chen et al., 2010; Motswere-Chirwa et al., 2014). If implementation of rapid testing is difficult for the entire population of KwaZulu-Natal, prioritizing the implementation for the adolescent and young women population would be critical. Lastly, collection of programmatic data should be collected and utilized to identify missing progress or regress information regarding the current state of KwaZulu-Natal's PMTCT services. Currently, there is a lack of data available regarding the specific identification of structural barriers that hinder the adolescent and young women population from accessing PMTCT services and the progress report for the proportion of exclusive breastfeeding in

the first six months of an infant's life. Information such as the knowledge score of PMTCT service healthcare workers, mothers and family members are needed about the entire province and by district, which would be an insightful tool to designing the educational program and locating the community health workers.

Figure 2. The HIV epidemic curve among antenatal women, KwaZulu-Natal, 1990-2019, Antenatal HIV Sentinel Survey



The prevalence reported in 2015, 2017 and 2019 is for both first and follow-up visit attendees.

Note. Woldesenbet, S.A., Lombard, C., Manda, S., Kufa, T., Ayalew, K., Cheyip M., and Puren, A. (2021). The 2019 National Antenatal Sentinel HIV Survey, South Africa, National Department of Health. Copyright 2021 by National Department of Health

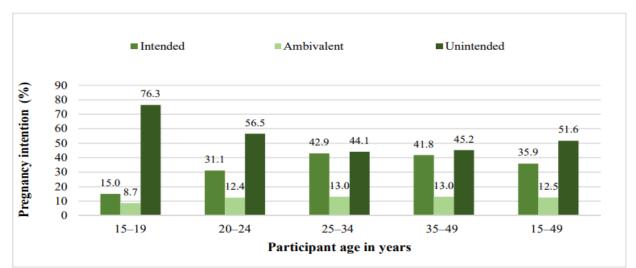
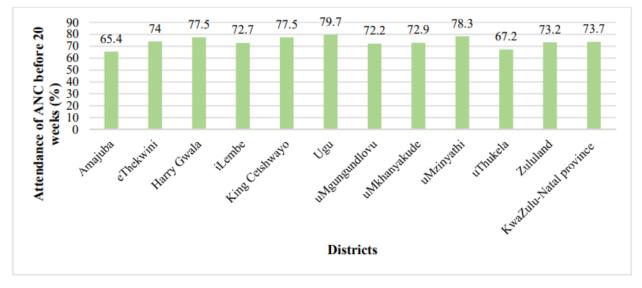


Figure 3. Pregnancy intention by age group in the 2019 Antenatal HIV Sentinel Survey, South Africa

The categories were defined as follows: Intended: response to both LMUP questions indicated pregnancy was intended; Unintended: response to both questions indicated pregnancy was unintended; Ambivalent: intended by only one response or at least one response indicated the woman was undecided about having a baby.

Note. Woldesenbet, S.A., Lombard, C., Manda, S., Kufa, T., Ayalew, K., Cheyip M., and Puren, A. (2021). The 2019 National Antenatal Sentinel HIV Survey, South Africa, National Department of Health. Copyright 2021 by National Department of Health

Figure 4. Attendance of antenatal care before 20 weeks of gestational age, in the 2019 Antenatal HIV Sentinel Survey, KwaZulu-Natal



Note. Woldesenbet, S.A., Lombard, C., Manda, S., Kufa, T., Ayalew, K., Cheyip M., and Puren, A. (2021). The 2019 National Antenatal Sentinel HIV Survey, South Africa, National Department of Health. Copyright 2021 by National Department of Health

DISCUSSION

One of the major strengths of Botswana's healthcare system regarding PMTCT services is the high attendance rates of antenatal care with a rate of 97%, which proved to be an effective leverage for implementation of HIV testing as the first African nation to implement routine HIV testing at each ANC visit (Creek et al., 2007; Ntombela et al., 2022). Integration of PMTCT into the broader healthcare system is an essential component in minimizing structural barriers and maximizing coordination to ensure smooth delivery of the "continuum of care" because it has the potential to strengthen other reproductive, maternal and child interventions (Nutman et al., 2013). Furthermore, the successful adoption of the Option B and B+ program was attributed to the support of early access to antenatal care, removing the barriers to rapid ART initiation by integration of ART into antenatal clinics (Dryden-Peterson et al., 2015). Especially in high HIV prevalence settings, routine HIV testing must be paired with primary HIV prevention interventions as part of the antenatal care programs to increase coordination of service delivery (Ortblad et al., 2022). Condom distributions, initiation of PreP, distributions of self-tests combined with HIV testing in antenatal clinics can improve clinics for pregnant women and reduce MTCT (Johnson et al., 2014; Ortblad et al., 2022).

In Botswana, among female adults aged 15-64 years, HIV prevalence ranges from 2.7% for 15-19 years group to 52.0% for 45-49 years group, which shows that the HIV prevalence peaks in the 45-49 years range (Republic of Botswana, 2022). Although the female adolescent population has lower HIV prevalence compared to other age groups, adolescent HIV infection rates remain high given that adolescents represent around 20% of

the total population and are identified as one of the most-at-risk groups for HIV acquisition due to risky sexual behavior (Barchi et al., 2022; Republic of Botswana Ministry of Youth, Sport and Culture, 2010). Given that 43% of pregnant women in ages 14-24 attended at least one ANC visit, there are ongoing efforts to increase contraceptive literacy and promote antenatal care (Barchi et al., 2022; PEPAR, 2022).

Regarding the goal to achieve 95-95-95 targets set forth by Joint United Nations Programme on HIV/AIDS (UNAIDS) where 95% of all people living with HIV will know their HIV status; 95% of all people with diagnosed HIV infection will receive sustained ART; and 95% of all people receiving ART will have viral load suppression, Botswana has reached 95.1%, 98.0%, 97.9% among adults (Republic of Botswana, 2022; UNAIDS, 2015). In 2021, Botswana was certified by WHO for achieving an important milestone in eliminating MTCT of HIV by achieving the target of reducing MTCT HIV transmission rate to under 5%, providing antenatal care and antiretroviral treatment for more than 90% of pregnant women and reducing the HIVcase rate of fewer than 500 per 100,000 live births (WHO, 2021). As the first high-burden country to receive this certification, Botswana's journey shows that elimination of PMTCT is possible.

Along with high ANC attendance in public facilities, training and employment of community health workers for PMTCT service counseling in public facilities dramatically increased the HIV testing coverage in Botswana between 2002 and 2003 reaching an uptake of 60% (Creek et al., 2007; Francistown District Health Team unpublished data). The positive contribution and cost-effectiveness of using community health workers to

provide HIV service delivery support in both prevention and treatment has been affirmed by many studies, highlighting the need to integrate community health workers into the wider healths systems to ensure scalability and sustainability of HIV services, especially for marginalized populations (Mukherjee and Eustache., 2007; Mwai et al., 2013). As mentioned above, the routine HIV testing adopted in 2004, and the availability of on-site rapid testing increased the national testing coverage to 95% in 2007 (Creek et al., 2007; Ntombela et al., 2022). The annual surveillance program that measures HIV prevalence trends among women aged 15-19 years who attend antenatal clinics provided representative data for the entire population showed that 10,000 child infections were averted through the PMTCT program between 2002 and 2007 and the MTCT was reduced to 3.7%, resulting in the dramatic decrease to 890 new annual child infections (Ministry of Health, 2005; National AIDS Coordinating Agency, 2007). The effective involvement of HIV-positive people in the process of counseling and recruiting for PMTCT service participation is also supported by multiple studies (Creek et al., 2007; Creek et al., 2006; Mfundisi et al., 2005).

Starting in 2005, Botswana implemented a Early Infant Diagnosis (EID) Program, through which infants of HIV-positive women are tested for HIV at age 6 weeks or at first health-care contact using PCR testing on dried blood spot specimens in order to diagnose increased the rate of early diagnosis, rapid initiation of treatment and retention in care, and provided psychosocial benefits, supporting the expansion of the EID into a national program (Motswere-Chirwa et al., 2014). The follow-up data from the first phase of implementation between 2005 and 2012 also underscored the importance of addressing

coordination issues across HIV services, such as reducing delays between HIV testing, post-testing counseling, and reducing time for referral in order to minimize loss to follow-up in the cascade of care (Chen et al., 2010; Motswere-Chirwa et al., 2014).

After the transition to infant feeding guidelines for exclusive breastfeeding for the first six months of life in 2016, the government of Botswana is making efforts to retract the spillover effects from the ineffective advice from the year of 1999, when the national PMTCT program recommended abrupt cessation of breastfeeding at 3-4 months if mothers chose to exclusively breastfeed the first few months of life along with the government provision of free commercial milk formulas until 6-12 months of age (Luo, 2002; WHO, 2016; Zash et al., 2016). Breastfeeding should be an integral part of PMTCT strategy, considering the nutritional value and subsequent reduction of risk of infant mortality (WHO, 2016). Despite the success of implementation of PMTCT programs, HIV-exposed and HIV-infected children at 24 months continue to account for most deaths at 24 months, highlighting the need to encourage early infant HIV testing and diagnosis especially in regions where formula feeding is common in order to support breastfeeding through counseling (Luo, 2002; WHO, 2016; Zash et al., 2016; Zash et al., 2016).

In light of Botswana's journey towards elimination of MTCT, it is important to consider the major contextual differences between Botswana and KwaZulu-Natal which inevitably affect the funding and implementation of PMTCT services. Botswana has a significantly lower population compared to KwaZulu-Natal (2,588,423 vs. 11,682,000) and a well-established transportation system that allows for smooth access to healthcare facilities

(Republic of Botswana, 2023; Statista, 2023; World Bank, 2023b). In addition, while South Africa has a higher GDP rank compared to Botswana as a nation, it scores higher on the Gini index, which indicates higher income inequality within the country (World Bank, 2023a). KwaZulu-Natal is a rural province with a history of ethnic violence and civil war especially in the 1980s and 1990s that has left present consequences both structurally and culturally (Mchunu, M. R., 2020). The present ethnically heterogeneous composition has its roots in the former apartheid system, when KwaZulu-Natal served as a legal homeland of the Zulus until 1994 (Britannica, 2020). Presently, more than four fifths of the population are Zulu, people of Black African descent and this impacts the resource allocation aspects of PMTCT funding.

In terms of PMTCT services, the greatest disparities of performance in KwaZulu-Natal seem to occur in the disproportionately low rates of ANC attendance among adolescent women, rooted in the societal pattern of high rates of unintended pregnancies and low levels of health literacy, which calls attention to the Botswana's utilized strategies such as self-testing, integration of ANC services involving routine HIV testing in the most accessible public families such as schools, development of communication strategies of educational materials to ensure minimum standard of knowledge (Luo, 2002; Ortblad et al., 2022). As highlighted by efforts in Botswana to reach the regions with high burden of HIV, communication strategies that encourage family involvement and participation, along with available information in local languages are essential. Strengthening outreach through the involvement of community health workers to reach adolescent women will be a beneficial approach as in the example of Botswana's efforts to train "lay counselors" for HIV

counseling services to specifically target the most vulnerable population groups (Creek et al., 2009; Luo, 2002). Involvement of HIV-positive people in the process of counseling and recruiting for PMTCT participation has also been proved to be effective (Creek et al., 2007). Along with the educational aspect, routine testing services combined with on-site rapid testing services in accessible ANC public facilities need to be prioritized in order to minimize missed opportunities and ensure high testing and ART coverage for especially adolescent and young women in KwaZulu-Natal (Creek et al., 2007; Stover et al., 2008). In addition, removal of barriers in the continuum of care, such as ensuring access to antenatal care and ART initiation before CD4 results will be an helpful approach to maximize the benefits of Option B+ implementation.

Regarding infant feeding practices, South Africa changed its national policy to align with WHO guidelines to support exclusive breastfeeding for 6 months and continued breastfeeding until 24 months for HIV-positive women receiving ART (Department of Health: Republic of South Africa, 2017). Despite this national policy, uptake of recommendation is suboptimal. According to an observational study in KwaZulu-Natal assessing the breastfeeding practices among HIV-positive women, around 70% of the participants practiced exclusive formula feeding due to reasons such as fear of HIV transmission to the infant, separation from infant due to work environment and absence or limited maternity leave, lack of social support and pressure from older generations to engage in formula or mixed feeding, fear of disclosure of HIV status and other HIV-related stigma (Remmert et al., 2020; Tuthill et al., 2017). From these, the major two reasons for lack of adherence to exclusive breastfeeding guidelines was fear of HIV transmission and

logistical and financial support, which highlights the importance of implementing trained healthcare providers such as community health workers to offer psychoeducation about the risks and benefits of breastfeeding. This approach is supported in reports from Botswana regarding the need to integrate breastfeeding counseling sessions into the broader PMTCT services (Motswere-Chirwa et al., 2014; Zash et al., 2016). Financial and logistic support from the government in regards to establishing breastfeeding-friendly work environments should also be a priority in combination with offering routine counseling sessions in public ANC facilities that encourage family involvement in infant feeding decision making process in order to strengthen social support (Remmert et al., 2020).

CONCLUSION

Effective delivery of PMTCT services is essential in ensuring elimination of HIV transmission from mother to child, and actions surrounding policy implementation, service coordination, availability and utilization of tests and treatments, HIV health literacy and infant feeding practices need to be prioritized in order to maximize the benefits. Botswana's successful journey shows that it is possible to eliminate mother to child transmission of HIV as a once high-burden HIV country through leveraging integration of PMTCT with the broader routine healthcare system through ANC attendance, dissemination of knowledge through community health workers, prioritization of removing structural barriers to PMTCT service access, and improving communication strategies. These areas of PMTCT work can be applied to KwaZulu-Natal's case, especially in regards to the highly vulnerable population of adolescent and young females. Targeted communication strategies that aim to educate the importance of PMTCT services through ANC attendance is the first step to achieving the maximum implementation of the PMTCT cascade of care. Cultural barriers surrounding stigma also need to be addressed through continued educational outreach in areas such as exclusive breastfeeding for HIV-positive mothers. Despite the limitations regarding the lack of discussion on the different political and economic aspects of healthcare in these two countries, there is value in drawing lessons learned from a successful example so that the evidence can be adapted and applied accordingly. In regards to KwaZulu-Natal, there is a need for future research work specifically identifying the structural and cultural barriers that result in performance gaps regarding ANC attendance, infant feeding practices and health literacy among pregnant women. In addition, collaboration between districts, regions and nations to strengthen

health governance structure and resource financing will be crucial to ensure sustainability, accessibility and availability of PMTCT and accurate reporting of progress.

APPENDIX

2002 Programme Review Team, PMTCT Advisory Group and Infant Feeding Study Group

Context

The first implementation of the PMTCT program in all public maternity units was in Francistown and Gaborone in 1999. During this time, the entry point to accessing the program was voluntary, confidential, counseling and testing (VCCT) to all pregnant women. After the evaluation of the pilot program in 2000, the PMTCT program was extended to all districts by November 2001, Botswana becoming the first African country with a population-based PMTCT program. During this time, HIV -infected women were provided oral AZT at 34 weeks of pregnancy and during labor, while the babies were provided AZT syrup until 4 weeks. Due to the PMTCT recommendation against breastfeeding, women were advised to practice abrupt cessation of breastfeeding at 3-4 months if they chose to exclusively breastfeed the first few months of life. Commercial milk formulas were provided until 6-12 months. The strength of Botswana's healthcare system was high rates of antenatal care usage (96%) and delivery in public facilities, which helped increase the access to the PMTCT program.

Lessons Learned

Program Improvement:

- Widespread and culturally appropriate communication strategies that encourage male and family involvement and participation, along with available information in local languages
- Address stigma and fear in PMTCT programs through effective communication

- Flexibility of quantify of formula for each woman for infant feeding
- Training all staff on PMTCT and infant feeding and training basic community-based workers to provide follow-up counseling for pregnant women in order to create effective workflow
- Encourage rapid testing on site with same day results

Infant Feeding:

- Reduce spillover effects of formula feeding to uninfected mothers through strategies such as Baby Mother Friendly Hospital Initiative
- Support breastfeeding mothers
- Train counselors on teaching and monitoring optimal feeding practices for infants and young children (emphasis on good hygiene, safe preparation of formula and proper diet)

2007 Creek et al.

<u>Context</u>

In 2003, Botswana's estimated HIV prevalence was 37.4% In addition to the short-course zidovudine (ZDV) that was available in 1999 (Botswana National AIDS Coordinating Agency, 2003), there was an addition of single-dose nevirapine(NVP) to the program in 2003 along with increasing ART uptake among pregnant women with AIDS (Nolan ML, Greenberg AE, Fowler MG, 2002). Despite the remarkable opportunity of PMTCT uptake through already established antenatal care uptake (> 95%), there were low HIV testing rates in 2002 (Francistown District Health Team unpublished data). Initially, PMTCT services were offered by trained midwives who had the responsibility to offer advice based

on weighted benefits and risks, but due to this unsuccessful approach, additional community workers (secondary school graduates with 4 weeks of training) were employed to offer counseling, which improved the testing uptake up to 60% (Francistown District Health Team unpublished data).

Lessons Learned

- High priority of ensuring minimum standard of knowledge for all pregnant women through educational material (ex. picture flip charts, radio messages)
- Involve HIV-positive people in the process of counseling and recruiting for PMTCT participation
- Encourage discussions on HIV testing with close people, including partners before antenatal visit
- Establishment of routine HIV testing as part of antenatal services in order to reduce stigma and offer easier access (supported by many countries such as US, Canada, Thailand, Brazil, Uganda, Kenya..etc)
- Standardization of post-test counseling content in order to ensure quality care and ARV uptake
- Encourage family planning to prevent pediatric HIV infections
- Support confidential testing and care for HIV among providers along with workplace protection

2007 Creek et al.

<u>Context</u>

Beginning in 2004, "routine but not compulsory" approach of HIV testing was implemented in healthcare facilities after Botswana's President Festus Mogae encouraged HIV testing and utilization of free HIV care and treatment during his New Year message in December 2003. This implemented a system which routinely tested people with signs and symptoms of HIV, patients with tuberculosis, pregnant women, persons with sexually transmitted infections and persons receiving routine medical examinations (Daily News, 2003). In 2004, Botswana government and CDC collaborated in the BOTUSA project in order to support the systematic introduction of routine HIV testing in antenatal clinics and evaluate the health outcomes impact of this implementation.

Lessons Learned

• Routine HIV testing resulted in dramatic increase in testing and PMTCT delivery and the addition of on-site rapid testing increased the testing coverage to 95%

2008 Stover et al.

Context

In 2005, the prevalence of HIV in Botswana was one of the highest in the world, reaching 24% (UNAIDS/WHO, 2006). The annual HIV surveillance program started in 1992 to provide information of HIV prevalence trends that is representative for the entire population by surveying women aged 15-19 years who attend antenatal clinics (Ministry of Health, 2005). Although the estimated number of new child infections was 4600 in 1999, more than 90% of HIV-positive women received antiretrovirals to prevent MTCT and more

than 10,000 child infections were averted between 2002-2007 though the PMTCT program (National AIDS Coordinating Agency, 2007). In early 2007, the program identified HIV status of all children born to HIV-positive mothers by using dried blood spots and PCR tests, which showed that the rate of MTCT was reduced to 3.7%, resulting in an estimated annual count of 890 new child infections.

Lessons Learned

- Expansion of the PMTCT program has resulted in successful treatment uptake among HIV-positive pregnant women, low rates of MTCT, and decline in child infections
- High coverage of ART program has resulted in the reduction in MTCT of HIV

2008 Creek et al.

Context

The initial recommendation from the Botswana PMTCT program was using the enzyme-linked immunosorbent assay(ELISA) test for 18 months old children to test for HIV antibodies. However, due to high rates of loss to follow-up and mortality, lack of trained staff and documentation, PCR on dried blood spots(DBR) was implemented as a large-scale demonstration project to accurately determine the HIV status of infants 6 weeks after exposure.

Lessons Learned

- Early infant testing using DBS PCR can be implemented as a national program
- There are clear benefits to early diagnosis, which as substantial psychosocial benefits to mothers and infants, improved morale among program staff, and

potential to improve health outcomes through early initiation of treatment for diagnosed infants

2010 Chen et al.

<u>Context</u>

According to 2006 WHO recommendations, all pregnant women who require treatment for their own health must take HAART as a combined treatment and PMTCT strategy (WHO, 2014). Considering the opportunity to maximize treatment leveraging the high antenatal visit rates, since 2002, the Botswana PMTCT guidelines have recommended CD4+ cell count testing during pregnancy and rapid referral and initiation of HAART at government facilities for those who qualify for treatment (Gadathe T., 2008). Women with CD4+ cell count below 200 per cubic millimeter (below 250 per cubic millimeter in 2008) or AIDS-defining illness met the criteria for HAART initiation, and if otherwise, intuition of short-course ZDV prophylaxis. The CD4+ cell count testing is free for all Botswana citizens.

Lessons Learned

 Structural barriers such as lack of transportation, lost or insufficient specimen, delay in CD4+ cell count results, delay in HAART referrals due to complication initiation process need to be addressed to address low rates of CD4+ cell count testing and HAART initiation during pregnancy.

2014 Motswere-Chirwa et al.

Context

In addition to the HIV testing through DBS PCR method at 6 weeks through the EID program, which was implemented nationwide in 2001, infants who were breastfed and initially were also retested for HIV 6 weeks after breastfeeding cessation. In 2011, the prevalence of HIV in Botswana was 30.4%. 98% of women in antenatal care tested for HIV, 93% of HIV-positive women who were pregnant received antiretroviral prophylaxis, and less than 4% of infants less than 18 months old tested by PCR were infected with HIV (Botswana Ministry of Health, unpublished data 2013). In Francistown, Botswana 71% of infants born to HIV-infected women were tested for HIV.

Lessons Learned

- Addressing the coordination issues across HIV services is important to reduce delays between HIV testing, post-testing counseling and ART initiation by strengthening the referral system to reduce time between cascade of care(prenatal care, postnatal care, EID testing, pediatric treatment) and educational, cultural and structural barriers need to be addressed as a part of comprehensive EID strategy
- Lack of breastfeeding is one of the reasons for high infant mortality in Francistown, where there is a high prevalence of pneumonia and diarrhea among children aged
 <5 years

2015 Dryden-Peterson et al.

Context

In 2013, WHO revised its previous recommendations and encouraged the adoption of Option B, which provides ART for all pregnant and breastfeeding women regardless of CD4 count and Option B+, which is continued lifelong ART(WHO, 2013). Option A, which provided antennal maternal zidovudine monotherapy, was no longer recommended. After a pilot program of Option B implementation in 2009, Botswana adopted Option B as its national policy in 2011(Botswana Ministry of Health, 2011). The Option B program was rolled out between 2011 and 2012. According to national policy, women with CD4+ cell count less or equal to 350 cells per microliter were eligible to receive ART for life, and women with less than 350 cells per microliter were eligible for ART during pregnancy and breastfeeding.

Lessons Learned

 Removal of barriers to rapid ART initiation by integrating ART into antenatal clinics, supporting early access to antenatal care and ART initiation before CD4 results can be helpful in successful implantation of Option B and B+

2016 Zash et al.

<u>Context</u>

In terms of feeding practices, there was a shift of guidelines in 2012 from exclusive formula feeding for HIV-infected mothers to being allowed to breastfeed for mothers on ART(Zash et al., 2016). Despite the success of implementation of PMTCT programs,

HIV-exposed and HIV-infected infants account for most deaths among children at 24 months.

Lessons Learned

- In addition to infant testing at 6 weeks, HIV testing at birth and HIV diagnosis within a few days of birth can support breastfeeding, especially in regions where formula feeding is common.
- Breastfeeding should be a component of PMTCT strategy, considering the high prevalence of diarrhea and pneumonia in settings where there is ART adherence.

2022 Ortbald et al.

Context

Botswana utilizes a robust health informatics system to monitor and evaluate HIV treatment and prevention systems (Monitoring and Evaluation and Health Information System). Botswana has a prevalence of 20% for HIV-positive adults (UNAIDS, 2019). In 2018, 91% HIV-positive people were aware of their status, 92% of these people received care, and more than 95% of these people were virally suppressed. In addition, there is a current implementation of PrEP delivery and a plan to implement HIV-self tests. Although the HIV incidence rate is lower in Botswana compared to other sub-Saharan countries, it remains above level so HIV epidemic control (equal or greater than 1 per 1000 person-years).

Lessons Learned

• In high HIV prevalence settings, routine HIV testing must be paired with primary HIV prevention interventions as part of the ANC programs

- Condom distributions, initiation of PrEP, distribution of self-tests combined with HIV testing in ANC clinics can improve outcomes for pregnant women and reduce MTCT
- Prioritized inclusion of old women and non-citizens for HIV prevention programs can improve HIV transmission in Botswana

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